

Abstracts

Abstracts of Theses Approved for the M.Sc., M.Med. and Phd. Degrees at the School of Medical Sciences, University Sains Malaysia, Health Campus, Kubang Kerian, Kelantan, Malaysia.

A COMPARATIVE STUDY BETWEEN DEXMETETOMIDINE AND MIXTURES OF MIDAZOLAM AND MORPHINE FOR POSTOPERATIVE SEDATION IN INTENSIVE CARE UNIT

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Introduction : The α_2 agonist dexmedetomidine is a new sedative and analgesic agent which is licensed in the USA for post-operative intensive care sedation. We compared dexmedetomidine with the mixture of midazolam and morphine for post-operative patient who required mechanical ventilation in intensive care unit (ICU).

Objective : To compare the effect of dexmedetomidine and midazolam-morphine mixture among post-operative patients in ICU; in term of the amount of analgesic (PCA morphine) requirement, sedation score, haemodynamic profiles and time of extubation.

Methodology : Prospective, double-blinded randomized controlled trial study design involved post-operative patients admitted to the Intensive Care Unit (ICU) of Hospital Universiti Sains Malaysia (HUSM) conducted from June 2003 to June 2004. Thirty-four mechanically ventilated post-operative patients were randomly assigned to receive short-term (minimum 4 hours) sedation with either continuous intravenous infusion of dexmedetomidine (group Dex, n=17) or midazolam-morphine mixture (group MM, n=17). Both groups received similar intraoperative anaesthetic regime. Patient controlled analgesia (PCA Morphine) was given to patient as rescue analgesic. Analgesic (PCA morphine) used (mg/hour), Ramsay sedation scoring, extubation time (minute), systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate were Medical Sciences, Universiti Sains Malaysia had approved this study on 9th April 2003.

Result : Mean extubation time of dexmedetomidine group was significantly lower than midazolam and morphine mixture group [mean (s.d.): 40.3 \pm 16.5 minutes versus 57.9 \pm 17.7 minutes, p=0.05]. Within the first 4 hours drug infusion, mean systolic blood pressure [mean (s.d.): 105 \pm 14 mmHg vs 127 \pm 24 mmHg, (p=0.000)], mean diastolic blood pressure [mean (s.d.): 59 \pm 8mmHg vs 66 \pm 13 mmHg (p=0.000)], mean arterial pressure [mean (s.d.): 76 \pm 9 mmHg vs 86 \pm 15mmHg (p=0.000)] and mean heart rate [mean (s.d.): 88 \pm 13 beats per minute vs 102 \pm 24 beats per minute (p=0.000)] were significantly lower in dexmedetomidine group than those in midazolam and morphine mixture. There was significant difference of mean Ramsay sedation score between dexmedetomidine and midazolam morphine mixture (p=0.000). However, there was no significant difference of mean dose of morphine per hour between dexmedetomidine groups and midazolam morphine mixture [(mean (s.d.): 1.4 \pm 0.7 mg/hour) versus mean (s.d.): 1.1 \pm 0.8 mg/hour), p= 0.157].

Conclusion : Dexmedetomidine provides safe, effective sedation and analgesia for postoperative long surgical patient in intensive care unit. Haemodynamic variables of dexmedetomidine group was more

stable than midazolam and morphine mixtures group. Thus dexmedetomidine provides better perioperative haemodynamic control or a long surgery. The use of dexmedetomidine also allowed for more rapid tracheal extubation.

Dr. Saedah Ali : Supervisor
Dr. Nik Abdullah Nik Mohamed : Co-Supervisor

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A COMPARISON OF THE LARYNGEAL TUBE WITH THE LARYNGEAL MASK AIRWAY DURING SPONTANEOUS VENTILATION IN PAEDIATRIC ANAESTHESIA

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Objectives : The purpose of this study is to assess whether the newly developed laryngeal tube is a reliable, easy and safe device for use in paediatric patients. We compared the use of the laryngeal tube with the laryngeal mask airway in spontaneously ventilating paediatric patients undergoing general anaesthesia during elective surgery.

Methodology : A randomized prospective study was conducted On 80 premedicated paediatric patients of ASA 1 and 2, aged between 2 to 10 years. They were divided into 2 groups (n = 40/group), receiving either LT or LMA as airway device. After inhalational induction of anaesthesia with sevoflurane followed by fentanyl 1.5 μ g.kg⁻¹, the LT or the LMA was inserted and the patients breathed spontaneously throughout the surgery. Anaesthesia was maintained with nitrous oxide, oxygen, and sevoflurane. The airway device was removed at the end of surgery with the patients fully awake. The speed and ease of insertion and the number of attempts needed to successfully secure the airway was recorded.. The quality of ventilation as assessed by incidence of oxygen desaturations, frequencies of airway manipulations throughout the surgery and the end-tidal CO₂ at various time intervals were recorded. Systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate at different time intervals were recorded. The incidence of complications was also recorded.

Results : We found that there was longer time and more number of attempts required for successful insertion for LT group as compared to LMA. which difference was statistically significant. The number of manipulations of device or patients after first attempt and the ET CO₂ recorded at various time intervals was higher with the LT group and the difference was significant. There was no statistical difference in episode of desaturation and haemodynamic changes. There was no difference in the incidence of complications between the two groups.

Conclusions : We conclude that during spontaneous ventilation in paediatric patients undergoing general anaesthesia the laryngeal tube is not as reliable in providing a satisfactory airway and we consider it is not a suitable alternative to the laryngeal mask airway.

Dr. Nik Abdullah Nik Mohamed : Supervisor
Dr. Rhendra Hardy Mohd Zaini : Co-Supervisor

A COMPARISON STUDY OF THE HEALING TIME OF DIABETIC PODIATRIC WOUNDS SUBJECTED TO FAR INFRARED LIGHT AND POVIDONE-IODINE DRESSINGS AND POVIDONE-IODINE DRESSING ALONE

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Introduction : Wounds have been the bane of physicians since time immemorial. The use of light of various colours (i.e. wavelengths) has shown potential as an adjuvant to be used in the armament of the surgeon treating wounds. The utility of infrared radiation is a relatively newer modality which shows encouraging promise, especially in the setting of diabetic wounds, which are unique and nefariously more complex due to poorly understood pathophysiology and systemic derangement. These wounds often run an indolent course and readily recur.

Objectives : This study attempts to assess the augmentation to wound healing the utility of a far-infrared device confers on diabetic wounds of Wagner grade 2.

Methodology : The study performed was a double-blinded non-randomized controlled trial, comparing two cohorts; a control cohort of diabetics undergoing standard treatment of wound care, inclusive of antibiotics, sharp surgical debridement and povidone-iodine and saline. dressings The second cohort was comparable to the first, except these patients were also subjected to exposure of pulsed far-infrared light over the involved foot (dressed) for a daily exposure of 30 minutes.

Results : From November 1st, 2003 till October 31st, 2004 a total of 66 patients were chosen for this study based on inclusion criteria; type 2 diabetic with a Wagner grade 2 wound, haemoglobin (Hb) level of at least 100 gm/dL, absolute lymphocyte count (ALC) of $\geq 1500 \text{ ml}^{-1}$, serum albumin of $\geq 25 \text{ gm/L}$, serum AST of $\leq 80 \text{ units/L}$, absence of endstage renal failure, and transcutaneous oxygen tension (TcO_2) of $\leq 30 \text{ mm Hg}$. Dropout criteria was necessity for a repeat debridement, poor sugar control of $> 20 \text{ mmol/L}$ on 3 consecutive readings and adverse reactions to either treatment modalities. The studied variable in this study was the readiness of the debrided wound for split-thickness skin grafting or secondary surgical closure of wound (end point) as measured from the time of the debridement till the end point. A total of 33 patients were enrolled in the Povidone cohort, of which 3 dropped out. Thai of the Infrared cohort enrolled 33, of which 4 dropped out. Parameters considered were age, sex, smoking status, exposure to smoking, comorbid medical illnesses, duration of diagnosis of diabetes, region of wound involvement, area of ulceration after debridement, Hb, ALC, albumin, AST, TcO_2 , HbA_{1c} and creatinine. Cohorts were comparable from the evaluation of independent t-test testing differences in means, with a strong significance of $P = 0.007$ in readiness of wound for SSG, comparing the infrared cohort to that of the povidone cohort. A mild significance was also arrived at in consideration of HbA_{1c} ($P = 0.36$). However, in the ANCOVA, with readiness for SSG as the backdrop, the cohort was found to be strongly significant ($P = 0.004$), while all other parameters were not, except for TcO_2 , which was also significant at $P = 0.007$, as has been repeatedly demonstrated by earlier studies on healing of diabetic wounds. The 4 patients who had dropped out of the Infrared cohort were all noted to have large sole and heel wounds and borderline albumin and TcO_2 levels. All developed dessication of wound and all but one developed blisters.

Conclusion : The utility of pulsed far infrared light as an augmentation to wound healing in type 2 diabetics with Wagner grade

2 wounds seems to result in accelerated wound healing at an exposure of 30 minutes daily through the dressed wound. A word of caution is added, however that the optimum duration of exposure is yet to be ascertained in those wounds denuding the calcaneum and associated with borderline levels of TcO_2 and serum albumin.

Dr. Abdul Halim Yusof : (Supervisor)
Dr. Mohamad Iskandar Mohamad Amin : (Co-Supervisor)

A PILOT COMPARATIVE STUDY BASE ON CLINICAL PERSPECTIVE UPON THE EFFECTS OF DECREASING MAS ON IMAGE QUALITY IN PAEDIATRIC CT BRAIN

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Introduction : Radiation exposure to the patient during computed tomography (CT) is comparatively and relatively high, and this has caused concern especially in paediatric patients. In addition, there is no known consensus about the optimal milliampere-second (mAs) and no established method for measuring diagnostic image quality settings for computed tomography (CT). Most institutes choose tube-current settings either by following the manufacturer's recommendations or by following their own experience without assessing the effect on image quality in detail or any clinical evidence. Thus, these standard protocols used by many imaging departments tend to be biased toward higher mAs and shorter pitch factors than is actually required for adequate imaging in the majority of children. Thus, it is important to optimize the radiation dose so that it is as low as possible achievable but still consistent with required diagnostic image quality.

Objective : To determine whether a lower radiation dose technique (using a lower mAs; in this study, 60% reduction) could be used in computed tomography (CT) of the paediatric brain without jeopardising the diagnostic accuracy of the images.

Methodology : This is a randomised cross sectional prospective trial. Data were obtained for a group of 50 children aged 0-12 who required non-contrast-enhanced computed tomography (CT) brain examinations between February 2004 and October 2004. The children were divided randomly into 2 groups. In this study, the variable parameter was mAs, with one group using 190mAs and the other, 70mAs (60% reduction). Other technical parameters such as kVp, pitch, collimation, section thickness, and total number of sections were fixed. Patient data also included age, sex and ethnicity. Anatomical details, resolution with less noise detected and the confidence level in reaching a diagnosis were evaluated by two radiologists in a double-blinded manner using a 4-point scoring system.

Results : For both observers, the Kappa statistics is 0.818, indicating that was perfect agreement between the two observers, and no statistically significant difference in the confidence level for reaching a diagnosis between the two groups. 56% of study group (using mAs of 70) was considered acceptable (by mutual agreement of both observers), revealing that mAs of 70 could be used. Total acceptability by first and second observers were 84% and 74% respectively. It was best shown in structures of high contrast resolution.

Conclusion : CT radiation dose reduction is an important issue when considering CT examination by balancing the benefits against possible radiation risk, especially as there is marked increased in utilization of CT scan. In this study, it was shown that it was possible to reduce the radiation dose of CT brain in paediatrics, lower than mAs of 190, however, not lower than mAs of 70. This dose reduction of 60% is

possible in certain conditions. It was especially useful in gross abnormalities, follow-up cases and in those conditions in which CT was not the primary diagnostic imaging modality.

Dr. Noreen Norfarahen Lee Abdullah : Supervisor
Assoc. Prof. Dr. W. Ahmad Kamil Abullah : Co Supervisor

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A PILOT STUDY ON RED CELL IMMUNIZATION IN MULTIPLY TRANSFUSED THALASSAEMIC PATIENTS

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Introduction : One of the risks of blood transfusion was formation of antibodies against one or more red cell antigens. The development of alloantibodies and autoantibodies complicates transfusion therapy in multiply transfused thalassaemia patients.

Objectives : To study the frequency, causes and prevention of this phenomenon were studied among thalassaemia patients. Clinical and serological data of 63 multiply transfused thalassaemia patients who sought their treatment in Hospital Universiti Sains Malaysia and Hospital Kota Bharu were collected and analyzed prospectively. Blood samples were subjected to standard blood bank procedure for screening of antibody and subsequent antibody identification.

Results : Of these patients, 49 (77.8%) were Hb E/_ thalassaemia, 10 (15.9%) were _ thalassaemia major, 3 (4.7%) were Hb H Constant Spring and one (1.6%) were Hb H disease. All patients received blood matched for only ABO and Rh(D) antigens. Overall, 7.9% of the patients had clinically significant alloantibodies and 1.6% had autoantibodies. Three patients develop one type of antibody, one patient developed 2 types of antibodies and one patient developed 4 types of antibodies. The specificities of the alloantibodies were anti E, anti c, anti K, anti Jka, anti N and anti S. There was no significance effects of ethnicity, splenectomy, frequency of transfusion and age at the start of transfusion on red cell immunization in this study due to small sample size. However we observed that all the 5 patients that developed alloantibodies had their first transfusion after the age of one year old and none of them had undergone splenectomy. Twenty-three patients were positive for direct antiglobulin test, of which 2 were positive for Ig G and C3d and 21 were positive for Ig G only.

Conclusions : Transfusion of matched blood was essential for chronically multi-transfused patients in order to avoid alloimmunisation. Considering the high frequency of anti E, it is advisable to match red cell unit for E antigens in multiply transfused thalassaemia patients. Therefore, all thalassaemia patients who had been started on transfusions should have RBC antigen phenotyping.

Dr. Rosline Hasan : (Supervisor)
Dr. Ariffin Nasir : (Co-Supervisor)

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A PILOT STUDY: CORRELATION OF CT PERFUSION PARAMETER WITH CLINICAL STROKE SCORE IN ACUTE ISCHAEMIC STROKE PATIENTS

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Introduction : Many recent advances have taken place in the diagnosis and management of acute stroke patients. One of the major breakthroughs is the introduction of acute thrombolysis therapy with intravenous recombinant tissue plasminogen activator (rtPA) within three hours of clinical stroke onset. This recent development has triggers many researches in cerebral perfusion during this hyperacute stage of stroke in an attempt to understand the perfusion disturbances during tissue ischaemia- infarction for an early diagnosis of stroke. Current clinical trials are using the National Institute of Health Stroke Scale (NIHSS) score to quantitatively measure the acute neurological deficit prior, during and post drug trial. Its baseline score can prognosticate the future outcome of stroke patients.

Objective : This pilot study aimed to investigate the correlation of CT Perfusion parameters (cerebral blood volume, cerebral blood flow and mean transit time) with the NIHSS score in acute ischaemic stroke patients.

Methodology : Twelve patients with first presentation of acute ischaemic stroke at less than 72 hours of clinical onset with no contraindication of intravenous contrast media were enrolled with an informed written consent during study period of February 2004 till October 2004. CT Perfusion and NIHSS scoring were performed by the researcher in the same setting. Perfusion parameters (cerebral blood volume, cerebral blood flow and mean transit time) and baseline NIHSS scores were analyzed to ascertain their correlation.

Result : A statistically significant and good strength of correlation noted between CBV ($r = -0.720, p = 0.008$) and CBF ($r = -0.723, p = 0.008$) with NIHSS score. Meanwhile a statistically insignificant and poor strength of correlation seen between MTT ($r = 0.136, p = 0.673$) with NIHSS score.

Conclusion : Findings from this pilot study may give an added value to CT Perfusion imaging in acute stroke patient; cerebral perfusion assessment with simultaneous prognostication of future stroke outcome.

Assoc. Prof. Dr. Nurul Azman Ahmad Alias : Supervisor
Assoc. Prof. Dr. John Tharakan : Co-Supervisor

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A STUDY OF ASSOCIATION BETWEEN MATERNAL PERIODONTITIS AND LOW BIRTH WEIGHT INFANTS AMONG MALAY WOMEN IN KOTA BHARU, KELANTAN

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Introduction : Worldwide, low birth weight (LBW) is a significant risk factor for neonatal and infant mortality. The adverse consequences of LBW, which include a variety of chronic medical conditions and neurodevelopmental disorders that may lead to long term health problems for the infants, not only cause a tremendous impact on the family but also on the health care system. Current studies have suggested maternal periodontal infection as a risk factor for LBW.

Objectives : The objectives of this prospective cohort study were to determine the incidence of LBW infants among pregnant women with periodontitis and the association between maternal periodontitis and LBW.

Methodology : Screening periodontal examinations were carried out on all pregnant women attending Klinik Kesihatan Ibu dan Anak (KKIA) Bandar Kota Bharu and KKIA Wakaf Che Yeh for antenatal health care during the study period of December 2003 to June 2004 who fit the inclusion and exclusion criteria. Systematic random sampling was utilized for selection of 250 study subjects for each study group.

Results : Of 500 women enrolled in the study, 28 (5.6%) were either lost to follow-up or excluded. Of the remaining subjects, 240 women had healthy periodontium while another 232 had periodontitis. Due to ethical considerations, the gestational duration at which the exposed and non-exposed subjects were recruited into this study was not equal, and hence the duration of follow-up was also different between the two groups. The follow-up duration for the exposed and non-exposed group was 9.6 weeks (SD 1.14) and 22.5 weeks (SD 0.97) respectively. The incidence of LBW was 14.2% (95% CI: 9.7-18.8) in women with periodontitis, and 3.3% (95% CI: 1.1-5.6) in women without periodontitis. The relative risk of having LBW infants was 4.27 times for women with periodontitis than for those without periodontitis (RR=4.27, 95% CI: 2.01-9.04). Significant association was found between maternal periodontitis and LBW at both univariable (OR=4.81, 95% CI: 2.17-10.65) and multivariable level analyses (OR=3.84, 95% CI: 1.34-11.05). The results of this study provide additional evidence that pregnant women with periodontitis are at a significantly higher risk of delivering LBW infants.

Conclusions : It is hoped that this study would stimulate and motivate further research that explores the role of oral diseases in human health. Ultimately, it should help to establish the groundwork for better communication between the medical and dental colleagues to improve the quality of antenatal health care in Malaysia.

Dr. Norsa'adah Bachok : Supervisor
Dr. Nik Hazlina binti Nik Hussain : Co-Supervisor

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A STUDY OF FEASIBILITY OF ENTONOX AS AN ANALGESIC IN THE EMERGENCY DEPARTMENT, HUSM

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Objectives : The main objective of this study was to assess the effectiveness and feasibility of Entonox in providing pain relief for patients who complain of acute pain seen in the Emergency Department (ED) HUSM. The specific objectives were to determine the level of pain reduction based on Visual Analogue Scale (VAS) score after the inhalation of Entonox as an analgesic. It was also aimed to assess the patient's acceptance in using Entonox as an analgesic.

Methodology : This prospective study was done in June, 2003. The patients who complain of acute pain that came to HUSM were randomly selected. A total of 55 patients (approved by the Ethical Committee USM in the 104th meeting, 2003) were chosen. Cause of pain and type of medications prior coming to EDHUSM were recorded. The severity of pain before and after treatment with Entonox was measured using VAS. Time taken by medical personnel to start the patient on Entonox after being ordered by a doctor was recorded. The changes in blood pressure and pulse rate before and after the treatment were also recorded. The patient was asked about the level of pain reduction after the use of Entonox, and the level of comfortness while using it. The data were analyzed using Paired t-test, Student t-test and ANOVA.

Results : It was noted that time taken by a medical personnel to start the patient on Entonox after being instructed by a doctor was 2.24 ± 0.69 minutes. This study showed that the overall mean for pre-treatment VAS score was 6.35 ± 0.79 , and the overall mean for post-treatment VAS score was 2.42 ± 0.71 . Analysis showed significant reduction of VAS score after the treatment of Entonox ($p < 0.05$). The pulse rate was significantly increased after the inhalation of Entonox but there were no significant changes in blood pressure before and after the treatment. All the patient claimed that the pain that they experience reduced after

using Entonox. 98.2% of the patients said that the pain was only partially relieved, and one patient declared complete pain relief after Entonox inhalation. Fifty

Conclusions : The administration of Entonox was relatively quick and easy, whereas the effectiveness of it as analgesia was proven. At present, the Entonox is still under-utilized in the emergency room. The protocol for the usage of entonox should be developed so that it can be widely used in the emergency room for the sake of the patient.

Dr. Wan Aasim Wan Adnan : Supervisor
Dr. Sharina binti Dir : Co-Supervisor
Dr. Azmany binti Wahab : Co-Supervisor

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A STUDY OF WORK STRESS IN THE EMERGENCY DEPARTMENT, SELAYANG HOSPITAL

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Introduction : Work related stress is a threat to the health of working people and to the healthiness of their work organizations. Recent evidence has shown that 30% of health care workers will experience psychological dysfunction.

Objective : To assess the level of occupational stress of Selayang Hospital Emergency Department medical personnel.

Methodology : Cross-sectional questionnaire survey. Main outcome was measured based on the data collected from self-explanation validated questionnaire forms which were based on the "Personal Stress Inventory" containing the score for occupational factors, the frequency of the stress factors within 6 months, the family stress factors score and stress symptom checklist score.

Results : Of 90 valid responders (100%). 56 person completed the form, 30 person declined to participate while 4 person did not complete the form. 37 (66.1%) personnel scored the occupational factors between 4 to 6 indicating moderate level of stress, 11 (19.6%) scored more than 6 indicating high level of stress. Twelve most stressful occupational factors were identified (score between 5.07 to 6.11), amongst were insufficient personnel to handle an assignment, personal insult from patient, patient's relatives or colleague and inadequate salary. 5 of the identified most stressful occupational factors appeared to be frequent in 6 months period, amongst were poorly motivated coworkers, insufficient personal time and lack of recognition for good job. Two stressful family factors identified were poor salary and not enough time spent with family. Most stressful symptoms complained were headache, back pain, muscle tension, stomachache or upset, heartburn and grinding teeth (all scored less than 2). The most stressful job was medical assistant (5.6), followed by attendant (5.2) and medical officer (5.0). Male was more stressful than female (5.32 vs 4.51). Stress score was moderate in Indian (4.6), which was higher compared to Chinese and Malay. Marital status has no effect on stress. Those who have children were more stressful than those without children. Stress was more in the older age group (5.3). Stress was more for new personnel. Those who did not take medical leave were more stressful.

Conclusion : There are moderate level of stress in medical personnel working in this department particularly the medical assistants and the attendants. There is unlikely to be an effect on staff morale and career longevity. Interventions to improve the working condition in emergency department is required particularly to increase the number of staff, to improve the salary, to implement crisis intervention program and motivational program as well as increasing the security support.

Prof. Madya Kamaruddin Jaalam : (Supervisor)
Dr. Sharifuddin Osman : (Co-Supervisor)

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A STUDY ON RISK FACTORS OF REPEATED ADMISSIONS AMONG SCHIZOPHRENIC PATIENTS IN HOSPITAL UNIVERSITI KOTA BHARU

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Introduction : The number of people with psychological problems in the world has reached 1.5 billion in 1996, but only one percent of them have received treatment (10th International Psychopathology Conference). Schizophrenia is a difficult disease that many choose to conceal. Relapse and frequent readmissions among schizophrenic patients are common and various risk factors have been associated with them. These further enhance the existing societal stigma which causes pain to the patients, their family and friends.

Objective : To identify the risk factors of readmission in less than 6 months from the previous admission among schizophrenic patients in Hospital Kota Bharu.

Methodology : A total of 120 outpatients who had repeated admission within 6/12 months and 120 inpatients who fulfilled DSM IV criteria for schizophrenia from Hospital Kota Bharu between 1st October 2002 until 31st March 2003 were interviewed using a validated questionnaire. The questionnaire includes questions on patients' sociodemographic data, compliance, insight, family support and life events.

Results: Using multiple logistic regression, it was shown that young age (OR: 0.94, p: 0.004), number of previous admission (OR: 1.163, p: 0.001), good compliance (OR: 0.046, p: 0.001), poor insight (OR: 7.32, p: 0.001), partial insight (OR: 3.08, p: 0.023), importance of follow up (OR: 2.94, p: 0.043) and family remind follow up (OR: 0.17, p: 0.001) were significant risk factors of repeated admissions. Other variables such as marital status, income, education, distance and life events showed no significant associations.

Conclusions : Age, number of previous hospitalization, poor compliance, poor insight and poor family support were important factors in determining repeated admissions among schizophrenic patients. In the management of these patients, good family supports need to be emphasized.

Dr. Mohd Raza Merchant : Supervisor
Dr. Shaiful Bahari Ismail : Co-Supervisor

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A STUDY ON THE PREVALENCE AND CLINICAL CHARACTERISTICS OF MALE PARTNERS IN INFERTILE COUPLES WITH UNEXPLAINED INFERTILITY HAVING ANTISPERM ANTIBODIES ATTENDING INFERTILITY CLINICS IN HOSPITAL USM AND HOSPITAL KOTA BHARU, KELANTAN.

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Introduction : Antisperm antibody can be a cause of male infertility

(Rumke et al 1974; Hendry et al 1977; WHO 1984; Bronson et al. 1984). Research over the last three decades has unraveled some of the mechanisms of sperm antibody- mediated infertility which include impaired sperm penetration through the cervical mucus (Kremer & Jager 1976, 1981), increased sperm attrition in the female genital tract and exclusion of viable sperm from the site of fertilization (Adeghe 1987), and inhibition of sperm penetration into the human ova (Bronson et al, 1984). Clinical management of this subgroup of infertile men still remains unsatisfactory. Despite this prevalence of immune based infertility, controversy exist over which patients should be tested for the presence of antisperm antibodies. As noted by Jarow and Sanzone (1992), the specific indication for antibody testing of infertile men have been based upon reports and studies using outdated antibody assays. Presently multiple risk factors, including vasectomy, infection, trauma, surgery, torsion and the presence of vancocoele are associated with an increased risk of antisperm antibodies. However the relationship between these risk factors and antisperm antibodies awaits confirmation by modern day assays directed at detection of antibodies.

Objectives : To determine the local prevalence of antisperm antibodies among men attending the infertility clinics in Hospital USM and Hospital Kota Bharu. To correlate these men with antisperm antibodies to various clinical features eg diabetes mellitus, sexually transmitted disease, genital infection, lower abdomen surgery, genital trauma and smoking habits.

Methodology : This is a prospective study involving 180 men receiving treatment at the infertility clinics in Hospital USM and Hospital Kota Bharu between 1st. January 2004 and 30st. October 2004. Patients are selected based on their record of unexplained infertility. These patients have been on follow up between 1st January 2002 till 30st. October 2004. Upon consent and recruitment, a sample of three cc of venous blood is taken from the right forearm. The blood is transported to the immunology laboratory in Hospital USM and processed to obtain a sample of serum. The serum is then pooled and later tested for the presence of antisperm antibody using the Anti-Spermatozoa- Antibody (ASA) ELISA test. (Pharmacia Diagnostics: Varelisa Sperm Antibodies). Meanwhile the patient is interviewed by the researcher and a checklist (Appendix i) is filled up.

Results : The prevalence of antisperm antibodies in this studied population is 6.1% (11 patients out of 180 patients). This is marginally lower than the reported incidence of 10-26% in other countries. Of all the parameters correlated with antisperm antibody, only genital trauma is significantly associated with antisperm antibody.

Conclusion : The prevalence of antisperm antibodies among the subfertile male is low in our study group. Hence routine screening is not encouraged as it is not cost effective. Corellation of antisperm antibody to genital trauma is significant and can be used as a marker for selective screening of men with antisperm antibody. The result may not be representative of the Malaysian population as it is a hospital based study. A larger scale study involving a few centres is required in order to obtain a national consensus.

Dr. Shah Reza Johan : (Supervisor)
Dr. Adibah Ibrahim : (Co-Supervisor)

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AN INTERVENTION STUDY OF PRESCRIPTION WRITING ERRORS AMONG DOCTORS AT SELECTED OUTPATIENTS CLINIC HOSPITAL UNIVERSITI SAINS MALAYSIA, KUBANG KERIAN, KELANTAN

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Introduction : Most studies have established normal values for Acoustic Rhinometry (AR) analysis of the nasal passage based on a primarily Caucasian. Since consistent anatomic differences do occur in anthropomorphic measurements of the nose of different races and in various ages.

Objectives : AR analysis was performed on Malay subject age between 12 and 18 years old in Kubang Kerian, Kelantan. The study was done in two parts. The objective of part I was to look at the mean airway resistance among Malay children with healthy nose without malocclusion and to describe the total minimal cross-sectional area (MCA) in relation to age and sex. Meanwhile part II was to look at the association between malocclusion and nasal airway resistance.

Methodology : All subjects included in this study were interviewed, screened undergone oral and nasal examinations and AR measurements were taken. Two hundred and twenty and twenty Malay students (107 male and 113 female) aged between 12 and 18 years in Sekolah Menengah Kubang Kerian, Kelantan with no nasal problems was selected in part I study.

Results : Out of 220, 190 was randomly selected as for normal occlusion group and another 63 subjects with untreated malocclusion from Orthodontic Clinic, Universiti Sains Malaysia was selected to participate Part II study. The mean MCA on the right side was 0.47 cm² (SD 0.108) and situated at 1.52 cm (SD 0.565) while left side, 0.45 cm² (SD 0.095) and situated 150 cm (SD 0.560) from the anterior nares. There was an increasing trend of total MCA with increasing age and males had significantly higher total MCA than female. Part two results showed nasal airway resistance (total MCA) was associated with malocclusion (OR=0.96, 95% CI=0.94, 0.97)

Conclusions : AR is a valuable method of assessing the geometry of the nasal cavity and was found to be well tolerated by the children and adolescent. In conclusion result of this study enable us to determine the mean value of the total MCA for healthy nose among Malay children aged between 12 and 18 years old in Malaysia and in the presence of nasal obstruction, malocclusion had a significant association with nasal airway resistance.

Dr. Than Winn : Supervisor

Dr. Suzina Sheikh Abd. Hamid : Co-Supervisor

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ASSESSING GLYCAEMIC CONTROL : A RANDOMIZED CONTROL TRIAL BETWEEN FASTING AND 2 HOURS POSTPRANDIAL BLOOD GLUCOSE MONITORING IN TYPE 2 DIABETIC PATIENTS ATTENDING KLINIK RAWATAN KELUARGA, UNIVERSITI SAINS MALAYSIA, KELANTAN

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MMed (Family Medicine)*

**Department of Family Medicine,
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Health Campus, Kelantan, Malaysia**

Introduction : The goal in management of patients with type 2 diabetes is to control fasting plasma glucose (FPG) and HbA1c. Unfortunately, the majority of patients with diabetes fail to achieve their glycaemic goals. Elevated postprandial glucose (PPG) concentrations may contribute to suboptimal glycaemic control. Postprandial hyperglycaemia is actually one of the earliest abnormalities in type 2 diabetes. Emerging data indicate that modulation of postprandial plasma glucose levels plays an important role in overall glycaemic control, such as glycosated hemoglobin, lipid abnormalities and the risk of macrovascular dan microvascular complications.

Objectives : This study was a prospective, randomized control trial designed to determine which blood glucose monitoring (either fasting blood glucose or 2 hours post taking standard meal for breakfast) can

leads to a better glycaemic control in type 2 diabetic patients and the correlation between these two glycaemic profiles with HbA1c and fructosamine, to evaluate the sensitivity, specificity and positive predictive values between glycaemic profiles in predicting good glycaemic control and to find out either demographic, socioeconomic or disease characteristic factors that associate with glycaemic control.

Methodology : A total of 82 patients from Klinik Rawatan Keluarga were assigned to either postprandial group (PP) or Fasting group (FG), and follow-up was done for 6 months. For Fasting group, they are monitored using fasting blood sugar (FPG) whereas postprandial group are monitored using 2 hours postprandial blood glucose (PPG). They were instructed to come for monthly blood glucose monitoring (FPG and PPG) and treatment was given or adjusted accordingly depends either FPG or PPG result. HbA1c, fructosamine and Fasting Lipid Profiles (FLP) were taken from each subject at baseline, month 3 and month 6. Demographic, socioeconomic and disease characteristics data were also collected from patients via interview during the first visit.

Results : With regards to glycaemic control for 6 months duration, 58.5% subjects in PP and 43.6% in FG were with the good control of HbA1c (HbA1c \leq 7.0%). So as for fructosamine, 48.8% subjects in PP and 33.3% in FG were with the good control of fructosamine ($<$ 285 μ mol/L). Subject in PP group only reduce about 0.1% (7.09 reduced to 6.99%) whereas subject in FG showed more reduction in HbA1c which was 0.42% (7.92 reduced to 7.49%). There was significant difference in mean glycaemic control (HbA1c and fructosamine) between both groups ($p=0.029$, $p=0.034$). As a whole, means of HbA1c and fructosamine levels in PP group at the end of study much more lower compared to FG. The estimated marginal mean showed reduction in HbA1c for both groups, FG more than PP but for fructosamine, only in PP group. PPG showed better correlation to HbA1c ($r=0.604$ vs 0.575 , $p=0.001$) whereas FPG correlated better to fructosamine ($r=0.566$ vs 0.551 , $p=0.001$). The sensitivity, specificity and positive predictive value of were 75%, 80.6% and 82.5% whereas FPG were 81.8% 58.3% and 70.6%. Multivariate analyses showed factors that associated with poor glycaemic control include younger age, increase in type of or hypoglycaemic agents took by the patients and patients with no nephropathy.

Conclusions : These results suggest that in overall, postprandial blood sugar (PPG) was better than fasting blood sugar (FPG) in monitoring type 2 diabetic patients who require oral hypoglycaemic agents. PPG correlated better than FPG with both HbA1c and fructosamine levels. Compared to HbA1c, fructosamine correlated least well with mean glucose profile results. So, using of HbA1c in monitoring overall glycaemic control is better than fructosamine. PPG predicted overall glycaemic control better than Fasting Blood sugar. Factors that associated with poor glycaemic controls are younger age, increase in type oral hypoglycaemic agents took by the patient and absent of nephropathy.

Assoc. Prof. Mutum Samarendra Singh : Supervisor
Dr. Saleena Awang : Co-Supervisor

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COMPARISON OF ARTERIAL AND VENOUS BLOOD GAS VALUES IN THE INITIAL EMERGENCY DEPARTMENT EVALUATION OF PATIENTS WITH DIABETIC KETOACIDOSIS

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MMed (Emergency Medicine)*

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Introduction : Diabetic Ketoacidosis is one of the most serious acute metabolic complications of Diabetes Mellitus. It is considered to be

an endocrinology emergency. Diagnostic criteria of Diabetic Ketoacidosis are plasma glucose of more than 13.5 mmol/L, arterial pH equal or less than 7.30, serum bicarbonate less than 15 mmol/L and the presence of ketone in plasma or urine. Arterial puncture can be quite painful and it needs a skillful personnel to do it. The objective of the study is to determine whether venous blood gas values correlate and show a high level of agreement with arterial blood gas values that can be used in the initial Emergency Department evaluation of patients with suspected DKA.

Methodology : A prospective cohort study was conducted on 50 patients presenting to the Emergency Department with clinical diagnosis of DKA. Other than plasma glucose and urine ketone sampling being taken, a venous and arterial blood gas were also obtained on arrival. Both samples were measured and analyzed to see whether they were highly correlated to each other. The venous and arterial blood gas will be evaluated to seek the level of agreement of one and other.

Results : Data from 50 patients exclusively diagnosed as DKA were analyzed. The mean difference between arterial and venous pH was only -0.0230 and -0.572 for HCO₃⁻. There was strong association between arterial and venous pH values ($r = 0.965$, $p < 0.0005$, $r^2 = 0.931$) and arterial and venous HCO₃⁻ values ($r = 0.967$, $p < 0.0005$, $r^2 = 0.935$). The pH and HCO₃⁻ values were highly correlated and show a high measure of agreement between each other.

Conclusions : Venous blood gas measurements can be used to replace arterial blood gas in the evaluation of pH and bicarbonate levels of DKA patients in the Emergency Department.

Dr. Rashidi Ahmad : (Supervisor)
Dr. Wan Asim Wan Adnan : (Co-Supervisor)

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COMPARISON BETWEEN INTRAVENOUS DEXMEDETOMIDINE (PRECEDEX™) INFUSION VERSUS INTRAVENOUS MORPHINE INFUSION FOR ANALGESIA IN PREEMPTED POSTOPERATIVE (ABDOMINAL LAPARATOMY) GYNEACOLOGY PATIENTS

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Objectives : This study was done to compare the clinical efficacy of dexmedetomidine intravenous infusion with morphine as postoperative analgesia in major gynaecology operation.

Methodology : In a prospective, randomized, double blind study, we evaluated 46 adult gynaecology patients scheduled for elective abdominal laparotomy with general anaesthesia. Preoperatively, patients were randomized into two groups of subjects. Patients in dexmedetomidine group were given preemptive oral rofecoxib 50 mg while patients in morphine group were given placebo. Postoperatively, in the recovery room, the selected patients were immediately given either dexmedetomidine or morphine slow bolus followed by intravenous maintenance infusion respectively. The allocated infusion were titrated to achieve analgesia. A PCA morphine was allocated to each patient as a self rescue analgesia in case having inadequate analgesia. The patients were followed hourly for first 4 hours and subsequently two hourly for next 20 hours for verbal pain score, Ramsay sedation score, analgesic dose, PCA dose, blood pressure, pulse rate, respiratory rate, nausea, vomiting, pruritus, rescue drug for side effects and finally satisfaction questionnaire.

Results : Patients in dexmedetomidine group received 0.5 µg/kg loading dose followed by 0.51 µg/kg/hr as maintenance dose. Where as patients in morphine group received 0.08 mg/kg loading dose

followed by 0.02 mg/kg/hr as maintenance dose. Patients obtained adequate and comparable analgesia with either drug (41.3% vs 39.1%, $p > 0.05$). Dexmedetomidine did not cause hypotension ($p > 0.05$), however cause slowing of pulse rate ($p < 0.05$) than those patients in morphine group. More nausea (28.3% vs 10.9%, $p < 0.05$) and vomiting (21.7% vs 6.5%, $p < 0.05$) was evident in morphine group than in dexmedetomidine group. Thus, more patients in morphine group required rescue antiemetic drug than those in dexmedetomidine group ($p < 0.05$). Both groups of patients had comparable sedation score and pruritus ($p > 0.05$). None of the patients from both groups had respiratory depression.

Conclusion : Dexmedetomidine intravenous infusion with preemptive oral rofecoxib can provide effective analgesia following major gynaecology surgery. Provided vigilance monitoring of its haemodynamic effects, it is safe to use and better tolerability for less causing nausea and vomiting.

Dr. Nizar Abdul Jalil : (Supervisor)
Ass. Prof. Dr. Nik Abdullah Nik Mohamad : (Co-Supervisor)

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COMPARISON OF THREE DIFFERENT TARGET BLOOD CONCENTRATIONS OF PROPOFOL FOR GENERAL ANAESTHESIA USING TARGET CONTROLLED INFUSION (TCI) TECHNIQUE

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MMed (Anaesthesiology)

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Objectives : To compare success rate of induction within 3 minutes, induction time and haemodynamic changes between three different target blood concentrations (TBC) of propofol in a predominantly Malay Malaysian population.

Methodology : In this prospective study, 135 ASA I and II patients in age between 18-55 years old and underwent any elective surgery were randomized into 3 groups. Group I received initial TBC of 2 µg/ml ($n = 45$), group II received initial TBC of 3 µg/ml ($n = 45$) and group III received initial TBC of 4 µg/ml ($n = 45$) for induction of anaesthesia. All patients were premedicated with oral midazolam 7.5 mg in the ward 30 minutes before induction and were given IV alfentanil 30 µg/kg bolus as analgesia. Induction time was measured from starting of infusion until loss of verbal contact and induction was considered successful if loss of verbal contact was achieved within 3 minutes from starting of infusion. Haemodynamic parameters (SBP, DBP, MAP and HR) were recorded at baseline, 1 minutes, 3 minutes and 5 minutes after induction. Patients were subsequently paralyzed with IV rocuronium 0.6 mg/kg and intubated. Maintenance of anaesthesia was continued with total intravenous anaesthesia using TCI of propofol at TBC of 1.5-6 µg/ml and alfentanil infusion at 30-60 µg/kg/h.

Results : Success rate of induction was 55.6% in TBC 2 µg/ml, 86.7% in TBC 3 µg/ml and 91.1% in TBC 4 µg/ml, which showed significant difference between 3 groups ($p = 0.000$). However from multivariate analysis using logistic regression method, success rate were only significantly difference between TBC 2 µg/ml and TBC 4 µg/ml ($p = 0.001$) but were not significantly difference between TBC 3 µg/ml and TBC 4 µg/ml ($p = 0.898$). Estimated marginal means and 95% confidence interval of induction time were 73.63 (59.08, 88.18) s in TBC 2 µg/ml, 74.12 (62.58, 85.65) s in TBC 3 µg/ml and 55.25 (40.76, 69.75) s in TBC 4 µg/ml which showed no significant difference ($p = 0.101$). There were significant changes within all haemodynamic parameters but no significant differences between the groups.

Conclusions : TBC 3 µg/ml was comparable with TBC 4 µg/ml for induction of anaesthesia with no significant differences in success rate

of induction, induction time or haemodynamic changes. TBC 2 µg/ml is not recommended for initial induction.

Dr. Shamsul Kamrlujan Hassan : Supervisor
Assoc. Prof. Dr. N. Abdullah N. Mohamad Co-Supervisor

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DOCTOR-SHOPPING BEHAVIOUR AMONGST ADULT PATIENTS ATTENDING FAMILY MEDICINE CLINIC, HOSPITAL UNIVERSITI SAINS MALAYSIA, KUBANG KERIAN, KELANTAN

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Introduction : Doctor-shopping refers to the changing of doctor without professional referral in a single episode of illness. It leads to some health risk and social problems.

Objectives : To determine the prevalence and associated factors of doctor-shopping behaviour amongst adult patients attending Family Medicine Clinic (FMC) Hospital Universiti Sains Malaysia (HUSM).

Methodology : It was a cross-sectional study conducted among 442 adult patients aged 18 years and above. It was conducted as face to face interview using questionnaires. Data were analysed using SPSS version 11.

Results : Fifty-six percents of these patients met our criteria for doctor-shopping patients. Most of the patients went to general practitioners for consultation prior to FMC visit. One-fifth of respondents went for alternative treatment for the current illness episode. The main reason for changing doctors was no improvement of the illness. Doctor-shopping behaviour was found to be significantly associated with older age group and employed patients. Doctor-shopping patients found to be high in married people, females and patients with low education level, but the associations were not significant. The significant associated factors of doctor-shopping behaviour were chronic duration of illness, and advice to seek treatment from somebody.

Conclusion : Prevalence of doctor-shopping behaviour amongst adult patients attending FMC was high. It is important to recognise and anticipate problems related to doctor-shopping behaviour. We need to emphasise on importance of a good doctor-patient relationship, and giving accurate explanation and health education to maintain a proper continuity of care.

Dr. Shaiful Bahari : Supervisor
Assoc. Prof. Dr. Syed Hatim Nor : Co-Supervisor

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DOES COLD THERAPY HAVE A ROLE EN THE MANAGEMENT OF ACUTE LOW BACK PAIN? - A PILOT STUDY

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MMed (Orthopaedics)

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Introduction : Therapeutic modalities are useful adjuncts in the rehabilitation of many patients commonly seen by orthopedic surgeons.

Therapeutic heat, electrical stimulation, infrared light and magnetic field treatments have been used extensively in the management of low back pain. The majority of therapeutic modalities have been investigated and their efficacy has been emphasized in the literatures. On the other hand, application of cold is not popular even though its role in the management of low back pain has been recommended in some literatures.

Objectives : The purpose of this study is to find out whether application of cold has beneficial effect in the management of acute low back pain. This research was conducted with an interest to identify cold therapy as a potential therapeutic modality in the rehabilitation program of low back pain particularly in acute cases. **DESIGN:** Prospective randomized control trial. **SETTING:** Hospital Universiti Sains Malaysia. **PARTICIPANTS:** 40 patients with acute presentation of low back pain.

Methodology : The study was carried out from March 2004 to August 2004. A special clinic staffed by a trained medical officer was established for the purpose of this study and a group of adult patients was selected. The patients were managed in accordance with standard recommendations. For the intention of this study, the patients were further divided into 2 groups. Group A patients was subjected to cold therapy (study group) whereas Group B patients was not subjected to cold therapy or any form of therapeutic modalities (control group). Data on pain intensity score and functional disability index were taken and collected before the initiation of treatment, on weekly basis, and at the end of the program (at 6 weeks). A comparative analysis was done ;tween these 2 groups.

Results : A total of 40 participants who met the criteria were included in the study. They were subsequently divided equally into 2 groups 20 patients 'ere in Group A and another 20 patients were in Group B. Results during the study period low a faster deceleration rate of pain level in Group A as compared to Group B. The pain level decreased significantly from week 2 in group A in comparison to Group B (P < 0.05). In contrast, the functional disability index was found to have similar deceleration between these 2 groups and does not carry any significant value (P > 0.05).

Conclusions : Cold therapy is beneficial by means of reducing the pain intensity early during the rehabilitation of low back pain, particularly in those with acute presentation. On the contrary, cold therapy was found out not to influence the functional disability index of these patients. Results indicate that application of cold was more effective by reducing the pain level more quickly than those who did not receive cold therapy or any form of therapeutic modalities. Cold therapy is not a placebo and may perhaps be considered as a potential therapeutic modality to reduce pain more rapidly while managing patients with acute low back pain.

Dr. Abdul Halim Yusof : Supervisor
Dr. Abdul Nawfar Sadagatullah : Co-Supervisor

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EFFECTS OF ACUTE-: AMMONIA TOXICITY ON NITRIC OXDE (NO), CITRULLINE-NO CYCLE ENZYMES, ARG1NASE AND OTHER RELATED METABOL1TES IN DIFFERENT REGIONS OF RAT BRAIN

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MMed (Chemical Pathology)

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Introduction : Nitric oxide (NO) is involved in many physiological and pathological processes in the brain. NO is synthesized From

arginine by nitric oxide synthase (NOS) enzymes. Citrulline, which is formed as a by-product of the NOS reaction, can be recycled to arginine by successive actions of argininosuccinate synthetase (ASS) and argininosuccinate lyase (ASL) via the citrulline-NO cycle. Hyperammonemia is known to cause poorly understood perturbations of the citrulline-NO cycle. Both ASS and ASL genes are reported to be induced in astrocytes but not in neurons of aggregates exposed to 5 mM ammonium chloride, suggesting that hyperammonemic brain might increase its recycling of citrulline to arginine.

Objectives : To understand the role of citrulline-NO cycle in hyperammonemia, NOS, ASS, ASL and arginase activities, as well as nitrate/nitrite (NOx), the stable end products of NO, and other related metabolites were estimated in cerebral cortex (CC), cerebellum (CB) and brain stem (BS) of rats subjected to acute ammonia toxicity (0.5mmol of ammonium acetate per 100g body weight).

Results : NOx concentration and NOS activity were found to increase in all the regions of brain in acute ammonia toxicity. The activities of ASS (CC, CB and BS) and ASL (CC and CB) also showed an increase whereas the activity of arginase was not changed. The concentrations of arginine and ornithine were increased in all the regions of brain in acute ammonia toxicity whereas citrulline concentration was not changed. Glutamine concentration was significantly increased in all regions of brain while glutamate and GABA concentrations were not changed.

Conclusions : The results of this study clearly demonstrated the increased formation of NO, suggesting the involvement of NO in the pathophysiology of acute ammonia toxicity. The increased activities of ASS and ASL enzymes indicate the increased and effective recycling of citrulline to arginine in acute ammonia toxicity, making NO production more effective and contributing to its toxic effects.

Dr. Mummedy Swamy : Supervisor
Prof. Dr. H. A. Nadiger : Co-Supervisor

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EFFECT OF PURE SEA-CUCUMBER EXTRACT ON HEALING PROCESS OF CLOSED SIMPLE LONG BONE (TIBIA) FRACTURE – ANIMAL STUDY (RABBITS)

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Introduction : Various researchers had shown the effect of sea cucumber {Gamat} on soft tissue healing. Effect of Gamat extract on fracture healing has never been evaluated previously.

Objectives : This is a pilot study done on animal model in anempi to assess if pure Gamat extract would promote fracture healing. Closed fracture is one of commonest injury encountered in orthopaedic practice which occasionally can be treated via closed manipulation and casting. The idea or biological stimulation in enhancing fracture healing for closed fracture is to avoid operative intervention and at the same time it would reduce time of immobilisation. This would lead to earlier functional mobility, thus less time out of work.

Methodology : The study consists of 10 rabbits, which was subjected to simulation of simple fracture of tibia with intramedullary wiring and casting for stabilisation. The rabbits then were divided into 3 groups. The first group was used as control and the second group was given low dose oral Gamat extract (1mg/Kg) in liquid form. The third group was given high dose oral Gamat extract (10mg/Kg) for comparison.

Results : Our gamat low dose group had demonstrated enhanced fracture healing as compared to subjects from other group shown delayed fracture healing as compared to the other groups at both 3 and

6 weeks.

Dr. Abdul Halim Yusof : (Supervisor)
Dr. Hasnan Jaafar : (Co-Supervisor)

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EFFICACY OF HYDRALAZINE BOLUS INJECTION VERSUS CONTINUOUS DRIP IN MANAGEMENT OF HYPERTENSIVE CRISES IN PREGNANT MOTHERS WITH PIH IN HOSPITAL SEREMBAN – A COMPARATIVE STUDY

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M.Med (Obtetrics & Gynaecology)

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School of Medical Sciences, University Sains Malaysia,
Health Campus, Kelantan, Malaysia.

Objective : To determine whether administering intravenous hydralazine in repeated bolus fashion is more effective in stabilizing the blood pressure in hypertensive crises of pregnant mothers with pregnancy induced hypertension, as compared to intravenous hydralazine in continuous drip.

Methodology : This is a single-blinded comparative prospective study conducted at Hospital Seremban, Malaysia from 20 October 2002 till 21 August 2003. Sixty nine pregnant mothers suffering from pregnancy induced hypertension with hypertensive crises, defined as diastolic blood pressure ≥ 110 mmHg (taken 15 minutes apart) with or without symptoms of impending eclampsia, admitted to Pre-Eclampsia Room, requiring potential hydralazine, were the target population. One arm received 25mg of hydralazine diluted in 500mls of Hartman's solution, commencing at 5 drops per minute and increased by 5 drops per minute every 15 minutes, titrating to diastolic blood pressure of 90-95mmHg (n=34). Another arm (m=35) received repeated bolus intravenous hydralazine, initial dose 5mg, then 2mg repeated every 15 minutes to titrate diastolic blood pressure to 90-95mmHg. Randomization was done by alternating patients. The main outcome measure is the time taken from commencement of intravenous hydralazine to stabilization of the blood pressure. The total cumulative dose of hydralazine required to stabilize blood pressure in each arm were also assessed.

Results : Results were compared and a "Student's test" performed to determine statistical significance, with a p value of <0.05 considered as significant. Both the groups were similar with respect to maternal age, parity, period of gestation, and their mean systolic and diastolic blood pressure much faster (mean 55.57 +/-SD 27.41 minutes) than the control arm (mean 22.35 +/-SD 37.36 minutes). The experimental arm also required less total cumulative dose of hydralazine (mean 10.62 +/-SD 1.98mg) compared to the control arm (mean 21.19 +/-SD 1.01mg) in stabilizing the blood pressure.

Conclusion : There was no overshoot hypotension or any side effects of treatment in both the groups. The data suggests that both methods of administering intravenous hydralazine are equally safe, but it appears that repeated bolus dose of intravenous hydralazine is more effective than continuous drip in the management of hypertensive crises in pregnant mothers with PIH .

Dr. Shah Reza Johan : (Supervisor)
Dr. Nik Mohamad Zaki Nik Mahmood : (Co-Supervisor)

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FACTORS INFLUENCING ANTENATAL MOTHERS' CHOICE OF HOSPITAL FOR DELIVERY AT HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) AND

HOSPITAL KOTA BHARU (HKB)

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Introduction : The selection of a hospital for delivery does not become an issue for women until they become pregnant. The main aim for promoting hospital delivery is to ensure safety to the mother and the newborn child.

Objectives : The main objective in this study is to determine the factors that influence antenatal mothers choice of hospitals for delivery at Hospital Universiti Sains Malaysia (HUSM) and Hospital Kota Bharu (HKB).

Methodology : The study was carried out in two phases. In phase one, a cross sectional study was conducted on 344 Malays, multiparty antenatal mothers who attended selected Maternal and Child Health Clinics (MCHC) in Kota Bharu district, from November 2003 to February 2004. Subjects were selected using two-stage sampling. Data were obtained using an interviewer guided, validated and piloted questionnaire. In order to ensure high quality of the interview, only one dedicated interviewer was involved. The questionnaire consists of a few domains namely socio-economic, accessibility, convenience, previous delivery experience, and interpersonal relationship with doctors and nurses, comfort of the patients and their relatives. The data were analyzed using logistic regression. Focus Group Discussions (FGD) were carried out in phase two in March 2004. FGD was carried out purposely to explore in depth the influencing factors, which cannot be explored through questionnaire. To fulfill this objective, 24 volunteered antenatal mothers were recruited in this phase after being consented and agreed to involve in this study. Four FGD sessions, each group consisted of six participants were conducted. Their responses were transcribed and analyzed based on the framework questions directed to them.

Results : The prevalence for choosing HUSM for delivery center was 38.0% and HKB 62.0% respectively. Based on the simple logistic regression, ten predictors variables namely health center, previous delivery hospital, distance to hospital, accessibility to hospital, good nursing care, short waiting hours, clean wards, children friendly (accept visitor under twelve) and fast admission to wards were significantly associated with the outcomes. Among these only three factors remained significantly influenced when analyzed through multiple logistic regression. The final model was tested and it was found fit. The factors derived from the final model were previous delivery hospital, accessibility and children-friendly hospital. The findings in FGD support the model above and were able to extract the underlying facts.

Conclusions : This study concludes previous delivery hospital; accessibility and children friendly hospital (hospital allows children under 12 years to visit their mothers in the wards) significantly influences the choice of hospital for delivery among antenatal mothers in Kota Bharu district.

Dr. Mohamad Hashim Mohamad Hassan : Supervisor
Dr. Mazlan Abdullah : Co-Supervisor

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HEALTH RELATED QUALITY OF LIFE AND THE ASSOCIATED FACTORS AMONG REPAIRED CLEFT LIP AND PALATE PATIENTS IN WILAYAH PERSEKUTUAN AND SELANGOR

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Introduction : Health related quality of life (HRQL) and the associated factors are now a topic of growing interest and have received increased clinical and research attention. Measurement of HRQL in the evaluation of treatment will give us broader insights into the patient's well being while discovering the associated factors can provide the focus of future intervention strategies.

Methodology : Therefore, a cross sectional study, exploratory in nature, was conducted from June to October 2004 among 120 repaired CLP patients aged 12 to 30 years old, recruited from six government orthodontic clinics in Wilayah Persekutuan and Selangor.

Objectives : This study was to determine the HRQL and its associated factors of repaired cleft lip and palate (CLP) patients in relation to five HRQL dimensions consisting of overall life satisfaction, physical functioning, social functioning, psychological well being and perception of general health status. After having piloted on 32 subjects, an assisted administered multidimensional HRQL questionnaire developed has shown good reliability and validity. Actual data collection was done at the clinics for the subjects who are still on treatment or at home for the subjects who had completed or defaulted treatments. Data was entered and analyzed using SPSS Version 11.5.

Results : Mean scores of HRQL in overall life satisfaction, physical functioning, social functioning, psychological well being and perception of general health status were 63.9 (95%CI:61.50, 66.31), 22.3 (95%CI:22.70, 23.93), 17.6(95%CI:16.90, 18.38), 37.2(95%CI:35.95,38.48) and 19.3 (95%CI:18.65,19.97) points, respectively. when score for each dimension was categorized into poor, moderate and good, majority of the subjects exhibited good HRQL score in physical functioning (56.3%), social functioning (53.3%) and perception of general health status (90.8%) dimensions. However, majority of the subjects had only scored moderate HRQL in overall life satisfaction (67.5%) and psychological well being (51.6%) dimensions. And compared to other dimensions, more subjects had expressed poor HRQL score in social functioning (4.2%). Function of nose and teeth, appearance of cleft related features, self confidence, feeling nervous, peaceful, occurrence of being teased, work accomplishment and opportunity to succeed in life were found to be affected by CLP and its treatments. Nine factors which consist of satisfaction with the treatment outcome and the information delivered by health personnel, types of cleft, mother's education level, religion, the perceived importance of appearance and community support, treatment status and race has emerged as the factors that were significantly associated with different HRQL dimensions.

Conclusions : HRQL of repaired CLP patients across five HRQL dimensions in both states vary from moderate to good. Some aspects in overall life satisfaction, psychological well-being and social functioning were found to be affected by CLP status. However, of the 46 items, CLP affected only 14 items in overall life satisfaction, psychological well-being and social functioning dimensions. Better or higher HRQL was associated with a few factors such as higher level of satisfaction with the treatment outcome and the information delivered by health personnel, having an isolated cleft lip, having a more educated mother, being a Buddhist and surprisingly being patients who defaulted treatment. On the other hand, a reduced or lower HRQL was associated with race and also how patients perceived the importance of appearance and community support in giving impact to their quality of life.

Dr. Nizam Abdullah : Supervisor
Dr. Mohd. Ayub Sadiq @ Lin Naing : Co-Supervisor

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IMMUNE STATUS IN PRETERM BABIES AND ITS ASSOCIATION WITH SEPSIS

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MMed (Pathology)

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Introduction : Preterm delivery is the most important risk factor for both mortality and morbidity due to infections. The risk of neonatal sepsis is 4-10 times higher in low birth weight infants than in full term neonates and varies inversely with gestational age.

Objectives : A cross sectional pilot study using convenient sampling method was conducted to evaluate various immunological parameters in preterm newborns, comparing them with term newborns and correlating them with the presence of neonatal sepsis.

Methodology : Cord blood from 36 preterm babies delivered at HUSM was analyzed. Cord blood from 36 term babies was also analyzed as control. For neutrophil function, we used Nitroblue tetrazolium (NBT) kit. For complement levels and immunoglobulin levels, we performed immunoturbidometry techniques. Lymphocyte subset analysis was performed by using tritest reagent and flowcytometric analysis.

Results : In both preterm and term groups, the numbers of boys were more than girls, majority of the babies were born via spontaneous vaginal deliveries and most of them were breastfed. The period of amenorrhoea (POA) of mothers of preterm babies ranges from 29 to 36 weeks and the mean POA was 34.47 weeks of gestation. In term babies, POA was between 37 to 41 weeks of gestation and the mean was 38.78 weeks. The mean weight of preterm babies was significantly lower than term babies. The gravidity of mothers of preterm babies ranges from gravida 1 to 9 whereas for term babies from gravida 1 to gravida 10. NBT was significantly reduced in preterm babies compared to term babies (7.5% versus 12.0%). Complement levels, C3 (0.5114 versus 0.7192g/l) and C4 (0.07 versus 0.14g/l) were significantly lower in preterm babies than in the term control group. Level of C3 was comparable with previous study but the level of C4 was lower, which may be due to different method performed. When we compared level of IgG in preterm and term babies, we found that the mean IgG level in preterm babies was lower than in term babies (9.5583 versus 14.2806 g/l). The IgG level of preterm babies in this study agreed with the previous study. In the study, IgM (0.1 versus 0.2g/l) and IgA (0.210 versus 0.225g/l) levels were lower in preterm than in term babies and the levels were significantly different between these two groups. The study has shown a number of differences between lymphocyte subsets of preterm and term babies. Only CD3% was significantly different between two groups (65.2917% versus 70.3153%). The percentages of CD4, CD8, CD 19 (B cell) and CD 16/56 (NK cell) were not significantly different. In the study, follow-up of the patients for two weeks after birth showed that sepsis occur in 11.1% of preterm babies. However, none of term babies developed sepsis. We also found that only NBT reduction and IgA level were associated with occurrence of sepsis in preterm babies. IgG level, IgM level, complement levels and lymphocyte subsets were not associated with occurrence of sepsis. However, this may be due to small numbers of babies. For association of immunological parameters and other variables including gravidity, sex, method of delivery, type of feeding or birth weight, we have found that NBT reduction, IgG, IgM, C3 and C4 levels were found to be associated with birth weight whereas CD3%, CD4% and CD 16/56 (NK cell) % were associated with gravidity.

Conclusions : We found that NBT reduction, IgG level, IgA level, IgM level, C3 level, C4 level and CD3% were significantly different between preterm and term babies. We also found that only NBT reduction and IgA level were associated with occurrence of sepsis in preterm babies. Other than that NBT reduction, IgG, IgM, C3 and C4 levels were found to be associated with birth weight whereas CD3%, CD4% and CD 16/56 (NK cell) % were associated with gravidity.

Dr. Che Maraina Che Hussin : Supervisor
Dr. Hans Amin Van Rosternberg : Co-Supervisor

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IMPACT ON THE WELLBEING OF PARENTS WITH CLEFT LIP AND PALATE CHILDREN ATTENDING KOTA BHARU COMBINED CLINIC

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Objectives : The aim of this study is to determine and compare the impact of CLP children on the wellbeing of their parents. The study also explores the factors associated with the impact on the wellbeing of fathers and mothers separately.

Methodology : The study was conducted using a cross sectional design for seven months (January 2004 to July 2004) at the Combined Cleft and Craniofacial Deformity Clinic (CCCDC), Jalan Mahmood, Kota Bharu Kelantan. A total of 223 parents (106 fathers and 117 mothers) attending the clinic were recruited into the study. This included ninety-seven married couples (97 fathers and 97 mothers), eight fathers, sixteen mothers, four single mothers and a single father. The tool of the study consisted of a set of validated self-administered questionnaire to be answered either at the clinic or at home. Six impact domains were explored in the study: disruption to social interaction, financial burden, disturbance to daily activities, effect on physical health, effect on mental health and disturbance to recreational activities. The responses from the ninety-seven married couples were used to determine and compare the impact of CLP children on the wellbeing of fathers and mothers. The response from both the married couples and the rest of the sample were used to determine the factors associated with the impact on parental wellbeing as a whole. To measure the impact on both parents, a percent impact score was constructed with more than 20 percent score as the indicator for the presence of impact.

Results : Four out of six domains showed impact on mothers among the married couples. This include disruption of social interaction, financial burden, disturbance to daily activities and effect on mental health with the Mean (SD) percent score of 22.2 (11.19), 22.7 (17.05), 21.1 (25.34), and 21.5 (15.02) respectively. In contrast, only two domains affect the wellbeing of fathers : disruption of social interaction and financial burden with the Mean (SD) percent score of 20.2 (10.53) and 21.9 (17.37) respectively. In terms of comparison between fathers and mothers, the overall percent score was significantly higher among mothers than fathers (p=0.004). However, mothers have significantly higher percent score on disturbance to daily activities (p=0.004), effect on physical health (p=0.021), and disturbance to recreational activities (p=0.011) compared to fathers. . The factors that influenced the mothers were number of dependents in the family and the presence of disease (s). One unit increase in the number of dependent in the family will reduce the impact percent score of the mothers by 1.07 (95 % CI: - 1.99, -0.14). The absence of disease(s) will reduce the impact percent score by 7.17 (-12.42, -1.91) units. The factors that influenced the impact on the wellbeing of fathers were age and marital status : being younger by one year will increase the impact percent score by 0.28 (95 % CI: -0.52, -0.42) and being single will significantly increase the impact percent score by 30.23 (95 % CI: 10.60, 49.85) units as compared to married fathers.

Conclusion : Among married couples, mothers of a cleft lip and palate children have a higher total percent score with a significant difference in the domains of disruption of social interaction, effect on physical health, and disturbance of recreational activities. Both fathers and mothers were found to have an impact on their social life and financial burden with an additional impact to mothers in the domains of disturbance to daily activities and effect on mental health. Among fathers, being one year younger increases the impact of wellbeing by 0.28 units and being single will increase the impact by 30.23 units. Among mothers, one unit increase in the number of dependent in the family will reduce the impact score by 1.07 units and the absence of

disease(s) reduces the impact score by 7.17 units.

Dr. Abdul Rashid Hj.Ismail : Supervisor
Assoc. Prof. Dr. Halim Salleh : Co-Supervisor

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INVITRO STUDY OF TEA TREE OIL EFFECTS ON TISSUE GROWTH AND COMMON ORGANISM IN CHRONIC SUPPURATIVE OTITIS MEDIA

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Introduction : Tea tree oil is known scientifically as malaleuca Alternofillia. It is a native Australian plant which is able to grow in Malaysia. Its major component is Terpinen-4-ol (30-40%) which is responsible for antibacterial, antifungal and antiviral properties. Other components are less than 5% for example 1,8-cineole, sesquiterpenes and paracymene which act as lipophilic solvents, penetration facilitators and antimicrobial synergistic. Widely used in Australia for cuts and bums as analgesic, used to treat mouth ulcer, abscess, impetigo, dandruff etc.

Objectives : The objective of this study was to determine the cytotoxic level of Tea Tree Oil and to determine the antimicrobial effect of TTO on common microorganism in CSOM.

Methodology : This was an in-vitro/laboratory, controlled and prospective study which was done in Craniofacial Lab of PPSG of USM and in Microbiology Lab of PPSP USM. Fibroblast cell culture passage 6 was used and the viability of cells was determined by MTT assay. Disc diffusion test was used to determine the antimicrobial effect of TTO. MHA media added with Tween 80 plates were prepared and selected organisms were lawn on the plate. Sterile blank disc was soaked with TTO and placed on the plate. Clear zone were measured after plate incubation for 24 hour.

Results : Results of cytotoxicity study was showed that LC₅₀ of Nambucca and Malaysia TTO is between 0.05 and 0.1% (v/v) and the result of Disc Diffusion Test showed presence of zone of inhibition on the 3 organisms tested (*E.coli*, *S. aureus* and *P.aeruginosa*).

Dr. Din Suhaimi Sidek : Supervisor
Prof. Dr. Rani Samsuddin : Co-Supervisor

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LIVE EVEN STRESS, PERSONALITY AND ILLNESS

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Objectives : The objective of this study is to identify the relationship between life event stress in the onset of illness (psychiatric illness and medical illness). This study would assess the nature, severity and frequency of the preceding life events in the onset of illness and determine the role of personality as a mediating factor between stress and illness.

Methodology : This comparative cross-sectional study used Interview for Recent Life Event Schedule, Impact Event Scale for the event instruments and personality traits is assessed by NEO Five Factor Inventory (Validated Malays Version) in 256 patients where 128 patients

each from psychiatric illness and medical illness at Hospital Universiti Sains Malaysia. The patients were equally divided into 4 subgroups that comprise of 64 patients each and these patients were recently diagnosed ie. Less than 1 year. Psychiatric illness comprised of psychotic subgroup and neurotic subgroup, while the Medical illness comprised of coronary heart disease subgroup and other medical illness subgroup.

Results : 206 reported at least one event prior to onset of illness. Out of 206 respondents, 179 reported independent event. Neurotic subgroup reported more independent event than other subgroups whereas psychotic subgroup reported more dependent even. Analysis on the independent sample revealed that medical group reported more significant event in family and social area (p=0.027) especially that was related to increased argumentation among family members. For the perceived stress in the independent sample, both groups reported more events with severe, marked and moderate severity in the months near the onset of illness (a month before the illness); however it was not statistically significant. Although neurotic subgroup reported more moderate and severe impact in IES score, it was not statistically significant. There was a significant association between two personality traits and illness. Neuroticism trait has significantly higher in neurotic subgroup than CHD subgroup (p=0.001). Neurotic subgroup has the high mean neuroticism score (mean=27.63, SD=6.64) as compared to other subgroup. High neuroticism trait has reported more negative impact (moderate to severe negative impact) (p=0.000) than other traits. Low openness trait mean score (mean=19.62, SD=3.83) has significant difference in CHD subgroup compared with other subgroups (p=0.000). However final multiple regression analysis did not revealed any significant association between life events stress, personality and illness except for age and sex.

Conclusions : This study found that the independent life event was not significantly related to the onset of illness when comparing with 4 diagnosis subgroups however there was a significant association between 2 personality traits and illness. Neuroticism trait was significantly higher in neurotic subgroup than in CHD subgroup. Neurotic subgroup has the high neuroticism mean score as compared to other subgroup. High neuroticism trait has reported more negative impact (moderate to severe negative impact) as showed by high IES score. CHD subgroup has low openness mean score when compared with other subgroups (p=0.000). However final analysis using multiple regression did not revealed any significant association between life events stress, personality and illness. The biological factor such as genetic that was not assessed in this study might play a more significant role in the pathogenesis of illness.

Prof. Dr. Hj. Mohd. Razali Salleh : Supervisor
Assoc. Prof. Dr. Hasanah Che Ismail : Co-Supervisor

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LOW DOSE BUPIVACAINE FOR UNILATERAL SPINAL ANAESTHESIA : A COMPARISON OF PLAIN BUPIVACAINE VERSUS HEAVY BUPIVACAINE

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MMed (Anaesthesiology)

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Objectives : The purpose of this study is to compare the effects of plain bupivacaine and heavy bupivacaine on performing unilateral spinal anaesthesia when a low dose is injected into adults patients.

Methodology : A randomized double blind controlled trial study on 72 padents with physical status base on American Society of Anesthesia classification, class I or U patients, aged 18 to 65 years. Patient were divided into 2 groups receiving either 10 mg 0.5% plain bupivacaine

or 10 mg 0.5% heavy bupivacaine as local anesthetic drug for unilateral spinal anaesthesia. Patient was placed in the lateral position with the limb to be operated on the dependent position. The lumbar puncture was performed at L 3-4 interspaced with a 21-gauge hypodermic-needle (B Braun Melsungen AG) as an introducer-needle preceding passage of the 27-gauge Pencan (pencil point tip) spinal needle (B Braun Melsungen AG) using the mid-line approach. After free flow of cerebrospinal fluid was observed, the needle hole was turned toward the dependent side and plain bupivacaine or heavy bupivacaine was injected slowly at a rate of approximately 0.1 ml/second. The lateral position was maintained for 10 minutes, and then patients were turned to supine position. An observer blinded to the anesthetic solution baricity recorded the evolution of sensory and motor blocks on both dependent and non dependent sides. Sensory level was evaluated by loss of pinprick sensation with a 21-gauge blunt hypodermic needle, while motor block was evaluated using modified Bromage scale. Sensory and motor blocks were tested every 3 minutes after bupivacaine injection until patients were turned to the supine position, then every 5 minutes interval until 30 minutes after patients were placed in supine position. Successful unilateral spinal anaesthesia was defined when there are loss of pinprick sensation at or above L1 dermatome level and complete motor block on the dependent side only, while the non-dependent side maintained both somatic sensibilities to the pinprick test and motor function. Unilateral spinal anaesthesia was assessed at the end of the 10 minutes lateral position and then 30 minutes after patients were turned supine.

Results : We found that there were significant differences in unilateral spinal anaesthesia in both groups. It seems that heavy bupivacaine is more reliable in providing unilateral spinal anaesthesia compared to plain bupivacaine in adult patient. In view of haemodynamic changes and used of rescue drugs there is no significant difference between both groups, but over all the haemodynamics changes were minimal in both groups in this study.

Conclusions : We concluded that when a small dose of 0.5% bupivacaine is injected slowly into adults patients placed in the lateral position, heavy bupivacaine provides more marked unilateral blocked compared to the plain bupivacaine.

Dr. Rhendra Hardy Mohamad Zaini : Supervisor
Assoc. Prof. Nik Abdullah Nik Mohamad : Co-Supervisor

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NON-TRAUMATIC ALTERED STATES OF CONSCIOUSNESS : A HOSPITAL BASED PROSPECTIVE STUDY

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Introduction : Non-traumatic ASC is a non-specific consequence of various etiologies. Awareness and understanding of the relative frequencies of the various etiologies of ASC in North-Eastern Peninsula of Malaysia can facilitate development of effective diagnostic and therapeutic approaches to patient management and promote efficient use of our resources in managing these patients. The Emergency Department (ED) of Hospital Universiti Sains Malaysia (HUSM) is a young department; it does not have sufficient epidemiological data on this group of patients presenting to the ED.

Objectives : The aim of this study was to collect and present data on the various etiologies responsible for non-traumatic ASC in an ED population and the factors associated with acute outcome.

Methodology : Patients with non-traumatic ASC were selected by purposive sampling according to pre-determined criteria. Data on

patient demographics, clinical features, investigations done, treatment given and outcome were collected prospectively over a six month period. Various risk factors were studied to determine association with 2-week outcome.

Results : 221 patients with non-traumatic ASC were seen from August 1st 2003 to January 31st 2004. 54.3 % of the patients were males. The mean age of the patients was 56 years old. The mean overall GCS score on presentation to ED was 10.3. The mean duration of ASC was 11.6 hours. 130 (58.8 %) patients experienced ASC secondary to general or focal cerebral disorders. The mortality rate was 40.3 % at 2 weeks after ED visit. 54.3 % of the patients were awake and considered to have good outcome whereas 45.7 % of the patients had poor outcome (comatose or dead) 2 weeks after ED visit. Mean overall GCS score, verbal and motor subscores had significantly decreased (worsened) after treatment in ED ($p < 0.05$). Subjective assessment of ASC, hypertension, current smoking, pupillary reflexes and acidosis were associated with 2-week outcome ($p < 0.05$). The mean age and WBC count was lower and the mean overall GCS score and eye, verbal and motor subscores were higher for the good outcome category ($p < 0.05$). There was significant agreement between subjective assessment of ASC and GCS scores in the assessment of non-traumatic ASC ($p < 0.05$).

Conclusion : Patients with non-traumatic ASC represented 1.2 % of the total number of patients seen in ED, HUSM. There were various etiologies responsible for non-traumatic ASC. There were certain variables associated with 2-week outcome that could be used to predict acute outcome. Both GCS and subjective assessment are recommended when assessing level of consciousness of non-trauma patients in order to reduce ambiguity when communicating with other parties. However, further study using a single investigator, patients presenting directly to ED, HUSM and multi-variate analysis can overcome selection and measurement biases, produce independent predictors of outcome and thus provide more reliable results and conclusions.

Dr. Wan Aasim Wan Adnan : Supervisor
Dr. Rashidi Ahmad : Co-Supervisor

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NOSOCOMIAL ACINETOBACTERIAL BLOOD STREAM INFECTION IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KELANTAN

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Introduction : Acinetobacter spp is a known nosocomial pathogen caused wide range of clinical diseases mainly pneumonia, wound infection and blood stream infection (BSI).

Objectives : A cross sectional descriptive study was performed to determine the prevalence of Acinetobacter infection in Hospital Universiti Sains Malaysia, Kelantan (HUSM).

Methodology : The risk factors and clinical outcome of Acinetobacter BSI were determined by 1:1 case control analytical study, involving fifty-eight confirmed cases Acinetobacter BSI patients compared to other Gram-negative infections.

Results : The prevalence of Acinetobacter infection in general in HUSM was 5.39% [95% CI 4.77-6.07%]. Acinetobacter pneumonia accounted 26.02% [95% CI 21.74-30.66%], central nervous system infection 11.60% [95% CI 5.14-21.57%], BSI 6.11% [95% CI 4.88-7.53%], wound infection 5.22% [95% CI 3.89-6.84%] and urinary tract infection 1.24% [95% CI 0.54-2.42%]. Acinetobacter BSI patients were mostly located in intensive care unit (OR 3.83 95% CI 1.40-4.07 $p=0.001$) and had longer intensive care unit stay (12.72 \pm 17.29 days compared to 2.97 \pm 7.88 days $p=0.010$). The risk factors for

Acinetobacter BSI include prior exposure to antimicrobial agents such as penicillins (OR 1.55 95% CI 1.04-2.29 p=0.026), aminoglycosides (OR 2.00 95% CI 0.98-4.08 p=0.048) and cephalosporins (OR 2.35 95% CI 1.52-3.64 p=0.000), mechanical ventilation (OR 2.40 95% CI 1.49-3.89 p=0.000), presence of nasogastric tube (OR 1.71 95% CI 1.21-2.42 p=0.001), arterial catheter (OR 1.90 95% CI 1.25-2.88 p=0.002) and urinary catheter (OR 1.70 95% CI 1.18-2.44 p=0.003). In multivariate analysis, the independent risk -factors for Acinetobacter BSI were prior treatment with cephalosporins (OR 3.836 95% CI 1.657-8.881 p=0.002) and mechanical ventilation (OR 3.164 95% CI 1.353-7.397 p=0.008). The crude mortality of Acinetobacter BSI was 47.2%, which was significantly more than other Gram-negative BSI (OR 1.89 95% CI 1.10-3.24 p=0.016) but there was no significant difference of the attribute mortality between both groups. Appropriateness of therapy did not seem to influence the clinical outcome of the patient but significantly reduce the attribute mortality (OR 0.20 95% CI 0.04-0.97 p=0.027). Prior exposure to carbapenems was not noted as a risk factor for Acinetobacter BSI but served as predictor of mortality in Acinetobacter BSI (p=0.003). Patient presenting with septic shock (OR 17.95 95% CI 3.36-95.84 p=0.001) and on central venous catheter (OR 12.48 95% CI 1.09-142.68 p= 0.042) were independently at higher risk of mortality.

Conclusions : This study revealed Acinetobacter as a common pathogen in this region and contributed to high mortality. Rational use of antimicrobial agents is of paramount importance to control the infection, thus reducing the mortality.

Dr. Azian Harum : (Supervisor)
Assoc. Prof. Dr. Mohd. Radzi Johari : (Co-Supervisor)

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PATIENTS' SATISFACTION TOWARD MEDICAL WARD SERVICES IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM) AND HOSPITAL KOTA BHARU (HKB)

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Objective : To compare patients' satisfaction toward medical ward services in Hospital Universiti Sains Malaysia (HUSM) and Hospital Kota Bharu (HKB).

Methodology : A cross-sectional study design which involved medical inpatients admitted to the medical wards of HUSM and HKB was conducted from April 2003 to September 2003. A validated, self-administered patients' satisfaction toward medical ward service (PSMWS) questionnaires were given to 376 eligible medical inpatients. Data entry was done using EpiInfo 6 while data analysis employed SPSS version 11.0.

Result : Demographic characteristics of the two groups were similar except median family income was higher among HUSM respondents (RM925 vs. RM775, p=0.050), median Patient's Out-of-Pocket Expenditure was higher among HUSM respondents (RM35 vs. RM20, p=0.001) and mean Length of Stay was longer among HUSM respondents (5.8 vs. 3.3 days, p=0.001). Level of patient satisfaction toward medical ward services in HKB was 14.4 percent compared to in HUSM was 17 percent (p=0.478). HKB medical inpatients were more satisfied with the services of nurses, doctors, other ward staff and financial aspect of medical ward services while HUSM medical inpatients were more satisfied with the clean and comfort (include medical ward facilities and infrastructure) aspect of medical ward services. Type of hospital (service hospital) and outside food expenses (more than RM5) were significantly associated with satisfaction score

of combined seven medical ward services domains.

Conclusion : Hospital managers should use satisfaction data to identify an improve specific medical ward services areas (e.g interpersonal communication skill of medical ward staff) in order to gain higher patient satisfaction and better utilization of their medical ward services.

Dr. Than Winn : Supervisor

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PREDICTING OUTCOME OF FEBRILE NEUTROPENIC EPISODES IN ADULT PATIENTS WITH ACUTE LEUKEMIAS AND LYMPHOMAS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction : Febrile neutropenia remains one of the major complications in cancer treatment. The risk of infection, serious infectious complications and overall outcome are influenced by the underlying disease and host profile. Recent studies have shown that febrile neutropenia can be stratified into different risk categories and managed accordingly.

Objectives : This historical cohort study was conducted to assess the association between the Multinational Association for Supportive Care in Cancer (MASCC) scoring system and the clinical outcome of febrile neutropenic episodes among patients with acute leukaemia and lymphoma. The microbiological characteristics in febrile neutropenia were also reviewed.

Method : This study included all episodes of febrile neutropenia in patients aged 12 years or more with underlying acute leukaemia or lymphoma at Hospital University Sains Malaysia from 1st January 1998 to 30th June 2004. Multiple entries for febrile neutropenia in the same patient were allowed provided patient had at least 5 days of afebrile period between the episodes. The required information such as patient characteristics (gender, severity and duration of neutropenia, duration of fever, control of cancer status, use of antibiotic prophylaxis and presence of indwelling intravenous catheter) and studied factors for MASCC scoring were extracted from patient's medical records and tabulated into a customized data collection sheet. Simple and multiple logistic regression were used to evaluate the MASCC score and its related factors.

Results : A total of 175 febrile neutropenic episodes from 76 patients were analysed. Gram negative bacteria were the most common pathogens (57.8%), followed by gram positive bacteria (43.3%) and fungal (16.7%). The most common gram negative bacteria were *E. coli* (15.6%), *Klebsiella sp* (12.2%) and *Pseudomonas sp* (8.9%). There were 5 episodes (5.6%) with extended spectrum beta-lactamases (ESBL) producing bacteria (2 *E. coli* and 3 *Klebsiella sp*). Methicillin resistant *S. epidermidis* (MRSE) and methicillin resistant *S. aureus* (MRSA) were the most common (31.1%) gram positive organisms isolated. Among fungus cultured, *Candida sp* contributed to 12.0% (14 isolates). Fever classification and total MASCC score category were associated with outcome of febrile neutropenia. Compared to microbiologically documented infection (MDI), fever of unknown origin (FUO) has 4.1 (p=0.001, 95%CI 1.73,9.94) and clinically documented infection (CDI) has 4.4 (p<0.001, 95%CI 1.98,9.64) folds increased chance to have favourable outcome. Patients with total MASCC > 21 were 5.4 times more likely to have favourable outcome as compared to those with score less than 21 (p=0.003, 95%CI 1.75,16.55). These odd ratios were adjusted to other possible contributing factors such as gender, severity and duration of

neutropenia, duration of fever before starting treatment, control of cancer status, use of antibiotic prophylaxis and indwelling central venous catheter. The final model of this prediction rule has sensitivity, specificity and positive predictive value of 67.2%, 72.8% and 57.0% respectively.

Conclusion : Gram negative bacterial infection was predominant in febrile neutropenia, however gram positive bacterial infection was also significant. The MASCC scoring system can predict the clinical outcome of febrile neutropenia in our population however; it has low specificity and positive predictive value. Although combination of the MASCC scoring system and fever classification is more accurate in predicting the outcome of febrile neutropenia than the MASCC score alone, their sensitivity, specificity and positive predictive value were still lower than in previous studies.

Prof. Dr. Abdul Aziz Baba : Supervisor
Dr. Abu Dzar Abdullah : Co-Supervisor

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PREVALENCE, CLINICAL FEATURES AND RISK FACTORS OF THYROID ASSOCIATED OPHTHALMOPATHY IN GRAVES' DISEASE WITHIN A MULTIETHNIC MALAYSIAN POPULATION

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Objectives : To determine prevalence, clinical features and risk factors of thyroid associated ophthalmopathy (TAO) in a cohort of patients with Graves' disease (GD) in Malaysia.

Methodology : This is a cross-sectional study involving 167 consecutive hyperthyroid GD patients attending the endocrine clinics of Hospital Universiti Sains Malaysia and Penang General Hospital (ages: 17-71; 124 females, 43 males). Patients were examined for TAO for a one year period from 1st October 2003 to 30th September 2004. Questionnaire was administered by the main investigator for assessment of potential risk factors and management characteristics of GD and TAO. Medical records were reviewed to determine patient health status, medications and investigation results.

Results : In this study, the prevalence of TAO using the American Association of Ophthalmology diagnostic criteria was 34.7%. The prevalence increased to 46.7% if lower lid retraction was taken as part of the diagnostic criteria. Thirty eight patients (65.5% of TAO) with TAO had exophthalmos, 31 (53.4%) upper lid retraction, 5 (8.6%) restrictive extraocular myopathy and none had optic neuropathy. Commonest presentation was exophthalmos, followed by, in decreasing order of frequency; lid retraction, combination of lid retraction and exophthalmos, combination of exophthalmos and myopathy and lastly combination of lid retraction and myopathy. Smokers at diagnosis of GD are at 2.8 times greater risk of TAO than non-smokers (p=0.019). Unit increase of low-density lipoprotein-cholesterol (LDL-C) decreases risk by 68.8% (p=0.005). Unit increase of weight increases risk by 3.9% (p=0.010). Body mass index however showed no significance (p=0.251). Hypertensives are at 0.342 times lower risk of TAO than non-hypertensives (p=0.041). Gender, race, age at diagnosis of GD and duration of GD had no impact on the development of TAO. Males were associated with TAO on univariate analysis (p=0.003) but smoking was found to be a confounder on multivariate analysis as more males smoke. There was no relationship found between type 2 diabetes mellitus, ischaemic heart disease, atrial fibrillation, cardiomyopathy, cerebrovascular accident, asthma and alcohol ingestion with TAO. Methods of treating GD and thyroid hormone levels were not relevant in TAO development.

Conclusion : TAO has a significant prevalence (34.7%) in Malaysian GD patients and may not be as rare in Asians as suggested by western literature (7.7%). Exophthalmos seems to be commoner in Malaysians than Caucasians. Upper eyelid retraction however is less common. Malaysians more readily develop lower eyelid retraction and this should be included in the diagnostic criteria for TAO in Malaysians. Smoking and weight increase risk of TAO. Hypertension and LDL-C are associated with a lower rate of TAO.

Dr. Elias Hussein : Supervisor
Prof. Wan Mohamad Wan Bebakar : Co-Supervisor

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PREVALENCE OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN CHILDREN WITH ADENOTONSILLAR PATHOLOGY IN USM – A PILOT STUDY

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Objective : The objectives were to study the prevalence of Obstructive Sleep Apnea Syndronn (OSAS) in children with adenotonsillar enlargement in Hospital Universiti Sains Malays (HUSM) and the association of adenoid and tonsillar pharyngeal ratio with severity of OSA in children at HUSM.

Methodology : This pilot study is a cross sectional study done from October 2003 to October 200 in children age 1 to 17 years old in HUSM, Kubang Kerian. History of symptoms c Obstructive Sleep Apnea Syndrome (OSAS) were obtained from the parents and all subject are subjected to a Ear, Nose and Throat examination , lateral soft tissue xray of nasopharynx and oropharynx and all are subjected to a Polysomnography. The Adenoids size was determine by measuring the adenoid to nasopharyngeal ratio and the tonsil size was determined by the Tonsillar to Pharyngeal ratio (T-P ratio) on the lateral soft tissue xray The severity of OSAS was assessed using Apnea Index (AI) in the ovemigh Polysomnography recording.

Results : A total of 12 males and 4 females with median age is 7 years were involved in this study. The commonest symptoms are snoring, restless sleep and mouth breathing during sleep and during daytime. Tonsillar enlargement present in 87.5% of the subjects. The prevalence of OSAS among patients with Adenotonsillar pathology in this study is 93.8%. The median for TP ratio was 0.83. The median Adenoid ratio was 0.58 and the median for Apnea Index was 12.05. The clinical tonsil size did not associated with AI. The TP ratio and Adenoid ratio also did not correlate with AI.

Conclusion : The prevalence of OSAS among children with Adenotonsillar pathology is high. The commonest symptoms of OSAS were snoring, restless sleep, mouth breathing during sleep and daytime mouth breather. Symptoms of OSAS should be asked regularly by the health provider to those children with Adenotonsillar pathology because certain symptoms of OSAS are under detected by the parents. It is important to recognized and treat the disease early.

Dr. Shamim Ahmad Khan : Supervisor
Assoc. Prof. Dinsuhaimi Sidek : Co-Supervisor

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PROGNOSTIC STUDY OF USING DIFFERENT MONITORING MODALITIES IN TREATING SEVERE TRAUMATIC BRAIN INJURY

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Objectives : The objective of this study was to determine that the multimodality monitoring made on severe traumatic head injured patients would result in better outcome score compared to the single modality monitoring patients.

Methodology : It was a prospective randomized study, included all adults with traumatic severe head injured cases who had a GCS of less than 9 and CT scan feature did not reveal significant intracranial pathology. We excluded patient who was on arrival had unilateral or bilateral fixed and dilated pupils believed to be due to an on-going herniation, a brain dead patient and patient known to have any condition that lowering his or her functional status score. The randomization process was made to allocate to either multimodality or standard modality monitoring. In the multimodality group, we monitored basic intensive care parameters and multiple cerebral parameters. In the standard monitoring group, only the intracranial pressure was monitored plus basic intensive care parameters. Monitoring proceeded for at least 3 days if uneventful. We noted the outcome at 6 months post treatment using the Barthel index score.

Results : 26 cases were included in each studied group, 47 males and 5 females to make a total number of 52 cases. The age ranged from 15 to 75 year-old with a mean value of 35 for multimodality group and 17 to 69 year-old with a mean of 33 for the single modality group. The sixth months outcome between those two groups was not statistically significant ($p < 0.479$). However, the percentage of cases who were independent at 6 months was higher in the multimodality group compared with the single modality group, 21.2% and 17.3% respectively. The multimodality group had also lower percentage of cases who were dependent at 6 months in comparison to the single modality group, 28.8% and 32.7% respectively. The univariate analysis revealed, age ($p < 0.03$), GCS on arrival ($p < 0.01$), 24 hours fluid balance at day two ($p < 0.01$), serum sodium ($p < 0.03$) and intracranial pressure at day 3 of monitoring ($p < 0.01$) were correlated with the outcome. The trends of the parameters disclosed younger, higher GCS, lower ISS and Marshall grade would have a higher chance to be independent at 6 months post trauma. Tachycardic, hyperthermic, hypo- and hyper-volumic patients during the first 3 days of monitoring tend to be dependent at 6 months post injury. The dependent patients also tend to be acidotic and alkalotic, have Pco_2 of < 20 mmHg or > 45 mmHg, blood haemoglobin level of < 8 g/dl, high blood urea and sodium. The persistently high ICP > 20 mmHg, CPP of < 55 mmHg, SJVO₂ $< 50\%$ or $> 75\%$, rCBF < 35 ml/100g/min, TCD MCA flow velocity < 35 cm/sec and $PtiO_2$ of < 15 mmHg were also associated with dependent outcome at 6 months. The data regarding the brain temperature, brain pH, brain carbon dioxide partial pressure and bispectrum EEG index (BISS) were inconclusive in term of their trends.

Conclusion : Despite there was no significant statistical difference between the multimodality and single modality groups. There may be still a possibility of better outcome obtained with multimodality technique because of higher cases with independent status observed in that group. This can be confirmed otherwise if larger cases were studied.

**Prof. Dr. Jafri Malin Dato Hj. Abdullah : Supervisor
Dr. Ghazaimie Ghazali : Co-Supervisor**

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RISK FACTORS FOR PULMONARY TUBERCULOSIS (TB) IN ADULT PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION: A CASE CONTROL STUDY

Dr. Narwani Hussin

MMed (Community Medicine)

Introduction : The HIV/AIDS epidemic has led to a rise in the incidence of TB particularly pulmonary TB and an epidemic of co-infection. The identification of risk factors, which may predict the occurrence of pulmonary TB, is needed. Hence, this study is done to identify factors associated with increased risk of contracting pulmonary TB in adult HIV patients.

Methodology : A case control study was conducted at infectious diseases clinic, Hospital Kota Bharu from November 2003 to August 2004. Ninety seven patients were cases (HIV and pulmonary TB) and ninety seven patients were controls (HIV only). No probability sampling method was applied. All patients who fulfilled the inclusion and exclusion criteria and who gave consent were recruited into the study due to limited number of patients. Interviewer guided questionnaire was administered and medical record was

Results : Cases were found to be more males, older and singles. The number of cases who smoked and consumed alcohol were higher than controls. High-risk behaviors such as intravenous drug users and having multiple sexual partners were found to be more in the cases compared to controls. The commonest mode of HIV infection in the cases was intravenous drug users (41.9%). Cases also had higher proportion of TB contact, past history of TB and other chronic diseases. They had lower hemoglobin, lymphocyte, CD4 and CDS but higher erythrocyte sedimentation rate (ESR) as compared to controls. In multiple logistic regression analysis, the significant risk factors detected were history of TB contact (OR=4.94, 95%CI=1.73, 14.07), past history of TB (OR=4.59, 95%CI=1.06, 19.78) and history of chronic diseases (OR=4.41, 95%CI=1.28, 15.20). Being females (OR=0.06, 95%CI=0.02, 0.24) and married (OR=0.06, 95%CI=0.01, 0.25) or widowed (OR=0.14, 95%CI=0.02, 0.84) had protective effect towards the risk to contract pulmonary TB. Other significant factors were CD4 (OR=0.996, 95%CI=0.993, 0.999), total white blood cell (TWBC) (OR=0.76, 95%CI=0.62, 0.92) and ESR (OR=1.04, 95%CI=1.03, 1.06).

Conclusions : The significant independent risk factors for pulmonary TB were male, single, had history of TB contact, had past history of TB, had chronic disease, low CD4, low TWBC and high ESR level. It showed that patients at high risk can be identified on the basis of demographic and clinical features.

**Assoc. Prof. Dr. Syed Hatim Noor : Supervisor
Dr. Rosemi Saleh : Co-Supervisor**

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RESPIRATORY SYMPTOMS, LUNG FUNCTION AND COGNITIVE PERFORMANCE OF THE PRIMARY SCHOOL CHILDREN EXPOSED TO SECONDHAND SMOKE AT HOME IN KOTA BHARU KELANTAN

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Introduction : In recent years, there has been concern that non-smokers may also be at risk for some of health affects from secondhand smoke exposure, especially children. Among the harmful effects of secondhand smoke exposure were increased risk of respiratory symptoms, middle ear diseases, sudden infant death, behavioral problems, neurocognitive decrements and becoming adolescent smokers.

Objectives : This study was aimed at determining the prevalence of secondhand smoke exposure at home, the association between secondhand smoke exposure and respiratory symptoms, lung function and cognitive performance among primary school children in Kota

Bharu, Kelantan.

Methodology : A comparative cross-sectional study was conducted from September 2003 to March 2004 on 795 primary school children who were randomly selected from 10 government primary schools in Kota Bharu, Kelantan. A self-administered questionnaire was used to obtain information on sociodemography status, respiratory symptoms and smokers in the household. Peak expiratory flow rate (PEFR), height and weight of the children were measured. Cognitive performances were assessed using Arithmetic, Digit Span Forward and Backward and Coding subtests of the Wechsler Intelligence Scales for Children-III (WISC-III). Analyses were conducted using SPSS version 11 and STATA.

Results : A total of 795 children involved in this study with 48.6% boys and 51.4% girls. The distribution by class was: Primary 4; 35.3%; Primary 5; 29.9% and Primary 6; 34.7%. 45% of the children lived with 1 smoker. 9.2% lived with 2 smokers, 1.1% lived with 3 smokers and 0.3% lived with 4 smokers. A total of 55.6% children lived with at least 1 smoker in the house. The most common source for the exposure was smoking by fathers. Significant associations were observed between secondhand smoke exposure and cough in the morning (OR=1.67, 95% CI=1.18, 2.39), cough at night (OR=1.59, 95% CI=1.10, 2.30), cough most days for the previous 3 months (OR= 1.76, 95% CI=1.16, 2.65), phlegm in the morning (OR=1.57, 95% CI=1.14, 2.17), phlegm during daytime or at night (OR=1.49, 95% CI=1.08, 2.07), nose problems in the morning (OR=1.38, 95% CI=1.03, 1.86), nose problems at night (OR=1.40, 95% CI=1.03, 1.90), throat problems in the morning (OR=1.57, 95% CI= 1.05, 2.36), throat problems during daytime (OR=1.81, 95% CI=1.15, 2.85) throat problems at night (OR=1.78, 95% CI=1.14, 2.78) and ever wheeze or diagnosed asthma by doctor (OR=1.55, 95% CI=1.06, 2.26). The odds ratios increased with increasing number of smokers at home for cough in the morning, cough most days for the previous 3 months, phlegm in the morning, ever wheeze or diagnosed asthma by doctor, throat problems in the morning, throat problems during daytime and throat problems at night. The PEFR was lower in exposed children but not statistically significant. Digit Span Forward, Digit Span Backward and Coding scores were lower in exposed children but also not significant.

Conclusions : More than half of the primary school children in Kota Bharu were exposed to secondhand smoke from at least one smoker in the house. The most common source of exposure was smoking by fathers. There was an association between secondhand smoke exposure and respiratory symptoms among the school children. No significant associations were observed between secondhand smoke exposure and PEFR and cognitive performance. In view of significant health risks posed to children by secondhand smoke exposure, public health policies and education are needed to protect this vulnerable population.

Assoc.Prof.Dr.Zulkifli Ahmad Supervisor
Assoc. Prof. Dr. Syed Hatim : Co-Supervisor

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ROAD TRAFFIC ACCIDENTS DURING FESTIVE SEASONS IN KELANTAN : ASSOCIATED FACTORS AND IMPACT OF INTERVENTIONAL PROGRAMMES

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MMed (Community Medicine)

Introduction : Road traffic accident (RTA) is one of the major causes of death and injuries in Malaysia. The adverse consequences of RTA, which include variety of chronic medical conditions and disabilities that may lead to long term health problems to road users, not only cause a tremendous impact on the family but also on the health system.

Objectives : The aim of this study was to describe mortality and morbidity pattern, and to determine the impact of interventional programmes (Ops Sikap) and associated factors contributing to road

traffic accidents (RTAs) cases during festive seasons in Kelantan.

Methodology : For the first parts of the study, monthly data were collected retrospectively from January 1997 to December 2003 using police records as the source of data. The second part of the study looked at daily accident data during the periods of "Ops Sikap" from 2002 to 2003. The first part of the study analyzed accident events, whereas the second part analyzed drivers' factors. A total of 40,452 accidents were reviewed during seven years period (1997-2003). The numbers of non fatal accidents showed an increasing trend from 1998 to 2003 except 2001, which showed decreased trend. Kelantan experienced a continuous increase of fatal accidents from 1997 until 2000, followed by a fluctuation between 2001 and 2003. The numbers of fatal and non fatal accident cases showed no pattern, but total cases for both accidents increased by months within the one calendar year. The impact of interventional programmes on non fatal injury cases were analysed for the yearly trend and was found to be statistically significant. The presence of interventional programmes caused 1.13 times increase of non fatal cases. The year to year increase of incidence rate ratio (IRR) was significant (1.27 to 1.45 times) and (1.09 to 1.27 times) of fatal and non fatal injury cases, respectively except in year 1999. In multiple logistic regression analysis, significant associated factors were safety measures either use of seat belt or helmet (OR=0.15, 95%CI=0.07, 0.31), motorcar and van drivers (OR=7.79, 95%CI=3.60, 16.83), vehicles went out of control (OR=4.58, 95%CI=1.67, 12.56) and road quality (OR=-0.04,95%CI=0.01,0.23).

Conclusions : There was no consistent seasonal pattern of the mortality and morbidity of accidents, but the trend was increased significantly throughout the months within one year calendar. The interventional programmes by police and other agencies did not have any significant impact on number of fatal cases. The four significant associated factors for severity of injury included safety measures such as using seat belt or helmet, motorcar and van accidents, vehicle out of control and road quality.

Dr. Mohamed Rusli Abdullah : Supervisor
Assoc. Prof. Dr. Abdul Aziz Al-Safi : Co-Supervisor

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SAFETY ASPECTS OF ANDROGRAPHIS PANICULATA AN INVESTIGATION INTO POSSIBLE MALE REPRODUCTIVE TOXICITY

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Introduction : *Andrographis paniculata* (AP) is one popular form of alternative therapy for diabetes mellitus in Malaysia. It is chosen by Ministry of Science and Technology, Malaysia to develop its standardized 95% ethanol extract (APE) as an effective and safe treatment of diabetes mellitus. Since previous studies have shown conflicting results regarding effects of AP on male reproductive system, this study was undertaken to investigate possible male reproductive toxicity of APE.

Objectives : To study effects of 95% ethanol extract of *Andrographis paniculata* (APE) on male reproductive health in Sprague Dawley rats.

Methodology : Fifty adult healthy male rats were randomly divided into 5 groups of 10 animals each. Group 1, 2 and 3 received three different doses of APE (10, 100 & 1000 mg/kg), group 4 received glibenclamide (5mg/kg) while group 5 received 2% CMC (vehicle). Treatment was administered once daily for 4 weeks pre-mating and a maximum of 2 weeks mating period. Body weight was recorded weekly. Four weeks pre-mating treatment was followed by mating of each male with 3 female animals until all females were sperm positive or a

maximum of 2 weeks. Male animals were then sacrificed. Reproductive organs were removed and weighed. Left testis was used for spermatid count, left caud.i for sperm count and morphology while right testis was used for histopathological examination.

Results : Testicular histology showed severe interstitial edema of testis with intact spermatogenesis in group 1; progressively severe disorganized arrangement of germ cells, sloughing of immature cells and significantly smaller tubular diameter in groups 2 and 3. However, Leydig cells showed mild hyperplasia in APE treated groups. Reproductive organ weight was high in group 1 and low in groups 2 and 3 when compared to control. Sperm count, spermatid count and daily sperm production were significantly low ($p<0.01$) in group 2 and were further reduced in group 3. Abnormal sperms were seen in groups 2 and 3. None of the above mentioned parameters showed significant differences between groups 4 & 5.

Discussions : APE adversely affects spermatogenesis by at least two different mechanisms: 1) Increase in capillary permeability 2) Damage to Sertoli cell functions. Increased capillary permeability has resulted into increased reproductive organ weight in group 1, while extensive damage to spermatogenesis in groups 2 and 3, caused primarily by damage to Sertoli cells has resulted into low organ weight and poor semen quality.

Conclusions : In conclusion, the results suggest that APE treatment adversely affects male reproductive functions in a dose-dependent manner in Sprague Dawley rats.

Prof. Dato' Mafauzy Mohamed : (Supervisor)
Assoc. Prof. Dr. Siti Amrah Sulaiman : (Co-Supervisor)

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SPECTRUM OF GASTROESOPHAGEAL REFLUX DISEASE (GERD) AMONG ENDOSCOPED PATIENTS IN HSPITAL USM AND ASSESSMENT OF CORRELATION BETWEEN ENDOSCOPIC AND HISTOLOGICAL GRADE

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MMed (Anatomi)

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Introduction : Many controversial issues exist regarding the diagnosis of gastroesophageal reflux disease (GERD).

Objectives : The aim of this study was to test the concordance between endoscopy and histological examination of the lower esophagus in the diagnosis of GERD and to determine the significance of gastric carditis in GERD. A secondary objective was to determine the prevalence of GERD in a sample of dyspeptic patients undergoing endoscopy in Hospital USM, Kelantan.

Methodology : The concordance between endoscopy (using standardised Los Angeles Classification) and histology (basal cell hyperplasia $>15\%$ of epithelial thickness and elongated papillary height of $>50\%$ of epithelial thickness) were assessed in a total of 81 patients with GERD symptoms referred for upper gastrointestinal endoscopy in HUSM within a one year period. Two biopsies were taken: one at 3 cm above the gastroesophageal junction (GEJ) and the other immediately below the GEJ (cardia mucosa), followed by routine staining with Haematoxylin and Eosin (H & E), and assessed by a single pathologist who was blind to the clinical findings.

Results : The subjects consisted of 81 (41 male, 39 female) patients, with a median age of 49 years old (range from 13 to 80 years old). The commonest presenting symptom was retrosternal pain (81.5%). Classical GERD symptoms of heartburn (43.2%), regurgitation (38.3%) and waterbrash (30.9%) showed significant association with endoscopically diagnosed GERD ($p<0.05$). Majority of patients

presented with mild symptoms (69.1%). GERD was diagnosed endoscopically in 36/81 patients (44.4%) whereby majority of subjects had LA Classification grade A (30.9%), while 8.6% had LA grade B, 1.2% had LA grade C and 3.7% had LA grade D. Using histology, 27/81 subjects (33.3%) had GERD. Only 15/36 patients who were diagnosed endoscopically had histological GERD, while 9/27 (23.1%) patients with histological GERD had normal endoscopy. The agreement between endoscopy and histology on the assessment of GERD in 81 esophageal biopsies occurred in only 18.5% (Kappa statistic 0.16). This discordance was seen through out all Grades A to D of the LA Classification. On assessing the histological parameters, intraepithelial neutrophils, eosinophils and lymphocytes were found to correlate well with histological GERD ($p<0.05$). Intraepithelial neutrophils were found to correlate with endoscopic GERD of severe grade (LA Classification grade D). In the gastric cardia, chronic inflammation was found to be significantly associated with histological GERD ($p=0.04$). Carditis with intestinal metaplasia however did not show any significant association with histological GERD.

Conclusions : This study shows poor concordance between GERD as determined by endoscopy and GERD as defined by histology, even though standard criteria were used. However, intraepithelial neutrophils infiltrate of esophageal mucosa is a reliable histological marker in the diagnosis GERD. An inflamed cardia mucosa may aid in the diagnosis of GERD.

Dr. Gurjeet Kaur : Supervisor
Dr. Syed Hassan bin Syed Abd. Aziz : Co-Supervisor

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THE EFFECT OF ADDING DEXAMETHASONE TO PCA MORPHINE ON POST OPERATIVE NAUSEA AND VOMITING

Objective : The aim of this study was to determine the effect of adding dexamethasone to PCA morphine on post operative nausea and vomiting as compared to PCA morphine alone.

Methodology : 60 female patients undergoing lower abdominal gynaecological surgery were randomized to receive either PCA morphine alone ($n = 30$) or PCA morphine added with 8 mg of dexamethasone ($n = 30$). The incidence of post operative nausea and vomiting were evaluated in both groups using numerical vomiting score every 4 hours for 24 hours. Data was analyzed by chi square with $p<0.05$ was considered significant.

Results : There were no significant differences in demographic data. The incidence of PONV at 0 to 4 hours was 33.3 % in both groups. At 4 to 8 hours the incidence were 26.6% in morphine groups and 26.7% in dexamethasone mixed with morphine group. At 8 to 12 hours both groups showed incidence of 6.6%. Morphine mixed with dexamethasone group showed earlier PONV free period beginning from 12 hours post operatively while morphine alone group at much later time from 16 hours onward. However, overall there were no statistically significant difference in term of incidence of PONV in both groups. Adding dexamethasone to PCA morphine also did not affect acute pain management as there was no significant difference in pain score in both groups.

Conclusion : Adding 8 mg dexamethasone to PCA morphine did not provide better prevention of PONV compared to PCA morphine alone.

Dr. Nik Abdullah Nik Mohamed : Supervisor
Dr. Mahamarowi : Co-Supervisor

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THE EFFECT OF LOW DOSE ESMOLOL AND NICARDIPINE MIXTURE ON HEMODYNAMIC CHANGES FOLLOWING LARYNGOSCOPY AND TRACHEAL INTUBATION

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MMed (Anesthesiology)

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Introduction : Adrenergic response manifested by tachycardia and hypertension are well known to occur following laryngoscopy and intubation. Various drugs have been used in attempts to attenuate this response but all have limitations. A more satisfactory approach for this situation might be to use smaller doses of combination of drugs which can provide good control for short period, have a short half life and also have complimentary actions. Many studies using esmolol (B-blocker) or nicardipine (calcium channel blocker) as a single drug to suppress these reflexes had shown promising results. As both esmolol and nicardipine had rapid onset and short duration of action, we formulated a study to evaluate the capability of this combination to attenuate the hemodynamic response to laryngoscopy and tracheal intubation.

Objectives : The objectives of this double-blinded, randomized study were to compare the effect of hemodynamic changes after laryngoscopy and tracheal intubation in patient pre-treated with placebo (saline as control group) and new lower dosage of esmolol and nicardipine mixture. Another objective of this study is to get the optimal range of esmolol and nicardipine mixture -for attenuation of hemodynamic changes after laryngoscopy and tracheal intubation.

Methods : Sixty patients, ASA physical status I or II, undergoing elective and emergency surgery assigned randomly in a double blind, placebo-controlled manner to received either saline (control group) or combination of esmolol-nicardipine (esmolol 0.5 mg/kg, nicardipine 10 µg/kg) as a pre-treatment prior to intubation. No patients were given pre-medication prior to surgical operation. All patients were induced in a rapid sequence intubation using i.v fentanyl 1.5 µg/kg, i.v thiopentone 4 mg/kg and i.v suxamethonium 1.5 mg/kg, 2 minutes after pre-treatment with the study drug. Intubation was performed 60 seconds following suxamethonium injection. Anesthesia was maintained with nitrous oxide in oxygen with a ratio 2:4 and 0.5% isoflurane. Intra venous vecuronium ±0.1 mg/kg was given after intubation as a long acting muscle relaxant. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded prior to pre-treatment with the study drugs as baseline TO, at 2 minutes after pre-treatment with study drugs as T1 and every minute after laryngoscopy and tracheal intubation (LTI) for 6 minutes duration (T2-T7). Patients were also monitored for complications such as bucking, moving limbs, bronchospasm, hypotension and arrhythmia.

Results : Both esmolol-nicardipine and control groups showed the increase of mean HR, SBP, DBP and MAP after laryngoscopy and tracheal intubation when compared to baseline. However esmolol-nicardipine group was able to reduce the mean SBP by 14.6 mmHg, mean DBP by 13.3 mmHg and mean MAP by 13.3 after laryngoscopy and tracheal intubation when compared to saline (control) group. All the reduction in blood pressure was significant statistically. Total overall complications also were significantly lower in esmolol-nicardipine group (20% overall intubation related complications) when compared to saline (control) group which has 46.7% total overall intubation related complications. Heart rate (HR) and rate pressure product (RPP) were increased in both groups and there was no significant difference between the two groups.

Conclusion : The low dose combination of esmolol-nicardipine was able to reduce the mean SBP, DBP and MAP after laryngoscopy and tracheal intubation when compared to saline (control) group. The total complications also were low in patients pre-treated with combination of esmolol-nicardipine.

**Assoc. Prof. Kamaruddin Jaalam : (Supervisor)
Dr. Nik Abdullah Nik Mohamad : (Co-Supervisor)**

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THE EVALUATION OF THE PREDICTORS OF DELAYED TRAUMATIC INTRACRANIAL HAEMORRHAGE (DTICH) AND PROGRESSIVE TRAUMATIC BRAIN INJURY (PTBI) IN TRAUMATIC HEAD INJURED PATIENTS FROM HOSPITAL KUALA LUMPUR

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MSurg (Neurosurgery)*

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Objectives : A repeat CT brain after 24 -48 hours from the 1st scanning is usually being practiced in Hospital Kuala Lumpur. This interval will be shortened if GCS deteriorates. The purpose of this study is to determine other important predictors for early detection of DTICH/PTBI before GCS drops. The most ideal timing of repeating CT brain is being determined at the same time.

Methodology : 81 patients were included in this univariate retrospective study by comparing the 1st and 2nd CT brain to diagnose the presence of DTICH/PTBI. The predictors tested are broadly categorized into patient factors, CT brain findings and laboratory investigations.

Results : Out of 81 patients in the study, mean age was 33.1 ± 15.7 years, male preponderance of 6.36:1, 81.5% of them suffered from MVA, Glasgow Coma Scale range from 4-15 (median of 12) upon admission and; mean time interval between trauma and 1st CT brain was 179.8 ± 121.3 minutes with PBI. In delayed traumatic intracranial haemorrhage (DTICH), 9.9% of the patients were found to have new clots. Significant predictors detected were different referral hospitals (p=0.02), GCS status (p=0.026), GCS status-motor component (p=0.05), haemoglobin level (p=0.001). Platelet count (p=0.023) and time interval between trauma and 1st CT brain (p=0.002). In progressive traumatic brain injury (PTBI), 42.0% of the patients were found to have new changes (new clot occurrence, old clot expansion and edema) in the repeat CT brain. Univariate statistical analysis had pointed out age (p=0.03), race (p=0.035), types of admission (p=0.024), GCS status (p=0.02), pupillary changes (p=0.014), no. of intracranial lesion (p=0.004), haemoglobin level (p=0.038), prothrombin time (p=0.011) and time interval between trauma and 1st CT brain (p=0.047) as the best predictors.

Conclusion : This study was shown to have 9.9% of patients having DTICH and 42% of PTBI. Early after traumatic head injury, the initial CT brain does not reveal the full extent of haemorrhagic injury and associated cerebral edema. Different referral hospitals, GCS status, GCS status with motor component, haemoglobin level, platelet count and time interval between trauma and 1st CT brain were the significant predictors for DTICH. Whereas the key determinants of PTBI were age, race, types of admission, GCS status, pupillary changes, number of intracranial bleed, haemoglobin level, prothrombin time and of course time interval between trauma and 1st CT brain. Any patients who had traumatic head injury are advised to have to repeat CT brain at 10 ± 2 hours from trauma regardless of the duration between trauma and initial scanning.

**Prof. Dr. Jafri Malin Dato Hj. Abdullah : Supervisor
Mr. Johari Siregar bin Adnan : Co-Supervisor**

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THE EXPRESSION OF P53 AND C-ERBB-2 IN INFILTRATING DUCTAL CARCINOMA WITH DUCTAL CARCINOMA IN-SITU COMPONENT

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MMed (Pathology)

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Objectives : This study aimed at analyzing the correlation between p53 and c-erbB-2 expression in infiltrating ductal carcinoma (IDC) of the breast having ductal carcinoma in-situ (DCIS) component.

Methodology : Thirty six cases of breast carcinoma with such histological features were identified. The median age of the patients was 45 years (range 29-69 years) and the median tumour size was 50mm in diameter (range 15-120mm). Standard immunohistochemical staining for both tumour markers was performed on tissue sections.

Results : There was a significant association between c-erbB-2 staining patterns with DCIS grade ($p < 0.001$) whereby the c-erbB-2 expression was associated with high grade DCIS, but this was not for IDC. There was no significant pattern seen in the expression of p53 in both parts of the tumour. We noted that there was no significant change in the expression of p53 and c-erbB-2 as the lesion progressed from in-situ to invasive carcinoma (McNemar $p = 0.625$ and 1.000 respectively). We also found that DCIS grade did not determine the IDC grade. In addition, we also noted that there was no significant difference in the expression of p53 and c-erbB-2 in DCIS component ($p = 0.146$) as well as in IDC part ($p = 0.344$).

Conclusions : We concluded that mutation of p53 and over-expression of c-erbB-2 occurred early in the carcinogenesis of breast cancer. There was possibility that abnormal expression of p53 protein caused genetic instability in the early stages of tumour development and resulted in subsequent expression of other oncogene (c-erbB-2). Other than that, we also found that the clinico-pathological features (mitosis, lymphovascular invasion, lymph node metastases, age and tumour size) did not significantly relate to the expression of both markers in the tumour. However, many of the other findings in this study were guarded, as the size of the studied group was small. Further studies in larger groups of patients maybe required to confirm some of the findings.

Prof. Madya Dr. Haji Hasnan Jaafar : (Supervisor)

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THE EXPRESSION OF P53 AND C-ERBB-2 PROTEINS AND THEIR RELATIONSHIP TO DUKES' STAGING IN COLORECTAL ADENOCARCINOMAS

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Introduction : Molecular studies on colorectal carcinoma has confirmed that tumourigenesis is a multistep process in which genetic alterations accumulate, and ultimately produce the neoplasm. Both proto-oncogenes and tumour suppressor genes are involved. Genetic alteration in *c-erbB-2 (HER-2/neu)* gene was found to have significant prognostic indicator in breast carcinoma while alteration *ofp53* (a tumour suppressor gene) has been found to occur in many type of human cancers including colorectal carcinoma. However, for a long period of time Dukes' staging has been used successfully in predicting disease outcome in patients with colorectal carcinoma.

Objectives : This study was carried out aiming at observing the expression of p53 and c-erbB-2 proteins by immunohistochemical method in relation to Dukes' staging in 51 cases of colorectal carcinoma cases registered at the Hospital Universiti Sains Malaysia over a span

of 5-year period between 1996 to 2000. Apart from Dukes' staging, other clinicopathological factors such as tumour grade, anatomical sites, and others were also analyzed against the expression of p53 and c-erbB-2.

Results : It was found that p53 expressions was seen in 65% of colorectal carcinoma cases while only 15.7% of the cases showed over expression of c-erbB-2. No significant correlation was found between the expressions of either p53 or c-erbB-2 with the Dukes' stage of the tumours with the p value of 0.169 and 0.909 respectively. No significant correlation was also found between the expressions of p53 and c-erbB-2 with tumour grade, anatomical sites of the tumour, right sided vs. left sided disease or local disease vs. advanced disease.

Conclusions : From these findings, it was concluded that p53 was involved in the course of colorectal carcinogenesis but it did not correlate with Dukes' stage in colorectal carcinoma. Since c-erbB-2 was over expressed by a very small number of the colorectal carcinoma, c-erbB-2 was not a common genetic event occurred in colorectal carcinoma.

**Assoc. Prof. Dr. M. Madhavan : Supervisor
En. Rosli Jusoh : Co-Supervisor**

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THE OUTCOMES OF PRIMARY UNREAMED INTERLOCKING NIL IN AN OPEN FRACTURES OF TIBIA IN HOSPITAL KUALA TERENGGANU.

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MMed (Orthopaedics)*

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Introduction : The used of nonreamed interlocking tibial nails in the management of open fractures of the tibial shaft has gained wide acceptance. It becomes a gold standard of the treatment of tibial diaphyseal fractures. This technique has been reported to have reproducible good results with low incidence of complications in Grade I, Grade II and Grade IIIA open tibial shaft fractures.

Objectives and Methodology : Forty (40) high energy open tibial diaphyseal fractures were treated with unreamed locked intramedullary nail in Hospital Kuala Terengganu from June 2002 until June 2004. They were reviewed at a minimum of 6 months to 1 year from injury.

Results : There were seventeen (17) patients of Grade I, sixteen (16) patients of Grade II and seven (7) patients of Grade IIIA. The mean diameter of intramedullary nail was 9 millimeters. The initial culture and sensitivity was positive in one (1) patients (2.5%). 67.5% of the wound were closed primarily and 32.5% were closed secondarily. The mean duration of clinical union was achieved at 15.7 weeks, where as the mean duration of radiological union was 22.4 weeks. One (1) patient had dynamization of distal screw at 16 weeks and the fracture united at 20 weeks postoperatively. All fractures united within 32 weeks postoperatively.

Conclusions : No delayed union, nonunion and malunion in this study. 7.5% (3) of fractures developed infection, 5% (2) developed superficial infection and 2.5%(1) developed deep infection in which required removal of intramedullary after the fracture had united. All infected cases were in Grade II open fractures. One (1) infection was seen in the wound closed primarily and two (2) infection were seen in the wound closed secondarily.

**Dr. Mohd Iskandar Mohd Amin : Supervisor
Mr. Mohd. Ros Mohd Ali Co-Supervisor**

THE PREVALENCE AND CLINICAL SIGNIFICANCE OF ANTIPHOSPHOLIPID ANTIBODIES (APA) IN NON-HODGKIN LYMPHOMA PATIENTS IN HUSM (A PILOT STUDY)

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Introduction : Cancer patients are at risk of developing thromboembolism (TE). Among all the malignancy, lymphoma is the fourth most likely cancer at risk to significant morbidity and mortality related to thrombosis. The association of antiphospholipid antibodies (APA) has been reported in several cases of patients with NHL and complete remission was associated with disappearance of APA after treatment. APA are group of autoantibodies which include anticardiolipin (ACA), anti-beta2 glycoprotein1 (anti-β2GPI) and lupus anticoagulant (LA). The presence of APA with occurrence of vascular thrombosis is known as antiphospholipid syndrome (APS). Study done by Zuckerman in 1995, found increased incidence of vascular thrombosis in APA positive cancer patient (22%). A pilot study was conducted in HUSM for one year period to recruit 53 selected NHL patients for detection of APA at presentation.

Objectives : The purpose of this study was to determine the prevalence of APA and its clinical significance.

Methodology : Patient's blood was tested for the presence of ACA and anti-p2GPI antibodies using ELISA technique. They were follow-up over a median period of 6 months to detect the occurrence of TE and bone marrow (BM) recovery after chemotherapy, especially for the platelet counts.

Results : We found APA in 23 out of 53 NHL patients (43.4%), with ACA 35.8% and anti-β2GPI antibodies 18.9%. From statistical analysis, the incidence of elevated APA increased with age especially for those with age more than 40 (91.3%). However positivity for APA was not associated with the gender, survival, histology and stage of lymphoma. There were three patients with APA developed TE in follow-up period; however there is no significant statistical association between APA and TE. However positive APA was found to correlate with development of thrombocytopenia at presentation and during follow-up before subsequent chemotherapy (p<0.05). This indicate, thrombocytopenia could be part of APA and there is a slow recovery of BM after chemotherapy for platelet count of APA positive lymphoma compared to APA negative lymphoma. Our observation from this study is that APA was prevalent among NHL patients. The presence of one APA or combination of these antibodies which are known to be correlated with thrombosis among APS patients, however were not significant in our patients.

Conclusions : We conclude that screening for APA to detect potential TE is not routinely recommended for all NHL patients in our institution. However, a finding of slow recovery of platelet count post chemotherapy probably indicate an underlying APA and confirmation by testing for APA and exclude other causes of thrombocytopenia could help in the patient's management

Dr. Wan Zaidah Abdullah : (Supervisor)
Dr. Narazah Mohd Yusoff : (Co-Supervisor)

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THE PREVALENCE OF EXTENDED-SPECTRUM BETA-LACTAMASE PRODUCING KLESIELLA PNEUMONIA (EPKP) IN HUSM AND RISK FACTORS AND CLINICAL OUTCOME OF EPKP BACTEREMIA

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Introduction : Prevalence of extended spectrum beta-lactamase producing klebsiella pneumonia (EPKP) has been reported worldwide, and generally known that different locality or hospital has different prevalence rate. Risk factors for EPKP infections and the outcomes of EPKP infections have been studied worldwide. The hallmark of this strain is resistance to the extended-spectrum cephalosporin but remain susceptible to beta-lactamase inhibitors.

Objectives : This study was conducted to determine the prevalence of EPKP isolates and EPKP bacteremia in HUSM. In this study also we determined the possible risk factors that influence the EPKP bacterimia and the outcome of EPKP bacteremia and non-EPKP bacteremia.

Methodology : A cross sectional descriptive study was done to determine the prevalence of EPKP isolate and EPKP bacteremia. A total of 501 of all significant isolate of Klebsiella pneumoniae were analysed between the study periods 1st January 2003 till 31st December 2003. All the isolates were tested for ESBL production using double disk synergy test.

Results : The prevalence of EPKP isolates in HUSM was 47.7% and among blood isolates was 52%. A case-control study was also conducted to determine the risk factors of EPKP bacteremia and its outcomes. Fifty-four cases of EPKP bacteremia and 56 controls of non-EPKP bacteremia were included in this study. Risk factors associated with EPKP bacteremia according to univariate analysis, included nosocomial acquisition (OR, 11.5; 95% CI, 1.420-93.451; p = 0.022) and day of admission before wpiodes of bacteremia of more than 28 days (OR, 3.085; 95% CI, 1.001-9.511; p = 0.05). Several protective factors were also identified, include no admission to intensive Care Unit (ICU) (OR, 0.323; 95% CI, 0.148-0.705; p= 0.005), no ceftazidime administration (OR,0.147; 95% CI, 0.611--.961; p = 0.00), no prior endo-tracheal tube (ETT) usage (OR, 0.147; 95% CI, 0.061-0.351;p<0.001) and no previous operation (OR, 0.009; 95%CI, 0.112-0.734; p = 0.009). On multivariate analysis, the final model revealed that nosocomial acquisition (OR, 9.63; 95% CI, 0.872-106.402 p = 0.065) was the risk factor EPKP bacteremia. However, no ETT usage (OR,0.145; 95% CI, 0.390-0.542; p < 0.001) and no ceftazidime usage (OR, 0.161; 95% CI, 0.390-0.542; p = 0.002) were the protective measure against EPKP bacteremia. This study showed that there was no significant difference in mortality of EPKP bacteremia compared non-EPKP bacteremia (p = 0.843).

Conclusions : Based on the findings, we concluded that the prevalence of EPKP in our setting is high and the significant risk factor was nosocomial acquisition whereas the protective factors against this infection were no prior usage of ceftazidime and ETT. Therefore, control of antibiotic usage and limiting nosocomial transmission of EPKP isolates may reduce the prevalence of this infection. In this study we found that the mortality rate did not differ between EPKP bacteremia and non-EPKP bacteremia.

Dr. Habsah Hassan : (Supervisor)
Assoc. Prof. Dr. Mohd. Radzi Johari : (Co-Supervisor)

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THE PREVALENCE OF SYMPTOMS AND THE DENTOFACIAL FEATURES OF OBSTRUCTIVE SLEEP APNEA SYNDROME AMONG ARMY PERSONNEL BASED IN KELANTAN

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Introduction : Obstructive sleep apnea (OSA) is repeated complete or partial upper airway obstruction during sleep, causing cessation of breathing (apnea) or reduction in airflow (hypopneas) despite persistent respiratory effort. It occurs in 9% and 24% middle-aged women and men respectively while obstructive sleep apnea syndrome, OSAS (OSA plus presence of symptoms such as excessive daytime sleepiness) occurs in 2% and 4% middle-aged women and men respectively.

Objectives : The objectives of the study were to determine the prevalence of symptoms of OSAS and the differences in dentofacial features of army personnel based in Kelantan who are at high risk and low risk of having OSAS, and to find factors associated with the risk of having OSAS.

Methodology : 911 army personnel based in the Desa Pahlawan camp were randomly selected to answer the Malay version of Berlin questionnaire. The distributions of symptoms of OSAS were determined and subjects were categorised as being either at high risk or low risk of having OSAS. Dental study models, lateral cephalometric radiographs and neck circumference for the determination of the dentofacial dimensions were taken from 35 high risk and 37 low risk subjects. A proportion of these subjects underwent overnight sleep studies.

Results : 661 questionnaires were returned. The mean age of total participants was 31.4 years (standard deviation (SD) 6.45) while the mean BMI was 24.4 kg / m² (SD 2.47). There was a range of prevalence of the main symptoms of OSAS with 45 subjects (6.8%, 95% CI: 5.0-9.0) categorised in the high risk group for OSAS. There were no significant differences in age and BMI between the 35 high risk and 37 low risk subjects that formed the subsequent comparison groups. The neck circumference, PNS_P (length of the soft palate), MPT (maximum soft palate thickness), MPH (distance between the mandibular plane and the hyoid bone), maxillary intermolar distance, mandibular intermolar distance and middle PAS (posterior airway space) were significantly different between both groups. There were significant associations between the following variables and the risk of having OSAS: mandibular intermolar distance, PNS_P and MPH.

Conclusions : The current study demonstrates presence of symptoms of OSAS and the distinct dentofacial features in subjects at high risk of OSAS. This study also confirms that symptoms of OSAS still exist even without the classical sign of OSAS, i.e. obesity. It also shows that greater attention should be paid to the evaluation of the dentofacial features in subjects with a low BMI at high risk for the disorder.

**Prof. Dr. Abd. Rani Samsudin : Supervisor
Dr. Mohd. Ayub Saddig @ Lin Naing : Co-Supervisor**

**THE USE OF THORACIC ULTRASOUND TO DETECT
PNEUMOTHORAX IN TRAUMA AND NON-TRAUMA
PATIENTS**

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Objective : To determine the sensitivity, specificity, positive and negative predictive value of thoracic ultrasound in the detection of pneumothorax in trauma and non-trauma patients, and to determine any significant difference of time taken by thoracic ultrasound and chest radiograph.

Methodology : We conducted a prospective study on 31 trauma and non-trauma patients presented to the Emergency Department, Hospital Universiti Sains Malaysia with symptoms suggestive of pneumothorax.

Informed consent was obtained from patients who met the inclusion and exclusion criteria before undergoing thoracic ultrasound examination of the chest. The thoracic ultrasound examination was carried out during secondary survey of physical examination. The chest X-ray was performed after the thoracic ultrasound examination, allowing the ultrasonographer to remain blinded during the examination. The result was later compared with the chest X-ray. Performance time of thoracic ultrasound and chest X-ray were recorded.

Results : Among the 31 patients, there were 8 patients diagnosed with pneumothorax, 7 of which were detected by thoracic ultrasound, thus study showed that the thoracic ultrasound has a sensitivity of 87.5% and a specificity of 91.3% in the detection of pneumothorax. The positive predictive value was 77.8% and the negative predictive value was 95.5%. There was significant mean difference of performance time between the thoracic ultrasound and chest radiograph (p<0.001). We found that the performance time of thoracic ultrasound was faster than performing a chest radiograph, and it can be learned easily and quickly. The disadvantage of the thoracic ultrasound is that it can cause false positive finding if the patient has a subcutaneous emphysema.

Conclusion : Thoracic ultrasound can be used to detect pneumothorax by the absence of "lung sliding" and "comet-tail" artifact. The future development and training of emergency physicians in this technique are useful in the emergency department setting.

**Assoc. Prof. Kamarudin Jaalam : (Supervisor)
Dr. Wan Asim Wan Adnan : (Co-Supervisor)**

**THE VALIDATION OF THE MALAY TRANSLATED
AUDIT OF DIABETES-DEPENDENT QUALITY OF LIFE
(ADDQOL)**

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Objectives : To translate the Audit of Diabetes-Dependent Quality of Life (ADDQOL) into the Malay language and to determine the feasibility, validity and reliability of the Malay translated ADDQOL.

Methodology : This was a cross sectional study. The respondents were patients with type 2 diabetes mellitus selected by systematic random sampling. Four clinics and 304 respondents were involved. The Malay translated ADDQOL and a previously Malay translated and validated Short Form 36 (SF-36) were self administered. The translation used forward, backward and respondent testing and has been reviewed for face and content validity. The Malay translated ADDQOL was self administered again one week later. Analysis included the determination of the scaling assumptions, feasibility, validity and reliability.

Results : Of 304 respondents, 288 were analyzed. The Malay translated ADDQOL has the floor effect of 1.4% and the ceiling effect of 0.0%. The 18 domains of the Malay translated ADDQOL have means ranging from -2.88 to -5.76 and standard deviation, sd ranging from 2.76 to 3.09. Means of the two overview items, Item I and Item II were 0.85 and -2.06 and sd were 0.87 and 0.76 respectively. Domains of the Malay translated ADDQOL showed highest Pearson correlation ranging from 0.52 to 0.78 with its own scale and lower with scales of the SF-36. The means and sd of the average impact Malay translated ADDQOL were -4.44 and 2.10 respectively. The Cronbach's alpha was 0.94 (95% CI 0.935, 0.943) and the intraclass correlation was 0.81 (95% CI 0.72, 0.87). Pearson correlations between the average weighted impact of the Malay translated ADDQOL were significant with four scales of SF-36 having correlations ranging from 0.01 to 0.18. Factor analysis with one-forced factor has factor loadings from 0.52 to 0.83. The means

of average impact Malay translated ADDQOL for respondents with HbA1c equals and below 7.5% was -4.15 and above 7.5% was -4.42 (95% CI of mean difference -0.37,0.93), for those on diet or one type of oral anti-diabetic and for at least 3 types of oral anti-diabetic or insulin were -4.35 and -4.82 respectively (95% CI of mean difference -1.25,0.34).

Conclusions : The translation of the ADDQOL was acceptable. The feasibility is present and the scaling assumptions met. The internal consistency and intraclass correlation were excellent. The content validity has been established with evidence of acceptable construct and criterion validity. The Malay translated ADDQOL should be used in the management and studies involving diabetic patients along with the Malay translated SF-36.

Assoc. Prof. Abd. Aziz Al-Safi Ismail : Supervisor
Dr. Lin Naing@Mohd Ayub Sadiq : Co-Supervisor

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TRENDS OF MOTORCYCLIST ACCIDENTS IN KELANTAN AND FACTORS ASSOCIATED WITH SEVERITY OF MOTORCYCLIST' INJURY SEEN IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM), KELANTAN

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Introduction : Motor vehicle crashes (MVCs) contribute large proportion of death and disability globally. In Malaysia, more than 50% of the registered vehicles are motorcycle and it becomes one of the most important forms of personal transportation. Approximately 52.2% of all fatalities and 70.9% of all casualties related to MVCs in Kelantan were motorcycle riders and pillion riders.

Objectives : The objectives of the study were to determine the trend of motorcycle crashes in Kelantan between 1998 and 2003 and to identify factors associated with the severity of injury sustained by motorcyclist accidents.

Methodology : This study has two parts. Part 1 was a retrospective record review of MVCs in Kelantan between 1998 and 2003. Part 2 was a cross-sectional study on associated factors of motorcyclist accidents, assessed through face to face interviewed-based questionnaire and, at the same time the severity of injury was determined through Revised Trauma Score.

Results : The study revealed that majority of road traffic injuries involved motorcycle users (58.5% to 63.1%). The proportion of fatality was between 8.6% and 10.7% and majority involved those aged 11-30 years (60.0% - 69.7%). About 90% of the fatal motorcycle injuries were male. The peak hour for fatality was between 4.00 and 8.00 in the afternoons. There was no seasonal pattern of motorcycle accidents but, there was significant linear increasing trend over time ($p < 0.001$) with an average increase of 9 cases every year. Age more than 50 years (OR=12.87, 95% CI: 1.85, 89.58), no motorcycle license (OR=14.32, 95% CI: 3.85, 53.23), no stressful condition (OR=4.73, 95% CI: 1.64, 13.69) and crash on two-way road (OR=4.78, 95% CI: 1.26, 18.10) increased the odds of getting low score (RTS<11). Accidents on straight roadways (OR=0.24, 95% CI:0.07, 0.75) or on wet roads (OR=0.09, 95% CI: 0.02, 0.55) and drivers sleeping six to less than nine hours at night prior to accidents (OR=0.11, 95% CI: 0.02, 0.64) reduced the odds for low score.

Conclusions : Based on the results above, we conclude that the trend motorcycle accidents was increasing in the years 1998 - 2003, but with no season, pattern. Most of the fatal motorcycle crashes involved young men riders and occurred in afternoons. Age more than 50 years,

no motorcycle license, no stressful condition and crashes on two-way road showed higher risk to sustain more severe injury. However drivers sleeping six to less than nine hours at night, crashes on straight roadways an wet road surfaces were associated with less severe injury. We recommend that public education, licensing and enforcement on accident prevention and safety riding should be given a priority.

Assoc. Prof. Dr. Abd. Manaf bin Hj.Hamid : Supervisor
Dr. Mohd. Ayub Sadiq @ Lin Naing : Co-Supervisor
Assoc.Prof.Dr. Nik Zaki bin Ibrahim : Co-Supervisor

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A STUDY ON MENOPAUSAL EXPERIENCES OF KELANTANESE WOMEN

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M.Sc Thesis

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Introduction : Menopause is associated with numerous transient typical and atypical symptoms. It is believed that Asian women suffer more of the atypical symptoms and fewer, and with lesser severity, the typical psychological and vasomotor symptoms than the western women.

Objectives : This study reports the incidence and nature of menopausal symptoms in Kelantanese women and the self-care actions taken by them.

Methodology : A semi-structured, self-administered questionnaire was administered to 326 postmenopausal women (aged, 57.01 ± 6.58 (SD) years) residing in the state of Kelantan. The subjects comprised of naturally menopausal, healthy women. Women with uncontrolled diabetes and hypertension were not included. Descriptive statistical analysis was performed on the data using SPSS programme.

Results : Mean age at menopause was 49.4 ± 3.4 (SD) years while both the mode and median were 50 years. The mode for the number of symptoms complained by each woman was 8 (range 0 - 16). The incidences for atypical symptoms was; tiredness (79.1%), reduced concentration (77.5%), musculo-skeletal aches (70.6%) and backache (67.7%). Night sweats (53%), headaches (49.4%) and hot flushes (44.7%) were the typical vasomotor symptoms, whereas mood swings (51%), sleep problems (45.1%), loneliness (41.1%), anxiety (39.8%), and crying spells (33.4%) were the main psychological symptoms. Majority of the women reported reduced vaginal secretion (50.9%). The commonest coital frequency was approximately 2-4 times per month (49.7%). Overall, 42.3% reported a decrease in the frequency of sexual activity postmenopausally. Over two-thirds (69%) of the women reported either reduced (39%) or absent (29.6%) sexual desire or interest. A similar pattern was also reported for libido. Varying degree of dyspareunia was reported by 34% of the women. Some women (23.3%) had noticed that their spouses' sexual interest in them had reduced compared to before menopause. A small percentage (7.1%) reported that their vagina was not able to accommodate completely an erect penis. A small percentage (2.1%) admitted to having sexual problems, which had an affect on their marital relationship and another group (9.5%) had spouses with sexual problems. A quarter of the women thought their sexuality could be improved while another quarter thought otherwise. More than half (52.6%) did not take any action to improve their sexuality. Those who did, took HRT, "Jamu", Evening Primrose Oil, Royal jelly, did regular exercises and controlled their diet. The percentage of women taking self-care actions depended upon the symptom, and ranged from 47.7% for reduced concentration to 100% for crying spells and anxiety. Their self-care actions included taking traditional medicine, alternative medicine, prescribed medications, getting actively involved in community work, and having peer support.

More than half (55%) did not seek any advice regarding their menopause. Those who did, mainly approached their friends. Some 13% of women were not aware of the menopause when it occurred. The sources of knowledge on menopause, according to the respondents, were friends, health professionals, and attending seminars.

Conclusions : Most of the respondents viewed menopause as biological event and placed it within the context of their development milestones. Those who viewed menopause as a marker of old age accepted it as a time frame within the lifespan. In conclusion, it appears that the menopause symptoms experienced by women elsewhere, albeit, with differing frequencies. Majority of the women accepted menopause as the beginning of the aging process and resorted to numerous self-care actions to help see them through this transition.

Dr. Nor Aliza Abdul Ghaffar : (Supervisor)
Assoc. Prof. Dr. N. Md. Zaki N. Mahmod : (Co-Supervisor)

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CHARACTERIZATION AND EVALUATION OF THE DIAGNOSTIC POTENTIAL OF THE ENCODED PROTEIN OF *BRUGIA MALAYI* 17DIII DNA SEQUENCE

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PhD Thesis

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Introduction : An estimated 13 million people worldwide are infected by *Brugia malayi*, and several times this figure are at risk of acquiring the infection. However the diagnosis of the disease still depends on the traditional microscopy detection method (McCarthy, 2000). In the effort to improve the diagnosis of this infection, *B. malayi* 17DIII DNA sequence (GenBank AF225296) has been previously reported to express a recombinant protein of diagnostic potential for detection of brugian filariasis.

Objectives : The aim of this study was to characterize the *B. malayi* 17DIII DNA sequence and to evaluate the potential of its corresponding BmR1 recombinant protein for diagnosis of *B. malayi* infection.

Methodology : Analysis by Vector NTI software showed that the *Bm 17DIII* DNA possessed a 618 bp ORF; and *via* Southern blotting this DNA sequence was detected in all stages of *B. malayi* i.e. L₃, L₄, mf, adult male and adult female. The application of monospecific antibody in conjunction with Western blotting and IEF, along with predictions using *PeptideMass* server demonstrated that the BmR1 native protein (expressed by adult worm) and the BmR1 recombinant protein (expressed by pPROEX™ HTb/Bm17DIII/TOP10F²) possessed MWs of 25 kDa and 30 kDa, and pI values of 4.46 and 4.85 respectively.

Results : Predictions based on various *in silico* tools and results from the immunolocalization experiment (involving monospecific antibody. IFAT and confocal microscopy) showed that the BmR1 native protein was probably an immunodominant transmembrane protein secreted by the epithelial cells of the uterus and *vas deferens* but remained localized within the epithelial membrane. By cloning and expression of each of the two halves of the DNA sequence, followed by determination of reactivity with mf+ serum samples, the antigenic terminus of BmR1 was detected at the N-terminus of the polypeptide. The recombinant antigen-based used in an ELISA format (*Brugia-ELISA*) demonstrated 100% specificity and sensitivity when evaluated against 151 mf- and 37 mf+ sera, however, the O.D. readings were not correlated to mf count. All (22/22) microfilaremic and *Brugia-ELISA* positive individuals were negative by *Brugia-ELISA* within the 21-month post-treatment period. In a treatment follow-up study on amicrofilaremic individuals who were positive by *Brugia-ELISA*, decline of IgG4 levels in all (13/13) individuals were detected by 21

months post-treatment. In contrast, 44% (7/16) of the untreated individuals were still IgG4 positive during the same study period. Field evaluation involving 1134 blood samples showed that *Brugia-ELISA* detected 9 times more positive cases as compared to microscopy observation. As a mapping tool, BmR1-based ELISA detected infection prevalence of 0.35% in eight schools in Pasir Mas, a level that could support active transmission of infection in the community (WHO, 1999). In an animal experimentation study, BmR1 recombinant antigen could detect *B. malayi* infection as early as day 8 post-infection; and showed sensitivity of ~94% (29/31) in detecting adult worms in gerbils irrespective of their microfilaria status. It was also able to differentiate between gerbils, which received live larvae and those which received live larvae antigens. An antigen detection ELISA was successfully developed to detect circulating BmR1 antigen. The assay was 100% specific but the sensitivity attained (50%) was not satisfactory. The low sensitivity may be due to the possibility that the antigen is only released into the host circulatory system during the release of mf or during larvae or worm death.

Conclusions : This study has succeeded in elucidating the physical characteristics of *Bm17DIII* DNA sequence and validating the diagnostic potential of its encoded protein in laboratory and field studies. In addition, this study also demonstrated the usefulness and versatility of the immunoassay based on the BmR1 recombinant protein in the diagnosis of *B. malayi* infection.

Prof. Dr. Rahmah Noordin : (Supervisor)
Prof. Dr. Zainul Fadziruddin Zainuddin : (Co-Supervisor)

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EMBRYOTOXICITY OF PERITONEAL FLUID FROM PATIENTS WITH ENDOMETRIOSIS ON REALY EMBRYONIC DEVELOPMENT: ROLES OF PRUVATE AND INTERLEUKINS

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M.Sc Thesis

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Introduction : The aetiology of endometriosis (E)-associated infertility remains poorly understood. In recent years, peritoneal fluid (PF) or its cellular components have been proposed to have toxic effects on pre-implantation embryos and therefore as possible mediators of infertility in endometriosis. However, to date, the precise factor/s responsible for the embryotoxicity in endometriosis has not been well clarified.

Objectives : This study therefore conducted to ascertain the embryotoxicity of peritoneal fluid from infertile women with endometriosis and to identify the possible embryotoxic factor/s that may be involved in the process.

Methodology : After receiving an informed consent, peritoneal fluid (PF) was obtained during laparoscopy or laparotomy from 21 infertile women at different stages of endometriosis (7: PF-minimal or mild-E, 7: PF-moderate-E, 7: PF-severe-E), and 7 infertile women without endometriosis (PF-NE). The PF was heat inactivated before use to inactivate the complement protein. Two-cell mouse embryos were obtained from superovulated mice (ICR strain). The embryos were cultured in modified Whitten's medium (mWM) in the presence of either PF-E, or interleukin (IL)-6 (at 1.6pg/ml and 100pg/ml) or IL-8 (at 16pg/ml and 1000pg/ml). For the control group, the 2-cell mouse embryos were cultured in mWM alone. To examine the effect of excess pyruvate on the embryotoxicity of PF, IL-6 and IL-8, 50pl of 1mmol/l pyruvate was added to each respective culture well. In cultures containing PF from patients with severe endometriosis, the effect of 50_1 of 2mmol/l and 5mmol/l pyruvate was also examined. The

embryos were observed at 24, 48 and 72 hours of culture to ascertain the number of surviving embryos. Concentrations of IL-6 and IL-8 in the PF-E and PF-NE were measured using ELISA technique and presented as mean \pm SEM. The number of surviving embryos in each group of culture is presented as percentage of the total number of embryos at time zero. The data were analysed using Fisher exact test, Mann-Whitney *U* test and Spearman's Rank correlation. A '*p*' value of <0.05 was considered significant.

Results : Addition of PF from all stages of endometriosis significantly ($p<0.001$) suppressed embryo growth at 24, 48 and 72 hours of culture. Addition of 50 μ l (1mmol/l) of pyruvate to the culture media significantly ($p<0.001$) reduced the embryotoxicity of PF-minimal or mild-E and PF-moderate-E at all time points of observation. However, in the PF-severe-E group, the effect of excess pyruvate was only evident at 24 hours of culture ($p<0.001$) even when 50 μ l of 5mmol/l of pyruvate was added to the media. Concentration of IL-6 was significantly ($p<0.05$) higher in PF-E when compared to its concentration in PF-NE and the levels increasing significantly with the severity of the disease. A positive correlation ($p<0.0001$) was noted between the levels of IL-6 and embryotoxicity (assessed as the percentage of degenerated embryos at 72 hours of culture) of PF from infertile women with endometriosis ($r = 0.7652; p<0.0001$). No significant differences were noted in the levels of IL-8 between the 2 groups. Addition of 50 μ l of IL-6 at 1.6 and 100pg/ml to the culture media significantly inhibited mouse embryo development at all stages of development ($p<0.001$). However, the embryotoxic effect of IL-8 at 16 and 1000pg/ml was only seen at 72 hours of culture ($p<0.001$). The effect of excess pyruvate in reducing the embryotoxicity of IL-6 was more marked when embryos were cultured with the lower dose of IL-6 (1.6pg/ml). The embryotoxicity of IL-8 that was observed at 72 hours, was reduced by excess pyruvate. The present study suggests PF from infertile women with endometriosis is embryotoxic and may be the cause of infertility in endometriosis. The increased levels of IL-6 in the PF-E together with the embryotoxicity of IL-6 and IL-8, suggests that interleukins (specifically IL-6) may mediate this embryotoxicity.

Conclusions : The similarity between the effect of pyruvate on IL-6, IL-8 and PF-E induced-embryotoxicity suggests that the mechanism of embryotoxicity might involve a disruption in pyruvate metabolism which can be overcome to some extent by the additional of excess pyruvate.

Prof. Gregory Tan Jin San : (Supervisor)
Prof. Harbindar Jeet Singh : (Co-Supervisor)
Assoc.Prof. Dr.Mohd. Shukri Othman : (Co-Supervisor)

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EXPRESSION OF PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR (PPAR) ISOFORMS AND CYTOKINE IN IMMUNE CELLS OF THE NON-OBESE DIABETIC (NOD) MICE

Mohd. Arifin Bin Kaderi
M.Sc Thesis

Introduction : The non-obese diabetic (NOD) mouse strain is a murine model for Type 1 diabetes mellitus, an autoimmune disease caused by the destruction of pancreatic β islet cells. The pathogenesis of the disease in these mice is believed to be caused by the unmodulated activity of immune cells such as macrophages as well as helper and cytotoxic T lymphocytes via several ways including the secretion of inflammatory cytokines. Peroxisome proliferator-activated receptors (PPARs) are transcription factors belonging to the nuclear hormone receptor superfamily. Activation of these PPAR isoforms by their ligands is believed to regulate the inflammatory responses of immune cells.

Objectives : The current study was carried out to investigate the possible relationship between the expression levels of mouse PPAR

isoforms, namely PPAR- α , PPAR- γ 1 and PPAR- γ 2 in selected immune cell subsets and the pathogenesis of Type 1 diabetes mellitus in NOD mice.

Methodology : Peritoneal macrophages, splenic CD4-positive and splenic CDS-positive lymphocytes were isolated from three different groups of NOD mice, specifically five weeks (NOD5) and nine weeks (NOD9) of age as well as diabetic (dNOD), from which total RNAs were isolated and cDNAs were synthesized. The same experiments were also carried out on similar groups of the non-obese resistant (NOR) mice, namely NOR5, NOR9 and dcNOR (diabetic-control NOR) which served as age-matched controls to the NOD mice. The expression levels of the aforementioned PPAR isoforms in each of the immune cell subsets of each mouse were quantified by Real-Time PCR technique using specifically developed homologous internal standards for each PPAR isoform. In addition, the expression levels of several selected cytokines were measured using the semiquantitative multiplex PCR technique.

Results : This research demonstrated the PPAR- α , PPAR- γ 1 and PPAR- γ 2 were differentially expressed in the peritoneal macrophages, the splenic CD4-positive and the splenic CDS-positive lymphocytes of NOD and NOR mice of selected age groups. Furthermore, the current observations suggest that these PPAR isoforms may play an important role in controlling the immunopathology of Type 1 diabetes mellitus. PPAR- α may be important in initiating the autoimmunity of peritoneal macrophages via its over expression in these immune cells. In contrast, PPAR- α may have a mixed role in the control of macrophage and CD4-positive lymphocytes from an early stage of Type 1 diabetes mellitus development, whereas PPAR- γ 1 may be important in the sudden progression of destructive insulinitis, which is believed to be due to the activity of CD8-positive lymphocytes. Cytokine gene expression levels were measured in the peritoneal macrophages, splenic CD4- and CD8-positive lymphocytes of NOD and NOR mice using multiplex PCR. In general, the observation on inflammatory cytokines gene expression in the peritoneal macrophages, CD4- and CD8-positive lymphocytes were consistent with the findings of earlier studies with regard to their roles in the progression of Type 1 diabetes mellitus.

Conclusions : Differential pattern of expression of PPAR isoform observed in the current study suggests differential roles of these receptor isoforms in Type 1 diabetes mellitus. PPAR- γ 2 may be important in regulating the gene expression of TNF- α , IL1- β and GM-CSF in the peritoneal macrophages as well as IFN- γ and IL-2 in the CD4-positive lymphocytes. Whereas, PPAR- γ 1 may be involved in the modulation of IFN- γ gene expression in the CD8-positive lymphocytes, especially the tissue-destructive stages of Type 1 diabetes mellitus in NOD mice. However, the existence of a direct relationship between the expression of PPAR isoforms and the production of cytokines by the specific cell subsets remains to be determined.

Assoc. Prof. Dr. Nik Soriani Yaacob : (Supervisor)
Prof. Dr. Norazmi Mohd. Nor : (Co-Supervisor)

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MOLECULAR SCREENING USING NON RADIOACTIVE DIFFERENTIAL DISPLAY TECHNIQUE IN MALAY KELANTANESE PATIENTS WITH PEPTIC DISEASE

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M.Sc Thesis

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Introduction : Peptic diseases are the most common chronic diseases of adulthood and proven to have a substantial multifactorial inherited components. Genetic influences play some role in the predisposition

to both forms of ulcers (gastric and duodenal ulcer). A small proportion of chronic gastric ulcers are susceptible to be transformed into malignancy. The possible somatic mutations that take place have not been extensively studied. The discovery of some genetic changes at the vicinity of the chronic benign inflammatory lesions is important in relation to the elucidation of the carcinogenesis of gastric cancers.

Objectives : The general aims of this study were to screen for differentially expressed genes in peptic diathetic patients and to apply a technique of non radioactive differential display analysis (DDRT-PCR). DDRT-PCR has been shown to be highly effective in identifying sequences that are differentially expressed in various cell types and this technique makes it possible to obtain reproducible result and efficiently identify specific mRNAs.

Methodology : Twenty tissue sample biopsies of gastric mucosa of the antrum were collected from peptic diathetic patients at Endoscopy unit. Total RNAs were extracted by using RNA extraction kit (RNeasy Mini Kit, Qiagen). The DDRT-PCR analysis was performed by a 2-step method which were reverse transcription and polymerase chain reactions (RNAimage Kit 1, GenHunter). Six percent denaturing Polyacrylamide Gel Electrophoresis (PAGE) was carried out in order to obtain the size of separation of cDNA fragments and visualized by silver staining. Once differentially expressed mRNAs were identified, the corresponding cDNAs were eluted from the band of the gel and reamplified. The sequence of cDNAs were determined using an ABI Prism DNA Sequencer. The sequences were searched for its homology using GenBank database provide by National Institutes of Health (NIH, USA).

Results : Two differentially expressed gene were identified, namely, ubiquinol-cytochrome c reductase complex (Complex III) gene and ribosomal protein L27 a gene in gastritis tissue compared to normal gastric tissue. The expressed genes can be analyzed to determine their involvement in the pathogenesis of peptic diathesis.

Conclusions : The determination of these genes will be used to study whether similar genetic derangement occur in gastric cancers in the future. This knowledge will enhance the understanding of carcinogenesis of chronic inflammatory lesions.

Assoc. Prof. Dr. Abdul Hamid Mat Sain : (Supervisor)
Prof. Dr. Mohd. Nizam Isa : (Co-Supervisor)

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LEVELS OF ENDOTHELIN-1, NITRIC OXIDE AND NITRIC OXIDE SYNTHASE ACTIVITY IN FETOPLACENTAL TISSUES FROM WOMEN WITH PRE-ECLAMPSIA

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M.Sc Thesis

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Introduction : The pathogenesis for pre-eclampsia remains incompletely understood but overwhelming evidence points to the presence of a placental abnormality contributing to placental insufficiency in pre-eclampsia. An imbalance of vasomotor factors in the placenta of women with pre-eclampsia is hypothesised.

Objectives : The aim of the study was to ascertain if there was any difference in the levels of endothelin-1 (ET-1), nitric oxide (NO) and nitric oxide synthase (NOS) activity between fetoplacental tissues from normotensive pregnant women (NTPW) and women with pre-eclampsia (PE). In addition, the genetic expression of ET-1 in these tissues was also examined to see if ET-1 was expressed in all these tissues.

Methodology : Supernatants of homogenates from fresh, vaginally delivered amnion, chorion, and placental cotyledon from 12

normotensive and 12 pre-eclamptic women were measured for ET-1, NO and NOS. ET-1 levels were measured using radioimmunoassay (RIA) whereas NO and NOS were measured using the Griess reaction technique. For the detection of ET-1 gene expression, RNA isolation and reverse transcriptase-polymerase chain reaction (RT-PCR) were carried out.

Results : There was no significant difference in the ET-1 levels in the amnion between the two. However, mean ET-1 levels in the chorion and placental cotyledon were significantly higher in placenta from women with PE when compared to its levels in similar tissues from NTPW ($p < 0.05$). When the women with PE were divided into those women with early onset PE (≥ 34 weeks) and those with late onset PE (< 34 weeks), it was found that levels of ET-1 in the placental tissues from women with early onset PE (< 34 weeks) were significantly higher than those in tissues from women with late onset PE (≥ 34 weeks) ($p < 0.05$). There was a significant correlation between ET-1 levels in the chorion and placental cotyledon of women with PE ($p < 0.05$) but no significant correlation was evident between ET-1 levels in the amnion and the chorion or between amnion and placental cotyledon in either of the groups. ET-1 gene expression was only evident in the placental cotyledon, but not in the amnion and chorion in either of the groups. There was no significant difference in the levels of NO or in the activity of NOS between the amnion, chorion and placental cotyledon from NTPW or PE or between corresponding tissues from both the groups. There was also no significant correlation between the levels of ET-1 and NO in the placental cotyledon in either of the groups. The NO:ET-1 ratio was slightly lower in placental cotyledon from women with PE.

Conclusions : Our observations appear to suggest that ET-1 is significantly elevated in the chorion and placental tissues from women with pre-eclampsia when compared to similar tissues from normotensive women. The principle site of ET-1 synthesis is the placenta. In addition, ET-1 is significantly higher in the placenta of women with early-onset pre-eclampsia, suggesting of a heterogeneous pathogenesis of pre-eclampsia. The absence of any significant difference in NO or NOS activity between tissues from both the groups, and a slightly lower NO:ET-1 ratio in tissues from women with PE suggest preponderance of vasoconstrictor activity in the intra-placental milieu of women with PE. This may, to an extent, be responsible for the hypothesized placental insufficiency in PE.

Prof. Harbindar Jeet Singh : (Supervisor)
Prof. Dr. Nizam Isa : (Co-Supervisor)

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UTILIZATION OF NEEDS ASSESSMENT TOWARDS PLANNING AND IMPLEMENTATION OF PROFESSIONAL DEVELOPMENT PROGRAMMES FOR STAFF NURSES IN THE QUEEN ELIZABETH HOSPITAL, KOTA KINABALU, SABAH

Bella Puvok
M.Sc Thesis

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Introduction : The Queen Elizabeth Hospital, Kota Kinabalu, Sabah, has programmes organized in its operating system for its nurses, which are believed to develop their knowledge and competence. Unfortunately, in most instances those programmes made available did not match with the nurses' actual needs. Often, the nursing division designed the programmes based on assumed or perceived needs. Nursing educational programmes were implemented mainly to fulfill its set criteria for the yearly staff performance appraisal. The existing continuous professional development unit in this hospital functions as

a coordinating unit for all the educational activities of the hospital staffs and had so far not carried out a survey that could provide accurate information for an effective professional development programme.

Objectives : This study was conducted to identify the actual development needs of the staff nurses in the Queen Elizabeth Hospital, Kota Kinabalu, Sabah, and to utilize needs assessment in shaping their development programmes.

Methods : The process of the study was divided into 3 phases consist of collection us wellas analysing data, implementation of planned professional development workshop and carrying out a post-workshop assessment and analysing of collected data ending with report writing.

Results : Out of the 200 randomly sampled subjects 192 or 96% participated in the study. The survey responses indicated the benefit of needs assessment as reflected in phase 1 findings. One of the glaring findings was on the needs of a majority of respondents to learn about use and care of an ophthalmoscope / aural scope which professional development providers might least consider. In section II, seven items out of 37, care of patients on artificial ventilator was the top choice. This finding indeed reflected on the unique situation in Queen Elizabeth Hospital where patients on life support are often seen in regular wards. Section III showed five out of 32 items rated by respondents as needing refresher course, with "interpretation of cardiogram" topping the list. Among the 16 items found in section IV, 6 were rated as needing refresher course with care and use of the manual resuscitation bag as the majority choice. In section V, out of its 9 items 6 were rated as needing refresher course. Items in section V, out of the 6 items ranked as needing refresher course the most popular item was counseling / communication skills. A one-day professional development workshop was held on 27th July 2004. All the 50 selected participants attended the day's workshop. The post-workshop study showed a remarkable positive learning outcome especially on topics that required less hands-on activities. There was a hundred percent achievement in knowledge, and ninety-eight percent in competence on the topic 'Calculation of drugs and intravenous infusion'. The least achieved was on the topic 'Interpretation of an electrocardiogram'. This activity requires learning both theory and practical aspects and required regular practice and familiarity over time.

Datin Dr. Rahimah Mohd. Said : (Supervisor)
Dr. Heric Corray : (Co-Supervisor)

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DEVELOPMENT OF DELTA AMINO LEVULINIC ACID AUXOTROPHIC OF VIBRIO CHOLERAEE O1 EL TOR OGAWA

Nur Haslindawaty bte Abd. Rashid
M.Sc Thesis

Introduction : Cholera is an important diarrheal disease in developing countries. WHO estimates that cholera caused 111,575 cases with 1,894 deaths in the year 2003 worldwide. To overcome that problem, a number of cholera vaccine candidates have been developed by mutation or deletion of various genes such as *ΔthyA* and *Δgln*. However, these auxotrophic strains were leaky and able to grow in the small intestine of experimental animal's *in-vivo*.

Objectives : This study done to develop an auxotrophic vaccine strains by mutating the housekeeping gene, *hemA* gene in *V. cholerae*.

Methodology : The *hemA* gene codes for glutamyl tRNA reductase. The *hemA* gene plays a major rate-limiting step in delta aminolevulinic acid (ALA). The *hemA* gene was PCR amplified from *V. cholerae* O1 El Tor and cloned into pAROISO vector at *£coRI* site. To mutate the *hemA* gene, a kanamycin cassette was inserted at the *BstXI* site. *Δ^mA-kan* was first subcloned into conjugative suicide vector pWM91 which was then, conjugatively transferred into *V. cholerae* O1 El Tor and the mutant obtained was designated as VCUSM3. hi order to

remove the kanamycin cassette, the *hemA* gene was inserted with GFP gene flanking with *SmI* site and subcloned onto pWM91. GFP gene was then excised and left a +1 frame shift mutation in *hemA* gene (*ΔhemA*/M*). *ΔhemA*/M* was conjugatively transferred to VCUSM3 and the mutant obtained was designated as VCUSM4. ALA auxotrophy of VCUSM3 and VCUSM4 were confirmed by their growth on ALA supplemented medium. The *hemA* mutants were confirmed by PCR using *hemA* specific primers and by DNA sequencing.

Results : Thus in this study ALA auxotrophs of *V. cholerae* O1 El Tor were created by mutating the *hemA* gene.

Dr. Manickam Ravichandran : (Supervisor)
Prof. Dr. Zainul Fadziruddin Zainuddin : (Co-Supervisor)