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Level of inpatients' satisfaction toward nursing care in five major public hospitals of Kuwait

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Introduction:

The purpose of this study was to determine:From a population of inpatients, the level of patient satisfaction with nursing care, in the inpatient setting at 5 major government hospitals in Kuwait; if there is any significant difference in patients' satisfaction with the nursing services among the 5 major public hospitals of Kuwait; and whether there is any association between demographic data and patient satisfaction towards the nursing care provided.

Methods:

This cross-sectional study enrolled 242 inpatients approached in 5 general hospitals in Kuwait. The study used self-administered questionnaire. The questionnaire was composed of 2 dimensions: socio-demographic and hospital information variables, as well as patient satisfaction and overall perception items. Values of each item in the patient satisfaction part were summed yielding a total patient satisfaction score. Association between the total score and other variables including socio-demographic and hospital information data was evaluated using non-parametric tests. Differences in regard to the total satisfaction score between the surgical and the medical wards of each hospital and between the different hospitals were also examined.

Results:

77. 7% of the sample scored above 51. Patients with a lower educational level received a higher satisfaction score than those with a higher educational level. Besides, private room inpatients scored higher in regard to satisfaction compared to non-private residents, although the association was "borderline" significant. No difference was found between medical wards' inpatients' satisfaction with the quality of nursing care. The same holds true for surgical wards. Also, there was no difference in the total patient satisfaction between surgical and medical wards in each hospital. An exception was Al-Sabah hospital in which surgical inpatients were more satisfied.

Conclusions:

A majority of the patients surveyed were satisfied with their nursing care.

2

Nurses knowledge of drug prescribing errors in Kuwait

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Introduction:
Four hundred and eight (408) randomly selected nursing staff members at three different medical centers in the Sate of Kuwait were surveyed to evaluate their experience in drug prescribing errors.

Methods:
A questionnaire was designed for this purpose.

Results:
Overall results indicated that drug prescribing errors is an underestimated problem that does exist. Nurses encountered this problem mostly in pediatric units. Almost one third of all nurses came across a wrong dose more than once during their practice in Kuwait. 5% of those have seen a serious complication (one case of death) as a result. Out of all nurses, only 68% would document any wrongly prescribed dose and 5% were not familiar with using the drug index book available in the unit. This last finding was not related to the level of education or to years of experience of the nurse.

Conclusions:
 Drug prescribing error is a problem encountered but under reported in Kuwait. The nurse should not transcribe or carry out an order as it is written if she/ he knows or suspect the order is wrong. Nurses should be able to use drug index books available to check all doubtful doses. This can only be achieved by continuous education of nursing staff and full cooperation of all physicians and surgeons.

3

A comparison study: health profile of male employee in oil refineries and ministries complex

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Introduction:

Objectives: To study and compare the prevalence of diseases and symptoms (respiratory, atopic, dermatological, auditory, musculoskeletal, gastrointestinal, and emotional /cognitive) among male employees in the oil refineries and in the ministries complex in Kuwait. Additionally, the study sought to assess associations between these symptoms and diseases the and occupational history of the oil refineries employees.

Methods:

This cross-sectional study surveyed male employees in the ministries complex and in the Kuwait National Petroleum Company (KNPC) oil refineries in Kuwait. A self-administered questionnaire was completed by employees in randomly selected ministries complex buildings and employees in accessible administrative zones that make up the three oil refineries of KNPC.

Results:

In both sectors, the most common reported symptoms were emotional/cognitive and musculoskeletal symptoms, however, the prevalence of these and other symptoms including respiratory, atopic, dermatological, auditory and gastrointestinal were found to be higher among oil the refinery employees than among the ministries complex employees. Logistic regression analysis showed statistically significant associations between symptoms and place of work after adjusting for age and smoking history. Also, many diseases as well as the knowledge of a co-worker with cancer were significantly more prevalent among oil refinery employees compared to those in the ministries complex. In addition, this prevalence was amplified after being employed in the oil refineries.

Conclusions:

The study supported our hypothesis that several symptoms and diagnosed diseases are more prevalent among oil refinery employees. Our results invite the health authorities to devise health promotion programs and to address the health issues of their employees.

4

Shoulder pain in diabetics – Role of Musculoskeletal Ultrasonogram in diagnosis and management

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Introduction:

Diagnosis and treatment of shoulder disorders in diabetics remains a challenge. All shoulder disorders present in a similar way. However it is the duty of the Physician to make a precise anatomical diagnosis in order to direct treatment towards it. Aim of this study is a)To find the correlation between shoulder disorders and diabetes mellitus. b)To make a precise anatomical and pathological diagnosis and to apply this knowledge in improving the management of shoulder pain

Methods:

All patients referred for musculoskeletal ultrasound diagnosis in PMR hospital between Jan 2007 and Aug 2007 were included in the study. Ultrasonogram was done using standardised methods.

Results:

Total number of patients = 102. 48 were diabetic and 54 non diabetic. Supraspinatus tendintis was seen in 80%, Biceps lesions in 39%, Bursal lesions in 28%, calcification in 27%, Degeneration in 58%, Impingement in 50%. 90% of our patients had more than one lesion. Compared to Non diabetics, diabetics had a significantly higher percentage of RC tendinitis ($p=.041$) and calcifications ($p=.006$). There is very strong evidence that degeneration is the most common cause of supraspinatus lesions ($p<.001$) and that Impingement is associated with bursal lesions ($p<.001$) The various findings are discussed with ultrasound images and how it helps in treatment decision making is also discussed.

Conclusions:

It is important to treat the underlying cause in Secondary adhesive capsulitis. Ultrasonogram is an effective and low cost non invasive tool for making correct diagnosis and it helps to make treatment decisions based on anatomy and pathology of lesion.

Key Words: Shoulder pain; Diabetes mellitus; Musculoskeletal ultrasonogram;
Funding Agency: None

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Management of non fracture related musculoskeletal pain in osteoporosis

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Introduction:

Osteoporosis is the most common metabolic bone disease. The relationship of osteoporosis to risk of fracture has been well established. Musculoskeletal pain without fracture is also found in osteoporosis. Aim of study is to 1) evaluate the pattern of non fracture related musculoskeletal pain in patients with Osteoporosis. 2)evaluate the coexisting medical problems and to plan appropriate treatment.

Methods:

Retrospective study of outpatients on pharmacotherapy for osteoporosis at PMR hospital. Period of study: Jan 2005 to June 2007. Details including Bone Mineral Densitometry, presence of coexisting medical problems and number of visits for various musculoskeletal problems were collected from patient records. Statistical analysis was done using SPSS 12. 0 version.

Results:

Total number of patients = 67. Mean age was 67 . 2 years. Mean BMD T score was – 2. 59(hip) and -2. 0 (spine). 92. 5% were post menopausal females. The most common sites of pain for which the patient visited the hospital were low back (mean visits = 2. 5) , neck (mean = 1. 24) knee (mean = 1. 36), heel and shoulder (mean = 0. 12). 61. 6% of the patients had pain in more than one site. Comorbid conditions included hypertension in 47. 8%, diabetes mellitus in 31. 3% and Ischemic heard disease in 16. 4%.   No significant difference in T score values was noted in any of these groups. Mean number of visits for back pain was significantly higher in patients with Ischemic heart disease (4. 7) compared to the rest (2. 1) with p value . 001.   Holistic treatment program included patient education, pharmacotherapy, diet plan, physical therapy program and lifestyle changes advice.

Conclusions:

Non fracture related musculoskeletal pain is not uncommon in Osteoporosis. Bone quality changes are affected by microvascular changes in diabetes. Hypertensive patients excrete higher amounts of calcium in urine which is replaced by increase in bone resorption leading to osteoporosis. Therapeutic lifestyle changes and a structured exercise program remain a common plan in management of all three conditions - Osteoporosis, Hypertension and Diabetes Mellitus.

6

Retrospective review of drotecogine alpha (Activated Protein-C) use and effectiveness at Al Jahra Hospital.

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Introduction:

Drotecogine alpha or activated protein-C has been approved by FDA for treatment of severe sepsis in 2001. It was first introduced in Kuwait in 2005. It has been seen that it reduces mortality in severe sepsis. However it is associated with life threatening hemorrhage and too expensive also. We designed this study to evaluate the appropriateness, safety and outcome of patients treated with activated protein-C (APC) at our ICU from January 2006 till January-2008.

Methods:

A retrospective chart review of patients records, who received APC were collected. Data collected included: Demographic data, APACHE-2 score, adverse events, length of stay and survival rate. These patients who received APC were known to have severe infections, three of four Systemic Inflammatory Response Syndrome Criteria, at least two of organ dysfunction and without any risk of bleeding.

Results:

Total of eight patients received APC till January 2008. Among them three patients had perforation peritonitis, one patient had acute necrotizing pancreatitis with abscess, one patient had severe chest infection, one patient had acute pylonephritis, one patient had infective endocarditis, and one patient had severe anterior abdominal wall cellulites following total abdominal hysterectomy. One patient with seratia marcecens pancreatic abscess received twice the course of APC in one week difference and she survived. Out of 8 patients 5(62. 5%) survived and 3(37. 5%) died. Those patients who died have mean APACHE-2 score was higher than those who survived 28. 3 vs 25. 5.

Conclusions:

Use of APC reduced the mortality in severe sepsis. Apache-II score predict the out come of effectiveness of APC in patient with severe sepsis. Higher Apache-II score during admission indicate increased mortality.

7

Time-dependent response of C6 glioma cells in culture to cisplatin.

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Introduction:

We developed a simple in vitro model to study response of C6 glioma cells to a single dose of cisplatin. In the course of cultivation period, three types of cell reactions, related to different kinds of programmed cell death (PCD) and survival, were observed. Ultrastructure of different PCDs is summarized in this poster.

Methods:

Cultures of astrocyte-like C6 glioma cells were treated with a 90 min pulse of Cisplatin (5-10 mg/ml) and examined by TEM at 1 to 10 days later. For electron microscopy, the cultures on coverslips were fixed in 2. 5 % phosphate-buffered glutaraldehyde, than postfixed in 2% buffered OsO4, dehydrated in ethanol, and embedded in Araldite CY212. Ultrathin sections were double stained with uranyl acetate and lead citrate and examined in a transmission electron microscope JEM-1200EXII (JEOL) at 80 kV.

Results:

Within 24 h post-treatment (p-t) the majority of cells in culture died by classical apoptosis (PCD Type-I) with nuclear condensation and cell shrinkage resulting in apoptotic bodies. The rest of the cell population, that survived the acute damage, demised by atypical mechanisms of programmed cell death. At 48 h p-t many surviving cells contained nuclei with bundles of microtubules and microfilaments and no signs of nuclear fragmentation (Type-III). By 72 h p-t the cells with nuclear microtubules disappeared from culture and within 96 h p-t many of surviving cells displayed multilobulated nuclei with micronuclei. Hetero and autophagocytosis was observed in these long-term surviving cells that eventually died by autophagic cell death (PCD Type-II).

Conclusions:

Our experiments demonstrate the wide range of C6 glioma cell response to a single dose of the cytotoxic drug cisplatin. These reactions were found cell cycle-dependent and resulted in classical apoptosis in majority of cell. A population of mis-targeted cell was capable of further cycling until some of them reached an atypical cell deaths (Types-II and III).

Key Words: Glioma cells; Cisplatin; Apoptosis;

8

Photosensitizing Activity of Novel Metalloporphyrins

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Introduction:

Photodynamic therapy (PDT) has succeeded as a minimally invasive approach, in treating both malignant and non-malignant tumors. Zn(II) N-methyl-porphyrins (ZnTM-PyP) can act as photosensitizers and kill human carcinoma cells and antibiotic-resistant bacteria. It is possible that increasing the hydrophobicity of the photosensitizing molecules will facilitate their cellular uptake, and thus increase their efficacy. To test this idea, N-butyl and N-hexyl analogs have been synthesized. The aim of the present study is to investigate photosensitizing activity of these compounds on cultured eukaryotic cells.

Methods:

LS174T adenocarcinoma cells were grown to 80-90% confluency. After adding the photosensitizer, cells were illuminated with visible light under standardized conditions. Cell viability was determined using both trypan blue (0. 2% w/v) exclusion and the MTT assay for metabolic activity.

Results:

Illumination of LS174T cells in the presence of Zn(II) N-methyl-porphyrins (ZnTM-PyP) incorporating alkyl substituents shows photo-mediated cell killing (Approximately 50% cell killing at Approximately 1 micromolar for 60 min light exposure for the hexyl derivative, 4 micromolar for the butyl derivative) without appreciable dark toxicity. This compares to Approximately 10 micromolar for 50% killing by the methyl derivative under similar conditions

Conclusions:

Alkyl substitution of Zn(II) N-methyl-porphyrins (ZnTM-PyP) generated agents showing high photosensitizer activity in cultured cancer cells without increased dark-toxicity. Hydrophobic zinc porphyrin compounds show promise as high activity photosensitizing agents.

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Circulating Plasma Nucleotides During Cardiac Surgery

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Introduction:
There are wide ranges of systems where adenosine and ATP are generated, utilised, or infused to achieve, diagnostic or therapeutic goals. Clinically, ATP and adenosine gained popularity for producing deliberate hypotension during surgery when administered intravenously. They have been also implicated in the contraction of human coronary bypass vessels and therefore, antagonism of these nucleotides receptors could be used to prevent vasospasm and re-stenosis in the saphenous vein during and after revascularisation surgery. we have attempted to measure the levels of ATP and ADP in the blood before and after cardiac surgery in order to relate levels to subsequent complications and outcome.

Methods:
122participants in this study were recruited from patients who underwent elective cardiac surgery. Blood samples were withdrawn before (baseline) and after (2 hours, day 1 and day 2) surgery. ATP and ADP were measured by the luciferase method . Fibrinogen was measured using Electra 1800 while MPM(mean platelet mass)and MPV (mean platelet volume) using ADVIA 120.

Results:
ATP started to increase insignificantly post-operatively at 2 hours ($p = 0.1$ Wilcoxon signed rank test) and reached higher levels at day 1 ($p = 0.002$ Wilcoxon signed rank test). Levels then declined from day 1 levels to day 2 $p < 0.001$ to reach baseline levels again p 0.9. Plasma levels of ADP didn't show any significant elevation . No correlation was found ($p > 0.05$ Spearman correlation) between measured levels of ATP or ADP with these platelet parameters or fibrinogen, except for border line association between pre-operative levels of MPM and baseline ADP ($p = 0.06$ Spearman correlation), preoperative MPV and 2hour ADP $p = 0.06$ Spearman correlation. Logistic regression for all samples time points showed $p = 0.08$, OR 2.4.

Conclusions:
 Measurement of ATP and ADP may be useful parameters to measure in the extracellular fluid of patients undergoing cardiac surgery.

10

Ecocardiography And Troponin I In Patients With Ischaemic Heart Diseases

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Introduction:
To study echocardiography reports for patients with ischemic heart disease in relation to troponin. Background: The analyzed images by echocardiography play a key role in helping the heart specialist to determine nature of the problem and in developing a plan for treatment.

Methods:
302 patients admitted and diagnosed with ischemic heart diseases were recruited. Findings from the admission echocardiography report were compared with troponin I (ADVIA Centaur).

Results:
Population median age 65 years (IQR: 55-75), with 60. 9 % were males, 43. 1 % hypertensive, and 23. 8 % diabetic. Chief presenting symptom was chest pain with 64. 9 % having typical cardiac pain. Patients with positive (n = 99) echocardiography findings showed higher levels of troponin I at admission and 12 hours than others ($p < 0.05$; Mann-Whitney)). Logistic regression models showed only admission troponin I to be significantly related to abnormal echocardiography findings (odds ratio 1. 1; $p = 0.02$).

Conclusions:
Combination of both tests may be more useful.

Key Words: Ecocardiography; Troponin I; Heart diseases;

Biochemistry
Category: Graduate (Basic Sciences)

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Detection of RXR α and its major nuclear receptor partners in the rat adrenals

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Introduction:

 Adrenal utilizes cholesterol to synthesize glucocorticoids in response to stress. The sources of cholesterol are derived from hydrolysis of cholesterol esters stored in subcellular lipid droplets, and carried by lipoproteins after internalization from the circulation. This hydrolysis liberates free cholesterol for steroidogenesis, but the fate of liberated free fatty acids remains obscure. Retinoid-X-receptor α (RXR α) is a nuclear receptor whose role is to regulate gene expression involving in fatty acid metabolism. To be functional, RXR α is homodimerized (RXR α /RXR α) or heterodimerized with peroxisome-proliferation activator receptor α (PPAR α). Furthermore, RXR α is degraded when it is dimerized with RARγ. The present work was aimed to investigate the glandular availability of these nuclear receptors.

Methods:

Wistar rats were used to harvest adrenals. Nuclear receptors were studied by Western blotting using specific antibodies. RXR ligands, namely, 9-cis-retinoic acid, cervonic acid, adrenic acid, docosapentadecanoic acid and arachidonic acid were determined by LC/MS or GC/MS. Adrenals were also collected from the rats stimulated with ACTH (30μg/100g BW) for four consecutive days. Rats injected with saline served as control.

Results:

Adrenal expressed RXR in two isoforms (RXR α and RXRβ), RAR in two isoforms (RAR α and RARγ), and PPAR in two isoforms (PPAR α and PPARβ). The polyunsaturated fatty acids were all detected; 9-cis-RA was not found. ACTH-stimulation of the rats resulted in an increase of RXR α.

Conclusions:

Adrenal expresses an array of nuclear receptors: RXR α, PPAR α and RARγ which are essential for fatty acid metabolism. The RXR α level is elevated by ACTH-stimulation. Thus, RXR/RXR, RXR/PPAR and RXR/RAR are possible dimers to deal with the liberated fatty acids during steroidogenesis.

Key Words: Retinoid-X-receptor α (RXR α); Adrenal; Peroxisome-proliferation activator

Biochemistry
Category: Basic Sciences

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Phytanic acid-mediated inhibition of IGF-1-induced mitogenic effects: Implications for Diabetes, Atherosclerosis and Cancer.

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Introduction:
Insulin-like growth factor-1 (IGF-1) is now known to control cellular proliferation, differentiation and regeneration, and its altered expression has been implicated in cancer, diabetes and cardiovascular disorders (CVD). Therapeutic manipulation of IGF-1-mediated effects has proven beneficial and we report for the first time that phytanic acid, a branched fatty acid synthesized in vivo during metabolic degradation of chlorophyll, attenuates growth factor-induced mitogenesis and IGF-1-mediated cellular events.

Methods:
Human dermal fibroblasts were grown from skin explants and cultures of rat aortic smooth muscle cells were established by enzymic digestion of the aortic tissue. Growth arrested quiescent cell cultures were treated with varying concentrations of phytanic acid in the presence or absence of IGF-1 and FBS. DNA synthesis in cells was measured by BrdU incorporation assay and NOX activity was measured in cell homogenates. Total RNA was extracted for RT-PCR analysis of PPAR-γ, NOX-1, IGF-1 and GAPDH.

Results:
Treatment of cell cultures with IGF-1 or FBS significantly ($p < 0.01$) increased the BrdU incorporation. Addition of phytanic acid to cell cultures significantly ($p < 0.01$) attenuated IGF-1- or FBS-induced increase in DNA synthesis. IGF-1 was observed to significantly reduce the mRNA levels of PPAR-γ and treatment of cell cultures with phytanic acid prevented IGF-1-mediated depletion of PPAR-γ. Phytanic acid did not have any significant effect on the gene expression of IGF-1. Enzyme activity of NOX and mRNA levels of NOX-1 were markedly increased in IGF-1 treated cells and phytanic acid markedly attenuated IGF-mediated increase in NOX activity, but failed to influence IGF-1-induced effects on NOX-1 mRNA levels.

Conclusions:
Our findings that phytanic acid exhibits anti-mitogenic characteristics and attenuates IGF-1-induced cellular effects underscore the therapeutic importance of this chlorophyll metabolite in CVD, cancer and diabetes.

Key Words: PHYTANIC ACID; IGF-1; PPAR-γ;

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Assessment of Urinary Iodine Excretion Among Normal Kuwaiti Adults

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Introduction:

Iodine is an essential component of thyroid hormones. Between 59 to 65% of total body iodine is contained in the thyroid hormones. Iodine deficiency (ID) is the world's leading cause of mental retardation, and data collected from 92% of the world's population indicated that, globally more than 1. 9 billion individual have inadequate iodine intake (<100μg/L). Little is known about iodine intake or its adequacy among the Kuwaiti population. Therefore, in a random sample of healthy adults the followings were investigated, urinary iodine excretion (UIE), thyrotropin hormone (TSH), free thyroxin (FT4) levels and thyroid antibodies (thyroid peroxidase (anti-TPOAb) and thyroglobulin antibodies (anti-TGAb).

Methods:

139 females and 86 males with mean age of 33 and 35 years for female and male, respectively were recruited. Random urine and blood samples were collected. Urinary iodine excretion (UIE), serum FT4, TSH, anti-TPOAb and anti-TGAb were analyzed.

Results:

Median urinary iodine excretion (UIE) was found to be within the recommended level by WHO (148 μg/L). However, some incidences of UIE <100 μg/L and <50 μg/L were detected in both male and female groups. Thyroid hormone analysis revealed normal levels of both TSH and FT4 for all participants except for one who had hyperthyroidism, which could be resulting from elevated iodine intake as reflected by increased UIE of 590 μg/L. Elevated Anti-TPOAb >75 IU/ml and anti-TGAb >150 IU/ml were detected in 15% and 34% of subjects investigated, and only 10% of them had elevated levels of both anti-TPOAb and anti-TGAb.

Conclusions:

The UIE median value of 148μg/L suggests that iodine intake is adequate for Kuwait, according to WHO recommendation as reflected by normal thyroid function test results. However, 20% and 3% of all participants had UIE <100μg/L and <50μg/L, respectively. Consequently, a nationwide study is reqiured

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Adrenal RXRβ: glandular and subcellular distributions

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Introduction:

Nuclear receptors are transcription factors regulating gene expression. Many of the receptors have been shown to translocate between cytosol and nucleus in response to ligand-activation. Retinoid X receptor-β (RXRβ) is a nuclear receptor, whose role is to mediate cholesterol homeostasis by enhancement of cholesterol-efflux from cells. RXRβ is activated by 9-cis-retinoic acid, arachidonic acid, adrenic acid, docosapentaenoic acid and cervonic acid. Adrenal zona glomerulosa and zona fasciculata utilize cholesterol for glucocorticoid and mineralocorticoid production, respectively. Adrenal glands express RXRβ. Investigations of the glandular and subcellular distributions of RXRβ can help in characterization of the receptor, with respect to control of cholesterol availability for adrenal steroidogenesis.

Methods:

Wistar rats were stimulated with ACTH (30μg/100g BW) for four consecutive days (control injected with saline). Adrenal distribution of RXRβ was investigated by immunohistochemical technique; subcellular distribution of the receptor was studied by Western blotting. 9-cis-retinoic acid and the polyunsaturated fatty acids were determined by LC/MS and GC/MS, respectively.

Results:

Adrenal RXRβ was immunostained heavily in the zona glomerulosa, but weakly in the zona fasciculata. The receptor was concentrated in the nuclear fraction, rather than the cytosol fraction. Arachidonic acid and adrenic acid were also detected in the nuclear fraction. 9-cis-RA was not found. Stimulation of rats with ACTH resulted in diminution of adrenal RXRβ, but its subcellular distribution remained unchanged.

Conclusions:

The ACTH-stimulated reduction of adrenal RXRβ can be postulated to minimize cholesterol efflux, thereby conserving cholesterol for steroidogenesis. Since the receptor is principally expressed in the zona glomerulosa, adrenal RXRβ is probably involved in controlling cholesterol availability for mineralocorticoid synthesis. The concentration of RXRβ in the nuclear fraction could be linked to the presence of arachidonic acid and adrenic acid in this fraction. The present data spotlight a future research direction on the role of adrenal RXRβ in glomerulosa steroidogenesis.

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Curcumin Ameliorates Experimental Colitis Through Suppression Of Toll Like Receptor-4

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Introduction:

 Toll like receptor-4 (TLR-4) mediates innate immune responses and is involved in the pathogenesis of inflammatory bowel diseases (IBD) through suppression of NFkB. Curcumin a commonly used as spice elicits anti-inflammatory properties through inhibition of NFkB. Whether curcumin inhibits inflammation through interaction with TLR-4 remains poorly understood.
The objective of the study was to investigate effects of curcumin on the TLR-4 signaling pathway in experimental colitis.

Methods:

 Colitis was induced in Sprague-Dwaley female rats by intra-rectal administration of trinitrobenzenesulphonic acid (TNBS) and followed for 5 days. The animals were treated orally with aqueous suspension of curcumin (100 mg/kg rat daily) 2 hrs before administration of TNBS. The controls animals received PBS orally in a similar fashion. On day 5, animals were sacrificed, colonic segments were taken out and frozen at -80oC until use. Colitis was characterized by measuring the levels of myeloperoxidase (MPO) activity and malondialdehyde (MAD) concentrations, and by histologic examination. The levels of TLR-4, NFkB and MyD88 proteins were examined using ECL western blot analysis, whereas TLR-4 m-RNA levels were measured using a semi quantitative competitive RT-PCR using a competitive control co-amplified with the target.

Results:

 Inflamed colon showed a significant increase in MPO activity and MDA levels, and the mucosal lining of colon was infiltrated with inflammatory cells. These changes were reduced significantly following curcumin treatments. Levels of TLR-4, NFkB and MyD88 proteins were also increased significantly in inflamed rat colon as compared to the control. Increase in the levels of these proteins was significantly reversed by curcumin treatment. Interestingly, the level of TLR-4 mRNA remained unchanged in all test groups.

Conclusions:

 These findings demonstrate reversal of colitis by curcumin through suppression of TLR-4 and MYD88 expression.

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In vivo effects of antioxidants: scavenging of free radicals or interference with protein expression

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Introduction:

It has been generally accepted that antioxidant additives exert beneficial effects by trapping free radicals. Calculations show, however, that in many cases tissue concentrations of antioxidants, combined with reaction rate constants, preclude any significant benefit from such additives. This is best illustrated by synthetic antioxidants, whose rate constants for reactions with free radicals are known and where tissue distributions are well characterized. Surprisingly, antioxidants with negligible free radical-scavenging capabilities perform in vivo as well as, or better than, antioxidants with superior radical-scavenging potentials. One possible explanation for such discrepancies is interference with cell signaling, leading to changes in gene expression. In this study the effect of a synthetic antioxidant, Mn(III) 5, 10, 15, 20-tetrakis(N-methylpyridinium-2-yl)porphyrin (MnTM-2-PyP), on protein expression was investigated.

Methods:

Diabetic and normal Wistar rats were used as a model system. MnTM-2-PyP was administered s. c. at a daily dose of 1. 0 mg/kg for two months. Protein expression was assessed by Western blotting. The Student's t-test was used for data analysis and $p < 0.05$ was accepted as statistically significant.

Results:

MnTM-2-PyP affected the expression of aconitase and inducible nitric oxide synthase (iNOS) in heart and endothelium. The antioxidant increased the expression of aconitase in both diabetic and normal rats. It suppressed iNOS expression, which was increased by diabetes. Among the proteins which were not affected were GAPDH and glucose transporter, GLUT 1.

Conclusions:

Apart from scavenging free radicals, antioxidants can lead to induction or suppression of certain genes. This effect depends on the nature of the antioxidant and on the redox state of the cells. These cellular effects of antioxidants may explain the often contradictory data obtained when antioxidants were used in different models of disease.

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The risk factors of multiple sclerosis in Kuwait

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Introduction:
Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease that can onset at any age, but most commonly among a younger population. It is characterized by destruction of the myelin sheath and gliosis in multiple areas. The etiology of MS is still unknown. However, both genetic and environmental factors seem to have a role in developing the disease. The objective of this study is to study different genetic and environmental risk factors of MS in Kuwait and assess relative importance of different risk factors as compared to the rest of the world.

Methods:
A case-control study, individually matched for age, sex and nationality, was carried out between the 13th and the 22nd of March, 2006. Cases were obtained from Ibn-Sina, Mubarak Al-Kabeer, and Amiri Hospitals, in addition to a conference held in Crown Plaza Hotel for MS patients. Controls were selected from the same hospitals. Regarding cases from the conference, their matched controls were selected from Al-Sabah Hospital. Information regarding exposures were obtained through a face-to-face interview or self administered questionnaire (depending on the condition of the patient). Only events taking place prior to the disease occurrence were taken into account. For each control a corresponding year of pseudo-diagnosis was established.

Results:
A total of 100 cases and their individually matched controls were approached. Family history of MS was strongly associated with MS (OR= 25. 000, lower 95% CI= 3. 75). Low fish products consumption was also positively associated with MS (Adjusted OR= 2. 914; 95% CI= 1. 36-6. 22). Family history of rheumatoid arthritis (RA) (Adjusted OR= 0. 472; CI= 0. 25-0. 90) and vicinity of equator (p = < 0. 0001) had a protective effect against MS.

Conclusions:
Family history of MS and low fish products consumption were positively associated with MS. On the other hand, positive family history of RA and living further away from the poles had a protective effect against MS.

Key Words: Multiple sclerosis (MS); Odds ration (OR); Confidence interval (CI);

Community Medicine
Category: Undergraduate

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Type 2 diabetes in Kuwaiti adult working population: prevalence rates and associated risk factors

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Introduction:

The aim of this study was to determine prevalence of type 2 diabetes among the Kuwaiti adult working population and to identify the risk factors associated with the disease.

Methods:

A cross-sectional survey with a sample size of 562 Kuwaiti public sector employees, using a gender stratified multi-stage cluster sample was carried out during March-April, 2007. Data were collected through a standardized self-administered questionnaire and a blood glucose test. Multiple regression analyses were used to evaluate the potential risk factors for diabetes.

Results:

The overall prevalence of diabetes was found to be 21. 4% of which 17. 3% were known to have diabetes, and 4. 1% were newly detected in this study. We found 10. 7% had impaired fasting glucose according to American Diabetic Association criteria. Multivariate logistic regression analysis identified the following risk factors for type 2 diabetes: increasing age (AOR = 2. 9, 95% CI 1. 5–5. 5), hypertension (AOR = 2. 1, 95% CI 1. 2–3. 9), sibling with diabetes (AOR = 1. 7, 95% CI 1. 1–2. 7), parents with diabetes (AOR = 2. 3, 95% CI 1. 4–3. 9), ex-smoker (AOR = 3. 0, 95% CI 1. 4–6. 4), increased waist circumference in female (AOR= 2. 2, 95% CI 1. 4–3. 6).

Conclusions:

Our study confirms a growing prevalence of type 2 diabetes in the Kuwaiti adult population. Age, hypertension, family history, smoking and increased waist circumference were significantly associated with type 2 diabetes. These subjects should be a primary target for preventive intervention strategies.

Key Words: Diabetes; Prevalence; Risk factors;
Funding Agency: None

Community Medicine
Category: Undergraduate

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Prevalence of Cardiovascular Risk Factors among Kuwaiti University Students

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Introduction:

The CVDs are the major cause of morbidity and mortality world wide. This cross sectional study aimed to study the prevalence of cardiovascular risk factors among Kuwait University students, and to evaluate the associations of these factors with the prevalence of elevated blood pressure.

Methods:

A total of 1000 students, male and female, aged 15-27 from 8 of 13 Kuwait University colleges were included in this study during September, 2006. The data were collected using a questionnaire and objectively measuring the height, weight, waist circumference and blood pressure for each participant. Dietary habits score, physical activity were measured. Prevalence and bivariate associaton of these risk factors were evaluated with elevated blood pressure both for male and female student groups.

Results:

The proportion of smokers is much higher in male students 23. 9% than female students 2. 3%. Students who reported exposure to passive smoking were 79. 5% of male and 63. 6% of female. Students with low physical activity were 48. 4% among male and 62. 4% among female. 47. 9% male and 34% female students were abdominally obese. Based on BMI, 54. 7% male and 26. 8% female students were either overweight or obese. Students who have one or more CVD risk factors were 75. 5%. Those with 2 or more CVD risk factors were 53. 3% and 31. 8% have 3 or more risk factors. In this study, 9. 1 % of male and 4. 6% of female students were having elevated blood pressure. For male students, age (OR=2. 6; 95% CI: 1. 2-5. 6), abdominal obesity (OR=2. 5; 95% CI: 1. 1-5. 7) were related to elevated blood pressure. For female students, BMI (OR=3. 0; 95% CI: 1. 2-7. 9) was significantly related to elevated blood pressure.

Conclusions:

This study record the high prevalence of modifiable CVD risk factors in this population and highlights the necessity to institute effective prevention and in Kuwait targeting at young age groups.

Key Words: Cardiovascular risk factors; Central obesity; BMI;
Funding Agency: none

Community Medicine
Category: Graduate (Basic Sciences)

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An exploratory study of basic life support and first aid knowledge among emergency medical professionals in Kuwait

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Introduction:

A cross-sectional study design was undertaken to assess the knowledge of Basic Life Support (BLS) and first aid among Emergency Medical Professionals (EMPs) in Kuwait.

Methods:

Participants were 64 Emergency Room (ER) physicians, 166 ER nurses and 91 paramedics from the six major government hospitals in Kuwait. The research tool included a self-administered questionnaire consisting of questions addressing sociodemographic factors and questions assessing BLS and first aid knowledge. The total median score was used for all analyses. A cut-off point of 60% was used to indicate a passing grade in the assessment.

Results:

The median score of the overall performance of the 321 EMPs was 64. 3% with an Interquartile Range (IQR) of [55. 4%, 75. 0%]. The median score in the BLS section was 60. 0% with an IQR of
[50. 0%, 73. 3%]. The median score in the first aid section was 61. 5% with an IQR of [61. 5%, 76. 9%]. Paramedics' knowledge of BLS and first aid (median score = 75. 0%) was better than that of ER physicians (median score = 67. 9%) or ER nurses (median score = 60. 7%) who were the least knowledgable of all the EMPs. The total median scores were significantly associated with occupation, nationality, first aid licensing, and a higher level of confidence in performing BLS and first aid. Our findings were consistent with earlier studies on the proficiency of BLS and first aid knowledge among the three groups of EMPs.

Conclusions:

Knowledge of BLS and first aid varied between ER physicians, ER nurses, and paramedics, yet insufficient knowledge in some aspects of BLS and first aid was noted across all groups. Appropriate and regular BLS and first aid training is crucial to ensure optimal management of acutely ill patients.

Key Words: Basic life support knowledge; First aid knowledge; Assessing emergency medical
Funding Agency: None

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Evidence Based Practise Among Primary Care Physicians in Kuwait.

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Introduction:

Evidence based medicine (EBM) is defined as the integration of best research evidence with clinical expertise and patient values.

Methods:

We conducted a cross sectional study with a sample of 332 primary care physicians in 57 primary care centers in Kuwait. A self-administered questionnaire was used to collect data with a response rate of about 93%.

Results:

Although half of the physicians self reported that they use EBP most of the time, adjusted analysis revealed that only about 24% had a reasonable understanding of EBM. Most of the clinical practice in the Kuwaiti primary care setting seemed to be based on the clinician's own judgment and traditional text books, rather than on evidence based sources such as the Cochrane Library or Medline. None of the physicians had internet connection at their work place and a vast majority of them had no access to international journals nor were they confident about the critical appraisal of published evidence.

Conclusions:

Overall, the level of awareness of EBM among primary care physicians in Kuwait was found to be considerably lower, despite the claim that almost half of them are evidence based. Training in the areas of EBM as well as making sure the Kuwaiti primary care centers have access to evidence based sources are critically important if primary care in Kuwait were to become evidence based.

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Prevalence and correlates of major chronic illnesses among older Kuwaiti nationals

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Introduction:

 Life expectancy of Kuwaiti nationals has increased to about 77 years. The corresponding salience of chronic illnesses in morbidity and mortality is increasing. This paper provides community based information on the prevalence of diabetes, hypertension and heart disease, and draws an epidemiological picture of the significant socio-demographic and behavioral correlates of such illnesses.

Methods:

 A household survey of Kuwaitis aged 50 and over was conducted during February 2005 to June, 2007. A proportionately representative sample from the relatively more urban (Capital) and less urban areas (Ahmadi) was selected. A total of 1451 individuals from the Capital and 1036 from Ahmadi were successfully interviewed. A proxy respondent was used in 5. 4% of the cases. Among the 3499 households approached for an interview, 1491agreed to participate (43%). Among the 2605 potential eligible persons approached for an interview, 2487 (95 %) participated.

Results:

 The doctor-diagnosed prevalence of diabetes, hypertension and heart disease was reported to be 51%, 53% and 18%, respectively, indicating a remarkable increase since 1996. Prevalence of each of the three diseases increased linearly by age among both sexes. With increasing age, co-morbidity of the three diseases increased markedly. The percentage of those with all three diseases increased from 4% among those aged 50-59 to 9% among those aged 60-69 and 21% among those aged 70+. Analysis according to major socioeconomic and behavioral factors indicates prevalence of chronic illnesses to be consistently higher among the relatively less educated, those with relatively higher levels of income, and those who participated in social activities less frequently.

Conclusions:

 Prevalence of diabetes, hypertension and heart disease has increased to alarmingly high levels among older Kuwaitis. There is a need to devise focused intervention programs for reducing morbidity and mortality.

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Prevalence of Metabolic Syndrome in Kuwaiti adolescents: Comparative evaluation of the International Diabetes Federation (IDF) and modified Adult Treatment Panel III (ATP III) diagnostic criteria

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Introduction:
The metabolic syndrome (MS) best predicts susceptibility to atherosclerotic disease. In this study, we attempted to evaluate the prevalence of MS in Kuwaiti adolescents. As there are no Arab diagnostic criteria, we evaluated comparatively the effectiveness of the IDF and the modified ATP III MS diagnostic criteria in the population.

Methods:
We evaluated 538 Kuwaiti students aged 10 – 19 years, recruited randomly from apparently healthy school students. Clinical evaluation included measurements of waist circumference (WC) and blood pressure (BP), and a fasting blood sample was collected for measurement of plasma lipids (including high density lipoproteins "HDL", triglycerides "TG"), and glucose.

Results:
The mean $\pm$ SD results obtained were: WC (75. 9$\pm$15. 2cm); TG (median 0. 64, range 3. 6-4. 8mmol/L); HDL (1. 2$\pm$0. 3mmol/L); glucose (5. 1 $\pm$ 0. 4mmol/L); BP (systolic 121. 9 $\pm$ 11. 3; diastolic 81. 7 $\pm$ 8. 4mmHg). By modified ATP III criteria, there was increased WC in 16. 9%, TG in 10%, Glucose in 2. 6%, BP in 61. 6%, and reduced HDL in 31. 4%. This corresponded to an MS prevalence rate of 11. 9% (frequency of individuals with at least 3 abnormal parameters). Using the IDF criteria, WC was increased in 31. 7%, TG in 3. 5%, Glucose in 13 %, BP in 51. 2 %, and HDL was reduced in 41. 9 %. This corresponded to an MS prevalence rate of 16. 9% (frequency of individuals with high WC + $\geq$2 other parameters).

Conclusions:
There is a relatively high prevalence rate of MS (> 10%) in Kuwaiti adolescents, whatever criteria are used, the IDF criteria tend to overestimate the prevalence of MS in comparison to the modified ATP III criteria (16. 9% vs. 11. 9%). These results indicate the need for MS diagnostic criteria specific for the Arab population. Nonetheless, the relatively high MS prevalence rates in Kuwaiti adolescents indicate an urgent need for intervention programs to prevent increasd ischemic heart disease rates.

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Mapping bioethical regulations in Kuwait: a collaborative UNESCO project

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Introduction:
The United Nations Educational, Scientific, and Cultural Organization (UNESCO) contacted our research group in Kuwait to participate in the multi-center collaborative study of the existence and content of bioethical regulations pertinent to selected topics for a comparative analysis in the Arab region.

Methods:
Data was collected from PubMed©, interviewed legal and administrative key governmental personnel in the Ministry of Health, and the MOH related rules and regulations in the State of Kuwait from 1960 up to 2007.

Results:
Only five out of the ten selected UNESCO topics (human reproductive and therapeutic cloning, embryonic stem cells, genetic test, human genome and gene analysis, research involving human subjects, organ transplant, assisted reproductive technology, pharmaceutical research, medical practices, and abortion) had existing regulations in the Arabic language currently found in the Ministry of Health in the State of Kuwait.

Conclusions:
There are many important health related issues that currently lack bioethical, legal and administrative regulations in the country. More over, there is currently no existing national ethics committee to guide and facilitate such a task. Based on the study's findings it is hoped that more effort is invested in the establishment of bioethical regulations in Kuwait as it is of grave importance for the advancement of health policies, practice and patients' care.

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Thyroid disease amongst nurses in Kuwait

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Introduction:

Thyroid disease has reached endemic proportions in the Middle East. It appears that medical personnel, particularly the nursing staff, might be at a higher risk of developing autoimmune thyroid disease. We undertook a cross sectional survey of nursing staff at a major tertiary center in Kuwait to study the prevalence of thyroid disease and it's associated risk factors.

Methods:

The survey was performed on 150 nurses working in Kuwait at the Mubarak Al Kabeer hospital. The wards in this hospital were selected as clusters and a stratified single stage cluster was done with a random selection of wards.

Results:

Of 150 nurses (female 79% and male 19%) 18% were Arab, 78. 7% were Asian and 3. 3% were other nationals. Two-thirds (63. 3%) of the nurses were below 35 years of age. The majority (40. 7%) were working in Kuwait for 5-9 years.

When asked about thyroid status, about half were asymptomatic and had not been tested (76 nurses). Of the other half that had been tested (71 nurses), 13 nurses (18%) had thyroid disease. No clear risk factor was noted.

Conclusions:

Our preliminary evaluation suggests that the prevalence of thyroid disease is higher than in the general population. Although no clear risk factor is forth coming, further analysis that is being done may provide the answers.

Full results will be updated in the
final poster presentation.

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Knowledge, Beliefs and Attitude Towards Consanguinity and Premarital Screening for Hereditary Diseases Among Kuwaiti University Students

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Introduction:

The aim of this study is to assess the three components of knowledge and attitude (knowledge of hereditary diseases, knowledge of premarital screening, and attitude towards consanguinity) in Kuwaiti university students that could potentially modulate their attitude towards premarital screening.

Methods:

A cross-sectional survey with a sample size of 592 Kuwaiti university students, using a gender stratified multi-stage cluster sample was carried out during March-April, 2007. Data were collected through a self-administered questionnaire. Multiple regression analyses were used to evaluate the independent associations in the study.

Results:

The overall rate of consanguinity between students' parents was 41.9%. Family history of a hereditary disease was present in 42.3% of the participants. 58.8% of participants were not in favour of consanguineous marriages. Customs and traditions were perceived to be the main factors behind the preference of consanguineous marriage (95.3%). 89% of participants were aware of the existence of premarital screening services. The majority of the participants agreed that premarital screening should be mandatory and that it does not conflict with religious teaching. Multivariate logistic regression analysis identified the following factors to be associated with the favourable attitude towards premarital screening: good knowledge of hereditary diseases (AOR = 1.8, 95% CI 1.2–2.7), good knowledge of premarital screening (AOR = 1.7, 95% CI 1.2–2.5), and non-favourable attitude towards consanguinity (AOR = 1.6, 95% CI 1.1–2.5).

Conclusions:

Premarital screening was perceived as an acceptable measure in the control of hereditary diseases not conflicting with religious, social, or cultural factors. This study found that a good knowledge of hereditary diseases, good knowledge of premarital screening, and non-favourable attitude towards consanguinity were independently related to a favourable attitude towards premarital screening.

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Prevalence of metabolic syndrome among healthy Kuwaiti adults

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Introduction:

Metabolic syndrome is the disease of the new millennium; its prevalence is increasing dramatically because of the rising number of people who are obese and inactive. The objective of the present study was to estimate the prevalence of metabolic syndrome among healthy Kuwaiti adults attending two primary health care centers in Kuwait.

Methods:

A convenience sample comprised of 434 Kuwaiti nationals, aged from 20-44 years who were attending the health centers for a routine check up and who were neither suffering from nor have ever been diagnosed with any chronic illness such as diabetes, hypertension, heart problems or dyslipidaemia was collected. The National Cholesterol Education Program Adult Treatment Panel III criteria of metabolic syndrome was used. Body mass index was determined. Waist circumference, levels of fasting blood glucose and fasting plasma lipids (triglycerides and high-density lipoprotein cholesterol), blood pressure were measured.

Results:

The total number of people who met the criteria of metabolic syndrome was 78 (18%), 62. 8% of them were males. The prevalence of overweight and obesity were 27% and 37. 3% respectively with no significant gender differences. Low HDL-C was found in 50. 7% (48. 5% of males and 54. 3% of females), central obesity was prevalent among 34. 6% and was significantly more common among females than males (45. 7% vs 27. 8% respectively). High TG was prevalent among 19% where males rated significantly higher than double females (28. 9% vs 14. 1% respectively). About 17% of the sample was suffering from either high blood pressure (17. 0% of males and 15. 9% of females) or/and impaired fasting blood glucose (18. 9% of males and 14. 0 of females).

Conclusions:

The prevalence of metabolic syndrome is high among healthy adults attending primary health care centers in Kuwait.

Key Words: Metabolic syndrome; Adults; Kuwait;

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Family history of breast cancer and its association with the practice of breast cancer screening

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Introduction:

Little is known about the prevalence of screening for early detection of breast cancer among women in Kuwait. The aims of this research were to: i. estimate the prevalence of practice of breast cancer screening by any method among working females, and ii. estimate the prevalence of history of breast cancer among family members and to evaluate its association with practice of breast cancer screening in this population.

Methods:

A cross sectional study was conducted among working women aged 35 years and older. A self-administered questionnaire consisting of 26 questions on demographic information, history of breast cancer among family members and among any close contacts and related aspects of breast cancer was used. We computed the prevalence of breast cancer screening practice and the history of
breast cancer among family members including close contacts.

Results:

Prevalence of the practice of breast cancer screening by any method was 28%. Of the 189 women, 47 (24. 9%) reported a history of breast cancer among the family members, while 73 (38. 6%) reported a history of breast cancer among close contacts. Upon univariate analyses, variables significantly associated with the breast screening practice were age 40 years and above (OR = 2. 0; 95% CI: 1. 02 – 3. 8) and positive personal history of any type of cancer (OR = 10. 9; 95% CI: 1. 2 – 100. 7). However, a positive family history or a history of breast cancer in close contacts was not significantly associated with the practice of breast cancer screening (OR = 1. 8; 95% CI: 0. 9 – 3. 6).

Conclusions:

Prevalence of breast cancer screening is low. Having a positive history of breast cancer among family members or close contacts does not seem to be a motivating factor for breast cancer screening in our study. Public health authorities need to accelerate their efforts to increase the awareness about the benefits of breast cancer screening practices among females.

Key Words: Breast cancer; Screening practice; Working females;

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Knowledge, Attitude and Practice of Kuwait University students about Avian Flu

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Introduction:

Avian flu is an emerging viral disease that poses the potential risk of a pandemic. We were interested in examining the awareness regarding this potential threat among Kuwait University students. The objective was to assess the knowledge, attitude and practice of Kuwait university students about avian flu.

Methods:

Students from six of twelve faculties of Kuwait University were selected as a sample for inclusion in our study including the faculties of Engineering, Science, Law, Business Administration, Allied health and Dentistry. Consenting students were selected as a sample of convenience and were approached between classes, cafeteria, and lobbies. Each one of the participants was provided with an information guide about Avian Flu after they filled in the questionnaire.

Results:

The prevalence of poor knowledge, negative attitude and poor practice score among Kuwait University students was 40. 2% (212/528), 21. 2% (111/524) and 33. 8% (178/527) respectively. Male gender, father being illiterate, living in a villa, and poor knowledge were significantly related with negative attitude. The factors significantly associated with poor practice of participants about Avian Flu were male gender, those living in a villa, and students with negative attitude. However, poor knowledge was not significantly associated with poor practice. There was no significant association between faculties and poor practice as well as negative attitude. The most common sources of information from where the participants heard about Avian Flu were the newspapers and magazine followed by TV and radio.

Conclusions:

Our research estimated prevalence of poor knowledge of negative attitude towards and poor practice regarding Avian Flu as, 40. 2 %, 21. 2%, 33. 8% respectively, among Kuwait University. Public health authorities should make efforts to create mass awareness about specific aspects of Avian Flu through print and electronic media.

Key Words: Avian flu; Knowledge; Students;
Funding Agency: None

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An Epidemiological study of dyslipidemia and assessment of coronary heart disease risk among working population in Kuwait

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Introduction:

Cardiovascular disease (CVD) is one of the most common cause of death worldwide. There are several risk factors for developing CVD, of which dyslipidemia is the most important. The aim of this study is to asses the prevalence of dyslipidemia and major cardiovascular risk factors to predict 10 year total cardiovascular risk among working population in Kuwait.

Methods:

Cross-sectional study of working population in private and government sector in Kuwait. Data were collected by self-administered questionnaire and measurement of blood pressure and cholesterol levels by CardioChek PA and Omron HEM 907. The questionnaire included sociodemographic characteristics, medical history and lifestyle habits.

Results:

Males had significantly higher abnormal levels of TC/HDL [OR: 5. 71; 95%CI: 3. 66- 8. 91], non-HDL [OR: 2. 02; 95%CI: 1. 13-3. 64] and HDL [OR 5. 49; 95%CI: 3. 54-8. 50] than females. Females showed an age trend in terms of prevalence of major CHD risk factors, while in males all age groups had the same prevalence of risk factors across several cholesterol dimensions. The 10-year CHD risk was assessed using Framingham score, 1. 1% of males had a 10-year risk >/= 25% , 2. 6% of males had a 10-year CHD risk between 15-25%. On the other hand, approximately 92% of females had 10-year CHD risk </= 1%.

Conclusions:

Men had abnormal levels of HDL, non-HDL and TC/HDL compared to women. The prevalence of major CHD risk factors were higher among males and the 10-year CHD risk in males exceeded that of females.

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Lack of evidence for the use of angiotensin receptor blockers as an angiotensin converting enzyme inhibitor substitute in high risk populations without heart failure

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Introduction:

Angiotensin receptor blockers (ARB) are widely used to treat patients without heart failure as a substitute for angiotensin converting enzyme inhibitor (ACEI), but their effect on cardiovascular morbidity and mortality has not been clearly determined.

Methods:

We conducted searches of the published literature. Criteria for inclusion in our meta-analysis included the use of a randomized control group not receiving an ARB and the availability of outcome data for either of four endpoints (myocardial infarction, stroke, cardiovascular death and all-cause death) which need not have been pre-specified. Of 44 potentially relevant studies, 36 trials met the inclusion criteria. We tabulated all occurrences of these four adverse outcomes.

Results:

Data were combined by means of a random-effects model. In the sub-group without heart failure, ARBs, as compared with the control group, had an odds ratio for myocardial infarction of 1. 09 (95% confidence interval [CI], 0. 98 to 1. 21), and the odds ratio for death from cardiovascular causes was 1. 01 (95% CI, 0. 93 to 1. 09).

Conclusions:

There is no evidence so far, after pooling more than 30, 000 patients, that ARBs confer cardiovascular protection akin to ACEI and the trend that emerged is not in favor of ARB therapy. Caution is therefore advised in the use of ARBs as a substitute for ACEI in patients without a heart failure indication.

Key Words: Meta-analysis; Angiotension receptor blockers; Myocardial infarction;
Funding Agency: None

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Intravenous magnesium improves survival in myocardial infarction: a quality effects meta-analysis

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Introduction:

Magnesium use in myocardial infarction had been discontinued based on the findings of two multi-centre mega trials. The problem with the meta-analyses including these two trials of magnesium to prevent mortality after myocardial infarction is that, using a fixed-effect model, there is no survival benefit for magnesium simply because they weigh heavily on the analysis. On the contrary, given the substantial heterogeneity created by these trials, the random effects meta-analysis finds a significant effect for magnesium, despite these two trials.

Methods:

In the wake of our recently proposed alternative to the random effects meta-analysis, we decided to run a quality effects meta-analysis in an attempt to resolve the magnesium stand-off. This was done by incorporating methodological differences within the meta-analysis.

Results:

We find, based on this new methodology, that magnesium is indeed effective in reducing mortality after myocardial infarction (OR 0. 78; 95% CI 0. 68-0. 9) and this translates to 1 life saved for every 62 patents treated given a 8% mortality in the control groups. These results are not sensitive to exclusion of either of the multicentre trials from the analysis

Conclusions:

Magnesium is effective in reducing mortality after myocardial infarction and should be re-instituted in standard protocols.

Dentistry
Category: Clinical

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A Questionnaire Survey on Halitosis (Bad Breath) Among the Population in Kuwait

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Introduction:

Halitosis is a major concern to the general public and a multimillion-dollar industry world wide. Following protein degradation in the oral cavity, there is a subsequent breakdown of certain amino acids to malodorous compounds like, hydrogen sulfide, methylmercaptan, cadaverine etc. A previous study on halitosis was conducted in Kuwait among the Kuwaitis only. Our study aims to compare its prevalence between Kuwaiti and Non Kuwaiti populations of various age groups.

Methods:

Questionnaires were distributed among Kuwaiti and Non Kuwaiti population aged 12 years and above. A total of 2556 questionnaires were distributed at various schools, government and private offices and university campuses in all six districts of Kuwait with a response rate (RR) of 70%. Data was analyzed using the Statistical Package for Social Sciences (SPSS) software (Chicago, IL, USA) version 14. 0. Frequency distribution and associations (using Chi-square test) between various parameters were calculated. Significance level used was $p<0.05$.

Results:

Prevalence of self reported halitosis was 55. 5% (n=989) among the population with 67. 2% (n=665) being Kuwaitis and 32. 8% (n=324) being Non Kuwaitis. A significant difference was seen between male and female respondents in the Kuwaiti population to the following questions: Do you have bad breath?, Can you smell your own breath?, Have you treated yourself for oral malodor?, Have you used traditional medicines for treating oral malodor?, Do you have relatives with bad breath?, Do you have white or yellowish deposits on your tongue? No significant difference was seen to these questions for the Non Kuwaiti population (Table 1). Further analysis revealed that the significant difference to the above mentioned parameters was mainly due to the female Kuwaiti population in particular (Table 2).

Conclusions:

Our data revealed the prevalence of halitosis was higher among Kuwaitis compared to the Non Kuwaitis and in particular among Kuwaiti females.

Dentistry
Category: Graduate (Resident)

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Referral of periodontal patient from primary health care providers in Kuwait.

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Introduction:
Periodontal diseases and caries are the most common oral infections and major causes of tooth loss worldwide. General dental practitioners (GDP) are the first line for oral care provision at the ministry of health in Kuwait (MOH). Our aim is to assess the basic knowledge of the GDP's in diagnosing periodontal conditions and to set referral basis for specialist periodontal care.

Methods:
 An anonymous self administrated questionnaire was completed by 67 GDP's, dental graduate residents. The questionnaire addressed the GDP knowledge of recognizing periodontal disease activity, ability of diagnosing and treating periodontal conditions. The need of further education in clinical Periodontology was also assessed.

Results:
The majority of the GDP's (88 %) have graduated within the last year and 94% were aware of the Basic Periodontal Examination (BPE) screening index. About 62 % felt confidant in diagnosing periodontal conditions, and 94 % would base their diagnosis on clinical and radiographic findings. Seventy four percent of the respondents agreed that probing depths, mobility and bleeding on probing are indicative of periodontal disease activity. Most of GDP's (97%) agreed on the importance of the medical history for their diagnosis. Only 71% of the respondents were confident in providing non-surgical periodontal therapy while 94% felt they need further education in diagnosing and treatment of periodontal conditions.

Conclusions:
 BPE index can be used clinically by most of the GDP's. This may help in identifying periodontal conditions effectively, hence improving oral care delivery. Referral guidelines for periodontal specialist centres maybe based on BPE index. Further periodontal education can be delivered to GDP during their resident internship year, or through continued education courses.

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Orthodontic treatment need and manpower requirements in Kuwait

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Introduction:

 Our purpose was to determine the orthodontic treatment need in adolescent Kuwaitis and to assess the orthodontic manpower requirement for meeting the need.

Methods:

 A population-based sample of 753 boys and 728 girls, representing about 7% of all 13-14-year-old Kuwaiti school-children, were selected according to cluster sampling methods. Information on nationality and orthodontic treatment experience was collected through subject and family interview. Treatment need was scored in a well lit classroom, or from initial study models of subjects with orthodontic treatment experience, according to the Aesthetic Component (AC) and Dental Health Component (DHC) of Index of Orthodontic Treatment Need (IOTN). The initiating occlusal feature of DHC as well as any mesial migration and loss of the first molars was also recorded.

Results:

 Orthodontic treatment need was categorized as definite in 31. 1%, as borderline in 28. 7%, and as no need in 40. 2% of the subjects. The need was similar in the different administrative areas, and no gender differences were detected ($P>0.05$). Impeded eruption, need for pre-prosthetic orthodontics and/or severe contact point discrepancy associated with mesial migration or loss of the first molars accounted for 22. 1% of the subjects with definite treatment need. However, the majority of these subjects demonstrated definite or borderline need also for other reasons. The current Kuwaiti birth cohorts of about 20, 000 will therefore imply an annual increment of about 6, 220 adolescents with definite need for orthodontic treatment. Assuming that each government employed orthodontist has capacity to start 100 comprehensive cases every year, Kuwait Ministry of Health must employ about 60 orthodontists to meet this need.

Conclusions:

 About 30% of each Kuwaiti birth cohort is likely to present with definite orthodontic treatment need at adolescence. The Ministry of Health will need a workforce of about 60 orthodontists to meet this need.

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Post-operative Complications Associated with the Placement of Implants

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Introduction:

The aim of this study was to assess post-operative complications associated with implant insertion.

Methods:

This was a prospective, two-center study of adult patients scheduled for the surgical placement of ¡Ý 1 implants. Mean swelling scores were evaluated through a 0-10 numerical scale during surgery, 24 hours after surgery, and after 1, 6, and 12 weeks. The incidences of other complications were also recorded.

Results:

A total of 510 implants were placed in 234 patients. Mean swelling scores were highest at 24 hours after the surgery (76. 9%), and gradually decreased at subsequent time-points. Factors significantly associated with pain included operator experience and Age (less than 45 years old). At one week, swelling levels were significantly associated with operator experience and prior augmentation. Only four cases developed altered sensation. The altered sensation resolved after 6 weeks. One implant perforated the maxillary sinus 3 months following placement. Three cases developed infection at week 6. most of these these cases were diabetic patients.

Conclusions:

Swelling experienced by patients following the surgical placement of dental implants is generally mild and gradually decreased with time. Other complications such as sinus perforation, infection and altered sensation are very uncommon and can be avoided with careful treatment planning.

Dentistry
Category: Clinical

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Posteroanterior cephalometric norms for adolescent Kuwaitis

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Introduction:

A comprehensive cephalometric analyses must include an evaluation of postero-anterior (PA) cephalograms in patients with transverse discrepancies or facial asymmetries. The aim of this study was to establish PA cephalometric norms for adolescent Kuwaitis of age comparable to common start of comprehensive orthodontic treatment, and to compare these norms to those of the common analysis systems.

Methods:

Digital lateral cephalograms made of 80 Kuwaiti boys and 79 Kuwaiti girls of mean age 13. 27 & 13. 21 yrs (SD 0. 42 & 0. 43), respectively, with ideal dental occlusion were evaluated. Anatomic landmarks were identified directly on the digital computer images. Linear and angular measurements were calculated electronically using the Dolhin version 9 software package.

Results:

While the mandibular intercanine width was clinically narrower than previously published norms, the remaining norms for dental widths as well as the norms for dental maxillo-mandibular relationships and symmetry were similar. All skeletal width measuremenst were also clinically similar to previous norms. However, the maxilla was clinically narrower relative to the mandible. In addition, the mandibular molars were more lingually positioned relative to the line connecting the skeletal bases. With the exceptions of molar relationship and dental midline, the ranges of all dental and skeletal Kuwaiti adolescent norms were larger than the respective clinical deviations previously presented.

Conclusions:

Our findings suggest that Kuwaitis have narower mandibular intercanine with, more lingually positioned mandibular molars relative to the skeletal bases, and a narrower maxilla relative to the mandible. Our findings also suggest a larger variation in the majority of the dental and skeletal transverse measuremenst than previously suggested in subjects with natural development of ideal occlusion.

Key Words: Cephalometric radiographs; Posteroanterior; Norms;

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Tooth-specific caries prevalence in Kuwaiti kindergarten schoolchildren

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Introduction:

The aim of this national dental survey was to determine the tooth-specific caries prevalence in Kuwaiti kindergarten schoolchildren.

Methods:

A national epidemiological survey of the 4- and 5-year-old kindergarten schoolchildren (n = 1, 277) was conducted in the five different governorates (Ahmadi, Farwaniya, Hawally, Jahra, Capital) in Kuwait. Five trained and calibrated dentists examined the children. Dental caries was scored using WHO criteria.

Results:

The proportion of caries-free 4- and 5-year-old children was 32% and 24% respectively. The corresponding mean dft/dfs for 4- and 5-year-olds were 3. 7/6. 9 and 4. 8/9. 6. The decayed component was the major contributor to these mean scores. The maxillary central incisors (37. 3%) were the most affected by caries followed by mandibular second molars (31. 1%), maxillary second molars (30%), mandibular first molars (28. 4%), maxillary first molars (27. 6%), maxillary lateral incisors (22. 4%), maxillary canines (11. 1%), mandibular canines (5. 9%), mandibular central incisors (4. 2%) and the mandibular lateral incisors (3. 5%) were the least affected teeth.

Conclusions:

Caries levels are lower or similar to those in neighbouring and other Middle East countries. A high percentage of carious maxillary incisors indicate an early childhood caries pattern in these children. Preventive services should be given high priority and needs to be at an earlier age to target the primary dentition. Access to dental care must be improved and the systematic preventive care program should be reinforced for infants and preschool children, as they are the high-risk groups for caries in Kuwait.

Dentistry
Category: Clinical

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The Awareness of the Diagnostic Value of Saliva among Dental Students, General Practitioners and Specialists

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Introduction:

The purpose of this study was to assess the level of dental practitioners' awareness of the diagnostic properties of saliva and assess the knowledge between different educational levels of dental professionals.

Methods:

A standardized questionnaire was equally distributed (n= 50) to clinical dental students, general practitioners, and specialists. A total of 150 questionnaires were collected, 52% females and 48% males. The descriptive statistics has been presented as median and inter-quartile apart from numbers and percentages, because continuous data for age, and years of practice were not normally distributed. Chi square test was used to find if there was any association between categorical variables. The probability level ($p<0.05$) was considered statistically significant.

Results:

the median age of our sample was 28 yrs (28- 37). The Kuwaiti and non-Kuwaiti participants were 69. 3% and 30. 7% respectively. The median years of practice inside Kuwait and outside Kuwait were 4. 5 yrs (4. 5-10. 0) and 2. 0 yrs (2-6. 75) respectively. 81. 3% of dentists and dental students agreed that saliva is a good marker to detect systemic diseases; however, only 18. 7% agreed that its diagnostic properties are as effective as blood test. Moreover, only 10. 0 % agreed that saliva can substitute blood test in the future. Highest knowledge was about the diagnostic susceptibility to dental caries (98. 0%) and periodontal disease (89. 3%) and the least knowledge was about the diagnosis of breast cancer by saliva (6. 7%). The knowledge of dental specialist about HIV detection by saliva was significantly higher than students ($p<0.05$). Students had significantly poor knowledge about detection of level of testosterone ($p<0.05$). However, they showed significantly high knowledge in saliva detection of Sjögren's disease ($p<0.05$).

Conclusions:

dentists and students require more knowledge about the diagnostic value of saliva.

Key Words: Saliva; Diagnosis; Systemic disease;
Funding Agency: None

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A Comparison of Root Canal Preparation Using NiTi Hand, K3, ProFile and ProTaper Rotary Instruments

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Introduction:

To overcome the existing shortcomings due to the use of the traditional stainless steel files a new standardization for endodontic instruments was introduced. Nickel titanium both hand and engine driven files were developed. The purpose of this study was to evaluate the shaping ability of various nickel titanium instruments in curved mesiobuccal canals of mandibular first molars.

Methods:

Sixty four teeth were randomly divided into four groups each having similar degrees of curvature. The mesial roots were sectioned horizontally at 2, 5 and 9 mm from the apex. The roots were reassembled and the canals were instrumented using ProTaper (group 1), K3 (group 2) and ProFile (group 3) instruments according to manufacturer's instructions. Group 4 were instrumented using hand NiTi instruments in step back technique. The pre and post preparation canal images were recorded and then assessed with an image analysis system. The amount of dentine removed, canal cleanliness, canal shape and the centering ratio were evaluated independently by two evaluators. Kruskal-Wallis, ANOVA and Post-Hoc tests were used for statistical analysis.

Results:

Rotary instruments resulted in cleaner canals when compared to hand instrumentation especially at the apical third ($p < 0.001$). ProTaper instruments removed more dentine at the three sections ($p < 0.01$). ProFile preparation resulted in better centering ratios at all canal sections ($P < 0.01$). There were more round canal shapes at the three section levels using rotary instruments. Hand instruments resulted in more irregular canal shapes at the apical third.

Conclusions:

ProFIle rotary instruments removed less amount of dentine and resulted in better centering ratios in all the sections when compared to other instruments. Rotary instruments resulted in much cleaner canals and more uniform canal shapes when compared to hand preparation.

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Orthodontic treatment need among patients accepted in Kuwait Ministry of Health.

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Introduction:

The aim of this study was to assess the Index of Orthodontic Treatment Need scores (IOTN), gender proportions and age distribution of patients accepted in the five government orthodontic units in the State of Kuwait.

Methods:

A cross-sectional study was conducted, in a randomly selected sample of 250 orthodontic diagnostic casts of patients from the five dental centers in the Ministry of Health, which are: Al-Amiri, Beneid Al-Gar, Al-Adan, Al-Farwaneya and Al-Jahra. Treatment need was assessed by author (M. A.) according to the Dental Health Component (DHC) of the Index of Orthodontic Treatment Need (IOTN) on a scale from 1 to 5. Patients were categorized as 'no need' (DHC 1-2), 'moderate or borderline need' (DHC 3), and 'definite need' for treatment (DHC 4-5). The examiner was calibrated in the use of IOTN prior to the study and demonstrated acceptable reproducibility.

Results:

A 'definite need' for treatment was recorded in 53. 6% of the cases and 32. 8% had 'border line' need on dental health grounds. Females constituted 68% of the sample. Only 48. 4% of the patients were in the age category 12-14 yrs. (golden age). No significant difference existed between
the five centres ($p>0. 05$).

Conclusions:

Our findings suggest that only half of the patients belonged to the 'definite need' and 'early adolescence' (12-14 yrs.) categories. In addition, females were over-represented in the three IOTN groups. Therefore, an objective method such as, the IOTN, is crucial to direct the resources in the ministry to those who are in real need for orthodontic treatment.

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Parental Attitude Toward Behavior Management Techniques Used in Pediatric Dentistry in Kuwait

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Introduction:
 The aim of this study was to evaluate the attitude of parents in Kuwait toward different behavior management techniques commonly used in pediatric dentistry.

Methods:
  One hundred-fifty parents participated in this study by answering a questionnaire and were asked to rank 11 behavior management techniques (BMT) according to their preference, from the most acceptable (rank 1) to the least acceptable (rank 11), after providing them with a verbal explanation of each technique. Techniques investigated were: Conscious sedation, Hand-over-mouth, Passive physical restraints, Active physical restraints, Parental presence/absence, Positive reinforcement, Non-verbal communication, Tell-show-do, Voice control, Distraction, and General Anesthesia.

Results:
  One hundred-fifty parents completed questionnaire forms for analysis. The ranking of the techniques in an order of decreasing acceptance as reported by the parents was in the following order: (1)Tell-show-do; (2)Positive reinforcement; (3)Parental presence/absence; (4)Distraction; (5)Non-verbal communication; (6)Voice control; (7)Sedation; (8)Active physical restrains; (9)Passive physical restraints; (10)Hand-over-mouth; (11)General anesthesia. The level of acceptance was not significantly associated with parent's gender, child's gender, order of the child between his/her siblings, and the presence of medical problems. However, parent's age, nationality, level of education, residency, occupation of mother, child's age, and place of receiving dental treatment were significantly associated with parental acceptance of certain BMT.

Conclusions:
  Parental attitude toward different behavior management techniques varies considerably between parents. A number of factors were found to significantly influence the parental level of acceptance of
 certain BMT.

Dentistry
Category: Undergraduate

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The Prevalence of Physical and Verbal Abuse Against Dentists in Kuwait

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Introduction:

The aims of this study were to examine dentists' awareness of the problem of abuse, and to evaluate the prevalence of physical and verbal abuse against dentists in Kuwait.

Methods:

This was a cross-sectional study of dentists from all governorates of Kuwait. A structured questionnaire that evaluated socio-demographic data, perception of stress associated with dentistry, awareness of the issue of abuse against dentists, dentist's definition of physical and verbal abuse, and the prevalence of this problem, was used. Descriptive statistics and univariate analyses were performed.

Results:

A total of 125 questionnaires were used in the study analysis. Of these, 66. 4% were males, 55. 2 % were Kuwaiti dentists, and 82. 3 % worked in the Ministry of Health. Dentistry was reported to be stressful by 84. 8 % of the subjects. A total of 91. 1% of the subjects were aware of the issue of abuse against dentists in the dental profession. Moreover, 62 subjects (49. 6%) thought that it was a common issue in general, and 72 subjects (57. 6%) thought it was a common issue in Kuwait. The majority of the dentists involved in the sample (76. 8%) stated that they had experienced one or more forms of physical and/or verbal assaults. Subjects were asked if they would change their profession if they had the chance, and 76. 4 % reported they would not.

Conclusions:

Abuse against dentists is common in Kuwait, and verbal abuse is the most common form. In addition, although most of the sampled dentists consider dentistry as being stressful, the majority of them do not want to change professions.

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US Dentists' Knowledge of Management of Luxation Dental Injuries in the Primary Dentition

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Introduction:

  Assess the knowledge of the US pediatric and general dentists with pediatric interest, of the International Association of Dental Traumatology (IADT) 2001 and the American Association of Pediatric Dentistry (AAPD) 2003 guidelines for managing luxation dental injuries in the primary dentition.

Methods:

 Questionnaires with three clinical scenarios and related questions with multiple answer options were mailed to 300 general and 300 pediatric dentists, randomly selected from the AAPD lists of members and general dentist affiliate members. Answers structured so that some options were consistent with the IADT and AAPD guidelines. Responses were rated as either consistent or inconsistent with these guidelines. Group knowledge was rated as follows according to the percentage of subjects who chose answers consistent with the guidelines: high >95%, adequate 95-75%, or inadequate <75%. Chi square tests were used to identify differences between pediatric dentists and general dentists with an interest in pediatrics.

Results:

 Responses were received from 203 pediatric and 142 general dentists. Both groups demonstrated high knowledge in managing primary tooth avulsion and luxation injuries. A difference in their knowledge, however, was detected in managing intrusion injuries, where pediatric dentists demonstrated high knowledge compared to an adequate knowledge in the general dentists group. This difference was not statistically significant (95% vs. 86%, P= 0. 076).

Conclusions:

  Both groups of dentists demonstrated satisfactory knowledge in managing luxation dental injuries in the primary dentition.

Dentistry
Category: Clinical

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Restorative care in Kuwaiti Kindergarten schoolchildren

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Introduction:
 The aim of the present national dental survey was to determine the restorative care among Kuwaiti kindergarten schoolchildren in government schools in the five different governorates (Ahmadi, Farwaniya, Hawally, Jahra, Capital).

Methods:
 A national epidemiologic survey of the 4- and 5-year-old kindergarten schoolchildren (n = 1, 277) was conducted in the five governorates of Kuwait. Five trained and calibrated dentists examined the children. The restorative care index in the primary dentition was measured as the percentage of the filled teeth and surfaces from all caries affected and filled teeth and surfaces.

Results:
 The restorative tooth index (f/dft%) was 9. 4% for 4-year-olds and 14. 1% for the 5-year-olds. The tooth index was highest in Hawally, 12. 6% for 4-year-olds and lowest in Ahmadi, 5. 3%. It was highest in Hawally at 25. 6% for 5-year-olds and lowest in Jahra, 6. 4%.
The restorative surface index (f/dfs%) was 11% for 4-year-olds and 16. 8% for the 5-year-olds. The
surface index was highest in Hawally, 15. 2% for 4-year-olds and lowest in Ahmadi 6. 8%. It was highest in Hawally at 29. 2% for 5-year-olds and lowest in Farwaniya, 8. 6%.

Conclusions:
 It is evident from this study that the restorative care has increased considerably compared to earlier surveys. It also showed differences in the delivery of restorative care between the governorates.

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Factors associated with adult rampant caries in Kuwait

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Introduction:

Contrary to expectation, the clinical impression in Kuwait is that rampant caries occurs in adults with normal salivary gland function. The aim of this work was therefore to investigate the relationship between caries etiological factors and occurrence of adult rampant caries in Kuwait.

Methods:

Forty-two rampant caries patients, attending polyclinics in Kuwait, were included in a cross-sectional study, and compared with 38 adult caries-free patients. The rampant caries patients were aged 16 years or older, and had a minimum of 8 open carious cavities, with the involvement of at least one anterior tooth; while the caries-free patients had at least 24 standing teeth, and no carious cavities. Resting and stimulated salivary flow rates, salivary buffering capacity, frequency of sugar consumption and oral hygiene index were measured; while lactobacilli and mutans streptococci counts were determined by the dip-slide method.

Results:

Chi-square or Fisher's exact test showed that rampant caries patients had significantly higher frequency of sugar consumption, plaque index, lactobacilli and mutans streptococci counts, when compared to the caries-free group. In contrast, no significant difference was observed in the stimulated salivary flow rates or buffering capacity between the two groups of patients. In the multiple logistic regression analysis, only frequency of sugar consumption, oral hygiene and mutans streptococci counts had significant effect on the occurrence of rampant caries. Of the demographic factors, only income level had significant effect on the occurrence of the disease, while age, gender, nationality and educational level had no effect.

Conclusions:

Adult rampant caries in Kuwait is not due to salivary gland hypofunction, but is the result of high frequency of sugar consumption and poor oral hygiene.

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Postoperative infection after surgical removal of impacted mandibular third molars without prescribing antibiotics: Analysis of 110 consecutive procedures at Kuwait University.

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Introduction:

In Kuwait there is a tradition always to prescribe antibiotics for surgical removal on impacted mandibular third molars (M3). The recently launched Oral & Maxillofacial Surgery (OMFS) unit at Faculty of Dentistry, Kuwait University uses a protocol with strict adherence to high aseptic techniques and without prescribing prophylactic perioperative systemic antibiotics for dento-alveolar surgeries. The aim of this study was to evaluate the rate of postoperative infection and other postoperative complications after surgical removal of impacted M3 following such a protocol.

Methods:

a total of 110 consecutive surgical removal of impacted M3 under local anesthesia in 90 patients performed by one specialist oral and maxillofacial surgeon was studied. Fifty nine were females, and 31 were males with average age of 25. 2 years. All surgeries were done under strict aseptic technique as adopted by operating room protocol. No systemic perioperative antibiotics were prescribed. The rate of postoperative infection and other complications were evaluated clinically.

Results:

Postoperative infection was found to occur after 6 surgeries of the 110 (5. 5%). Other complications were alveolar osteitis (8. 2%), postoperative pain lasting more than 1 week (4. 3%) and sensory dysfunction of inferior alveolar nerve (0. 8%). These figures are in accordance with similar worldwide studies.

Conclusions:

The low rates of postoperative infection and other complications encourage our OMFS outpatient clinic to continue surgical removal of impacted mandibular third molars without routine prescription of antibiotics unless indicated for medical reasons.

Key Words: Infection; Antibiotics; Wisdom teeth;

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Epigenetic Profiling of Colorectal Cancer Using Methylight Technology

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Introduction:

Introduction: Methylation is an enzyme-mediated chemical modification that adds methyl (CH3) groups at selected site on proteins, DNA and RNA. In humans, DNA methylation is the only known natural modification of DNA and only affects the cytosine base (C) when it is followed by guanosine (G). Abnormal methylation of normally unmethylated CpG islands leads to an excess of DNA damage and aberrant expression of certain genes that are involved in tumor suppression, differentiation and growth in cancers. A number of methods are available for determining DNA methylation status tissues e. g methylation specific PCR (MSP) and combined bisulfite restriction analysis (COBRA) to name a few. In this work, we established a quantitative method for determining methylation, termed Methylight. Methylight is based on Real-time quantification and allows the rapid screening of thousands of DNA samples with the added advantage of quantitating the amount of methylated DNA in a sample. We describe here, the application of methylight technology to DNA extracted from formalin-fixed paraffin-embedded (FFPE) colorectal cancer tissues in relation to MLH1 and CACNA1G genes.

Methods:The optimization has been performed on 83 FFPE
colon cancer tissues. Sodium Bisulfite modification of extracted DNA was utilized to chemically convert all unmethylated cytosine to uracil while maintaining the methylated cytosine.
Methylight Assay was optimized to measure the Percentage of methylated reference (PMR) for the MLH1 and CACNA1G promoters.

Results: The PMR was shown to be equivalent to the dose-response curve method used to quantitate methylation.
We measured the threshold cycle (Ct) in our methylight assay for each of the bisulfite converted samples. For MLH1 gene, of 83 samples, 7 (8 %) were 30-100% methylated, 5 (6%) were considered as low-methylated with PMR below 30%, while 48 (57. 8%) were considered as unmethylated. For CACNA1G, of 57 samples, 2 (3. 5%) were considered as methylated with PMR range of (30-100%), 3 (5. 2 %) low-methylation, while 50 (87. 7%) were considered as unmethylated.

Conclusion:The development of methylight assay should considerably enhance our ability to rapidly and accurately generate epigenetic profile of tumor samples.

Methods:

Results:

Conclusions:

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Whole Genome Amplification: A novel solution for preserving rare and precious DNA samples

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Introduction:

The availability of sufficient quantity and quality of DNA is crucial to any genetic analysis, especially with the current analytical tools that require high DNA input such as SNP analysis and microarray technology. Whole Genome Amplification (WGA) methods were developed in an attempt to immortalize DNA resources through multiplying nanogram amounts of DNA to give microgram quantities that are adequate for multi-stage genetic testing.

In this research we tested the ability of a DOP-PCR WGA methodology to representatively amplify the DNA without any bias.

Methods:

DNA samples were extracted from 35 breast and 15 colon cancer cases fixed in formaline and preserved in paraffin. The amplified and unamplified products were purified and assessed for quality by Agarose gel electrophoresis.

Both amplified and un-amplified forms of DNA from corrsponding samples were genotyped using metaphase and microarray-based comparative genomic hybridization.

In addition, Her2-neu gene copy number was quantitated using Fast Real Time PCR, in breast cancer cases.

To investigate the ability of WGA to maintain allelic ratios, SNP analysis was used on colon cancer representative DNA in relation to the RKIP gene.

Results:

Results obtained from each of these investigations were analyzed and compared , to detect any changes inflicted by the WGA technique. Results:

Results from HER2neu gene copy number quantitation using Real- time PCR assay, show that WGA method was able to maintain copy number with a sensitivity of 91% and specificity 71. 4% compared to Fluorescent in situ hybridization.

Results obtained from CGH analysis revealed that WGA method preserved areas of deletions or gains with an accuracy of 95. 65%.

Conclusions:

Our results established the ability of the WGA technique to faithfully maintain the DNA copy number and allelic ratio.

Such verification will have great impact on research, clinical services and genetic classification of rare samples by providing unlimited supply of DNA banks

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Molecular Diagnosis of Spinal Muscular Atrophy in Patients and Carriers

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Introduction:

Spinal muscular atrophy is the second most common lethal autosomal recessive disorder of childhood affecting approximately 1 in 10, 000 births, with carrier frequency of 1 in 50. It primarily affects the anterior horn cells of the spinal cord and motor cranial nerve nuclei, leading to progressive paralysis with atrophy. The International Consortium on Spinal Muscular Atrophy has distinguished three forms of childhood-onset spinal muscular atrophy (types I, II, and III) on the basis of age and severity of the clinical course as assessed by clinical examination, muscle biopsy, and electromyography. All three forms of spinal muscular atrophy were linked to survival motor neuron gene (SMN) localized on the chromosome 5q11. 2-q13. 3. According to the type of spinal muscular atrophy, 80 to 90% of patients show homozygous deletions of exons 7 and 8 of SMN1 gene, whereas homozygous deletions were found in 2-3% of carriers and controls.

Methods:

We analyzed DNA obtained from blood of 6 subjects of a family in which there are three affected boys by Werdnig-Hoffmann disease, one unaffected boy and no consanguineous parents. Molecular analysis of SMN gene was conducted by PCR amplification of exeons 7 and 8 of SMN followed by RFLP. Restriction enzyme digestion of exon 7 PCR products was done with DraI restriction enzyme and of exon 8 PCR products with DdeI restriction enzyme.

Results:

We demonstrate by PCR-RFLP homozygote deletions in exons 7 and 8 of survival motor neuron gene in affected patients.

Conclusions:

We discuss, through this report, prenatal diagnosis which is most frequently requested by families with spinal muscular atrophy type I. We demonstrate that the deletion analysis by PCR-RFLP and by quantitative real time PCR is a particularly useful tool for molecular prenatal diagnosis and genetic counselling.

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Establishment of high throughput screening for MLH1 and MSH2 gene mutations for detection of HNPCC

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Introduction:
 Colorectal Cancer (CRC) is the third most common cancer in the Western World. In Kuwait the incidence of CRC is 8 in 100, 000 individuals per year. CRC can either be sporadic or inherited. MLH1 and MSH2 genes are involved in the mismatch repair mechanism. Mutations in these genes have been linked to CRC development. This study aims to establish a high throughput algorithm to detect mutations in these genes via studying and coupling protein expression to targeted DNA sequencing. This approach provides more accurate risk calculation for members with a family history of CRC.

Methods:
 Immunohistochemistry for MLH1 and MSH2 proteins was performed on clinical samples from probands with positive family history of HNPCC.
PCR and capillary sequencing methods were optimised for all exons of the MLH1 and MSH2 genes. DNA was collected from members of a family with a history of CRC. Sequencing was carried out on DNA samples of family members and unrelated controls.

Results:
 We identified the defective protein in probands prior to sequencing of the target gene, which reduced the mutation detection time by 4-8 weeks. We tested this workflow algorithm on two families with HNPCC and found a significant reduction in time, effort and money. This approach enabled the confirmation of a heterozygous mutation (226 C>T) in MSH2 exon 2 that was found among affected members of a family with history of CRC.

Conclusions:
 This is the first high throughput sequence analysis optimised for MLH1 and MSH2 genes in Kuwait coupled to an intelligent protein based algorithm.
This approach serves in enhancing patients' care and counselling of family members on their risk
 of developing cancer.

Key Words: Colon cancer; MSH2; Sequencing;

Genetics and Molecular Biology
Category: Clinical

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Association of Insulin-like Growth Factor-1 gene polymorphism with rheumatoid arthritis

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Introduction:

Insulin-like Growth factor-1 (IGF-1) regulates several cellular processes such as proliferation, differentiation, survival and regeneration, and its plasma levels are linked to osteoporosis, type 2 diabetes and cardiovascular diseases. Rheumatoid arthritis (RA) is a multifactorial inflammatory disease where non-HLA genes have been suggested to play an important role in its susceptibility. Low plasma levels of IGF-1 have been suggested to contribute towards pathogenesis of RA. This is the first study to investigate an association between a genotype of IGF-1 and the susceptibility and pathogenesis of RA.

Methods:

60 RA patients were recruited and clinically characterized according to disease duration, disease severity, disease activity and American College of Rheumatology (ACR) functional class. 35 healthy controls (HC) were also enrolled in the study. IGF-1 gene polymorphism genotypes were determined in patients and HC using polymerase chain reaction (PCR).

Results:

We observed that 96% of the subjects studied carried a 192-bp allele, an IGF-1 genotype reported as the wild_type allele in Rotterdam study because of its presence in 88% of the population. In our study, 4. 2 % of the subjects investigated were non-carriers of the 192-bp allele and had RA whereas all healthy controls exhibited the presence of this wild_type allele. Interestingly, we observed that gender correlates significantly with allele frequencies as 16% of the male RA patients in our study were non-carriers of 192-bp allele, and this wild_type allele was present in 98% of the female RA patients. Our results also suggest a possible influence of the IGF-1 gene polymorphism on the RA disease activity, severity and functional class.

Conclusions:

This is the first report establishing an association between IGF-1 gene polymorphism and RA. Our results suggest that males have a greater frequency of IGF-1 gene polymorphism and non-carriers of the wild_type 192-bp allele have an increased risk of developing RA.

Key Words: IGF-1; Rheumatoid Arthiritis; Gene Polymorphism;
Funding Agency: NONE

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Microarray Profilling of siRNA-knockout of RKIP in primary HEK293s cell line

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Introduction:

The Raf Kinase Inhibitor Protein (RKIP) is a member of conserved group of proteins called PEBP. On the molecular level, RKIP is an inhibitor of the Raf/MEK/ERK signaling pathway. Initially, RKIP was identified as a metastasis suppressor gene in human prostate cancer. our laboratory demonstrated for the first time an association between loss of RKIP expression and reduced survival in early stage colorectal cancer and metastasis in breast cancer. Although the molecular mechanism by which RKIP inhibits the Raf signaling pathway has been partially delineated, little is known about the biological relevance and consequences of silencing RKIP in primary cells. Our research addresses a significant niche in the RKIP literature and present novel data on the mechanism of RKIP functions.

Methods:

RKIP was down regulated by transfecting normal HEK293 cells with pcDNA6. 2 Plasmids coding for RKIP-miRNA. The level of RKIP protein in standard HEK293 and miRNA-knockout cell line was detected by Western immunoblotting. Both the growth rate and migration assays were performed. In addition, HEK293 cells RNA was used in microarray profiling. U133 plus 2 Affymatrix GeneChip was utilized to determine the expression profile of the genes in relation to the expression or down regulation of RKIP. Finally, Real-time PCR was used to further confirm and quantify the detected gene expression changes.

Results:

The reduction of RKIP expression in miRNA-knockout cells was verified by Western blotting and real time PCR. In growth curve assay, miRNA-knockout cells grew faster. Moreover, miRNA–RKIP- silenced HEK cells had a higher migration index than control cells. To understand the molecular defects responsible for these phenotypic changes, we compared the expression profiling of control versus RKIP-silenced cells, in triplicates, using Affymetrix high density U133 Plus 2 Gene Chip. Our data show significant differences in expression profiling between the two cell lines ($p < 0.0000001$), mainly in relation to genes that control metabolism, growth, differentiation, apoptosis and oxidative stress. These novel data sets are discussed in relation to cancer growth, invasion and metastasis.

Conclusions:

We present novel data pertaining to the function of RKIP protein and the catastrophic consequences of its down regulation on the behavior of primary cells.

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Haptoglobin gene polymorphisms in Kuwaiti and Nigerian sickle cell disease patients

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Introduction:

Haptoglobin (Hp) is a sialoglycoprotein with hemoglobin-binding capacity that plays a key role in preventing the toxic effects of free haemoglobin (Hb) liberated in hemolytic states like sickle cell disease (SCD). There are 3 major functional Hp phenotypes: Hp 1-1, Hp 2-2 and the heterozygous 1-2. Hp 1-1 is the most effective in binding Hb, while 2-2 is the least and 1-2 is intermediate. Hp 2-2 is a recognized genetic risk factor for atherosclerosis, while 1-1 protects against vascular complications of diabetes mellitus. Its role in the pathophysiology of SCD has not been well documented.

Methods:

We have carried out Hp genotyping in Kuwaiti and Nigerian SCD patients and Hb AA controls using PCR amplification of DNA segments representing the Hp 1 and Hp 2 alleles, followed by agarose gel electrophoresis. The Kuwaiti subjects were attending the haematology clinic of Mubarak Hospital while the Nigerians were patients whose DNA samples were obtained from a previous study.

Results:

There were 82 Kuwaiti SCD patients and 50 controls while there were 56 Nigerian SCD patients and 32 controls. Hp 2-2 was most prevalent among Kuwaitis (52. 4% in SCD and 46. 9% in controls) compared to the Nigerians (16. 1% and 28. 1% respectively). Hp1-1 was found in 4. 9% of
Kuwaiti SCD and in 37. 5% of Nigerian SCD patients while the figures in controls were 4. 1% and 37. 5% respectively. The frequency of the Hp-2 allele was significantly higher among Kuwaitis
compared to Nigerians (either among SCD patients or control subjects).

Conclusions:

Hp polymorphism is a significant discriminating factor in the Nigerian and Kuwaiti groups. These differences probably reflect the ethnic backgrounds of the subjects. It will be interesting to see if the genotype distribution has any correlation with different SCD phenotypes e. g. frequent severe vaso-occlusive crisis, osteonecrosis and brain infarcts. This is the focus of ongoing research.

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Neuronal differentiation of two different pluripotent stem cell populations isolated from umbilical cord blood

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Introduction:

Human umbilical cord blood is considered as a rich source of pluripotent stem cells with practical and ethical advantages.

Methods:

We showed that umbilical cord blood contains at least two "non-haematopoietic" pluripotent stem cells populations with high potential for neuronal differentiation. One cord blood unit (CB187) formed niche-like structures which produced highly proliferating floating cells. The other cord blood unit (CB145) was rich in adherent mesenchymal stem cell-like cells. In order to isolate, select and expand the pluripotent stem cells, we isolated the mono-nuclear cells from the cord blood using the Lymphoprep™ solution and cultured them for 3 weeks in appropriate in-vitro environment that favoured the wanted stem cells and enhanced their proliferation. Following 3 weeks in expansion media, we placed the stem cells in media supplied with Retinoic acid (RA) and Brain derived neurotrophic factor (BDNF) for two weeks.

Results:

Cells from both cord blood units showed abilities to differentiate into neuronal-like cells. Confocal microscopy analysis showed that proliferating undifferentiated stem cells from both cord blood units expressed Octamer-4 (Oct-4), an embryonic stem cell marker, and nestin. Differentiated cells from CB145 expressed neurofilaments-200 (NF200), glial fibrillary acidic protein (GFAP) and doublecortin (DC) while differentiated cells from CD187 expressed NF200.

Conclusions:

These findings suggest that the umbilical cord blood is a rich source for pluripotent stem cells with high potential for neuronal differentiation which makes it a promising tool for future regenerative medicine applications.

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The use of ECG Gated Myocardial Perfusion SPECT in evaluation of septal wall perfusion defect in patients with LBBB.

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Introduction:

  Left bundle branch block (LBBB), affects the extent of septal wall thickening during systole. This is due to abnormal polarization pattern and contraction sequence of left ventricular myocardium. However, in patients with LBBB, frequent septal perfusion defects are reported even when there is no coronary stenosis on angiography. Some patients may have coronary artery disease and LBBB. GATED Myocardial Perfusion SPECT (Single Photon Emission Tomography) is an accurate indicator for perfusion status of cardiac walls, it has shown high sensitivity and specificity to diagnose CAD. Septal perfusion defect is intensified during stress perfusion scintigraphy. It is attributed to abnormal systolic phase in the septum, and abnormal conduction leading to reduced contraction of septum which gives a false appearance of reduced perfusion during systolic phase. PATIENTS AND

Methods:

  Stress-rest Gated Myocardial Perfusion SPECT using Tc99m myoview was performed in 20 subjects with LBBB with probability of CAD. Visual analyses of the slice images and revision of quantitative results of Gated SPECT study were done on end diastolic (ED), end systolic (ES) images, regional wall motion and wall thickness for evaluation of the perfusion of septum.

Results:

  Visual analysis of stress –rest slices: 1)Reversible septal hypoperfusion was noted in 13 (65%) patients 2)Fixed septal defect in 4 (20%) 3)Three patients (15%) had normal septal perfusion. Quantitative analysis of gated study: 1)Out of the 13 patients with reversible hypoperfusion, 8 (40 %) show normal findings on Gated SPECT and only the remaining 5 (25 %) patients had true reversible hypoperfusion. 2)The 4 patients with fixed septal defects show normal finding on Gated SPECT

Conclusions:

 The use of Gated myocardial perfusion scintigraphy can help in the evaluation of septal perfusion, wall motion and thickening and hence differentiate true perfusion defects from false pattern in cases
 of LBBB.

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MRI Lumbar Spine in Kuwait: Is there Abuse of the System?

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Introduction:

The objective of this study is to identify if there is an unnecessary demand of requesting magnetic resonance imaging (MRI) for lumbar spine (LS) studies causing abuse of the system and should we restrict writing the request form to a specialist.

Methods:

A retrospective review of 935 MRI LS scans of patients referred with low back pain to Al-Amiri hospital was assessed. The abnormalities seen in the images was identified and divided into the following categories: normal, non-neurologically significant findings and neurologically significant findings. The specialty of the referring physicians (orthopedicians, neurologist, rheumatologist or general physician) was identified as well as the nationality, age and sex of the patients.

Results:

MRI LS was the most frequently requested study in Al-Amiri hospital (28% of total). Thirteen percent of the cases were reported as normal, 48% were not neurologically significant and 39% were neurologically significant findings. The Kuwaiti to non-Kuwaiti ratio was 1: 6. 5. Age range was 11-86 years. Thirty-four percent of cases were referred by orthopedicians, 18% by neurologists, 3 % by rheumatologists and 45% by general physicians. There was no statistical difference between the numbers of identified neurologically and non- neurologically significant findings among all different referring clinicians.

Conclusions:

There is unnecessary increasing demand on MRI studies by Kuwaiti patients and by all clinicians, regardless of their specialty, which is considered abuse of the system. Remedial measures should be taken early to increase the awareness of both clinicians and patients of the indications of an MRI study.

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Interobserver variation in the detection of parenchymal lung disease on high resolution computed tomography

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Introduction:

This study was designed to measure the inter-observer and intra-observer variation between non-chest radiologists in a general hospital in the detection of parenchymal lung changes of patients with SLE using high resolution computed tomography (HRCT).

Methods:

The HRCT images of 65 patients with systemic lupus erythematosus (SLE) treated at the chest clinic in Al-Amiri hospital were retrospectively reviewed by 4 radiologists- 1 magnetic resonance (MR) radiologist (HK), 1 cross sectional radiologist (OS) and 2 general radiologists (RPA and PS). Each radiologist read the scans twice at least 6 months apart. Known SLE radiological lung features were noted and also recorded as normal or abnormal lung parenchyma.
The inter-observer variation among the 1st and 2nd readings of the 4 radiologists and the intra-observer variations of each radiologist's two readings were recorded and assessed by κ and p values.

Results:

There is statistically significant variation between the 1st and 2nd readings among all 4 radiologists. This was highest for the MR radiologist where the κ value was 0. 482; the other 3 radiologists had comparable κ values. The p value for all 4 radiologists was . 001 which indicated significant difference. There is statistically significant variation between all radiologists being the highest between the MR radiologist and the other 3 radiologists in which the κ value was ranging between . 362 - . 551.

Conclusions:

There is significant inter-observer and intra-observer variability among non-chest radiologists in evaluating the HRCT findings in patients with SLE. Initiating treatment based exclusively on HRCT interpretation may not always yield the desired clinical benefit and a review of indeterminate findings by a dedicated chest radiologist and in some situations, lung biopsy might be required.

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SLAP lesions of the shoulder: MRI approach and classification.

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Introduction:

Introduction: Superior labrum anterior and /or posterior (SLAP) lesions of the shoulder are peculiar types of injuries that involve the superior and anterior aspects of the glenoid labrum in the gleno-humeral joint with or without posterior extension. Radiologists interpreting MR images of the shoulder should be aware of the MR findings in SLAP tears as these can be a significant cause of patient disability and are difficult to diagnose clinically. The purpose of this study is to provide an MRI approach for the evaluation and classification of SLAP injuries based on our experience in Al-Razi Orthopedic Hospital hoping that this would provide a guide for the general radiologists in the conduction and interpretation of shoulder MRI studies.

Methods:

Methods: MRI scans of the shoulder performed in Al-Razi hospital during the year 2007 were retrospectively evaluated. Three Radiologists independently reviewed the scans using specific evaluation criteria. The controversial cases were excluded from our study. The MRI findings were correlated with the most recent 10-type classification system of SLAP injuries.

Results:

Results: 23 patients with SLAP injuries of the glenoid labrum were identified and categorized. 3 patients had type-I SLAP lesion, 5 patients had type-II, 3 patients had type-III and 5 patients had type IV injury. Seven (30%) of our patients, however, could not be classified into these routinely used categories. Therefore, the new classification system of ten types was applied to categorize them. 2 patients were found to have type V, 3 patients type VII, one patient type IX and one patient had type X. No patients could be identified as having type VI or type VIII.

Conclusions:

From the imaging point of view, the recent SLAP lesion classification system is extensive and is not easily applicable to MRI. However, it may be helpful to categorize lesions that would not correspond to the routinely used 4-type classification system.

Key Words: SLAP lesions; Glenoid labrum; MRI scans;

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Bone mineral density in Kuwaiti sickle cell disease patients

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Introduction:

Bone complications are common in sickle cell disease (SCD) and recent studies have reported low bone mineral density (BMD) in 79. 6% and 64% of American SCD adults and children respectively. There have been no previous BMD studies among Kuwaiti SCD patients, who generally have a milder phenotype because of their high Hb F levels.

Methods:

SCD patients and controls were recruited from hematology clinics of Mubarak Hospital. BMD was measured using dual X-ray absorptiometry (DEXA, Hologic) at the lumbar spine and the hip. T-scores were used to classify the adults as being osteoporotic, osteopenic or normal while a Z-score < -2. 0 was used to identify children with low bone mass.

Results:

Included in the study were 110 adults and 57 children. The adults (55 controls, 55 SCD patients) were aged 17 to 57 (mean of 31) years. The children (24 controls, 23 sickle patients) were aged 4 to 16 (mean of 10) years. In adults, the mean T-score was significantly lower in SCD patients than in controls at the lumbar spine (-1. 06 vs. -0. 15, $p < 0. 01$) but not at the hip (0. 04 vs. 0. 25, $p > 0. 05$). In children, the mean Z-score in SCD patients was not significantly different from that in the controls at the lumbar spine (-1. 08 vs. -0. 46, $p > 0. 05$) and at the hip (-0. 24 vs. -0. 11, $p > 0. 05$). However, low lumbar spine BMD was identified in 61. 3% (47. 7% osteopenia; 13. 6 % osteoporosis) of adults and in 22. 6% of children with SCD.

Conclusions:

The prevalence of low BMD is lower in Kuwaiti SCD patients than in American patients, especially in childhood. This may be related to the milder course of SCD among the former. However, early screening for low BMD is advised so that early intervention can be implemented to prevent bone fractures.

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Is there a relation between mammography breast density and bone mineral density?

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Introduction:

Mammography breast density (MBD) is a well-established and strong predictive risk factor for breast cancer. Bone mineral density (BMD) is another predictor of breast cancer risk in women. Both MBD and BMD are linked to a common pathway, which involves oestrogens, and are highly heritable. This study evaluated the relationship between MBD and hip and spine BMD in Kuwaiti women.

Methods:

Mammograms and BMD data of 248 women were studied. BMD was measured at total lumbar spine (L1-L4) and total left hip using dual energy X-ray absorptiometry. Women were classified using the World Health Organization (WHO) criteria for BMD evaluation as normal, osteopenic and osteoporotic. According to MBD, breasts were classified into fatty, fibro glandular, heterogeneously dense and extremely dense breasts according to their MBD and as defined by the Breast Imaging Reporting and Data System (BI-RADS). Data was analysed statistically to evaluate the relationship between BMD and MBD.

Results:

Statistical analysis showed no significant difference or correlation between the MBD and BMD even after adjusting for obesity and menopausal status. However, a highly significant difference was found between MBD and body weight ($p < 0.005$).

Conclusions:

There was no significant correlation between MBD and BMD in Kuwaiti women.

Imaging (Nuclear Medicine and Radiology)
Category: Clinical

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Spectrum of cross sectional imaging findings in cervical spine injuries

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Introduction:
 The radiological evaluation of suspected cervical spine injuries demands rapid evaluation and highly accurate imaging, given the potentially devastating consequences of erroneous or delayed diagnosis. Computed tomography and magnetic resonance imaging play a fundamental role in the assessment of patients with suspected cervical injury. Furthermore, cross-sectional imaging facilitates the recognition of accompanying injuries to the face, head, and vascular structures of the neck. A study was conducted to review the different patterns of cervical spine injuries sustained in blunt trauma in Kuwait.

Methods:
 A retrospective study of cervical spine injuries for 2-years in our trauma center was conducted. A General Electric (GE) spiral CT scanner was used, with reconstruction of the axial images to generate routine coronal and sagittal reformatted images. In patients who presented with a neurological deficit after experiencing trauma, MR imaging, using GE 0. 7 Tesla open magnet, was used for better evaluation of the cervical cord as well as the associated suspected ligament or facet joints injuries.

Results:
 A wide variety of cervical spine injuries has been found. The injuries included: 1) flexion injuries (e. g. facet dislocation, anterior subluxation and wedge compression fractures), 2) extension injuries (e. g. C1 posterior arch fracture, laminar fracture, pillar fracture, extension teardrop fracture,
 hyperextension fracture dislocation and hyperextension subluxation), 3) compression fractures (e. g. Jefferson's fracture and burst fracture), 4) complex fractures (e. g. odontoid fractures).

Conclusions:
 Computed tomography is the preferred primary imaging modality in blunt cervical spine trauma. It plays a vital role in the rapid detection and evaluation of cervical spine injuries. MR imaging is considered superior to other diagnostic techniques for examining patients with neurological deficit and for detection of ligamentous rupture.

Key Words: Cervical spine; Injuries; Imaging;
Funding Agency: NONE

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Use of Tc-99m labeled anti-granulocyte monoclonal antibody fragment (Leukoscan) in Pediatric Bone and Soft tissue Infection

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Introduction:

The aim of this study was to evaluate the diagnostic accuracy of Tc-99m labeled anti-granulocyte monoclonal antibody fragment Fab'(Leukoscan) for the detection of bone and soft tissue infection in pediatric population.

Methods:

This is a retrospective study of 18 patients (10males, 8 females) with the mean age of 5. 1years (range I to 14 years). These patients were referred to Nuclear Medicine Departments of Hussain Makki Al Jumma and Farwania hospitals, from July 2005 to November 2007, for hip pain (n=3), PUO (n=1), orthopedic implant infection (n=1) and osteomyelitis (n=13). Three phases bone scan and Leukoscan were carried out with maximum interval of 10 days. Imaging for Leukoscan was done at 3-4 hours and in 8 cases at 24 hours. The dose was age adjusted with a minimum dose of-3. 5mCi. The scintigraphic diagnosis was compared with clinical diagnosis and informations collected from routine blood test (erythrocytes sedimentation rate, full blood count & C-reactive protein), plain radiograph & microbiology. The final diagnosis was determined by above mentioned informations and complementary investigations like computed tomography/ magnetic resonance imaging and long term clinical follow-up. No adverse reactions were observed till 24 hours after Leukoscan injection.

Results:

The sensitivity, specificity, positive and negative predictive value for Leukoscan are 100%, 82%, 78% & 100% respectively. Accuracy of the scan is 89%. By adding delayed 24 hours imaging, in suspicious cases, the specificity and accuracy can be increased to 91% and 94% respectively.

Conclusions:

Conclusion: Leukoscan has high sensitivity and negative predictive values, so it can be used with confidence to rule out infection of bones and soft tissue in pediatric population. In case of positive study with faint radiotracer uptake, imaging after 24 hours can improve specificity.

Imaging (Nuclear Medicine and Radiology)
Category: Graduate (Resident)

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Estimation of Thyroid Volume Using a Pinhole Collimator

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Introduction:

  Different imaging modalities including nuclear medicine have been used to estimate thyroid gland volume. In nuclear medicine, planar scintigraphy performed with parallel hole collimation has been previously used while pinhole collimation has not, despite the fact that it is clinically the most commonly used collimator for thyroid imaging . The aim of this study was to evaluate the use of a pinhole collimator imaging technique for calculating thyroid gland volume in patients with Grave's disease, and compare the volumes calculated with those from an ultrasound technique.

Methods:

  Five thyroid phantoms with volumes ranging from 7 to 52 ml were constructed using clay material. The phantoms were filled with tectnetium 99m pertecthnetate and imaged with a gamma cameral equipped with a pinhole collimator. The phantom thyroid lobes were enclosed with the help of an automatic region of interest (ROI) detection tool with a 20% threshold being optimum for determining the thyroid's volume. The volume was calculated using an ellipsoid formula. The estimated volume of each phantom was compared and correlated with its known volume. After standardization of the technique with phantom studies, planar scintigraphy (with 20% threshold) in 40 patients with Grave's disease was performed to estimate their thyroid size. The thyroid size was also estimated by ultrasonography, which similarly applied the same ellipsoid formula for volume calculation.

Results:

  Pinhole Scintigraphy showed a strong and significant correlation with ultrasonography in measurement of the thyroid volume (r=0. 8, P-value<0. 01). The thyroid volumes calculated with pinhole scintigraphy and ultrasound were (mean+SD) 19. 3+8. 0 ml and 20. 2+12. 8 ml respectively.

Conclusions:

  Pinhole scintigraphy provided good results in measuring the thyroid volume; therefore, imaging thyroid gland and volume quantitation can be combined in a single study, especially in Grave's patients prior to their radioactive iodine therapy.

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Tc 99m(v)-DMSA in colorectal cancers: Values and relevant lesions' and imaging time 's factors analysis

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Introduction:

This prospective study aimed at evaluation of Tc 99m-(v) DMSA role in colorectal cancer (CRC) management compared to the standard lab, endoscopic and radiological investigations, determination of its ability to discriminate between CRC lesions and other benign colorectal lesions, fiding-out different factors that may affect lesion uptake, and find-out a cut-off value separating benign from malignant colorectal(CR) lesions.

Methods:

98male patients were the subjects of this study. They were classified into 2 groups (Gp). Gp 1 included 86 patients with histopathologically-proved CRC and Gp 2 patients included 13 cases with benign C R lesions , all were inflammatory bowel diseases(IBD). Gp 1 cases were sub classified into Gb 1 A including 50 patients with gross locoregional , nodal and /or metastatic CRC and Gp 1 B including 36 cases with no evidence of CRC after complete excision. All cases were subjected to thorough clinical examinations, standard and related lab, endoscopic and radiological investigations. All cases were subjected to Tc 99m-(v)-DMSA whole body (WB) scan, as well as spot views scan 2 hours (Hrs) and 4 Hrs. post-injection. Results were interpreted qualitatively, semi quantitatively and quantitatively using lesion/non-lesion (L/NL) ratios.

Results:

Tc 99m(v)-DMSA had 100% sensitivity and negative predictive value(NPV), 94 %positive predictive value(PPV), 70 %specificity and 92 % accuracy to localize gross active CRC (whether local residues and /or recurrence) that were comparable to computed tomography(CT) and ($p > 0. 05$) and significantly better than sonography($p < 0. 05$). Its abilities to detect nodal and liver deposits were much less than CT being 8% and !@ % respectively($p > 0. 05$). 4 Hrs. L/NL ratios were significantly higher than 2 Hrs. ratios(206+0. 9 vs 2. 0+0. 5 respectively with $p < 0. 05$). . there

were strong positive correlations between degree of Tc 99m(v)-DMSA uptake and pathological grades as well as Duke's stage of CRC. A cut-off value 2. 0+_ was found to separate between malignant and benign CR lesions ($p < 0. 05$).

Conclusions:

Tc 99m(v)-DMSA is a simple , sensitive , objective method that could differentiate benign from malignant CR lesions and capable of localizing metabolically-active CRC whether local residues and /or recurrence.

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Evaluation of Prostate Specific Antigen (PSA) as a Predictor of Extent of Bone Metastasis in Prostate Cancer Patients

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Introduction:

Objectives: This study was designed to evaluate correlation between Prostate Specific Antigen (PSA) levels and Bone Scan for assessment of skeletal metastasis in patients with prostate cancer and to determine whether PSA can accurately predict bone metastases in Adenocarcinoma of Prostate.

Methods:

32 patients (mean age 68. 1+9. 4years) with histopathological evidence of prostatic Adenocarcinoma were referred to CENUM Hospital, Lahore, Pakistan from January to October, 2007. PSA levels were measured by Radioimmunoassay (RIA). 99Tcm-MDP bone scan was done to identify and define the extent of metastatic lesions. Statistical means, percentages, Pearson's correlation coefficient (r) and t-test were used for data analysis. Patients are divided in to Group A with no bony metastasis and Group B with metastatic disease.

Results:

This study showed a significant correlation (N=32, r=0. 479/ P=0. 006) between number of metastatic bone lesions and PSA levels. Difference of means of PSA levels in Group A (N=11, 34%) and Group B (N=21, 66%) were also significant (P=0. 05). We found a significant correlation (r=0. 508/ P=0. 019) between extent of skeletal metastasis and PSA levels in Group B. There was no significant correlation between extents of bone metastasis and PSA levels in subgroups: Group B1, N=9, early metastasis (P=0. 977) & Group B2, N=12, advanced metastasis (P=0. 491). PSA levels were found 76% sensitive with a positive predictive value of 67% and a false positive rate of 73%. It was 27% specific with a negative predictive value of 38%. 20% of cases with appendicular metastasis & 22% of cases with vertebral metastasis had normal PSA levels.

Conclusions:

This retrospective study shows that we can not exclude bone scanning from diagnostic workup even if PSA levels are normal. This would help in prophylaxis of harmful consequences of complicated bone metastasis.

Key Words: PSA; Bone Metastasis; Prostate Adenocarcinoma;

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Prognostic value of dipyridamole sestamibi myocardial perfusion imaging in patients with left Bundle-Branch Block

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Introduction:
 The detection of myocardial ischemia in patients with preexisting left bundle branch block (LBBB) remains problematic. Myocardial perfusion scintigraphy (MPS) with Dipyridamole is the preferred non-invasive diagnostic modality for this group of patients.

Methods:
 Seventy six patients with preexisting LBBB underwent sestamibi perfusion imaging with dipyridamole infusion protocol (0. 56 mg/kg). Stress and rest SPECT studies were acquired using double head gamma cameras. Images were interpreted by consensus of two experienced observers and classified as, low risk group (normal MPS, small reversible/small fixed defect) and high-risk group (a large severe fixed or reversible defect and dilated LV cavity). 76 patients with mean age of 53 ± 10 years (range=39-72 years) were included in the study. These patients were followed up for 24 months $\pm$ 8 months and occurrences of hard cardiac events (MI or cardiac death) were asked by telephones.

Results:
 Out of 76 patients 52 had low-risk scans (68%) and 24 had high-risk scans (32%). In low risk group cardiac deaths were observed in 1/52 (1. 9%) and non-fatal MIs were seen in 2/52 (3. 8%). In
 high-risk scans, 5 suffered cardiac death (20. 8%) and non-fatal MIs in 3 (12. 5%). Over all survival rate was 98. 1% in the low-risk group compared with 79. 16% in the high-risk group with a significant difference (p=0. 0338). Conversely, the negative predictive value of a normal myocardial perfusion scintigraphy for the occurrence of death was 100%.

Conclusions:
  Myocardial perfusion imaging with dipyridamole stress provides important prognostic information in patients with left bundle-branch block, which is incremental to clinical assessment

Key Words: Sestamibi myocardial perfusion scintigraphy; Left bundle branch block; Coronary

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Effect of hyperthermia on the function of thyroid gland and its radionuclide evaluation

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Introduction:

Hyperthermia may be a consequence of environmental conditions, bacterial or viral infections and/or thyroid storm. The aim of this study is to investigate the effect of body temperature elevation on thyroid function and on its radionuclide evaluation.

Methods:

Thyroid scintigraphy studies were performed on fifteen New Zealand White rabbits weighing approximately 3-3. 5 kg. Each rabbit was injected with 115 MBq (3. 1 mCi) technetium-99m pertechnetate (99mTc pertechnetate). Static images were acquired using Gamma camera equipped with a low energy, high resolution, pin-hole collimator interfaced with a computer. Two days later the same protocol was repeated for the same rabbit after increasing the body temperature by 2°C. The experiment was repeated again after a 2 day interval at 3°C, and then after another 2 day interval at 4°C. Plasma Free thyroxine (FT4), free triiodothyronine (FT3) and thyroid stimulating hormone (TSH) were measured at control and at different hyperthermic temperatures (+2, 3, 4°C). Isometric tension of isolated rabbit thyroid artery strips were also recorded in organ baths during stepwise temperature elevation.

Results:

During hyperthermia the significant decrease in thyroid function and thyroid scintigraphy studies were proportional to body temperature. The reduction was more than 50%. The recording of isometric tension in rabbit thyroid artery strips in organ baths, showed vasoconstriction during hyperthermia which is significantly proportional to the heating temperature, (n=10; *$p < 0.05$). Plasma FT4 and FT3 level were decreased while TSH levels were not affected by acute fever.

Conclusions:

Our results indicate that acute hyperthermia causes a transient decrease in thyroid gland function and its scintigraphic patterns. Thus, body temperatures must be measured before radionuclide studies in order to ensure that interpretation of data is not influenced by hyperthermia.

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Does water-pipe smoking affect Tc-99m DTPA aerosol in lung epithelial clearance?

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Introduction:

Increased pulmonary epithelial permeability is evaluated by the rate of clearance of the Tc-99m DTPA aerosol from lung to blood. The effects of cigarette smoking have been widely studied, however, little is known regarding the effects of smoking water-pipe. A sharp increase in the use of water-pipe has been noted in recent years in Kuwait. The aim of this study was to evaluate the effect of water-pipe smoking on lungs permeability after the inhalation of (99m Tc-DTPA aerosols)

Methods:

A total of 46 subjects were divided into 3 groups: water pipe smokers (27), cigarette smokers (9) and non smokers (11). The 27 water-pipe smokers were further divided into 2 subgroups: 16 who smoked water-pipe few days earlier (A) and 11 who smoked few hours prior to the test (B) The cigarette smokers and non-smokers were the positive and negative control groups. Tc-99m DTPA aerosols inhalation scintigraphy was performed in all subjects. Following the inhalation of radiotracer through a nebulizer for 5 minutes while seated; dynamic images in the posterior view of the thorax (1 frame/min, for 30 min) were taken from both lungs using a gamma camera linked to a computer. ROIs were drawn over both lung areas and time activity curves were obtained. The half time (T1/2) of 99m Tc-DTPA aerosols clearance was calculated by placing a monoexponential fit on the curves.

Results:

The mean average T1/2 values of 99m Tc-DTPA aerosols clearance was 74. 0, b8. 0, 32. 7, b12 , 65. 1, b19 , 95. 2, b13 for the non smokers, cigarette smoker, water pipe smokers A and B respectively.

Conclusions:

Water-pipe smoking seemed to decrease the epithelial permeability and the alveolar clearance temporally. There is no significant association between the average T1/2 and the study parameters including the age, duration and amount of smoking. The only association was between the time of smoking and the imaging.

Key Words: Tc-99m DTPA aerosols clearance; Water-pipe smoking; Bronchepithelial

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Localization of intraductal masses by wire guided ductography technique

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Introduction:
  A guide wire technique is described for localizing intraductal masses.

Methods:
  The materials used are a 2-0 Prolene/Surgipro guide wire, plastic intravenous cannulas ranging from 20G to 26G, Kopans breast localization hook wire, Omnipaque 240mg I/I, a magnification lens mounted on a headpiece and a high intensity light source. Under aseptic condition and with the patient in the supine or recumbent position, 1-2cm of the guide wire is inserted into the discharging duct orifice. When the guide wire is properly placed, it passes freely and painlessly into the duct. 26G plastic cannula is then passed over the guide wire into the duct. With the cannula in place, the guide wire is removed. 0. 2-0. 4ml of contrast is injected. Magnified craniocaudal view of the breast is taken. Intraductal mass location is verified and then the guide wire is passed again and the 26G cannula removed. A 24G cannula is passed over the guide wire. This process is repeated using a 22G and then 20G cannula. Through the 20G cannula, the hook wire is inserted into the intraductal mass and then the hook wire is cut 2cm from the nipple. Patient is sent to the theatre with the hook wire in place.

Results:
  This technique has been successfully carried out in two patients in the year 2007 in Radiology Department, Al- Jahra Hospital, Kuwait. This technique is more precise and accurate in intraductal mass localization for the surgeon than the methylene blue technique in which lobules had to be removed. This technique enables microsurgery to be done with selective removal of the involved duct and mass.

Conclusions:
  This is a simple and easy technique for localization of intraductal mass lesions with little discomfort to the patient. It also enables the surgeon to do microsurgery with minimal cosmetic effects to the patient.

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Scintigraphic Patterns of Poliomyelitis on Bone Scan

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Introduction:

Post-poliomyelitis syndrome causes variable musculoskeletal manifestations including pain, muscle weakness and fatigue. These manifestations are commonly secondary to overuse and misuse of muscles and joints and could follow patient's falls. Bone scan can be useful in determining the underlying cause and follow up. The objective of this study was to identify the scintigraphic patterns of poliomyelitis on bone scan.

Methods:

Bone scans of 7 adult patients (6 females and one male), aged 35 to 53 years known to have paralytic poliomyelitis were studied. Six patients had unilateral while one had bilateral disease. All patients had three phase bone scan and five had SPECT study as well. Studies were reviewed by 2 qualified nuclear medicine physicians and findings were recorded and analyzed.

Results:

Several patterns were consistently identified: (a) significantly decreased uptake of blood pool activity on the affected lower limb of all patients. (b) Deformed ipsilateral hemi pelvis with reduced uptake on the affected side in all patients which was less prominent in the patient with bilateral disease. (c) Stress changes with increased uptake in the bones of the contra-lateral lower extremity. (d) Degenerative changes of multiple joints (shoulder, knee, hip, ankle and spine). Significant scoliosis was only noted in the patient with bilateral disease.

Conclusions:

Poliomyelitis related scintigraphic patterns on bone scan were identified. Awareness of these characteristic scintigraphic findings is important for proper interpretation thereby avoiding misinterpretation.

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A picture is worth a thousand words: introducing pattern recognition to first year medical students

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Introduction:

The New Medical Programme starts in Phase II with a vertically integrated organ-system based course which introduces students to disciplines they would normally meet 3 years later. Nuclear Medicine (NM) is one of the disciplines that is being introduced but there is little experience on how it should be presented and assessed a this level. A NM Skills Lab teaching station supported by a Learning Topic (LT) was delivered. At the first assessment, NM material was tested in 4 levels of skill in one OSCE station to determine the success of the teaching strategies employed.

Methods:

106 students took the formative OSCE-OSPE examination. An NM station was constructed using a computer loop on a series of computer screens representing medium to high cognition testing levels. The 4 incremental levels tested were: (1) a pure knowledge test using one A-type multiple-choice question; (2) 4 thyroid scans clearly showing common pathologies and 4 matching diagnoses; (3) four thyroid scans and a probing question testing deductive reasoning; (4) one thyroid scan with 4 explanatory statements related to the scan pattern.

Results:

The knowledge test resulted in 52% correct answers; matching 4 scans with common pathological diagnoses, 78%; high level reasoning, 21%; and matching the best of 4 explanatory statements with a single NM scan, 31%.

Conclusions:

After one teaching session of 20 minutes and provision of one LT, the formative test outcomes were considered encouraging. Whereas, the second level of pattern recognition was easily within the student's mastery, the two most complex levels were beyond a first year medical student's ability. Pattern recognition is the way experts practice and students soon learn that they must develop these skills. As NM is very much pattern driven 3 levels of complexity were used to determine the appropriate level for 1st year medical students. This information is useful for the planning of an incremental NM programme of study

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Can you create a thoughtful doctor?

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Introduction:

 Assessments drive exam preparation and other student study strategies. At Kuwait University, course memorization has been rewarded by assessments that seldom test higher levels of cognition. The FOM curriculum reform is changing this. What is unknown is whether students are ready for this change. The first 5/6 major summative assessments have been reviewed to determine what levels of cognition were tested and how the students performed.

Methods:

 530 A-type multiple-choice items, best 1:5 options, all summative exams with an internal reliability >0. 80 were used (n=5). Items were reviewed and edited to remove ambiguities and item writing flaws and then classified as testing recall and comprehension (K1) or higher order cognition such as analysis or application of knowledge (K2). The level of cognition tested was determined either by eight or more Angoff judges, or a consensus group of no less than four. When Angoff judgments were used, a majority decision decided the cognitive level tested. The consensus group arrived at their agreement by an iterative process. The proportion of candidates marking the correct answer (p-value) was noted and again for the top, middle and bottom achieving student groups. When 2/3 group results agreed the conclusion favoured this majority.

Results:

 The average frequency of K2 items across the five examinations was 25%, range 15% - 39%. The p-values for K1 items were equal with K2 in two module exams; higher than K2 in the End of Year exam and one module exam and lower in one module exam. Bottom group K1 p-values were higher in 1/5 exams, for the top group, 2/5 and better K2 p-values, 1/5.

Conclusions:

 We found no evidence that students only memorise what they learn in the New Curriculum. However, the majority of exam questions would still encourage this. While students easily cope with advanced forms of testing, if we want thoughtful doctors we must also use assessment items that promote those skills.

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What is the value of a formative OSCE?

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Introduction:

Formative assessment is an important educational strategy in the New Medical Curriculum at FOM. FOM has delivered two formative OSCE-OSPEs with over 45 active stations. These assessments fulfill several important goals: (1) introduce students to unfamiliar exam formats, (2) provide feedback and diagnostic information about student progress and (3) indirectly serve as an evaluation of the teaching process. We also wished to determine the relationship between in-course formative OSCE station performance and eventual performance in the high stakes End of Year Exam.

Methods:

Three OSCE-OSPE examinations have been delivered, two formative and one summative. 256 medical students went through the process and 66 medical students presented themselves three times. Thirty two stations from three assessments (June and October 2007, formatives; and January 2008, summative) measuring students' developing clinical skills were available for analysis. Our Observer-Examiners used a Borderline Group Method (BGM) to set the standard for the Clinical skills' stations.

Results:

There was an incremental improvement at each time point for all clinical skills. The greatest improvement of 18. 1% + 15. 2% was observed between October 2007 and January 2008. Thirteen medical students have required a Resit Examination. Their clinical performance in June was lower than those who passed in January, 46. 4% versus 54. 7%, $p<0.01$; and again in October, 49. 3% versus 60. 3%, $p<0.001$. We also found using the BGM standard set, resit students failed 43% of stations, while passing students failed 21%.

Conclusions:

There was a predictable improvement between the last formative and summative exam. A formative cut score of 50% diagnosed weak students who failed twice as many stations in the January summative exam. The overwhelming majority of students met the standard set by our experienced clinical examiners. Therefore, we believe we have met the three criteria for formative assessments.

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Chromium supplementation Improves Glucose and Lipid Variables of Diabetics in Kuwait

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Introduction:
Chromium (Cr) deficiency is a cause of impaired glucose tolerance. Supplemental Cr induced improves glucose and/or lipid concentrations in diabetes mellitus type 1 (T1DM) and type 2 (T2DM) and glucose intolerance. Diabetes causes abnormal Cr metabolism. Despite increased intestinal absorption, the three-fold increase in urinary Cr excretion in diabetics might contribute to negative Cr balance, probably indicated their significantly (60%) lower plasma Cr. The study the aimed to examine the effect of supplementing Cr to free living T2DM and glucose intolerant (GI).

Methods:
A total of 102 aged 35 – 65 overweight / obesity and T2DM/GI were recruited. Divided into two intervention (a: Cr supplemented and b: Cr not supplementation) and c: control group. Group a instructed to improve their mode of life (reduce weight and do ½ hr. exercise) and take 1 tab (200µg /3. 84 µmol) elemental Cr three times daily. Group b, improve mode of life only. Whereas, group c no supplemental Cr nor mode of life improvement. All recruited maintained their normal life and medication

Results:
A significant improvement noticed in serum FBG, HbA1c, total and LDL cholesterol and TG in group a after 2, 4 and 6 months compared with base line values, as well as when the 6 months' and between 6 months' and 2 months' Cr supplementation. Group a HDL cholesterol increased significantly only after 6 months of Cr supplementation.

Conclusions:
 Supplemental of 600µg Cr daily as chromium picolinate (200 µg three times daily) improved diabetes control. Thereby decreased the risk of cardiovascular and other long term diabete's complications. Seemingly the key point favouring the remarkable response of Cr supplementation group is the right selection of Cr deficient cases that need supplementation. Additional studies are required to delineate and document the clinical signs and symptoms for hypochromia diagnosis.

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Attitude of physicians toward use of electronic medical record system in primary care providing diabetes care and barriers in system implementation

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Introduction:
Studies have shown that successful implementation of an electronic medical record (EMR) may require a set of interrelated system and technology factors in primary care practices for ensuring high-quality diabetes care. We carried out this study to identify the attitude of physicians toward use of EMR system in Primary Health Care (PHC) providing diabetes care, and to determine the barriers in system implementation.

Methods:
Diabetes Care Programme (DCP) was established to improve the quality of care in the PHC in Kuwait through several strategies. EMR has been installed by the Ministry of Health at the PHC. We conducted cross-sectional survey from 41 PHC centers and 118 physicians were surveyed to assess their attitude toward the EMR system, to describe the main themes of improvement, and to identify the main barriers faced into practice reality.

Results:
The participants were 118 physicians caring for diabetic patients within PHC setting (mean age = 45. 5 years; 55. 1% male). The majority of physicians (86 %) thought that EMR system will improve quality of diabetes care. Attitude was not related to age or years of practice. The main themes expected for improvement were in: i) saving and extracting data, ii) follow-up, iii) referral system, iv) screening for complications, v) investigations, vi) drug prescription policy and cost's reduction, vii) implementation of guidelines, viii) statistics, ix) research, audit and quality assurance, and x) connection to other clinics, departments and hospitals. The main barriers identified in system implementation included limitations in technology, software, hardware, and system users.

Conclusions:
Our study have shown that primary care physicians have a positive attitude toward implementation of EMR which may lead to improvements in patient health record and implementation of guidelines set by the DCP. Efforts should focus on overcoming the identified barriers to establish an efficient and effective system.

Key Words: Electronic medical record; Diabetes; Primary care;

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Clinical and immunological characteristics of young Arabs (aged 12-30 years) with newly diagnosed diabetes

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Introduction:

To describe the clinical and immunological characteristics of young Arabs with newly diagnosed diabetes, and to establish the prevalence of glutamic acid decarboxylase (GAD) antibodies among young Arabs with type 1 diabetes.

Methods:

We evaluated 28 young Arabs (aged 12-30 years at diagnosis) with newly diagnosed diabetes that were referred to Diabetes outpatient clinic at Al-Sabah Hospital from 1997 to 2006 and followed up for at least one year. The clinical features documented were age of onset, BMI, BP, family history of diabetes, and modality of treatment within the first year of diagnosis. Patients were clinically diagnosed to be type 2 diabetes if they did not require insulin within the first year of diagnosis. Laboratory investigations included presenting blood glucose, diagnosis of ketoacidosis by serum bicarbonate or arterial PH, HbA1c%, triglycerides, HDL- and LDL-Cholesterol, GAD antibodies, thyroid function parameters (T4, TSH, and thyroid antibodies).

Results:

Out of the 28 patients, 25% were diagnosed as having type 2 diabetes. Diabetic ketoacidosis (DKA) was present in 75% of type 1 diabetic patients at diagnosis, whereas none of type 2 diabetics had DKA. Compared with type 2 diabetics, type 1 diabetics had significantly lower BMI (22. 8 +/- 7. 8 vs. 31. 8 +/- 4. 9 kg/m2, $p < 0.05$), lower LDL cholesterol (2. 7 +/- 0. 8 vs. 3. 6 +/- 1. 0 mmol/l, $p < 0.05$), and higher presenting plasma glucose (32. 1 +/- 12. 9 vs. 16. 0 +/- 2. 9 mmol/l, $p < 0.005$). Prevalence of GAD antibodies in type 1 diabetics was 58. 3 %, whereas none of type 2 diabetics was GAD positive. There was no statistical difference in other parameters.

Conclusions:

This study shows that type 2 diabetes in young Arabs is an emerging alarming health problem. Presenting plasma glucose, DKA, BMI, LDL level, and GAD antibodies are helpful distinguishing clinical and immunological features

Key Words: Diabetes; GAD antibodies; Arabs;

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Serum fructosamine and haemoglobin A1C in pregnant women

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Introduction:

Serum fructosamine (FRA) and haemoglobin A1C (HbA1C) are commonly used in monitoring the control of diabetes mellitus. HbA1C and FRA indicate diabetic control for the past 6-8 weeks and 2-3 weeks, respectively. Therefore, FRA is suggested to be a rapid indicator of glycemia, and may be used to monitor control in diabetic pregnancies. The objective of this study was to find out if serum FRA is a superior indicator of gestational diabetes in comparison to HbA1C.

Methods:

The study was conducted at Maternity Hospital in Kuwait. A total of 122 pregnant women were studied. Seventy eight (Group I) women were tested once for both FRA and HbA1C. Forty-four women (Group II) were tested for 2-hour glucose tolerance (GTT) and serum FRA. Fasting blood sugar (FBG), HbA1C and FRA were quantitatively determined on COBAS autoanalyzer system. Reference ranges for FBG, HbA1C and FRA were between 3. 9-6. 1 mmo1/l, < 5. 9% and < 2. 83 umol/l, respectively.

Results:

In the Group I, 50% of the women had diabetes with a mean ($\pm$ SD) FBG, 7. 2 ($\pm$2. 86) mmol /l, HbA1C and FRA were 5. 9% ($\pm$1. 4) and 252. 2 ($\pm$59. 7) umo1/l, respectively. In the same group I, the 50% non-diabetic women, the mean ($\pm$ SD) FBG, HbA1C and FRA, respectively were 5. 49 ($\pm$1. 0) mmo1/l, 5. 29% ($\pm$0. 56) and 224. 9 ($\pm$40. 7) umo1/l. FBG, HbA1C and fructosamine values
were all significantly different between the diabetic and non-diabetic women. As a whole, HbA1C was significantly correlated to FBG (p<. 001) and fructosamine (p<. 003) in the group I. In the group II, serum FRA values after GTT were significantly higher (p<. 003), compared to before GTT.

Conclusions:

HbA1C and FRA were significantly correlated among all the group I pregnant women. FRA values before and after GTT were significantly different in the group II. However, an indepth study with a larger sample size is required to determine the superiority of FRA over HbA1C

Key Words: Fasting blood sugar (FBG); Hemoglobin A1C (HbA1C); Serum fructosamine (FRA);

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Prevalence of cardiovascular risk factors and development of a risk score for screening hypertension in Kuwaiti adult Population.

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Introduction:

The aim of this study was to describe the prevalence of some of the main cardiovascular risk factors in the Kuwaiti adult population and to develop a risk score for hypertension.

Methods:

A cross-sectional survey was conducted among Kuwaiti employees in the ministry complex using gender stratified multi-stage cluster sampling. Data was collected through a self administered questionnaire; glucose measurements and waist circumference were measured. The prevalence of diabetes, hypertension, obesity, increased waist circumference, and smoking were estimated. Multivariate logistic regression was done to identify independentatly associated risk factors for hypertension and a ROC curve(Receiver Operating Curve) was done to develop a score.

Results:

The following prevalences were found: hypertension was 12. 1%, known diabetes was 17. 3%, undetected diabetics was 4. 1%, overweight was 37. 2%, 27. 9% were found to have obesity, 4. 8% were found to have morbid obesity, 54. 1% were found to have increased waist circumference, and smoking was 18. 7%. Our score for hypertension consisted of three variables and had a sensitivity of 67% and a specificity 87%.

Conclusions:

Given the evidence that suggests high prevalence of cardiovascular risk factors in the target population compared with other data reported in the literature, our population should be screened and thereby possibly minimizing the public health burden.

Key Words: Cardiovascular risks; Risk Score; Hypertension;

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Waist circumference cut-off points for identification of abdominal obesity among the Kuwaiti adult population.

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Introduction:

  There are no data on optimal cut-off points to classify obesity among Kuwaiti. The existing cut-off points were obtained from studies of European populations. OBJECTIVE: Waist circumference (WC) is a convenient measure of abdominal adipose tissue. It itself is a cardiovascular disease (CVD) and diabetes-risk factor and is strongly linked to other CVD risk factors. There are, however, ethnic differences in the relationship of WC to the other risk factors. The aim of this study was to determine the optimal cut-off points of WC at which cardiovascular risk factors can be identified with maximum sensitivity and specificity in a representative sample of the Kuwaiti adult population.

Methods:

  A community-based cross-sectional study of 20 years or older. WC, BMI (Body mass index), Blood glucose were measured and hypertension was recorded. Receiver operating characteristic (ROC) curve analysis was used to identify optimal cut-off values of WC to identify with maximum sensitivity and specificity the detection of diabetes, impaired fasting glucose (fasting glucose 6. 1- 6. 9 mmol/l), hypertension and increased body mass index (BMI>/=25).

Results:

  ROC curve analysis suggested WC cut-off points of 93 cm in men and 86 cm in women for the optimum detection of diabetes and impaired fasting glucose (fasting glucose 6. 1- 6. 9 mmol/l), hypertension and increased body mass index (BMI>/=25). The cut-off points recommended for the Caucasian population differ from those appropriate for the Kuwaiti population.

Conclusions:

  Based on the ROC analysis, we suggest a WC of 93 cm for men and 86cm for women as appropriate cut-off points to identify central obesity for the purposes of CVD and diabetes-risk detection among Kuwaiti adult population.

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Weather and Asthma: A Twelve-Month Retrospective Study in Kuwait.

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Introduction:

We investigated the relationship between daily hospital admissions and emergency visits for Asthma and Rhinitis (AR) and the possible confounding and modifying effects of metereological factors in Kuwait.

Methods:

Age groups 0-20, 20-40, 40-60 and 60+ years were studied, SPSS package was used to see the levels of daily AR admissions and emergency visits associated with climatological factors.

Results:

Total number of 2, 740 AR attacks and 15, 948 emergency asthma visits were registered during 2005. AR cases recorded was high in the months of June 313, September 275, October 252 and November 318 and emergency asthma cases recorded was high in the months of September 2, 024, October 2, 124 and November 1, 942. Moderate average temperatures (270C -400C) and maximum temperatures (330C-490C), high percentage of maximum relative humidity (40%- 100%), low precipitation except November month (36. 60mm), high wind speed range (11mps- 13mps) and wind direction from north west were the major meteorological factors investigated, which may enhances AR levels during the above specific months. Percentage of Kuwaiti females (37%) were higher then the Kuwaiti male patients (27%) and percentage of Non-Kuwaiti males (25%) were higher then the Non-Kuwaiti females (10%), AR cases (41%) were high when compared with individual asthma (39%) and rhinitis cases (20%), AR admissions were high from the central region (72%) of Kuwait and high percentage AR cases about 47% was recorded among the 20-40 years age group. Spearman's Rank Order Correlation analysis shows that there was a significant positive association between total patient readings and temperature ($r= 0. 064$, $p< 0. 035$) and emergency cases where significantly positively correlated with minimum and maximum humidity ($r= 0. 087 – 0. 092$, $p< 0. 04$).

Conclusions:

Temperature, relative humidity and wind direction found to have significant associations with daily hospital admissions and emergency visits of AR patients.

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Effects of lipid lowering drugs on proteinuria.

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Introduction:

 Lipid abnormalities are one of the non-immunological factors that contribute to the development and progression of glomerulosclerosis and nephropathies. Recent studies suggested that in addition to lipid lowering effect, hypolipidemic drugs decrease glomerulosclerosis and improve nephropathies by different mechanisms.

Objectives: The aim of this study is to clarify the effects of ezetimibe and atorvastatin on proteinurea.

Methods:

 28 male Sprague-Dawely rats were enrolled in this study. They were randomly divided into 4 groups, each of seven rats: In group 1 (normal diet control), the rats fed on standard chow diet. Induction of hyperlipidemia and renal damage were carried out by feeding the rest 21 rats (group 2, 3 and 4) hypercholesterolemic diet (4% cholesterol-enriched diet plus 1% cholic acid) for 8 weeks . At the end of 8th week, group 2, 3 and 4 were treated (together with hypercholesterolemic diet) with one of the followings for the next 4 weeks: distilled water (hypercholesterolemic control), atorvastatin (10mg/kg/day) and ezetimibe (5mg/kg/day) respectively. Proteinurea and total serum cholesterol (TSC) were measured. At the end of the experiment (12 weeks), all animals were sacrificed. Renal tissue oxidation markers namely malondialdehyde (MDA) level, superoxide dismutase (SOD) activity and reduced glutathione (GSH) level were determined.

Results:

  The cholesterol-enriched diet induced a significant increase in TSC ($p<0.001$). Likewise proteinuria increased in rats fed on hypercholesterolemic diet ($p<0.001$). Furthermore, MDA levels ($p<0.01$) and SOD activity ($p<0.01$) were significantly increased in renal tissues of hypercholesterolemic rats where as GSH levels were significantly decreased ($p<0.01$). TSC was significantly decreased by atorvastatin ($p<0.001$) and ezetimibe ($p<0.01$) treatment. In addition, proteinuria was significantly decreased by atorvastatin ($p<0.001$) and ezetimibe ($p<0.001$) administration. Atorvastatin administration produced significant decreases in MDA level ($p<0.05$) and SOD activity ($p<0.05$) . Ezetimibe also produced significant decreases in MDA levels ($p<0.05$) and SOD activity ($p<0.05$). There were small, but statistically significant ($p<0.05$), increases in GSH levels produced by atorvastatin and ezetimibe administration.

Conclusions:

  Atorvastatin was significantly better than ezetimibe in reducing TSC. Also it was obvious that both drugs produced significant antioxidant properties. Therefore, our data suggesting that in addition to their lipid lowering effect, atorvastatin and ezetimibe improved proteinuria probably by their antioxidant effect.

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Epidemiology of Crohn's Disease in Kuwait

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Introduction:

Crohn's Disease (CD) is believed to be rare among the Arabs. We conducted this study to determine the pattern of CD in Kuwait.

Methods:

The study included a continuous series of 224 CD patients seen in two major hospitals in Kuwait. Information was collected through personal interview and review of case notes with regard
to clinical features, results of diagnostic tests, treatment and clinical course.

Results:

Among the 224 CD patients, the majority (92%) were of Arab origin (114 (51%) males, 110 (49%) females; sex ratio: 1:1). The average age at diagnosis (± s. d.) was 22. 7 ± 10. 2 years (range
1-64 years); the median age was 20 years. The mean duration of symptoms prior to the diagnosis of CD was 6. 1 ± 5. 6 months. Family history of CD was reported by 39 (17. 4%) patients. The disease was limited to the small bowel in 123 (54. 9%) patients, whereas in 71 (31. 7%) it involved both the small bowel and colon; 30 (13. 4%) patients had only Crohn's colitis. The behavior of the disease was non-stricturing, nonpenetrating in 128 (57. 1%) patients, whereas 55 (24. 6%) had stricturing and 41 (18. 3%) penetrating disease. The commonest clinical features included abdominal pain (87. 5%), diarrhea (81. 7%), weight loss (61. 2%), rectal bleeding (37. 1) and perianal disease (16. 5%). Medical treatment for the disease included 5'aminosalasilytes (78. 6%), systemic steroids (70. 1%), azathioprine/6MP (67. 5%), infliximab (30. 3%), methotrexate
(7. 1%) and adalimumab (3. 5%). A total of 74 (33. 0%) patients had had some surgery for the disease (42 for perianal disease, 33 for strictures, and 5 for medically unresponsive disease).

Conclusions:

These data show that Crohn's Disease in Kuwait is equally common in males and females, presents at a younger age, and in about 50% is limited to the small bowel. The latter two features may be an indication of an underlying genetic predisposition for the disease in this population.

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Scimitar syndrome: The impact of interruption of anomalous systemic arterial supply on further management of symptomatic infants.

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Introduction:

There are conflicting sporadic reports in the literature on the impact of interruption of anomalous systemic arterial supply (ASAS) in the management of scimitar syndrome presenting during infancy. No systematic study has been undertaken so far on this issue.

Methods:

Out of 25 children diagnosed to have SS during the past 25. 5 years, 17 symptomatic infants had ASAS. After interrupting ASAS (coil embolization -15, surgical ligation -2), they were prospectively evaluated to decide on further management strategies.

Results:

All 17 infants had sizable ASAS and 9 had variable scimitar vein (SV) stenosis. Sixteen (94%) had pulmonary hypertension and significant left to right shunt. Post intervention, there was variable reduction of shunt in 15 and pulmonary artery pressure in 16 cases. All showed varying clinical improvement. One died of septicemia shortly afterwards. Definitive surgery was deferred for optimal results in 7 children for a mean period of 8 months (range 1 month to 3 years). Remaining 9 children did not require definitive surgery. One among them had closure of stenosed partial SV by Amplatzer duct occluder ('physiologic correction'). Three children on short term, and 6 children on long term follow up (mean 5. 2 years; range 3. 3 to 10. 3 years) are doing well.

Conclusions:

Interruption of ASAS helps to avoid or defer definitive surgery for SS during infancy. Therefore, we recommend coil embolization of ASAS as initial palliation, and long term medical follow up to assess need for further intervention.

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Quality of Life and Clinical Profile of Thalessemia Patients in Kuwait : A Case Control Study

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Introduction:

Thalassemia is an increasingly serious public health problem throughout the the Middle East including Kuwait. It is estimated that there are currently 200-300 patients with Thalassemia major in Kuwait. This study aimed at describing the quality of life of patients with Thalassemia major in Kuwait and to describe their socio-demographic characteristics, disease profile, and treatment profile.

Methods:

A case–control study with 75 cases and 75 age and gender matched controls was carried out in March 2007. Coded data were analyzed using STATA 8. 0 and SPSS. Descriptive statistical analysis was used for quantitative variables, variability between case and control was demonstrated using conditional logistic regression. The cut off level for statistical significance was used as p-value < 0.05 with a 95% CI.

Results:

The study showed that 65% of cases had a quality of life score less than the median population score, compared to 35% of controls after the adjustment for the confounding factors. Consanguinity was found to be 63% compared to 30% in general population in Kuwait. Although known to have a very significant family history of carrier and affected individuals, 68% of the patients were diagnosed only after the emergence of the disease symptoms. During the course of their treatment, 27% of all the patients became hepatitis C positive due to repeated blood transfusions. Despite the fact that oral chelation therapy is the most convenient treatment modality available for patients with Thalassemia major, only 31% of the patients involved in this study were on this treatment which was only available for Kuwaiti nationals.

Conclusions:

Thalassemia major in Kuwait has a negative impact on the perceived physical, emotional, social and school/work functioning. More understanding and support from health authorities, school administration, and the society in general is crucial to enhance the quality of life of patients with chronic illness.

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Hips do lie - Paradoxical associations of hip circumference with Coronary Heart Disease (CHD) risk factors and CHD in patients with type 2 Diabetes.

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Introduction:

Recently waist hip ratio (WHR) has been shown to be the best anthropometric risk factor for CHD. This could be due to relatively large waist, small hip or both. This study aimed to identify the separate associations of waist circumference (WC), hip circumference (HC) and WHR with the incidence and risk factors for CHD in 248 (109 M and 139 F) patients with Type 2 diabetes mellitus and 313 (119M and 194F) matched control subjects.

Methods:

We measured fasting CRP (high sensitivity assay - hs-CRP), adiponectin, leptin, resistin, glucose, insulin, β-cell function (%B), insulin sensitivity (% S) and resistance (homeostasis model assessment (HOMA-R)), HbA1c and lipid profile. Univariate and multivariate regression analyses were used to find the associations of these variables with each other and CHD.

Results:

In male and female patients and control subjects, HC showed significant (p<0. 05) correlations with factors that increase the risk of CHD such as hs-CRP (r = 0. 44), insulin (r = 0. 35), %S (r = - 0. 32), HOMA-R (r = 0. 26), triglyceride (r = 0. 23); adiponectin (r = - 0. 46), leptin (r = 0. 53) and resistin (r = 0. 49). Paradoxically, HC showed a significant graded protective association with CHD (odds ratio (OR) 0. 65; 95% CI 0. 45 to 0. 93 after adjustment for confounders. Patients in the
bottom quartile of HC had the highest WHR and, in this group, the OR (95% CI) for the association of HC with CHD was 2. 64 (1. 18 to 5. 93). WHR showed poor, insignificant correlation with body mass index (r = 0. 1) and insignificant association with CHD (OR (95% CI) = 0. 98 (0. 95 - 1. 02)).

Conclusions:

We conclude that larger HC is associated with increased number of CHD risk factors but paradoxically associated with reduced incidence of CHD. Having a small HC is the factor associated with increased CHD risk. These paradoxical effects are poorly captured in the WHR in our cohort in whom the WHR is a poor risk factor for CHD.

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Detailed evaluation of symptoms in women admitted for coronary angiography and found to have no significant coronary artery disease - Analysis of 100 patients.

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Introduction:
 It is well-known that atypical presentation of Coronary artery disease (CAD) is seen more often in women than in men. There is also the possibility of their non cardiac symptoms being ignored if they are found to have no significant CAD. We have analysed the symptoms in 100 consecutive women who underwent Coronary Angiography and were found to have non significant CAD.

Methods:
 Demographic details and risk factors were recorded. Coronary and left ventricular angiograms were done and all the cine angio films were analyzed by two Cardiologists. An alternate explanation of symptoms was sought by detailed history, physical examination and if necessary through special investigations.

Results:
 91% were Arabs (74 % Kuwaitis). Mean age was 52. 6 (+/- 10. 22), BMI greater than 30 was found
 in 77%, Hypertension and Diabetes were seen in 74% and 54% respectively. 11% gave history of smoking. A definite alternative explanation for symptoms was found in 61%. This was related to musculoskeletal causes (27%), obesity (26%) , physical de-conditioning (5%) and gastrointestinal causes (3%).

Conclusions:
 A definite alternative explanation was found in most of the patients admitted for coronary angiography and found to have no significant CAD. In the majority, symptoms were related to obesity and musculoskeletal causes.

Medicine
Category: Clinical

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Sero-epidemiology of Hepatitis A Virus in Kuwait

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Introduction:

  Hepatitis A virus (HAV) is often a self limiting disease that can be associated with fulminant hepatic failure (FHF). The mortality rate tends to increase with age, in particular when greater than 40 years of age. (1) Various data from the world showed that with the improvement in hygiene and quality of life there is a shift in the epidemiology of HAV to older people exposing them to the risk of serious HAV infection.
Hepatitis A virus HAV is the predominant form of viral hepatitis. The aim of this study is to find the current seroepidemiology of HAV in Kuwait.

Methods:

  Kuwaiti adult from both sex applying for new job was studied. Each individual completed a questionnaire. Thereafter, 5 ml of blood was obtained. Blood samples were collected from different
 centers and sent to the Virology Unit – Public Health Laboratories. Axsym HAVAB 2. 0 kit from
 ABBOTT LABORATORIES was used for the detection of IgG anti-HAV from all samples . The
 procedure followed as indicated by the manufacturer. In addition, the samples were tested for anti-hepatitis B surface antigen (HBsAg), anti-Hepatitis C virus and antiHIV. Data is descried using descriptive statistical method namely counts and percentages of screened subjects

Results:

  Total of 2851 Kuwaiti applied for new jop were screened. HAV positive cases were 28. 8%
, 59%were males and 41% were females . The highest prevalence was in Ahmadi area . High prevalence was among the group of non educated than the educated parents.

Conclusions:

 This is the first study in Kuwait demonstrating shifting epidemiology of HAV in Kuwait. This study reflects the need of the Kuwaiti population for HAV vaccine.

Key Words: Hepatitis A Virus; Fulminant Liver Failure,; HAV vaccine;

Medicine
Category: Clinical

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Quality of life in multiple sclerosis: the Kuwaiti experience using a disease-specific questionnaire.

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Introduction:

  In Kuwait, a rising incidence and prevalence of multiple sclerosis (MS) has been reported recently. There are no studies from the Arab world on the quality of life of MS patients using a disease-specific instrument, and there is paucity of reports on the impact of family caregiver attitudes. QOL issues present the opportunity to measure the disease effect more broadly and to include psychosocial factors in the clinical setting, in order to enhance the quality of care. We compared the QOL self-ratings of relapsing remitting (RRMS) and progressive (PMS) MS patients with those of a matched general population sample; and assessed the association of demographic, clinical, and caregivers' variables with patients' QOL.

Methods:

  Consecutive clinic attendees at Ibn Sina Hospital were assessed with the 54-item MSQOL, the Beck's Depression Inventory, and the Expanded Disability Status Scale (EDSS). Caregivers rated their impression of patients' QOL (using the 26-item WHOQOL) and attitudes to patients' illness.

Results:

  Of 170 patients (35. 5% m, 64. 5% f; mean age 32. 4 years; 23. 9% unemployed), 85. 3% had RRMS and 14. 7% had PMS. Mean EDSS was 2. 7 (SD 1. 8). Subjects' characteristics were similar to the national epidemiologic sample. The questionnaires fulfilled standard criteria for reliability and validity. RRMS subjects had higher QOL domain scores (P < 0. 001). Patients had lower QOL than the controls (P < 0. 001). Depression was the commonest significant covariate of QOL domains. After controlling for depression and disability, differences between the MS groups were less significant. Predictors of overall QOL were caregiver impression of patient's QOL, depression, and treatment side effects.

Conclusions:

  The findings call for programs that address depression, disability, the impact of treatment side effects, and caregiver attitudes about illness at the clinic. QOL issues should be included in routine care in order to enhance the quality of care.

Key Words: Quality of life; Multiple sclerosis; Kuwait;

Medicine
Category: Clinical

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Spectrum of bone mineral density in Arab women resident in Kuwait

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Introduction:

It is well known that bone mineral density (BMD) differs at different sexes and age groups. At both sexes, BMD tends to increase from childhood and reaches its peak at about 26 ± 4 years of age. Subsequently, it plateaus and declines at a variable rate in different population and ethnic groups. Due to the fact that data on BMD status of Arab women are deficient on literature, this study aimed to assess the spectrum of bone mineral status in Arab women who reached their maximal BMD (i. e. aged >/= 30 years).

Methods:

All Arab women (aged >/= 30 years, not known to have bone disease and were not taking any medication that may alter bone status for 12 months prior to study) who were referred for assessment of BMD in between January 1998 and January 2002 at Mubarak Al-Kabeer Hospital, were included in the study. Their BMD of the AP spine L2-L4 and of the proximal right femur were measured using Dual Energy X-Ray Absorptiometry (DEXA-Lunar). WHO criteria for definition of normal, osteopenic and osteoporotic BMD were used with T-scores (ratio of patient's BMD and that of young adult population).

Results:

805 Arab women (aged >/=30 years) were included in the study. They were stratified according to age as follows: 30-39 years (n=158), 40-49 years (n=248), 50-59 years (n=276) and >/= 60 years (n=123). Their (mean$\pm$SEM) BMI respectively are: 28. 6$\pm$0. 5, 30. 6$\pm$0. 4, 31. 6$\pm$o. 4 and 32. 4$\pm$0. 5 kg/m2. The results of their BMD of L2-L4 and of the right femur are tabulated below:

	30-39 yrs	40-49 yrs	50-59 yrs	>/= 60 years
L2-L4	N=152	N=245	N=269	N=121
Normal	92 (60%)	146 (60%)	122 (45%)	35 (29%)
Osteopenic	48 (32%)	82 (33%)	105 (39%)	44 (36%)
Osteoporotic	12 (8%)	17 (7%)	42 (16%)	42 (35%)
Rt femur neck	N=114	N=210	N=242	N=111
Normal	57 (50%)	124 (59%)	111 (46%)	33 (30%)
Osteopenic	42 (37%)	76 (36%)	106 (44%)	51 (46%)
Osteoporotic	15 (13%)	10 (5%)	25 (10%)	27 (24%)

Conclusions:

After the achievement of peak BMD age, percentage of low BMD (combined osteopenia and osteoporosis) of L2-L4 spine in Arab women increases progressively from a younger age (40 years) than that age (50 years) observed for increased percentage of low BMD of the right femur. This would suggest the need for assessment of BMD of large cohorts of Arab females throughout their life span.

Key Words: Bone density; Age; Kuwaiti women;
Funding Agency: None

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The Incidence of Angiotensin-converting Enzyme (ace) Gene Insertion-deletion (i/d) Polymorphism In patients with Primary Knee Osteoarthritis

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Introduction:

Angiotensin converting enzyme (ACE) plays an important role in a number of inflammatory and immune related disorders. ACE is present as a membrane-bound enzyme in endothelial cells, in different types of epithelial cells and synovial fluid. A biallelic polymorphism (insertion-deletion, I/D) was identified in the intron 16 of the ACE gene and it has since been associated with marked differences of serum of ACE levels in unrelated healthy individuals. Knee osteoarthritis (OA) is one of the most common musculoskeletal disorders world wide. It is estimated that 10% of people older than 55 years will have disability knee symptoms. Recent community studies have shown that osteoarthritis is a common problem in Kuwait. This study was undertaken to investigate an association between ACE gene I/D polymorphism and primary knee osteoarthritis (OA) in Kuwait and to find out a possible correlation between clinical subgroups of OA and ACE I/D polymorphism genotypes.

Methods:

The prevalence of ACE gene I/D polymorphism was determined in 115 patients with primary knee OA and 111 healthy controls using PCR of the genomic DNA. The association of ACE gene I/D polymorphism genotypes with age of onset of disease, its functional and radiological grading was also investigated.

Results:

There was no significant difference in the frequency of ACE gene I/D polymorphism genotypes and alleles between patients and controls. The frequency of ACE gene polymorphism genotypes was also studied in subgroups on basis of clinical parameters of age of onset of disease, function and radiological grading and no significant difference was detected between subgroups of OA patients and controls. This is in sharp contrast to a previous report from Korea in which a significant association had been found between ACE gene polymorphism and OA.

Conclusions:

There was no significant association between ACE gene I/D polymorphism in patients with knee osteoarthritis in Kuwait.

Key Words: Knee Osteoarthritis; ACE Gene Polymorphysm; Genetic Rescarch;
Funding Agency: Nil

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Effect of Smoking Habit on Circulating Adipokines in Diabetic and Non Diabetic Subjects.

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Introduction:

 Background and objectives: Despite the well known inverse association between smoking and body weight, there have been conflicting reports on the association between smoking and adipokines such as leptin and adiponectin.

Aim of the study : To determine and compare whether tobacco smoking (cigarettes or sheesha) affects circulating levels of adiponectin and/or influences leptin and leptin receptor (sOb-R) concentrations and free leptin in diabetic and non-diabetic subjects.

Methods:

  Fasting plasma adiponectin, leptin, sOb-R, glucose and lipid profile were determined in 236 subjects grouped as control subjects (n = 53); non diabetic cigarette smokers (n =34), non-diabetic sheesha smokers (n = 38), diabetic non smokers (n =75) and diabetic smokers (n =36).
 Uni- and multi-variate regression analyses were used to determine the associations of these variables with body mass index (BMI) and smoking.

Results:

 When compared to control subjects, smoking cigarettes or sheesha was associated with significantly higher glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C) and lower serum leptin, sOb-R and free leptin. The effects of smoking on the BMI, leptin and sOb-R were dose dependent. Binary logistic regression analysis showed that smoking is a significant determinant of BMI; leptin, sOb-R, free leptin index, adiponectin and LDL-C.

Conclusions:

  We conclude that smoking sheesha does not reduce the metabolic effects of smoking. Smoking may modify leptin receptors and modulate leptin synthesis but the weight-lowering effect may not be related to leptin-induced anorectic signals.

Medicine
Category: Undergraduate

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A Kuwaiti Diabetes Risk Score for Targeted Screening

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Introduction:

Introduction: Type 2 diabetes is common, costly and often goes unrecognized for many years. When patients are diagnosed, the majority exhibit associated tissue damage or established cardiovascular risk. Evidence is accumulating that earlier detection and management of diabetes and related metabolic abnormalities may be beneficial. We aimed to develop and evaluate a score base on routinely collected information to identify people at risk of having undetected diabetes.

Methods:

Methods: A cross-sectional survey was conducted among 562 Kuwaiti employees in the ministry complex using a gender stratified multi-stage cluster sampling. Data was collected through a self administered questionnaire and researchers carried out a blood glucose test using a glucose meter.

Results:

Results: The overall prevalence of diabetes was found to be 21. 4% of which 17. 3% were known to
have diabetes, and 4. 1% were undetected diabetics. We found 10. 7% were pre-diabetics (impaired
fasting glucose) according to American Diabetic Association (ADA) criteria of 1997. The performance of the screening tools (i. e. The Thai, Omani, ADA, Indian, Rotterdam, Danish, Finnish and Cambridge

Conclusions:

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Incidence, Risk factors, and Causative agents of Hospital Acquired Pneumonia (Nosocomial Pneumonia) in adult Hospitalized Patients in Medical Wards of a General Hospital in Kuwait

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Introduction:
Pneumonia is the second most frequent nosocomial infection. The incidence ranges from four to 50 cases per 1000 hospital admissions. In this study we attempted to identify the incidence and the most common pathogens causing hospital acquired pneumonia. We also wanted to increase the awareness regarding identification of susceptible patient likely to develop these infections, aiming for early diagnosis and deciding proper empirical antimicrobial agent.

Methods:
Retrospective study of all adult patients'admitted to four general medical wards and developing pneumonia 48 hours or more after admission with no previous evidence of infection by symptoms or signs. The data were analyzed and reported by age, sex, risk factors, and causative agents from January to June 2005.

Results:
Out of a total of 1971 patients admitted over a six months, 132 patients (6. 6%) developed nosocomial pneumonia. The commonest risk factors detected were the use of H2 blocker (75. 8%), smoking (40. 2%), diabetes mellitus (39. 4%), and chronic obstructive pulmonary disease (38. 6%).
The commonest organisms detected were Pseudomonas aurginosa (45. 2%), Klebsiella pneumoni (24. 2%).

Conclusions:
Overall incidence of hospital-acquired pneumonia was 6. 6% in all-medical cases reviewed. Use of H2 blocker was the most significant risk factor for the development of HAP in this study. Cigarette smoking, diabetes mellitus and COPD were the other risk factors. Associating the type of organism to the number of risk factors showed high percentage of infection occurring in patients with multiple risk factors.

Key Words: Hospital acquired infections; Nosocomial pneumonia; Pseudomonas aurginosa;
Funding Agency: None

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Adipocyte enhancer-binding protein 1 (AEBP1) is a critical stromal factor in regulation of mammary gland development, inflammation, and tumorigenesis.

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Introduction:
 A complex interplay between epithelial and stromal compartments of mammary tissue is critical in mammary gland development. Disruption of epithelial-stromal communication is linked to breast cancer. Adipocyte enhancer-binding protein 1 (AEBP1) is a multifunctional protein that up-regulates NF-κB activity. The objective of this study is to elucidate the molecular mechanism undertaken by AEBP1 to modulate mammary gland development and promote tumorigenesis. This study also investigates the role of macrophages in such biological processes.

Methods:
AEBP1-transgenic mice (AEBP1sup TG endsup) with targeted AEBP1 over-expression in stroma and AEBP1-null (AEBP1sup-/-endsup) mice were used as invaluable tools to assess AEBP1 role in mammary gland development and tumorigenesis. The influence of AEBP1 on such processes is evaluated by Western blot analysis of whole-cell and nuclear extracts, immunohistochemical analysis, electrophoretic mobility gel shift assay, RT-PCR, and mammary gland transplantation experiments.

Results:
 Ablation of AEBP1 causes defective mammary gland development with premature involution during pregnancy. Stromal restoration of AEBP1 expression is sufficient for normal mammary gland development in AEBP1sup-/-endsup mice. AEBP1TG mice display spontaneous growth of mammary tumors. Treatment of mammary epithelial cells with AEBP1TG and AEBP1sup-/-endsup macrophage-conditioned media results in increased and decreased NF-kapaB activity and survival signal, respectively.

Conclusions:
AEBP1 is a critical factor that regulates mammary gland development and promotes mammary tumorigenesis by activation of survival signal via TNF α -mediated NF-κB activation. Our results highlight the need for further elucidation of AEBP1 role in the signaling pathways involved in mammary tumorigenesis, which should improve manipulations of these processes towards design of prevention and treatment strategies for breast cancer.

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The effect of Ramadan fasting in Kuwaiti T2DM on the control of diabetes, blood Pressure and dyslipidemia.

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Introduction:
 Ramadan fasting is 1 of 5 pillars of Islam. Fasting is a religous obligation for all Muslims.
However, Islam excempts sick from duty of fasting including diabetic patients. But in fact most of
 the diabetic patients do fast despite the advise. Fasting entails major changes in metabolism both
 in healthy and diseased, and these changes most probably due to the changes in eating pattern,
frequency and sleep pattern. The aim is to study the effect of Ramadan fasting in type 2 diabetic
patients on the control of diabetes, blood pressure, dyslipidemia and body weight.

Methods:
 Observational study conducted in the month of Ramadan year 2006. 56 Kuwaiti patients were
asked to enroll in the study all were T2DM on either diet control alone or diet and oral anti
diabetic therapy, 36 accepted, but only 16 (8 males and 8 females) completed the 2 phases of the
study.
Patients were studied before (within a month before Ramadan) and at the end of Ramadan (within
the last 5 days of the month) for changes in the following variables:
Body weight, Blood pressure, HbA1C, Total Cholestrol, LDL cholestrol, HDL cholestrol,
Triglycerides, and the total daily caloric intake.

Results:
 We observed NO significant changes in the total daily caloric intake, weight, glycemic control,
blood pressure, and lipid control.

Conclusions:
  Ramadan fasting in the current dietary pattern did not lead to a significant changes in the control
of diabetes, blood pressure, dyslipidemia, and body weight in Kuwaiti patients with T2DM.
Because of the limited number in our cohort, further studies are needed to be conducted in this
field.

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Safety and efficacy of infliximab in patients with active systemic systemic lupus erythematosus: a pilot study

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Introduction:

New treatments for systemic lupus erythematosus (SLE) are urgently needed. As disease activity in SLE correlates well with increased serum levels of tumor necrosis factor α (TNF-α, we assessed the safety and efficacy of TNF blockade in patients with active SLE.

Methods:

15 patients with active SLE were allocated to treatment and control arms randomly. In addition to conventional treatment, treatment arm received Infliximab infusions 3 mg/ kg body weight at 0, 2, 6 weeks and then q 8 weeks for a total of 24 weeks. Clinical, laboratory and treatment data were entered into a pre-designed proforma. Health status (SF 36), patient global assessment (PGA) of disease activity, disease activity scores by SLEDAI, and organ damage by SLICC/ACR-DI were measured at baseline and end of the study. Relevant immunological studies included C3 & C4 complement levels, IgM, IgG and IgA anti-dsDNA antibody titers, IgG, IgM, and IgA isotypes of anticardiolipin and anti-β2GPI antibodies, and serum levels of TNF-α and sTNF receptors 1 and 2.

Results:

The treatment group showed significantly greater improvement in several SF-36 subscales (role physical, bodily pain, vitality, social, mental, overall physical component and overall mental component), SLEDAI, VAS fatigue, hemoglobin, complement proteins C3 and C4 and anti-dsDNA titers. PGA and mean SLICC/ACR-DI scores did not change significantly in either group. Paradoxically, reduction in 24h proteinuria was more in the control group. The mean levels of sTNFa, sTNFr1 and sTNFr2 were significantly higher in the SLE group compared to healthy controls. However, no significant differences emerged between the treatment and control SLE patients over the study period. We did not face any safety issues with infliximab in this study.

Conclusions:

Anti-TNF α therapy is an interesting candidate approach for treating SLE , with improvement in several parameters with a good safety profile.

Key Words: Systemic lupus erythematosus; Treatment; Infliximab;

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Does the glomerular filtration rate affect circulating adipokines in patients with type 2 Diabetes Mellitus and varying degrees of Nephropathy?

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Introduction:

Obesity and insulin resistance contribute to the progression of renal disease via several mechanisms. We postulate these mechanisms may involve retention of low molecular weight adipokines when glomerular filtration rate (GFR) decreases. The main objective of this study was to evaluate the relationships between adiponectin (30kDa), resistin (12. 5 kDa) and leptin (16 kDa) concentrations with estimated GFR (eGFR) in patients with Type 2 diabetes (T2DM) and varying degrees of diabetic nephropathy.

Methods:

Fasting adiponectin, resistin and leptin were determined in 210 T2DM patients who were classified as normo- (n = 139) or micro-albuminuric (n = 71). eGFR was determined by the Modification of Diet in Renal Disease equation. Uni- and multi-variate regression (with inclusion of age, gender, waist circumference (WC), coronary heart disease, hypertension and smoking status as potential confounders) analyses were used to determine the associations of eGFR with adipokine concentrations.

Results:

37% of patients had eGFR < 60 ml/min/1. 73 m2 and in these patients mean WC (105 vs 107 cm) was lower but mean adiponectin (15. 8 vs 14. 3 ng/ml), resistin (24. 7 vs 23. 3 ng/ml) and leptin (39. 9 vs 39. 2 ng/ml) were higher than in patients with eGFR > 60 ml/min/1. 73 m2. Adiponectin (r = -0. 38), leptin (r = 0. 45) and resistin (r = 0. 49) were significantly correlated with WC and these correlations remained significant after correction for eGFR and the above confounders. In regression analyses, no significant associations were found between adiponectin, leptin and resistin and eGFR. Sub-group analysis of patients with eGFR < 60 ml/min/1. 73 m2 failed to show associations between adipokines and eGFR.

Conclusions:

Our results reject the hypothesis that there is GFR dependent retention of adipokines in patients with T2DM in whom the degree of adiposity appears to be the most significant determinant of circulating adipokines.

Medicine
Category: Clinical

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Does preoperative serum creatinine predict early postoperative mortality after open heart surgery?

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Introduction:

Acute renal failure (ARF) is a frequent and serious complication of cardiac surgery associated with increased mortality. The purpose of this study was to find out the impact of preoperative serum creatinine on the early postoperative mortality (within 30 days) after open heart surgery.

Methods:

The following data were collected from 500 successive open heart surgeries: age, gender, co-morbidities, operative and postoperative data. Data were analyzed using SPSS for windows.

Results:

369(73. 8%)were males, 163(32. 6%)above 65 years, 36. 4% were diabetics, 57. 4% were hypertensives, 40. 2%had chronic obstructive airway disease (COAD), 9. 45had chronic renal impairment(CRI)with preoperative creatinine above 150μmol/l, 22. 6% had recent myocardial infarction, 65. 2% had ejection fraction(EF)below 35%, 17. 6% had combined coronary and valve surgeries, 5. 8% had post operative hemorrhage, 9. 0%had postoperative infection, 38. 6%had extracorporeal circulation time(ECCT)>100 minutes, 40. 8%had aortic cross clamp time CCT>60 minutes, 17. 4% had postoperative ARF(>25%increase in serum creatinine) and 12% required dialysis. The overall mortality was 34(6. 8%, it was 28. 7%(25 cases)in those developed postoperative ARF and 33. 3%(20 cases)in those required dialysis. Univariate analysis showed: female gender, hypertension, COAD, CRI, EF below 35%, ECCT>100 minutes, CCT>60 minutes, post operative hemorrhage and infection, use of more than two vasopressors, postoperative ARF, prolonged ventilation and MOF as factors contributing to early mortality. Multivariate analysis detected female gender (P=0. 01), preoperative creatinine(P=0. 007)and MOF(P< 0. 001)as the only independent variables determining the early post operative mortality. Among them, high preoperative creatinine was the most significant and the best predictor for early postoperative mortality.

Conclusions:

This study confirmed a strong link between preoperative renal impairment and early postoperative mortality after cardiac surgery.

Key Words: Acute renal failure; Open heart surgery; Outcome;

Medicine
Category: Clinical

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Epidemiology and outcome of acute renal failure in KUWAIT(a single center study)

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Introduction:

Acute renal failure (ARF) is a serious complication in hospitalized patients with a mortality exceeding 50% among those requiring dialysis. The epidemiology and outcome of ARF in different regions of the world is not well established. The aim of this study was to define the epidemiology and outcome of ARF in Kuwait.

Methods:

A prospective study was conducted in Al-Sabah Medical Region (2003 to 2005). All cases presented with ARF were enrolled in the study. Patients' clinical data and outcome were statistically analyzed

Results:

476 patients had ARF, 269 (56. 5%) were males, 254 (53. 4%) were Kuwaiti, 168 (35. 3%) were Other Arabs and 54 (11. 3%) were Non-Arabs. Mean age was 59. 7±17. 25 years. 264 (55. 5%) were

diabetics, 310 (65. 4%) had ischemic heart disease, 324 (68. 1%) had hypertension, 173 (36. 4%) had chronic kidney disease, 73 (15. 3%) had obstructive airway disease, 60 (12. 6%) had neoplastic diseases, 223 (46. 8%) had sepsis, 235 (49. 4%) were hemodynamically unstable, 238 (50%) were mechanically ventilated, and 130 (27. 3%) had multi organ failure. Regarding the cause of ARF; 60 (12. 6%) had open heart surgery, 98 (20. 6%) had contrast nephropathy, 40 (8. 4%) had recent myocardial infarction, 98 (20. 6%) had septic shock, 49 (10. 3%) had drug induced nephotoxicity, 23 (4. 8%) had obstructive uropathy, 24 (5%) had abdominal surgeries, 19 (4%) had tumor lysis, 14 (2. 9%) were volume depleted, 46 (9. 7%) were multifactorial, 3 (0. 6%) had rhabdomyolysis, and 2 (0. 4%) had hepatorenal syndrome. Continuous venovenous hemofiltration (CVVH) was conducted in 224 (47. 1%) of cases. The overall mortality was 135 (28. 4%). Mortality with CVVH was significantly higher than in those treated conservatively 78 (34. 8%) vs 57 (22. 6%) (P = 0. 002)

Conclusions:

ARF is a life threatening condition. The main underlying causes in Kuwait were septic shock, contrast nephropathy. Mortality rate is high with a higher mortality rates among those treated with CVVH

Key Words: Acute renal failure; Sepsis; Outcome;
Funding Agency: None

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Allopurinol reduces renal injury in nitric oxide inhibition model.

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Introduction:

  It is increasingly recognized that oxidative stress is important factor in the development of nephropathies. Recent studies suggested that xanthine oxidase inhibition is an emerging pharmacological strategy to reduce oxidative stress and to provide renoprotection. Objectives: This study aims to evaluate the renoprotctive effect of allopurinol.

Methods:

  In this study, a total of 24 New Zealand white male rabbits, aged 3–4 months and weighing 2. 0 to 2. 4 kg, were used. They were randomly divided into three groups, each of eight animals. Group C (Control), receiving no treatment throughout the course of the study. Group N, orally treated with NO inhibitor, Nw-L- nitroarginine methylester (L-NAME) 0. 5 mmol/L dissolved in drinking water, corresponding to daily intake of 30mg/kg, for 3 weeks. Group N+A, receiving L-NAME (30mg/kg/day) and allopurinol (50mg/ kg/day) orally for 3 weeks. Proteinuria was measured (on day 1, 7, 14 and 21). At the end of experiment, all animals were sacrificed. Plasma fibrinogen level (acute phase reactant) and serum uric acid (SUA) were measured. Renal cortical tissues were homogenized to asses the tissue oxidation markers namely malondialdehyde (MDA) level, superoxide dismutase (SOD) activity and reduced glutathione (GSH) level.

Results:

  Treatment with L-NAME promoted massive proteinuria ($p < 0.001$). Plasma fibrinogen levels ($p < 0.001$) and SUA ($p < 0.01$) were significantly higher ($p < 0.01$) in group N than group C. Compared to control group (C), MDA levels ($p < 0.01$) and SOD activity ($p < 0.05$) were significantly increased in renal tissues of group N where as GSH levels ($p < 0.01$) were significantly decreased. Proteinuria was significantly decreased ($p < 0.001$) with allopurinol treatment. Also it was obvious that allopurinol administration significantly reduced plasma fibrinogen levels ($p < 0.01$) and SUA ($p < 0.001$). Additionally, allopurinol significantly decreased renal tissue's MDA levels ($p < 0.01$) and SOD activity ($p < 0.05$). Furthermore, renal tissues had significantly higher GSH levels ($p < 0.01$) in allopurinol treated group.

Conclusions:

  Our findings suggesting that allopurinol posse's ant inflammatory and antioxidant properties. It is therefore we concluded that allopurinol reduces oxidative stress mediated renal injury.

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The Excitotoxin Qunolinic Acid Induces Tau Phosphorylation in human neurons

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Introduction:

 Tryptophan catabolites produced through the kynurenine pathway (KP), and more particularly the excitotoxin quinolinic acid (QA), may play an important role in the pathogenesis of Alzheimer's disease (AD).
It has been reported that: (1) QA synthesis is increased in AD brain; (2) high levels of QA in brain are associated with neurodegeneration and dementia; (3) QA leads to neurotoxicity by at least 4 different mechanisms; (4) tau hyperphosphorylation and its subsequent aggregation into neurofibrillary tangles is the hallmark pathology in AD-related neurodegeneration and dementia. Based on these reports, we hypothesize that tau hyperphosphorylation may be a new mechanism for QA neurotoxicity.

Methods:

 We investigated the effect of QA on tau phosphorylation in vitro using primary cultures of human fetal neurons. Neurons were cultured without or with various concentrations of QA.

Results:

 We found that QA increased the phosphorylation of tau at serine 199/202, threonine 231 and serine 396/404 in a dose dependent manner using Western blot. Increased accumulation of phosphorylated tau was also found by immunocytochemistry. This increase in tau phosphorylation was parallelled with a substantial decrease in the total protein phosphatase and PP2A activity in the cultures treated with QA at 400-1200 nM. QA treatment decreased the expression of major tau phosphatases, protein phosphatase-1 (PP1), PP2A and PP5, in a dose-dependent manner.

Conclusions:

 These data demonstrate that QA in pathophysiological concentrations induces phosphorylation of tau at residues present in the paired helical filaments from AD brain. A reduction in the expression of major tau phosphatases appears to be the mechanism for tau hyperphosphorylation. These observations suggest a new role for QA in the neuropathology of AD. These results bring a novel therapeutic target for the treatment of AD.

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Role of tigecycline in the control of outbreaks of carbapenem-resistant Acinetobacter baumannii infections in the ICU of Mubarak Hospital, Kuwait

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Introduction:

Control of Acinetobacter baumannii (MRAB) infections in an ICU setting is often problematic mainly because of limited available therapeutic options. We report 3 different episodes of nosocomial outbreaks of multi-resistant A. baumannii in our ICU successfully controlled with tigecycline.

Methods:

Three outbreaks occurred in February and April, 2006 and April 2007. Patients' demographics were carefully recorded. Samples of endotracheal tube (ET) secretions, sputum, blood, urine, CSF and wound were collected and cultured as appropriate. Identification was achieved with automated VITEK II ID system. Susceptibility testing was done by the Etest method. Molecular typing of the isolates was determined by PFGE. Patient and environmental screening strategies were followed.

Results:

Twenty-one patients, aged 19-75 years, were involved. Time-of-admission to time-of-acquiring infection ranged from 3-31 days. All isolates were resistant to 15-17 antibiotics, including carbapenems (MRAB-C) but susceptible to tigecycline with MIC_{90} of 2mcg/ml.
Overall mortality rate was 14. 3%. The first outbreak involved 6 cases. Time-to-clearance of the MRAB-C after therapy with amikacin and ciprofloxacin was 8. 3 days and was associated with a mortality rate of 50%. The second outbreak involved 10 patients. All patients received tigecycline. Time-to-clearance was 2. 8 days and all survived. Five patients were involved in the third outbreak. Time-to-clearance with tigecycline was 3. 1 days and all survived. Environmental screening revealed gross contamination on many surfaces and equipment within the unit. Genotypic characteristics demonstrated 2 clonally related strains. Other measures of control included closure of the ICU to new admissions during the second outbreak.

Conclusions:

Two clones of MRAB-C were responsible for the outbreaks and the outbreaks successfully controlled with the use of tigecycline and aggressive infection control strategies.

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Expression of pathogenic Mycobacterium tuberculosis-specific RD1 proteins in non-pathogenic Mycobacterium smegmatis to develop mycobacterial vector-based vaccines against tuberculosis

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Introduction:

  Tuberculosis (TB) is among the top ten causes of death worldwide. With the rapid increase in drug-resistant TB and poor efficacy of BCG vaccines, there is an urgent need to develop new vaccines against TB. BCG vaccines lack 11 genomic regions that are conserved in Mycobacterium tuberculosis. One of these regions is RD1 that contains several open reading frames (ORFs) important for protective immunity. Four of these ORFs, i. e. ORF3, ORF5, ORF6 and ORF7 are major targets for recognition by protective T cell. The aim of our research was to express these RD1 ORFs in the fast-growing Mycobacterium smegmatis in order to develop non-pathogenic mycobacterial-vector based vaccines against TB.

Methods:

  Recombinant shuttle plasmids with cloned orf3, orf5, orf6 and orf7 genes were used to transform M. smegmatis cells using electroporation. The transformed cells were selected by growing on selective media under the pressure of antibiotic hygromycin. Polymerase chain reaction was used to detect the presence of desired inserts in the growing organisms and the identity of amplified DNA was confirmed by size identification using agarose gel electrophoresis. The expression of the proteins in M. smegmatis, as recombinant proteins fused with hemagglutinin, was detected by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) and western immunoblotting using anti-hemagglutinin antibodies.

Results:

  M. smegmatis transformants were obtained with recombinant plasmids containing orf3, orf5, orf6 and orf7 genes. The identity of transformed cells was confirmed by their ability to selectively grow in solid and liquid medium containing hygromycin, followed by positive PCR using gene-specific primers.

Conclusions:

 The expression of the recombinant proteins was successfully detected by SDS-PAGE and Western immunoblotting. The recombinant M. smegmatis strains available through this work are ready for evaluation as candidate vaccines against TB.

Key Words: Tuberculosis; Shuttle plasmids; M. smegmatis;

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Application of molecular methods for identification and characterization of *Streptococcus agalactiae* from environmental isolates.

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Introduction:

 Streptococcus agalactiae has assumed considerable importance in recent years because of the high economic losses in both wild and culture fish. Molecular techniques were used to identify and characterize isolates of S. agalactiae from environmental samples.

Methods:

  Direct PCR amplification method was used to identify Streptococcus isolates. Amplification of genomic DNA for genotyping was performed with a single RAPD primer and Ribotyping was used for species conformation.

Results:

  Total of 66 samples was analyzed from 7 different fish species, isolates from different organs and 5
 sewage samples from two different locations in Kuwait bay were studied. These samples were cultured on BHI agar. Fifty seven positive from 66 fish isolates and 3 positive from 5 sewage isolates were identified as Streptococcus by culture and biochemical tests. Forty three positive from 66 fish isolates and 5 out of 5 positive from sewage isolates were identified as *S. agalactiae* by PCR. 66% of positive fish isolates and 100% of positive sewage isolates were conformed by PCR and 86% of positive fish isolates and 60% positive sewage isolates were conformed by culture method for Streptococcus. Seventeen different samples were used for DNA typing using RAPD on 12 samples from fish and 5 samples from sewage. Relative high similarity was seen between the band pattern of all isolates, 4 (80%) of sewage isolates analyzed by RAPD showed high similarity with fish isolates. Ribotyping was used to conform the species
 of all PCR positive isolates.

Conclusions:

  This study was able to demonstrate that DNA based techniques are invaluable in identifying and
 characterize bacterial associated with disease spread in human, animal and environment

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Trends in susceptibility pattern of Mycobacterium tuberculosis strains isolated from tuberculosis patients over a ten-year period (1996 to 2005) in Kuwait

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Introduction:

Continuous nationwide monitoring of drug-resistance levels is important for proper control/management of tuberculosis (TB). The aim of this study was to determine the prevalence of pulmonary and extrapulmonary TB and trends in drug resistance patterns among all Mycobacterium tuberculosis strains isolated over a ten-year period in Kuwait.

Methods:

Drug susceptibility data for M. tuberculosis isolates recovered from all pulmonary and extrapulmonary TB patients in Kuwait from January 1996 to December 2005 were collected and analyzed. Patients were divided into Kuwaiti nationals and expatriates. Prior treatment status was not recorded.

Results:

From 1996 to 2005, 5399 nonrepetitive culture-positive TB cases (56% from pulmonary sites and 44% from extrapulmonary sites) among 917 (17%) Kuwaiti nationals and 4482 (83%) expatriates were identified. Although the total number of TB cases remained nearly same, downward and upward trends in the rate of M. tuberculosis isolates recovered from pulmonary and extrapulmonary specimens, respectively, were observed. Overall resistance rates were as follows: any drug, 12. 5%; isoniazid, 9. 1%; rifampicin, 1. 1%; ethambutol, 2. 0%; streptomycin, 4. 3% and multidrug resistance (MDR), 0. 9%. The resistance rates over the study period remained nearly same. However, significantly higher resistance rates for rifampicin and MDR among pulmonary versus extrapulmonary cases and for any drug, isoniazid and ethambutol among isolates recovered from expatriate versus Kuwaiti patients were observed.

Conclusions:

The total number of active TB cases from 1996 to 2005 remained nearly same in Kuwait. Moderate and stable single drug resistance (<10%) and low MDR rates (<1%) were found among M. tuberculosis strains. The increasing incidence of extrapulmonary cases also suggests that majority of active TB cases in Kuwait are occurring due to reactivation of previously acquired infection.

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Detection of galactomannan, (1-3)-β-D–Glucan and species-specific DNA in sera samples from suspected patients of invasive aspergillosis

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Introduction:

Invasive aspergillosis (IA), an increasingly common mycosis among immunocompromised patients, is associated with high mortality. Early diagnosis of IA is crucial for improved prognosis. The aim of this study was to detect non-invasive markers (DNA and antigens) in serum samples of clinically suspected patients of IA.

Methods:

Fifty-seven serum samples from 35 patients suspected of Aspergillus infection/colonization and 10 sera of normal subjects were used. The DNA from serum specimens was extracted by using DNA extraction kit. The presence of galactomannan (GM) by ELISA test, DNA specific for Aspergillus fumigatus, A. terreus and A. flavus by nested PCR and (1-3)- β-D –glucan (BDG) by Fungitell colorimetric assay was detected. The cut-off values for GM and BDG were 0. 5ng/ml and 80 pg/ml, respectively. The amplicons of nPCR were detected by agarose gel electrophoresis. The sensitivity and specificity were determined using the results obtained from control sera.

Results:

All control sera were uniformly negative for GM, Aspergillus species-specific DNA and BDG. Among the serum samples from suspected patients, the positivity for GM, Aspergillus DNA and BDG was 35 (61%), 36 (63%) and 23 (40%) of 57 samples, respectively. The samples positive for DNA included A. fumigatus (n=20), A. flavus (n=12) and A. terreus (n=4). Nineteen serum samples were positive for two markers and 11 additional samples for all the three markers. On the basis of positive markers, the diagnosis of IA was made in 4 patients who also yielded Aspergillus by culture of respiratory specimens.

Conclusions:

The data suggest that detection of GM, DNA specific for Aspergillus species and BDG in serum samples may be used for early diagnosis of IA in clinically suspected patients. Furthermore, use of serum samples may be preferable in patients where tissue biopsy can not be obtained. Further studies with serially collected serum samples are suggested.

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Imipenem resistant Pseudomonas aeruginosa - A two year study from Adan

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Introduction:

Imipenem is a carbapenem, a betalactam antibiotic. Introduction of imipenem in 1980s was for treating infections by drug resistant bacteria including P. aeruginosa. However, P. aeruginosa strains resistant to imipenem and other carbapenems emerged worldwide largely due to indiscriminate use of carbapenems. Imipenem resistance may be due to porin mutations, altered penicillin binding proteins, increased efflux with or without production of metallo betalactamases. The data on imipenem resistant P. aeruginosa from Kuwait are scanty and results of recent two years study are presented.

Methods:

The strains represented isolates from inpatients of Adan hospital, Ahmadi area polyclinic patients and from Adan hospital environmental sources. The culture was identified using MicroScan. Strains showing intermediate susceptibility or exhibiting resistance to imipenem in MicroScan were checked routinely by disc diffusion technique as part of our antibiotic susceptibility reporting policy. P. aeruginosa ATCC 27853 was used as a control.

Results:

While 906(77. 44%) of 1170 P. aeruginosa strains were found to be sensitive to imipenem, 252 strains (21. 54%) were imipenem resistant. A few strains 12(1. 02%) showed intermediate susceptibility. Analysis of comparative data suggested an increase from 16. 09% imipenem resistant Ps. aeruginosa strains in 2006 to 25. 14% in 2007.

Conclusions:

The emergence and increase in imipenem resistant P. aeruginosa in this environment is a cause of concern. Further data from other hospitals may give more information on the magnitude of the problem in Kuwait. We presently recommend that imipenem should be judiciously used to contain imipenem resistant strains.

Key Words: Imipenem resistant; Pseudomonas aeruginosa; MicroScan;

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Metallo-betalactamase detection in Pseudomonas aeruginosa strains isolated from hospitalized patients in Kuwait.

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Introduction:
 Pseudomonas aeruginosa is one of the most common nosocomial pathogens and is also notorious for antibiotic resistance. Carbapenems were considered very effective for such infections. However,
 recently resistance to carbapenems is globally reported. Such resistance may be due to porin mutations, efflux pumps and or due to production of metallo betalactamases which hydrolyse carbapenems. The present pilot study is conducted to screen for metallo betalactamase production in Pseudomonas aeruginosa as data from Kuwait are lacking.

Methods:
 Initial screening for imipenem resistance was carried out in MicroScan for twenty non-repetitive strains isolated from inpatients of Adan Hospital. They were confirmed to be imipenem resistant by disc diffusion technique. Metallo betalactamase production was detected by at least four fold reduction in Minimum Inhibitory concentration (MIC) with imipenem-ethylene diamine tetra-acetic acid (EDTA) and by zone enhancement by more than 5mm with EDTA impregnated imipenem and ceftazidime discs. Pseudomonas aeruginosa ATCC 27853 was used as a control strain.

Results:
 Six out of twenty strains (30%) were found to be positive for metallo betalactamase production by both the techniques used. Fourteen (70%) strains showed negative results. The control strain also did not show any reduction in MIC and also showed no zone enhancement.

Conclusions:
  More studies are needed to assess the magnitude of the problem in strains from hospitalized patients in Kuwait. Routine screening by the techniques used is also recommended as the usual antibiotic susceptibility testing does not detect metallo betalactamase mediated drug resistance.

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Construction of a novel vector for precision cleavage of fusion proteins and its application in expression and homogeneous purification of recombinant mitogillin from Aspergillus fumigatus

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Introduction:

  Mitogillin (MIT), a low molecular weight secretory protein of Aspergillus fumigatus is found in urine of immunocompromised patients with invasive aspergillosis (IA). The availability of MIT and anti-MIT antibodies may help in non-invasive early diagnosis of IA. The aim of this study was to clone and express MIT gene as fusion protein with two affinity tags in Escherichia coli and to purify it by precision cleavage of the fusion partner by constructing a novel expression vector.

Methods:

  A novel expression vector, pGES-PH with glutathione S-transferase (GST) and 6xHis affinity tags and cleavage site for PreScission Protease was constructed using pGEX-6P1 as backbone. The two-exonic MIT gene devoid of signal sequence was PCR amplified, cloned in pGES-PH and expressed as GST-MIT-6xHis fusion protein. GST-free, pure MIT was obtained by a combination of GST-Sepharose chromatography, PreScission Protease cleavage of fusion protein and further purification on Ni-NTA agarose. The identity of purified MIT protein was confirmed by N-terminal protein sequencing.

Results:

 The construction of the novel expression vector with the desired features was confirmed by its molecular characterization. The MIT gene was successfully cloned and expressed at high levels as GST-MIT-6xHis fusion protein in E. coli. The purified fusion protein bound to GST-Sepharose matrix was cleaved by highly specific PreScission Protease to release MIT. Further purification on Ni-NTA agarose yielded >99% pure MIT. The amino acid sequence of N-terminal 12 amino acid residues matched completely with MIT protein of A. fumigatus.

Conclusions:

 A novel expression vector with the desired features was successfully constructed. The utility of newly constructed vector was demonstrated by efficient expression and purification of recombinant MIT protein of A. fumigatus which could now be used as an antigen probe and also to generate anti-MIT antibody probes for the non-invasive diagnosis of IA.

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The immunodominant sequence of PPE68 encoded by M. tuberculosis-specific RD1 DNA segment is completely identical between pathogenic Mycobacterium tuberculosis and M. bovis BCG vaccines

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Introduction:
The region of difference (RD)1 of Mycobacterium tuberculosis can potentially encode 14 M. tuberculosis-specific open reading frames (ORFs). However, it has previously been shown that one of the major antigenic proteins of RD1, i. e. PPE68, was recognized equally well by peripheral blood mononucelar cells (PBMC) from TB patients and M. bovis BCG vaccinated healthy subjects. The aim of this study was to confirm the major recognition of PPE68 by Th-1 cells and identify the immunodominant epitope.

Methods:
Antigen-induced T-cell lines were established using peptides of RD1 and PPE68 and PBMC from M. bovis BCG vaccinated healthy subjects. The T-cell lines were tested in Th1-cell assays in response to peptide pools of RD1 and ORF proteins. Furthermore, the peptides of PPE68 were tested individually in Th1-cell assays with PBMC to identify the immunodominant peptide and the sequence was searched using the appropriate data base.

Results:
All of the predicted ORF proteins in RD1 were recognized by T-cell lines, but the most recognized antigen was PPE68 and its peptide 121-145 VLTATNFFGINTIPIALTEMDYFIR was immunodominant. The search with this peptide seqnuence in data base showed that a 14 aa stretch, i. e. aa 124-137 (ATNFFGINTIPIAL) was completely identical in several PPE-family proteins of M. tuberculosis and M. bovis BCG. Testing of the peptide aa 124-137 with PBMC from a group of HLA-heterogeneous donors showed that this peptide was presented promiscuously to Th-1 cells and the magnitude and frequency of recognition was comparable to the full-length immunodominant peptide aa 121-145.

Conclusions:
The peptide ATNFFGINTIPIAL is the promiscuous and immunodominant epitope region of PPE68 and is present both in M. tuberculosis and M. bovis BCG vaccines. Because of its strong Th1 cell reactivity, the peptide ATNFFGINTIPIAL could be useful as a new peptide-based vaccine against TB.

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Mycobacterium tuberculosis-specific region of difference 1 genes encode sero-reactive peptides recognized by antibodies in tuberculosis patients' sera

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Introduction:

  The antigens ESXA and ESXB encoded by Mycobacterium tuberculosis-specific region of difference (RD)1 genes have previously been shown as major antigens useful for the diagnosis of tuberculosis (TB) in cell mediated immunity (CMI) assays. However, CMI assays are cumbersome, time-consuming and costly. On the other hand, serological assays based on antibody detection are cheap, less demanding and easy to perform. The aim of this work was to identify the seroreactive peptides encoded by 12 RD1 genes, which could be exploited later to develop serological assays for the diagnosis of TB.

Methods:

  A total of 220 peptides covering the complete sequence of 12 proteins of RD1, i. e. Rv3871 (39 peptides), PE35 (6 peptides), ORF4 (9 peptides), PPE68 (24 peptides), ESXB (6 peptides), ESXA (6 peptides), ORF8 (9 peptides), Rv3876 (44 peptides), Rv3877 (36 peptides), Rv3878 (18 peptides), ORF14 (17 peptides) and ORF15 (6 peptides), were designed and synthesized. The wells of 96-well ELISA plates were coated with individual peptides at a concentration of 10 micro g/ml. A pool of sera obtained from 10 TB patients was tested with individual peptides for antibody reactivity in ELISA using standard procedure for antibody detection. The promising peptides were further tested with another batch of pooled serum from 14 TB patients to confirm their seroreactivity.

Results:

  The primary screening of a batch of pooled serum from 10 TB patients showed that 44 peptides had significant ELISA reactivity. The subsequent experiments with the same batch of serum showed that only 12 of 44 peptides showed antigen-specific antibody reactivity. Retesting of these peptides with another batch of pooled serum confirmed seroreactivity of 10 peptides encoded by four different ORFs. T

Conclusions:

 hese results show that several RD1 region genes encode seroreactive peptides, which may be evaluated for diagnostic potential.

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Septicemia in neonatal intensive care unit: Etiology and antimicrobial susceptibility

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Introduction:

   Neonatal septicemia is a common cause of morbidity and mortality especially in intensive care units (NICU) as these neonates are compromized hosts. Prematurity, low birth weight, early rupture of membranes and prolonged labour are major factors predispoing to infections. Early culture and susceptibility testing of the causative agents is an integral part of management. We present here recent data on septicemia in NICU in Adan hospital.

Methods:

   3177 blood culture samples were received from NICU of Adan hospital during 2006 and 2007. The culture bottles were incubated in BactAlert / Bactech for 7 / 5 days respectively as per protocol. The positive cultures were inoculated on standard culture media and identification and susceptibility testing was carried out in MicroScan and/by conventional methods. However, no antimicrobial susceptibility for Candida spp. was carried out.

Results:

   Out of 3177 blood cultures, 449 (14. 13%) were culture positive. Of the positive cultures, S. epidermidis (43. 88%) was the commonest isolate followed by K. pneumoniae (9. 58%), E. coli (8. 69%), Candida spp. (6. 24%), A. baumanii/haem. (5. 57%) and Enterococcus spp. (4. 45%). In addition, a few isolates included S. agalactiae, S. viridans and other members of enterobacteriaceae. While susceptibility varied for different antimicrobial agents for different bacterial isolates, no vancomycin resistant gram positive organisms were encountered in the present study. Another distinct observation was sudden appearance of A. baumanii/haem. in 2007 as we did not report even a single such isolate form blood culture from NICU in 2006.

Conclusions:

   S. epidermidis was found to be the commonest isolate causing septicemia in NICU. The study of septicemia in NICU is useful in framing antibiotic guidelines.

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Termination of an outbreak caused by community-acquired methicillin-resistant Staphylococcus aureus in neonatal intensive care and special care baby units

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Introduction:

Although community-acquired methcillin-resistant Staphylococcus aureus (CAMRSA) has been isolated previously in Kuwait hospitals, it had not been reported to cause hospital outbreaks. This paper describes an outbreak of CAMRSA in a neonatal intensive care unit (NICU) and a special care baby unit (SCBU) and the measures adopted to terminate it.

Methods:

From 10 April to 30 April 2007, 15 neonates were infected or colonized with MRSA in a 16-bed NICU and 36 bed SCBU of a Kuwaiti teaching hospital. Surveillance cultures were obtained from all babies twice weekly and on all new admissions. Colonized babies were isolated, placed on contact precautions and decolonized. Infected patients were treated appropriately. In total, 137 healthcare workers (HCWs) were screened and those found to be carriers were decolonized. All MRSA isolates were typed using antibiogram, coagulase gene polymorphism (coa-RFLP), staphylococcal cassette chromosome mec (SCCmec) typing and pulsed-field gel electrophoresis (PFGE). A multifaceted infection control approach was implemented to terminate the outbreak.

Results:

Twenty seven MRSA isolates were obtained from 15 neonates, two nurses, two doctors and a cleaner. All 22 isolates obtained from the 15 neonates had identical antibiogram, coagulase RFLP, SCCmec and PFGE patterns and were different from those obtained from HCWs. Isolates from the neonates were resistant to gentamicin, kanamycin and fusidic acid. They belonged to coagulase RFLP 104, SCCmec type V and PFGE type A. The carriage of SCCmec type V genotype identified the clone as CAMRSA.

Conclusions:

The results showed that a CAMRSA clone belonging to SCCmec type V colonized or infected all 15 neonates. However, its source was not identified. Aggressive infection control measures were necessary to terminate the outbreak.

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Dissemination of Potentially Pathogenic Bacteria into the Environment

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Introduction:

 Under certain conditions, untreated wastewater is released into the sea discharging pathogenic microorganisms into the marine environment exposing receivers to different types of infectious diseases. Thus, it is very important to legislate rules and penalties to avoid and prevent the dumping of such hazardous bacteria into the environment. The aim of the present study was to examine seawater samples collected from Kuwait bay for the presence of Gram negative bacteria originating from untreated wastewater.

Methods:

 Seawater samples were collected aseptically and transported directly to the lab for analyses. Gram negative bacteria were isolated on EMB and MacConkey agar and identified by 16S sequencing. Antibiotic susiptibility testing (AST) was determined according to the NCCLS protocol. The diversity of isolated bacteria was examined by restriction fragment length polymorphism (RFLP) analysis of 16S rDNA sequences. In addition, the survival of isolated bacteria in seawater was investigated by monitoring their growth (absorbance at 600 nm) and activity (amount of carbon dioxide evolution).

Results:

 Total of 121bacteria were isolated and identified. Phylogenetic analyses indicated the dominance of three ---proteobacteria phylotypes: Enterobacter, Pantoea and Klebseilla. Furthermore, 16S-RFLP analysis showed the high diversity of the three isolated genera. All isolated bacteria exhibited resistance to penicillin and demonstrated the potential to survive in seawater for 750 hours.

Conclusions:

 Analysis of seawater samples indicated the presence of bacteria originating from human activities such as the dumping of untreated wastewater into the sea. This study exemplified the importance of monitoring seawater that may represent latent source of hazardous and highly diverse bacterial communities.

Key Words: Pathogenic; RFLP; PCR;

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Occurrence of Pseudomonas aeruginosa in Kuwaiti Environment

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Introduction:
Deliberate and accidental releases of opportunistic pathogens such as Pseudomonas aeruginosa into the environment increase the likelihood of spreading infectious diseases. Also, P. aeruginosa is responsible for nosocomial infections and usually harbour several antibiotic resistance genes. Therefore, it is important to elucidate the linkage between the environmental and the medical strains as a step towards the containment of such pathogenic bacteria.

Methods:
In the present study total of 76 strains of P. aeruginosa were characterized (54 strains were isolated from soil samples collected from crude oil contaminated site located north of Kuwait and 22 strains were isolated from medical samples). All strains were identified using VITEK 2 system (bioMérieux) and 16S rDNA sequencing. Bacterial antibiotic susceptibility testing (AST) was determined. Furthermore, the similarity between the strains was investigated using multilocus sequence typing (MLST) and restriction fragment length polymorphism (RFLP) of 16S PCR products. The ability of bacteria to utilize crude oil was determined by respirometry.

Results:
Whereas the phenotypic characterization such as the biochemical tests using VITEK 2 system (bioMérieux) and AST showed the high similarity between the medical and the environmental strains, the molecular analyses based on MLST and RFLP revealed the heterogeneity of isolated P. aeruginosa as demonstrated by the presence of different clusters or phylotypes. MLST fingerprints showed that the medical and the environmental strains belong to different phylotypes indicating the week linkage between the two groups of bacteria tested. However, 16S-RFLP fingerprints showed that 88% of the medical strains and 98% of the environmental strains were closely related. In addition, results demonstrated that environmental strains are better adapted to crude oil contaminated sites.

Conclusions:
The high virulence of P. aeruginosa warrant more investigations to elucidate the relation between the environmental and the medical strains in order to reveal the points of release of pathogenic bacteria into the environment. The environmental strains may be better adapted to stress conditions such as crude oil pollution but may represent hidden reservoirs for pathogenic traits that may disseminate to other bacteria in the environment.

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Varying prevalence of embB codon 306 mutations in ethambutol-resistant clinical Mycobacterium tuberculosis isolates from Beirut and Dubai

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Introduction:

Ethmbutol (EMB) is a bactericidal, first-line drug for the treatment of tuberculosis (TB). EMB-resistant M. tuberculosis strains contain mutations in several genes, notably embA, embB or embC encoding arabinosyltransferases. However, mutations at embB codon 306 (embB306) are more common, accounting for nearly 60% of resistance conferring mutations in clinical EMB-resistant M. tuberculosis strains isolated from TB patients in Western Europe and North America. This study detected embB306 mutations in 14 and 17 EMB-resistant and 14 and 15 EMB-susceptible strains of M. tuberculosis isolated from TB patients in Beirut, Lebanon and Dubai, UAE, respectively.

Methods:

The phenotypic drug susceptibility testing of M. tuberculosis isolates to EMB was determined by BACTEC 460 TB system. The presence of wild-type (ATG) or mutant embB306 was detected PCR amplification of the embB306 DNA region from M. tuberculosis isolates followed by restriction digestion of amplified fragments with Nla III to generate restriction fragment length polymorphism (PCR-RFLP). The results of PCR-RFLP analyses were confirmed by DNA sequencing.

Results:

Ten of 14 (71%) EMB-resistant M. tuberculosis strains from Beirut but only three of 17 (18%) EMB-resistant M. tuberculosis isolates from Dubai contained a mutated embB306. The mutation ATG306GTG (M306V) was the most common mutation at embB306 in EMB-resistant strains. None of the EMB-susceptible strains from Beirut or Dubai contained a mutated embB306.

Conclusions:

The prevalence of embB306 mutations in EMB-resistant M. tuberculosis strains in Beirut and Dubai varied considerably. This is most likely attributable to the ethnic origin of TB patients since all isolates in Beirut were recovered from Middle Eastern patients while those from Dubai were mostly from South Asian patients.

Microbiology and Immunology
Category: Graduate (Basic Sciences)

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Antibody Responses to Antigenic Peptides in Sera of Immunized Rabbits, Mice, and Sera from TB patients and Healthy Subjects

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Introduction:

To identify the antigenic peptides of five immunodominant proteins of Mycobacterium tuberculosis in antibody assays using sera from actively immunized rabbits and mice and sera from pulmonary TB patients and M. bovis BCG-healthy subjects

Methods:

The pure proteins, peptide mixtures representing each protein and individual peptides of ORF3, ORF5, ORF6, ORF7 and RD903 were tested for antibody reactivities in ELISA assays using sera from rabbits immunized with purified recombinant proteins and mice immunized with recombinant DNA plasmids pUMVC6 and pUMVC7. In addition, sera from pulmonary TB patients and healthy subjects were also tested for antibody reactivities in the same assays. The optical density (OD) was measured at 405 nm and the ratios of $OD_{experimental}$ / $OD_{control}$ (E/C) >2. 0 were considered positive, where
$OD_{experimental}$ = OD405 in presence of antigen or peptide plus serum and
$OD_{control}$ = OD405 in presence of serum alone.

Results:

Sera from rabbits showed antigen-specific antibody reactivities with all of the immunizing proteins and their peptide mixtures. Sera with individual peptides showed positive ELISA reactivity with ORF3 peptides P1, P2, P5 and P6, ORF5 peptides P9, P11, P14, P22, P23, P24, all peptides of ORF6, ORF7 and RD903 peptides P1, P2, P3, P5, P6. Antibodies to all proteins were detected in sera of mice immunized with the recombinant pUMVC6 and/or pUMVC7 DNA. With respect of peptides, only P6 of ORF3 and P18, P24 of ORF5 showed antibody reactivity with sera of mice. The peptides of ORF3, ORF6 and ORF7 did not react with antibodies in human sera, whereas peptides P11, P14, P22, P23, P24 of ORF5 and peptides P4, P5, P6 of RD903 showed positive reactivity with sera from TB patients and healthy subjects.

Conclusions:

The antibody responses to various immunodominant proteins of M. tuberculosis are heterogeneous with respect to the peptides recognized by antigen-specific antibodies raised in the tested mammalian species in response to active immunization or natural infection.

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Characterization and Immunogenicity of RD1 Encoded Antigens of Mycobacterium tuberculosis

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Introduction:

There is an urgent need to identify and characterize new Mycobacterium tuberculosis antigens useful for specific diagnosis and developing safer vaccines against TB. This study aimed to investigate whether the major/moderate antigens of M. tuberculosis encoded by RD1 genes, i. e. ORF3, ORF5, ORF6, ORF7 and RD903 could be useful in the specific diagnosis and/or developing new vaccines against TB.

Methods:

 DNA corresponding to all genes were cloned in plasmid vectors and expressed in Escherichia coli. The expressed proteins were purified and used to generate antigen-specific antibodies in rabbits and reverse transcriptase-PCR were used to detect gene expression in mycobacteria at protein and mRNA levels, respectively. The diagnostic potential of the proteins was investigated by studying delayed type hypersensitivity (DTH) responses in guinea-pigs infected with M. tuberculosis, BCG, M. avium and M. vaccae. Constructed DNA vaccines (pUMVC6 and pUMVC7) based on these genes were evaluated for their effectiveness in mice by studying Th1 and Th2 cytokine responses.

Results:

RT-PCR and antigen-specific antibodies showed that mRNAs and proteins corresponding to all ORFs were expressed in M. tuberculosis, however only RD903 was expressed in BCG and none were expressed in M. avium and M. vaccae. In guinea-pigs, DTH responses to all proteins were observed in animals immunized with M. tuberculosis, to RD903 only in BCG-immunized animals and to none of the proteins in animals immunized with M. avium and M. vaccae. Immunization of mice with DNA vaccine constructs of all ORFs sensitized spleen cells to proliferate in response to in vitro stimulation with the purified proteins and cocktails of overlapping synthetic peptides. Spleen cells secreted the protective Th1 cytokine IFN-γ but did not secrete non-protective/pathological Th2 cytokines IL-5/IL-10 in response to the immunizing antigens.

Conclusions:

This study confirms in vitro and in vivo expression of RD1 ORF3, ORF5, ORF6, and ORF7, and RD903 in M. tuberculosis and suggests their potential as reagents for specific diagnosis and/or developing safer vaccines against TB.

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Colonization and Subsequent Development of Methicillin-Resistant Staphylococcus aureus (MRSA) Infection in Intensive Care Unit Patients

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Introduction:

 Asymptomatic colonization with MRSA has been recognized as an important risk factor for subsequent MRSA infection. The objective of this study was to determine the impact of MRSA colonization on the occurrence of subsequent infection among intensive care unit (ICU) patients.

Methods:

  All patients admitted to medical/surgical ICU from January 2004 through October 2007 were screened for MRSA colonization by obtaining samples from nares, axilla and groin at the time of admission and weekly thereafter. In addition specimens from other sites such as endotracheal aspirate, blood, wound/pus etc. were also collected for culture whenever clinically indicated. Isolation of MRSA from a site showing evidence of infection or no infection was recorded as community-or hospital-acquired infection and colonization, respectively.

Results:

  During the study period surveillance specimens were obtained from 2429 pts. & 45 (1. 9 %) were found to be positive for MRSA. Anterior nares were found to be the commonest site for colonization in both, community (40 %) and hospital (44 %) acquired MRSA. Of 45 pts. who were MRSA positive 10 developed infection (OR, 0. 454; 95% CI, 0. 101-2. 046) & among 25 pts who were negative for MRSA screening at admission 8 developed subsequent infection (OR, 0. 135; 95% CI, 0. 015-1. 212) during their stay in the ICU. Coagulase-typing of all MRSA isolates revealed that 92% patients acquired type 36 MRSA during their stay in the ICU whereas 95% of pts. were colonized with MRSA other than type 36 at the time of admission to the ICU. Only 47% of coagulase type 36 correlated with PFGE 1 pattern.

Conclusions:

 Since only 17. 8% of pts. colonized with MRSA developed subsequent infection it does not appear to be a major problem in our ICU. Coagulase type 36 & PFGE 1 pattern was observed more often among MRSA acquired by patients during their stay in the ICU.

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Major outer membrane proteins (MOMPs) from many species of Campylobacter cross-react with cholera toxin

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Introduction:
 Campylobacter species are major foodborne diarrhoeal pathogens. It was believed that a cholera toxin-like toxin (CTLT) produced by the major species, C. jejuni contributes to watery diarrhoea. We showed that C. jejuni strains do not produce a functional CTLT, but the 53-kDa MOMP cross-reacts with cholera toxin (CT) antibody in ELISA and immunoblot. This would have led to the erroneous conclusion of CTLT production by C. jejuni strains. We investigated whether other species of Campylobacter behaved in a manner similar to C. jejuni.

Methods:
 Two strains each of C. jejuni, C. coli, C. lari, C. foetus, C. hyointestinalis, and C. upsaliensis were studied. CTLT production was determined in Casamino Acids yeast extract broth shake culture in a microaerophilic condition at 42oC and testing the filtrates on Chinese hamster ovary (CHO) cell monolayer. Elongation of ¡Ý50% of monolayer at a ¡Ý1:4 filtrate dilution was considered CTLT-positive. Cross-reactivity of crude MOMP and Sarkosyl-purified MOMP (SMOMP) with rabbit CT antibody and normal rabbit serum was determined by immunoblot.

Results:
 Filtrates from all species were negative for CTLT production in CHO cell assay. Crude MOMPs from all species produced common bands of 53-kDa and 79- kDa on immunoblot on reaction with CT antibody. There were additional bands in C. foetus and C. upsaliensis. Immunoblot with normal rabbit serum showed the 79-kDa band from all species and two higher molecular weight bands from C. upsaliensis. When SMOMP was reacted with CT antibody, all species showed only the 53-kDa MOMP, with C. foetus showing additional bands excluding the 79-kDa band. SMOMP from any species did not react with normal rabbit serum.

Conclusions:
 Like C. jejuni, other Campylobacter species did not produce a functional CTLT, and their MOMPs reacted with CT antibody. This might lead to the erroneous conclusion of their CTLT production. Immunoprophylaxis with CT may be explored against campylobacteriosis

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Antimicrobial resistance surveillance among clinical isolates of anaerobic bacteria in Kuwait

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Introduction:

Anaerobes are exotic and important human pathogens especially in those with impaired body defense systems. In this surveillance study, we investigated the trend in the antibiotic resistance pattern of anaerobes submitted to the Anaerobe Reference Laboratory over a period of 6 years, 2002-2007.

Methods:

Isolates sent from all the government hospitals in Kuwait for identification and susceptibility testing were studied. The identification were carried out using conventional, API 20A and GLC methods. Susceptibility testing was carried out by estimating the minimum inhibitory concentrations (MIC) using E test method. Metronidazole-resistant strains were investigated for carriage of nim genes by PCR technique and the PCR product subjected to PCR-RFLP analysis.

Results:

During this period, 2619 isolates were received, out of which 803 (30. 7%) were Bacteroides fragilis, 667 (25. 5%) Bacteroides spp. , 543 (20. 7%) Prevotella spp. , 24 (0. 9%) Porphyromonas spp. , 496 (18. 9%) Peptostreptococcus spp. and 22 (0. 8%) Clostridium spp. B. fragilis and the Bacteroides spp. were the most resistant isolates. Antibiotics with the poorest activities were clindamycin with resistance rates of 39. 3%, 49. 4%, 28% and 19. 6% against B. fragilis, Bacteroides spp. , Prevotella and Clostridium spp. , respectively, followed by piperacillin. The overall resistant rate of B. fragilis to metronidazole was 1. 4%. Resistance to the carbapenems was seen mostly in B. fragilis with rates as high as 3. 9% and 6. 1% for imipenem and meropenem, respectively. The highest level of resistance was noted in year 2005 and lowest in 2007. Seven metronidazole-resistant Bacteroides spp. , carried nimA and nimE genes.

Conclusions:

Metronidazole resistance among the clinical isolates remains low in spite of the sporadic isolation of nim genes-carrying Bacteroides spp encountered in 2005. Resistance to clindamycin, piperacillin and, to a lesser extent, amoxicillin-clavulanic acid remains unacceptably high.

Microbiology and Immunology
Category: Graduate (Basic Sciences)

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Heterogeneous Adenovirus Serotypes Cause Conjunctivitis in Kuwait

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Introduction:

Different adenovirus (AdV) serotypes cause variable forms of conjunctivitis. Fifty-two human AdV were identified based on neutralization assay. A neutralization epitope has been located on the hypervariable region-7 (HVR-7) of the hexon protein. Hence, HVR-7 has been used as target for typing of AdV by sequencing. Despite the significance of AdV eye infections, they have never been investigated in Kuwait. Here we used PCR-sequencing of HVR-7 to type AdV from conjunctivitis patients, and subsequently identify the amino acids of the neutralization epitope within the HVR-7.

Methods:

A total of 163 eye swabs were collected from 131 patients with conjunctivitis. Samples were screened for AdV by PCR using primers specific for the hexon gene conserved region. DNA form AdV positive samples was amplified by PCR using HVR-7 specific primers. The HVR-7 was sequenced and analyzed by Beckman Coulter CEQ 8000. The amino acid epitope sequence was deduced from nucleotide sequences within the HVR-7, and both nucleotide and amino acid sequences were compared to sequences available at the GenBank.

Results:

Sixty eight samples (41. 7%) were positive for AdV DNA by PCR. Out of 52 randomly selected samples investigated by sequencing, serotypes 7, 3, 11, 8, 37, 4 and 5 were identified in 21, 11, 10, 4, 3, 2 and 1 sample, respectively. The HVR-7 of local isolates varied in serotypes 7, 11, and 3, while showed 100% homology among serotypes 4, 37 and 8. A case of AdV transmission was confirmed based on identical sequences of isolates from first degree relatives. HVR-7 neutralizing epitope was identical in local isolates of serotypes 3, 4, 11, 8 and 37, while showed distinctive conservative and non-conservative variations among serotype 7 isolates.

Conclusions:

This study has identified, for the first time in Kuwait, a heterogeneous population of human AdV serotypes causing eye disease. Serotype 7 was the most dominant AdV causing conjunctivitis cases in Kuwait.

Key Words: Adenovirus; Conjunctivitis; DNA sequencing;

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High Prevalence of Antibacterial Resistance and Virulence Determinants in Staphylococcus aureus obtained from Food Handlers in Kuwait Restaurants.

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Introduction:

Food handlers are important sources of bacteria causing food poisoning. It is important to identify and treat carriers to prevent food poisoning. The purpose of this study was to determine the antibacterial susceptibility patterns and the carriage of genes for virulence factors in S. aureus obtained from food handlers in Kuwait City restaurants.

Methods:

Two hundred S. aureus isolates were isolated from stool, nasal and hand swabs of food handlers in different restaurants in Kuwait City. Susceptibility to antibacterial agents was done by disk diffusion and Etest. PCR was used to detect genes for accessory gene regulator (agr); capsular polysaccharide serotypes (cap) 5 and 8, staphylococcal enterotoxins (SE), toxic shock syndrome toxin-1 (TSST-1) and Panton-Valentine leukocidin (PVL).

Results:

A total of 188 (94. 0%) isolates were resistant to at least one antibacterial agent and 138 (69. 0%) were resistant to two or more antibacterial agents. Majority (78. 5%) of them were resistant to penicillin, 63. 5% were resistant to cadmium; 19. 0%, 9. 5% and 2. 5% were resistant to tetracycline, trimethoprim and kanamycin and streptomycin respectively. Fifty-seven and 38. 0 percent of them belonged to cap8 and cap5 respectively. Fifty, 20 and 23. 5 percent of them belonged to agr types I, II and III respectively. Genes for SE, TSST-1 and PVL were detected in 70. 5, 4. 0 and 9. 0 percent respectively. Genes for SEI, SEG, SEC, SEH, SEB, SEA, SED and SEE were present in 36. 5, 27. 0, 24. 5, 23. 0, 12. 5, 12. 0, 1. 5 and 1. 5 percent respectively. Most (45. 5%) of them contained genes for two to four SEs. Genes for PVL were detected in isolates from different sources, and different genetic background but none carried gene for TSST-1.

Conclusions:

The study demonstrated a wide variation in susceptibility to antibacterial agents and the distribution of virulence determinants, including PVL. It justifies the need for regular screening of food handlers to detect and treat carriers and protect restaurant customers from food poisoning.

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Neonatal bacteremia: bacteriological profile and antimicrobial susceptibility pattern

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Introduction:

Neonatal bacteremia remains a significant cause of morbidity and mortality in the new born. This study was carried out to determine the bacteriological profile, the antimicrobial susceptibility of the blood isolates and the change in the trends over the study period.

Methods:

All blood isolates from cases of neonatal bacteremia (single isolate per episode) were taken over a period of 5 years (January 2002- December 2006) at the Maternity hospital, Kuwait. Routine identification and susceptibility testing were performed mainly by using VITEK II system. E test was used for some isolates.

Results:

There were 1551 episode of bacteremia during the study period. The most common isolated organism was coagulase-negative staphylococcus (45%). Gram-negative organisms were isolated in 464 (30%) of cases and the most common isolate was Klebseilla pneumoniae (37. 1%). Other Gram-negative isolates were Escherichia coli (14. 2%), Enterobacter spp (14%) and Acinetobacter spp (15. 3%). All Gram-positive cocci were susceptible to vancomycin and most Gram-positive cocci other than staphylococci were susceptible to ampicillin. No methicillin- resistant Staphylococcus aureus was isolated. Most of the Gram-negative organisms were sensitive to amikacin (95. 7%), ciprofloxacin (95. 3%), tazobactam-piperacillin (95. 3) and for meropenem (99. 1%) while they were more resistant to cefotaxime (46. 9%) and ceftazidime (34. 9%) and only 10. 9% were resistant to gentamicin.

Conclusions:

The bacteriological profile of organisms causing neonatal bacteremia is comparable to profiles from other reports in literature. Over the study period we observed a trend of increasing resistance to commonly used antibiotics among Gram-negative isolates.

Key Words: Neonatal Bacteremia; Bacterial etiology; Resistance patteren;

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Inhibition of replication of different enterovirus types in stably transfected Vero cells expressing human MxA protein

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Introduction:

Enteroviruses (EVs) are highly prevalent in patients with aseptic meningitis, febrile illness or cardiac diseases. In Kuwait, genotyping of detected viral sequences in clinical samples showed the presence of different types of EVs. MxA protein, an intracellular protein induced by type I interferons, has been shown to inhibit the replication of one type of EV, coxsackievirus B4. The main aim of this study was to investigate the susceptibility of different types of EVs commonly found in Kuwait to MxA protein expressed in stably transfected cell line.

Methods:

An eukaryotic expression vector containing the full-length coding sequence of human MxA gene has been designed to allow high level constitutive expression of MxA protein. Vero cells have been transfected with the expression vector by using Lipofectamine. Transfected cells have been selected in culture medium containing Geneticin. Resistant clones have been examined for MxA expression by detection of MxA protein by indirect immunofluorescence. MxA-transfected and mock-transfected Vero cells have been incubated in the presence of different types of EV. The EV-induced cytopathic effects (CPE), the expression of EV VP1 protein and the progeny virus titers in infected cells have been assessed at various time points.

Results:

Stably transfected Vero cells expressed MxA protein in more than 98% of cells. Compared with control cells, the replication of all types of tested EVs was dramatically reduced in MxA-transfected cells as evidenced by the reduction of CPE, VP1 expression and progeny virus titers. However the susceptibility of different EV types to the antiviral activity of MxA was not the same, with coxsackievirus B5 being the most susceptible serotype.

Conclusions:

Our results clearly indicate that the antiviral activity of MxA protein extends to different types of enteroviruses, but, at the same infectious viral dose, this antiviral activity is not equally exerted.

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First detection of human astroviruses in raw sewage samples in Baranya County, Hungary

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Introduction:

Enteric viruses, including human astroviruses (HAstVs) are excreted in high titer in human feces resulting in their accumulation in community sewage. Viruses in sewage can contaminate drinking water resources, recreational and natural waters, potentially causing a high public health risk. One of the most resistant enteric viruses is the HAstV. Due to the mild form of infection, its impact is certainly underestimated. Because sewage plants collect and treat community and industrial wastewater, sewage samples may be used as good indicators for numerous viruses, including HAstVs present in the community.

Methods:

To obtain data on whether HAstVs are shed in the environment, 35 raw sewage samples from 22 sewage plants in different regions of Baranya County, Hungary were tested for HAstVs using the polyethylene glycol method for concentration and the guanidinium thiocyanate-silica procedure for extraction of viral RNA. RT-PCR with HAstV-specific primer pairs Mon2/PRBEG and Mon2/JWT4 was used for amplification and the specificity of amplicons was confirmed by sequence analysis.

Results:

Among the 35 raw sewage samples, 15 (43%) contained HAstV and by sequence analysis, 10 HAstV genotype 1 and 1 HAstV genotype 2 were identified. HAstV strains detected in sewage samples clustered with the corresponding Hungarian strains found in clinical specimens, but were slightly different from them. Thus far we have not detected HAstV genotype 2 in clinical samples.

Conclusions:

Our results suggest that HAstVs are more common cause of gastrointestinal infections than it can be expected from clinical diagnostic practice, and most of these infections are probably mild or asymptomatic. According to our knowledge, this was the first investigation where a molecular method was used to detect HAstVs in sewage in Hungary.

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Toxoplasmosis in the Arabian Gulf: nuisance or a significant disease ?

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Introduction:

Toxoplasmosis is a zoonotic disease of man world-wide. In the Middle East, the dietary habits, close contact with domestic felines, kidney transplants and HIV/AIDS results in asymptomatic to acute infections. However, toxoplasmosis appears to be unappreciated, unrecognized or underdiagnosed for several reasons which we elaborate. We discuss a variety of clinical presentations in patients infected with Toxoplasma gondii: the outcome in a pregnant female who had significant IgG and IgM antibody titres from the first trimester; an adult male who presented with swollen cervical lymph nodes; a female who had a "lump on the shoulder" and a female child who had both ocular lesions and zoonotic onchocerciasis.

Methods:

To assess the significance of the disease, we report the presence of antibodies in normals and various groups of patients diagnosed with toxoplasmosis, as measured by the "VIDAS Toxo IgG II" and "Toxo IgM".

Results:

In 150 sera from normals of all age-groups, significant IgG antibody was present in over 25 %. A total of 196 sera were submitted for a diagnosis of toxoplasmosis; 82 were from pregnant females of which 45 (55%) had IgG and 4 (4. 9%) had IgM antibodies; of 93 with a diagnosis of"recurrent abortion" , 26 (30%) had a significant IgG titre but none had IgM antibodies. Of eight sera from an eye clinic one patient had a significant IgG titre. Seventy four pregnant females, of which 34 (46%) had significant IgG titres, were followed up over three trimesters and one (1. 4%) sero-converted over the period. The clinical outcome in kidney transplant patients and those with HIV/AIDS diagnosed with toxoplasmosis is discussed.

Conclusions:

T. gondii is being transmitted on a wide scale but diagnosis, treatment and prevention are problematic. We developed a question and answer brochure to ensure some appreciation of toxoplasmosis thus alleviating concern amongst pregnant mothers in Kuwait.

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Developing and Optimizing a PCR-Based Method for Screening Cervical Samples for the Presence of Human Papilomavirus

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Introduction:

Human Papilomavirus(HPV) is a small DNA virus, strongly associated with the development of cervical cancer. More than 100 different genotypes of HPV were detected by molecular techniques.

In this study a Real-Time Polymerase Chain Reaction(PCR) Method was optimized to determine the presence of HPV in cervical scrapes taken from women attending Obstetrics and Gynecology (Obs&Gyn) Clinics.

Methods:

Cervical scrapes were collected from women attending Obs& Gyn Clinic for routine check-up. All required data was collected from the patient. Cervical scrapes were taken by using cervex brush and collected in 20 ml ThinPrepVial. Cytology Examination:Cervical cells were deposited onto glass slides using ThinPrep 2000(Cytyc, USA) and stained by Papanicolaou staining method. Cervical slides were screened by cytotechnologist and reported using The Bethesda System 2001. The remaining of the cellular sample was used for PCR. General Primers:The universal (consensus) GP5+/6+ primers were used. DNA detection:Genomic DNA was extracted from cervical scrapes using Nucleospin Kit, (MN, Germany). Negative & positive controls were included in each run. Real-Time PCR was performed using Applied BioSystems machine (ABI Prism 7000).

Results:

985 cervical samples were analysed. Cytological abnormality was reported in 4. 1% of the samples. HPV was detected in 73% of the samples with abnormal cytology report and in 10% of samples with normal cytology report.

Conclusions:

This study shows that Real-Time PCR is very sensitive and effective method for the detection of HPV in cervical samples. It also shows that the majority of samples with abnormal cytology reports were infected with HPV, as described previously. This study suggests that further characterization of HPV into High-risk and Low-risk genotypes will determine the current situation of HPV infection in women in Kuwait.

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Evaluation of procalcitonin, a novel marker of sepsis, in a tertiary care hospital in Kuwait

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Introduction:

 Procalcitonin (PCT), a prohormone of calcitonin, is one of the earliest markers of sepsis. Evaluation
 of PCT in the workout of sepsis bundle was done at Ibn-Sina hospital. The main objective was to
 evaluate the sensitivity and specificity of PCT in the diagnosis of sepsis and compare it with
other routine markers such as fever and leukocyte count. The value of PCT as a prognostic
indicator was also evaluated.

Methods:

 All patients with clinical diagnosis of sepsis from January to March 2007 were included in the
survey. Patients with blood culture positive and elevated PCT value were analyzed. PCT level of
0. 5ng/ml and above was considered as a cut off point indicating sepsis. The sensitivity, specificity
and positive and negative predictive values of PCT in relation to blood culture positivity and
clinical sepsis were calculated. Follow up of the patients and their PCT level were done.

Results:

 Out of a total of 338 blood cultures, 109 were positive. Out of 502 PCT results, 256 were more
than 0. 5 ng/ml. In comparison with blood culture results, the sensitivity, specificity and positive
and negative predictive values of PCT were 72. 4%, 81%, 71. 8% and 81. 5%, respectively. PCT
had better correlation with sepsis compared to both fever and leukocyte count. Follow up of the
PCT levels in 16 patients with either clinically diagnosed or blood culture proven sepsis after
starting of antimicrobial chemotherapy showed dramatic reduction proving the role of PCT as a
valuable prognostic indicator. Five patients with culture proven sepsis had either increase or no
reduction in PCT levels following antimicrobial chemotherapy all had expired, showing the
prognostic value of PCT

Conclusions:

 PCT is an effective marker for the early diagnosis and further management of sepsis.

Key Words: Procalcitonin; Marker; Sepsis;

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An epitope delivery system using M. vaccae to identify Mycobacterium tuberculosis-specific proteins candidates to be included in improved BCG vaccine

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Introduction:

 Besides being the world's most widely used vaccine, and being directed against the world's leading cause of infectious disease mortality, BCG is the most controversial vaccine in current use. Estimates of protection imparted by BCG against pulmonary TB vary greatly. One approach to improve the current BCG vaccine is to express additional M. tuberculosis-specific antigens that are not present in BCG. Our previous studies have shown that four open reading frames (ORFs): ORF3 (rv3872), ORF5 (rv3873), ORF6 (CFP10), and ORF7 (ESAT6) encode proteins that are major targets for T cell recognition in humans and animals infected with M. tuberculosis and M. bovis, respectively. The aim of this study is to express these ORFs in M. vaccae and evaluate their ability to induce specific immune responses in mice.

Methods:

 The appropriate ORFs were amplified using M. tuberculosis genomic DNA as fused to hemagglutinin (HA) DNA tag. The amplified ORFs were ligated to the shuttle vectors pSMT3, pAU151, and pDE22 at the appropriate restriction sites. Ligated as such, the expression of the proteins was directed to the cytoplasm, cell wall, or the outside of the host, respectively. The recombinant vectors were then cloned in M. vaccae. Expression of the corresponding proteins was detected with western blotting using anti-HA antibodies. Recombinant M. vaccae were injected in Balb/C mice, spleens were removed, and specific immunity to the recombinant antigens was assessed using standard spleenocytes culture and cytokines quantitation assays.

Results:

 We were able to amplify the M-tuberculosis – specific ORFs, ligate them to the shuttle vectors, and clone them in M. vaccae in which they were expressed. Recombinant M. vaccae were evaluated for immunogenicity in Balb/C mice.

Conclusions:

 Delivery of M-tuberculosis –specific epitopes in M. vaccae using shuttle vectors proved to be a promising system to identify candidate antigens to develop improved BCG.

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Molecular characterization of isoniazid resistance in multidrug-resistant clinical Mycobacterium tuberculosis isolates in Kuwait

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Introduction:

 Isoniazid (INH) and rifampin (RIF) form the cornerstone of tuberculosis treatment, and Mycobacterium tuberculosis strains resistant to INH and RIF are defined as multidrug-resistant (MDR). Infections with MDR M. tuberculosis (MDR-TB) have low cure rate and often relapse. Resistance of M. tuberculosis to INH is caused by mutations in several genes, however, mutations at codon 315 of katG (katG315) and regulatory region of inhA occur most frequently in clinical isolates. In this study, presence of mutations at katG315 and inhA regulatory region were investigated for rapid detection of INH resistance in MDR-TB strains in Kuwait.

Methods:

 The M. tuberculosis H37Rv was used as reference strain. A set of 36 pansusceptible and 47 phenotypically documented MDR-TB strains were analyzed. Mutations at katG315 were detected by restriction digestion of PCR amplified fragments with Msp I and MspA1 I and confirmed, for selected isolates, by DNA sequencing. The mutations in inhA regulatory region were identified by DNA sequencing of PCR amplified product containing this region.

Results:

  All pansusceptible M. tuberculosis strains contained wild-type sequences at katG315 and the regulatory region of the inhA gene. A Mutation at katG315 was found in 29 of 42 MDR-TB strains with 27 and 2 isolates containing AGC to ACC and AGC to ACA (both S315T) mutations, respectively. The mutations -15C • ¨T, -8T • ¨G and -8T • ¨A in the inhA regulatory region were found in 14, 1 and 1 MDR-TB strains, respectively. Three isolates contained mutations in both the genes. Thus, 42 of 47 MDR-TB strains were identified as INH-resistant.

Conclusions:

 Analysis of katG315 and inhA regulatory region correctly identified INH-resistant status of most (42 of 47, 89%) of MDR-TB strains in Kuwait. Rapid detection of resistance of M. tuberculosis strains to RIF and INH confirms the MDR status of the isolate and is useful for adjustment of therapy for proper management of MDR-TB.

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Nested PCR for the detection of Fusarium solani DNA and its evaluation in the diagnosis of invasive fusariosis using an experimental mouse model

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Introduction:

The Fusarium species are important and emerging fungal pathogens of immunosuppressed patients. They enter the body through the lungs or through a cutaneous source and disseminate through the bloodstream. Fusariosis is now the second most common mould infection in immunocompromised patients and Fusarium solani accounts for nearly half of these infections. The aim of this study was to develop a specific nested PCR (nPCR) assay for the detection of F. solani DNA in culture and in clinical specimens.

Methods:

The nPCR assay was developed by using genomic DNA isolated from Fusarium species and from other common pathogenic and environmental fungi. The nPCR assay was evaluated by using DNA isolated from bronchoalveolar lavage (BAL) and serum samples from mice infected intravenously with F. solani conidia and sacrificed on day 1 and then on every third day up to 25 days post-infection. The lung homogenate, BAL and blood samples were also cultured for F. solani.

Results:

The nPCR assay was specific for F. solani and the lower limit of detection was 450 fg of template DNA corresponding roughly to 11 F. solani cells. Cultures of lung homogenate of infected animals up to day 16 yielded F. solani with decreasing fungal load and were negative thereafter. The nPCR positivity in BAL was 100% concordant with culture results. Although detection of F. solani DNA in serum was less sensitive than in BAL, it could be detected for longer duration, i. e. up to 22 days.

Conclusions:

We have developed a sensitive and specific nPCR assay for the detection of F. solani DNA. Our data from experimental mouse model show that detection of DNA in BAL and to a lesser extent in serum by nPCR offers a sensitive and specific diagnostic approach for invasive F. solani infection.

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Polymerase Chain Reaction and RAPD Genotyping of clinical isolates of Streptococcus agalactiae from Kuwait.

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Introduction:

 The aim of this study was to develop a simple and specific method for direct detection of Streptococcus agalactiae from clinical specimens without any apparent clinical symptoms, but reports of neonatal infections, causing significant morbidity.

Methods:

 84 different clinical and environmental samples were studied. Direct PCR amplification method was used to identify epidemiologically unrelated group B Streptococcus using F1 IMOD primer for 16s RNA. The genotyping of the isolates were performed using RAPD analysis. Antibiogram was prepared using six different antibiotics.

Results:

 A total of 84 samples were analyzed of material collected from clinical (HVS) and environmental (FK) samples. These samples were cultured on BHI agar (Brain Heart Infusion). 63 positive and 21 negative reported for Streptococcus by culture method. Out of 84 samples 41 from High Vaginal Swab and 15 environmental samples showed positive report for the antibiotic tests. From 84 clinical isolates (90%) were identified as S. agalactiae by PCR and (60%) were positive for S. agalactiae by culture method. These strains were then studied using designated primer RAPD/P2 which showed high relative profiles, The RAPD method appears to be more discriminatory than conventional antibiogram assay.

Conclusions:

 This study was able to demonstrate importance of RAPD and PCR in the investigation and the genetic polymorphism of the pathogenic isolates belonging to the species S. agalactiae from environment and clinical source.

Key Words: Agalaciae; PCR; RAPD;
Funding Agency: None

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First isolation and characterization of Candida orthopsilosis among Candida parapsilosis strains isolated from clinical specimens in Kuwait

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Introduction:

 Recent studies showed that phenotypically identified Candida parapsilosis strains represent three distinct genotypes with varying virulence characteristics. These genotypes have now been recognized as three distinct species viz. C. parapsilosis, C. orthopsilosis and C. metapsilosis. The prevalence of C. orthopsilosis and C. metapsilosis in Kuwait and the region remains unknown. The aim of this study was to study genotypic heterogeneity among 114 clinical yeast isolates identified as C. parapsilosis by conventional yeast identification methods.

Methods:

 A randomly selected set of 114 C. parapsilosis isolates and identified by Vitek2 yeast identification system were analyzed. The C. parapsilosis complex and species-specific identification of each isolate was carried out by PCR using complex- and species-specific primers targeting variable sequences in rDNA. The results were validated by species-specific profiles obtained by PCR-RFLP of SADH gene. The species-specific identification of selected isolates was also confirmed by DNA sequencing of rDNA.

Results:

 Five of 114 (4%) isolates previously identified as C. parapsilosis by conventional yeast identification methods were found as C. orthopsilosis strains by species-specific amplification of rDNA and by PCR-RFLP studies. The identification of all C. orthopsilosis isolates was confirmed by direct DNA sequencing of rDNA. The results for the remaining 109 (96%) isolates were concordant with their phenotypic identification.

Conclusions:

 Five of 114 (4%) phenotypically documented C. parapsilosis isolates were identified as C. orthopsilosis by molecular characterization. The study underscores the limitation of the current yeast identification methods in discriminating closely related yeast species. This is also the first report of isolation of C. orthopsilosis from clinical specimens including blood from the Middle East.

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Activity of tigecycline and 9 others against clinically significant Gram-negative bacteria, including ESBL-producing strains

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Introduction:

The problem of multi-drug resistant microorganisms is increasing worldwide and the treatment options are limited. Thus, the activity of tigecycline, the first glycylcycline with broad-spectrum profile, and 9 other antibiotics, was investigated against clinically significant Gram-negative bacteria.

Methods:

Over a period of 6 months, 292 consecutive bacteria isolated from various infected body sites, were studied for their susceptibility to 10 antibiotics, including tigecycline. MICs of the antibiotics were determined by E-test and the results interpreted according to the recommended guidelines. Extended-spectrum beta-lactamase (ESBL) was detected by the ESBL E-test and PCR techniques.

Results:

All members of the Enterobacteriaceae family, including the ESBL-producers, and the Acinetobacter spp, were susceptible to tigecycline, with MIC_{90}s ranging from 0. 25 - 1 and 2 mcg/ml, respectively. ESBL production was confirmed in 72% of the Escherichia coli and Klebsiella pneumoniae isolates; they were all susceptible to imipenem and meropenem (MIC_{90}s = 0. 038 and 0. 05 mcg/ml, respectively). MIC_{90}s of ciprofloxacin for these strains were each >32 mcg/ml, but were 0. 06 mcg/ml for the non-ESBL-producers. Unlike tigecycline with MIC_{90} of 2 mcg/ml, MIC_{90}s of imipenem and meropenem for the Acinetobacter spp. were 16 and 32 mcg/ml, respectively with resistance rates of 35 and 65%. Strikingly, 88 and 96% of A. baumannii were resistant to amikacin and gentamicin.

Conclusions:

Comparatively, tigecycline had excellent in vitro activities just as the carbapenems against ESBL-producing Enterobacteriaceae and demonstrated superior activity against Acinetobacter spp. The drug thus holds promise as alternative therapy for ESBL-producing isolates and for treating multi-drug resistant Acinetobacter spp.

Key Words: Tigecycline; Susceptibility; Gram-negative bacteria;

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Incidence of Malaria and Filaria Among Expatriates Coming to Kuwait

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Introduction:

Introduction: Our aim was to detect the prevalence of malaria and filaria, among 300, 000 immigrants come to Kuwait every year from developing countries where infectious diseases are endemic, and also to control the spread of these diseases.

Methods:

Methods: Thick and thin blood films were made from all the immigrants coming from malaria and filaria endemic countries and stained with Giemsa. These stained slides were checked by microscopy for malaria and filaria.

Results:

Results: About 682, 713 immigrants were checked for malaria and filaria during 2005 – 2007 and 452 (0. 066%) were found positive. Out of 452 positive cases 226 (0. 033%) were infected with malaria and the same number 226 (0. 033%) with filaria. All the four species of malaria were detected and their distribution was found as; P. vivax 38. 05%; P. falciparum 32. 32%; P. ovale 6. 64; P. malariae 2. 65% and mixed infection of P. falciparum and P. vivax 19. 02%. Wuchereria

bancrofti was the only prevalent species found in infected cases of filaria.

Conclusions:

Conclusion: The rate of infection was (0. 15%) and (0. 08%) for malaria and filaria, respecitively, among immigrants detected in 1991 – 1999. This decline is due to proper screening of the immigrants in their home countries before coming to Kuwait. The immigrants infected with malaria were treated in Infectious Diseases Hospital, whereas, those with filaria were sent back to their home countries because of the risk of transmission.

Miscellaneous
Category: Basic Sciences

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Planning the physicians and dentists workforce in Kuwait to the year 2020

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Introduction:
This study addresses the supply and demand for physicians and dentists in the light of emerging variables such as projected population, economic growth, and changes in public and private healthcare strategies. The aim of the study was to project the future demand for physicians and dentists for the years 2007 to 2020 based on the past period 1994 to 2006.

Methods:
Population projections were derived using an average annual population natural increase rate. The future need of physicians and dentists were projected using the average physician or dentists to population ratios for the years 1994 to 2006 (one physician to 581 population and one dentist to 2967 population respectively). The projected number of Kuwaiti physicians or dentists at a given year was calculated by incrementing the number of Kuwaiti physicians or dentists of the previous year by the average annual growth rates of Kuwaiti physicians (4. 08%) or dentists (5. 58%) during the past period 1994 to 2006.

Results:
The average growth rate per annum of Kuwaiti physicians for the period 1994 to 2006 was 4. 08% compared to 2. 83% for non-Kuwaiti physicians. The average annual growth rate for Kuwaiti dentists was 5. 58%, while for non-Kuwaiti dentists it was 3. 19%. This indicates that the number of Kuwaiti physicians or dentists is growing at faster rates. The disparity between the projected number of physicians needed and the number of Kuwaiti physicians that will be available is likely to decline from 62. 14% in 2007 to 48. 1% in 2020. In the case of dentists the disparity is expected to fall from 54. 42% in 2007 to 24. 67% in 2020.

Conclusions:
The supply of Kuwaiti physicians and dentists will remain insufficient to meet the projected demand until the year 2020. Physician and dentist to population ratios in Kuwait are low compared to most Western countries and require to be improved.

Key Words: Demand and supply of healthcare workforce; Dynamics of healthcare strategies; Funding Agency: None

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Projection of the nurses' workforce in Kuwait to the year 2020

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Introduction:

Periodic review of supply and demand for nurses should be undertaken in the light of emerging variables such as projected population, economic growth, and changes in healthcare strategies. The aim of the study was to project the future demand for nurses, with special reference to the supply of Kuwaiti nurses, for the years 2007 to 2020 based on the past period 1994 to 2006.

Methods:

Population projections were derived using an average annual natural increase rate. The future need of nurses was projected using the average nurse: population ratios for the years 1994 to 2006 of one nurse to 256 population. The projected number of Kuwaiti nurses at a given year was calculated by decrementing the number of Kuwaiti nurses of the previous year by -3. 33%, the average decrement rate of Kuwaiti nurses during the period 1994 to 2006.

Results:

The average decrement rate (-3. 33%) per annum for Kuwaiti nurses indicates that the number of Kuwaiti nurses is declining. There is a substantial gap between the numbers of Kuwaiti and non-Kuwaiti nurses, and this gap is expected to become wider with time due to the decline in the number of Kuwaiti nurses. Of the total demand of nurses in year 2006, Kuwaiti nurses only constituted 6. 6%. The supply of Kuwaiti nurses is projected to decline to 3. 37% in year 2020.

Conclusions:

It is unlikely that Kuwait will achieve self-reliance with respect to the supply of nurses by the year 2020. On the contrary, it is expected that the gap between the demand for nurses and the supply of Kuwaiti nurses would progressively increase in view of the projected decline in the number of Kuwaiti nurses that will be available. Public education programs are required to educate the community about the role of nurses in the healthcare delivery system in order to minimize the public negative perception about the nursing profession and hence increase the number of Kuwaiti nurses.

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Effect of obesity on Outcome of antioxidant thearapy in men with Asthenozoospermia

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Introduction:
 Obesity has been associated with male infertility, but the mechanisms are still not fully understood.
Objective of study: To determine the effects of Obesity on the outcome of antioxidant therapy in the treatment of asthenozoospermic men and effect on oxidative stress and apoptosis and sperm fertilising capacity in male subfertility

Methods:
 Forty-one men with asthenozoospermia i. e < 20 million/mland > 40 percent are immotile, were randomized into four weight related therapy groups using the Body Mass Index (BMI) Kg/m2 </=18, 18. 1-25. 9, 26-29. 9, >/=30
Methodology: Semen analysis according to WHO guidelines. MDA, TNF-α, Total antioxidant Capacity (TAC), superoxide dismutase (SOD) and glutathione peroxidase were determined in the semen and serum. Sperm chromatin integrity was measured using Sperm Chromatin Structural Assay (SCSA) to assess acid-induced denaturation of sperm DNA and acridine orange staining and evaluated by light microscopy. The second portion was fixed in glutaraldehyde and evaluated by electron microscopy.

Results:
 Obesity was significantly associated with oxidative stress, compared to normozoospermia, with higher seminal levels of MDA and TNF-α, and low TAC, SOD and GPX. Markers of oxidative stress, apoptosis and DFI were significantly more common in obese men than those with normal BMI. Although antioxidant therapy was generally associated improved sperm parameters, there was significantly less improvement in obese men in terms of reduction of oxidative stress, apoptosis and sperm DNA fragmentation.

Conclusions:
 Obesity was significantly associated with seminal oxidative stress, apoptosis and sperm DNA fragmentation and their reduction by Antioxidant therapy was significantly less in obese men than in men with normal body weight.

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Bi-directional role of glucose in sperm capacitation.

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Introduction:

Glucose increases sperm capacitation but the mechanism has not been elucidated.
Objective of the study is to evaluate the role of lipid peroxidation in sperm capacitation with
glucose and the effect of antioxidants.

Methods:

20 men with infertility, but with normal sperm parameters and normal blood glucose levels were
evaluated with semen analysis, fasting blood and seminal glucose; glucose concentrations of 0
mM, 2. 5 mM, 5 mM, 7. 5 mM, 10 mM, 12. 5 mM and 15 mM in RPMI. (1) plus 100, 000
sperm to each concentration and incubated for 1 hour at 37degreeC and (2) glucose vitamin E.
Semen analysis, MDA and Acridine Orange denaturation and Electron Microscopy. (EM) of
Sperm.

Results:

Blood glucose concentration was 4. 4±0. 8 (95% CI; 3. 8, 4. 9) but not detectable in semen. Sperm
concentration 98 x 105/ml; Progrssive motility 46±11%, Sperm immotility 15±6% and Blood
MDA 2. 3±0. 4 nmol/ml and seminal plasma MDA 2. 4±0. 3 nmol/ml. Sperm motility increased
by 20% at 7. 5 mM glucose concentration and thereafter declined from 10 mM to 15 mM by 30%.
MDA level increased from 1. 5±0. 4 nmol/ml at glucose level of 0 mM to 4. 5±1. 2 nmol at 15
mM glucose concentration. Sperm DNA fragmentation Index (DFI) increased by 23%. Electron
microscopy showed increased disruption of the acrosome and midpiece. Most of the abnormalities
of MDA, sperm motility, DFI and ET were significantly reduced by vit E.

Conclusions:

Low concentration of glucose increased sperm capacitation but high levels increased lipid
peroxidation and sperm damage, which were reversed by vitamin E through its antioxidant
activity.

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The effects of oxidative stress on pregnancy outcome of assisted reproductive techniques

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Introduction:

 Aerobic metabolism is associated with the generation of prooxidant molecules called free radicals or reactive oxygen species (ROS) that include the hydroxyl radicals, superoxide anion, hydrogen peroxide, and nitric oxide. There is a complex interaction of the prooxidants and antioxidants, resulting in the maintenance of intracellular homeostasis. There is a complex interplay of cytokines, hormones, and other stressors that affects cellular generation of free radicals. Whenever there is an imbalance between the prooxidants and antioxidants, a state of oxidative stress is initiated. Free radicals can influence the oocytes and embryos in their microenvironments. This study addresses how oxidative stress influences the outcomes of assisted reproductive The aim is to investigate the impact of oxidative stress and cytokine profile on pregnancy success by monitoring malondialdehyde, TNF-a, IFN, IL4, IL10 levels in follicular fluid.

Methods:

 54 couples were enrolled in this prospective study. Following long protocol of GnRH analogues and r-FSH treatment, oocyte retrieval and intracytoplasmic sperm injection were performed. Malondialdehyde levels were assayed by thiobarbutiric acid reacting substances test. Measurement of cytokines:TNF-α, IFN-γ, IL4, IL10 was performed by ELISA

Results:

 Patients were divided into two groups; group I (pregnancy positive, n = 20), group II (pregnancy negative, n = 34). There was no statistical significant difference in terms of age, infertility period, FSH levels on the third day, number of oocytes retrieved and fertilization rates between the two groups. Pregnancy rates were found to be decreasing in higher malondialdehyde levels. All 4 Cytokines were below level of detection in follicular fluid.

Conclusions:

 Malondialdehyde can be used as a marker of oxidative stress and a potential marker in predicting assisted reproductive techniques outcome.

Key Words: Oxidative stress; Follicular fluid; MDA;
Funding Agency: none

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Measurement of IGF-1 in follicular fluid and its predictive value of pregnancy outcome in patients with PCOS undergoing in vitro fertilization

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Introduction:
Polycystic ovary syndrome (PCOS) is characterized by hyperandrogenism and impaired ovarian folliculogenesis. PCOS is frequently associated with insulin resistance. Insulin may act through its own receptor in the ovary or via the homologous type I insulin-like growth factor (IGF) receptor.. Our objective is to investigate intrafollicular insulin-like growth factor I (IGF-I) in patients with PCOS) in comparison with women of other infertility causes and to explain a relationship between concentrations of IGF-1 in follicular fluid, oocyte quality, and outcomes of in vitro fertilization--embryo transfer (IVF-ET)

Methods:
376 follicular fluid samples were collected from 54 women undergoing IVF/ICSI treatment during the year 2007. IGF-1 results were analyzed. The patients were then classified as either PCOS or non-PCOS according to roterdam`s criteria. 1. GnRH long protocol used. Ovarian stimulation with exogenous gonadotropins is started 2. Cycle monitoring: By transvaginal sonography. HCG was given when the leading follicles achieved a diameter of 18 mm; a transvaginal ultrasound–guided oocyte retrieval was scheduled 35 h later. Embryos were transferred.

Results:
Analysis of demographic data (age and infertility duration and FSH level) of PCOS and non-PCOS group showed no statistical significance. No difference was observed in terms of number of Amps of gonadotrophin consumed or Duration of stimulation. Statistically higher No. of oocytes retrieved, higher No. of embryos obtained and higher level of E2, lower Fertilization rate in PCOS group. The implantation rate and clinical pregnancy rate were similar in both groups. Miscarriage rate was higher among PCOS. IGF-1 level in PCOS group was higher.

Conclusions:
Higher IGF-1 levels among PCOS group can be explained by higher number of immature follicles during stimulated cycles. This can explain the lower fertilization rate in PCOS group

Key Words: PCOS; IGF-1; Follicular Fluid;

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The role of Bishop Score in the Outcome of Labour in Induction of Labour

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Introduction:

Previous studies have indicated that Bishop Score had some influence on the methods and outcome of Induction of Labour{IOL). A low Bishop Score has been associated with an increased risk of caesarean section and adverse maternal and perinatal outcome. The objective of our study was to ascertain the impact{if any} of Bishop Score in our patients undergoing induction of labour.

Methods:

The Bishop Score of all patients admitted for IOL(Study Population) in a Unit at Maternity Hospital, Kuwait, was estimated by experienced residents over a three-month period{ November 1, 2007-January 26, 2008}. The patients admitted in spontaneous labour immediately after the cases of IOL over the same period served as Control. All the patients studied (study/control) had singleton pregnancies in cephalic presentation. The biodata, social status, present and past obstetric history and the past medical history were extracted from the files. The patients were followed through induction/labour and the maternal and perinatal outcome documented.

Results:

This is the initial report of an on-going prospective study. 110 study and 100 control patients were studied. 99. 1% of the study population had unfavourable cervix and a Bishop Score of <7. There was no statistical difference in the mean age of the study and control patients [29. 25±5. 545 vs 28. 31±5. 516, p=0. 220] and the gestational age at delivery [39. 42±1. 778 vs39. 19±1. 297]. Although, there was no significant difference in the birth weight of the study and control population, the caesarean section rate was significantly higher in the study group: 20% vs 8. 1%, p=0. 017; the incidence of vaginal delivery was significantly higher in the control group [83. 6% vs 77. 0%, p=0. 026. There was a case of ruptured uterus in the study group. The maternal and perinatal were comparable.

Conclusions:

Low Bishop Score was significantly associated with increased incidence of caesarean section. The
maternal and perinatal outcomes were satisfactory.

Key Words: Bishop Score; Induction Labour; ;

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Implication of Alteration in Blood Flow on Leucine Transport in Human Placenta: Search for Toxemia Model

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Introduction:
 Previous reports from our laboratory had shown that maternal-fetal status of some nutrients are altered in pre-eclamptic pregnancies. Transport behaviour of an esential amino acid, L-leucine was studied in toxemia model placental perfusions, with altered perfusate flows, to evaluate role of reduced perfusion per se on its transfer from maternal to fetal circulation.

Methods:
 Human placentae, were collected post-partum. 0. 50 uCi of 14C-labelled L-leucine(specific activity: 54 mCi/mmol; Amersham, UK) along with 1 uCi of tritiated water (specific activity : 5 mCi/mmol; Amersham, UK) as reference marker were then injected as a single bolus (100ul) into the maternal arterial circulation of perfused placental lobules and perfusate samples collected from maternal and fetal circulations over a period of 5 minutes. National culture and tissue collection (NCTC) medium was used as the perfusate. The experiment was repeated after a period of 10 minutes with reduction in maternal perfusion rate of 50 percent than control phase to mimic a toxemic state. Concentration of substances studied in perfusate samples was assessed using liquid scintillation spectrometry using double window counting(LKB Wallac Model, Denmark) and transport and pharmacokinetic parameters analyzed using standard established parametres

Results:
 Differential transport rates of tritiated water and l-leucine differed significantly (Student's t-test; p<0. 05) in 8 control and toxemia model perfusions. TR50 index of leucine of compared to reference marker averaged 1. 16+/-0. 03 in control phase series while in toxemic model phases the index averaged 0. 86+/-0. 04. Leucine transport index averaged 48. 2+/-2. 2 % of reference marker value while in toxemia model perfusions, leucine transport inex averaged 39. 2+ /-2. 1% of water trasnport value. Indices of various pharmacokinetic parameters such as area under the curve, clearance, elimination constant, absorption rate, and elimination rate of leucine compared to tritiated water showed variable differences between control and toxemia model perfusions. Absorption rate and elimination rate indices of leucine differed significantly(Student's t-test; p<0. 05) between control and toxemia model perfusions as well.

Conclusions:
 Our studies show for the first time that transport behaviour of essential amino acids could be compromised in preeclamptic states, with potential harmful effects on fetuses or infants of afflicted mothers.

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Characterisation of apoptotic responses in a pituitary derived cell line

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Introduction:

A novel pro-apoptotic mediator gene was recently identified in pituitary tumour cell lines and named the Pituitary Tumour Apoptosis Gene (PTAG) for its role in the apoptosis pathway. PTAG was shown to be under-expressed in most pituitary adenomas, and methylation of its promoter region leads to gene silencing and oncogenic transformation in pituitary adenomas. While genetic alteration is usually irreversible, epigenetic methylation is potentially reversible and provides the possibility for future treatment interventions. This study aims to determine if PTAG expression is regulated by bromocriptine-induced apoptotic stimuli, and to investigate the relationship between PTAG expression and the activity of its promoter region.

Methods:

Bromocriptine-induced apoptotic response was assessed using Hoechst staining. Ribonucleic acid (RNA) extraction was performed on pituitary tumour cells treated or untreated with bromocriptine up to 48 hours of treatment, and PTAG expression was determined employing quantitative Real Time-Polymerase chain reaction (qRT-PCR). PTAG promoter activity was examined using transient transfection of PTAG promoter-reporter (luciferase) constructs and the Renilla construct, and reporter activity was determined through chemiluminescence.

Results:

Treatment with increasing doses of bromocriptine induced a proportional increase in apoptotic cells. Maximal PTAG promoter activity was found to be produced from the 5' flanking region between -170 and -135. This activity did not increase upon exposure to bromocriptine-induced apoptotic stimuli.

Conclusions:

Mapping of the PTAG promoter sequence identified a region of 35 base pair sequence, located between nucleotides -170 and -135 as the PTAG basal promoter. Further sequencing analysis showed the sequence to harbour transcription factor-binding sites.

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HER2neu gene copy number quantitation assay in breast cancer cases unresolved by FISH

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Introduction:

 Fluorescence Insitu Hybridization (FISH) is a standard FDA approved method widely used to aid in selection of patients for HERCEPTIN therapy based on HER2neu gene amplification status.
It has been understated worldwide the number of breast cancer cases in which FISH assay failed to give results even after test repetition. This leaves out patients with Her2/neu amplification without the appropriate treatment.
In this research we have introduced an "in-house" Relative quantitation assay for HER2neu copy number assessment using Real Time PCR System as an adjunct technique to FISH.

Methods:

 To investigate the accuracy of HER2/neu relative quantitation assay, tumor tissue was microdissected from deparaffinized microscopic slides corresponding to 30 breast cancer cases, and DNA was extracted, amplified and purified. Using 7500 Fast Real Time PCR System, a relative quantitation assay was performed using two target sequence detection primers (Her2B and HER2neu introns-1), two endogenous normalizing control primers (TOPO-A2 and RNase-P) and three normal reference DNA samples. Specialized software calculates the quantification results. These cases were also examined by FISH for the gene copy number. We executed the same quantitative assay on other 8breast cancer cases that were undiagnosable by FISH.

Results:

 Results from 30 breast cancer cases confirmed that quantitation assay was able to successfully detect 90% (18 out of 20) amplified states diagnosed by FISH, with a sensitivity of 94. 7% and specificity of 66. 6 %.
While 7 out of 8 samples, unresolved by FISH, had normal copy number of HER2/neu gene and one sample was found positive for the amplification.

Conclusions:

  HER2/neu Relative Quantitation copy number assay enables determining amplification status of the gene, in cases which fails FISH analysis. Thus, Real time PCR offers a valuable, quick and less expensive tool that can complement FISH in diagnosing breast cancer.

*Key Words: Fluorescence Insitu Hybridization (FISH); Breast Cancer; HER2neu gene;
Funding Agency:*

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Metastatic Tumor Antigen 1 (MTA1) and MTA1 Short Form (MTA1s) mRNA in Human Breast Cancers: any Clinical Significance?

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Introduction:

Metastasis-tumor antigen (MTA1) is correlated with invasiveness or aggressiveness in several types of cancers, including breast cancer. A naturally occurring C-terminal truncated variant of MTA1, MTA1 short (MTA1s), has also been identified. MTA1s is localized in the cytoplasm of ER-α negative breast cancers, that is, cancers that do not express any nuclear-localized estrogen receptor (ER) -α. MTA1s binds and inhibits the nuclear functions of ER-α by sequestering it in the cytoplasm. However, ER-α sequestered in the cytoplasm remains functional and promotes the non-genomic action of ER-α in the cytoplasm. In the present study, the levels of MTA1 and MTA1s expression in breast cancer tissue was studied.

Methods:

FFPE breast cancer samples from 50 patients were used in this study. For RNA extraction a kit by Stratagen was used. This was followed by DNase treatment and reverse transcription. cDNA was then amplified with specific MTA1 and MTA1s primer sets using real time PCR (ReT-PCR). The PCR reactions were prepared using the SYBR GREEN master mix. At the end of the ReT-PCR cycles a dissociation curve (melting curve) was generated which showed the peak for the amplified gene at the specific melting temperature (Tm). The dissociation curve provides us with a peak derivative that reflects the intensity of the band.

Results:

MTA1 and/or MTA1s were detected in 40 breast cancer samples, however, no significant difference in detection level was seen. When correlated with results from pathology reports on ER status, no correlation was found between ER status and MTA expression.

Conclusions:

Although MTA1 and MTA1s have been demonstrated to modulate ER mediated gene transactivation and signal transduction further studies need to be performed on a larger number of samples to address the relationship of MTA1 and ER.

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Real Time PCR (ReT-PCR) a Novel Method for the Detection of Estrogen Receptor (ER) α and β Isoforms and their Variants

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Introduction:

Estrogen receptors -α and -β mediate the actions of estrogens. Several mRNA splice variants exist for both receptors and the normal estrogen function results from a balance between the wild-type ERs and their functional variants that may interfer with the coexpressed wild-type forms in a dominant negative manner, or by becoming ligand-independently activated. In addition, ER-α and ER-β isoforms can exert opposite biological activities, as it is evident that ER-α stimulates cell proliferation while ER-β can inhibit ER-α -stimulated cell proliferation.

Methods:

45 FFPE breast cancer samples were used in this study. ReT-PCR analysis was conducted using ER-α primer sets detecting wild type (wt) and exon deleted 3, 5, 6 and 7 variants. The ER-beta primer sets used detected the wt ER-β 1 and the ER-β 2 and ER-β 5 variants. At the end of the ReT-PCR cycles a dissociation curve (melting curve) was generated which showed the number of peaks for each sample at specific melting temperatures (Tm). If more than one peak is obtained at the higher meting temperatures then this indicates the presence of variants for the specific gene of interest. In addition the dissociation curves provide us with a peak derivative that reflects the intensity of the band.

Results:

Using this method minimal amounts of mRNA could be detected and many samples expressed not only the wt ER isoforms but also their variants. The Tm value served as a cut-off point for determination of wt versus variant ER expression. Wild type to variant ratio was easily calculated from the peak derivatives.

Conclusions:

This method allowed us to detect both ER isoforms and their variants in FFPE breast cancer tissue. This method, by showing wt and variants, can be used as an invaluable tool in the clinical field to predict the response of patients to antiestrogen therapy.

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Optimal timing of PBSC collection in Lymphoma and Myeloma patients after standard dose of chemotherapy and/or G-CSF mobilization

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Introduction:

Background: It would be a clinical and economical advantage if the optimal time point of peripheral blood stem cell (PBSC) collection following chemotherapy and/or G-CSF mobilization was known in advance.

Methods:

Patients and Methods: A total of 43 harvests from 22 patients with Hodgkin's disease (n = 9), Non-Hodgkin's Lymphoma (n = 10), and Multiple Myeloma (n = 3) were included in this prospective study. Leukapheresis procedure was initiated when the peripheral blood CD34 $^+$ cell count reached ≥10 cells/µl and performed daily until a target number of ≥ 2. 0×10 ^{6} CD34 $^+$ cells/kg was collected. The yield of CD34 $^+$ cells was monitored on hour 3, 4 and 5 of receiving G-CSF injection.

Results:

Results: The median patient age was 44. 5 years (range 14-59), and the median weight was 74. 5 kg (range 44-119). Univariate analysis showed that there was a significant correlation between hour 3, 4 and 5 from receiving G-CSF injection and the yield of CD34 $^+$cells (0. 36 × 10 ^{6} cells/kg versus 0. 85 × 10 ^{6} cells/kg versus 1. 43× 10 ^{6} cells/kg P < . 001, respectively). In multivariate analysis including (PB) Plt, MNC, and WBC counts, a high yield of CD34 $^+$ cells can only be predicted by the number of circulating CD34 $^+$ cells (P < . 001). The target of harvesting ≥ 2. 0×10 ^{6} CD34 $^+$ cells/kg was achieved in 16/43 (37. 2%) collections with a median number of 66 circulating CD34 $^+$ cells/µl (range 23-169).

Conclusions:

Conclusion: These results showed that measuring peripheral blood CD34 $^+$ cell count and starting the collection after 4 hours from receiving G-CSF injection are the main parameters for successful, efficient and economical PBSC harvesting.

Key Words: CD34 $^+$cells; Peripheral Blood Stem Cell collection; Lymphoma and
Funding Agency: None

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Epidemiological evidence for a link between dental X-rays and thyroid cancer

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Introduction:

An increasing incidence of thyroid cancer has been reported over the last few decades. Much of this increase may be due to increased ascertainment, but there may be other contributing factors. The thyroid gland is highly susceptible to radiation carcinogenesis. Dental radiography, a common source of radiation exposure in the general population, is often overlooked as a source of radiation to the gland and may be associated with the risk of cancer. An increased risk of thyroid cancer has been reported in dentists/dental assistants and exposure to dental X-rays have been associated with an increased risk of meningiomas and salivary tumours. The objective of this study was to investigate the relationship between dental X-rays and risk of thyroid cancer.

Methods:

Design: Population based case-control study. Setting: Kuwait Cancer Registry, Kuwait Cancer Control Centre. 313 patients with thyroid cancer; 313 control subjects individually matched to each thyroid cancer patient for age, gender, nationality, and district of residence. Information on dental X-rays and other relevant exposures was collected through a personal interview with the cases and controls, and the data were recorded in a structured questionnaire. The main outcome measure was to determine the risk of thyroid cancer associated with exposure to dental X-rays.

Results:

There was an approximately 2-fold significantly increased risk of thyroid cancer in individuals who were exposed to dental X-rays (OR=2. 1; 95% CI: 1. 4-3. 1) (P= 0. 001). There was also a statistically significant dose-response relationship which showed an increasing trend in risk with increasing number of dental X-rays (P-trend <0. 0001). This relationship remained after controlling for sociodemographic factors (gender, nationality, education), number of live births, or age at diagnosis.

Conclusions:

These data support the hypothesis that exposure to dental X-rays is associated with an increased risk of thyroid cancer.

Key Words: Thyroid; Cancer; Dental X-ray;
Funding Agency: None

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Factors affecting mobilization of peripheral blood progenitor cells in patients with Non-Hodgkin's Lymphoma

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Introduction:

Background: The objective of this study was to identify factors influencing the efficacy of peripheral blood progenitor cell (PBPC) collection in patients with non-Hodgkin's lymphoma.

Methods:

Fifty-five patients with low-grade (n = 7) and high-grade (n = 48) non-Hodgkin's lymphoma underwent initial PBPC collection at Kuwait Cancer Control Center (KCCC) between 2000 and 2007. PBPCs were mobilized with either granulocyte-colony stimulating factor (G-CSF) alone (n = 23) or G-CSF following combination chemotherapy (n = 32). After mobilization, the CD34 $^+$ cells were harvested using COBE Spectra continuous-flow blood-cell separators (COBE laboratories Ltd, Gloucester). Univariate and multivariate analyses were used to assess potential factors affecting CD34 $^+$ cell yield (collection of more than a target number of > 2. 0×10^6 cells/kg) such as age, gender, lymphoma grade, disease stage, weight, prior chemotherapy, bone marrow status at baseline and mobilization regimen.

Results:

The target of collecting > 2. 0×10^6 CD34 $^+$ cells/kg was achieved in 37/55 (67. 3%) patients with a median of two apheresis procedures (range 1-5). In a univariate analysis, only the mobilization regimen was predictive of a high yield CD34 $^+$ cells (3. 7×10^6 cells/kg of chemotherapy plus G-CSF versus 2. 3×10^6 cells/kg of G-CSF alone; P = . 021). However, in a multivariate analysis, mobilization regimen, lymphoma grade and bone marrow status at baseline were the factors associated with high CD34 $^+$ cell yield (P < . 01, P = . 036 and P = . 043, respectively).

Conclusions:

These data suggest that mobilization regimen, lymphoma grade and bone marrow status at baseline were the only factors affecting the efficiency of PBPC collection.

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Determinants Of Serum Creatinine And The Need For Population-Appropriate Creatinine Reference Ranges In Kuwait

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Introduction:

Serum creatinine (Cr) is the most commonly used marker of Glomerular Filtration Rate (GFR). Guidelines specify five classes of kidney diseases based on estimation of GFR (eGFR) from Cr using the Modification of Diet in Renal Disease (MDRD) equation. The MDRD equation was developed in Americans and may not be accurate across racial groups. For accurate classification, proper age and gender stratified reference ranges are needed but the Mubarak Hospital (MKH) uses externally determined manufacturer's reference range. Therefore, the aims of this study are to: determine age and gender stratified reference ranges for Cr and eGFR in consecutive patients seen in MKH; determine the prevalence of low Cr, which could affect the eGFR.

Methods:

We determined fasting Cr and full clinical biochemistry profiles on healthy 309 (154 females and 155 males) subjects and 186 (73 female and 113 male) inpatients. Clinical details were recorded and eGFR was calculated with the MDRD. Reference ranges for Cr based on age and gender were determined.

Results:

Age and gender were significant determinants of Cr. In males, age-stratified Cr ranges are (<20years: 48. 5 (13. 0-77. 0), 20-39years: 75 (26. 9-113. 1), 40-59years: 83 (58. 1-111. 1), >/=60years: 88 (29. 3-117. 7). In females, age-stratified serum Cr ranges are (<20years: 48. 5 (5. 2-63. 0), 20-39years: 57. 0 (35. 5-87. 0), 40-59years: 66. 0 (40. 8-119. 6), >/=60years: 68. 0 (31. 0-119. 5)). These ranges are significantly different from the uniform reference range of 60-120 µmol/L
used in MKH. 1. 8% of male inpatients, 4. 1% of female inpatients and 1. 3% of female outpatients
had low Cr concentration. The commonest cause of low Cr was diabetes and high Cr is mainly caused by renal disease.

Conclusions:

The reference ranges in use in Kuwait are inappropriate and can lead to significant misclassification of patient's renal disease status. We report locally applicable reference ranges for Cr concentration appropriate for use in the Kuwaiti population.

Key Words: Creatinine; Reference ranges; Kuwait;
Funding Agency: None

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Significance of periclavicular haemorrhage at the origin of sternocleidomastoid muscle in hanging

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Introduction:

Hanging is a common method of suicide. Various studies in the forensic literature have reported considerable differences in the frequency of hyoid bone or thyroid cartilage fractures and injuries to the musculature and vasculature of the neck. Haemorrhage at the periosteal-clavicular origin of sternocleidomastoid muscle has seldom been employed as a diagnostic feature of hanging. The present study was carried out to evaluate the incidence and significance of periclavicular haemorrhage in hanging cases and compare it with other commonly described cervical injuries in such instances.

Methods:

A study was undertaken of 43 deaths due to suicidal hanging (23 males and 20 females; aged between 22 and 58 years) and 30 control subjects (19 males and 11 females; aged between 17 and 63 years), at the Department of Forensic Medicine, Ministry of Interior, Kuwait, during the period January 2005 through December 2007. The study entailed scene of incident examination, cervical radiological investigations, autopsy examination including cervical soft tissue dissection, histopathological examination, and toxicological screening.

Results:

Hanging was complete with full body suspension in 30 (69. 8%) and incomplete in 13 (30. 2%) of the cases. Periclavicular haemorrhage at the origin of sternocleidomastoid muscle was demonstrated in 28 of the cases (65. 1%) and was associated with the localization of the highest point of suspension in 15 cases (53. 6%). Laryngo-hyoid fracture was detected in 10 cases (23. 3%),
while soft tissue cervical haemorrhage was established in only 8 of the cases (18. 6%).

Conclusions:

The present study further highlights the value of periclavicular haemorrhage at the origin of sternocleidomastiod muscle as a reliable and more significant ante-mortem finding than other frequently employed cervical injuries in hanging. Extension of force by the suspended body weight is the likely causative mechanism of periclavicular haemorrhage in such conditions.

Pathology
Category: Clinical

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Medico-legal aspects of infant death in Kuwait

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Introduction:

  Infant mortality is a sensitive index of the health and welfare of any community. The conditions and events that may be associated with infant death are extremely varied. The objective of this study is to recognize the various aspects of infant death among cases referred for medico-legal autopsy in Kuwait in an attempt to provide more accurate forensic-medical documentation of such cases.

Methods:

  Data was collected on infants dying under the age of one year and referred for medico-legal examination during the period 2003-2006 at the Department of Forensic Medicine, Ministry of Interior, Kuwait. Analysis involved clinical and epidemiologic data, scene examination and complete autopsy investigations. Statistical records on infant death from the Ministry of Health were also obtained.

Results:

  There were 220 medico-legal infant deaths included in this study (129 Kuwaitis: 91 non-Kuwaitis). They constituted 12. 5% of the overall infant mortality figures in Kuwait during the study period(1760 deaths; 997 Kuwaitis: 763 non-Kuwaitis). Natural infant death accounted for 133 cases (60. 5%), while violent deaths were recorded in 87 cases (39. 5%). Of the natural causes, there were 21 stillbirths (9. 5%), but the commonest cause of natural death was due to infections (52; 23. 6%). Sudden infant death syndrome comprised 38 (17. 3%) of the cases, while congenital heart defects were reported in 15 cases (6. 8%). Of the violent infant deaths, domestic mishaps formed the commonest group (32; 14. 5%), while road traffic accidents were documented in a fairly large number of cases (30; 13. 6%). Infanticide was reported in 25 cases (11. 4%).

Conclusions:

  Our preliminary study identifies the medico-legal pattern of infant death in Kuwait in recent years. Infections were recognized as the commonest natural cause of infant death. A disturbing finding is the relatively high incidence of violent infant deaths. Further in-depth investigations are recommended.

Key Words: Infant death; Stillbirth; Sudden infant death syndrome;
Funding Agency: None

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Kuwait National Antenatal RBC grouping and antibody screening program: A 3 year study.

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Introduction:

Kuwaiti national antenatal screening program established in June 2003 aiming to identify pregnancies at risk of fetal and neonatal hemolytic disease of new born (HDN) and to identify Rh-D negative women who need anti-D prophylaxis. Guidelines for the prevention and management of red cell antibodies (Abs) during pregnancy were established too. Accordingly, all patients attending antenatal centers in Kuwait were tested at booking and at 28 weeks gestation. Testing of samples was centralized at Kuwait central blood bank antenatal laboratory, anti-D is still the main cause of HDN among other Abs implicated. This will be the first statistical study assessing the prevalence of Rh-D immunization and the effectiveness of anti-D prophylaxis program in Kuwait after the implementation of the program.

Methods:

Patient samples (PS) received during 2004 until 2006 were analyzed. All samples were tested using Gel and beads card methods for ABO, Rh and kell antigens, and screened for the presence of RBC Abs. antibody identification is performed for PS screened positive and titration is done for Anti-D, Anti-c, and anti-K only. Patients with anti-D were classified into low, moderate and high risk for HDN according to anti-D titration. PS with low anti-D titer (titer2) are clinically insignificant and were excluded. Data were recorded using customized Oracle based software and statistical reports were issue. A comparison of date between the 1st and 3rd year of the screening program was done.

Results:

A total of 57. 818 PS were studied during 3 years. Study shows a decreased prevalence of Abs in 2006 with a significant decrease in clinically significant Abs (CSA). There was also a significant decrease in anti-D immunization in Rh-D negative patient, while the percentage of patients with high risk increased.

Conclusions:

The Kuwait national antenatal screening program is proven to be effective in decreasing the Rh-D immunization and the management of HDN. A review study every 2 years period recommended.

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Associations of markers of low-grade inflammation and Insulin resistance - A study of type 2 Diabetic subjects and their first-degree relatives.

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Introduction:

Non-diabetic relatives of patients with Type 2 diabetes (T2DM) are susceptible to develop diabetes and low-grade inflammation is a factor in the development of insulin resistance. This study evaluates the associations of inflammatory markers with metabolic abnormalities and whether T2DM probands and their first-degree relatives (FDR) differ from control subjects without a family history of diabetes.

Methods:

We studied 172 non diabetic FDR of 81 T2DM probands and 32 healthy nondiabetic control subjects matched for age, sex, and BMI. Fasting complement C3, CRP (high sensitivity assay), insulin, glucose, and full lipid profile were determined. Insulin sensitivity (%S) and insulin resistance (HOMA-R) were assessed using the homeostasis model assessment formula.

Results:

When the cohort was examined as a whole, C3 showed significant (all $p < 0.01$) correlations with (CRP ($r = 0.41$); BMI ($r = 0.41$); waist circumference (WC) ($r = 0.47$); insulin ($r = 0.27$); HOMA-R ($r = 0.29$); %S ($r = -0.32$); Total cholesterol ($r = 0.42$); LDL Cholesterol ($r = 0.29$) and Triglycerides ($r = 0.30$). CRP showed similar correlations with these variables. T2DM and FDR had significantly higher C3, CRP, BMI, WC, Insulin, HOMA-R and significantly lower %S and HDL-Cholesterol than the control subjects. However, although T2DM patients had significantly higher C3, CRP, BMI and WC than their normoglycemic FDR, the differences in %S and HOMA-R were not statistically significant. Partial correlation analysis, correcting for WC, abolished the associations of C3 and CRP with insulin, %S, HOMA-R and lipid parameters except Triglycerides which remained significant (partial $r = 0.25$; $p = 0.005$).

Conclusions:

Normoglycemic FDR of T2DM patients were already more insulin resistant than controls because of obesity-associated increases in C3 and CRP. This suggests that in subjects at high risk of T2DM, the insulin-resistant state is related to obesity-dependent low-grade inflammation.

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The Predictive Value of Hepatic Stellate Cell Count Used for Assessing Fibrosis and Disease Activity in Patients with Chronic Hepatitis.

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Introduction:

The activation of hepatic stellate cells (HSCs) is a critical event in hepatic fibrosis, a characteristic of most types of chronic liver diseases. The identification of these cells is therefore important to our understanding of the pathogenesis of hepatic fibrosis. The objectives of this study were first to find out if CD38 expression on HSCs can be demonstrated immunohistochemically in liver biopsies from patients with chronic liver diseases and second to find out if CD38 positive HSC count is correlated with Metavir inflammatory and fibrosis scores.

Methods:

Immunohistochemical stainings for áSMA (á-Smooth Muscle Actin) and CD38 expression are performed on 100 liver biopsies from patients with different chronic liver diseases using monoclonal antibodies against CD38 and áSMA. The CD38 and áSMA positive HSCs were identified and counted. áSMA is a known stain for HSC and was therefore used to confirm that the CD38 positive cells were HSC.

Results:

The CD38 positive HSC count , as well as, the áSMA positive cell count was found to be positively associated with both the Metavir activity and fibrosis scores. The CD38 positive HSC count was able to discriminate between no fibrosis and stages 2, 3 or 4 fibrosis but could not discriminate between no fibrosis and stage 1 fibrosis. Using Receiver Operating Characteristic (ROC) curves a cut-off point of 10 HSCs per 10 high power field or 25 per 100 hepatocytes is 80% sensitive and 70% specific for predicting fibrosis. The specificity rose to 100% in patients with HCV.

Conclusions:

We conclude that HSCs can be demonstrated immunohistochemically in liver biopsies and that CD38 positive HSC count is highly predictive of hepatic fibrosis.

Key Words: Hepatic stellate cells; Liver fibrosis; CD38;

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The Hypercoagulable State and Methylene Tetrahydrofolate Reductase (MTHFR), C677T mutation, in Patients with Beta Thalassemia Major in Kuwait.

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Introduction:

Beta Thalassemia major is a relatively common genetic disorder in Kuwait. Thalassemia major patients can present with hypercoagulable state, the pathogenesis of which is vague. Inherited deficiencies of Protein C (PC), Protein (PS), antithrombin (AT); or acquired presence of lupus anticoagulant (LA), in addition to hyperhomocysteinemia, which is related to the prevalence of MTHFR, C677T mutation, have been suggested to be risk factors for hypercoagulability in thalassemia major. This research aims to study these factors on Beta thalassemia major patients in Kuwait to determine whether they are contributory factors to the hypercoagulable state in these patients.

Methods:

We studied certain risk factors of hypercoagulability in 50 Beta thalassemia major patients (mean age 22. 04 years) and 50 apparently healthy controls (mean age 21. 86 years). Coagulation inhibitors PC, PS, AT levels were performed on ACL 9000 analyser. LA was detected by using a manual method. Total plasma homocysteine was analysed by a competitive immunoassay. PCR was done on extracted DNA from samples that were treated with Hinf I restriction enzyme to detect MTHFR, C677T, mutation.

Results:

The natural coagulation inhibitors, PC ($P<0.0001$), PS ($P<0.0001$) and AT ($P=0.0173$) were significantly decreased in the patients. On the other hand, none of them presented with the presence of acquired anticoagulant LA. Only 4% of the patients had hyperhomocysteinemia thus total plasma homocysteine was not significantly higher in thalassemic patients compared to controls ($P=0.60$). 32% patients were heterozygous and 4% were homozygous for MTHFR, C677T, thrombophilic mutations.

Conclusions:

Deficiencies of the natural coagulation inhibitors PC, PS, AT are the most significant risk factors for hypercoagulable state in thalassemia major. As few patients had mutations in MTHFR, C677T mutation and hyperhomocysteinemia, these factors may not be significant contributors to the hypercoagulable state in these patients.

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CD10 expression in follicular patterned thyroid nodules

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Introduction:

Follicular patterned thyroid nodules are a common problem in thyroid pathology and sometimes distinguishing benign from malignant nodules can be challenge. CD10 was studied and founded to be expressed in 79% of follicular patterned malignant thyroid nodules (i. e. follicular carcinoma and follicular variant of papillary carcinoma) and negative in benign counterparts. However, no further evaluation has been done in literature of this stain. Therefore, we conducted this study to evaluate CD10 expression in follicular patterned thyroid nodules

Methods:

Fifty four cases of follicular patterned thyroid nodule were selected from Farwaniya hospital files as follow: Nodular hyperplasia 18 cases, follicular adenoma 16, follicular variant of papillary carcinoma 17 and follicular carcinoma 3 cases. CD10 was tested on one representative block from each case. The stain was reviewed by the two authors to reach an agreement and 10% was considered a cutoff point for positive result.

Results:

The CD10 was expressed in different follicular patterned thyroid nodules as follow: 6/18 nodular hyperplasia, 2/16 follicular adenoma, 4/17 follicular variant of papillary carcinoma and 0/3 of follicular carcinoma. CD10 was expressed in 23. 5% of benign nodules and 20% of malignant nodules.

Conclusions:

CD10 is neither sensitive nor specific for distinguished follicular patterned thyroid nodules.

Key Words: CD10; Thyroid; Follicular;
Funding Agency: None

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Solitary rectal ulcer syndrome: a clinico-pathological study of 13 cases

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Introduction:

Solitary rectal ulcer syndrome (SRUS) is a rare disorder and has a wide spectrum of clinical presentation and variable endocscopic findings. To further characterize the clinical and pathological features, a retrospective, hospital based clinico-pathological study was conductted

Methods:

All cases of SRUS diagnosed at Farwania Hospital, Kuwait between 2002 and 2007 were retrieved. The histological slides were reviewed by two authors to confirm the diagnosis. Immunohistochemical stain for smooth muscle actin (SMA) was performed. The clinical files were reviewed for clinical features and endoscopic findings.

Results:

Thirteen cases were identified 8 males and 5 females. The age range was 15-85. Rectal bleeding, constipation and abdominal pain were the most common clinical presentation and were seen in 92% of cases combined or isolated. Rectal ulceration was the most common endoscopic findings which seen in 61% of the cases. Thirty seven percent of these cases had multiple ulcerations. Two patients (15%) had rectal polyps one of them was multiple. The histological examination revealed that all cases had surface serration, fibromuscular obliteration of lamina propria and crypts distortion. Fifty four percent of the cases had diamond crypts. Ectatic mucosal vessels were a common finding. Postivity for SMA was seen in all examined cases.

Conclusions:

SRUS is a rare disorder and only 13 cases were diagnosed in Farwania hospital over 6 years period. The clinical presentation of our patients is typical for SRUS. The presence of polyps and multiple ulcerations in the endoscopic findings further support that SRU is a misnomer. Surface serration, fibromuscular obliteration and crypts distortion are the most diagnostic features. Presence of Diamond crypts are additional diagnostic feature.

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Does Insulin-like Growth Factor 1 Play a Role between Obesity and Cancer Development in the Kuwaiti Population?

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Introduction:

Insulin like growth factor 1 (IGF1) is a peptide hormone that plays a role in cell cycle progression, proliferation and death. IGF1 stimulates proliferation of several types of cancer cells, inhibits apoptosis and interacts with a variety of molecules that are critically involved in cancer development such as sex steroid hormones, products of tumor suppressor genes and other growth factors. This study examines the association between circulating IGF1 and cancer in the Kuwaiti population.

Methods:

Fasting IGF1 was determined in 237 cancer patients (breast, prostate, and colon) and 123 sex and age matched apparently healthy control subjects. Uni- and multi-variate regression analyses were used to find the associations between IGF1 and other variables (insulin, insulin resistance (HOMA), body mass index (BMI) and waist circumference (WC)) and the Mann-Whitney U test was used to examine the difference in IGF1 levels between cancer patients and control group. The association between levels of IGF1 and cancer risk was determined by calculating the odds ratio (OR) and 95% confidence interval (CI) using binary logistic regression.

Results:

The distribution of IGF1 was positively skewed. There was a very highly significant ($P<0.001$) difference in the levels of IGF1 between cancer patients (median of IGF1 (152 ng/mL, intraquartile range (IR) = 112. 38 ng/mL) and controls (median of IGF1 in control group (189 ng/mL, IR=87 ng/mL). There is highly significant association between IGF1 and cancer (OR (95% CI) = 0. 995 (0. 993-0. 998), $p<0.002$). IGF1 was negatively correlated with BMI and WC with ($r = -0.22$, $p = 0.001$; $r= -0.151$, $p = 0.016$) respectively. In this cohort, IGF1 was not significantly associated with insulin and HOMA-IR.

Conclusions:

We conclude that markers of obesity are the most significant determinants of IGF1. As IGF1 is significantly associated with cancer, we conclude that it may play a role in the link between obesity and risk of developing cancer.

Pathology
Category: Clinical

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Expressions of Estrogen Receptor α and Estrogen Receptor beta in Fine Needle Aspirates from Breast Carcinoma.

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Introduction:

  Estrogen receptor (ER) is one of predictors for response to endocrine therapy in breast cancer. The role of estrogen receptor – α (ERα) has been studied in depth but little is known of the recently discovered estrogen receptor - β (ERβ). Most of the studies on ERβ are on tissue sections. Objective:This study aims to evaluate the expression of ERβ in fine needle aspirates (FNA) and correlate with its expression in tissue sections.

Methods:

  In 38 cases of breast carcinoma with available material for cytohistologic correlation, ERα and ERβ were studied by immunocytochemical methods. Their expression in aspirates and tissue sections were correlated with the cytologic and histologic grade of the tumor.

Results:

  In tissue sections, ERα and ERβ were expressed as nuclear staining in 80% and 90% of the cases respectively. In FNA, ERα and ERβ were expressed in 47% and 45% of the cases respectively and were equally distributed in the different cytologic grades. However, in tissues sections both histologic grade 1 and grade 2 tumors showed greater expression of ERα(Grade 1-81%; Grade 2-100%) and ERβ(Grade 1-94%; Grade 2-100%) as compared to Grade III tumors (ERα-50%; ERβ-70%). In aspirates 30% of ERα negative tumors were positive for ERβ and when both ERα positive and ERβ positive tumors were combined the expression increased to 63% (24 of 38 cases). Also, in tissues 75% of ERα negative tumors were positive for ERβ (p-0. 007).

Conclusions:

 Demonstration of ERβ on FNA smears is feasible by immunocytochemistry and it significantly increases the percentage of ER positive tumors. We recommend that it be incorporated into the panel of prognostic markers studied in FNA of breast cancers. Also, its demonstration may be important as it has been proposed that ERβ may have the potential to become a therapeutic target in the specific subcohort of ERα negative breast cancers.

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Role of Fine Needle Aspiration Cytology in Pediatric and Adolescent Thyroid Tumors

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Introduction:

Thyroid nodules are uncommon in childhood and adolescence, their prevalence being 5-10 times lower than adults, however, the frequency of malignancy among thyroid nodules is higher than in adults. Furthermore, thyroid cancer is the third most common solid tumor in childhood and adolescence in the West. Scarce and controversial data on the role of FNAC in palpable thyroids in the pediatric age group is available. The aim of this study was to determine the usefulness of FNAC in documenting thyroid neoplasms in the pediatric and adolescent patients.

Methods:

Over a period of 15 years (1993 to 2007) the cytology reports of 717 satisfactory thyroid aspirates (64 males and 653 females) performed on children and adolescents (ranging from 4 to 21 years) at Mubarak Al-Kabeer Hospital were reviewed. Aspirates were done in the clinic on palpable thyroids. Forty-five of these were reported as a neoplasm.

Results:

The spectrum of disease seen in the thyroid aspirates included benign follicular cells (4%) goiter (47%), cystic change (2%), hyperplasia (6%), thyroiditis (40%), neoplasms (0. 5%) and miscellaneous lesions (1%). Distribution of the thyroid neoplasm (45 cases) in the age group 4-<12, 12<16, 16-<19 and 19-21 years was 2, 4, 9 and 30 cases respectively and they comprised 0. 3, 0. 6, 1. 3 and 4. 2% of the total aspirates in that age group. There were 41 females and 4 males. In 25(55. 6%), 12(26. 7%), 6(13. 3%) and 2(4. 4%) cases papillary carcinoma, follicular neoplasm, follicular lesion and hurthle cell neoplasm was reported. All the four males in this study were reported to have papillary carcinoma. The clinical presentation was a solitary thyroid nodule in 38 (88. 4%) cases.

Conclusions:

FNAC significantly contributes to the diagnosis of cancer in children and adolescents with palpable thyroid masses. It is a safe technique and is recommend

Key Words: Thyroid neoplasms; Fine needle aspiration cytology; Pediatric and adolescents;
Funding Agency: None

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A Lipid Clinic audit – Do dyslipidaemic patients respond satisfactorily to conventional lipid lowering guidelines?

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Introduction:
 The importance of Lipid Clinics in controlling dyslipidaemia in at-risk populations is not controversial. What is unclear is to what extent these Clinics have been fulfilling these roles. This study was therefore designed to audit the effectiveness of a Lipid Clinic in Kuwait and also determine what biochemical parameters are most sensitive to clinic intervention.

Methods:
 We reviewed the lab data and clinical records of 277(102m, 175f)Kuwaiti patients who presented in, and were followed up at the Lipid Clinic for at least 6 months. Of these patients, 144(52%) were diabetic, comprising 48(33. 3%)males and 96(66. 7%)women. Treatment was with statins alone in 208 and fibrates alone in 69, with additional medications for diabetes and hypertension, as appropriate. The lipid profile(TC, TG, HDL, LDL, non-HDL, apoA1, apoB)and weight were noted at
presentation and on follow-up.

Results:
 In all the patients there was a significant reduction in TC, LDL, non-HDL and apoB($p<0.05$)irrespective of medication deployed. Levels of HDL, apoA1 and weight did not change significantly in the whole group. In subgroup analysis however, HDL levels decreased significantly($p<0.05$)in males–diabetic and non-diabetic, but did not change with treatment in any group of females. On correlative analyses, delta Apo A1(0-6mo)was significantly related to deltaHDL and non-HDL(both $p<0.001$)but not LDL or weight. Similarly, deltaApoB correlated significantly with deltaHDL, non-HDL and LDL all($p<0.001$)but not weight.

Conclusions:
 Current Lipid Clinic guidelines appear effective, even in the short-term, in promoting reduction in circulating levels of TC, non-HDL, LDL and apo B in both diabetic and non-diabetic subjects–these could be satisfactorily monitored with serial apo B levels. The treatments appear less effective in modulating HDL levels or body weight loss, both of which contribute to the atherogenic burden. It is important that Lipid Clinics improve on current modalities for HDL and weight control.

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Differentiating criteria on liver biopsy in the diagnosis of late complications of Living Donor Liver Transplantation

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Introduction:

Potential causes of late liver allograft dysfunction can be difficult to interpret because of overlapping clinical, biochemical, serological and pathological features. More than one lesion can contribute to allograft dysfunction

Methods:

Follow up biopsies and clinical data of 180 cases of living related liver transplantation performed in Wadi El Neel hospital from October 2001 until December 2007 were retrospectively reviewed.

Results:

There were 23 pediatric and 157 adult recipients. Microscopic features were studied and correlated
with the final diagnosis. Differentiating microscopic criteria were identified for the most common and problematic causes of late liver allograft dysfunction, including acute and chronic rejection, recurrent and new-onset viral and autoimmune hepatitis, idiopathic post-transplant hepatitis, and biliary strictures. Results were discussed with Banff Working Group on Liver Allograft Pathology and criteria were finalized by consensus. A discussion of differential diagnosis of such criteria is also presented.

Conclusions:

By clearly defining the differentiating criteria of diagnosis of the late complications of Living Donor Liver Transplantation, the role liver biopsy in identifying such complications is enhanced and lead to improve therapy, and better understanding of pathophysiological disease mechanisms

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Scalp lesions - diagnosis by fine needle aspiration and scrape cytology : HMJCSS experience

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Introduction:

  Scalp lesions are frequently encountered in clinical practice, and when present must be carefully evaluated. A variety of benign and malignant lesions have been reported from the scalp. The aim of
 this study is to assess the effectiveness of Fnac and scrape cytology in the diagnosis of scalp lesions.

Methods:

 A total of 36 cases of scalp lesions subjected to cytological evaluation(FNA/Scrape) over a period
 of 2 years(2006-2007) at HMJCSS were reviewed. The lesions were categorised as nodules and ulcers. Fnac was performed on the nodular lesions while scrape cytology was done on the ulcers. Multiple slides were made and either air dried and stained with Diff-Quik reagent and/or fixed in alcohol and stained by Papanicolaou method. A histologic correlation was available in 5 cases.

Results:

 Seven of the 36 cases reviewed were for scrape cytology and 29 were subjected to fine needle aspiration. There were 21 females and 15 males with age range from 16–75 years. Out of the 36 cases 18 were benign(1 scrape), 15 malignant(5 scrape), and 3 were nondiagnostic(1 scrape). Epidermal inclusion cyst(11), benign lipomatous lesion(5) and one case each of hematoma and tuberculous abscess comprised the benign cases. Of the 15 malignant cases 8 were primary and 7 metastatic. The primary cases included basal cell carcinoma(4), malignant melanoma(2), squamous
 cell carcinoma(1)and dermatofibrosarcoma protruberanse(1). Tumours metastatic to the scalp included one each of Ewing's sarcoma, non-Hodgkins lymphoma of thyroid, colonic adenocarcinoma, ductal carcinoma of breast, chloroma, uterine malignant mixed mullerian tumour
 and an unknown primary.

Conclusions:

  The results of this study demonstrate that cytology is an effective method to evaluate both cutaneous and subcutaneous lesions of the scalp. Fine needle aspiration or scrape cytology should be the diagnostic method of choice for scalp lesions for both patients with and without prior history of malignancy.

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Prevalence and determinants of low HDL-Cholesterol levels in dyslipidaemic patients attending a Lipid Clinic in Kuwait

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Introduction:

Low HDL-cholesterol is a major independent cardiovascular disease risk factor that has been recognized as a therapeutic target in recent guidelines. This study aimed to assess the prevalence of low plasma HDL levels (men <1. 03mM; women <1. 29mM) in dyslipidaemic patients referred to the Lipid Clinic in Kuwait.

Methods:

Anthropometric (weight, BMI, WHR), clinical (medical history, BP) and biochemical parameters (fasting plasma levels of lipids (TC, TG, HDL, LDL) and glucose) were evaluated in a total of 762 patients (384m, 378f). About 61 % of these patients (215 m, 253 f) fulfilled the ATP III criteria for the diagnosis of the Metabolic Syndrome.

Results:

84 % of males were overweight/obese with (mean+/-SD) body wt (81. 4+/-15. 0 kg); BMI (28. 8+/-4. 9 kg/m^2); about 87 % of females were also obese/overweight with (mean+/-SD) body wt 74. 2+/-15. 6 kg and BMI 30. 8+/-6. 3kg/m^2. Additionally, 245 of the 762 patients (32. 2% (with 41% males & 59% females) were diabetic. With respect to low HDL levels in men, the determinants appeared to be: diabetes (diabetic (61%) vs. non-diabetic (57%)) and hypertriglyceridaemia (high TG (67%) vs. normal TG (43%)) but not WC (WC >/=102cm (59%) vs. WC <102cm (58%)). This pattern of low HDL levels was similar in women: diabetic (70%) vs. non diabetic (62%); high TG (73%) vs. normal TG (51%) although WC also appeared to contribute in women (WC >/= 88 cm (65%) vs. WC <88cm (62%)

Conclusions:

Low HDL cholesterol is common in dyslipidaemic patients and associates consistently with other components of the metabolic syndrome (particularly diabetes and hypertriglyceridaemia). The association with WC appears gender specific. Management strategies control should include assessment and correction of these abnormalities in an attempt to reduce atherogenic risk.

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CT guided fine needle aspiration cytology of lung lesions: HMJCSS experience

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Introduction:

 CT guided FNAC is a useful tool for evaluatinglunglesions. In view of the relative paucity of published audit studies on CT guided lung aspirates in Kuwait this study was undertaken to assess the utility of guided FNAC in the diagnosis of lung lesions in HMJCSS

Methods:

 Over a period of one year (2007), 75 CT guided FNA from lung lesions were reviewed. Multiple slides were either air dried and stained with Diff Quik reagent and/or fixed in alcohol and stained by Papanicolaou method. Histological correlation was available in 6 cases.

Results:

 Of the75 total cases 17 were females and 58 males with age range from 23 to 78 years. In 16 cases the aspirate was unsatisfactory. Adequate aspirates (59)were reviewed and categorized as benign not otherwise specified (18;); inflammatory (11); tuberculosis (2) and malignant (38). Nine of the 38 malignant cases were metastatic from sites such as urinary bladder (1); ovary (1); prostate(1); opposite lung (2); larynx(1) & lymph nodes (1) and unknown primary sites (2). The 29 primary lung tumors were further categorized as small cell carcinoma(3); neuroendocrine tumor(3); adenocarcinoma(13); bronchioloalveolar carcinoma (3); squamous cell carcinoma (1); Non Hodgkins lymphoma (1); spindle cell tumor(2)and poorly differentiated carcinoma(3). In 4 of the 6 cases the cyto-histological correlation was consistent. One case of Non small cell carcinoma probably adenocarcinoma, histologically proven to be pulmonary blastoma. A case of squamous cell carcinoma diagnosed by cytology was histologically reported as BOOP. There was no reported major complications with CT- guided lung FNAC except for mild asymptomatic pneumothorax and blood tinged sputum.

Conclusions:

 Our experience in HMJCSS shows that CT-guided FNAC is a useful, simple, safe, cost-effective, rapid and reliable technique in the diagnosis of lung masses

Key Words: CT-Guided; Lung; Fine needle aspiration;
Funding Agency: none

Pathology
Category: Clinical

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Inflammatory and other predictors of atherosclerosis susceptibility in Kuwaiti adolescents: influence of body mass

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Introduction:
 Some markers of inflammatory response (e. g. CRP and adhesion molecules ICAM & VCAM) and oxidant activity (e. g. homocysteine (Hcy) and its determinants, vitamin B12 & folate) have been implicated as predictors of atherosclerosis susceptibility. There is a high prevalence of childhood obesity in Kuwait that constitutes an increased risk for atherosclerotic vascular disease in adult life. This study explores the relationship between body mass and circulating levels of these biochemical risk markers in Kuwaiti adolescents.

Methods:
 We recruited 514 Kuwaiti adolescents aged 10–19 yr randomly from selected schools. 226 of them were non-obese, and 288 overweight/obese. In all subjects, BMI was measured (wt/ ht²), and a fasting blood sample was collected and analyzed for Hcy, vit B12, folate, CRP, ICAM and VCAM.

Results:
 Results of non-obese vs. overweight/obese for each of the parameters:(i)Hcy-6. 6±2. 3 vs. 6. 4±2. 2µM, p NS; (ii)vit B12-median 349 (range132-1196) vs. 299 (136-1177)pg/ml, p<0. 001; (iii)folate-15. 4±4. 4 vs. 15. 0±5. 0ng/ml, p NS; (iv)CRP-0. 03 (0. 01-1. 57) vs. 0. 16 (0. 01-5. 06)mg/dL, p<0. 001; (v)ICAM-230. 1±77. 6 vs. 244. 7± 81. 4ng/ml, p=0. 040; (vi)VCAM-1142. 4±344. 7 vs. 1151. 8± 247. 6ng/ml, p NS. In correlation analysis, BMI had significant (p<0. 01) correlation with Vit. B12(r= -0. 255), folate(r= -0. 18) and CRP(r= 0. 65). Homocysteine, as expected, was significantly correlated with vit B12(r= -0. 30) and folate(r= -0. 42). ICAM had significant correlation (p<0. 05) with Hcy(r= -0. 19), vit B12(r=0. 10), folate(r=0. 12)and CRP(r=0. 1).

Conclusions:
 Predictors of atherosclerosis (CRP, adhesion molecules, not homocysteine) are increased in obese adolescents; There were significant correlations between BMI and ICAM-1 and the other mediators, suggesting possible pathogenetic interconnectivity of these parameters. Apparently healthy Kuwaiti adolescents have elevated levels of atherosclerotic mediators, particular when obese. This is an obvious target for intervention.

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Statistical and immunophenotypic association of chronic lymphocytic thyroiditis with papillary thyroid cancer

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Introduction:

 Papillary thyroid cancer (PTC) is the second most common cancer in Kuwaiti women. It is often associated with thyroiditis but a definite link between the two conditions is still controversial. Objectives: to determine a definite statistical relation between chronic lymphocytic thyroiditis (CLT) and PTC in Kuwait and to evaluate the role of high grade CLT (Hashimoto's thyroiditis (HT)) in the pathogenesis of PTC.

Methods:

 We carried out a retrospective review of 721 cases diagnosed as PTC, Nodular Goiter (NG) and Follicular Adenoma (FA) at Mubarak Al-Kabeer Hospital between the years 1982 and 2005. Grading of chronic lymphocytic thyroiditis was performed using the criteria of Williams and Doniach. Immunohistochemistry using antibodies specific for PTC-associated proteins (CK19, HBME-1, GAL3 and RET) was performed on 50 cases of PTC with different thyroiditis grades and 15 cases of HT.

Results:

 The prevalence of high grade CLT was significantly higher in PTC (35 %) than in patients with NG (11 %) or FA (13 %) ($p < 0.01$). Focal expression of PTC-associated proteins was detected in all cases of HT specifically in the follicular cells with PTC-associated nuclear alterations. Normal follicles were negative for all markers.

Conclusions:

 Significant statistical association exists between CLT and PTC in Kuwait. The PTC-like immunophenotypic changes seen in Hashimoto's thyroiditis suggest that these altered thyroid follicles may represent sites of early focal premalignant transformation in the development of PTC.

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Fine Needle Aspiration Cytology Of Non-Neoplastic Lesions Of The Thyroid In Children And Adolescents: A Fifteen-Year Review Of Cases From Mubarak Al-Kabeer Hospital.

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Introduction:

 Scarce and controversial data on the role of Fine Needle Aspiration Cytology (FNAC) in palpable thyroids in the pediatric and adolescent age is available. Studies point to the increasing prevalence of Hashimoto's thyroiditis/ juvenile autoimmune thyroiditis in this age group. The aim of our study was to document the efficacy of FNAC in the diagnosis of palpable thyroids in the pediatric and adolescent patients.

Methods:

 Over a period of 15 years (1993 – 2007), 11181 patients underwent FNAC of thyroid in the in the cytology laboratory of Mubarak Al-Kabeer hospital. Of these 763 (6. 8%) aspirates were performed on children and adolescents (ranging from 4-21 years). Of these 717 (93. 97%) satisfactory aspirates, 672 (93. 74%) were diagnosed to have a non-neoplastic lesion and 45 (6. 28%) as malignant. The files of these non-neoplastic cases were reviewed.

Results:

 Of the 672 non-neoplastic lesions, 27 (4 %) cases were reported as benign aspirate (NOS), 328 (48. 81%) cases were colloid goiter, including 13 cases with cystic change, 43 (6. 4%) cases as hyperplastic nodule, 266 (39. 6%) cases as thyroiditis and 8 (1. 2%) cases as miscellaneous lesions. Of the 266 cases of thyroiditis, 147 (55. 26%) cases were reported as lymphocytic thyroiditis, 3 (1. 1%) cases as granulomatous thyroiditis and 116 (43. 61%) cases as Hashimoto's thyroiditis/ autoimmune thyroiditis.

Conclusions:

 FNAC is a safe, cost effective diagnostic technique in the evaluation of euthyroid patients in the pediatric and adolescent age group. In our study 48. 8% and 39. 6% of the aspirates showed colloid goiter and thyroiditis respectively.

Key Words: Aspiration cytology; Non-neoplastic lesions thyroid; Pediatric and adolescents;

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Effect of green tea on cellular proliferation and the expression of growth factors in the intestinal mucosa of fasting rats

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Introduction:

In previous studies we showed that green tea protects the intestinal mucosa of fasting rats from free radicals-induced damage. The aim of this study is to understand the role of green tea on cellular proliferation and the expression of growth factors (FGF, IGF, TGF-β) and epidermal growth factor receptor (EGFR) in the intestinal mucosa of fasting rats

Methods:

Three groups of male Wister rats were used (n=12 per group)

G1-Normal controls, on rat chow diet and water ad libitum.

G2-Animals on rat chow diet and water ad libitum were fasting for 3 days (only i. p. 10% glucose 40 ml/day).

G3-2 weeks of drinking green tea solution ad libitum (instead of water) and rat chow then fasted for 3 days.

On day 4 of fasting, the animals were euthanized and 2 inches of jejunum was removed for histological and immunohistochemical analysis of markers of cell proliferation (PCNA, Ki-67), growth factors (FGF, IGF, TGF-β) and EGFR.

Results:

Compared to G2 (fasting) group, the intestinal mucosa of G3 rats showed a significant increase (p<0. 05) in the expression of proliferating markers, PCNA and Ki-67. Of the growth factors, as compared to G2 group, the intestinal mucosa of G3 rats showed a significant increase in the expression of FGF (p=0. 004) and significant decrease in the expression of IGF (p<0. 0001) and TGF-β (p=0. 003). However, there was no significant change in the expression of either EGF or EGFR in G2 and G3 as compared to G1.

Conclusions:

Green tea helps in repairing and maintaining the intestinal mucosa of fasting rats by increasing cellular proliferation, probably by inducing the expression of growth factors such as FGF.

Key Words: Green tea; Fasting; Growth factors;

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Gastrointestinal stromal tumors: A clinicopathological study from Jahra Area

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Introduction:

Gastrointestinal stromal tumors (GISTs) are unique mesenchymal neoplasms of the gastrointestinal tract that characteristically express c-Kit (CD117) protein. To our knowledge, there are very few published reports regarding the clinicopathological profile of GISTs in Kuwait. We undertook this study to analyse the clinicopathologic features of GIST diagnosed in Jahra hospital and to compare our findings with the previously published data from Kuwait.

Methods:

A total of 8 cases of GIST diagnosed during the period of 2000 to 2007 were retrieved from the departmental archives. H&E sections were reviewed and the tumors were categorized into very low risk, low risk, intermediate risk and high risk groups using Fletcher's criteria. Immunohistochemical staining was performed using CD34, CD117, vimentin, desmin, SMA, S-100, neurofilament and NSE.

Results:

The mean age of the patients was 50 years(range 21-84years). There were 3 males and 5 females. Stomach was the most common site (3 cases,) , followed by small intestine (2 cases), rectum (1case), omentum(1 case) and mesentery (1 case). The average tumor size was 6. 62cm(range 3. 5-22 cm). Histologically, 6 cases had predominantly spindle cell morphology and the remaining 2 had mixed spindle and epithelioid cells. Based on standard criteria 4 cases belonged to low risk group, 1 intermediate risk group and 3 high risk group. Both the extraintestinal tumors belonged to high risk group. CD 117 expression was seen in 7 cases (87. 5 %) and CD34 in 5 cases (62. 5 %). The tumors showed smooth muscle differentiation in 3 cases, neural in 4 cases and both smooth muscle and neural differentiation in 1 case.

Conclusions:

The results of the present study are similar to the previously published data from Kuwait: stomach is the most common location; both CD117 and CD34 are useful defining markers. Our female: male ratio was slightly higher and we found that extra intestinal GISTs are more likely to be malignant.

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Hodgkin's Lymphoma: Diagnostic Difficulties in Fine Needle Aspiration (FNA) Cytology.

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Introduction:

Hodgkin's lymphoma (HL) is diagnosed in fine needle aspiration (FNA) smears based on the pathognomonic Reed-Sternberg (R-S) cells and Hodgkin cells in a background of reactive lymphoid cells, myeloid cells, and histiocytes. However, certain non-Hodgkin lymphomas (NHLs) like anaplastic large cell lymphoma (ALCL) and T-cell-rich B-cell lymphoma (TCRBCL) create confusion with HL because of morphological similarities. Since the management protocols of these two entities (NHL vs. HL) are different, we attempted to find out the differentiating clinical and cytomorphological features between the two NHL subtypes on one hand and HL on the other.

Methods:

38 HL and 10 NHL (9 ALCL and 1 TCRBCL) cases with morphological similarities with HL were obtained in a review of FNA smears of 133 lymphoreticular malignancies and 10 cases of atypical lymph node cytology. These groups were compared in respect of various clinical and cytomophological features. Fisher's Exact Test and ANOVA were utilized for finding out the statistical significance.

Results:

Age of ALCL and TCRBCL cases (37.8 ± 13.49 years) did not differ significantly from HL (31.6 ± 18.51 years, $p= 1.000$) but the frequency of extranodal disease in these NHL subtypes (30.0%) was significantly higher than that of HL (2.6%, $p= 0.0245$). ALCL and TCRBCL cases, when compared cytomorphologically with HL, showed higher frequency of pleomorphic blast cells (60.0% versus 0.0%, $p< 0.0001$), Doughnut cells (80.0% versus 21.1%, $p= 0.0010$), and mitotic activity (40.0% versus 2.6%, $p= 0.0048$). In Hodgkin's lymphomas, there was higher frequency of Hodgkin cells (92.1% versus 50.0%, $p= 0.0060$), R-S cells (100.0% versus 60.0%, $p= 0.0011$),), histiocytes (44.7% versus 0%, $p= 0.0086$), and eosinophils (55.3% versus 10.0%, $p= 0.0134$) than those in ALCL and TCRBCL.

Conclusions:

Despite their morphological similarities, nonHodgkin lymphomas like ALCL and TCRBCL differed from Hodgkin's lymphoma in respect certain clinical and most of the cytomorphological features.

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Association of the HPA1 Polymorphism of Platelet Glycoprotein IIIa with risk for Coronary Heart Disease in a Kuwaiti Population

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Introduction:

 Platelets are important in atherogenesis, possibly through changes consequent on their glycoprotein IIIa (GPIIIa) polymorphisms. The human platelet antigen (HPA) 1 polymorphism is the most extensively studied, with 2 allelic isoforms (a and b), and is believed to influence platelet aggregation. Here, using a larger control group in comparison with our previous report on the subject, we have again tested, in a Kuwaiti population, the hypothesis that HPA1 polymorphism associates with increased risk of development of coronary heart disease (CHD).

Methods:

 We studied 2 groups of subjects; Group A: 257 patients who were confirmed with CHD within 24 hr of admission (CHD); Group B: 254 apparently healthy control subjects recruited from the Central Blood Bank (HC). Genotyping was done for all the subjects by the Polymerase Chain Reaction – Restriction Fragment length polymorphism (PCR-RFLP) method. Results obtained for HC and CHD were compared using Fishers' Exact test.

Results:

  HPA-1a1a was the most frequent genotype in both groups, but was present at higher frequencies in HC compared to CHD (75. 5% vs. 83. 0%, p= 0. 04). Additionally, heterozygote genotype 1a1b frequency was significantly higher in CHD (23. 3% vs. 15. 0 %, p=0. 02). In view of the relatively
small numbers of 1b homozygotes (n=8 - 3 CHD, 5 HC), we further assessed if frequencies of 1b carriage (homozygous & heterozygous) differed between HC and CHD. The results indicated that 1b allele carriers were seen in higher frequencies in CHD than in HC (24. 5% vs. 16. 9%, p= 0. 04).
 suggesting a possible association of 1a1b heterzygotes and 1b allele with CHD.

Conclusions:

  Our results suggest that, in the Kuwaiti population: (i) HPA1a1b genotype and 1b allele appear to associate with increased risk for development of CHD; (ii) Homozygous HPA1a genotype possibly confers a protective effect against atherogenesis.

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Process improvement by error management

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Introduction:
Error management is a part of continuous Quality Improvement. A good error management system includes the key elements of detection, documentation, investigation, evaluation, corrective action, communication and prevention. The success of an error management system, however, depends on the people involved in the process. In the Laboratory, errors are usually due to the failure of following written Standard Operating Procedure (SOP). Kuwait Central Blood Bank (KCBB) went through number of changes in error management during the last 10 years to reach the highest level of system improvement. A Report of error is written to provide a process to capture, assess, investigate, and monitor events that deviate from accepted policy or procedure or that fails to meet the requirement of KCBB and other applicable regulations and requirements.

Aim:
The aim is to use the report of error to capture the common causes of errors, and to perform the proper corrective action.

Methods:
Reports were collected and analyzed during the period from January to December 2006. Errors were documented, investigated and a complete follow-up was done. Most of the errors were solved with a thoroughly studied system improvement.

Results:
Results show that more than 80% of errors were managed, controlled, and supported with a comprehensive policy in Quality Plan.

Conclusions:
• Failure to follow written SOP is the most common cause. Therefore SOP must be strictly followed to prevent the occurrence of errors.
• Implementation of Data Management System DMS reduced the wrong data entry errors.
• Error management plays an important role to control and capture the Near miss/ Variance events, which leads to reach highest possible level of safe transfusion service.

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Child abuse in Kuwait

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Introduction:
Child abuse is becoming a serious emerging problem in Kuwait. Every 30 seconds, one child is abused worldwide. In September 2007, KUMSA held a scientific conference entitled Bridging the Know-Do Gap that addressed many controversial issues including child abuse. It was attended mainly by medical students and medical interns.

Methods:
A questionnaire was distributed to the attendees on the specific day that Child Abuse was discussed. The questionnaire asked students about some of their basic knowledge concerning child abuse. Questions in the questionnaire concerned witnessing and reporting abuse, shelter for abused children, and hitting for discipline. One question was about if they experienced verbal, physical, or sexual abuse.

Results:
96 questionnaire were completed. 97. 9% of those who completed the questionnaire declared that child abuse does exist in Kuwait. 7 of the attendees self-reported episodes of abuse and almost all of them by someone they know, be it a parent or a relative. Mostly, all agreed that a safe shelter for the abused children should be available. Moreover, all agreed that a reporting system should be available nationally so when child abuse is suspected it can be reported.

Conclusions:
 Child abuse is increasing but nonetheless its awareness needs to increase as well. People should be on the lookout for any signs of abuse and this can only happen with education. The establishment of the child abuse law is a must if we want the statistics to stop increasing. A national hotline for the child protection authority should be assigned where children or anyone else can report child abuse immediately.

Pediatrics
Category: Undergraduate

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Association of Insulin Delevering Modalities and Regimen with Compliance and Quality of Life in patients with Type 1 Diabetes in Kuwait

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Introduction:
Our hypothesis states that: patients with type 1 diabetes that use insulin pen injectors as a delivery method and the basal-bolus regimen are more compliant to treatment and have better quality of life.

Methods:
A cross-sectional sample survey was conducted in December 2007 covering type 1 diabetes outpatient clinics in 4 general hospitals across Kuwait, in addition to Diabetes Society Clinic in Keifan. Children and adolescents below the age of 18 years were included in the study. Data was obtained through personal interview using a structure questionnaire. Glycosylated hemoglobin, HbA_{1c} %, measurements were provided by the treating diabetologists in each clinic.
Scores were devised to measure the compliance and quality of life in type 1 diabetes patients.

Results:
A total of 130 children with type 1 diabetes were included with a response rate of 95%. Out of the 130 participants 51. 6% used syringes while 48. 4% used pens. With increasing age, patients tended to switch from conventional to basal-bolus regimen. Most of syringe users were following the conventional regimen. Pen users were found to be more compliant to insulin treatment. Also, the basal-bolus regimen had better compliance. Being male or have an older age group was found to improve compliance. HbA_{1c} %proved to be closer to normal range ($< 8. 0$ %)
when patients had a good compliance score, $p < 0. 001$. There was no strong association between compliance to insulin treatment and quality of life.

Conclusions:
The study supported the hypothesis that compliance of children with type 1 diabetes to insulin treatment is improved through using pen injectors and the basal-bolus regimen. Compliance to insulin treatment is enhanced when a patient is male or is of an older age group. However, pen injector use among males is possibly a confounding factor.

Key Words: Diabetes Type 1; Compliance; Quality of Life;
Funding Agency: None

Pediatrics
Category: Clinical

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Measles outbreak in Kuwait: 2007

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Introduction:

  The last outbreak of measles in Kuwait was in 1998; with 90 cases reported. Since then, the national reported cases have been maintained below 20 cases / year. In 2007, 156 cases of measles were reported between January and April. The aim is to describe the epidemiology, clinical features and outcome of children admitted to the Infectious Diseases Hospital with measles.

Methods:

 A retrospective chart review of all patients' ages between 0-12 years admitted with serological evidence of measles during the outbreak period.

Results:

  There were 117 children who presented with measles. Only 86 children (74%) were hospitalized. The outbreak started on January 15th and lasted until April 20th. Majority of the cases (52%) were admitted during the month of February. Seventy five percent of the cases were from Al- Jahra area (North of Kuwait). Seventy percent of children were less than one year of age. The median age is 11 months. The affected nationalities were distributed as follows: Kuwait (52%), Non-Kuwait (20%), Saudi (13%), Arabic (7%), and Asian (2%). The major clinical presentations were: fever (100%), rash (95%), cough (77%), conjunctivitis (31%), and coryza (18%). Symptoms were present for mean of 5 days prior to presenting to medical care. There was history of exposure in 60% of the children, and 75% were non-vaccinated. Mean days of hospitalization was 6 ±3 days. Complications wee present in 30 patients (35%) and included bronchopneumonia (18), pneumonia (5), hepatitis (2) and diarrhea (5). There were 4 children admitted to the ICU. There were no mortalities.

Conclusions:

  Ensuring that the entire population is vaccinated and decreasing the number of susceptible persons in the population are the keys to avoid outbreaks.

Key Words: Measles; Children; Kuwait ;
Funding Agency: None

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L-Ascorbic acid partially nullifies two cycles of cisplatin chemotherapy-induced epididymal damage and spermato-toxicity in a mouse model

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Introduction:

L-Ascorbic acid is an antioxidant with a wide variety of protective roles in vivo. The present study investigates the effects of L-Ascorbic acid on cisplatin-induced damage of epididymis and spermatozoa in a mouse model.

Methods:

Adult male BALB/C mice were used in the present study. One group was treated i. p. with water (control) and four groups with two cycles of 5 days each of cisplatin (1 and 2. 5 mg/kg), with a recovery period of 17 days between the cycles. Among them, two groups were also treated with 10 mg/kg L-Ascorbic acid. One group was treated only with L-Ascorbic acid. All animals were sacrificed within 72h, after the last treatment. The sperm samples were obtained from the epididymis and sperm count, motility and sperm abnormality tests were conducted. The epididymis was processed for microscopical analysis, and structural changes in the head, body and tail region were documented. The data were analyzed by Kruskall-Wallis test and Mann-Whitney 'U' test with the level of significance set at $P<0. 05$.

Results:

The weight of epididymis was decreased in 1 mg/kg and 1 mg/kg + L-Ascorbic acid treated groups, whereas the sperm count, and motility were decreased in both treated groups ($P<0. 05$). L-Ascorbic acid treatment was able to restore the sperm count ($P<0. 05$), but not the sperm motility. The sperm abnormalities were increased in cisplatin treated groups, but recovery following L-Ascorbic acid treatment was seen only at 2 mg/kg dose-level ($P<0. 05$). Structural changes such as nuclear pyknosis, epithelial degeneration, vacuoles in the epithelium and stereocilia disruption were noticed in the epididymis. Immature germ cells and decreased sperm concentration were seen in the tubular lumen.

Conclusions:

Cisplatin at human therapeutic dose-levels adversely affects the structure, number and functions of spermatozoa and the structure of epididymis, and that L-Ascorbic acid only partially protects them.

Key Words: Anticancer drugs; Reproductive toxicity; Testis;

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Imidazoline I1 receptor and α-2 adrenoceptor dependent effects of moxonidine.

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Introduction:

Moxonidine, an imidazoline I1 receptor agonist, effectively reduces blood pressure, particularly in patients with the metabolic syndrome X. However, its administration to heart failure patients was associated with increased mortality despite significant reduction of sympathetic overactivity. Hypothesis was tested that some side effects caused by the stimulation of α-2 adrenoceptors could be responsible for the negative consequences in heart failure patients.

Methods:

Wistar male rats were implanted with telemetric transmitters to monitor blood pressure, ECG, pre-ejection time, respiratory rate, body temperature and animal moving activity. Moxonidine alone as well as in combination with equimolar doses of yohimbine and efaroxan was applied s. c. in 7 successive days. Heart rate and blood pressure variability were calculated with the Wigner-Ville transform. Complex demodulation was used to estimate baroreflex sensitivity.

Results:

Low doses of moxonidine (0. 04, 0. 12, 0. 36 mg/kg) reduced the overall intensity of the cardiovascular autonomic modulation. Sympathetic system was affected more than the parasympathetic system. High doses (1. 08, 3. 24 mg/kg) had stronger sympatholytic activity than the low doses, but the parasympathetic modulation was intensified. Baroreflex sensitivity was increased as well. A dose dependent reduction in the heart rate, myocardial contractility, respiratory frequency and body temperature was registered after high doses. When yohimbine, an α-2 adrenoceptor antagonist, was applied before moxonidine, these effects were not present. However, the sympatholytic effect was blocked only with efaroxan, an imidazoline I1 receptor blocker.

Conclusions:

Higher moxonidine doses have several adverse effects. Dose dependent activation of miscellaneous receptors, i. e. imidazoline I1 and α-2 adrenergic receptors, could be responsible for the different outcomes of moxonidine application.

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Angiotensin-(1-7) Contributes to the Effect of AT1 Receptor Blockers in Reducing Diabetes-Induced Vascular Dysfunction

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Introduction:

Angiotensin (Ang) II plays an important role in the development of vascular complications in diabetes. Ang-(1-7) acts as an endogenous antagonist of Ang II. The aim of this study was to investigate the role of endogenous Ang-(1-7) in mediating the beneficial effects of angiotensin-converting enzyme inhibitors and AT1 receptor blockers (ARBs) in preventing vascular dysfunction in diabetes.

Methods:

6 groups of male Wistar rats were used. Group I: Vehicle-treated control rats. Group II: vehicle-treated diabetic rats (diabetes was induced by an ip injection of STZ). Group III: diabetic rats treated with captopril (300 mg/l in drinking water). Group IV: diabetic rats treated with captopril and an Ang-(1-7) antagonist, A779 (1 mg. kg-1. day-1 ip). Group V: diabetic rats treated with losartan (300 mg/l in drinking water). Group VI: diabetic rats treated with both losartan and A779. Animals were treated for four weeks and at the end of the study, they were sacrificed and the

isolated mesenteric beds were perfused to measure the vasodilator response to carbachol and sodium nitroprusside (SNP).

Results:

The vasodilator response to carbachol was reduced in the mesenteric beds of diabetic rats ($P<0.05$). Inhibition of Ang II synthesis by captopril and blockade of AT1 receptors by losartan increased the vasodilator response to carbachol in diabetic rats. Significant attenuation of the vasodilator response to carbachol was induced by chronic administration of A779 in losartan-treated but not captopril-treated diabetic rats. The vasodilator responses to SNP were similar in all the groups studied.

Conclusions:

Ang-(1-7) partly contributes to the beneficial effects of ARBs in diabetic mesenteric vascular beds.

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Role of Prostaglandin in Mediating the Protective Effect of Angiotensin-(1-7) in Diabetic Renal Vasculature

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Introduction:

Angiotensin-(1-7) [Ang-(1-7)], an endogenous antagonist of Angiotensin II (Ang II), prevents diabetes-induced cardiovascular dysfunction. The aim of this study was (1) to investigate the effect of endogenous Ang-(1-7) in the renal artery of diabetic rats, and (2) to examine the role of prostaglandins (PGs) in mediating Ang-(1-7) renoprotective effect.

Methods:

6 groups of male Wistar rats were used. Group I: Vehicle-treated control rats. Group II: vehicle-treated diabetic rats (diabetes was induced by an ip injection of STZ). Group III: diabetic rats treated with an Ang-(1-7) antagonist, A779 (1 mg. kg-1. day-1 ip). Group IV: diabetic rats treated with an Ang-(1-7) synthesis inhibitor, DX-600 (5 ìg. day-1 ip). Group V: diabetic rats treated with Ang-(1-7) (1 mg. kg-1. day-1 ip). Group VI: diabetic rats treated with Ang-(1-7) and indomethacin
(1 mg. kg-1. day-1 ip). The animals were sacrificed at the end of the four-week study, and ring segments of the isolated renal arteries were mounted to measure changes in tension in response to phenylephrine (PE) (mg/mg tissue weight).

Results:

Induction of diabetes resulted in an increased vascular reactivity to PE in the renal artery segments (P<0. 05). Chronic treatment of the diabetic rats with DX-600, but not A779, resulted in a significant increase in the vasoconstrictor responses to PE. Chronic treatment with Ang-(1-7) produced a significant reduction in PE-induced vasoconstriction. The attenuated vasoconstrictor response to PE in Ang-(1-7)-treated diabetic rats was significantly prevented by indomethacin.

Conclusions:

Endogenous Ang-(1-7) contributes to the vascular responsiveness of the renal artery, and this effect is mediated partly by PGs.

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In Vitro and In Vivo Anti-Inflammatory Effects of Andrographolide: Inhibition of the Release of Cytokines Relevant to Asthma

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Introduction:

Andrographolide is the major active principle isolated from the plant Andrographis paniculata. Pharmacological investigations of the drug have shown that it possesses a strong anti-inflammatory activity. However, the possibility that andrographolide may affect asthmatic inflammation, through inhibition of the release of some mediators involved in the disease, has not been explored. The purpose of this study was therefore to investigate the in vitro and in vivo anti-inflammatory effects of the drug by testing its ability to inhibit the release of cytokines relevant to asthma.

Methods:

The effect of andrographolide was studied in vitro on LPS-induced release of tumor necrosis factor-
α (TNF-α) and granulocyte macrophage colony-stimulating factor (GM-CSF) from
isolated peritoneal macrophages of male BALB/c mice. The effect of the drug on the expression of mRNA for the two cytokines was investigated by RT-PCR followed by agarose gel electrophoresis. In the in vivo study, the effect of the drug on cytokine and cellular content of bronchial lavage fluid was investigated in a mouse asthma model in which mice were immunized and challenged with ovalbumin.

Results:

The LPS-induced TNF-α and GM-CSF release from mouse peritoneal macrophages was inhibited by andrographolide in a concentration-dependent manner (IC_{50}: 0. 6 micro M and 3. 3 micro M, respectively and maximal inhibition at 50 micro M was 77% and 94%, respectively). The drug was as efficacious as dexamethasone, but less potent. The results also showed that the drug suppressed the expression of mRNA for the two cytokines, suggesting that this effect may contribute to its mechanism of action. In the in vivo study, treatment of ovalbumin-sensitized mice with intraperitoneal andrographolide dose-dependently inhibited ovalbumin-induced elevation of TNF-α and GM-CSF levels, as well as accumulation of eosinophils and lymphocytes, in the bronchial lavage fluid.

Conclusions:

These results, therefore, provide evidence that andrographolide is an effective anti-inflammatory drug that is active in vitro and in vivo, and affects non-specific as well as inflammation resulting from antigen-antibody interaction. Thus, andrographolide has the potential to be used as an anti-asthmatic drug as well as in other inflammatory conditions.

Pharmacology and Toxicology
Category: Basic Sciences

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Evaluation of the Random Amplified Polymorphic DNA (RAPD) for the detection of DNA damage and genotoxicity effect of oil polluted desert soil in Kuwait

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Introduction:
 A huge amount of oil-contaminated soil remains unremediated in the Kuwait desert with potential to cause pollution and to affect the health of people in the neighborhood. The effects of environmental pollutants on organisms may be monitored in a number of ways and at different levels. In the case of genotoxic chemicals, the effects on the DNA may be monitored using a number of assays. Recent developments in molecular biology such as DNA fingerprinting and gene amplification by the polymerase chain reaction (PCR) offer new possibilities for detecting DNA damage.

Methods:
 We investigated, whether an alternative assay can reveal differences in the DNA fingerprints of sample from control and polluted areas investigated. We investigated the feasibility and potential usefulness of an integrated approach to genotoxicity analysis of oil contaminated soil. The approach employed the RAPD assay to evaluate the DNA damage produced by soil extracts in bacterial cells.

Results:
 Extracts of uncontaminated and contaminated soil were incubated with E. coli bacterial cells. Four oil-contaminated locations were tested and 8 soils were sampled from these various sites of oil-contaminated soil in Kuwait and tested for genotoxicity to bacterial cells. The results indicate that DNA fingerprinting by arbitrarily primed PCR offers a useful alternative biomarker assay for detection of the genotoxic effects of oil contaminated soil. The changes occurring in RAPD profiles following genotoxic treatments that are seen included variation in band intensity, appearance of new bands, loss of bands and increase in band intensity were also evident in the RAPD profiles generated by the soil extracts.

Conclusions:
 In this study, we established that the oil contaminated desert soil could support chemicals with genotoxic potential and that the random amplified polymorphic DNA (RAPD) assay could be used to detect genotoxicity potential of oil contaminated soil.

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Micro-array based transcriptome analysis reveals global gene upregulation associated with kidney damage in DOCA-salt-induced hypertensive rats occurs via signaling cascades involving epidermal growth factor receptor and RasGTPase.

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Introduction:

End organ damage including renal dysfunction is a natural consequence of hypertension. In an attempt to understand the molecular mechanisms leading to renal dysfunction, we analyzed global gene expression changes in the kidneys of deoxycorticosterone acetate (DOCA)-salt–induced hypertensive rats with and without treatment with AG1478, an inhibitor of epidermal growth factor receptor tyrosine kinase (EGFR), or with FPTIII, an inhibitor of RasGTPase.

Methods:

Microarray-based global gene expression analysis was performed in triplicate for each rat kidney taken from the following four animal groups: 1) Normal (non-hypertensive) Wistar rats, 2) DOCA-hypertensive (DH) rats, 3) DH rats treated with AG1478 and 4) DH rats treated with FPTIII. Amersham Codelink arrays housing 10, 000 rat genes were hybridized with RNA taken from rat kidney samples as per manufacturers' instructions. Microarrays were scanned using an Affymetrix Scanner and data analyzed using Imagene and Genowiz (Ocimum Biosolutions) softwares.

Results:

Upregulation of 2398 genes and downregulation of only 10 genes by more than 2-fold was observed in hypertensive rat kidneys compared to non-diseased controls. Interestingly, treatment of animals with AG1478 or FPTIII prevented up-regulation of all of genes associated with hypertension in the rat kidney implying that EGFR and RasGTPase signaling are important mediators of renal damage in hypertension. Histopathological examination confirmed that renal damage induced by hypertension was prevented following treatment with either AG1478 or FPTIII.

Conclusions:

EGFR and RasGTPase-mediated signaling appear to be important cascades leading to multiple gene changes that ultimately cause renal dysfunction and end-organ damage in hypertension. Therapeutic strategies inhibiting either of these signaling molecules may represent novel paradigms for the treatment of renal disease associated with hypertension.

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Angiotensin 1-7 modulates PPAR-γ in kidneys of diabetic spontaneously hypertensive rats: Role of peroxisomes

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Introduction:

 Peroxisome proliferators activated receptors (PPAR) are a novel class of nuclear receptors and PPAR γ is the therapeutic target of several diabetic drugs. Recently antihypertensive drugs such as ACE inhibitors (ACEI) and angiotensin receptor blockers (ARBs) have been reported to modulate PPAR γ. We have therefore investigated the effect of angiotensin1-7 (Ang-(1-7)), an antidote of angiotensin II (Ang-II), on PPAR γ in diabetic hypertensive rats.

Methods:

 Diabetic and non-diabetic WKY and SHR were treated with Ang-(1-7) and kidneys subjected to RT-PCR for measurement of PPAR γ mRNA levels. Enzyme activities of key peroxisomal enzymes, catalase and acyl CoA oxidase were also assayed in the kidney homogenates.

Results:

 RT-PCR analysis revealed that kidneys of diabetic and SHR had significantly ($p < 0.05$) lower levels of PPAR γ mRNA as compared to WKY rats. Treatment with Ang-(1-7) markedly attenuated the diabetes- or hypertension-induced down regulation of PPAR γ. Angiotensin 1-7 treatment significant increased catalase activity in WKY rats and alleviated inhibition of catalase in diabetic hypertensive rats. Ang-(1-7), however had no significant effect on the diabetes- and hypertension-induced elevation of acyl CoA oxidase activity.

Conclusions:

 These results suggest that Ang-(1-7) besides its known antihypertensive effects might also be exerting antidiabetic and antioxidant effects via activation of PPAR γ and catalase respectively.

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Prostaglandins Contribute to the Cardioprotective Effect of Angiotensin-(1-7) in Diabetes

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Introduction:

Diabetes is a major predisposing factor to cardiovascular disorders like myocardial infarction and hypertension. Angiotensin-(1-7) [Ang-(1-7)] exerts vascular and cardio-protective effects in various
animal models of ischemia/reperfusion. This study examined the role of prostaglandins in mediating the cardioprotective effects of Ang-(1-7) in the diabetic heart.

Methods:

Wistar male rats were used and divided into four groups. Group 1: Vehicle-treated control animals [C], Group 2: Diabetic animals [D], Group 3: Diabetic treated with Ang-(1-7) [D+Ang-(1-7)], Group 4: Diabetic treated with Ang-(1-7) and indomethacin (Indo) [D+Ang-(1-7)+Indo]. Diabetes was induced by an ip injection of streptozotocin. Animals in groups 3 and 4 received their treatment starting on first day of inducing diabetes and were sacrificed after 4 weeks. Hearts were isolated, mounted on a Langendorff Perfusion Assembly and exposed to 30 min perfusion followed by 40 min ischemia and 30 min reperfusion.

Results:

Table 1: Mean % post-ischemic recovery of LV contractility and hemodynamics.

Group	Pmax	LVEDP	CF	CVR
C	54±2	337±19	48±2	263±13
D	5±1. 7*	665±36. 9*	9±1. 3*	635±39. 2*
D+Ang-(1-7)	22±2#	471±19#	24±2#	551±22
D+Ang-(1-7) + Indo	11±1. 8†	620±19. 6†	13±2†	662±24

Pmax: maximum developed pressure, LVEDP: left ventricular end diastolic pressure, CF: coronary flow, CVR: coronary vascular resistance. *Value significantly different compared to C, #value significantly different compared to D, value significantly different compared to D+Ang-(1-7).

Conclusions:

The beneficial effect of Ang-(1-7) in reducing cardiac dysfunction in diabetes is mediated partly by prostaglandin release.

Key Words: Prostaglandins; Angiotensin-(1-7); Cardiac dysfunction;

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Role of Angiotensin-(1-7) in Mediating the Cardioprotective Effect of Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers

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Introduction:

 Angiotensin-(1-7) [Ang-(1-7)] has been found to exert vascular and cardioprotective effects in various animal models of ischemia/reperfusion. This study examined the role of Ang-(1-7) in mediating the cardioprotective effects of angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARBs) in the diabetic heart.

Methods:

 Wistar male rats were used and divided into 6 groups. Group 1: Vehicle-treated control animals [C], Group 2: Diabetic animals [D], Group 3: Diabetic treated with captopril (Cap) [D+Cap], Group 4: Diabetic treated with Cap and A779 [D+Cap+A779], Group 5: Diabetic treated with losartan (Los) [D+Los], Group 6: Diabetic treated with Los and A779 [D+Los+A779]. Diabetes was induced by an ip injection of streptozotocin. Groups 3 to 6 received their treatment starting on first day of inducing diabetes and were sacrificed after 4 weeks. Hearts were mounted on a Langendorff Perfusion Assembly and exposed to 30 min perfusion followed by 40 min ischemia and 30 min reperfusion.

Results:

 Table 1: Mean % post-ischemic recovery of LV contractility and hemodynamics.

Group	Pmax	LVEDP	CF
C	54±2	337±19	48±2
D	5±1.7*	665 ± 36.9*	9±1.3*
D+Cap	20±1.7#	503±19#	22±2.4#
D+Cap+A779	16±1.2##	579±16.6##	18±1.2
D+Los	19±1.3#	530±21.9#	18±1.2
D+Los+A779	11±0.6†	635±14.7	12±1.6

Pmax: maximum developed pressure, LVEDP: left ventricular end diastolic pressure, CF: coronary flow. *Value significantly different compared to C, #value significantly different compared to D, ##value significantly different compared to D+Cap, †value significantly different compared to D+Los.

Conclusions:

 These results suggest that Ang-(1-7) contributes to the cardioprotective effect of ACEI and ARBs in diabetes.

Key Words: Diabetic heart; Captopril; Losartan;

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Accidental Poisoning Among Children with Pharmaceuticals and Chemical Agents in Kuwait: A Retrospective Survey

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Introduction:

 Accidental poisoning by pharmaceutical and chemical agents in childhood is a worldwide problem and one which is amenable to public health preventive measures. Past studies in Kuwait have suggested differences in admission rates and pattern of poisoning at general hospitals which could impact on the implementation of public health interventions. The objective was to compare the admission rates, case demographics and pattern of poisoning in pediatric patients at public general hospitals in Kuwait.

Methods:

 A retrospective survey of all pediatric (Less than 12 yrs) poisoning cases at the six main government general hospitals in Kuwait was carried out for January 2004 to December 2005. Patient demographic data, toxic exposure details and case presentation were documented.

Results:

 A total of 978 children were admitted due to poisoning. The median age was 2. 3 years and 92. 4%
 were five years of age or younger. Just over half the cases were male and 70. 9% Kuwaiti. 64. 6% were poisoning from medicines, 35. 4% with chemicals with the remainder due to other causes. Jahra, Sabah and Amiri hospitals had the highest proportion of chemical-related cases (39. 8%, 45. 8%, 47. 6% respectively) with kerosene a major problem at Jahra hospital (35. 2% of chemical exposures). The most common medicine exposures involved non-opioid analgesics (22. 3% of medication exposures) with hormones and drugs affecting the autonomic nervous system also common.

Conclusions:

 Case demographics do not vary significantly between the hospitals but there are differences in the nature of toxic agents to which children are exposed. This suggests that public health interventions may need to be tailored to local needs. Continuous education of parents of young children is important to reduce the chances of accidental poisoning.

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Anti-inflammatory Effect of Some Novel Enaminones – Inhibition of LPS-stimulated TNF-α Release from Mouse Peritoneal Macrophages

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Introduction:

The enaminones are synthetic amino compounds whose structures contain a ketone group adjacent to a carbon-carbon double bond. In addition to their use as synthetic intermediates, enaminones have been shown to display a range of pharmacological activities such as anti-convulsant, Pgp modulatory, histaminergic, and molluscicidal activities. However, relatively little is known about their possible anti-inflammatory effect. The purpose of this study was to screen a series of novel enaminones for anti-inflammatory activity in vitro and to explore their mechanism of action.

Methods:

The ability of the studied enaminones to inhibit lipopolysaccharide (LPS)-induced TNF-α release from peritoneal macrophages isolated from male BALB/c mice was determined as index of anti-inflammatory activity. TNF-α release was measured by enzyme-linked immunosorbant assay (ELISA) method. Possible inhibition of TNF-α mRNA expression by enaminones was studied using molecular biology techniques.

Results: α

Of the 17 compounds tested, 3 (BRG12, BRG13, and E166) were found to be active in inhibiting TNF-α release in vitro, with IC_{50} values of 4. 2, 4. 6, and 0. 9 μM, respectively, and almost complete inhibition by all the 3 compounds at 30 μM. These 3 active compounds were the only ones characterized by the presence of NH-NH functional group in their structure. Dinitrobenzyl-substitution on the simple aromatic ring attached to the amino group resulted in complete loss of activity. The anti-inflammatory activity of enaminones could not be explained by induction of cell death and was characterized to be reversible and appeared to be exerted at the early stages of cell activation. However, LPS-induced TNF-α mRNA upregulation was unaffected.

Conclusions:

These results show for the first time that some enaminones, especially those with NH-NH functional group, possess strong anti-inflammatory effect exerted on cytokine production in vitro, but this effect is not a result of inhibition of TNF-α expression at the mRNA level.

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Discovery of a novel pharmacological action for Q8-KU001: A drug with in vitro and in vivo bronchodilator activity

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Introduction:

β_2 bronchodilator therapy is one of the main stay treatments for respiratory diseases such as asthma and although they are relatively effective, their use has downsides such as tachyphylaxis and also associated with increased death. There is therefore a need for equipotent drugs with less risk. The objective of this study is to investigate the bronchodilator effect of the novel drug Q8-KU001.

Methods:

Bronchioles were isolated from guinea pigs and mounted in an organ-bath set-up to record isometric contractions. Cumulative concentration response curves (CRC) to salbutamol (10^{-9}- 3×10^{-4} M) or Q8-KU001 (10^{-9}-10^{-4} M) were established after pre-contracting the bronchioles with carbachol (3 microM), and repeated after one hour. The effects of the two agonists were tested after incubating the bronchioles with 1 microM of propranolol or glibenclamide for 60 mins. Bronchodilator activity of Q8-KU001 was also assessed, in vivo, using a citric acid-induced airway obstruction guinea pig model in a whole body plethysmograph set-up.

Results:

Results form in vitro experiments are summarised in table 1. Results from in vivo experiments showed that pre-treatment with Q8-KU001 dose dependently inhibited the citric acid-induced airway obstruction in guinea pigs.

Table 1

	-Log EC$_{50}$
E121	-7. 3+/-0. 1
E121 Repeated	-6. 8+/-0. 2#
E121+ Propranolol	-6. 4+/-0. 2#
E121 + Glibenclamide	-6. 7+/-0. 2#
Salbutamol	-7. 7+/-0. 1
Salbutamol Repeated	-6. 3+/-0. 1*
Salbutamol + Propranolol	-5. 6+/-0. 1*
Salbutamol + Glibenclamide	-7. 3+/-0. 2

significantly different compared to E121, * significantly different compared to salbutamol, $p < 0.05$. EC$_{50}$ indicates the log of Molar concentration of the agonist required to reduce the induced tone by 50%.

Conclusions:

These results show that Q8-KU001 has a bronchodilator activity, both in vivo and in vitro, and also exhibits less tachyphylaxis than salbutamol. Q8-KU001 induces bronchodilation via both $\beta2$ receptors and K$_{ATP}$ channels.

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Angiotensin-(1–7) Prevents Activation of NADPH Oxidase and Renal Vascular Dysfunction in Diabetic Hypertensive Rats

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Introduction:

Overproduction of reactive oxygen species is associated with renal dysfunction in diabetics and hypertensives. The objective of this study was to examine the influence of chronic treatment with angiotensin-(1-7) [Ang-(1-7)] on renox (renal NADPH oxidase, NOX-4) and the development of renal dysfunction in streptozotocin (STZ)-treated spontaneously hypertensive rats (diabetic SHR).

Methods:

Male SHR and WKY rats were used in this study and divided into five groups (n = 15/group): group 1, WKY; group 2, SHR; group 3, SHR treated with Ang-(1–7) (576 μg/kg/day i. p.); group 4, STZ-treated SHR; group 5, Ang-(1–7)-treated diabetic SHR. Diabetes was induced by a single intraperitoneal injection of 55 mg/kg body weight STZ. At the end of the 4-week treatment period, NADPH oxidase activity, mean arterial pressure (MAP), urinary protein and vascular responsiveness of the isolated renal artery to vasoactive agonists were studied.

Results:

Ang-(1-7) decreased the elevated levels of renal NADPH oxidase (NOX) activity and attenuated the activation of NOX-4 gene expression in the diabetic SHR kidney. Ang-(1-7) treatment increased sodium excretion but did not affect MAP in diabetic SHR. There was a significant increase in urinary protein (266 +/- 22 mg/24hrs) in the diabetic compared to control SHR (112 +/- 13 mg/24hrs) and treatment of diabetic SHR with Ang-(1-7) reduced the degree of proteinuria (185 +/- 23 mg/24hrs, p<0. 05). Ang-(1-7) treatment also attenuated the diabetes-induced increased in renal vascular responsiveness to endothelin-1 and norepinephrine in SHR, and significantly increased the vasodilation of the renal artery of SHR and diabetic SHR to the vasodilator agonists.

Conclusions:

These results suggest that treatment with Ang-(1-7) constitutes a potential therapeutic strategy to alleviate NOX-mediated oxidative stress and reduce renal dysfunction in diabetic hypertensives.

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Pharmacological characterization of theophylline derivatives as putative nootropic agents.

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Introduction:

Dementias, e. g. Alzheimer's disease, are characterized by pathophysiological changes in the cortex
and hippocampus that are associated with impairment in memory and other cognitive processes. We tested the hypothesis that theophylline analogs may be cognitive enhancers by examining their ability to modify population spikes (PS) in the hippocampus, a region that is involved in memory and cognitive processing. TH analogs with different carbon chain length (m=2-4) substitutions bearing different terminal rings on the nitrogen at position 7 of the theophylline ring were tested including terminal hexahydroazepin-2-ones: TH-9 (m=4), TH-8 (m=3) and TH-7 (m=2); piperidin-2-one: TH-6 (m=4) and pyrrolidin-2-ones: TH-3 (m=4) and TH-1 (m=2).

Methods:

350 um coronal slices of the forebrain containing the hippocampus were generated from male rats. Evoked, population spikes were recorded extracellularly in current clamp mode using NaCl-filled electrodes.

Results:

TH-9, TH-8 and TH-7 all increased PS amplitude by 56. 5±18. 0%, 42. 4 ±14. 2%, 40. 9±14. 0%, respectively. TH-3 and TH-1 had no effect(6. 4±4. 4% and 2. 0±2. 4%), while TH-6 caused a reversible depression of -25. 9±4. 6%. TH-9 and TH-6 effects were concentration-dependent with estimated EC50 values of 2. 0uM and 0. 06uM, respectively. The effect of TH-9 was blocked by atropine (0. 2±2. 8%) and d-tubocurarine (-2. 5 ±2. 8%) but not by CGP55845(55. 4±15. 5%)or CPT(47. 9 ± 22. 7%). The effect of TH-6 was blocked by CGP55845(1. 7±10. 5%) but not by CPT(-27. 6 ± 6. 5%).

Conclusions:

Our data indicate that the carbon chain length does not affect the neuroactivity of these compounds. By contrast, the terminal ring substituent on the carbonyl group strongly influences neuroactivity and the type of effect produced. The hexahydroazepin-2-ones cause enhancement, piperidin-2-ones cause inhibition while pyrrolidin-2-ones are devoid of neuroactivity. Therefore, hexahydroazepin-2-one analogs have potential use as cognitive enhancers.

Key Words: Hippocampus; Cholinergic mechanisms; Population responses;
Funding Agency: None

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Potassium bromate - induced thyrotoxicity in adult albino rats and the protective effect of Resveratrol

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Introduction:

Potassium bromate ($kBrO_3$) is widely used in cosmetics and food products. It is carcinogenic in rat thyroid. It is known to be an oxidizing agent. Resveratrol (R) is a natural polyphenolic compound present in several plant derivatives including mulberries, peanuts, grapes, pines and legumes. It is known to have antioxidant and antitumour activities. The aim of this study was to examine the effects of resveratrol on thyroid stimulating hormone (TSH), tetraiodothyronine and histopathology of thyroid tissue induced by potassium bromate.

Methods:

This study was conducted on 40 adult male albino rats randomly divided into 4 equal groups. First group was used as a control, second group (R), third group (potassium bromate) and fourth group (R+ potassium bromate). Rat in (R), potassium bromate and (R+ potassium bromate)were given Resveratrol (10 mg /kg) , potassium bromate (30 mg/kg) and Resveratrol (10 mg/kg) plus potassium bromate (30 mg/kg) orally once daily all for 12 weeks. After that, rats were anesthetized, blood samples were collected for biochemical analysis and thyroid glands were obtained for histopathological examination by light and electron microscopes.

Results:

In potassium bromate group TSH was higher, while tetraiodothyronine was lower than the control group ($p < 0.001$) for both. In (R+ potassium bromate) group, both TSH and tetraiodothyronine moved toward normal compared to potassium bromate group ($p < 0.001$) for both. Light microscopical examination of the thyroid of potassium bromate group showed severe damage of thyroid follicles with cellular infiltration. Electron microscopical examination showed distorted thyroid follicles, apoptotic nuclei and fragmented rough endoplasmic reticulum. In (R+ potassium bromate) group, most of thyroid follicles were preserved and full of colloid substance.

Conclusions:

It can be concluded that resveratrol protects against thyrotoxicity induced by potassium bromate in adult albino rats.

Key Words: Resveratrol; Potassium Bromate; Thyrotoxicity;
Funding Agency: none

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Higher dose of enteric coated mycophenolate sodium (EC-MPS) in kidney transplantation; tolerability, efficacy and pharmacokinetic correlation.

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Introduction:
 EC-MPS is known to improve mycophenolic acid (MPA) related gastrointestinal (GI) symptoms with therapeutic equivalence to mycophenolate mofetil (MMF) in kidney transplant recipients (KTRs). The aim of the study is to assess the effect of higher dose of EC-MPS on its efficacy, tolerability and pharmacokinetic properties.

Methods:
 Twenty two KTRs were randomly selected to receive either 50% increased dose of EC-MPS 1080 mg bid (study group, n=10) or regular dose of MMF 1000 mg bid (control group, n=12) in addition to prednisolone and cyclosporine as triple immunosuppressive therapy. Rejection in the first 3 months post transplant was taken as a parameter of efficacy while GI disorders, hematological abnormalities and infections were used to assess tolerability. A severity score system was used to assess GI disorders. Pharmacokinetic profiles were performed in 6 patients in each group to compare MPA trough concentration (C0), maximum concentration (Cmax), time to maximum concentration (Tmax) and area under the concentration curve (AUC) for both drugs.

Results:
 Four patients in EC-MPS group had acute rejection versus one in MMF group. None of them lost the graft. Eight patients (80%) on EC-MPS versus 6 patients (50%) on MMF developed GI symptoms with severity index of 0. 32 versus 0. 11 respectively. Dose reduction due to adverse events was attempted 1. 4 times per patient on EC-MPS versus 0. 42 per patient on MMF. AUC was 39 ug. h/ml for EC-MPS group versus 23 ug. h/ml for MMF group (p=0. 004). C0 (1. 59 versus 0. 69 ug/ml, p=0. 049) , Cmax (9. 87 versus 5. 85 ug/ml, p = 0. 011) and Tmax (2 versus 1 hour, P = 0. 001) were significantly higher in EC-MPS compared to MMF groups respectively.

Conclusions:
 Higher dose of EC-MPS was associated with reduced tolerability and efficacy. Higher AUC and/or Cmax in the study group could be the reason for increased adverse events.

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Therapeutic Drug Monitoring: A time to change the current practice.

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Introduction:

Standards for Therapeutic Drug Monitoring (TDM) must address the factors required for a valid TDM result. That is test ordered with an appropriate indication, samples obtained at the appropriate time, analysis is precise and accurate, and the result interpreted in right clinical context. Indications for ordering drug concentrations are to assess patient compliance, lack of response, adverse effects, initial or new baseline concentration after steady state has been achieved and drug interactions. Interpretation of TDM results requires data related to patient (age, sex, weight, ethnicity, disease state, etc) and drug (pharmacokinetics, dosage regimen, interactions) so that the deviation from the normal therapeutic range can be ruled out and most effective dose determined.

Methods:

A retrospective study was conducted in RNLMC to asses the manner of TDM requesting. Results obtained after analysis of drugs (Amikacin, Aminophylline, Carbamazepine, Digoxin, Paracetamol, Phenobarbital, Phenytoin, Valproic Acid, Vancomycin) were scrutinized for the data given on the form for one month. The data included Clinical diagnosis, date and time of Sample collection after last dose, Subject's demographics (age, sex, weight, ethnicity) and the hospital wards from where the request was raised. The data was sorted and pie charts generated to give a concise picture of TDM requesting.

Results:

It was observed through the study that 54% of the TDM request forms had no time of sample collection specified, which is the most important factor required for interpretation of the result. Also data related to patient's demographics, other disease states, comedications given and dosage regimen (dose, dosing interval and frequency) was absent.

Conclusions:

The aim of this study was to highlight and change the current practice of requesting TDM so that the process is completed in more qualitative and economical manner achieving its ultimate goal i. e. Effective Therapeutic Management.

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Toxicogenomics of cationic delivery systems: the influence of polymer architecture on genocompatibility and siRNA-mediated gene silencing

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Introduction:

Short interfering RNA (siRNA), a Nobel prize winning technology, is being evaluated in clinical trials for the silencing of disease-causing genes. However, siRNAs are macromolecular polyanions that require efficient delivery systems for efficacy in target tissues. Recent toxicogenomics studies have shown that delivery systems are not biologically inert but can markedly alter gene expression in cells. Here, we show that the delivery system-induced toxicogenomic fingerprint is dependent on the architecture of the cationic delivery system.

Methods:

Human A431 epithelial cells were exposed to different architectures of three different polymer delivery systems and their global gene expression profile analyzed 24h later using micro-array based transcriptome profiling. For in vivo studies, linear (L) or branched (B) polyethylenimine (PEI) architectures were directly administered to A431 xenografts and microarray-based transcriptome analyses performed 24h later.

Results:

The L and B architectures of PEI elicited multiple but markedly different gene expression changes in A431 tumour xenografts. A comparison of fractured and intact generation 6 polyamidoamine (PAMAM) dendrimer architectures led to markedly different gene changes in A431 cells that in some cases (e. g. epidermal growth factor receptor (EGFR) expression) actually led to opposing effects on gene and protein expression. Subsequent evaluation of these PAMAMs for siRNA-mediated gene silencing showed that the apparent potency of an anti-EGFR siRNA could be enhanced 10-fold when using the architecture that also inhibited EGFR expression.

Conclusions:

Cellular recognition and toxicogenomic response is determined by delivery system architecture. Separate to enhancing cellular uptake, delivery system-induced gene changes can also alter the apparent gene silencing potency of siRNA and thus, the 'genocomptibility' of delivery system should be studied prior to use with siRNAs in the clinic.

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Formulation of sustained release ketorolac tromethamine

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Introduction:

Because of the short biological half-life of the potent nonsteroidal anti-inflammatory Ketorolac tromethamine (KT), frequent dosing of KT is necessary to maintain a therapeutic effect. The objective of this work is to prepare sustained release formulation to reduce side effects and improve patient's compliance.

Methods:

Non-pariel were initially coated with Eudragit®-RS. KT solution; containing Eudragit- RL/RS, talc, and propyl gallate, was then applied onto the non-pariel pellets in coating pan. KT pellets (2 mm) were coated using different proportions of Eudragit®-RL and Eudragit®-RS. Drug content and drug release was measured spectrophotometry at 323 nm. The pellets were stored at 40degreeC/75%RH, 30degreeC/70%RH, and shelf conditions. The pellets were assessed physically and chemically, by stability-indicating HPLC method, to evaluate the effect of various storage conditions.

Results:

Drug release followed the orde: Eudragit®RS<RL: RS; 1:3<RL: RS; 1:2<RL. Eudragit®-RS generally reduced drug release. Formula-III (RL: RS of 1:3) showed KT-extended release over 12 h. KT release followed Higuchi diffusion controlled model. Storage of the selected formulation at 40degreeC/75% RH resulted in a color change from white to yellowish white ending with dark yellow pellets after three months of storage. Flow of such pellets was diminished, which could be attributed to the elevation of moisture content from 2. 29% to 2. 99% after two months. The storage at 25degree C/60%-RH maintained the physical parameters, under 40degree C/75%-RH, resulted in acceleration of drug release, which is attributed to the elevated moisture content of the pellets. Storage of pellets at 30degree C/ 70% RH did not result in appreciable change in the dissolution characteristics. Storage of the prepared pellets under the three conditions of temperature and % RH didn't affect the chemical stability of the drug.

Conclusions:

The proposed formulation provided sustained KT-release over 12 hours and characterized by good physical and chemical stability.

Key Words: Ketorolac; Non-pareil; Sustained release;

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Preparation and In- Vitro Evaluation of Extended Release Aspirin Tablets Using Air Fluidization Technique

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Introduction:

Aspirin is a potent inhibitor of both prostaglandin synthesis and platelet aggregation. Sustained release formulation decreases gastrointestinal side effects encountered with regular oral preparations. The aim of this work was to prepare modified release aspirin tablets based on ethyl cellulose coated aspirin particles using air fluidization technique.

Methods:

Factorial design (8 trials) was constructed to study the effect of coating process variables on ethyl cellulose-coated aspirin microcapsules. Factors investigated; %-weight gain (2. 4-5%), concentration of polymer coating solution (1. 2-5%), air temperature (40-60°C) and sparying rate (3-7 mL/min). The properties of the prepared microcapsules were assessed and compared to commercial product. Tablets were prepared by direct compression employing the developed coated aspirin microcapsules. The physical properties, release and free salicylic acid content were investigated; in comparison with reference commercial tablets.

Results:

The hardness of the tablets of all the prepared trials is generally higher than that of the commercial reference tablets. All trials, except trial VII and III, showed slower release patterns compared with the reference tablets, where trial VII showed a faster release pattern with a 100% release after only 90 minutes. Trial III tablets exhibited almost identical release profile to the reference product. The free salicylic acid content of trial III is 0. 22% compared to 0. 15% for the reference product.

Conclusions:

The conditions adopted in the formulation of particles of trial III were the best among all the conditions in preparing a product having a similar release profile as the reference (1. 2% coating solution concentration, 2. 4% weight gain, 40°C fluidization air temperature and 3ml/min. spraying rate).

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Synthesis and antibacterial activity of piperazinyl oxazolidinones containing 5-(4-methyl-1, 2, 3-triazole)

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Introduction:

 The bioisosteric replacement of the 5-acetamidomethyl group of linezolid by 5-triazolylmethyl yielded compounds with superior antibacterial activity against Gram-positive bacteria strains. Replacing morpholine by acylpiperazinyl yielded compounds including PH038-PH047 with improved activities compared with PH-027 and linezolid. Furthermore, methyl substitution at 4-position of the triazole exhibited reduced monoamine oxidases and mitochondrial protein synthesis inhibition, while retaining good antibacterial potency. In this study we investigated the antibacterial activity of novel 5-(4-methyl-1, 2, 3-triazolyl)methyl oxazolidinones (PH-series) bearing morpholine and acylpiperazinyl moieties.

Methods:

 Novel 5-(4-methyl-1, 2, 3-triazole)methyl oxazolidinones were synthesized and evaluated against Gram-positive clinical isolates in comparison to linezolid, vancomycin and PH-027. Organisms tested included methicillin-susceptible (MSSA, n=10) and -resistant S. aureus (MRSA, n=10); methicillin-susceptible (MS-CNS, n=6) and -resistant coagulase-negative staphylococci (MR-CNS, n=3); and vancomycin-susceptible (VSE, n=6) and -resistant enterococci (VRE, n=4) and standard reference strains (n=3). Minimum inhibitory concentrations (MIC's, ug/ml) were determined by agar dilution method on Brain Heart Infusion agar with the medium containing dilutions of antibacterial agents ranging from 0. 12 - 64 ug/ml, with and without 50% human plasma.

Results:

 The most active compound, isopropylcarbonylpiperazino derivative (PH-121, ClogP: -0. 097) with MIC range 0. 5-1 ug/ml showed comparable activity to linezolid and PH-27 (MIC, 0. 5-1 ug/ml) against all strains. This was followed by the morpholino (PH-84, Clog P: 0. 900) and dichloroacetylpiperazino (PH-119, Clog P: 1. 494) derivatives with MIC ranges of 0. 5-2 ug/ml, respectively. Substitution with bulky acyl groups at the distal piperazine 4-position gave PH-108 (R=tert-butoxycarbonyl), PH-128 (R=heptanoyl) and PH-131 (R=trans-cinnamoyl) with reduced antibacterial activity and MIC ranges of 2-8, 4-8 and 8-16 ug/ml, respectively. Most of the new compounds showed increased MIC values in the presence of 50% human plasma suggesting plasma instability or binding.

Conclusions:

  All the compounds tested exhibited moderate to strong antibacterial activity against all Gram-positive cocci evaluated. The study highlighted significant structure-antibacterial activity relationships.

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Metabolism Study of Yohimbine by Bacillus cereus var. fluorescens

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Introduction:

Microbial cultures are known for being biocatalysts. In addition, microbial models may be used to predict metabolic pathways in mammals. Moreover, microbes are capable of giving an array of derivatives in adequate quantities that are difficult to obtain from mammals or synthesis. Yohimbine, a natural alkaloid, is promoted as a natural aphrodisiac.

Insufficient reports about yohimbine microbial metabolism made it an attractive drug for investigation using different microorganisms to get possible metabolites.

Methods:

The microbial cultures were originally obtained from the American Type Culture Collection, USA. All the preliminary screening and preparative-scale experiments were carried out according to the standard two-stage protocol. Yohimbine was prepared as a 10% solution in N, N-dimethylformamide and added to the 24-h-old stage II culture medium of the microorganisms at a concentration 0.1 mg/mL of medium. Substrate control was composed of sterile medium to which the substrate was added and incubated without microorganisms. Culture controls consisted of fermentation blanks in which the microorganisms were grown under identical conditions but without the substrate addition. After two weeks of incubation, each control was harvested and analyzed.

Of eight microbial cultures screened for their ability to convert yohimbine, Bacillus cereus var. fluorescens showed definite metabolism, thus, it was selected for preparative-scale fermentation.

Results:

Yohimbine was transformed by Bacillus cereus var. fluorescens affording two metabolites. These metabolites were isolated by solvent extraction, purified by chromatography and subjected to spectral analyses.

Conclusions:

B. cereus var. fluorescens transformed yohimbine into two metabolites. These metabolites are yet to be biologically evaluated.

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Health professionals' attitudes towards medication errors and possible consequences at a Kuwait hospital.

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Introduction:

To assess the attitudes and perceptions of healthcare professionals regarding medication errors and their possible consequences on the employee.

Methods:

Self-administered questionnaires on healthcare professionals' attitudes and perceptions regarding medication errors were distributed anonymously to gather information from nurses, physicians and pharmacists at the Armed Forces Hospital in Kuwait. Data were analyzed using the Statistical Package for the Social Sciences (SPSS v12) and EpiCalc 2000 (v 1. 02).

Results:

One hundred and forty-nine (74. 5%) questionnaires were completed and returned. Physicians and nurses tended to have more work experience than pharmacists. There were no significant differences in the demographics of respondents of all three groups regarding length of time in practice or duration of employment with the hospital. Most respondents (70. 5%) thought that medication errors should be investigated but there was inter-professional variation between the different groups. All pharmacists, the large majority of physicians (85. 5%) and slightly more than half (52. 6%) of the nurses thought that errors should be investigated. Nurses had a more negative perception of administration's support (mean = 2. 22 (0. 86); 2. 79 (1. 31); 3. 08 (0. 78); $p < 0.001$),
and a greater fear of consequnces (2. 99 (1. 01); 2. 62 (1. 39); 2. 21 (1. 76); $p = 0.026$) than physicians and pharmacists respectively. Physicians had the most positive perception of their ability to openly communicate their opinions regarding patient care practices (3. 11 (0. 91); 2. 32 (0. 86); 2. 63 (0. 97); $p < 0.001$) compared to nurses and pharmacists respectively. Pharmacists were more in favor of investigating and reporting medication errors. All participants perceived graver consequences based on severity of harm to patient.

Conclusions:

Professional perception of the consequences of committing medication errors may depend on each profession's relative position in the institution's hierarchy.

Key Words: Medication error; Questionnaire; Percetption;

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Comparative assessment of drug-drug interactions using different drug databases.

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Introduction:

Identification of drug-drug interactions (DDIs) during the prescribing process may help to prevent serious adverse effects on patients.

Methods:

A total of 123 DDIs previously identified using the Micromedex Drug-Reax® database (MDRx) were examined using interaction checkers available through Clinical Pharmacology, Drugs. com, Medscape and Multum. Criteria compared between the various databases were ability to detect the interaction, availability of a classification system for severity rating of the interaction, and quality of documentation of the interaction within the database. Severity descriptions in each database were used to normalize a numerical rating scale for comparative purposes. The scale ranged from 0 (unknown) to 4 (contraindicated for concurrent use) using the MDRx system as the reference.

Results:

Some drugs were not found resulting 4. 1% of DDIs not being identified in Clinical Pharmacology and Multum, 3. 3% in Drugs. com and 6. 5% in Medscape. Concordance of DDI severity between MDRx and the other databases were: major interaction - Clinical Pharmacology: (57. 1%), Drugs. com and Multum (66. 7 each) and Medscape (33. 3%); moderate interaction - Clinical Pharmacology (75. 9%), Drugs. com (72. 4%), Medscape (26. 4%) and Multum (75. 9%); and minor interaction - Clinical Pharmacology (66. 7%), Drugs. com and Multum (73. 3% each), and Medscape (26. 7%). Clinical Pharmacology rated 14. 3% of the major and 13. 3% of the minor DDIs higher than MDRx according to the scale established. DDIs found in MDRx but not recognized as DDIs by the other databases were as follows: Clinical Pharmacology 5. 7% (3 major, 2 moderate and 2 minor); Drugs. com 9. 8% (1 major, 8 moderate and 3 minor); Medscape 70. 7% (6 major, 57 moderate and 10 minor); and Multum 8. 9% (8 moderate and 3 minor).

Conclusions:

There is considerable variability in the abilities of different drug interactions checkers to detect DDIs or to distinguish clinical significance of severity.

Key Words: Drug interactions; Database; Interaction checker;

Pharmacy
Category: Basic Sciences

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Monoamine oxidase inhibitory activity of novel oxazolidinone antibacterials

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Introduction:

One of the unwanted side effects of the oxazolidinone antibacterial agents is inhibition of monoamine oxidases (MAO) due to their structural similarity with MAO inhibitors such as toloxatone. The aim of this study was to investigate the MAO inhibitory properties of some newly synthesized oxazolidinone antibacterials.

Methods:

Oxazolidinones were synthesized as previously described (Phillips et al. 2003, Bioorg Med Chem 11:35). MAO activity was determined by a continuous peroxidase linked spectrophotometric assay. The in vitro effect of the compounds (50 and 200µM) was tested on rat brain homogenates. Experiments were repeated five times with good reproducibility and accuracy.

Results:

A total of nine oxazolidinones were tested. At the higher concentration (200µM), the 5-(aminomethyl) morpholino(PH-99) and [5-(4-methyl-1, 2, 3-triazolylmethyl)] morpholino(PH-84) derivatives did not cause significant MAO inhibition. However, the 5-(aminomethyl)4-tert butoxycarbonyl piperazino derivative(PH-100) was the most potent MAO inhibitor followed by the 5-[(N-hydroxyamino)methyl] morpholino(PH-18) and 5-(N-hydroxyacetamidomethyl) morpholino(PH-23) derivatives. Three of the tested oxazolidinones, [5-(1, 2, 3-triazolylmethyl)] morpholino(PH-27), [5-(4-methyl-1, 2, 3-triazolylmethyl)] morpholino(PH-84) and [5-(4-methyl-1, 2, 3-trioazolylmethyl)]4-tert-butoxycarbonyl piperazino(PH-108) derivatives displayed good activity against gram-positive bacterial strains (MIC range 1-8µg/ml). However, compound PH-23 was only active against M. tuberculosis H37Rv (MIC 1. 38µg/ml).

Conclusions:

This preliminary study shows that our experimental method is suitable for rapid screening of potential MAO inhibitors. Methyl substitution at the 4-position of the 5-triazolyl moiety was found to reduce MAO inhibition. However, further investigations on pure MAO-A or MAO-B and in animal models are needed to determine the selectivity, potency and reversibility of MAO inhibition

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Audit of the quality of documentation in diabetic outpatients in Kuwait

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Introduction:
The prevalence of type 2 diabetes mellitus in Kuwait ranks amongst the highest in the world at about 15%. Since diabetes is a major risk factor for cardiovascular disease (CVD), which is the leading cause of death in Kuwait, the high incidence of diabetes has major social and economic impact. This impact can be minimized by good glycaemic control and appropriate management of cardiovascular disease risk factors.
To help facilitate this, patients are seen at regular intervals in specialist diabetic outpatient clinics at the major hospitals in Kuwait. Some polyclinics also hold clinics for diabetic patients.

Methods:
Design: Retrospective audit of patient medical notes.
Main Outcome Measures: Percentage of patients for whom different parameters were recorded in medical notes during the 12-month period up to, and including, the scheduled outpatient appointment. SettingAll patients aged 40 years or older who had been scheduled to attend the diabetic outpatient clinic at a major hospital in Kuwait during the period September 2006 to March 2007 were included in the study.

Results:
Out of the 201 patients included in the study, recent blood pressure, HbA1C, body weight and plasma total cholesterol were documented in 97%, 92%, 87. 1% and 76. 1% of records, respectively. Corresponding values for smoking status, urine albumin concentration, waist circumference and height were 41. 3%, 31. 8%, 24. 4%, and 24. 1%, respectively.

Conclusions:
Implicit to good care is good documentation, so that any change in a patient's health status can be monitored and in order to improve seamless care between health care professionals. Some important parameters were found to be inadequately recorded.
Introduction of a standard patient monitoring record form, to be completed at each outpatient visit, may help improve documentation.

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In vitro permeation study on enantioselective penetration enhancing effect of carvone on transdermal permeation of nicorandil

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Introduction:
 The objective of the investigation was to study the possible enantioselective penetration enhancing effect of carvone (a chiral terpene) on transdermal drug permeation using nicorandil as a model drug.

Methods:
 The in vitro permeation study was carried out across excised rat skin using an automated flow-through diffusion apparatus. The drug reservoir formulation used was HPMC gel drug reservoir containing 4%w/w of nicorandil and 12% w/v of either R-carvone, S-carvone or RS-carvone (1:1). A control in vitro permeation study was also carried out without carvone in the HPMC gel drug reservoir. The amount of nicorandil permeated across the rat skin at different time intervals was estimated by HPLC. The flux of nicorandil and the lag time to achieve steady state flux were determined.

Results:
  The flux of nicorandil in control study without carvone was 18. 2±0. 2 $\mu g/cm^2$. h.
The mean penetration enhancement ratio (ER) values with R-carvone, S-carvone and R-S-carvone were 39. 4, 33. 3 and 32. 3 respectively. R-carvone showed highest ER, but no significant difference was observed in ER value obtained with R-S-carvone when compared to S-carvone. However, there was a significant difference in the lag time so as to produce a steady flux of the drug across the skin when different enantiomers of carvone were used at the same concentration.

Conclusions:
 The in vitro permeation studies indicated that the chiral terpene enhancer, carvone showed enantioselective penetration enhancing effect on transdermal permeation of nicorandil. Further studies are needed to understand the observed difference in the enantioselective penetration enhancing activity observed with various enantiomers of carvone.

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Chromatographic Behavior of Uric Acid and Methyl Uric Acids on a Diol Column in Hydrophilic Interaction Chromatography

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Introduction:

Retention behavior of uric acid and methyl uric acids on a diol column in hydrophilic interaction chromatography(HILIC) is presented and effects of parameters such as organic solvent and salt concentration in the mobile phase and column temperature were systematically investigated using a design of experiment(DOE). Retention prediction models are derived in order to gain insights on the retention mechanisms involved.

Methods:

The retentions of the analytes were obtained under HILIC conditions. Multiple Linear Regression(MLR) analysis is applied to the data and optimal number of predictors and best regression equations were selected. Validity of the derived MLR models was tested by cross validation procedures.

Results:

DOE results revealed that the content of organic solvent acetonitrile had the most influence on retention of the analytes. Effect of salt concentration indicated possibility of electrostatic repulsion between negatively charged analytes and deprotonized residual silanol groups on the surface of the stationary phase. Van't Hoff plots were constructed to further study the effects of column temperature on retention. Nonlinear van't Hoff plots were observed for all the analytes in the temperature range (0-60ºC) signifying that the retention on the diol column is governed by mixed retention mechanisms.

Conclusions:

Retention prediction models derived by MLR showed that the retention of the analytes is dependent on the percentage of acetonitrile in the mobile phase and two solute-related descriptors namely ovality(Ov) and lowest unoccupied molecular orbital(LUMO). Among the three predictors, the percentage of acetonitrile had the most significant effect on retention indicating hydrophilic partitioning as the major interaction responsible for the retention behavior. The incorporation of Ov, a shape parameter, in MLR equation signified the importance of the shape/size of the compounds on the observed retention on the diol phase.

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Preparation, characterization and optimization of probucol self-emulsified drug delivery system (PBSEDDS) applying Response Surface Methodology

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Introduction:

Self-emulsifying drug delivery system (SEDDS) has proved its efficacy to improve the solubility, dissolution and hence the bioavailability of poorly water soluble drugs. The system is emulsified rapidly in stomach presenting the drug as fine O/W emulsion and promote wide distribution of the drug throughout the GIT. Probucol (PB) is a lipid regulating drug with limited and variable absorption from GIT. The objectives of this study were to prepare and characterize of PBSEDDS to get an optimized formulation applying Response Surface Methodology (RSM) Experimental Design (EP).

Methods:

A three-factor (X1-X3), three-level (Y1-Y3) Box-Behnken EP was used to explore the quadratic response surfaces and construct a second-order polynomial model. Series of PBSEDDS were prepared by mixing different proportions of soybean oil (X1), Labrafil (X2) and Capmul (X3). The resulted formulations were characterized for droplet size (Y1), turbidity (Y2) and drug dissolution after 30 min (Y3). Response surface plots were used to demonstrate the effect of factors (X1-X3) on the response (Y3).

Results:

Amounts of X1-X3 showed a significant effect on the emulsification rates and on the physical properties of the resultant emulsions (droplet size and turbidity). Observed and predicted values of Y3 obtained from the constructed equations were in close agreement. Response Surface Methodology (RSM) was then used to predict the levels of factors X1-X3 under the constrained variables for an optimum response. The predicted values were 0. 0704 um, 18. 95 NTU and 88. 87% for Y1, Y2 and Y3, respectively. Two new formulations were prepared according to the predicted levels. The observed and predicted values were in close agreement.

Conclusions:

The findings indicated that PBSEDDS with high drug release and acceptable physical characteristics could be prepared and the quantitative RSM applied in this study helped in understanding the effects and the interaction effects between the three factors applied.

Key Words: Self-emulsifying drug delivery system; Probucol; Optimization;

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Characterization and In-Vitro Dissolution Studies of Solid Dispersion Systems of Gliclazide with Macrogols

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Introduction:

The objective of the present investigation was to improve the aqueous solubility and dissolution rate of Gliclazide (GLC), a hydrophobic anti-diabetic drug by solid dispersion (SD) technique, using a water soluble carrier (Macrogol).

Methods:

Preliminary screening of various grades of PG's (4000, 10000 and 20000) at different concentrations (0. 5, 1, 2, 5 and 10%) was done by phase solubility studies to analyze their influence on solubility of GLC. SD's of GLC and PG in different ratios (1:1, 1:2, 1:5 and 1:10) were prepared by the fusion technique. The SD's were compared with the original drug as well as the physical mixtures (PM) in the same ratios for in-vitro dissolution release. DSC studies were performed to identify the physicochemical interaction between the drug and the carrier. SD with satisfactory characteristics was used for the formulation of tablets by wet granulation method and compared with a commercial brand.

Results:

It was evident from the phase solubility studies that the drug solubility increased linearly with increasing PEG concentrations indicative of the AL type of phase diagram. Intrinsic solubility of GLC in water was found to be only 6. 144 µg/ml. Dissolution of GLC improved significantly in solid dispersions as compared with the original drug and physical mixtures. SD's of GLC with various grades of PEG in 1:2 w/w ratio showed almost 100% release in phosphate buffer (pH 7. 4) in 30 mins, as compared to 23% dissolution of plain GLC. Results of DSC studies demonstrated that enhanced dissolution of GLC from SD might be due to a decrease in crystallinity of GLC in the molten state while its formulation by fusion method. SD tablets of GLC and PEG 20, 000 in 1:2 w/w ratio exhibited a better dissolution profile (54. 21%) than the commercial brand (30. 26%).

Conclusions:

This study reveals the possibility of preparing SD tablets of GLC with improved aqueous solubility and dissolution rate.

Key Words: Gliclazide; Macrogols; Solid Dispersions;

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Quantification of Levetiracetam in human plasma by liquid chromatography-tandem mass spectrometry: application to therapeutic drug monitoring

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Introduction:

Levetiracetam (LEV), (S)-á-ethyl-2-oxo-1-pyrrolidine acetamide, is structurally unrelated to existing antiepileptic drugs (AEDs). LEV is indicated as adjunctive therapy in the treatment of partial seizures, with or without secondary generalization that are refractory to other established first-line AEDs. The objective of the present study was to develop and validate a rapid, reliable, and accurate electrospray MS-MS method for the determination of LEV in human plasma.

Methods:

The drug and IS were extracted by solid phase extraction (SPE) technique and analyzed on Symmetry® C18 column (5 µm, 3. 9 x 50 mm) using a mobile phase of methanol-water-formic acid. Quantitation was achieved using a positive electrospray ionization (ESI+) interface employing multiple reaction monitoring (MRM) mode at MRM transitions m/z 171>126 and m/z 268>136 for LEV and IS, respectively.

Results:

The method was validated over the concentration range of 1. 0 – 40 µg/ml (r > 0. 99) with a limit of quantification of 1. 0 µg/ml (RSD, %; 4. 1 and Bias, %; -9. 0 to + 11. 0 %). Intra- and inter-run precision of LEV assay at three concentrations ranged from 0. 6 to 8. 9% with accuracy (bias) varied
from -4. 0 to 8. 6% indicating good precision and accuracy. Analytical recoveries of LEV and IS from spiked human plasma were in the range of 91. 7 to 93. 4% and 80. 2 to 84. 1%, respectively. Stability of LEV in human plasma samples at different conditions showed that the drug was stable under the studied conditions. Matrix effect study showed a lack of matrix effect on mass ions of LEV and IS.

Conclusions:

The described method compared well with the commercial HPLC-UV method of Chromsystem (r2 = 0. 99). The present method has been successfully utilized in our TDM-CT lab for therapeutic drug monitoring of LEV by analysis of plasma samples of patients treated with LEV.

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Metastatic Tumor Antigen 1 (MTA1) and MTA1 Short Form (MTA1s) mRNA Expression in Rat Placenta during Gestation

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Introduction:

  MTA1 was originally identified in rat metastatic breast tumors. A C-terminal truncated form, known as MTA1s has also been identified. The functional significance of the MTA family in development is beginning to emerge; MTA1 up-regulates β-catenin and cyclin D1 indicating an activation of Wnt pathway promoting cell growth. During pregnancy, placental growth arrest is spared despite the high levels of circulating maternal estrogens. This can be attributed to MTA1 and MTA1s interaction with the estrogen receptor (ER) as it has been demonstrated that MTA1 inhibits the ligand induced transactivation effect of estradiol on ER. The level of expression of both MTA1 and MTA1s in rat placenta was studied in an attempt to better understand their role in placental growth and development.

Methods:

  Maternal serum, amniotic fluid and placental samples were collected at 16, 19 and 21 days gestation (dg). MTA1 and MTA1s mRNA expression was studied using Real-Time PCR.

Results:

  Placental weights increased between 16 and 21 dg ($p<0.001$). Maternal serum and amniotic fluid estradiol levels increased between 16 and 21 dg ($p<0.05$). MTA1 and MTA1s were detected from 16 dg. Although the developmental changes were not significant, there was a trend, especially for MTA1, to increase by 21 dg. However, when the expression of both genes were compared at each gestational period, MTA1 was significantly more expressed than MTA1s at both 16 and 21 dg ($p<0.05$).

Conclusions:

  Estradiol, acting through its receptor, may play a direct role in inhibiting placental growth. However, expression of MTA1 and its truncated form in rat placenta suggests that they may play a role in inhibiting the ligand induced transactivation effect of ER and hence spare the placenta from growth arrest. Indeed, increased MTA1 expression may contribute to placental growth via other mechanisms including the activation of β-catenin and cyclin D1.

Physiology
Category: Basic Sciences

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Gender Differences in Diabetes Knowledge among Kuwaiti University Undergraduates.

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Introduction:

The prevalence rate of diabetes in Kuwait is 22. 4% (WDF, 2007). It has been shown by a large number of studies that diabetes is significantly more common in women than men (WHO, 2007). In this context, this study aims at examining gender difference in diabetes knowledge among Kuwait University undergraduate students.

Methods:

The sample of (569) undergraduate students of Kuwait University, including (244) males and (325) females were selected for the study. Their age ranged between 17-28 years (M=19. 64, SD=2. 29). The Arabic version of the Diabetes Knowledge Scale DKN-B (Beeney, Dunn & Welch, 1996) was used for assessing diabetes knowledge. The α coefficients of the DKN-B in the present study sample is (α=. 72) denoting good internal consistency of the Arabic DKN-B. The data were analyzed using SPSS-V. 15.

Results:

The mean score for diabetes knowledge in men and women (4. 84± 2. 62) and (6. 20±2. 83) respectively. It was significantly lower in men (t=5. 95, p<. 001). Also, the score of diabetes knowledge was rated as "Good" (> 60%) in only 3. 3% of males, compared with 12. 8% in the females.

Conclusions:

[1] Diabetes knowledge is poor among those who took part in the study. [2] There is a gender difference, with the men being significantly less informed about diabetes. [3] These findings do not relate directly to the aetiology and prevalence of diabetes. [4] However, this study highlights the urgency of improving the awareness of diabetes and, in general, health education among the Kuwaiti population at different levels.

Key Words: Gender; Diabetes Knowledge; Kuwait;

Physiology
Category: Basic Sciences

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Maximal O2 uptake relationship to fat free mass in Athletes and Sedentary subjects.

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Introduction:

A strong correlation between maximal oxygen consumption (VO2max) and fat free mass (FFM) reflects the relationships between muscle, the major component of FFM, and oxygen delivery systems. Training may alter this relationship. We characterize the VO2max to FFM relationship in Kuwaitis participating regularly in sports compared to sedentary subjects.

Methods:

Subjects were adult males athletes (n=85, means ±SD: 26. 2±4. 2 years, 175. 4±7. 4 cm height) or sedentary urban office workers reporting no regular physical activity in the last six months (n=61, 31±7. 4 years, 170. 7±6. 4 cm height). Aerobic sports were classified in a scale from 0 (weight lifting) to 1(marathon). Maximal oxygen uptake was measured using calibrated oxygen and ventilatory flow meters during graded treadmill exercise tests to exhaustion. Mid trunk flexibility was measured (cm) using a sit and reach instrument (Lafayette Co.). Height, weight and seven skin-folds (John Bull caliper) were measured to estimate FFM. Subjects signed prior informed consent.

Results:

The significant correlation ($R2=0. 34$, $p=0. 005$) between FFM, (67±8. 7 Kg FFM) and VO2max (4±0. 68 L/min) in athletes was absent ($R2= 0. 19$, $p=0. 15$) in sedentary subjects (61. 9±7. 1 Kg FFM, VO2max 3. 2±0. 66 L/min). Stepwise regression analysis indicated that VO2max was predicted ($R2=0. 48$) as 0. 255+0. 048 (FFM)-0. 012 (Resting Heart Rate)+2. 115(Aerobic Component of Sport) +0. 015 (Flexibility) in athletes but not in sedentary subjects ($R2=0. 23$) where VO2max=2. 68+ 0. 024(Flexibility). Maximal heart rates (181±1. 1 and 185±1. 6 beats/min) and respiratory exchange ratios (1. 15±0. 12 and 1. 10±0. 11) in athletes and sedentary subjects did not differ.

Conclusions:

FFM relates to the oxygen delivery systems in athletic but not in sedentary subjects. Joint flexibility has more of an influence on peak oxygen uptake in sedentary than in athletic subjects.

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Prevalence, severity, co-morbidity and unmet need for treatment of anxiety and depression among 3303 Kuwaiti nationals in the general population.

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Introduction:

Health planners need information on the occurence of common mental disorders, for resource allocation in the planning psychological services. This is the first nation-wide epidemiological study of mental disorders in Kuwait. We present national general population data on the prevalence and severity of generalized anxiety disorder (GAD), major depressive disorder (MDD) and related sub-threshold disorders, their severity, co-morbidity, associated factors and unmet need for treatment.

Methods:

A one-in-three systematic random proportionate sample of consenting Kuwaiti nationals attending popular open places, such as the large cooperative stores, in all six governorates participated. We used self-report questionnaires keyed to making American DSM-IV diagnoses of GAD and MDD – the PHQ-8 and PHQ-9, respectively. We manually scrutinized their responses, thus using the questionnaires as diagnostic instruments. Data were analyzed by SPSS.

Results:

The 3303 subjects consisted of 44. 8% men and 55. 2% women, aged 16 -87 years. Majority (59. 9%) had a college education. The questionnaires fulfilled standard criteria for reliability and validity. The prevalence rates for GAD and MDD were 10. 7% (95% C. I. = 9. 6% - 11. 8%) and 5. 7% (C. I. 4. 9 - 6. 6), respectively; and for sub-threshold disorders, 11. 6% and 7. 1%, respectively. Co-morbidity was common. The following had significantly higher prevalence of disorders: women, the elderly, the less educated, the unemployed and the divorced. Only 9. 7% with MDD and 8. 4% with GAD were receiving help from doctors. Using standard criteria, 26. 5% with GAD and 37. 6% with MDD had severe disorders. Compared with international data, the sample had higher levels of anxiety.

Conclusions:

The findings should interest policy makers and call for public mental health education. In view of the noted difficulty of house-to-house surveys in this culture, future studies should be planned in collaboration with the national census office.

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Prevalence and correlates of posttraumatic stress disorder among Kuwaiti veterans and their wives according to level of involvement in the Gulf War.

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Introduction:
Although the Gulf War that ended with the liberation of Kuwait has given rise to several reports on posttraumatic stress disorder (PTSD) among Western veterans, there are no reports specifically focused on Kuwaiti military men. We compared the prevalence of PTSD among Kuwaiti veterans and their wives, divided into four equal groups (50 men each, and their wives) according to increasing degree of exposure to combat, viz: the retired, an active –in-the-army group (AIA) (involved in duties at the rear); an in-battle group (IB) (involved in combat); and a prisoners –of-war (POWs) group. Also, we compared the severity of impact of events (IES), co-morbid depression and anxiety; and evaluated the contribution of self-esteem and locus of control. We assessed the relationship between wives' PTSD and family adjustment, husbands' level of combat exposure, and PTSD status.

Methods:
Subjects were interviewed 6 years after the war, using: the PTSD Scale (CAPS) for DSM-IV diagnosis, the Impact of Events Scale (IES), Hopkins Anxiety/Depression, Locus of Control (LOC) and Self-esteem scales. The 200 men were a representative sample selected randomly. Their 176 wives completed the DSM –IV PTSD Checklist.

Results:
63(31. 5%) men fulfilled criteria for PTSD, with the rate significantly higher among the POWs (48%) than the retired (24%) and IB(22%), reflecting the severity of IES. Avoidance symptoms were the most pronounced. Self-esteem was significantly lowest among the POWs and those with PTSD. External LOC was associated with PTSD, anxiety and depression. 50(28. 4%) wives fulfilled criteria for probable PTSD. The prevalence was significantly associated with husbands' combat exposure, but not with husbands' PTSD status. Wives' PTSD was mostly predicted by their depression /anxiety scores.

Conclusions:
PTSD characteristics showed similarity with those from elsewhere. Interventions should focus on self-esteem, avoidance symptoms and women empowerment issues.

Key Words: Posttraumatic stress disorder; Veterans - wives; Kuwait;

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Olanzapine in the treatment of behavioral problems associated with autism an open-label trial in Kuwait

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Introduction:

Autism is a lifelong disorder that affects communication and daily routines. The nature and causes still remain unknown. There is no total cure for autism as yet. Olanzapine which is proven to be beneficial in treating schizophrenic patients with behavioural disturbances could be effective for autistic children with similar behaviors. An open-label trial study was adopted to examine the clinical efficacy of olanzapine in the treatment of disruptive behavior associated with autism.

Methods:

The current prospective open-label trial was conducted on 40 male children mean age12. $2 \pm 2. 2$ who met DSM-IV-TR criteria for autism. Patients received olanzapine treatment (5-10mg/day) dose for a 13-week treatment period. The primary efficacy measures were the Aberrant Behavior Checklist and the Clinical Global Impressions-Severity done at baseline and at the end of treatment. At entry point and at the end of treatment, the patients underwent laboratory and physical investigations.

Results:

Paired comparison of baseline and 13 weeks endpoint scores showed a significant reduction of the ABC subscale scores irritability, hyperactivity and lethargy($p < 0. 0001$), and stereotyped behavior and inappropriate speech ($p < 0. 005$). Of the 40 patients 12(30%) were considered as improved and the difference was statistically significant ($p < 0. 005$). There was no enzyme elevation or serum biochemistry changes after treatment. Olanzapine treatment was not associated with significant body weight changes or with any other treatment-emergent side effects.

Conclusions:

This study shows that olanzapine treatment can be beneficial in alleviating some behavioural symptoms associated with autism and should be considered an appropriate therapeutic option as part of a comprehensive treatment strategy for children with autism. The short period of this trial limits inference about adverse effects such as body weight increase and APS. Further long term placebo-controlled studies of olanzapine are required.

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Prevalence of eye trauma in Squash players in Kuwait

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Introduction:

The Gulf Arab countries including Kuwait have seen a surge in the number of young people who are being attracted to amateur and professional sports. Squash playing is such a sport gaining wide popularity, however, an increasing number of eye injuries related to it have been reported. Very little is known about the prevalence of eye trauma related to playing squash and the prevalence of using protective eyewear in Kuwait.

Methods:

A nation-wide survey was distributed to all sport clubs in Kuwait with recognized squash teams. A total of 123 players returned a self administered questionnaire in Arabic. Coded data obtained from the questionnaires were entered and analyzed using (SPSS) software, version 14. 0.

Results:

The majority of players in this study (85%) had more than one year of experience playing squash. Of the total, 68% were $\leq$ 19 years of age. Eighty percent of respondents did not wear protective eyewear. Of those who did; only 40% used it at all times during games, practice, and playing in Kuwait or abroad. Three players had history of eye surgery and 15% were known to wear regular eye glasses or contact lenses to improve their vision. Nineteen players reported current eye problems needing treatment with drops or ointments (inflammation, infection, allergies, others). The prevalence of eye trauma while playing squash in this study was 22%. Among those players, 12% reported severe eye trauma requiring admission to hospital. The majority of players (84%) never read any educational material about eye protection while playing squash. Finally, when asked if they will use protective goggles if provided by own clubs, 49% agreed compared to only 31% who agreed to purchase such protective eyewear themselves if requested by their clubs.

Conclusions:

The prevalence of eye trauma while playing squash is high in Kuwait. If appropriate preventive measures are taken, squash playing should not entail any significantly higher dangers than other games.

Key Words: Squash; Eye Trauma; Protective eyewear;
Funding Agency: None

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Retinopathy of prematurity: Incidence, Risk factors and treatment outcomes in Kuwait

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Introduction:

Retinopathy of prematurity (ROP) is the leading cause of preventable blindness in infants. Advanced neonatal care in a country like Kuwait results in better survival of even extremely low birth weight infants. This results in more eligible babies for screening of ROP. We analyzed our data to estimate the incidence, risk factors and treatment outcomes in ROP babies.

Methods:

The study was conducted at neonatal intensive care unit of Jahra Hospital, Kuwait. We analyzed the charts of babies who were screened for ROP from September 2006 to August 2007 in a retrospective study.

Results:

Two hundred and nine infants were examined. ROP was diagnosed in eighty nine infants (42. 6 %). The most important independent risk factor for the development of ROP was the gestational age at birth. Eleven babies needed laser therapy. One of the babies had adverse structural outcome.

Conclusions:

Our study shows incidence and risk factors of ROP similar to the developed countries. Results of treatment show that incidence of adverse outcome is low in our series.

Key Words: Retinopathy of prematurity; Laser; Gestational age;

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Extruding glaucoma drainage devices:double layer repair

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Introduction:

 To describe a novel method of repair of extruding of Glaucoma Drainage Devices (GDD)using a donor scleral allograft in conjunction with Amniotic Membrane Transplantation (AMT).

Methods:

 Description of the clinical outcomes of consecutive case series of 7 GDD erosions presenting to the one glaucoma specialist over a 3 year period. Each case was repaired using double layer technique of scleral allograft plus AMT. In 2 cases, repair was combined with resiting of the GDD via pars pana.

Results:

 Successful repair was achieved with 7 cases(follow up range from 6 months to 3 years). Intra-ocular
 pressure control was maintained in 6 cases without medication and in one case with additional topical medication. One GDD re-eroded and was repaired by repeating the procedure.

Conclusions:

 There are a limited number of options to avoid removal of an extruding GDD. AMT is a useful substitude to conjunctiva in this situation to cover the scleral allograft and prevent GDD re-exposure.

Key Words: Glaucoma; Drainage devices; Scleral Allograft;
Funding Agency: No

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Desensitization protocol in highly sensitized prospective kidney recipients using immunoadsorption (IA) or plasma exchange (PE) and intravenous immunoglobulin (IVIG)

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Introduction:

Transplantation of renal allograft into highly sensitized recipients has become increasingly successful over the past several years. In order to prevent antibody mediated graft damage, desensitization prior to transplantation is now done with either IA or PE and IVIG.

Methods:

We describe the characteristics of five highly sensitized kidney recipients who underwent successful desensitization prior to transplantation. The mean panel reactive antibody (PRA) titer was 33% for class I histocompatability antigens (HLA) and 50% for class II. Donor/recipient cross match was positive by flowcytometry but negative by cytotoxicity tests for all recipients except one who was positive for both. The desensitization protocol started by giving tacrolimus and mycophenolate for 3 weeks prior to antibody removal either by IA in 2 or PE in 3 patients for another week, which was subsequently continued for 4-6 weeks post transplantation. Donors were live in 4 and cadaveric in one transplant with median HLA mismatch of 3. Surgery was done 4 hours after negative cross match. All patients received induction immunosuppression with polyclonal anti T cell antibody. IVIG was given for two days after transplantation. Donor specific antibody titer was monitored post transplant according to the protocol and kidney biopsies were performed at 3 and 6 months post transplant.

Results:

All recipients had immediate graft function except one who had slow graft function. One patient had acute rejection (Banff IA) that responded to steroid pulse. Infection occurred in two patients (one had urinary tract and the other had bacteraemia) both responded to antibiotic treatment. The mean hospital stay was 35 days and the latest mean serum creatinine was 85 umol/l.

Conclusions:

Desensitization using IA or PE with IVIG is an impressive option for successful transplantation in highly sensitized prospective kidney recipients.

Key Words: Kidney transplantation; Desensitization; Immunoadsorption;
Funding Agency: None

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Addition of single dose Amikacin to Prophylactic Quinolones significantly reduces infectious complications of transrectal ULTRASOUND GUIDED BIOPSY OF THE PROSTATE GLAND.

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Introduction:

A rising incidence of infectious complications in our unit following transrectal ultrasound guided biopsy (TRUSB) of the prostate gland has prompted us to review our prophylactic antibiotic regimen in patients undergoing such procedures. This study compares infectious complication rates in these patients given prophylactic ciprofloxacin only or ciprofloxacin combined with a single dose of intravenous (IV) amikacin.

Methods:

Between 2001 and 2005, 300 consecutive patients (Group1) undergoing TRUSB of the prostate were given oral ciprofloxacin 500mg BD one day before and for 2 days after the biopsy. From 2006 to 2007, 194 patients (Group 2) in addition to ciprofloxacin as above also received IV amikacin 500mg 30 minutes before the biopsy. Patients had standard 6-12 core prostate biopsies. Patients were required to report: high fever (T > 39oC), chills or if they felt generally unwell with low grade pyrexia within 168 hours of the procedure. Blood and urine samples were sent for microbiological analysis in patients admitted with septicaemia post biopsy.

Results:

In group 1 patients, the incidence of septicaemic episodes after TRUSB of the prostate rose from 1. 6% to13. 3% in 2001 and 2005 respectively. Feeling unwell with low grade pyrexia within 168 hours was reported by 21/300 (7%) and 3/194 (1. 6%) in groups 1 and 2 patients respectively (p<0. 001). Septicaemia occurred in 14/300 (4. 7%) and 1/194 (0. 5%) in groups 1 and 2 patients respectively (p<0. 001). E. coli resistant to quinolones was responsible for 13/15 (86. 7%) septicaemic cases, while one case each was due to E. faecalis and Klebsiella spp resistant to quinolones.

Conclusions:

Increased incidence of septic complications after TRUSB of the prostate in our unit is due to quinolone resistant bacteria, particularly E. coli. The addition of IV amikacin to quinolone prophylaxis significantly reduces infectious complications of TRUSB of the prostate.

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Functional endoscopic dilatation of paranasal sinus ostia (balloon sinuplasty):Patient selection and surgical technique

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Introduction:

 A new, minimally invasive technique-balloon catheter dilation of paranasal sinus ostia (balloon sinuplasty)-has been described by Brown. (2006). Astenotic sinus ostium can be enlarged by the pressure applied by a small balloon catheter.

Methods:

 15patients suffering from chronic sinusitis with failed medical treatment despite of proper antibiotics, topical steroids, and allergic managements beside abnormal CT findings suggestive chronic sinusitis were subjected to balloon sinoplasty alone or in combination with FESS in ENT department AL Jahra Hospital. The procedure done under general anaesthesia with the application of a vasoconstrictor such as 1:1, 000 topical epinephrine on a cotton pledget. A hollow, plastic sinus guide cannula is placed near the entrance of the involved sinuses(maxillary ;frontal and sphenoidal) under videoendoscopic visualization usually with a 0 [degrees] or 30[degrees] telescope. With the aid of a fluoroscopic C-arm, a sinus guide wire is inserted through the sinus guide cannula into the sinus ostium. A catheter with an attached balloon is fed over the sinus guide wire into the sinus. After the balloon has been accurately placed, an assistant inflates it to 6 to 10 atmosphere. The balloon is left inflated for several seconds and deflated; it can be moved slightly and reinflated if necessary, particularly in the frontal recess. The involved sinus can be lavaged if necessary. After the balloon has been deflated and removed, the endoscope is used to inspect the frontal recess or sinus ostium.

Results:

 The dilated sinus ostium was patent in all cases. There were no serious adverse events. No associated problems such as bleeding, scarring, and orbital or intracranial complication.

Conclusions:

 Sinus ostia balloon dilation is a useful safe new option with minimal mucosal injury and scar formation without serious orbital nor intracranial comlications.

Key Words: Functional endoscopic dilatation.

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Duration of hospitalization and associated factors among burn patients in Kuwait

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Introduction:

The duration of hospitalization or length of stay (LOS) for patients has been an important factor among health care providers all over the world. We, therefore, attempted to study LOS among burn patients, admitted at Al-Babtain Burn Center, Kuwait, during the period 1993 to 2006. The objective was to determine the factors associated with higher average length of stay (ALS).

Methods:

This prospective study was based on a total of 3175 cases of burn patients. The data on duration of hospital stay was taken from in-patient records, and related with other available variables; such as, age, gender, nationality, cause of burn, total body surface area (TBSA), and patient's outcome. The statistical software, SPSS (15. 0), was used for analysis and presentation of significant findings.

Results:

The median length of stay, in a total of 3175 burn patients, was found to be 12 days, being significantly higher among survivors than non-survivors (12 vs 7 days; $p < 0. 001$). Among fatal cases, 40% died within 3 days. The length of stay was highest (19 days) among patients aged 60 years and above, and lowest (9 days) in those less than 15 years ($p<0. 001$). On gender and nationality grounds, females and non–Kuwaiti patients had significantly higher duration of stay. Also, considering the cause of burn, patients with flame burns had higher duration of stay (15 days) as compared to any other cause ($p< 0. 001$). However, the longest duration of 38 days was found among patients with 30-69% TBSA.

Conclusions:

Our study showed that factors which influenced LOS among burn patients were higher age, flame burns and TBSA (50+20%). These patients need to be given special attention during in-patient care so as to reduce the ALS among burn patients. There is also a need to find new, effective and more efficient treatment modalities.

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Steroid Avoidance in Renal Transplantation – A Prospective open labeled controlled study.

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Introduction:

 Steroids have remained the mainstay of immunosuppression in renal transplant recipients(RTR). Initial studies reported a higher incidence of acute rejection episodes(ARE)on steroid withdrawal/avoidance. More recent data indicate that early elimination or steroid free regimens are feasible in RTR, thereby reducing the side effects and improving compliance. This is a prospective, open labeled and controlled study to assess the safety and efficacy of steroid avoidance in RTR.

Methods:

 The inclusion criteria were the following :severe diabetes mellitus, ischemic heart disease, gross obesity and bone complications like osteoporosis or avascular necrosis. Primary end point was biopsy proven acute rejection (BPAR). Total number studied was 50 with 25 RTR each in steroid free group and control group. Induction was done with thymoglobulin or basilixmab. Steroids were given only for 5 days and then discontinued. Maintenance immunosuppression included a combination of mycophenolate mofetil, MMF and calcineurin inhibitor, CNI, tacrolimus or cyclosporine, /Rapamicin. These subjects were compared to matched controls who received similar induction therapy and triple drug maintenance therapy with steroids, MMF and CNI or Rapa . They were followed up for a median period of 18 months.

Results:

 Demographic features were comparable in both groups. Patient survival and graft survival were 100% in both the groups. BPAR episodes were 3(12%)in each groups with a mean serum creatinine of 107. 8 umol/L in the study group and 118. 2 umol/L in the control group. Prevalence of post transplant hypertension, requirement of increased antihypertensive medications, weight gain and post transplant diabetes mellitus were more common in the control group.

Conclusions:

 Steroid avoidance in selected RTR using newer immunosuppressive protocols provides comparable graft survival, patient survival and rejection episodes with low incidence of steroid related morbidities.

Key Words: Steroid avoidance; kidney transplantation; Immunosuppression;
Funding Agency: None

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Retransplantation after renal allograft loss to polyoma virus-associated nephropathy (PVAN)

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Introduction:

Polyomavirus-associated nephropathy (PVAN) is an emerging cause of kidney transplant failure affecting 1-10% of patients. Limited data exists concerning retransplant in patients who lost their previous graft due to PVAN.

Methods:

Live donor retransplantation was done in four recipients who lost their grafts due to PVAN at a mean of 10 months after graft failure. Graft nephrectomy was done in all except one who was negative for viraemia and viruria and did not require dialysis prior to transplantation. Induction immunosuppression was given for thee patients (2 monoclonal and one polyclonal antibody). Post transplant immunosuppression was similar to the current center policy during the first three months (Prednisolone, Mycophenolate and either tacrolimus in three or cyclosporine in one patient). Immunosuppression was tapered over the next 3 – 9 months to the minimum that keeps normal graft function. Follow up to detect virus reactivation in blood and urine was done monthly for the first 3 months then every 3 months for the first year using polymerase chain reaction (PCR).

Results:

The follow up period was 3, 6, 15 and 50 months post transplant with mean serum creatinine 85 umol/l. All patients tolerated reduction of immunosuppression without rejection episodes. Viral reactivation was observed in two patients one turned negative and the second remained viruric on further reduction of immunosuppression.

Conclusions:

Retransplantation with reduced immunosuppression is a successful therapeutic option in recipients who lost earlier graft due to PVAN.

Key Words: Kidney transplantation; Immunosuppression; Polyoma virus;
Funding Agency: None

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Tracheotomy in children: our experience in Jahra

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Introduction:

The surgical treatment of airway diseases in children has improved significantly over the two past decades. Correct diagnosis together with greater likelihood of curative therapeutic procedures has optimised the result of tracheostomy. There has been a significant change in the indications of tracheostomy. Long-term intubation and subglottic stenosis are now the most frequent indications. Objective: retrospective study to review our experience in tracheostomy in children

Methods:

review of records of 37 children who underwent a standard tracheostomy between 1994 and 2007. Clinical, radiologic and endoscopic evidences as well as the surgical procedure were noted. C-T scan was undertaken in 21 patients. Informed consent was obtained.

Results:

total patients=37 (female =21, male =16). The age range was from 6 months to 14 years with a mean age of 6. 9 years. Indications; long-term intubation(65%), subglottic stenosis(13%), congenital airway anomalies(14%) and central nervous system disorders(4%). 11 patients(32%) were less than one year. Concomitant endoscopy was performed in 27 children. Patients were followed up for an average of 2 years post-surgery. The procedure was elective in all cases. 21 children were decannulated. Complications;wound infection, accidental decannulation, tube obstruction, tracheoctaneous fistula and 1 pneumothorax. The choice of tracheostomy tube depended on clinical requirements.

Conclusions:

Good airway is easily achieved to good effect in children requiring tracheostomy. Tracheostomy in children is not a simple procedure. It carries a higher risk than in adults. Improved surgical techniques and involving the family in the postoperative care have helped to optimise the result of the procedure. There is a shift in the indications in recent decades. Infectious diseases are no more the principal reasons for tracheostomy. The availability of a modern intensive care is an important determinant.

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Outcome of Cadaveric Renal Transplantation in Kuwait

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Introduction:

An active programme to expand the donor pool by procuring cadaveric organs was started in March 1996. The aim of this paper is to analyze the outcome of cadaveric kidney transplantation performed in Kuwait.

Methods:

The medical records of 236 recipients of cadaveric kidney grafts, since March 1996 were retrospectively reviewed. 106 recipients were males, and 40 were children under the age of 18 years. Many patients had, beside renal failure, one or more other high risk factors. Renal grafts were transplanted after a short ischaemia (mean 12. 5 hours), and the procedure was a re-transplantation in 29 recipients. Induction immunosuppression was mainly with antithymocyte globulin, and the diagnosis of acute graft rejection was based on histopahtological findings.

Results:

Recipients were followed up for 3 months to 140 months. Primary graft function was observed in (81%) of cases. Pos-transplantation complications were: (a) 81 (35%) surgical, (b) 40 (17%) systemic bacterial and viral infections, (c) 64 (28%) episodes of acute rejection, and (d) 5 (2. 1%) cases of malignancy. Twenty-eight recipients died with functioning graft at 1 month to 62 months after transplantation, and 45 more grafts were lost at one day to 87 months after transplantation. The 5- and 10-year actuarial survival rates were 89% and 88% respectively for recipients, and 75% and 69% respectively for grafts.

Conclusions:

The kidney transplantation programme in Kuwait is steadily growing. Kidney grafts procured from cadaveric donors contributed to 29% of transplantation activity and were associated with a high rate of primary function. The overall actuarial recipient and graft survival rates were comparable to those reported by other larger centers.

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Etiology and management of adult giant hydronephrosis

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Introduction:

Giant hydronephrosis is the massive dilation of the kidney and renal pelvis, it most commonly arises from severe and chronic ureteropelvic junction (UPJ) obstruction, but it can also occur as a consequence of other etiologies. This work is conducted to study giant hydronephrosis of varied etiology with an emphasis on the operative techniques used in their management.

Methods:

Eleven adult patients with giant hydronephrosis were included in the study. Nine patients had unilateral and two had bilateral hydronephrosis. The etiology was stricture disease in 9 renal units (UPJO in 6 patients, lower ureteral stricture in 2 patients) and stone disease in 4 renal units. The preoperative evaluation included urinalysis & CS, biochemical profile and imaging studies (US, CT scan, contrast studies and radionuclide scan). Percutaneous nephrostomy (PCN) was used to drain infected cases, to decompress tense hydronephrosis especially in cases with bilateral obstruction or in cases with elevated serum creatinine. Definitive surgery was performed either primarily or after drainage by PCN.

Results:

The mean patient age was 45±11. 2 years (27-68 years). Five patients required PCN before definitive surgery, nephrectomy was performed in 4 patients (3 laparoscopic and one open), ureterovesical reimplantaion was used in three units and pyeloplasty in one unit and four patients underwent surgery for stone disease. One patient lost follow up and 0ne died in the early postoperative from pulmonary embolism. Postoperative evaluation showed reasonable improvement in clinical, biochemical and imaging parameters.

Conclusions:

The etiology of giant hydronephrosis in adult is different than that in young patients. Initial nephrostomy is used to improve the renal function in uremic patients and to predict more accurately the recoverability of function. With the advent of new imaging tools and minimally invasive surgery, renal-conserving approach becomes more feasible.

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Clinical fact or fiction: urinary calculi become impacted mostly at 3 sites of anatomic narrowing in the ureter only?

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Introduction:

Anatomically, the ureter is described as having 3 narrowest sites at which ureteric calculi tend to become impacted. These sites are: pelvi-ureteric junction (PUJ), at the crossing of the iliac vessels and at the uretero-vesical junction (UVJ). The aim of this study is to determine whether ureteric calculi causing obstruction and requiring treatment in our unit are found mostly at the 3 narrowest points of the ureter.

Methods:

Patients with ureteric calculi who required surgical removal of symptomatic obstructing ureteric caculi were studied. All the patients had pretreatment intravenous urography (IVU) or spiral CT scan of kidneys, ureters and bladder (KUB). Stone localization on KUB was categorized according to 10 levels outlined in a designed diagram. Histogram was constructed to plot the distribution of stones within the ureter. Exclusion criteria were previous history of ureteric surgery and patients with congenital anomalies of KUB.

Results:

50 patients were analysed so far. The male to female ratio was 4:1 with calculi equally distributed between the right and left side. Calculi were less than 1cm. in 78% and more than 1cm. in 22%. Two peaks in calculous distribution in the ureters were confirmed; the first above the ischial spine i. e. the proximal part of the lower ureter (42%), while a second was recognized at the level between L-3 and L-4 lumbar vertebrae (36%). There was an absence of the peak in stone location over the iliac vessels.

Conclusions:

This study illustrates two different peaks of calculi distribution in the ureter: one in the upper ureter, below the PUJ and a second in the lower ureter, more proximal than the UVJ. Our findings indicate an absence of the peak predicted by the classic 3 known anatomic sites of ureteric narrowing.

Key Words: Urinary calculous; Ureter; Anatomical narrowing;
Funding Agency: Departmental resources

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Stenting is not essential after ureteral dilatation during uncomplicated ureteroscopy: A randomized study

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Introduction:

The rationale for routine use of ureteral stents after ureteroscopy originates from assumption rather than evidence based medicine. This study is conducted to assess the need for routine double –J ureteral stenting after balloon dilatation during non complicated ureteroscopic stone extraction for lower ureteric stones.

Methods:

This is a prospective randomized study of series of patients who underwent ureteroscopy from January 2004 to Jan 2007. A total of 220 patients, were divided into two groups; group I double –J stented (n=110), group II non-stented (n=110) all of whom had ureteric orifice balloon dilatation during ureteroscopy. Standard ureteroscopic stone extraction with or without intracorporeal lithotripsy was performed through an ureteroscope (Storz, 10. 5 Fr). Tested variables were patients' sex, age, stone characters and previous surgery. The operative and postoperative variables were also tested.

Results:

There was no significant difference between the groups with regard to age, sex, or stone burden. Operative time was less in the group II than in the group 1 (33. 77±6. 50 minutes; 46. 73±9. 92 minutes; respectively with P<0. 05). Dysuria and urgency were significantly less in group II. Also, average length of hospital stay was lower in group II (28. 30±10. 81 hours vs. 47. 54±15. 39 hours in group I with P<0. 05). There was no significant difference in postoperative consequences of flank discomfort or fever with need for rehospitalization among the study groups (P=0. 689).

Conclusions:

In patients undergoing ureteroscopy for distal ureteral stones with routine balloon dilatation, double–J ureteric stenting can be safely omitted, thereby reducing operative time, surgical costs, and patient morbidity. Balloon dilatation during uncomplicated ureteroscopy for lower ureteric stones is not an indication for stenting.

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Comparison Between Laparoscopic Pyelolithotomy and Percutaneous Nehrolithotripsy in Management of large Renal Stones. Double Center Experience

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Introduction:

We compared laparoscopic Pyelolithotomy (LP) and Percutaneous Nehrolithotripsy (PCNL) in the treatment of renal pelvic stones >2mm in diameter.

Methods:

Between June 2004 and Jan 2007, 91 patients having big solitary renal calculi with certain inclusion criteria were chosen and non-randomized controlled into two groups . Group (1) For Laparoscopic Pyelolithotomy and group (2) for percutaneous nephrolithtripsy. Two procedures were done in two separate centers. Operative time, blood loss, residual stones , need for auxiliary treatment time to oral intake, dose of analgesic, surgical complications, conversions, hospital stay and return to normal activities were compared.

Results:

There was no difference between the two groups regarding the characteristics of the patients and the stones. All procedures were successfully completed. Operative mean time was 1. 8 h and 1. 3 h for both groups respectively ($p < 0.05$). There were no differences in analgesia, hospital stay and time for return to normal activities. Complications were observed in group 1 as (hypercarbia in one patient, peritoneal lacerations as well as gonadal vessel injury each in one patient). blood transfusion is (in group (1) 0 % and group 2 was needed in two patients 4. 6% and one patient in need for selective embolization). No residuals in group 1 but only one patient was in need for ureteroscopy to remove migrating fragment in group 2. Urinary leakage occurred in 5 patients in group 1 and 1 patient in group 2 ($p > 0.05$).

Conclusions:

There are no relevant differences between laparoscopic Pyelolithotomy LP and percutaneous nephrolithotomy PCNL. Laparoscopic Approach is suitable for patients with large non-staghorn stones without history of recurrent pyelonephritis or prior surgery and PCNL remains the procedure of choice for these indication

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Laparoscopic Pyelolitotomy: Comparison OF Transperitoneal And Reteroperitoneal Approaches

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Introduction:

We compared transperitoneal laparoscopic pyelolithotomy (TLP) and retroperitoneal laparoscopic pyelolithotmy(RLP) for the treatment of renal pelvic stones >20 mm in diameter.

Methods:

Between June 2002 and jan 2008, 48 consecutive cases (male, 37; female, 12) with solitary renal calculi had undergone TLP (27) or RLP (21). Patients were chosen to be treated laparoscopically on economic grounds or when the stones has not responded to treatment with extracorporeal shock wave lithotripsy or percutaneous nephrolithotomy. Operative time, blood loss, time to oral intake, dose of analgesic, surgical complications, conversions, hospital stay and return to normal activities were compared.

Results:

There was no difference between the two groups regarding the characteristics of the patients and the stones. All procedures were successfully completed. Operative mean time and time to oral intake were 2. 2 h and 24 h for the transperitoneal and 1. 8 h and 12 h for the retroperitoneal approach (p<0. 05). There were no differences in blood loss, analgesia, hospital stay and time for return to normal activities. Complications were observed in two patients in the TLP(gonadal vessel injury and ileus) and there were three events in the RLP (hypercarbia, peritoneal lacerationas well as gonadal vessel injury). Urinary leakage occurred in 3 patients in TLP group and 2 patients in RLP group (p> 0. 05). No conversions occurred in both groups.

Conclusions:

There are no relevant differences between the transperitoneal and retroperitoneal approaches. Choice of the laparoscopic approach rests upon particular aspects of each case or upon the surgeon's preference.

Key Words: Renal stone; Laparoscopy; nephrolithotomy;

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Current indications and results of percutaneous nephrostomy: The Mubarak Hospital, Kuwait experience.

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Introduction:

 The insertion of percutaneous nephrostomy (PCN) tube is often a useful emergency radiological procedure to relieve urinary tract obstruction associated with uraemia or septicaemia. The major advantage of PCN is that it can be performed under local anesthesia even in very ill patients. We analyzed the indications and results of PCN tube insertion in our unit over a 7- year period.

Methods:

 228 patients with acute ureteric obstructions who had PCN tubes inserted in our Hospital between 2000 and 2007 were prospectively studied. On admission urine and blood samples were sent for microscopy, culture and sensitivity (MCS). Intravenous ceftriaxone or amikacin was given prophylactically prior to PCN tube insertion. The fluid obtained from the obstructed renal pelvis during PCN insertion was also sent for MCS. Serum creatinine on admission and 168 hours post PCN insertion were estimated. The indications for PCN, the effect of PCN on renal function and complications encountered were also analyzed.

Results:

 Ureteric calculus and ureteric stricture due to schistosomiasis were the commonest causes (70% and 13% respectively) of ureteric obstruction requiring urgent PCN tube insertion. There was significant bacterial growth in 20% of the cultured urine specimens. E. coli was isolated in 45% of these, with sensitivity of 82%, 73% and 60% to amikacin, ofloxacin and ceftriaxone respectively. Minor complications occurred in 11. 4% of the patients. Renal function normalized in 90% of patients within 168 hours of PCN tube insertion.

Conclusions:

 The commonest indication for PCN insertion in our unit is ureteric obstruction secondary to calculus. The commonest isolated bacterium is E. coli. Amikacin is an effective empiric prophylactic antibiotic. We therefore advocate the use amikacin as a first choice antibiotic in urinary tract sepsis.