

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 DESFLURANE AND SEVOFLURANE IN RECOVERY TIME AND RECOVERY CHARACTERISTICS ON PATIENTS FOR ELECTIVE ORTHOPAEDIC PROCEDURE

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Introduction : The safety of anaesthetic recovery is closely related to the *speed* of which the patient reaches a state of stable circulation, respiration and well maintained reflexes. Apart from the risk of surgical complications, the risk of residual anaesthetic effects, are the reason for keeping patients in a highly staffed, and high surveillance recovery unit. With the new rapidly eliminated inhalational anaesthetic agent, such as desflurane, having low blood gas solubility coefficient (0.42), it is supposed to offer a rapid recovery. The so-called fast-track concept means that the patient is so well recovered when he leaves the operating theatre that the recovery unit may be by-passed without any risk for the patient.

Objectives : The objectives of the study were to compare the effect of desflurane versus sevoflurane as inhalational agent for maintenance, on recovery time and side effects. A randomized single blinded prospective study was conducted in Hospital Universiti Sains Malaysia from June 2004 to June 2005 involving a total of 60 ASA I patients planned for elective orthopedic procedures with duration of surgery less than 2 hours. The patients were allocated into 2 equally numbered groups, desflurane (n=30) and sevoflurane (n=30).

Patients and Methods : All patients were induced with intravenous fentanyl, propofol and atracurium. Intravenously, either desflurane 6% or sevoflurane 2% (which are equivalent to 1MAC of both agents in 100% oxygen) was used together with 30% oxygen and 70% nitrous oxide. Atracurium infusion was used as a muscle relaxant and fentanyl was given for analgesia. Hemodynamic parameters (blood pressure and heart rate) were recorded on arrival, pre-intubation, post-intubation and every 10 minutes until the end of the surgery. Bispectral index scale (BIS) was used to monitor anaesthetic depth. During emergence, stimulation of patients was limited to verbal encouragement to open eyes with a tap on Ac shoulder at 10 seconds interval. Time was recorded from discontinuation of anaesthetic until patients opened their eyes and obeyed simple commands. The changes in BIS values with time were recorded as the inhalational agent was discontinued. At the same time, patients were observed for any complications during emergence and at Ac recovery room.

Results : From this study, there was significant difference between desflurane and sevoflurane in terms of recovery time, which included time to open eyes (7.21 ± 1.82 minutes, for desflurane versus 12.55 ± 2.70 minutes, for sevoflurane with $p < 0.001$) and time to obey command (8.33 ± 1.77 minutes, for desflurane versus 13.52 ± 2.65 for sevoflurane with $p < 0.001$), with the duration of operation within 2 hours. The changes in BIS values with time showed significant difference between the groups, which was faster with desflurane groups. However,

there was no significant difference in term of hemodynamic parameters between the groups. There were 5 (16.7%) incidence of complications during emergence/recovery in patients who received sevoflurane. However it was not statistically significant.

Conclusions : In summary, this study showed that desflurane has a faster recovery time with similar hemodynamic and side effects as compared to sevoflurane.

Assoc. Prof. Dr. Nik Abdullah Nik Mohamad : Supervisor
Dr. Mahamorowi Omar : Co-Supervisor

A COMPARATIVE STUDY OF DEXMEDETOMIDINE AND PROPOFOL FOR SEDATION IN CARDIOTHORACIC INTENSIVE CARE UNIT

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Introduction : The intensive care unit (ICU) is an uncomfortable and often frightening environment for patients. Many new sedative agents are being developed to fulfill the criteria of an "ideal" sedative agent.

Objectives : The aim of this study was to compare the efficacy of a new sedative agent, dexmedetomidine to current sedative agent used, propofol in the provision of sedation and analgesia and their haemodynamic and respiratory effects in post open heart surgical patients. We also aimed to justify the cost-effectiveness of these sedative agents.

Patients and Methods : A prospective, randomized single-blinded trial was conducted on post open heart surgery patients whom were being mechanically ventilated in the cardiothoracic intensive care unit (CICU) of Hospital Universiti Sains Malaysia (HUSM) between January 2003 and July 2005. Thirty two patients were randomized to receive short-term sedation with either dexmedetomidine (n=16) or propofol (n=16). The infusion rate was titrated to achieve bispectral index of 65 to 85. Analgesic requirement, haemodynamic and respiratory parameters, and extubation time were measured and compared. Mean rate of infusion to achieve adequate sedation were used to justify the cost-effectiveness of these two agents.

Results : No differences in the demographic characteristic, use of intraoperative analgesia, type of operations, and duration of sedation were observed between the two groups. Patients sedated with dexmedetomidine required significantly lower dose of morphine compared to propofol [mean (sd): 12.80 (2.61) versus 15.86 (1.87) pg/kg/min, $p=0.00$]. Mean heart rate was also significantly lower in dexmedetomidine group compared to propofol group [mean (CI): 74.48 (70.38,78.59) versus 83.85 (79.61,88.09) per minutes, $p=00$]. However there were no significant differences in the mean level of bispectral index score, mean systolic and diastolic blood pressure, PF ratio, PCO₂ level, serum lactate, pH and extubation time between the two groups.

Cost involved in the mean rate of infusion of dexmedetomidine was slightly higher compared to propofol (RM 9.57 versus RM8.94).

Conclusions : We concluded that dexmedetomidine is comparable to propofol in the provision of sedation, and its effect on haemodynamic and respiratory parameters. However it has added advantages in the provision of analgesia, and caused a significant reduction in heart rate. Significant reduction in heart rate is beneficial in these patients by reducing myocardial oxygen demand, and hence subsequent ischaemia and infarction. However, further larger studies are needed to evaluate the effect of dexmedetomidine on perioperative cardiac morbidity and mortality.

Assoc. Prof. Dr. Nik Abdullah Nik Mohamad : Supervisor
Dr. Saedah Bt Ali : Co-Supervisor

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A COMPARISON FOR EASE OF INSERTION AND ADEQUACY OF VENTILATION BETWEEN LARYNGEAL TUBE SUCTIONING (LTS) AND AIRWAY MANAGEMENT DEVICE (AMD)

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Objectives : The purpose of the study is to assess whether the recently introduced modified version of the airway management device (AMD) is easy, reliable, and safe as claims by the manufacturer. We compared the use of the airway management device (AMD) with the laryngeal tube suctioning (LTS) in spontaneously ventilating adult patient undergoing general anaesthesia. Ease of insertion, the effectiveness of ventilation and incidence of airway complication when using the tube for airway maintenance were evaluated between the two groups.

Materials & Methods : A randomized single blinded prospective study was conducted involving a total of 80 patients premedicated, ASA I or II patients, aged 18 to 65 years and were divided into 2 groups either LTS or AMD as for airway management during elective surgery. After a standardized induction of anaesthesia with intravenous fentanyl 1.5 mcg.kg⁻¹ and intravenous propofol 2 mg.kg⁻¹, a size 3 or 4 LTS or AMD was inserted and the patients breathed spontaneously throughout the surgery with no muscle relaxant given. Anaesthesia was maintained with nitrous oxide, oxygen and isoflurane. The airway device was removed at the end of surgery with the patients fully awake. The ease of insertion (easy: require one attempt; difficult: require 2 or 3 attempts; or failed), the rate of successful insertion and the incidence of airway trauma were recorded. Episodes of airway manipulations and desaturation intraoperatively were also recorded.

Results : We were able to achieve a clear airway in 36 patients (90.0%) in the LTS group and in 38 patients (95%) in the AMD group. In the LTS group, the LTS was considered easy to insert in 25 patients, difficult in 11 patients, and it was easy in 33 patients, difficult in 5 patients in the AMD group. The ease of insertion and success rates of insertion between the two groups were not significantly different (p=0.156 and 0.338 respectively). There was no significant difference in the incidence and severity of the postoperative airway complications between the two groups. Although, the incidence of airway manipulation and desaturation were higher in AMD compared to the LTS but it is not likely to be clinically relevant in this study.

Conclusions : We conclude that LTS and AMD performed equally well in the ease of insertion and atraumatic to the airway.

Assoc. Prof. Dr. Nik Abdullah Nik Mohamad : Supervisor

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THE EFFECT OF EPHEDRINE PROPHYLAXIS IN TWO DIFFERENT DOSES ON THE HAEMODYNAMIC RESPONSE TO INTRAVENOUS PROPOFOL

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Introduction : Propofol anaesthesia is commonly used because of the ease and reliability of its use together with its short duration of action and minimal hangover effect and good in daycare surgery. It can however cause deleterious effect of hypotension and bradycardia because of decrease in systemic vascular resistance and cardiac output caused by a combination of venous and arterial vasodilatation, impaired baroreceptor and sympathetic response and depression of myocardial contractility. Many studies have been done using sympathomimetic drug such as ephedrine, metaraminol, phenylephrine, dopamine and dobutamine to counteract the hypotensive effect of propofol. Ephedrine is used in this study because it has been shown to attenuate the hypotensive effect of propofol when given as prophylaxis. Ephedrine causes less vasoconstriction of the arterial and venous system (compared to other sympathomimetic agents eg. phenylephrine, metaraminol), increase in heart rate and cardiac output due to direct and indirect action to adrenergic receptor. As both ephedrine and propofol have rapid onset and short duration of action, we formulated a study to evaluate the effect of ephedrine prophylaxis at different dosage (0.3mg/kg and 0.4mg/kg) to attenuate the haemodynamic response to propofol induction in adults.

Objectives : The objectives of this double-blinded, randomized study were to compare the haemodynamic changes (Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Pressure, and Heart Rate) in adult patients induced with propofol with two different doses of ephedrine (0.3mg/kg and 0.4mg/kg) given 1 minute before induction for patients undergoing evacuation of products of conception (ERPOC) under general anaesthesia.

Patients and Methods : 72 adults female patients, ASA physical status I, undergoing evacuation of products of conception under anaesthesia were assigned randomly in a double blind study and they were divided into two groups to receive prophylactic ephedrine 0.3mg/kg (Group A) or 0.4mg/kg (Group B) before induction with propofol. All patients were induced with fentanyl 1 µg/kg followed by propofol 2mg/kg. Patient's breath a mixture of 60% nitrous oxide in oxygen, and anaesthesia was maintained using transparent facemask in all patients for 5-10 min after induction of anaesthesia. During the study period anaesthesia were maintained with increments of propofol 0.5 mg/kg given whenever there were signs of insufficient anaesthesia. Selected parameters like systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) heart rate (HR), were recorded prior to injection of study drugs as baseline data (TO), and at every one minute until 5 minutes post induction (as T1, T2, T3, T4, T5). Hypotension and bradycardia, if any was recorded, rescue drug ephedrine 0.1 mg/kg or atropine 0.02mg/kg was given as required.

Results : Ephedrine in a dose of 0.3mg/kg (Group A) or 0.4mg/kg (Group B) given intravenously shows a minimal rise in blood pressure (SBP, DBP, MAP) (5%) after 1 minute of induction with fentanyl and propofol, but then there was a gradual decrease in SBP, DBP, MAP until 5 minutes after induction. There was a decrease in HR from the baseline until 5 minutes of induction. The percentage of drop in HR from the baseline (TO) to T5 was 13.3%. The percentage drop at the end of 5 minutes of SBP was (10.9%), DBP was (23.4%), MAP was (18.9%). from baseline data (TO). It was noted that there was no significant difference in attenuations of SBP, DBP, MAP and HR in comparing both doses of ephedrine 0.3mg/kg and 0.4mg/kg in Group A and Group B.

Conclusion : Ephedrine given at the dose of 0.3mg/kg or 0.4mg/kg one minute before induction causes transient rise in blood pressure (SBP, DBP, MAP) at one minute and thereafter there was a decrease in blood pressure till five minutes and values were comparable and they were not statistically significant ($P>0.05$). There was a decrease in heart rate in both groups from induction until five minutes and this value was also comparable and they were not statistically significant ($P>0.05$). There is attenuation of hypotension (SBP, DBP, MAP) with the use of ephedrine at 0.3mg/kg or 0.4mg/kg body weight in response to propofol and fentanyl induction in adult.

Dr. Gnandev Phutane : Supervisor
Assoc. Prof. Dr. Nik Abdullah Nik Mohamad : Co Supervisor

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A COMPARISON OF THE EFFECTIVENESS OF INFRACLAVICULAR AND SUPRACLAVICULAR APPROACHES FOR BRACHIAL PLEXUS BLOCK USING 0.5% ROPIVACAINE

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Objectives : To search for an effective upper extremity block technique which could provide higher rates of successful blockade.

Patients and Methods : A one year study was carried out on eighty patients scheduled for upper limb surgery in Hospital Universiti Sains Malaysia where they were randomly allocated into two groups to receive brachial plexus block using 0.5% ropivacaine either via supraclavicular plumb-bob method or vertical infraclavicular block. The unique of these two techniques is the vertical insertion of the stimulating needle perpendicular to the operation table. The performance time was clocked and, the sensory and motor blocks were assessed every 5 minutes till a complete block established, defined as the present of analgesia at the operation site.

Results : From the analysed data, we concluded that the onset of complete sensory block and the numbers of successful block were not significant between supraclavicular plumb-bob method and vertical infraclavicular block with $p > 0.05$, but the blockade performance via supraclavicular plumb-bob method is significantly faster with the $p < 0.001$.

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

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PATIENT CONTROLLED EPIDURAL ANALGESIA VERSUS CONTINUOUS EPIDURAL ANALGESIA FOR POST OPERATIVE PAIN MANAGEMENT AFTER MAJOR GYNAECOLOGICAL SURGERY

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Introduction : Patient-controlled epidural analgesia (PCEA) has proven to be a safe and satisfactory method to provide labour analgesia and post-operative analgesia. However research regarding efficacy and

safety of this technique is still limited. The analgesic regime also varies and still unsure which one is the best choice.

Objectives : The goal of this study was to find out to what extent using PCEA could reduce the amount of local anaesthetics and opioids for postoperative pain management after major gynaecological surgery in comparison to continuous epidural infusion (CEI). Also we wished to compare the efficacy and safety of PCEA and CEI for management of pain after major gynaecological surgery

Patients and Methods : 30 patients were allocated to two groups in this randomized, double-blind study, given 15 patients in each group of PCEA and CEI. The PCEA group could demand a bolus of 4 ml of 0.1% bupivacaine plus fentanyl 2 µg/ml solution, with lockout interval of 10 minutes and background infusion of 2 ml per hour continuously. While the CEI group received 7 ml per hour of the same solution and could also demand a bolus of only 0.5 ml of the solution with the same lockout interval. All patients could demand a rescue drug i.e intramuscular pethidine. The patients were interviewed at the recovery room at 0 hour and subsequent 6 hour, 12 hour and 24 hour after the start of PCEA or CEI. The total analgesic consumption, the intensity of pain at rest and on movement, spread of sensory block, motor block and side effects were recorded.

Results : Thirty patients completed the study. The bupivacaine and fentanyl consumption during 24 h was smaller in the PCEA group, [mean±SD 103.7±30.7] as compared to [182.5± 17.6; $P < 0.001$] in the CEI group. The need for rescue pethidine was similar in both groups. There were no significant differences between the PCEA and EPI groups regarding the pain score and the incidence of side effects.

Conclusion : It is clear in study that PCEA could reduce 0.1% bupivacaine plus fentanyl 2µg/ml solution requirement compared with CEI without affecting the quality of post-operative analgesia for major gynaecological surgery

Dr. Nizar Abdul Jalil : Supervisor
Assoc. Prof. Dr. Nik Abdullah Nik Mohamad : Co-Supervisor

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A COMPARISON BETWEEN FENTANYL AND ESMOLOL IN PREVENTING INCREASES IN INTRACRANIAL PRESSURE DURING ENDOTRACHEAL SUCTION IN SEVERE HEAD INJURY PATIENT

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Introduction : Preventing increases in intracranial pressure while maintaining adequate cerebral perfusion is a primary goal in the treatment of adults with a severe head injury. Routine nursing interventions can trigger reactive intracranial hypertension. For example, endotracheal suctioning causes a progressive increase in intracranial pressure with each insertion of the suctioning catheter. In current practice fentanyl, a rapid onset opioid was given before suctioning to blunt responses to noxious stimuli. Esmolol, a rapid-onset and short-acting selective beta₁-adrenergic receptor antagonist is utilized to attenuate the cardiovascular response to laryngoscopy and as an adjunct to controlled circulatory techniques.

Objectives : The goals of this study were to observe the effect of fentanyl and esmolol on the changes in intracranial pressure, cerebral perfusion pressure, mean arterial pressure and heart rate responses during endotracheal suctioning in adults with severe head injuries and to compare the effect of fentanyl and esmolol in preventing increase in intracranial pressure during endotracheal suction.

Methods : Sixty two patients who are admitted to neurointensive

care unit with Glasgow Coma Scale (GCS) of 8 and less, with intracranial pressure monitoring in place and mechanically ventilated. The patients were then randomly received either esmolol (1mg/kg) or fentanyl (1mcg/kg) before endotracheal suction. Arterial blood pressure (ABP), mean arterial pressure (MAP), heart rate (HR), intracranial pressure (ICP), cerebral perfusion pressure (CPP), arterial blood gases (ABG) and bispectral index (BIS) were recorded at baseline, immediately after and 5 minutes, 10 minutes and 15 minutes after endotracheal suctioning.

Results : There were no significant difference in ICP and BIS in patients who are given either fentanyl or esmolol in preventing a raise in intracranial pressure during endotracheal suctioning. A significant difference was seen in mean arterial pressure, cerebral perfusion pressure and heart rate.

Conclusion : We conclude that in patients with severe head injury who are well sedated and had a normal intracranial pressure, the used of fentanyl or esmolol in preventing a raise in intracranial pressure during endotracheal suction has no advantage. However, esmolol (1 mg/kg) is better than fentanyl (1mcg/kg) in control mean arterial pressure and cerebral perfusion pressure during endotracheal suctioning.

Assoc. Prof. Dr. Nik Abdullah Nik Mohamad : Supervisor
Prof. Dr. Jafri Malin Abdullah : Co-Supervisor

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THE PREVALENCE AND ASSOCIATED FACTORS FOR CARIES EXPERIENCE AMONG 16-YEAR-OLD SCHOOL CHILDREN IN TUMPAT DISTRICT, KELANTAN

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Introduction : Dental caries is a multifactorial disease and is a major problem among children and adolescents in many parts of the world. It has a considerable impact on individual's health leading to low self-esteem, poor eating ability and nutrition and it causes a lot of pain and suffering.

Objective : The objectives of this study were to determine the prevalence of dental caries, the differences in knowledge, attitude and practice (KAP) level among caries experience group as well as to determine the associated factors for caries and high caries experience among 16-year-old school children in Tumpat district.

Methodology : This two-stage study was conducted from July, 2004 to February, 2005. The first part was a cross-sectional study to determine the prevalence of caries. In this study, 1087 16-year-old school children from nine Sekolah Menengah Kebangsaan in Tumpat district were examined intraorally following the WHO criteria using DMF index. Based on DMFS score, subjects were categorized into three groups, namely, caries free group (DMFS=0), mild caries group (DMFS 1-7) and high caries group (DMFS 8). The second stage of this study was a case-control study. The caries groups formed the cases and the caries free group formed the control. Simple random sampling was used to obtain 163 subjects from each group. 156 subjects were in the caries free group, 157 subjects were in the mild caries group and 160 of the subjects were in the high caries group. Self-administered questionnaire were used to assess the KAP (for subjects) and to obtain data on sociodemographic background, deciduous teeth status, birth order and birth weight (for parents). Salivary unstimulated and stimulated flow rate, buffering capacity, pH and viscosity were tested. Gingival inflammation was assessed using GI. Subsample of subjects from each group was done for testing of salivary mutans streptococci and

lactobacilli level using the same sampling method. There were 32 subjects in caries free group, 33 subjects in the mild caries and 33 in the high caries group. Analyses were conducted using SPSS version 11 and Stata version 7.

Results : The prevalence of caries among 16 year old school children in Tumpat was 82.1% (95% CI: 79.8; 84.4). Attitude was the only factor found to be statistically significant different between caries free and high caries group (p=0.001) in the KAP study. The factors associated with caries and high caries experience determined using multiple ordinal logistic regression analysis were found to be educational level of parents (OR=1.55, 95% CI: 1.06; 2.28), deciduous teeth status (OR=2.84, 95% CI: 1.92; 4.20), gingival inflammation (OR=3.49, 95% CI: 2.36; 5.16), saliva viscosity (OR=2.12, 95% CI: 1.36 ; 3.29), saliva pH (OR=1.55, 95% CI: 1.07; 2.58), saliva buffering capacity (OR=3.54, 95% CI: 2.37; 5.29), salivary mutans streptococci level (OR=8.14, 95% CI: 2.78; 23.9), salivary lactobacilli level (OR=4.18, 95% CI: 1.31; 13.32), attitude level (OR=0.62, 95% CI: 0.43; 0.91) and dietary practice (OR=0.97, 95% CI: 0.95; 0.99).

Conclusion : The prevalence of dental caries was high among the study group in Tumpat. Low educational level of parents, unhealthy deciduous teeth and salivary factors were important factors determining the caries experience. Positive dental attitude and low frequency of sugar intake had protective effect against caries experience. The knowledge on factors associated with caries experience is very useful in planning effective preventive dental program especially for group experiencing high caries.

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

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TOOTH WEAR : PREVALENCE AND ASSOCIATED FACTORS AMONGST 16-YEAR-OLD SCHOOL CHILDREN IN KOTA BHARU, KELANTAN

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Introduction : Tooth wear describes the non-carious loss of tooth tissue that results from the interaction of three processes, which occur singly or in combination that are attrition, erosion and abrasion. The amount of wear that accelerates the physiological tooth wear called pathological tooth wear.

Objective : The study was designed to determine the prevalence and mean scores of raw tooth wear (RTW) and pathological tooth wear (PTW). compare Knowledge, Attitude and Practice (KAP) between cases and controls and determine associated factors of PTW amongst 16-year-old school children in Kota Bharu, Kelantan.

Patients and Methods : This was a two-stage study. The first stage was a cross-sectional study involving 688 children who were selected using systematic random sampling. All children were examined intraorally. The Smith and Knight Tooth Wear Index was used for charting tooth wear and WHO criteria for dental caries. Data were analyzed using a simplified Microsoft Excel Programme based on the score to quantify PTW. The second stage adopted a case-control design, involving 116 cases and 460 controls that were resampled from the first stage using simple random sampling in the ratio of 1:4. Cases were children with PTW having at least one tooth surface scoring 1 for PTW (PTW score 1). Controls were children with no PTW indicated by zero scores on all tooth surfaces (PTW score=0). Validated self-administered questionnaire provided family socio-demographic profile, general information, KAP and associated variables for tooth wears. Saliva analysis utilized the standard method recommended by 'GC'

Asia Dental.

Results : The prevalence of RTW and PTW was 100% and 20.1% (95% CI: 17.1-23.2) respectively. The proportion of children with exposed dentine in RTW was 23.5%. The highest mean score of RTW was in the upper incisal quadrant with mean score of 0.95 and the highest mean score of PTW was in the lower incisal quadrant with mean score of 0.16. There was no significant difference in KAP between cases and controls. Multivariable analysis showed nine significant variables associated with PTW which were male (OR=2.19, 95% CI: 1.35-3.55), monthly household income, RM0-500, (OR=5.11, 95% CI: 1.01-25.79). '100 Plus' drink, 4x/week, (OR=2.89, 95% CI: 1.23-6.81), duration of intake of orange juices (OR=1.17, 95% CI: 1.05-1.28), hydration (normal flow rate of saliva, OR=2.13, 95% CI: 1.30-3.52 and low flow rate of saliva, OR=9.20, 95% CI: 2.76-30.69), viscosity (frothy bubbly saliva, OR=2.23, 95% CI: 1.33-3.74 and sticky frothy saliva, OR=5.15, 95% CI: 1.99-13.31) and pH of saliva (pH 5.0-6.9, OR=0.49, 95% CI: 0.25-0.96), caries experience (DMFS 1-7, OR=1.98, 95% CI: 1.15-3.41 and DMFS 8, OR=2.88, 95% CI: 1.49-5.57) and swimming, >3x/week, (OR=3.17, 95% CI: 1.24-8.13).

Conclusion : In conclusion, all children had some degree of wear with high proportion already affected by PTW. The lower anterior quadrant was mostly affected by PTW. The level of awareness regarding tooth wear amongst some children was still low. Associated modifiable factors were SES, lifestyles, caries and diet. Oral health promotion should emphasize on this information. The erosive potential of some foods and drinks require further investigation.

Dr. Noorliza Mastura Ismail : Supervisor
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SOLVENT EXPOSURE AND RESPIRATORY HEALTH STATUS AMONG WORKERS IN A TIRE RETREADING FACTORY

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Introduction : Rubber industry is known to have abundant chemicals, mainly solvents, in their working environment. Although the effects of these substances on respiratory health are well known, there is limited local information. This study was aimed to explore the respiratory health status among workers, solvent exposure in the workplace, level of KAP, and associated factors, which potentially impair the lung function among workers in a tire retreading factory.

Methods : In this cross sectional study, questionnaires were distributed to available 95 male production workers to obtain sociodemography, personal and work related information, respiratory symptoms and KAP. Physical examination and lung function test were conducted. Area samplings were done for toluene, benzene and xylene, followed by personal air sampling and urine sampling for toluene. Toluene was selected to be checked because toluene level was highest in area sampling.

Result : All participants were Malay with mean (SD) age of 36.6 (6.29) years and median (IQR) working duration was 133.8 (63.53) months. Chest tightness (32.6%) was the commonest symptom followed by phlegm production (27.4%), morning cough (10.5%) and shortness of breath (10.5%). Physical examination revealed normal findings whereas mean (SD) of FVC, FEV₁, FEV₁/FVC ratio and FEF_{25-75%} were 3.6 (0.56) litre, 2.9 (0.45) litre, 80.4 (7.82) percents and 3.5 (1.52) litre/second, respectively. Known associated factors for lung function such as age, height and weight, and occupational factors such as exposure to dust and work shift were noted to be significantly

associated with at least one parameter of lung functions. In KAP assessment, prevalence for both knowledge level below 80 percent score were 45.3% and 21.1%, whereas prevalence for attitude level below 70 percent score was 25.3% and prevalence for practice level below 80% score was 89.5%. In environmental sampling, toluene level was ranged from undetectable to 300 ppm, level of personal sampling ranged from undetectable to 5.5 mg/m³ and range of urine hippuric level was from 0.02 to 3.63 with median (IQR) of 0.26 (0.40) g/g creatinine.

Conclusion : The study demonstrated an evidence of toluene exposure and mild effect on respiratory health among workers. It also revealed the needs for intervention in order to improve KAP in this workplace.

Dr. Lin Naing @ Mohd. Ayub Sadiq : Supervisor
Prof. Dr. Rusli Nordin : Co-Supervisor

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THE USE ETHYL CHLORIDE AS TOPICAL ANESTHETIC FOR INTRAVENOUS CANNULATION IN THE EMERGENCY DEPARTMENT

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Introduction : Intravenous cannulation is one of the procedures frequently performed in the emergency department. In the emergency department, it is usually done without the use of a local anesthetic to reduce the pain. This may be due to the fact that drugs usually used e.g. EMLA, require a time of at least 60 minutes to be effective. For the majority of cases in the emergency department intravenous cannulation has to be done immediately. Ethyl chloride is a chemical substance, which has a localizing anesthetic effect that is immediately effective. This drug has been studied for intravenous cannulation but its effectiveness and use in the emergency department setting is still not confirmed.

Objectives : The objective of this study was to study the effectiveness of this chemical substance as a local anesthetic for intravenous cannulation.

Methods : A randomized prospective study was conducted on 216 patients who had come to the emergency department and required intravenous cannulation. Patients who fulfilled the criteria for inclusion were randomized to receive either ethyl chloride or isopropyl alcohol. The pain experienced by the patient during cannulation was measured using the visual analogue scale.

Result : The results from the 216 patients requiring intravenous cannulation showed that patients randomized to ethyl chloride had significantly less pain compared to those randomized to isopropyl alcohol. The p value for pain during intravenous cannulation was less than 0.05 showing a significant difference in pain score. Mean pain score for ethyl chloride was 13.20mm ± 19.61 and for isopropyl alcohol 35.63mm ± 21.01. A difference in pain score of more than 20 mm was obtained. Out of 108 patients randomized to ethyl chloride, four had the side effect of pain on spraying ethyl chloride.

Conclusion : Ethyl chloride is an effective drug for reduction of pain during intravenous cannulation in the emergency department. Its relative inexpensiveness and easy application should make its use for intravenous cannulation in the emergency department routine.

Dr. Wan Asim Wan Adnan : Supervisor
Dato' Dr. Abu Hassan Assari Abdullah : Co-Supervisor

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PATTERN OF INJURY AND PREVENTABILITY OF HOSPITAL DEATH AMONG MOTORCYCLIST

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Objective : To examine the pattern of anatomical injury in victims of road traffic accident fatalities involving motorcyclists (rider and pillion rider) who die prior to reaching hospital and to determine the possibility of preventable death.

Patients and Methods : A retrospective review of post mortem cases at the Penang Hospital Forensic Department , of motorcyclists (rider and pillion rider) who died in motorcycle crashes between 1 January 2000 and 31 December 2001. Those cases where the victim died in the prehospital phase were examined. The Abbreviate Injury Scores and Injury Severity Scores were calculated in each case.

Result : There were 140 motor road crash fatalities identified that underwent post mortem at the Penang Hospital Forensic Department in the study period. Seventy five of these (57%) were prehospital deaths involving motorcyclists, which satisfied specified criteria. There are 92% of victims who sustained head injury of which 66.7% of them had AIS 4 to 6, 72% abdominal injury and 44% of them had AIS of 4 to 6, 94.7% of victims sustained chest injury and 42.7% of them had AIS 4 to 6, 82.7% of victims had extremities or pelvic injuries and 4% of them had AIS 4 to 6. The minimum ISS score calculated was 21 and the highest 75 with mean of 50.28 ±18.6 standard deviation. 35 (66.7%) had ISS above mean and 23 (30.7%) had ISS of 75 (unsalvageable). 32 victims (42.7%) had ISS of 5-44, 16 victims (21.3%) had ISS of 45-54, 27 victims (36%) had ISS of 55-75. Percentage of mortality is calculated using the injury severity score against age. Result showed that 27 victims (36%) had 100% mortality, 19 victims (25.3%) had 50-99% mortality, 29 victims (38.7%) had mortality less than 50%. From this, it is inferred that preventable calculated prehospital death occur in 29 victim (3 8.7%).

Conclusion : In motorcycle crash fatalities, most motorcyclists die before reaching hospital because of severe injury, with the head and abdomen the commonest regions involved. Almost one third of victims died before reaching hospital despite immediate or best treatment at the site of accident. 38.7% of victim may survive from the accident Further study need to be done in Malaysia to strengthen the result of this study.

**Dr. Nik Hisamuddin Nik Ab. Rahman : Supervisor
Dr. Mohd. Idzwan Zakaria : Co-Supervisor**

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THE ROLE OF BETA 2-ADRENERGIC RECEPTOR POLYMORPHISMS IN ACUTE EXACERBATION OF BRONCHIAL ASTHMA ON THE EMERGENCY ROOM VISITS AT HOSPITAL USM

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Introduction : The short acting beta 2-agonists have become standard bronchodilators and are the most potent bronchodilators currently available to relieve bronchoconstriction during acute, life-threatening asthmatic attacks. Nevertheless, following inhalation of

short acting 2-agonist. 60-70% of patients show variable response from slight to good while about a third fail to respond at all. Our hypothesis is that the variable response may be due to variable binding to beta 2-adrenergic receptor (2AR). Therefore, we studied the role of p2AR polymorphism and their influence on p2-agonists during asthmatic exacerbation. In this study, we focused on two of the most common p2AR polymorphisms at Codon 16 and Codon 27.

Objectives : The objective we to determine the prevalence of 2AR polymorphisms at Codon 16 and 27 in Malay patients with acute exacerbations of bronchial asthma, as well as determine the association between 2AR polymorphisms and the visits to emergency room for acute exacerbations of bronchial asthma. We also sought to find the association between 2AR polymorphisms at Codon 16 and 27 and response to short acting beta 2-agonists, as well as to ascertain the association of 2AR polymorphisms among acute exacerbations of bronchial asthma and healthy non-asthmatics.

Methodology : One hundred and thirty-two asthmatic patients presenting to Department of Emergency Medicine at HUSM for acute exacerbations of bronchial asthma fulfilling the inclusion and exclusion criteria were chosen during a study period of 15 months. Patients' vital signs were assessed and PEFr was performed before and 30 minutes after short acting beta 2 agonist nebulization treatment. Five mls of venous blood was taken for DNA extraction and PCR genotyping for B2AR polymorphisms. Demographic data were also collected. All data were available for analysis using various descriptive studies from the Statistics program for Social Studies (SPSS)® version 11.0. The demographic data was analyzed using descriptive analysis and the responses post nebulization using the non-parametric test.

Results : Of the 132 patients, at codon 16, 17 (12.9%) earned Arg-Arg16 genotype. 112 (84.8%) carried Arg-Gly16 genotype and 3 (2.3%) carried Gly-Gly16 genotype. At codon 27, 104 (78.8%) carried Gln-Gln27 genotype. 26 (19.7%) earned Gly-Glu27 genotype and 2 (1.5%) carried Glu-Glu27 genotype. There was significantly high prevalence of homozygous Gly-Gly16 genotype in asthmatic cohorts when compared to normal non-asthmatic healthy cohorts, (p=0.029). whereas at codon 27, there was no significant association found between genotype prevalence. (p=0.113). There was no significant association between p2-AR polymorphisms at both codon 16 and 27 and acute exacerbation of bronchial asthma and the number Emergency Room visits (p=0.639; p=0.533 respectively). There was also no significant association between 2-AR polymorphisms at both codon 16 and 27 and response to Salbutamol (short acting 2-agonist nebulization) (p=0.268 and p=0.825 respectively).

Conclusions : We found B2AR at codon 16 was more commonly associated with asthmatic exacerbations. Nevertheless, B2AR polymorphisms at both codons 16 and 27 poorly predicted recurrent relapses of acute exacerbations of bronchial asthma and Emergency Room visits for it. B2AR polymorphisms also poorly predicted response to inhaled salbutamol.

**Dr. Wan Asim Wan Adnan : Supervisor
Assoc. Prof. Rusli Ismail : Co-Supervisor**

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SURVIVAL AND PROGNOSTIC FACTORS OF HOSPITALIZED ACUTE MYOCARDIAL INFARCTION PATIENTS IN DISTRICT OF KOTA BHARU, KELANTAN : A RETROSPECTIVE COHORT STUDY 2000-2003

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Introduction : Acute myocardial infarction (AMI) remains a major public health problem in Malaysia despite advances in medical management and technology. Local prognostic data on AMI will provide an essential information for effective preventive measures. The objectives of the study were to determine the survival of hospitalized acute myocardial infarction patients in Kota Bharu and identify the prognostic factors that influence the risk of death.

Methodology : A retrospective cohort study was conducted involving 368 hospitalized AMI patients from the district of Kota Bharu who were admitted in two tertiary hospital; Hospital Kota Bharu and Hospital Universiti Sains Malaysia from 1st January 2000 to 31st December 2003. Additional follow up of one year after the recruitment of the subjects was done from 1st January 2004 to 31st December 2004. All patients who fulfilled the criteria were included in the study. Hospital medical records and physician clinic records were reviewed by a researcher. The required information on variables of interest and patients' survival status until 31st December 2004 was recorded into a data collection form. Telephone calls were also conducted to obtain the information on survival status of some patients who were discharged alive but loss to follow up.

Results : The overall cumulative survival for hospitalized AMI in Kota Bharu were 91.0 (95% confidence interval (CI): 87.6, 93.5), 88.8 (95% CI: 85.2, 91.7), 86.6 (95% CI: 82.6, 89.7) and 83.9 (95% CI: 79.6, 87.5) percent for 1 day, 2 days, 1 week and 1 month respectively. The long-term survival rate for 6 months, 1 year, 2 years, 3 years and 4 years after AMI were 80.7 (95% CI: 76.1, 84.6), 77.5 (95% CI: 72.6, 81.7), 76.2 (95% CI: 71.2, 80.6), 71.9 (95% CI: 66.0, 76.9) and 69.2 (95% CI: 62.7, 74.8) percent respectively. Based on Cox Proportional Hazards Regression multi variable analysis after adjusting other variables, the significant prognostic factors that influenced the risk of death in hospitalized acute myocardial infarction patients in Kota Bharu were age at diagnosis (HR=1.03, 95% CI: 1.01, 1.06), diabetes mellitus (HR=1.60, 95% CI: 1.03, 2.46), left ventricular failure (HR=2.15, 95% CI: 1.38, 3.34), thrombolytic therapy (HR=0.48, 95% CI: 0.31, 0.73) and first contact of care (HR=0.47, 95% CI: 0.24, 0.91).

Conclusion : Survival rate of hospitalized AMI patients in the district of Kota Bharu was comparable with other developed countries. All significant independent prognostic factors identified were considerably similar to other countries, except a few important factors such as gender and drugs prescribed on discharge. Interestingly, first site contact of medical care was also identified to significantly influence the risk of death of AMI in Kota Bharu.

Assoc. Prof. Dr. Abdul Aziz Al-Safi Ismail : Supervisor
Assoc. Prof. Dr. Syed Hatim Noor : Co-Supervisor
Assoc. Prof. Dr. Zurkurnai Yusof : Co-Supervisor

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FACTORS INFLUENCING DELAYED TREATMENT AMONG SMEAR POSITIVE PULMONARY TUBERCULOSIS PATIENTS

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Introduction : TB remains a great challenge to public health in Malaysia and worldwide. Delay in treatment commencement can result in significant increase morbidity, mortality and transmission. Hence this study is aimed to determine the prevalence of various delays (patient, health service, diagnosis, initiation and total delay) and to identify the factors influencing the patient delay and health service delay.

Methodology : A cross sectional study was done from October 2004

to June 2005 among 178 smear positive pulmonary TB patients in four districts in Kelantan (Kota Bharu, Tumpat, Bachok and Pasir Mas). All patients who fulfilled the inclusion and exclusion criteria and gave consent were recruited due to limited number of patients. Interviewer guided questionnaire was administered and medical record was reviewed to gather patient's information.

Results : The median and inter-quartile range of patient delay, health service delay, diagnosis delay, initiation delay and total treatment delay in days were 30.0(76.00), 7.0(14.50), 3.0(4.00), 3.0(4.00) and 64.0(90.25) respectively. Furthermore, the prevalence and 95%CI of unacceptable delays; patient delay, health service delay, diagnosis delay, initiation delay and total treatment delay were 46.6%(39.3, 53.3), 45.5%(38.2, 52.8), 48.3%(41.0,55.6), 37.6%(30.5,44.8), 61.8%(54.7,68.9) respectively. In multiple logistic regression analysis, the significant factors associated with unacceptable patient delay were age (OR: 3.88; 95%CI: 1.35, H.18;p= 0.012), distance from home to first health facilities attended (OR: 3.98; 95%CI: 1.56, 10.15;p= 0.004), attending the T/CM practitioners (OR: 10.51; 95%CI, 1.80, 55.39; ^=0.006), attending the private practitioners (OR: 0.24, 95%CI: 0.09, 0.60; p= 0.002) and stigma (OR: 4.81; 95%CI: 1.59, 14.60; ^=0.006). On the other hand, the significant factors associated with unacceptable health service delay were negative results of initial sputum smear (OR:14.48; 95%CI: 2.30, 91.34; /?=0.004), number of visits to health facilities (OR: 4.99 95%CI: 2.76, 9.03; p= 0.001) and types of first health care facilities attended (OR: 5.78; 95%CI: 1.58, 21.11;;?= 0.008)

Conclusion : This study showed that there was a substantial delay in case finding in Kelantan. Raising public awareness about symptoms of TB, curability and benefit of utilizing available governmental health facilities through health education campaign might shorten the patient delay. Health care personnel in both private and government sectors should be reminded on the important of early diagnosis and prompt treatment of TB. Traditional and complementary practitioners should be well-cooperated in contributing to Malaysian health care system by interacting with both private and governmental health sectors.

Prof. Madya Dr. Syed Hatim Noor : Supervisor
Dr. Muhammad Rusli Abdullah : Co-Supervisor

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A STUDY ON THE PREVALENCE OF CORONARY ARTERY DISEASE PATIENTS WHOM DID NOT ACHIEVE THE TARGETED LIPID LEVEL AND ITS ASSOCIATED FACTORS

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Introduction : Lupus nephritis increases the morbidity and mortality associated with systemic lupus erythematosus. Over the last 4 decades, changes in the treatment of Systemic Lupus Erythematosus (SLE), especially in lupus nephritis have greatly improved overall survival in SLE patients. With decreased morbidity and improved mortality, the gonadal dysfunction observed become a problem faced by SLE patients. There had been several studies looking at the menstrual irregularities found in SLE patients; in which the prevalence, the type and risk factors of menstrual irregularities were evaluated.

Objectives : The aim of this study was to determine the prevalence and the types of menstrual irregularities among SLE patients, and to identify factors that influence the development of their menstrual irregularities.

Methodology : The study was a cross-sectional and observational study. All SLE patients attended medical clinics at Hospital University Science of Malaysia who fulfilled our selection criteria were

interviewed using a set of questionnaires. Their blood pressure, height, weight and other clinical parameters were reviewed by the attending doctor. Blood sample was taken for evaluation, such as; hemoglobin, renal function, proteinuria, C3C4 level and ANA. Participants' records which included current and past were then reviewed by principal investigator.

Results : A total of 61 patients were evaluated. The patients' age was ranging from 16 to 53 completed years, and majority of them were aged between 21 to 30 completed years. The mean age was 33.23 (SD: 10.96). Majority were Malay ethnic group, and unemployed. Majority of them had severe SLEDAI score on initial presentation (75 percent), and majority of patients had class IV lupus nephritis (50.8 percent). Sixty-five-point-six percent of patients received combination of steroids and immunosuppressive therapy; with majority of them on cyclophosphamide (59 percent). Majority of patients who were on cyclophosphamide had standard induction of intravenous cyclophosphamide (50.8 percent), whereas 4.9 percent of patients had extended induction, and 3.3 percent of patients had oral cyclophosphamide therapy. From our study; 49.2 percent of study population have menstrual irregularities. Majority of patients who had menstrual irregularities aged between 41 to 50 years old (21.3 percent), followed by patients aged 31 to 40 years old (16.4 percent). Majority of patients with menstrual irregularities had sustained amenorrhea (60 percent); with majority of them aged 41 to 50 completed years (30 percent), followed by patients aged 31 to 40 completed years (20 percent). During active phase of SLE, 21.3 percent of patients had menstrual irregularities, and oligomenorrhea was commoner than amenorrhea (18.0 percent versus 3.3 percent). During inactive phase of SLE; 49.2 percent of patients had menstrual irregularities, and amenorrhea was commoner than oligomenorrhea (27.9 percent versus 21.3 percent). From the study, cyclophosphamide was recognized as one of the risk factors for menstrual irregularities in SLE patients, beside age. Majority of patients with menstrual irregularities were patients who had cyclophosphamide (83.3 percent); and majority of them had sustained amenorrhea (46.7 percent). Cumulative dose of cyclophosphamide influenced the prevalence of menstrual irregularities in SLE patients; with dose higher than 10 gram played a major risk. Nine patients with sustained amenorrhea had hormonal assay which confirmed diagnosis of premature menopause.

Conclusions : This study showed that SLE patients have a higher risk of developing menstrual irregularities in comparison to normal / healthy population. The risk was higher in older age group especially those aged more than 30 years old. The risk became higher once patients had cyclophosphamide therapy; especially if cumulative dose of cyclophosphamide was more than 10 gram. There were variable types of menstrual irregularities recognized in this study; with sustained amenorrhea being the commonest.

Assoc. Prof. Dr. Zainal Darus : Supervisor
Dr. Aniza Abdul Aziz : Co-Supervisor

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A STUDY ON THE PREVALENCE OF CORONARY ARTERY DISEASE PATIENTS WHOM DID NOT ACHIEVE THE TARGETED LIPID LEVEL AND ITS ASSOCIATED FACTORS

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Introduction : Aggressive lipid lowering prevents recurrent cardiac events and lowers total mortality in patients with significant hyperlipidaemia and known CAD. Despite abundant evidences that

LDL-C should be less than 2.6 mmol/L, there continues to be inadequate management of this modifiable risk factor.

Objective : This study was conducted to assess the effectiveness of the management of hyperlipidaemia in coronary artery disease patients. The prevalence of patients with CAD whom did not achieve the targeted lipid levels and its associated factors were the focus of this study.

Methods : A cross sectional study was designed and patients who presented with unstable angina, non-ST elevation myocardial infarction, ST elevation myocardial infarction and those who were found to have significant lesions on coronary angiography were included into this study. The study period was from January 2004 till December 2004. The number of study subjects were 174. The medical records were reviewed for appropriate data. Their LDL-C were recorded to see if the target of less than 2.6 mmol/L was achieved or not. If the target was not achieved, the possible associated factors were probed in the medical records.

Results : This study showed a total of 41.4% did not achieve the targeted LDL-C level of less than 2.6 mmol/L. Dietician involvement in the management of hyperlipidaemia along with lipid lowering therapy showed a significant positive impact on the outcome.

Conclusion : The treatment success in this study, is similar to or better than prior reports, however there remains a substantial room for improvement.

Dr. Tee Meng Hung : Supervisor
Assoc. Prof. Zurkurnai Yusof : Co-Supervisor

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A PILOT STUDY ON SENSITIVITY AND SPECIFICITY OF QUANTIFERON-TB GOLD TEST ON NEWLY DIAGNOSED MYOBACTERIUM TUBERCULOSIS INFECTION IN KELANTANESE POPULATION

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Introduction : Diagnosis of tuberculosis infection has not been simple, commonly diagnosis been made after reviewing several investigation results. Unfortunately delay in diagnosis and hence treatment has made tuberculosis infection not treated early. Therefore a new test with reliability and rapidity is required.

Objective : This study was carried out to compare between *Quantiferon-TB gold* test and sputum culture for the detection of active *Mycobacterium tuberculosis* infection.

Patients and Methods : Twenty four suspected active tuberculosis infected patients enrolled in this pilot cross sectional study and each patient was required to provide sputum and 5 mls of blood. The T-cells from the patient's serum were stimulated in-vitro with antigens specific for *M tuberculosis* (ESAT -6 and CFP-10). Hence, interferon gamma, (a cytokine that is released during tuberculosis infection) was detected after the in-vitro stimulation and using the *Quantiferon-TB gold* kit, the level was quantified via ELISA method. It was analyzed using a computer software provided by the Cellestis (Manufacturer of *Quantiferon-TB gold test*). Simultaneously sputum samples were obtained from the same patient and cultured for *M tuberculosis*.

Results : The results showed that when compared to sputum Acid Fast Bacilli culture, *Quantiferon-TB gold* assay is 94.7 % sensitive and 80% specific, positive and negative predictive values of 94% and 80%. While the likelihood ratios were 4.73 for positive cases and 16.7 for negative cases for M tuberculosis infection. Our study suggests that *Quantiferon-TB gold* assay is a useful diagnostic kit for diagnosis of active tuberculosis infection in our country which is endemic for *M tuberculosis* infection and in which most of the population had been

vaccinated with BCG. The sensitivity 94.7% obtained in this study is high in comparison to other study carried out in Japan, USA and Australia in which each represents 89.5%, 91.3% and 83.3% (in pulmonary TB cases). While the specificity of 80% in this study is considered low as compared to other studies, 98.1% (Japan), 97.8% (Australia) and 99.8% (USA). The increasing numbers of reported cases and delay in diagnosis due to delay in obtaining culture results are reasons for carrying out this study. Delay in diagnosis has made tuberculosis difficult to eradicate in our country.

Conclusion : This study will provide evidence on the usefulness of *Quantiferon-TB gold* assay as a rapid diagnostic tool kit in diagnosing new tuberculosis cases in our country. It will provide a useful supporting diagnostic instrument to the clinician for fast and accurate result.

Assoc. Prof. Dr. Mustafa Musa : Supervisor
Dr. Che Wan Aminudin Hashim : Co-Supervisor

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PREVALENCE AND RISK FACTORS OF ANTITUBERCULOSIS DRUG-INDUCED HEPATITIS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction : Tuberculosis is one of the major diseases worldwide, affecting about one-third of the world's population- The introduction of antituberculosis drugs decades ago has improved tremendously the outcome of those infected with tuberculosis. Among the drugs, isoniazid, rifampicin and pyrazinamide had been proven to be effective, but not without the side effects, of which hepatotoxicity is the most important. Antituberculosis drug-induced hepatitis has been reported and many risk factors had been recognized.

Objectives : This case control and observational study was conducted to determine the prevalence of antituberculosis drug-induced hepatitis in Hospital Universiti Sains Malaysia, to determine the risk factors in relation to the development of drug-induced hepatitis as well to observe the clinical course in patients with antituberculosis drug-induced hepatitis.

Method : This study examined the evidence of antituberculosis drug-induced hepatitis in patients treated for tuberculosis in Chest Clinic for a period of 30 months from January 2003 until June 2005. Eligible cases of drug-induced hepatitis were selected and compared with controls which were selected by Simple Random Sampling in terms of demographic data and risks involved such as age, gender, body mass index, hepatitis B carrier, HTV infection, sites of tuberculosis, and pretreatment liver biochemistries such as serum albumin, globulin, AST, ALT and bilirubin. The clinical course of patients of hepatitis was also examined in term of onset, severity and duration of hepatitis, as well as the presence of Jaundice. Data were evaluated by khi square and independent *t* test (univariate) and binary logistic regression analysis (multivariate).

Results : A total of 473 patients were registered during the period of the study, 46 patients were noted to have antituberculosis drug-induced hepatitis and eligible for the study. 138 patients were selected as controls. The prevalence of drug-induced hepatitis was 9.7%. Among the risk factors evaluated, the presence of HTV infection ($p=0.05$), extrapulmonary tuberculosis ($p=0.08$), lower serum albumin ($p=0.023$) and higher serum globulin ($p=0.025$) were noted to be significant at univariate analysis. On binary logistic regression analysis, the presence of HTV infection ($p=0.018$) and extrapulmonary tuberculosis ($p=0.017$) were noted to be significant risk factors. Observation of the clinical course of patients who had drug-induced tuberculosis, showed that

most of them had mild hepatitis (58.7%) and moderate hepatitis (32.6%). The onset of hepatitis mostly occurred between one to two weeks (32.6%) and two to three weeks (17.4%). The duration of hepatitis was mostly from one week (34.8%) to two weeks (32.6%). The occurrence of jaundice was 32.6 percent.

Conclusion : The prevalence of antituberculosis drug-induced hepatitis was 9.7 percent. The presence of HIV infection and extrapulmonary tuberculosis were significant risk factors for the development of hepatitis. Most of the patients who developed antituberculosis drug-induced hepatitis had mild symptoms and signs. Patients with risk factors should be monitored closely for the development of drug-induced hepatitis.

Assoc. Prof. Dr. Nazmi Mohd. Noori : Supervisor
Prof. Dr. Mustafa Embong : Co-Supervisor

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COMBINATION THERAPY FOR OPTIMUM GLYCAEMIC CONTROL : A RANDOMIZED OPEN LABEL TRIAL COMPARING ROSIGLITAZONE WITH COMBINATION SULPHONYLUREAS AND METFORMIN TABLETS IN TYPE 2 DIABETES MELLITUS IN RELATION TO PEPTIC ULCER DISEASE

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Introduction : As it is often difficult to achieve and maintain glycaemic goals, multiple drug therapy is eventually required in most patients. Combination therapy, involving an insulin secretagogue and an insulin sensitizer, can address the metabolic effect of this disease. The use of two sensitizers with different but complementary mechanisms of action may provide additional glucose control. The addition of thiazolidinedione may improve glycaemic control in patients who failed to achieve glycaemic control with a combination of sulphonylureas and metformin. There is scarce data on efficacy, safety and cost effectiveness of adding third agent to patients who failed to achieve glycaemic control on maximum combination therapy.

Objectives : To determine the efficacy, safety and cost effectiveness of adding Rosiglitazone to patients with type 2 diabetes mellitus on maximum dose of sulphonylureas and metformin who had not achieved glycaemic control

Methodology : This was a randomized, open label study. The subjects with T2DM who refused insulin therapy were randomized into treatment group and control group. The treatment group received adding a dose of rosiglitazone 4 mg once daily for 6 months while the control group was maintained on maximum dose of metformin and sulphonylureas. HbA1c, FBS, Total Cholesterol, LDL and HDL were taken at baseline and at 6 month.

Results : A total of 75 diabetic patients were included in this study. There was significant reduction in HbA1c (9.61 ± 1.37 % to 8.20 ± 1.87 % ; $p < 0.001$) and FBS (9.6 ± 3.69 mmol/L to 7.93 ± 3.46 mmol/L ; $p = 0.002$) in treatment group after 6 months of therapy. However, in control group, there was a significant increased in HbA1c (9.75 ± 1.33 % to 10.06 ± 1.77 % ; $p = 0.023$) but no significant change in FBS (10.81 ± 3.38 mmol/L to 10.48 ± 3.29 mmol/L ; $p = 0.95$) at 6 months. There was greater reduction in HbA1c level and FBS in treatment group compared to control group - 1.37 % vs + 1.70 % and - 0.24 % vs + 0.41 % respectively. Twenty eight percent (28 % ; $p < 0.001$) (11/ 40) of patients of the treatment group achieved HbA1c < 7 % while no one in control group achieved this target. For FBS, 51 % ($p < 0.001$) (19 / 37) of patients in the treatment group achieved FBS < 7 mmol/L

compared with the control group, only 12 % (3 / 25) of patients achieved FBS < 7 mmol/l at 6 months. There were no significant changes in lipid profiles at 6 months in both groups. In addition, for every improvement of 1 % HbA1c, there was 13.3 times better chance in improvement of HbA1c (OR 13.3, adjusted 17). The cost effectiveness (CE) ratio between the treatment and the control group was not significant (z = - 0.79, p= 0.43)

Conclusion : The addition of rosiglitazone improves glycaemic control, when compared to patients in control group, allowing more patients to achieve HbA1c < 7 % with greater reduction of HbA1c. In addition, adding rosiglitazone to patients on maximum metformin and sulphonylureas were efficacious but not cost effective.

Prof. Dato' Wan Mohamed Wan Bebakar : Supervisor
Dr. Mazlan Abdullah : Co-Supervisor

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DETECTION OF P1A2 GENE POLYMORPHISM IN GLYCOPROTEIN IIIA IN PATIENTS WITH MIGRAINE

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Introduction : Glycoprotein IIIa (GP IIIa) is a platelet membrane receptor, which when activated leads to platelet adhesion. Platelet alloantigen (P1A) is normally represented on the GPIIIa of human platelet membrane in the more common homozygous allelic state (P1A1/A1), or the rarer polymorphic state (P1A1/A2). The latter polymorphic P1A1/A2 polymorphic state renders the platelet hyperadhesive leading to increased incidence of coronary events and possibly migraine as well. Migraine is also a disorder wherein platelet hyperadhesion and serotonin release have been observed. Migraine is a common headache disorder exhibiting a prevalence of 9% in the Malaysian population.

Objectives : This study was designed to identify the prevalence of the homozygous (P1A1/A1) and the polymorphic (P1A1/A2) state in the population at Kelantan and to determine whether the polymorphic state (P1A1/A2) is more common in our migraine patients.

Patients and Methods : A case control study was conducted between September 2004 and October 2005. Eighty (80) patients who fulfilled the International Headache Society (IHS) criteria for migraine with or without aura, and a group of eighty healthy volunteers were recruited for the study. The P1A1/A2 genotype pattern of all these 160 individuals was analysed by polymerase chain reaction (PCR) using the AUEle Specific Oligonucleotide (ASO) technique and the results compared with the migraine symptoms in the patients concerned.

Results : It was found that 77 (of the 80) controls and 76 (of the 80) cases with migraine possess the homozygous (P1A1/P1A1) configuration, indicating that in the population here the homozygous state is more common (i.e present in 153 out of 160 individuals studied). Secondly the occurrence of the P1A1/A2 polymorphism in only four (of the 80) migraine cases and also three (of the 80) controls suggest that the polymorphic (P1A1/A2) state is not more frequent in the migraine cases. Thirdly, of the four cases positive for P1A1/A2 polymorphism three had classical visual aura (75%). Earlier studies have reported that migraine with aura has an increased familial incidence when compared with migraine without aura suggesting that migraine with aura could well be related to the inheritance of this P1A1/A2 polymorphic state.

Conclusions : Although our findings do not totally support the hypothesis that the P1A2 polymorphism represents an added inherited platelet risk factor for migraine or even migraine with aura, further searches for such a factor are clearly warranted, because of the familial

aggregation of migraine headache cases. Thus this preliminary study shows that P1A1/A2 polymorphic state on the GPIIIa platelet membrane receptor does not increase the risk of inheriting migraine. However if present, it is more likely to manifest as migraine with aura in the migraineurs with this polymorphism.

Assoc. Prof. Dr. Atul Prasad : Supervisor
Prof. Jafri Malin Abdullah : Co-Supervisor

EVALUATION OF MICROSCOPY, POLYMERASE CHAIN REACTION (PCR) AND IMMUNOASSAY TESTS FOR THE DETECTION OF *CRYPTOSPORIDIUM PARVUM* IN STOOL SPECIMENS OF HIV-INFECTED PATIENT

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Objectives : In this study we evaluated the sensitivity and specificity of nested PCR method for the detection of *Cryptosporidium parvum* in fecal specimens of HTV infected patients and also the practicality of PCR to be used as routine diagnostic tool in our laboratory.

Patients and Methods : Fifty-nine fecal specimens were collected from HIV infected patients admitted to medical ward in General Hospital Kota Bharu during the study period. A part of stool sample was used for microscopy examination and the other portion was preserved in 2.5% potassium dichromate for PCR analysis and immunoassay (BD ColorPac). Two methods of DNA extraction were assessed; phenol-chloroform method and boiling method with polyvinylpyrrolidone (PVPP), a modified method from Morgan *et al* 1998. Nested PCR assay targeting 18SrRNA gene that is specific for *Cryptosporidium parvum* was used in this study.

Results : Compared with the phenol-chloroform method, the boiling method with PVPP was found to be simple, less time consuming and gave clearer bands on gel electrophoresis. The sensitivity and specificity of nested PCR was 33.3% and 94.6% respectively. We found two samples, which were strongly positive by microscopy but repeatedly negative by PCR. Since we considered microscopy as a gold standard, false negative by PCR could be due to infection with different species of *cryptosporidium* that cannot be amplified by 18SrRNA primers, which is specific for *Cryptosporidium parvum*.

Conclusions : We concluded that nested PCR using 18SrRNA is less sensitive but specific to detect *Cryptosporidium parvum* in clinical samples. Further test such as DNA sequencing is required to confirm the species. From this study, we found that PCR assay is not practical to be as a routine diagnostic tool since it is tedious and required skill personnel.

Professor Madya Dr. M. Ravichandran : Supervisor
Dr. Zeehaida Mohamed : Co-Supervisor
Dr. Maheran Mustafa. :Co-Supervisor

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COMPARISON OF MICROSCOPY AND POLYMERASE CHAIN REACTION (PCR) IN THE DETECTION OF *PNEUMOCYSTIS CARINII* IN HIV INFECTED PATIENTS ADMITTED AT GENERAL HOSPITAL KOTA BHARU (GHKB)

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MPath (Microbiology)

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Introduction : *Pneumocystis carinii* pneumonia (PCP) has become the most common opportunistic infection involving Human Immunodeficiency Virus (HTV) patients with CD4 count less than 200. The prevalence among HTV patients is about 5 to 20%. A current method of diagnosis is based on clinical condition of the patients, chest x-ray finding and by looking at the level of oxygen saturation. As far as laboratory investigation is concerned, many centers at the moment rely on the microscopy method. However, microscopy method stained with Grocott's methanamine silver (GMS) is able to give a good detection rate only if the samples is bronchoalveolar lavage (BAL).

Objectives : In this study Ac PCR based method for the detection of *P. carinii* were used and compared the results with microscopy methods in term of their sensitivity and specificity.

Methodology : For this study induced sputum samples were taken because this samples are known to be less invasive than BAL. One hundred and thirty five induced sputum samples were collected from HIV infected patients admitted at General hospital Kota Bharu after obtaining ethical approval and informed consent The inclusion criterion was HIV patient aged more than 18 years. For microscopy methods, the smear was stained with Giemsa stain and GMS stain. The slides were observed by an expert microscopist and reconfirmed by a clinical parasitologist. Deoxyribonucleic Acid (DNA) extraction from induced sputum sample was performed using a commercial kit. Polymerase chain reaction was performed using PAZ102X and PAZ102Y primers. The amplified DNA fragment of 252bp was detected by agarose gel electrophoresis. No positive reaction was seen with DNA from different microorganisms typically found in the respiratory tract.

Result : *P. carinii* DNA was demonstrated in only 8 out of 135 patients by PCR method. Microscopy on the other hand was not able to detect any *P. carinii* trophozoite or cysts from all the induced sputum samples. The sensitivity of the microscopy and PCR cannot be calculated because of the zero positivity of microscopy. However using Poisson Probability showed that the chances to get zero positive are 0.00034. Therefore the conclusion was that, zero positive cases detected by microscopy was not an occurrence by chance. It would be a very rare chance to give zero positive result if microscopy would have been a good diagnostic tool for the diagnosis of *P. carinii* infection.

Conclusion : The use of PCR for detection of *P. carinii* using induced sputum is a useful and non-invasive method for the early diagnosis of PCP.

**Professor Madya Dr. M. Ravichandran : Supervisor
Dr. Maheran Mustafa : Co-Supervisor**

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**THE OUTCOME OF HIV INFECTED PREGNANT
MOTHER AND THE RATE OF MATERNAL TO CHILD
TRANSMISSION OF HUMAN IMMUNODEFICIENCY
VIRUS**

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Introduction : An estimated 39.4 million people are living -with HIV by the end of 2004 as reported by UNAIDS. Almost half of them are woman, mofority are in the reproductive years. As they become pregnant, HIV virus can be transmitted to the babies by vertical

transmission and through breast feeding. About 2.2 million children are living with HIV with 600,000 infected annually. Almost 90% of them infected through maternal to child transmission (MTCT). Because of that reason, aiming to reduce the risk of transmission by antiretroviral monotherapy (Zidovudine) in pregnancy and post portion as well as advising the mother for elective caesarean section and abstinence from breastfeeding become a standard of practice without possibly increase the risk to the mother and the baby.

Objectives : The aim was to identify any significant adverse outcome in pregnancy particularly towards increase risk of premature delivery, low birth -weight and stillbirth among babies delivered. We also interested to hum the rate of vertical transmission (MTCT) in our state of Kelantan

Methodology : This is a prospective cohort study started in Jan 2003 until December 2004 conducted at Obstetric and Gynecology Clime Hospital Kota Bharu. Only HIV positive mother that gave birth during this periods, would be enrolled m this study after fulfilling the exclusion and inclusion criteria. The study group was divided into two groups, the HIV positive mother and other was the control group. The HIV positive mother would be started on Zidovudine monotherapy 500mg daily (300mg in the morning and 200mg in the evening). Any abnormality during pregnancy would be documented and followed - up closely by serial blood investigation and serial ultrasound for the baby. At term mother was advised/or elective caesarean section. Baby delivered by HIV positive mother would be started on Zidovudine therapy 2 mg/kg until 6 weeks of life. A serial PCR test would be done at birth, 6 weeks and 6 months of fife to determine status of infection. Samples were analyzed by using SPSS version 12. A p value of less than 0.05 was considered significant.

Results : There were 102 patient enroll in this study with HIV positive mother represent 50% of the study sample There was no significant different m the demographic characteristics between the two groups. There are 9.8% HIV positive mother had VDRL positive and 2 of them were confirmed by TPHA test and none of HIV negative mothers were tested positive (p value 0.02). During ante partum periods 9.8% of HIV positive mother developed urinary tract infection and gestational diabetes, 7.8% experienced premature contraction and all were not statistically significant compared to HIV negative mothers with p value > 0.05. Mild anaemia with hemoglobin 8-9.9g/dl occurred in 21.6% in HIV positive mother and 11.8% in HIV negative mother(p value 0.02).None of HIV positive mother recorded an increase of AST level more than 3 folds of the normal value with only 29.4% had 2 fold increase in level. When the mean baby weight delivered (2.8kg) and low birth weight(21.6%) in HIV positive mothers were compared to the control group, mean weight (3.1kg) and low birth weight (11.8%) it was statistically significant (p value is 0.04). There was no significant development of post operative complication, where postoperative fever (6.2%) and wound injection (3.1%) develops among HIV positive mother. No stillbirths "were recorded and 7.8% in HIV positive mother develop IUGR, 3.9% sepsis and 2% f^fAS. At 6 months follow-up two babies were detected positive by PCR test (5% transmission rate) -with each delivered vaginaify and emergency caesarean section respectively.

Conclusion : The HIV infection in pregnancy -with antiretroviral treatment does not increase any adverse pregnancy and neonatal outcome. However there are possible association with tow birth weight baby and development of mild anaemia. The vertical transmission rate in this study population was 5%

**Assoc. Prof. Dr. Nik Mohd. Zaki Nik Mahmood : Supervisor
Dr. Zainalabidin Hanafiah : Co-Supervisor
Dr. Wan Zahanim Wan Yusoff : Co-Supervisor**

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**A COMPARATIVE STUDY BETWEEN ROUTINE
CATHETERIZATION AND NON-CATHETERIZATION IN
ELECTIVE CAESAREAN DELIVERY**

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Introduction : In the patients who were undergoing elective caesarean section, several preoperative preparation were made such as insertion of Foley’s catheter for urinary drainage intra operative and postoperatively. The indication for the regular practice however was of doubtful benefit even though some may think that the procedure facilitates surgery on the lower segment during caesarean section. This routine practice however entails the cost of Foley’s catheter and urine bags, urinary symptoms in patients and antibiotic therapy if urine microscopy suggests infection.

Objectives : To evaluate role of routine Foley’s catheter during and after caesarean section and compare the outcome of routine use of urinary catheterisation and non catheterisation in patient undergoing elective caesarean section.

Methods : This study was a case control study conducted from 1st January 2005 until September 2005. All patients who underwent elective caesarean section were included in this study. The patients were divided into 2 groups i.e. control group containing 70 patients who had Foley’s catheter inserted preoperatively and were kept during and until day 1 postoperatively and another 70 patients Foley’s catheter were not inserted prior to caesarean section but instead the patients were asked to pass urine one hour before start of caesarean section to empty the bladder. The two groups of patients were compared in terms of duration of caesarean section, intra-operative difficulty and also post operative outcome namely time of first void, discomfort at first void, duration of ambulation time postoperatively and incidence of urinary tract infection after caesarean section.

Results : In this study, the main ethnic group involved was Malay 93.6% followed by Chinese (3.6%), Indian (0.7%) and Siamese 2.1%. The commonest indication for elective caesarean section was repeat caesarean section (40%) followed by breech (19%) and placenta praevia (12.4%). Regional anaesthesia was given in 82.9% of patients while 17.1% were given general anaesthesia. There was no significant difference in terms of duration of caesarean section (46.67 minutes in control versus 44.49 in patients without Foley’s catheter in situ), difficulty encountered during performance of caesarean section and mean length of hospital stay after operation (3.10 day in control as compared to 3.17 day in case group). There was however significant difference in discomfort at first void, mean ambulating time and incidence of urinary tract infection in both groups.

Conclusion : Continuous urinary catheter by using Foley’s catheter is not necessary in patients undergoing elective caesarean section as it does not show any significant difference in terms of mean operating time, difficulty in performing caesarean section but it creates discomfort at first void, delay mean ambulating time and higher to urinary tract infection related to CBD.

Assoc. Prof. Dr. Mohd. Shukri Othman : Supervisor
Dr. Habsah Hassan : Co-Supervisor

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RESPIRATORY SYMPTOMS AND PULMONARY FUNCTION IN MALE WOODEN FURNITURE WORKERS EXPOSED TO WOOD DUST IN KOTA BHARU, KELANTAN

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Introduction : Wood industries such as wooden furniture factory are one of the major socio-economic development of rural Kelantan. There are significant proportions of workers involved in wooden furniture factories. Majority of factories are lack of supervision by DOSH and have low compliance of the OSHA 1994 and its regulations. COPD and smoking are the leading causes of morbidity and mortality in industrialized and developing countries. Prolonged occupational exposure to wood dust at workplace can increase susceptibility of developing COPD in future.

Objectives : This research was aimed to study respiratory symptoms, level of knowledge, attitude and practice in relation to wood dust exposure and factors associated with respiratory function in male wooden furniture workers in Kota Bharu, Kelantan.

Methods : A comparative cross-sectional study of 97 male wooden furniture (exposed) workers and 97 male office workers (non-exposed) was conducted from May till July 2005. Data was collected through a questionnaire on respiratory symptoms, knowledge, attitude and practice of health hazards of wood dust exposure in workplace and spirometry test. Chi-square test was used to determine the significant difference in the prevalence of respiratory symptoms and independent *t* test was used to compare means *F* *K* *P* score and result of respiratory function parameter between exposed and non-exposed group. Multiple linear regression was used to determine factors associated with FEV₁ in exposed group.

Results : The prevalence of respiratory symptoms were significantly higher among exposed compared to non-exposed group. The most frequent symptoms among exposed group were skin itchiness (47.4%), followed by chest tightness (39.2%), morning cough (35.1%) and morning phlegm (35.1%). The mean total knowledge score in exposed group was significantly lower [95.7(10.8)] compared to non-exposed group [99.8(10.3)]. Exposed group had significantly higher mean score for total practice score [24.8(4.8)] compared to non-exposed group [22.2(4.7)]. There were no significant differences for mean total attitude and KAP scores between exposed and non-exposed group. About 71 % of exposed group had abnormal respiratory function whereas only 24% of non-exposed group had abnormal respiratory function. Of the 69 (71.1%) exposed group with abnormal spirometry test, 30 (30.9%) exhibited mild restriction, 24 (24.7%) with moderate restriction and 15 (15.5%) with severe restriction. Duration of smoking (*P*<0.001), height (*p*<0.001), duration of work (*p*=0.002) and number of cigarettes smoke perday (*p*<0.001) were significantly related to FEV₁ and FVC. Only age (*p*=0.049) was significantly related to FEV₁/FVC.

Conclusion : We therefore conclude that the level of knowledge, attitude and practice in relation to the health hazards of wood dust exposure in the exposed group was unsatisfactory compared to the non-exposed group and chronic occupational wood dusts exposure can lead to higher prevalence of respiratory symptoms and abnormal respiratory function among exposed group.

Prof. Dr. Rusli Nordin : Supervisor
Assoc. Prof. Dr. Razlan Bin Musa : Co-Supervisor
Dr. Mohd Ayub Saddiq : Co-Supervisor

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A STUDY OF JOB STRESS, ANXIETY AND DEPRESSION AND ASSOCIATED FACTORS IN AUTOMOTIVE ASSEMBLY WORKERS

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Introduction : In automotive assembly-line work, workers have less control, do repetitive job and are exposed to physical hazards such as noise, vibrations and dangerous machines that will lead to depression, anxiety and stress. Therefore, the present study attempts to compare the prevalence and associated factors of stress, anxiety and depression in two prominent governmental flagship automotive assembly plants in Selangor (Factory A) and Pahang (Factory B).

Methodology : A cross sectional study was conducted on 300 automotive assembly workers (Factory A: 150 workers and Factory B: 150 workers) from March till May 2005. The Malay version of the questionnaires consisting of demographic factors, JCQ and DASS 42 were validated and used.

Results : The results showed that all automotive assembly workers were Malays (100%), males (95%) and aged between 19-42 years. The prevalence of job strain in Factory A and B were 27.3% and 19.5%, respectively. The prevalence of depression for Factory A and B were 34.0% and 41.3%, respectively. The prevalence of anxiety for Factory A and B were 61.3% and 70.7%, respectively. The prevalence of stress for Factory A and B were 26.0% and 25.3%, respectively. Associated factors of depression in Factory A were: shift work, job insecurity, skill discretion, supervisor support and toxic exposures, whereas in Factory B: job insecurity, psychological job demand, hazardous condition and interaction between psychological job demand and job insecurity. Associated factors of anxiety in Factory A were job insecurity, shift work, skill discretion and supervisor support, whereas in Factory B job insecurity, hazardous condition, physical exertion, created skill and psychological job demand. Associated factors of stress in Factory A were job insecurity, created skill, hazardous condition and supervisor support, whereas in Factory B; job insecurity, psychological job demand, skill discretion and hazardous condition. Predictive factors of depression, anxiety and stress in Factory A were job insecurity and supervisor support Shift work and skill discretion were predictive factors of both depression and anxiety. Whereas in Factory B, predictive factors of depression, anxiety and stress were job insecurity, hazardous condition and psychological job demand.

Conclusions : We conclude that the predictive factor for depression, anxiety and stress for automotive assembly workers in Factory A and B was job insecurity. Predictive factor of stress in both Factory A and B was a hazardous condition. We also concluded that the predictors of depression, anxiety and stress were different in different workplaces.

Prof. Dr. Rusli Nordin : Supervisor
Dr. Lin Naing : Co-Supervisor

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A PILOT STUDY OF BOVINE BONE FOR ORBITAL IMPLANTS IN RABBITS

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Objective : To assess the biocompatibility of bovine bone xenograft as ocular implants in rabbits. At the same time, to determine the presence of histopathological and clinical rejection towards bovine bone xenograft as ocular implant in rabbits.

Methodology : Eviscerations with and without bovine bone orbital implantation were performed onto the right eye of 12 New Zealand white rabbits. Group A (n = 6) was eviscerated without implant whereas Group B (n = 6) was eviscerated with insertion of an orbital implant using bovine bone. Observation was done at day 1, day 7, day 14, day 28 and day 42. Serial clinical examination was done based on a few fixed criteria including rate of infection, implant migration, any

evidence of wound breakdown and any restriction of intraocular movements. The implanted eyes were then enucleated on day 42. The enucleated eyes were sent for histopathological evaluation to record the type of inflammatory reaction and rate of fibro vascular ingrowth.

Results : Serial clinical examination showed presence of minimal infection in all eyes both in the control group and the implanted first post operative day, which responded well with antibiotics. Infection occurred after first post operative day but there was no evidence of orbital migration or extrusion of implant, wound breakdown, restriction of extra ocular movement, severe infection or any physical abnormality of implanted groups. Histopathological examination revealed good fibrovascular ingrowth in implanted groups, with minimal reaction of rabbit eye towards bovine bone implant.

Conclusion : Orbital bovine bone implants was highly biocompatible with minimal infection during the early period and no evidence of clinical rejection. Histopathology examination supported the evidence of good fibrovascular ingrowth and minimal inflammatory reaction towards the implants. We can thus conclude that this bovine bone implant has a high potential for use clinically with the added advantage of being cost effective.

Dr. Wan Hazabah wan Hitam : Supervisor
Prof. Dr. Abd. Rani Samsudin : Co-Supervisor
Assoc. Prof. Dr. Hasnan Jaafar : Co-Supervisor

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THE ROLE OF BETA 2-RECEPTOR POLYMORPHISMS ON PRESSURE LOWERING EFFECTS OF TOPICAL TIMOLOL MALEATE IN GLAUCOMATOUS PATIENTS

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MMed (Ophthalmology)

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Introduction : Topical timolol maleate is an essential medication for treatment of glaucoma. Nevertheless, the response to timolol varies with individuals. As timolol acts on the beta receptors in the eye, therefore, beta 2-receptor (p2AR) polymorphisms may play a role in the varied response to timolol.

Objectives : To determine the frequency of R2AR polymorphism in glaucoma patients and to study the association of R2AR polymorphisms with responsiveness to timolol in glaucoma patients.

Methods : A prospective cohort study was conducted, involving newly diagnosed POAG and NTG patients who were planned on monotherapy with timolol maleate-XE 0.5%. After the baseline data was recorded, timolol was started and the patients were followed up at 1, 3, 6 and 12 months. During each visit, the intraocular pressure (IOP), cup-to-disc ratio (CDR), optic disc photography and visual fields were assessed. Based on the response to timolol (using the last IOP reading from the baseline), the patients were grouped into 3 categories; good responder (30% reduction), moderate (15% and <30% reduction) and poor (<15% reduction). Control subjects were matched with glaucoma patients according to age, race and sex. Five milliliters of blood was obtained from each patient. DNA extraction and single tube Multiplex PCR was carried out to analyze the blood samples for _2AR polymorphisms in allele 16, 27, 164, -20 and -47.

Results : From 100 glaucoma and control patients (28 POAG, 22 NTG and 50 controls) analyzed, the frequency of alleles, among the glaucoma subjects, were (72%) Arg16, (28%) Gly16, (92%) Gln27, (8%) Glu27, (100%) Thr164, (40%) -20C, (60%) -20T, (8%) -47C and (92%) -47T. The association between glaucoma and control subjects was not significant for allele 16 (p=0.757), -47 (p=0.480) and allele 164. There was a significant overrepresentation of allele -20C (p=0.000) and Gln27 (p=0.037) in glaucoma patients compared to control subjects. Although

not statistically significant, the heterozygous genotype of alleles 16, 27, -20 and -47 appeared to be associated with lower IOP reduction during 1-year follow-up. The association of β 2AR polymorphisms with responsiveness to timolol was not statistically significant.

Conclusions : The frequencies of Gly16 and Glu27 in our patients were relatively lower compared to other population. There is a significant association between allele -20C and Gln27 with POAG and NTG. There was no significant association between β 2AR polymorphisms with responsiveness to timolol though heterozygosity of alleles 16, 27, -20 and -47 appeared to be associated lower IOP reduction in glaucoma patients on timolol.

Dr. Liza Sharmimi Ahmad Tajuddin : Supervisor
Mr. Ho Boon Peng : Co-Supervisor

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PROSTANOID (FP) RECEPTOR POLYMORPHISMS : THE ASSOCIATION OF NOVEL SINGLE NUCLEOTIDE POLYMORPHISM WITH THE RESPONSIVENESS OF GLAUCOMA PATIENTS TO TOPICAL LATANOPROST

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Introduction : Diversity in clinical response among glaucomatous patients in response to topical latanoprost is not a new issue, many researchers attributing it to the different races, treatment regimes, glaucoma types, and some genetic variants.

Objective : The objective of this study is to determine the presence of polymorphism in exon of PTGFR gene and its role in responsiveness of glaucoma patients to topical latanoprost treatment.

Methodology : Glaucoma patients started on topical latanoprost were followed up for 6 months. Pattern of IOP and rate of good responder (30% reduction or more), moderate responder (15-30% reduction) and poor responder (less than 15% reduction) were determined. Polymorphism of the PTGFR protein coding region was identified among the glaucoma patients and the controls using denaturing High Performance Chromatography (dHPLC). The identified polymorphisms were associated with glaucoma and the pressure-lowering effect of topical latanoprost among glaucomatous patients on treatment.

Result : From 76 glaucoma patients and controls screened, no exon SNP was found. One novel intron nSNP^(A-T) at 5 flanking region of exon-3 with frequency of 46% was identified. Among the glaucoma patients, mean IOP reduction was 33.1% and there was as high as 47.4% good responder, 28.9% of moderate responder and 23.7% of poor responder. The Intron SNP was statistically found to be neither associated with the responder rate, the race nor with glaucoma patients.

Conclusion : Topical latanoprost is effective among glaucoma patient in our local set up. The novel intron SNP found within the PTGFR gene does not statistically associate with glaucoma and clinical IOP lowering effect among glaucoma patients receiving topical latanoprost.

Dr. Liza Sharmimi Ahmad Tajuddin : Supervisor
Dr. Wan Hazabah Wan Hitam : Co-Supervisor

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A STUDY OF ASSOCIATION BETWEEN FUNCTIONAL ORAL STATUS AND NUTRITIONAL STATUS AMONG ELDERLY LIVING IN "PONDOK" IN KELANTAN

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Introduction : The relationship between oral health status and nutritional status among elderly people have been explored by various researchers. However the exact nature and strength of the relationship were not fully described.

Objectives : This cross-sectional study were to investigate the dentition status, prosthetic needs and functional oral status of elderly people, to assess the nutrient intake, to determine the distribution of body mass index, to determine correlation between daily calorie intake and body mass index and to investigate the association between functional oral status with inadequate calorie intake and underweight in elderly people living in "Pondok" in Kelantan.

Methodology : A cross-sectional study was conducted from Jun 2004 to January 2005. and a simple random sampling was utilized for selection of 386 subjects. Subjects were interviewed using a structured form to collect information about the subjects' demographic background and self-reported health status. For the anthropometric measurement; the subjects' weight and height were measured, then, body mass index was calculated. The 24-hour recall method was used to provide information on the subject's exact food intake during the previous 24 hours. Finally, it was followed by oral examination whereby the assessment of natural teeth and prosthetic status were done. The "Nutritional Software" was used for nutrient calculation, followed by SPSS version 11.5 for data analysis.

Results : The response rate was 95.6% and majority of the respondents were female (92.4%). The percentage of edentulism was 81.0% (95% CI: 77.0 . 85.0) with high prosthetic need. 47.2% (95% CI: 42.1 . 52.3). Compromised functional oral status was experienced by 48.2% (95% CI: 43.1 . 53.3) of the subjects. Majority was contributed by edentate elderly without dentures (23.6%) or with defective dentures (56.2%). Regarding nutritional status. 70.7% (95% CI: 66.1 . 75.3) of the subjects had inadequate calorie intake, that is less than 66.7% or 2/3 of the Recommended Nutrient Intake and 25.7% (95% CI: 21.2 . 30.2) were underweight. The odds of having inadequate calorie intake and getting underweight among elderly with a compromised functional oral status was 3.7 times and 42.0 times respectively, compared to non-compromised functional oral status.

Conclusion : This study has shown that dentition status of elderly living in "Pondok" in Kelantan was not satisfactory with high percentage of edentulism, compromised functional oral status and prosthetic needs. Mean intakes of calorie and all nutrients were below the Recommended Nutrient Intake (RNI), while the prevalence of underweight was 25.7%. There was a positive correlation between calorie intake and body mass index. Significant associations were noted between functional oral status with inadequate calorie intake and underweight among elderly living in "Pondok" in Kelantan.

Assoc. Prof. Dr. Abdul Manaf bin Abdul Hamid : Supervisor
Dr. Abdul Rashid bin Haji Ismail : Co-Supervisor

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A COST-EFFECTIVENES ANALYSIS OF GLASS IONOMER CEMENT AS FISSURE SEALANT IN SCHOOL-BASED FISSURE SEALANT PROGRAMME IN THE DISTRICT OF PONTIAN, JOHOR

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Health Campus, Kelantan, Malaysia.

Introduction : Community oral Health Care mainly focused on preventive measures such flouridation, oral health promotion, oral

cancer screening and school-based fissure sealant programme. To date, there has been no local evaluation of fissure sealant effectiveness especially in term of its cost.

Objectives : To determine the status of occlusal surface of lower left FPM in sealed group and unsealed group after 5-year follow up, to determine the extra cost for sealed group, cost of complication and cost per averted occlusal caries for both groups and to compare the status of lower left permanent molar between sealed and unsealed groups.

Methodology : This was a retrospective cohort study conducted in Pontian from June 2004 to October 2005. There were two phases in the study i.e. phase 1 for descriptive and cost analysis which involved 618 high caries risk group and phase 2 for questionnaire component which involved 322 high caries risk school children. Phase 1 only focused on dental treatment record (LP8) and financial data from administrative office and the data was collected from 1998 to 2003. For phase 2, subjects who were selected by a random sampling technique were given questionnaire for socio demographic status. Costing analysis was done based on the specified programme for the fissure-sealant preventive measure only.

Results : The total retention rate of glass ionomer cement as fissure sealant in this study was 19.4% and the total loss was 80.6%. The status of sound occlusal lower left FPM in the sealed group was 88.4% and in the unsealed group was 76.8%. There was 11.6% of sealed teeth and 23.3% of unsealed teeth which developed caries after a 5-year follow up. For cost analysis, the extra cost for the sealed group was RM 1,294.73, cost complication for the sealed group was RM 988.83, cost complication for the unsealed group was RM 1,927.10 and lastly cost per averted occlusal caries in the sealed group was RM 8.37 (95%CI 8.03-8.72) and cost per averted occlusal caries in the unsealed was RM 8.35 (7.98-8.72).

Dr. Mazlan Abdullah : Supervisor
Dr. Abdul Rashid Hj. Ismail : Co-Supervisor

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IN VIVO STUDY OF SEA CORAL MATERIAL AS BONE REPLACEMENT IN RABBITS

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

Objectives : This study was designed to assess the biocompatibility of the coral graft processed by the National Tissue Bank, School of Medical Sciences, Universiti Sains Malaysia as a bone substitute in rabbit models. The effects of coral graft in host were studied by means of behavioral observation, macroscopic evaluation and scanning electron microscopy evaluation.

Method : This was an experimental animal study involving 24 New Zealand White Rabbits. The coral graft was implanted into their right mandible for a period of one month, two months, three months and four months before harvesting the graft. The harvested grafts were examined macroscopically and were evaluated using scanning electron microscopy.

Results : There was no significant immunological reaction noted in rabbits. The macroscopic evaluation showed that the graft was well incorporated within the bony defect. The scanning electron microscopy evaluation showed a good cellular growth and cellular incorporation within the implanted corals

Conclusion : This study confirmed the biocompatibility of the processed coral as a bone material replacement with no significant immunological reaction, and good bone and soft tissue incorporation within the graft.

Prof. Dr. Abd. Rani Samsudin : Supervisor
Dr. Rosdan Salim : Co-Supervisor

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THE ROLE OF PERIOPERATIVE ANALGESIA (INTRAVENOUS MORPHINE VERSUS INTRAMUSCULAR DICLOFENATE) IN DECREASING THE INCIDENCE AND/OR SEVERITY OF PHANTOM LIMB PAIN

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Health Campus, Kelantan, Malaysia.

Objectives : To evaluate the perioperative intravenous morphine and intramuscular diclofenate in reducing the incidence of phantom limb pain as well as the severity of phantom pain following lower limb amputation. In addition, to evaluate the association between phantom limb pain and the pain suffered before the amputation, the duration of diabetic mellitus and the duration of various feet or legs problems prior to amputation.

Method : This was a non-randomised observational study involving a total 55 patients. 27 patients were selected for intravenous morphine infusion. The patients' blood pressure, heart rate, respiratory rate, sedation score, blood oxygen saturation were monitored closely. The other 28 patients were selected for intramuscular diclofenate. The drug was given to those patient who had pain score at 2 or more before operation and at regular dose after amputation. The rescue intramuscular tramadol was added if the pain was not adequately controlled in diclofenate group. Both medications were continued till day-3 post-amputation. The characteristic, intensity and location of pain encountered before analgesia, after analgesia and after amputation was documented. The modified numerical pain score was used to quantify the intensity of pain. The phantom sensation, phantom pain and stump pain following lower limb amputation was identified in both groups. The patients were followed up at one week, 1, 3 and 6 months after amputation via phone.

Results : Patients in both groups experienced comparable pain intensity before and after the operation ($p > 0.05$). However, two patients in diclofenate group required rescue i/m tramadol 50 mg for post-amputation pain control. Overall, 50 out of 55 patients (90%) experienced phantom limb sensation and 33 patients (60%) encountered phantom pain after amputation. Twenty one patients (75%) out of 28 in diclofenate group had phantom limb pain compared with 12 patients (44%) out of 27 in morphine group. The phantom sensation in diclofenate and morphine group was 89% and 92% respectively. In 16 patients with phantom limb pain (48%), the symptom subsided within 6 months. Most of the phantom pain encountered was low pain score and only 2 patients required medical treatment. Patients in morphine group was 0.176 time (odd-ratio) less likely to develop phantom limb pain as compared to diclofenate group ($p < 0.05$). Intravenous morphine significantly reduced the severity of phantom limb pain after adjusting possible confounding factors like sex, age, race and presence or absence of diabetic mellitus ($p < 0.05$). The maximal phantom pain score in morphine and diclofenate groups was 1.57 and 2.37 respectively.

The severity of pre-analgesia pain and the duration of various leg and foot problem encountered prior to amputation did not significantly relate to phantom pain. However, the longer history of diabetic mellitus had less risk or incidence of phantom pain ($p=0.03$)

Conclusion : This study showed perioperative intravenous morphine infusion reduced the incidence and severity of phantom limb pain as compare to

Prof. Dr. Zulmi Wan : Supervisor

Assoc. Prof. Dr. Hasnan Jaafar : Co-Supervisor

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EVALUATION OF NASAL CAVITY EOMETRY USING ACOUSTIC RHINOMETRY: A CROSS-SECTIONAL STUDY AMONG NORMAL SUBJECTS AT HOSPITAL UNIVERSITI SAINS MALAYSIA, KELANTAN

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Introduction : The symptom of nasal obstruction is a common subjective complaint among patients. Such complaint can be extremely complex that can mislead both the patient and clinician as the symptom of nasal obstruction is often inconsistent with clinical rhinoscopic findings. Acoustic rhinometry is the recommended technique for assessment of nasal patency. It quantified this subjective symptom of nasal obstruction and this will be useful in choosing the best appropriate treatment in managing the nasal disease.

Objectives : The objective of this study is to develop a preliminary local database for normal values of the Minimal Cross-sectional Area (MCA) in the nasal geometry in a group of healthy adult subjects using acoustic rhinometry instrument. It intended to compare the MCA among the Malay, Chinese and Indian ethnic groups. It is also to determine other associated factors namely the sex, age, height, weight, head circumference. Body Mass Index (BMI) and Body Surface Area (BSA) that may influence the MCA.

Methodology : This is a cross-sectional study of a total of 150 healthy volunteer adult subjects comprising 25 males and 25 females of each ethnic groups of Malay, Chinese and Indian which were seen at Clinic of Otorhinolaryngology - Head and Neck Surgery (ORL-HNS) Hospital Universiti Sains Malaysia. All the subjects were given a brief explanation regarding the procedure before an informed consent were taken. A primary assessment with thorough history was undertaken, followed by systemic and ENT examination including rigid nasoendoscopy were performed for each individual at the same setting. Measurements of nasal patency using acoustic rhinometry were done before and after the application of nasal decongestant. The acoustic rhinometry results were analyzed using two-tailed unpaired T-test and a *p-value* less than 0.05 was considered to be significant

Results : The mean value of MCA 1 for Malay males are 0.59 ± 0.14 . Malay females are 0.56 ± 0.22 , Chinese males are 0.56 ± 0.91 . Chinese females are 0.46 ± 0.12 . Indian males are 0.50 ± 0.10 and Indian females are 0.46 ± 0.10 . The MCA 1 for males are 0.55 ± 0.92 and females are 0.50 ± 0.13 . There were significant difference of MCA between males and females ($p = 0.022$). The MCA between Malay and Indian also shows significant difference ($p = 0.038$) but no significant difference of MCA between Malay-Chinese and Chinese-Indian. The MCA has a weak significant correlation with age ($p = 0.042$) and also with Body Mass Index ($p = 0.042$). However there were no correlation between MCA with height, weight, head circumference and Body Surface Area (BSA).

Conclusion : Acoustic rhinometry is a valuable method of assessing geometry of nasal cavity which is well tolerated by the subjects. The result of this study enables us to develop a local database on normal geometric value of the nose among Malaysians. The mean value of MCA in healthy adult in this study is comparable with previous studies. There is a significant difference of MCA between sex and between Malay-Indian ethnic groups. We observed that acoustic rhinometry is less sensitive to detect nasal narrowing beyond the distance of MCA 2. Acoustic rhinometry is sensitive but not a diagnostic tool for nasal diseases. In the nutshell, the acoustic rhinometry information may be employed to substantiate rhinoscopic finding and symptomatology in

treating nasal disease.

**Dr. Shamim Ahmed Khan : Supervisor
Prof. Dr. Rani Samsudin : Co-Supervisor**

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THE ACCURACY OF STEREO LITHOGRAPHY MEDICAL OF SINONASAL ANATOMICAL STRUCTURE COMPARE TO 3D CT SCAN MEASUREMENT

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Introduction : Stereolithography is a relatively new tool in medicine. It has been used to produce many anatomical models in various fields. The accuracy of Stereolithography is thus essential to provide real replacement and time saving procedure.

Objectives : The objectives of this study were to develop Stereolithography model for sinonasal region for ENT and craniofacial teaching and to assess the accuracy of Stereolithography model produced by our stereolithographic apparatus. It is also to evaluate the suitability of Stereolithography model to be used as pro surgical planning for endoscopic sinus surgery together with an Image Guided System. If appropriate the model also will be used for surgical training for resident.

Methodology : Data with normal paranasal sinus was collected from USM craniofacial CT scan database. The images were processed with a specific procedure using MIMIC software. A Stereolithography model was produced using the data. The model was compared with 3D CT scan image using specific landmark. The landmarks were divided into general craniofacial measurements and sinonasal measurements. The model was tried for simulated endoscopic sinus surgery using Image Guided System.

Results : The stereolithography model shows an accuracy of 99.82% for general craniofacial measurement and 99.68% for sinonasal measurement. Lamina papyracea thickness produces the largest error of 28.71%. There is no pattern to indicate internal measurement group is opposite to the value of external measurement group. The stereolithography model is not suitable to be used as planning of endoscopic sinus surgery, since the anatomy requirement is very critical in the related area.

Conclusion : Stereolithography model is accurate in the dimensions that were measured. The model is suitable for planning in craniofacial surgery. However to be used as presurgical planning in endoscopic sinus surgery, it is still not detail enough. Further improvement in material used in stereolithography is needed before it can be utilised as presurgical model for endoscopic sinus surgery.

**Prof. Dr. Rani Samsudin : Supervisor
Assoc. Prof. Dr. Din Suhaimi Sidek : Co-Supervisor**

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YOUNG CHILDHOOD ACUTE GASTROENTERITIS IN QUEEN ELIZABETH HOSPITAL, KOTA KINABALU: DEMOGRAPHIC PROFILE AND RISK FACTORS

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Objective : To describe the demographic profile and to identify the risk factors for developing acute gastroenteritis (AGE) in children aged 1 month to 60 months old admitted to Queen Elizabeth Hospital, Kota Kinabalu

Methodology: This case-control study was conducted from 1st September 2003 till 31st May 2004 in Queen Elizabeth Hospital, Kota Kinabalu. There were 180 children aged 1 month to 60 months old with AGE and 180 controls from paediatric clinic and health clinic were selected according to criteria. The demographic profile of AGE cases was analyzed using central tendency and dispersion from frequency of descriptive statistics. AGE cases and control group were then compared and analyzed for risk factors of AGE by using logistic regression. As to identify factors associated with increased risk of developing AGE independently, a multivariate analysis was done to adjust for confounder effect of variables.

Results : The number of AGE cases in this study was highest in one to twelve months old which contributed 59.4% of total cases followed by thirteen to twenty four months old with 26.1%. There was male predominance with 79.1%. Most of the patients were bumiputra Sabah (76.1%) and followed by immigrants from Philippines (26.1%). Among the common places where the AGE cases came from were Menggatal (14.44%), Penampang (10.0%), Putatan (8.89%), Inanam (8.89%) and Pulau Gaya (7.78%). Overall from September 2003 till May 2004, the mean was 20 patients per month and mode was 29 patients per month. The risk of developing AGE was higher among wasted children (OR =2.91; 95% CI: 1.65-5.11), low household income (OR =5.53; 95%CI: 1.57-19.48 in total income <RM685), crowded family (OR = 3.84; 95% CI: 2.04-7.22 in family with 3-4 young children), sending child to day care center (OR = 18.24; 95% CI: 1.98-168.28), never breastfed (OR = 17.61; 95% CI: 4.08-76.10), weaning period (OR = 6.00; 95% CI: 2.27-15.86 in 3-6 months old) and positive contact history with AGE patients (OR = 6.46; 95% CI: 2.32-18.02).

Conclusion : This study helped in demonstrating the demographic profile of patients with AGE in QEH, Kota Kinabalu. The risk factors associated with AGE were malnutrition, low household income, and crowded family with children less than 5 years old, sending child to nursery care, weaning period and contact with AGE patients. Breastfeeding conferred a protective effect against AGE. Knowing these risk factors could help in planning the preventive measures to reduce the incidence and severity of young childhood AGE in Sabah.

**Dr. Noorizan Abdul Majid : Supervisor
Dr. Soo Thian Lian : Co-Supervisor**

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**EFFECTS OF MORINDA CITRIFOLIA ON ISCHEMIC-
REPERFUSED MYOCUTANEOUS FLAPS IN AN
ANIMAL MODEL**

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Introduction : Oxidative stress is a constant threat to all living organisms. Ischemia and reperfusion is characterized by a significant oxidative stress and characteristic changes in the antioxidant defense. Ischemia underlies many of the most important problems faced by the microvascular and replantation surgeons. Many of these ischemic episodes can be reversed at an early stage by surgical or pharmacological means with the ultimate aim of preventing infarction and cell necrosis in the ischemic tissues. However, reperfusion of

ischemic areas, in particular the readmission of oxygen, may contribute to further tissue damage (ischemia reperfusion injury). Ischemia reperfusion injury is a multifactorial process. An understanding of the mechanisms involved is essential for the design of therapeutic strategies for outcomes improvement. The generation of reactive oxygen species subsequent to reoxygenation inflicts tissue damage and initiates a cellular cascade leading to inflammation, cell death and ultimate organ failure. The inflammatory-like response that follows the onset of reperfusion involves intense interactions with tissue. Neutrophils have been implicated as primary and secondary mediators of lethal injury after reperfusion. This has led to the introduction of an array of treatment modalities in managing this problem. Most living organisms possess various defense systems against excessive production of reactive oxygen species. Recently, more attention has been paid to the role of natural antioxidants. *Morinda citrifolia* (Noni), has been extensively used in folk medicine by the Polynesians for over 2000 years, it has been reported to have broad therapeutic effects, including as an antioxidant Noni is unique in view of the large number of medical claims that have been made for its efficacy; nevertheless, little is known about its pharmacological potential compared with other popularly used botanicals.

Objective : The aim of this study is to evaluate the effect of *Morinda citrifolia* on ischemic reperfusion myocutaneous flaps in an animal model. Forty male Sprague Dawley rats were randomly divided into four groups (10 rats per group). Two groups were given Noni extract via gavaging, and another two groups were given distilled water. One group of Noni treated animals and one group of controlled animals, were rendered ischemic by clamping the femoral vessels supplying the gracilis muscle for four hours, followed by periods of reperfusion for 24 hours. The gracilis myocutaneous flaps were then harvested and muscle biopsy were taken for viability test, edema test and neutrophil infiltration count. The data were analysed statistically, p value is taken as 0.05.

Results : This study showed that there are significant increase in muscle viability and reduction in muscle edema in rats pretreated with Noni, but not statistically significant in reducing neutrophil infiltration.

**Assoc. Prof. Dr. Ahmad Sukari Halim : Supervisor
Prof. Dato' Dr. Ahmad Ridzwan Arshad : Co-Supervisor**

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**PREVALENCE, TYPES AND RISK FACTORS OF
MENSTRUAL IRREGULARITIES AMONG SYSTEMIC
LUPUS ERYTHEMATOSUS PATIENTS**

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Introduction : Lupus nephritis increases the morbidity and mortality associated with systemic lupus erythematosus. Over the last 4 decades, changes in the treatment of Systemic Lupus Erythematosus (SLE), especially in lupus nephritis have greatly improved overall survival in SLE patients. With decreased morbidity and improved mortality, the gonadal dysfunction observed become a problem faced by SLE patients. There had been several studies looking at the menstrual irregularities found in SLE patients; in which the prevalence, the type and risk factors of menstrual irregularities were evaluated.

Objectives : The aim of this study was to determine the prevalence and the types of menstrual irregularities among SLE patients, and to identify factors that influence the development of their menstrual irregularities.

Methodology : The study was a cross-sectional and observational study. All SLE patients attended medical clinics at Hospital University Science of Malaysia who fulfilled our selection criteria were

interviewed using a set of questionnaires. Their blood pressure, height, weight and other clinical parameters were reviewed by the attending doctor. Blood sample was taken for evaluation, such as; hemoglobin, renal function, proteinuria, C3C4 level and ANA. Participants' records which included current and past were then reviewed by principal investigator.

Results : A total of 61 patients were evaluated. The patients' age was ranging from 16 to 53 completed years, and majority of them were aged between 21 to 30 completed years. The mean age was 33.23 (SD: 10.96). Majority were Malay ethnic group, and unemployed. Majority of them had severe SLEDAI score on initial presentation (75 percent), and majority of patients had class IV lupus nephritis (50.8 percent). Sixty-five-point-six percent of patients received combination of steroids and immunosuppressive therapy; with majority of them on cyclophosphamide (59 percent). Majority of patients who were on cyclophosphamide had standard induction of intravenous cyclophosphamide (50.8 percent), whereas 4.9 percent of patients had extended induction, and 3.3 percent of patients had oral cyclophosphamide therapy. From our study; 49.2 percent of study population have menstrual irregularities. Majority of patients who had menstrual irregularities aged between 41 to 50 years old (21.3 percent), followed by patients aged 31 to 40 years old (16.4 percent). Majority of patients with menstrual irregularities had sustained amenorrhea (60 percent); with majority of them aged 41 to 50 completed years (30 percent), followed by patients aged 31 to 40 completed years (20 percent). During active phase of SLE, 21.3 percent of patients had menstrual irregularities, and oligomenorrhea was commoner than amenorrhea (18.0 percent versus 3.3 percent). During inactive phase of SLE; 49.2 percent of patients had menstrual irregularities, and amenorrhea was commoner than oligomenorrhea (27.9 percent versus 21.3 percent). From the study, cyclophosphamide was recognized as one of the risk factors for menstrual irregularities in SLE patients, beside age. Majority of patients with menstrual irregularities were patients who had cyclophosphamide (83.3 percent); and majority of them had sustained amenorrhea (46.7 percent). Cumulative dose of cyclophosphamide influenced the prevalence of menstrual irregularities in SLE patients; with dose higher than 10 gram played a major risk. Nine patients with sustained amenorrhea had hormonal assay which confirmed diagnosis of premature menopause.

Conclusions: This study showed that SLE patients have a higher risk of developing menstrual irregularities in comparison to normal / healthy population. The risk was higher in older age group especially those aged more than 30 years old. The risk became higher once patients had cyclophosphamide therapy; especially if cumulative dose of cyclophosphamide was more than 10 gram. There were variable types of menstrual irregularities recognized in this study; with sustained amenorrhea being the commonest.

Assoc. Prof. Dr. Zainal Darus : Supervisor
Dr. Aniza Abdul Aziz : Co-Supervisor



THE PATHWAYS TO HEALTH CARE A COMPARISON BETWEEN PSYCHOTIC ILLNESS AND EPILEPSY

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Introduction : Identifying the pathways which patients take to reach health care is important, as patients' experience of the first pathway to care may determine their future compliance and progression of the illness. Understanding the type of pathways, which patients take and the associated factors that influence the selection are crucial information for future intervention to improve the quality of health care. Studies

on pathways to care were sparse and pathways to care among local psychiatric patients had not been explored.

Aim : The aim of the study was to describe the pathways to health care of psychotic patients (schizophrenia and schizophreniform disorder) to the tertiary health center (psychiatry and medical specialized clinics in HUSM); and to examine the demographic, social, clinical and other factors influencing the pathway to care. Similar assessments were done in epilepsy patients for comparison.

Methodology : The number and type of previous healers (modern and traditional) visited by patients since onset of illness were assessed using multiple sources of information in 60 psychotic (schizophrenia and schizophreniform disorder) and 60 epileptic patients attending the respective specialist clinics for the first time during the study period. The pathways taken by the patients before reaching the clinics were explored by using semi-structured interview questionnaires and charted on a common diagram. Patients' sociodemographic data, details of the illness, and information regarding the decision makers were also gathered during the interview from patients, and family members.

Results : Sixty patients in each psychotic and epileptic group entered the study; all of them were Malays. Schizophreniform disorder formed the majority (76.7%) of the psychotic patients. Four types of pathways were identified from the studied population. The pathway involving consultation of traditional and/or alternative healers was the most popular (44.3%) and was significantly higher in psychotic than epileptic patients. 61.7 % and 26.7 % of the psychotic and epileptic patients consulted traditional and/or alternative healers respectively. Most of them consulted Malay traditional healers (bomoh) and only 2 patients consulted homeopathic practitioners in addition to bomoh. Other pathways were direct access (24.2%), which was the second most popular, followed by private General Practitioner (18.3%), and other government's doctors (13.3 %). Direct pathway was equally represented by patients from both groups, while General practitioner and other doctors pathways were predominated by epileptic patients. The demographic variables between those who had consulted traditional and/or alternative healers and those who did not were not significantly different. Belief in supernatural caused of mental illness and availability of traditional and/or alternative healers were the factors that significantly influenced the decision of seeing traditional and/or alternative healers. There was no significant difference in contact delay between the diagnostic groups. There was significant difference in treatment delay between epileptic and psychotic patients regardless whether they had consulted or not consulted traditional and/or alternative healers.

Conclusions : Epileptic and psychotic illness such as schizophrenia and Schizophreniform disorder have a slight different pathway in help seeking behavior. A significant higher number of psychotic than epileptic patients consulted traditional/alternative healers. As a complementary treatment in Malay society, bomoh is more popular than the well-established alternative medicine in treating such illness. The author concluded that the study of pathway to health care could provide a framework for better understanding of health services utilization and the associated factors that affect the services utilization. The effects of socio-cultural belief on the studied population were not much different as compared to the findings from the earlier studies. Hence there is a need for further understanding about traditional, complementary and alternative medicine and collaboration between traditional/alternative and modern health services.

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



PSYCHIATRIC MORBIDITY AMONG CHILDREN AND ADOLESCENTS LIVING IN ORPHANAGES AROUND KOTA BHARU, KELANTAN.

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Introduction : Child psychiatric morbidity are common and treatable, but often go undetected and therefore remain untreated. Children living in orphanage are more likely to have problems.

Objective : To characterize the psychiatric morbidity and associated factors among children and adolescents at risk living in orphanages around Kota Bharu.

Method : This study involving two-stage study design. First, screening of all the children and adolescents living in orphanages were done using the Malay version of Strengths and Difficulties Questionnaire. Both of self-rating and teacher-rating were used in this study. In the second stage, all the children and adolescents who were identified as high-risk group (extreme 10 % of population) and selected cases from the low risk group (90% of population) were interviewed for diagnoses using ICD 10.

Results : Based on the SDQ scoring in the screening phase, for the self-rating data, 27 (12%) of children and adolescents scored in the high risk group and 193 (88%) scored in the low risk group. Teacher rating data of SDQ reported that 25 (11%) children and adolescents scored in the high risk group and 195 (88%) scored in the low risk group. In the second stage, for the self rating data 24 (10.9%) of respondents had a psychiatric diagnosis and for the teacher rating data, 18 (8.2%) had a psychiatric diagnosis.

Conclusions : Psychiatric morbidity were relatively frequent among children and adolescents living in orphanage. This results indicate that increased focus on prevention and early recognition of children and adolescents in need of treatment seems crucial. The screening programmes was found to be useful for the detection of child psychiatric morbidity, thereby improving access to effective treatment.

**Dr. Mohd. Jamil Yaakob : Supervisor
Dr. Sarimah Abdullah : Co-Supervisor**

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THE ASSOCIATION BETWEEN DEMOGRAPHY, ANTHROPOMETRY, SERUM ESTROGEN AND BREAST DENSITY IN PATIENTS HAVING MAMMOGRAPHY IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction : Breast cancer is the most common cancer in female. Report from Malaysia National Cancer Registry (NCR) 2002 showed that breast cancer account for 30.4% of all cancers followed by cervical cancer (12.4%). Many contributing factors have been identified to increase the risk of developing breast cancer. One of the factors is breast density. Dense breast tissue by mammography is associated both with epithelial proliferation and with stromal fibrosis. The relationship between these histological features and risk of breast cancer may be explained by the known actions of growth factors (hormones) that are thought to play important roles in breast development and carcinogenesis. The risk might be partly due to masking of tumors by dense tissue. Other factors such as nulliparity, late age at first birth, younger age, parity, age and duration of menopause, body mass index, hormone replacement therapy and serum estrogen may potentially affect breast cancer risk through their indirect effect on breast density.

The aims of the study were to determine the characteristics of patients with mammography in Hospital Universiti Sains Malaysia and to determine the independent variables associated with breast density.

Methods and Materials : This study was a cross-sectional study conducted for one year duration from May 2004 to May 2005. Data were taken from patients who came for mammography in Radiology Department, Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan during the study period. Data from 84 patients were collected.

Results : Significant association noted between body mass index ($p=0.033$), parity ($p=0.002$) and breast density. Body mass index showed inverse relationship with breast density meaning that patients with higher body mass index had lower chance of being associated with dense breast. Results showed that for every one unit increase in body mass index, there is 0.86 times chance of association with dense breast. Inverse relationship also noted between parity and breast density. One unit increased in parity was associated with 31% reduction in chances of having dense breast (95% CI, risk reduction range from 12% to 46%). Serum estrogen however was not a significant independent variable for breast density.

Conclusion : Body mass index and parity but not serum estrogens were significantly associated with breast parenchyma when adjusted for potential confounding factors.

**Dr. Latifah Mohd. Basheer : Supervisor
Dr. Nik Hazlina Nik Hussain : Co-Supervisor**

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DUPLEX DOPPLER ULTRASOUND OF THE CEREBRAL VESSELS IN HEALTHY NEONATES BORN IN HUSM, KELANTAN : ESTABLISHMENT OF NORMAL VARIABLES MEASUREMENT

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MMed (Radioology)*

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Health Campus, Kelantan, Malaysia.**

Objectives : The aims of this study were to establish the mean and standard deviation of RI and PI values of both ACA and MCA in healthy term neonates born in HUSM, Kelantan and to compare it to the established data. This study who also done to determine the relationship of the RI and PI of both vessels with participant's demographic data such as gestational age.

Methodology : 95 healthy term neonates undergone duplex Doppler ultrasonography through the anterior fontanelle using a7.5MHz sector transducer from December 2004 to November 2005.

Results : For the Anterior Cerebral Artery (ACA): The mean (standard deviation) values of Resistive Index (RI) and Pulsatility Index (PI) are 0.71 (0.080), and 1.14 (0.215) respectively. For the Middle Cerebral Artery (MCA): The mean (standard deviation) values of RI and PI are 0.73 (0.096) and 1.18 (0.248) respectively.

Conclusions : The mean and standard deviation values of RI in the ACA determined from this study showed no statistical differences with three previous study and statistically significant different with another three published studies. No relationship observed with participants' demographic data including birth weight, head circumference, gestational age, postnatal age, oxygen saturation and heart rate with the RI and PI of both vessels.

**Dr. Noreen Norfaraheen Lee Abdullah : Supervisor
Assoc. Prof. Dr. Nurul Azman Ahmad Alias : Co-Supervisor**

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THE INCIDENCE OF MALIGNANT INFILTRATION IN HUMAN OSTEOSARCOMA BIOPSY TRACT

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MMed (Orthopaedics)

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Introduction : Osteosarcoma is the most common non-haemopoietic primary bone malignancy afflicting the young. Biopsy remains the gold standard in the confirmation of the diagnosis. The placement of the biopsy is of utmost importance as the tract is removed en bloc with the tumour during limb sparing surgery, with the assumption that it is contaminated by the tumour. Tissue conservation, to ensure adequate soft tissue cover, and preservation of function still remains a challenge for musculoskeletal oncology surgeons. This study aims to investigate the incidence of tumour infiltration in osteosarcoma biopsy tract, namely in the pseudocapsule, surrounding muscle, fascia, subcutaneous tissue and skin; in order to explore the margin of tumour infiltration for safe resection of the biopsy scar.

Patients and methods : This is a prospective cross sectional study, carried out from May 2003 to March 2005 at Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan. A total of twenty six cases which had undergone either limb salvage surgery or amputation by the Orthopaedic Oncology and Reconstructive Unit, School of Medical Sciences, University Science Malaysia, with the histopathological diagnosis of osteosarcoma were collected. The biopsy tracts were submitted as a whole and examined histologically for tumour presence.

Results : Of the 26 cases examined, twenty one cases (80.8%) did not show any tumour infiltration in the biopsy tract. One case (3.8%) had tumour infiltration in the pseudocapsule, two cases (7.7%) had infiltration to the muscle and another two cases (7.7%) had infiltration up to the subcutaneous tissue. None had skin infiltration

Prof. Dr. Zulmi Wan : Supervisor
Dr. Wan Faisham Nu'man Wan Ismail : Co-Supervisor

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COMPOSITION OF 148 URINARY STONES OF PATIENTS AT HOSPITAL ALOR STAR KEDAH

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Introduction : Urinary calculi disease is a common problem encountered in clinical practice worldwide. The term urolithiasis or urinary tract calculi are applied to a group of biominerals that are formed as a result of multifactorial process. Urinary calculi are crystals formed mainly of one or more of three components, oxalate, phosphate and urate.

Objective : The objectives of this study are to determine various clinical characteristic of the stone former in Hospital Alor Star. There are epidemiologic feature, presentation and urine investigation. We also want to determine urinary stone composition and to correlate this stone composition with urinary pH and radiological features.

Methodology : A cross sectional study was undertaken. One hundred and forty eight stone formers were recruited from Hospital Alor Star Kedah. The data as per study proforma were obtained from the surgical record of the stone former attending Surgical Department Hospital Alor Star Kedah from 1st July 2002 to 31st June 2003. The patient's urinary stone were collected. Surgical record and the first radiograph done for

kidney, ureter and bladder were then traced. Radiograph films were interpreted by a researcher, identifying the location, opacity and the size of stone. The urinary stone were sent to the FTIR laboratory, PPSK (Pusat Pengajian Sains Kesihatan) Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan.

Results : During the study period from 1st July 2002 to 31st June 2003, we consecutively collected urinary stones from 148 patients who fulfilled the inclusion criteria. The mean age of the study population was 53.9 (range 41-60 years). In this study, ninety patients (60.8%) were male and fifty eight (39.2%) were female. The racial distribution of the study subjects were 100 patients (67.6%) Malay and another 48 patients (32.4%) were from other ethnic groups (18 Chinese, 18 Indian and 12 were other ethnic for example Siamese and Bangladeshi. Eighty seven patients (58.8%) complained of pain whereas another sixty one patients (41.2%) were painless. Sixty patients (40.5%) had macroscopic haematuria. Forty six patients (31.1%) have had family history of urolithiasis while the other hundred and two patients (68.9%) had no such family history. Fifty eight patients (38.8%) had history of concurrent medical illness for example diabetes mellitus, hypertension and gouty arthritis. None of the patient or their family members have ever been investigated for genetic diseases that were associated with urolithiasis e.g Dent's disease, Batter's syndrome and X-linked hypophosphatemic rickets. Ninety four patients (63.5%) had upper tract stone, fifty two patients (35.1%) lower tract stone and two patient (1.4%) had both upper and lower tract urinary stone. The percentage of calcium oxalate (CaOx) in upper tract stone was 34% and in the lower tract stone was 9.6%. Upper tract stone had significantly greater amount of CaOx content compared to lower tract stone (P=0.036). In contrast, the percentage of uric acid in upper tract was 11.7% and in lower tract was 17.3%, suggesting that lower tract stone had significantly greater proportion of uric acid stone (P<0.05). Sixty out of one hundred forty eight subjects (40.5%) had positive urine culture. Among the patients who had positive urine culture 35.7% had urine pH of less than 5.9, 46.1% had urine pH of 6-7 and 34.1% had urine pH of more than 7. Pearson Chi Square shows no significant correlation. Sixty one (41.2%) subjects showed acidic urine (pH<7.0) and eighty three (58.8%) had alkaline urine (pH>7). Urinary pH was categorized into three groups i) <5.9, ii) 6-7 iii) >7. 18.9% of the subjects showed urine pH less than 5.9, 51.4% subjects showed urine pH 6-7 and 29.7% subjects had had urine pH of more than 7. Patients with uric acid stone were having urine pH of less than 5.9 and patient with CaO, CaO + CaP were having urine pH of 6-7. The correlation of urine pH with urinary stone constituent was statistically significant (p=0.006). Seventy urinary stones (47.3%) were radiopaque on radiograph finding, twenty four stones (16.2%) were radiolucent and 36.5% were faintly radiopaque. Majority of calcium oxalate stones were radiopaque (34.5%) but there were also radiolucent and faintly radiopaque on plain radiograph finding for calcium oxalate stone. Uric acid stone were seen faintly radiopaque in 20.4% of the urinary stones collected radiolucent in 16.7% of stones and radiopaque in 7.1% of stone. These correlation is found statistically not significance. The composition of most of the stone formers were calcium oxalate mixed with calcium phosphate, which accounted for 33.8%. 25.7% was pure calcium oxalate stone, 12.2% calcium phosphate stone, 13.5% uric acid stone and 14.9% struvite stone.

Conclusion : Accurate diagnosis is important as the diagnosis of "stone-former" has important life-style implications. Once the diagnosis is confirmed, management is dependent on the patient's symptoms, the size and location of the calculus, as well as the inter-calyceal anatomy. Therefore, the chosen imaging technique should not only have a high diagnostic accuracy but also provide a clear demonstration of the local anatomy. Ideally the investigation should also provide information on the nature or composition of the calculus. From this study, we noticed a lot of limitation of plain abdominal radiograph (KUB) in the diagnosis of stone as well as identifying the types of the injury stone. Despite this modest accuracy, the KUB is irreplaceable in the management of a known radiopaque ureteric calculus especially in planning fluoroscopically-guided, extracorporeal shockwave

lithotripsy (ESWL) or monitoring the progress of stone fragments after ESWL

Dr. Mohd Nor Gohar Rahman : Supervisor
Dr. Murali Mohan : Co-Supervisor
Dr. Mohan Nallusamy : Co-Supervisor



A COMPARATIVE STUDY BETWEEN SYRINGE PRESSURE IRRIGATION WITH NORMAL SALINE AND SIMPLE CLEANSING WITH TOPICAL POVIDONE IODINE FOR REDUCING POST OPERATIVE WOUND INFECTION

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Introduction : Cleansing of a contaminated wound using high pressure saline irrigation has been shown experimentally and clinically to be effective in decreasing bacterial and particulate matter as well as reducing wound infection rate. The use of topical 1% povidone-iodine solution has been advocated for cleansing post-appendicectomy wounds in Hospital Alor Setar for some time.

Objective : The objective of this study was to evaluate the effectiveness of syringe pressure irrigation with normal saline in the prevention of post-appendicectomy wound infection as compared to povidone iodine cleansing.

Patients and methods : A prospective study of 207 patients admitted to Department of Surgery, Hospital Alor Setar with the clinical diagnosis of appendicitis and undergoing appendicectomy was undertaken. After removal of the appendix and closure of external oblique aponeurosis, patients were randomized to receive one of the two wound cleansing methods.

Results : One hundred and nine patients were included in the saline irrigation group and 98 patients in the povidone iodine group. Out of 109 patients in the saline irrigation group, 5 patients (4.6%) had wound infection as compared to 11 patients (11.2%) who developed wound infection from the povidone iodine group. Demographic data and wound infection rate was compiled and analysed using SPSS version 11.0. Analysis suggested that there are no statistically significant differences in infection rates between the wound cleansed with topical povidone iodine and syringe pressure irrigation with normal saline. Although there is an increase in wound infection rate found in wounds cleansed with povidone iodine compared to syringe pressure saline irrigation, the difference is not statistically significant.

Conclusion : Syringe pressure saline irrigation can be an effective alternative for patients with hypersensitivity to topical povidone-iodine solution. In the present environment of cost-conscious health care delivery, there has been a trend towards using physiological solutions which are inexpensive, cost-effective, easily available and do not impair the wound healing process. This research support the use of saline wound irrigation as an alternative to povidone-iodine swabbing in an attempt to reduce wound infection rates. Further research should explore the combination of syringe irrigation with an antiseptic solution (povidone iodine) to see if a farther reduction in wound infection rate can be obtained.

Dr. Mohan Nallusamy : Supervisor
Dr. Zainal Mahamood : Co-Supervisor
Dr. Kamal Yatiban : Co-Supervisor



A CROSS-SECTIONAL STUDY ON THE PREVALENCE AND FACTORS CONTRIBUTING TO RECURRENT LARYNGEAL NERVE INJURY AND HYPOCALCAEMIA AFTER THYROIDECTOMY IN HOSPITAL UNIVERSITI SAINS MALAYSIA (1996-2003)

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Objective : Morbidity is today's concern in thyroid surgery. RLN injury and hypocalcemia are the two most common complications nowadays following thyroidectomy. This study evaluates the prevalence and factors contributing to these complications in patients submitted to thyroidectomy during 8 years period in our local setting that is HUSM.

Patients and methods : This study is a cross sectional review of all cases of thyroidectomy performed by General Surgeons in the University Hospital (U.S.M), Kubang Kerian, Kelantan for a period of eight years, from January 1996 to December 2003. The items of interest pertaining to this study, namely: the patients' characteristics; age, race and sex, the preoperative diagnosis, the FNAC results, the type or extent of operation performed, the experience of the surgeons, the structures which had been identified intraoperative, the histopathological results, the pre and post operative calcium levels, the results of the pre and post operative indirect laryngoscopy for recurrent laryngeal nerve status, the length of stay of the patients in the hospital and the follow up outcomes were recorded in a table form. The duration of complications, that is hypocalcemia and RLN palsy were determined from the follow up whether they were less than six months or more and were classified as temporary and permanent as permanent complications are when they persist for more than 6 months. The type of symptoms presented by the patients in case of hypocalcemia has also been included in the study. Lastly, the data obtained were then analyzed for prevalence of the morbidities and tested for statistical significance to determine the factors contributing to them. The data were further regrouped and univariate and multivariate analysis were carried out for each complication separately. Each complication was further divided into temporary and permanent and was then subjected to Univariate and multivariate analysis again.

Results : From January 1996 to December 2003, 492 patients were operated in HUSM for thyroidectomy. Eighty-five (19.9%) patients were having postoperative serum calcium less than 2 mmol/L. Out of them, fifty three (12.4%) cases were hypocalcemic for a period of less than 6 months and were labeled as temporary hypocalcemia and thirty-two (7.5%) cases were hypocalcemic for more than 6 months and were thus labeled as permanent hypocalcemia. Seventy-two (14.8%) had hoarseness of voice postoperative with sixty (12.3%) being less than 6 months duration and labeled as temporary RLN palsy and twelve (2.5%) being more than 6 months duration and labeled as permanent RLN palsy. There were no cases of bilateral vocal cord palsy. Sex, age and race were not factors which contributed to these complications. For hypocalcemia in general, the factors contributing were presentation of a patient and extent of operation while in RLN injury, they were presentation of patient preoperatively and structures identified intraoperatively. For temporary hypocalcemia, extent of operation and presentation of patient were significant, while in permanent hypocalcemia only extent of operation was significant. The factor contributing to temporary RLN injury was presentation of patient while structures identified intraoperative and final HPE results were contributing factors for permanent RLN injury. Our results favored STT or NTT rather than TT for bilateral benign diseases and hemithyroidectomy could be a very interesting alternative in malignant

diseases of young aged group if the other side was not involved. Finally we could appreciate that trainees under supervision in our institution were doing quite well as their morbidities were comparable to the senior surgeons but provided they were supervised.

Conclusion : Our results for RLN Injury and hypocalcemia were well within international accepted values. Presentation of patient preoperatively and extent of operation seemed to be the strongest contributing factors in hypocalcemia, temporary or permanent and presentation of patient, nerve identification and final HPE results were the strongest contributing factors in RLN injury, temporary or permanent. STT or NTT rather than TT were favored for bilateral benign diseases and hemithyroidectomy could be an interesting option in young patients having malignant disorder; if only unilaterally involved. Finally, trainees under supervision in HUSM were quite acceptable in performing thyroidectomies for selected cases; their good outcome might be due to selection bias of cases.

Dr. Myint Tun : Supervisor
Dr. Shwe Baw : Co-Supervisor
Dr. Mohammed Nor Gohar : Co-Supervisor

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THE CLINICAL PATTERN OF STAGHORN CALCULI TREATED IN HOSPITAL UNIVERSITI SAINS MALAYSIA AND THEIR OUTCOME

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Introduction : Urinary stone is a common problem encountered in clinical practice in Kelantan.

Objectives : This study is carried out to determine the epidemiology and outcome of staghorn calculi patients that were managed in Hospital University Sains Malaysia (HUSM).

Results : Between January 1995 and December 2003, there were 95 patients followed up in HUSM for staghorn calculi. The prevalence of staghorn calculi as observed in HUSM was 38.4 per 100 000 admissions. The commonest mode of treatment during that period was pyelolithotomy (60.5%). This was followed by percutaneous nephrolithotripsy (PCNL) (25.3%), nephrectomy (8%), nephrolithotomy (5.7%), extracorporeal shock wave lithotripsy (ESWL) (3.4%) and partial nephrectomy (1.1%). However towards the end of this study period there was a change in trend of management. Pyelolithotomy was being replaced by PCNL as a common mode of treatment for staghorn calculi. Post operative mortality rate was 1.1% (lease) with major and minor complication observed in 21(24.1%) cases and 29(33.3%) cases respectively. Residual stone were noted in 46(61.3%) cases which were further treated with various modalities. The common modes of treatment for residual stone were ESWL (52-2%) followed by stone chemolysis (37%), ureterorenoscopy (6.5%) and secondary PCNL (43%). Total of 39(52%) cases achieved stone free status. Out of these 39 cases, 3(7.7%) cases developed recurrence in long term follow up. About half of the patients (46%) had various degree of renal impairment at presentation. 6(7.1%) cases had further deterioration, 27.1% had improved renal function and other 65.8% had no change in renal function between 3 to 6 months post treatment. After 1 year follow up, we noted that, 4.8% of cases had deterioration in renal function, 32.3% improve and 62.9% of cases had static renal function.

Conclusions : In contrast to previous study done by Nazmi et al⁶⁴, Ac out come of staghorn calculi cases that were managed in HUSM from January 1995 to December 2003 were good and comparable with Western figures.

Dr. Mohammed Nor Gohar Rahman : Supervisor

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VASCULARIZED SOFT TISSUE ENGINEERED CONSTRUCTS: AN EXPERIMENTAL MODEL IN RATS.

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Introduction : Synthesizing autogenous tissue for use in reconstructive surgery will significantly decrease donor site morbidity and allow for greater flexibility in generating specific tissue to replace the anatomical defect. Tissue engineering has allowed us to experiment with various factors and scaffolding material to better our understanding regarding the interplay required to generate autogenous tissue.

Objective : In this experiment, we are trying to invent a model chamber for autogenous tissue synthesis.

Methods : The inferior epigastric vessels of twelve Sprague-Dawley rats were dissected out Lyostypt (medical grade bovine collagen) was wrap around each of the pedicle. Six of the rats had a muscle tissue taken from the ipsilateral rectus femoris muscle and transplanted between the pedicle and the lyostypt. The composite material was then placed into a modified silicon construct that was then placed subcutaneously in the rat's groin. The chambers were harvested at two weeks and at four weeks.

Results : All twelve pedicles were patent. There was new tissue formation surrounding the pedicle as observed by the presence of inflammatory cells, new blood vessels and replacement of the lyostypt by the host collagen. Mean weight of harvested tissues with muscle biopsy at two weeks and at four weeks were 0.17gms and 0.132 gms respectively (not statistically significant). Mean weight of harvested tissues without muscle biopsy at two weeks and at four weeks were 0.132 gms and 0.118 gms respectively (not statistically significant). Distance of tissue migration at two weeks and at four weeks were 1.949 and 2.874 respectively (statistically significant).

Conclusion : Using lyostypt as the scaffold, tissue could be generated in the modified silicon chamber. The distance of the newly generated vascularized tissue from the pedicle was statistically significant between the 2 weeks and the 4 weeks group. There was no difference in the composition of the vascularized tissue comparing between the group with the muscle tissue and the group without muscle tissue.

Prof. Dr. Ahmad Sukari Halim : Supervisor
Assoc. Prof. Dr. Hasnan Jaafar : Co-Supervisor

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A STUDY ON PAIN MANAGEMENT FOR ACUTE ORTHOPAEDIC FRACTURE IN EMERGENCY DEPARTMENT, HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction : Pain is the most common chief complaint of patients presenting to Emergency Department (ED). This is not surprising to anyone working in ED. What is surprising is the fact that emergency health care providers have not established themselves as champions in

the treatment of acute pain. Pain is not simply a signal for tissue injury, but also a signal to seek repair and recuperation.

Objective : The aim of this study is to assess the pattern of analgesics use for managing fracture pain of extremities and clavicles for adult patients; and determine the association between type of fracture (upper limb vs lower limb) with adequacy of pain management.

Methodology : A study was conducted from July to October 2005 in ED, Hospital Universiti Sains Malaysia (HUSM). All patients were triaged by the paramedic. Patients who fulfill the inclusion criteria were selected for the study. Paramedics in charge are the assistants; at the same time become the observer. The paramedic then completes the questionnaire before patients leave the ED.

Results : 42 patients were enrolled. 85.7% (n=36) were male and 14.3% were female with 97.6% Malays. Mean age is 29.6 years old. Only 4.76% (n=2) of doctors practice proper pain assessment. 71.4% (n=30) patients were given analgesics. Mean NRS before leaving the ED was 3.88; with 14.3% and 33.3% were in severe pain and moderate pain respectively. There was no statistically significant association between fracture sites and analgesic administration (p value=0.300). There was also no statistically significant association between fracture sites with adequacy of pain relief (p value= 0.902). The mean duration of time for analgesic administration was 34.67 minutes for those who were unable to achieve adequate pain relief, whereas for those who were able to achieve adequate pain relief was 57.22 minutes.

Conclusions : 71.4% of patients were given analgesics, yet 10% of them did not achieve adequate pain relief. Overall data analysis showed that before leaving ED, 14.3% and 33.3% patients were having severe pain and moderate pain respectively. We also identified that there was no statistically significant association between fracture sites and analgesics administration; no association between fracture sites and type of analgesic; and no association between fracture sites with adequacy of pain relief.

Dr. Rashidi Ahmad : Supervisor
Dr. Nik Hisamuddin bin Nik Rahman : Co-Supervisor

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THE EFFECTIVENESS OF SPECIFIC HEALTH EDUCATION IN PROVIDING BETTER QUALITY OF LIFE AMONG ASTHMATIC PATIENTS AT A PRIMARY CARE SETTING IN HUSM.

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Introduction : The global increase in asthma morbidity requires a closer examination on the aspects of asthma management. The cornerstone of asthma management is achieving adequate symptom control, better quality of life and patient education.

Objective : The aim of this interventional study was to evaluate the effectiveness of a specific health education programme in the asthmatic patients. An interventional study was enrolled among asthmatic patients in Klinik Rawatan Keluarga, HUSM from April 2004 through end of January, 2005.

Patients and Methods : A hundred and thirty asthmatic patients were recruited, 60 of whom were assigned to the intervention group and another 70 to the control group. The outcomes measured were the quality of life. The Malay version of Asthma Quality of Life (AQLQ) Questionnaire was used to assess the quality of life among the asthmatics. The intervention group attended the programme as scheduled which was conducted individually in the first health education and followed by group counseling of five to ten participants each in the second health education. They were carried out in an interactive way. The programme included information about asthma,

instruction on the appropriate use of medication and training in the metered dose inhaler (MDI) technique and information about the identification and control of asthma attacks and the recognition of early signs of exacerbation. The control group was submitted to the standard care provided at the clinic, with usual asthmatic advice regarding asthma control.

Results : The intervention group showed significant differences when compared to the control group with respect to the overall quality of life comprising of activity limitations, symptoms, emotional function and environmental stimuli. The global rating of each questionnaire also showed an increase number of those who scored 'better' in the intervention group compared to the control group. However, no significant differences observed in terms of PEFR measurements in the intervention group.

Conclusions : The educational programme led to a significant improvement in the quality of life of the asthmatics and the implementation of such programme is possible at the primary care level.

Dr. Harmy Mohamed Yusoff : Supervisor
Dr. Azmani Wahab : Co-Supervisor

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THROMBOLYSIS FAILURE WITH STREPTOKINASE IN ACUTE MYOCARDIAL INFARCT ECG CRITERIA – HUSM EXPERIENCE

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Introduction : Streptokinase has high thrombolysis failure rate despite being cheap and widely used in acute myocardial infarction. Electrocardiogram criteria using more than 50% reduction in ST elevation in the worst infarct lead predicted TIM I III flow with good sensitivity and specificity.

Objective : The primary objective of this study was to determine the failure rate of thrombolysis with Streptokinase in acute myocardial infarction using electrocardiogram criteria in Hospital Universiti Sains Malaysia (HUSM). The secondary objective was to compare the association between independent variables, treatment and outcome parameters with failure of thrombolysis with Streptokinase.

Patients and Methods : A total of 192 subjects were recruited into this retrospective cohort observational study.

Results : 109 patients (56.8%) has failed thrombolysis with Streptokinase. Seven variables were significantly associated with thrombolysis failure using Streptokinase in a univariate analysis including anterior location of myocardial infarct (p<0.001), longer symptom-to-needle time (p=0.01), longer door-to-needle time (mean 114 ± 82.9 min, p=0.03), history of hypertension (p=0.04), higher heart rate (mean 79.3 ± 18.3 beats per min, p=0.01), higher systolic blood pressure (mean 136.7128.9 mmHg, p=0.02) and higher diastolic blood pressure (mean 83.8 ± 20.9 mmHg, p=0.003). Five variables were associated with streptokinase failure as thrombolytic agent in multiple logistic regression analysis (backward stepwise method) including anterior location of -lyocardial infarct (p<0.001; OR 0.07, 95% CI 0.03 - 0.16), longer door-to-needle time (p=0.02; OR 1.01, 95% CI 1.00 - 1.02), diabetes mellitus (p=0.03; OR 3.13, 95% CI 1.13 - 8.69), hypertension (p=0.08; OR 2.06, 95% CI 0.92 - 4.60) and high total white cell count (p=0.03; OR 1.12, 95% CI 1.01 - 1.24). Both recurrent acute coronary syndrome (p=0.02; crude OR 2.49, 95% CI 1.16 - 5.32) and death after one year (p= 0.04; crude OR 7.61, 95% CI 0.95 - 61.24) were associated with increase in the rate of thrombolysis failure with streptokinase in univariate analysis.

Conclusions : The result of this study has shown that streptokinase

has higher failure rate of thrombolysis in acute myocardial infarction using electrocardiogram criteria in HUSM. History of diabetes mellitus, history of hypertension, anterior location of myocardial infarction, longer door-to-needle time and high total white cell count were highly predictive of increase in the rate of thrombolysis failure using streptokinase. This group of patients may benefit from other early reperfusion strategy including tissue plasminogen activators (tPA), PCI or CABG.

Dr. Tee Meng Hun : Supervisor
Prof. Madya Zurkurnai Yusof : Co-Supervisor

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DEPRESSION AMONG END STAGE RENAL DISEASE PATIENTS ON REGULAR HAEMODIALYSIS; COMPARING THE HAEMOGLOBIN, NUTRITIONAL STATUS, BLOOD PRESSURE CONTROL, FLUID INTAKE AND ADEQUACY OF DIALYSIS THERAPY BETWEEN THE DEPRESSED VERSUS THE NONDEPRESSED PATIENTS

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Introduction : Depression is the most commonly encountered psychiatric problem in patients with end stage renal disease (ESRD) and has been shown to have a significant impact on the morbidity and mortality of these patients. The prevalence rate of depression in ESRD patients on haemodialysis as quoted by Kimmel et al (1998) was 50%. Unfortunately there was no local data on the prevalence of depression in ESRD patients undergoing haemodialysis; hence this study was conducted to address this issue. The objective of the study was also to compare the differences in parameters such as haemoglobin, nutritional status, blood pressure control and adequacy of dialysis between the depressed versus the non depressed ESRD patients.

Methodology : This was a cross sectional study conducted on all ESRD patients undergoing haemodialysis in Hospital University Sains Malaysia (HUSM) and Renal Care dialysis centre. The subjects were interviewed using a validated Malay version of Hospital Anxiety and Depression Scale (HADS) questionnaire as a screening tool for depressive illness. The blood and dialysis parameters such as haemoglobin, serum iron, renal function, serum albumin, interdialytic weight gain and blood pressure were obtained and analyzed. Amount of dialysis delivered was measured by urea kinetic modeling (Kt/V).

Result : The local prevalence of depressive illness among ESRD on regular haemodialysis (using 11 as the cutoff point) obtained from this study was 56.8%. On univariate analysis, this study had shown a significantly lower haemoglobin level (10.4 vs 11.5; $p < 0.009$) and higher systolic blood pressure (149.0 vs 138.6; $p < 0.031$) among the depressed group as compared to the non depressed group of patients. Univariate analysis had also significantly showed more proportion of female in the depressed group as compared to the non depressed group (32.1% vs 24.7%; $p < 0.027$). On further analysis with multivariate analysis, the haemoglobin and systolic blood pressure control remain statistically significant with $p < 0.023$ and $p < 0.008$ respectively. Multivariate analysis had also significantly showed more proportion of diabetics had depression as compared to non diabetics with $p < 0.033$.

Conclusion : In conclusion, local prevalence of depressive illness amongst end stage renal disease patients on haemodialysis was comparable to previous studies. We also found that depressive state was significantly associated with lower haemoglobin level and higher systolic blood pressure. Diabetes was also shown to become an

independent risk factor of developing depression.

Assoc. Prof. Zainal Darus : Supervisor
Dr. Kamarul Imran : Co-Supervisor

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SURVIVAL ANALYSIS AND FUNCTIONAL OUTCOME AT 6 MONTHS IN SURGICAL TREATMENT OF SPONTANEOUS SUPRATENTORIAL INTRACEREBRAL HEMORRHAGE (ICH)

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Objectives : The aim of this study is to evaluate the role of surgery in patients with spontaneous supratentorial intracerebral hemorrhage and to identify predictors of outcome and survival including radiological, genetic, biochemical and treatment factors.

Study design and method : This is a prospective cohort study, involving patients with spontaneous supratentorial intracerebral hemorrhage, who fulfill the inclusion criteria for surgical evacuation of the hematoma. This study was conducted over a 13 month period, from February 2004 to March 2005. Surgery consisted of evacuation of hematoma using craniotomy and microsurgical techniques, as well as in some cases, a decompressive craniectomy. The ventriculostomy for intracranial pressure monitoring and drainage and regional cortical cerebral blood flow (rCoBF) monitoring and microdialysis were performed in all subjects. In addition, the association between Apolipoprotein E (APOE) e4 and outcome was also studied. The study end points were survival time and functional outcome at 6 months based on a dichotomised Glasgow Outcome Scale (GOS). GOS of 1-3 was defined as poor or unfavorable outcome and GOS of 4-5 was defined as good or favorable outcome. The selected clinical, radiological, genetic, biochemical and treatment factors that may influence the survival and functional outcome were analysed for its significance. The univariate analysis of the relation between various variables and GOS at 6 months were analysed using the chi-square test and the survival time was analysed using the Kaplan Meier and log rank test. In multivariate analysis, the binary logistic regression for functional outcome and Cox regression analysis for survival function were performed.

Results : 36 patients were recruited into the study during the period of February 2004 and March 2005. All of those were followed-up for a period of 6 months. There were 19 males and 17 females with age ranged from 39 to 76 years and a mean age of 58.6 (± 10.1) years and a median age of 61 years. 27(75%) patients had Glasgow Coma Score (GCS) between 5 to 8 on admission and 9(25%) were admitted with GCS of 9 on admission. The survival time ranged from 2 to 180 days with a mean survival time of 105.36 \pm 76.4 days. At 6 months, 20 (55.6%) patients had GOS I, 1 (2.8%) patient had GOS II, 10 (27.7%) patients had GOS III and 5 (13.9%) had GOS of IV. None of the patients in this study had GOS of V. The mortality rate at 6 months was 55%. 86 % had a poor or unfavorable outcome (GOS I-III) and 14% had good or favorable outcome (GOS IV-V). The study of Apolipoprotein E showed that the APOE e4 allele was not detected in all patients. In the univariate analysis for the functional outcome based on GOS, 3 significant variables were identified, the midline shift ($p=0.009$), regional cortical cerebral blood flow (rCoBF), ($p=0.034$) and tracheostomy status ($p=0.047$). The univariate analysis for survival function revealed that the regional cortical cerebral blood flow (rCoBF), ($p=0.0143$), midline shift ($p=0.0064$) and pupillary status on admission ($p=0.0016$) were significant predictors of survival function. The selected variables were then incorporated into models generated by

binary logistic regression and Cox regression analysis to identify significant predictors of functional outcome and survival function. Midline shift was the single significant predictor of functional outcome at 6 months (OR=20.8; 95% CI = 1.90-227.26; p=0.013), and the pupillary status was sole significant predictor of survival function (HR = 2.298; 95% CI 1.168 - 4.523; p=0.016). Patients with midline shift > 5mm has almost 21 times higher chances of being associated with poor outcome (GOS I-I-III) and patients with abnormal pupil on admission has 2.3 times risk of mortality compared to patients with normal pupillary reaction on admission.

Conclusion : Surgical treatment for spontaneous intracerebral hemorrhage in this group of patients only benefited a small number of patients in terms of favorable outcome (14%) and in the majority of patients (86%), the outcome was unfavorable. Patients with midline shift > 5mm has almost 21 times higher chances of being associated with poor outcome (GOS I-III) at 6 months and patients with an abnormal pupil on admission had an increase in mortality risk of about 2 times compared to patients with normal pupillary reaction on admission.

Prof. Dr. Jafri Malin Datuk Abdullah : Supervisor
Assoc. Prof. Dr. John Tharakan KJ : Co-Supervisor

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RISK FACTORS FOR AND ADEQUACY OF SYMPTOM CONTROL AMONG CHILDREN WITH ACUTE ASTHMA PRESENTING TO THE EMERGENCY DEPARTMENT HOSPITAL USM

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Objective : To determine the adequacy of asthma control among children with asthma presenting to Emergency Department Hospital USM and to identify the risk factors for frequent visits to Emergency Department for acute asthma and the risk factors for poorly controlled asthma.

Method : This is a cross sectional study, of 260 children between 5 to 12 years old who presented to the Emergency Department (ED) for acute asthma between September 2003 until May 2005 who requiring nebulised p2 agonist and were enrolled in this study. Parents who consented for the children were interviewed in the ED, pediatric clinic or pediatric ward depending on the availability of the investigator. All information including the demographic data, asthma history, medication history and risk factors for frequent presentation at the Emergency Department and for poorly controlled asthma were listed using a standard Proforma and entered into a computer database.

Result : Almost one third (27.2%, 71/260) of the children reported daytime asthma symptoms more than one per week in the previous 4 weeks. Thirty percent (30.4%, 79/260) and 22.7% (59/260) of the children reported nocturnal cough and nocturnal wheeze more than twice per month during the previous one month, respectively. Inhaled β_2 agonist was used at least once per week in 34.9% (66/189) of the children during the last one month. Overall, 15.4% (40/260) of the children required hospital admission in the previous one year and 2.5% (1/40) of them had more than one admission. Single emergency department visit was reported in 26.2% (68/260) of children and 73.9% (192/260) required at least one revisit to ED for the last one year. About half (50.9%, 114/224) of the children had school absenteeism at least one day in the previous one year. About one third of the children who reported having well controlled asthma were actually having persistent asthma according to the GINA guideline classification. The risk factors for frequent visit to ED were frequent use of β_2 agonist bronchodilator (OR= 16.76; CI 95% 6.56-42.83), family history of eczema (OR=2.67;

CI 95% 1.28-5.61), family history of asthma (OR=1.94; CI 95% 0.98-3.84) and poor compliance to treatment (OR=2.56; CI 95% 1.37-4.77). The risk factors for poorly controlled asthma were family history of asthma (OR=2.57; CI 95% 1.34-4.94), family history of allergic rhinitis (OR=2.05; CI 95% 1.03-4.08) and presence of allergic rhinitis (OR=2.78; CI 95% 1.32-5.82).

Conclusion : The children who present with asthma symptoms to the ED at HUSM are overall not well controlled. Many of them still are disturbed by day or nocturnal symptoms. The perception of asthma control differs between the parents and GINA guideline. Several factors for frequent ED visits were identified such as poor compliance to treatment, frequent use of β_2 agonist bronchodilator, family history of asthma and eczema. Presence of allergic rhinitis is also a risk factor for poorly controlled asthma along with family history of asthma and allergic rhinitis.

Prof. Quah Ban Seng : Supervisor

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

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Introduction : 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.

Study design and method : 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 infratentorial 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 Pco2 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 PtiO₂ 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 if larger cases were studied.

Prof. Jafri Malin Abdullah : Supervisor
Dr Ghazaim Ghazali : Co-Supervisor

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EFFECT OF COMMERCIALLY AVAILABLE VITAMIN E PREPARATIONS ON ARTERIAL COMPLIANCE AND SELECTED CARDIOVASCULAR PARAMETERS

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Doctor of Philosophy

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Introduction : Vitamin E is a potent lipid soluble antioxidant. It is the principal chain breaking antioxidant in human tissues, membrane and plasma. Vitamin E comprised of two families, the tocopherols and tocotrienols, each family is further divided into the alpha, gamma, delta and beta isomers.

Objectives : This PhD thesis aimed to address some of the unresolved issues on vitamin E use in vascular health.

Patients and Methods : For tocopherol, a randomised, crossed over, double blind, placebo controlled clinical trial involving 20 healthy post menopausal women was conducted to assess the effect of alpha tocopherol on arterial compliance, an index of vascular health in a group of high cardiovascular risk subjects who has no overt vascular disease. Subjects were randomised to either placebo or tocopherol 400 IU daily for ten weeks, before being crossed over for treatment for another ten weeks. At intervals of 5 weeks, subjects attended afternoon sessions where measurements of arterial compliance, blood pressure and plasma vitamin E level were taken.

Results : Mean age of these women were 54.59 ± 1.22 years. After 10 weeks treatment, plasma vitamin E level was 24.22 ± 2.1 / μ g/ml and 11.89 ± 0.68 / μ g/ml respectively with vitamin E and placebo ($p = 0.001$). There was no significant difference in pulse wave velocity [PWV] after ten weeks treatment with tocopherol compared to placebo, PWV values being 9.04 ± 0.29 m/s versus 9.14 ± 0.29 m/s respectively. Similarly, no difference in systolic and diastolic blood pressures was seen between placebo and vitamin E at the end of ten weeks. For tocotrienols, two clinical trials were conducted. The first study was a randomised, placebo controlled, blinded end point clinical trial with a parallel design involving 36 healthy male subjects. This study aimed to determine the effects of a normal preparation of tocotrienol rich vitamin E [TRE] on the primary parameter, arterial compliance as assessed by aortic femoral PWV. Other measurements taken were augmentation index [AI], plasma total antioxidant status [TAS], plasma vitamin E levels, serum total cholesterol [TC] and low density lipoprotein [LDL-C]. Subjects were randomised to four treatment, either placebo or TRE at doses of 80 mg, 160 mg, or 320 mg mixed tocotrienol daily for two months. The TRE contained 34.56%, 24.63%, 15.00% and 26.17% respectively of alpha-tocotrienol, gamma-tocotrienol, delta tocotrienol and alpha-tocopherol. Mean age of subjects were 23.28 ± 0.25 years. There were no significant differences between the groups in their change in PWV and AI with treatment

[ANOVA, $p = 0.467$ and $p = 0.092$ respectively]. There were also no significant differences between groups in other measurements taken. Group 160 mg however, showed a small but significant improvement in AI after treatment compared to baseline. The TRE capsules used in this study were well tolerated by subjects. The second clinical trial on TRE aims to determine the effect of three doses of a special formulation of tocotrienols (SF-TRE) [claimed to enhance tocotrienol absorption] on arterial compliance. This study was a randomised, placebo controlled, blinded end point clinical trial with a parallel design involving 36 healthy male subjects. Other measurements taken were AI, plasma TAS, plasma vitamin E levels, serum TC and LDL-C. Subjects were grouped into four groups, each group were prescribed either placebo, or SF-TRE at doses of either 50 mg, 100 mg, or 200 mg tocotrienols daily for two months. The SF-TRE contained 23.54%, 43.16%, 9.83%, 23.50% respectively of alpha, gamma, delta tocotrienol and alpha tocopherol. Mean age of subjects were 23.86 ± 0.39 years. There were no significant differences between groups in their change in PWV with treatment; change for each group being -0.06 ± 0.29 , -0.44 ± 0.20 , -0.77 ± 0.19 and -0.65 ± 0.14 m/s respectively for groups placebo, 50 mg, 100 mg and 200 mg [$p = 0.117$]. However, groups 100 mg and 200 mg showed significant improvement in PWV after treatment compared to baseline [$p = 0.007$ and $p = 0.002$]. Analysis of variance [ANOVA] for change in AI treatment was of borderline significance at $p = 0.048$, change for groups placebo, 50 mg, 100 mg and 200 mg being 2.22 ± 1.54 , -6.59 ± 2.84 , -8.72 ± 3.77 and -6.27 ± 2.67 respectively. However, post-hoc analysis showed a borderline p value of 0.076 between groups placebo and 100 mg. All treated groups showed significant improvement in AI after treatment compared to baseline. There were no significant differences between groups in the other parameters measured. The SF-TRE used was well tolerated by subjects.

Conclusion : Supplementary vitamin E for ten weeks at 400 IU daily increased plasma level of alpha tocopherol but has no effect on arterial compliance in healthy post menopausal women. For tocotrienol rich vitamin E, treatment with all groups treated with TRE and SF-TRE produced significant elevations of alpha, gamma and delta tocotrienols. The conventional preparation of TRE did not have an effect on arterial compliance in healthy male subjects. Overall, the SF-TRE also did not show significant effect on arterial compliance. However, there was a trend towards improvement in arterial compliance as suggested by the borderline significance value observed for the measurement of AI with SF-TRE. Significant within group improvement were also observed for all treated groups compared to baseline. Future studies to investigate the effect of TRE on arterial stiffness in patients with clinically manifest cardiovascular disease is suggested.

Prof. Abdul Rashid Abdul Rahman : Supervisor
Prof. Madya Dr. Zurkurnai Yusof : Co-Supervisor

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ANTI-NUCLEOSOME ANTIBODIES AS A DISEASE ACTIVITY MARKER IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction : The clinical aspect of measuring the level of anti-nucleosome antibodies in patients with systemic lupus erythematosus (SLE) has been well established and it is claimed that their presence is associated with the disease activity.

Objectives : The overall aim of this study was to measure the level of anti-nucleosome antibodies in the SLE patients, to determine the sensitivity as well as the specificity of these antibodies in the diagnosis

of the disease. The evaluation of the relationship between the levels of anti-nucleosome antibodies, the disease activity as well as and other markers (anti-dsDNA antibodies, C3, C4 and CRP) were also compared and assessed.

Patients and Methods : In this cross sectional study, all patients were selected from Hospital Universiti Sains Malaysia (HUSM), who were either attending the medical specialist's clinic or have been admitted to the medical wards. Ninety SLE patients, forty-five other connective tissue diseases (e.g., rheumatoid arthritis, mixed connective tissue disease, scleroderma, Raynaud's syndrome and Sjogren's syndrome) and ninety normal controls were tested for anti-nucleosome antibodies by enzyme linked immunosorbent assay (ELISA), anti-dsDNA and ANA by Immunofluorescence (IF), C3, C4 and CRP by immunoturbidometry techniques. SLE diseases activity was evaluated by using SLE-Disease Activity Index (SLEDAI) score. A patient is defined as having active SLE when SLEDAI score is more than 5.0.

Results : Out of 90 SLE patients, anti-nucleosome antibodies were positive in 52% of patients, whereas these antibodies were positive in 7% of patients with other connective tissue diseases. The median concentration of anti-nucleosome antibodies was significantly different between SLE patients and other connective tissue diseases. None of the normal controls was found to be positive for these antibodies. Anti-dsDNA antibodies were positive in 37% SLE patients, whereas these antibodies were positive in 8% of patients with other connective tissue diseases. None of the normal controls was found to be positive for these antibodies. ANA was found to be positive in 81% SLE patients, in 61% of patients with other connective tissue diseases and 7% in normal controls. Anti-nucleosome antibodies had a sensitivity of 52%, whereas anti-dsDNA antibodies had a sensitivity of 37%. The specificity of anti-nucleosome and anti-dsDNA antibodies was 98% and 97% respectively. ANA had sensitivity and specificity of 81% and 75% respectively. Anti-nucleosome antibodies were positive in 98% of patients with active SLE, whereas these antibodies were positive in 14% of patients with inactive SLE. The median concentration of anti-nucleosome antibodies was significantly different between active and inactive SLE patients. Anti-dsDNA antibodies were found to be positive in 61% of patients with active SLE and in 16% of patients with inactive SLE. Anti-nucleosome antibodies had a stronger correlation than anti-dsDNA antibodies with SLEDAI score. The median concentration of C3 and C4 was significantly different between active and inactive SLE patients, and showed an inverse and significant correlation with SLEDAI score, whereas the median concentration of CRP was not significantly different between active and inactive SLE.

Conclusions : Anti-nucleosome antibodies test is a recently developed test that may help in diagnosis of SLE patients. Anti-nucleosome antibodies are highly sensitive and specific for the diagnosis of SLE, especially when the anti-dsDNA antibodies are absent. Thus anti-nucleosome antibodies test can be a better tool for the diagnosis of SLE. Anti-nucleosome antibodies have a stronger and significant correlation with SLEDAI score than other traditional disease activity markers. Therefore, it can be a useful and additional disease activity marker to other laboratory tests that can help in the assessment SLE disease activity.

Dr. Che Maraina Che Hussin : Supervisor
Assoc. Prof. Dr. Kamaliah Mohd. Daud : Co-Supervisor

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**BILIRUBIN-URIDINE DIPHOSPHATE
GLUCURONOSYL TRANSFERASE (UGT1A1) GENE
MUTATIONS AMONG NEWBORN BABIES IN THE
MALAY POPULATION IN KELANTAN WITH
HYPERBILIRUBINAEMIA.**

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Introduction : Gilbert syndrome is caused by defects in the uridine diphosphate-glucuronosyltransferase 1A1 (*UGT1A1*) gene. These mutations differ among different populations and many of them have been found to be genetic risk factors for the development of neonatal jaundice.

Objectives : The objectives of this study were to determine the frequencies of the following mutations in the *UGT1A1* gene: A(TA)₇TAA (the most common cause of Gilbert syndrome in Caucasians), G71R (more common in the Japanese and Taiwanese populations) and G493R (described in a homozygous Malay woman with Crigler-Najjar syndrome type 2) in a group of Malay babies in Kelantan with hyperbilirubinaemia and a group of normal controls and to compare the frequencies of these mutations between these group.

Patients and Methods : The Gene Scan fragment analysis was used to detect the A(TA)₇TAA variant. Mutation screening of both G71R and G493R was performed using denaturing high performance liquid chromatography (DHPLC).

Results : Fourteen out of 55 neonates with hyperbilirubinaemia (25%) carried the A(TA)_yTAA mutation (10 heterozygous, 4 homozygous). Seven out of 50 controls (14%) carried the mutation (6 heterozygous, 1 homozygous). The allelic frequencies for hyperbilirubinaemia and control patients were 16% and 8% respectively (p = 0.20). Heterozygosity for the G71R mutation was almost equal among both groups (5.5% for hyperbilirubinaemia patients and 6.0% for controls; p = 0.61). One subject (1.8%) in the hyperbilirubinaemia group and none of the controls were heterozygous for the G493R mutation (p = 0.476).

Conclusions : The A(TA)₇TAA seems more common than the G71R and G493R mutations in the Malay population in Kelantan. Even though the allelic frequency of the A(TA)₇TAA mutation in the hyperbilirubinaemia group was twice that of the non hyperbilirubinaemia group, the difference did not reach statistical significance.

**Assoc. Prof. Dr. Hans Amin Van Rosternberghe :
Supervisor**
Dr. Narazah Mohamad : Co-Supervisor

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**AGE-RELATED CHANGES IN THE OXIDATIVES
STATUS AND ANTIOXIDANT CAPACITY IN
DEFFERENT BRAIN REGIONS OF SPONTANEOUSLY
HYPERTENSIVE RAT**

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Introduction : Oxidant/antioxidant imbalance has been implicated in the pathogenesis of neurological disorders associated both with aging and hypertension.

Objectives : We determined oxidative status and antioxidant capacity in a time-course manner in the cerebral cortex (CC), cerebellum (CB) and brain stem (BS) of spontaneously hypertensive rats (SHR) and Wistar-Kyoto rats (WKY).

Methodology : Six animals from WKY and SHR strains were sacrificed at 8, 16, 24, 32, 40, 48, 56 and 64 weeks of age after measuring their blood pressure and body weight. CC, CB and BS were dissected out, homogenized and used for the following estimations : thiobarbituric acid reactive substances (TBARS), protein carbonyl (PCO), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR), glutathione S-transferase

(GST), reduced glutathione (GSH), oxidized glutathione (GSSG), total antioxidant status (TAS) and membrane-bound enzymes activities (Na, K -ATPase, acetylcholinesterase - AChE).

Results : SHR showed higher blood pressure and lower body weights at all time points studied. When compared to control, TBARS from week 24 and PCO from week 32 onwards increased significantly in all brain regions of SHR. GSH content and GSH/GSSG ratio were lower in SHR from weeks 16 and 24 onwards respectively in all brain regions. TAS and activities of SOD and GST were significantly decreased in all brain regions from 24 weeks onwards in SHR. GPx activity showed significant decrease in CB and BS from week 24 and CC from week 56 onwards in SHR. CAT activity was significantly lower in CB from week 32 and CC from week 56 onwards in SHR. There was no difference in CAT activity in BS at all time points studied. GR activity showed significant decrease in CC, CB and BS from weeks 48, 16 and 24 onwards respectively in SHR. Na⁺,K⁺-ATPase showed significant decrease in its activity from week 32 onwards in all brain regions of SHR. AChE activity was significantly lower in CC, CB and BS from weeks 24, 32 and 48 onwards respectively in SHR. All three brain regions had similar SOD activity. BS of WKY and SHR had significantly higher TAS, activities of CAT and GPx. and lower TBARS and PCO levels in comparison to CC. Similar PCO levels and GPx activity were found in CB and BS, but significantly higher TAS and CAT activity, and lower TBARS levels were found in BS compared to CB. However, GSH contents, GSH/GSSG ratio and activities of GST and GR were significantly lower in BS compared to CC and CB. CC and CB had similar TBARS and PCO levels, GSH contents and TAS, but activities of GPx, CAT and GR were significantly lower in CC compared to CB.

Conclusions : It is suggested that the brain regions toward oxidative stress is in the order: CCB>BS>BS. Along with progression of hypertension, there is increased oxidants level and decreased antioxidants capacity with alteration in membrane-bound enzymes activities in CC, CB and BS of SHR. Thus, oxidative stress may play a role in hypertension-associated neurological diseases.

Dr. K.N.S. Sirajudeen : Supervisor
Assoc. Prof. Nor Akmal Wahab : Co-Supervisor

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EFFECT OF ETHANOL EXTRACT OF ANDROGRAPHIS PANICULATA (BURM.F.) NEES ON STREPTOZOTOCIN-INDUCED DIABETIC FEMALE RATS

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Introduction : Diabetes mellitus (DM) is a chronic disease, characterised by hyperglycemia and other metabolic abnormalities. Insulin resistance is believed to be one of the pathogenic factors in the development of diabetic complications. Most published data showed that both of aqueous and ethanol extract of *Andrographis paniculata* (AP) which were prepared via freeze dried vacuum technique, have strong antihyperglycemic effect in the short term to reduce blood glucose level in STZ-induced diabetic male animals. However, studies of long term effects (six weeks) of AP ethanol extract which prepared via spray dried technique on female diabetic animal is not only essential but of significant importance.

Objectives : The main objective of this study is to evaluate the standardized of 95% AP ethanol extract on streptozotocin (STZ)-induced female Sprague Dawley (SD) rats and on estrous cycle of normal female SD rats.

Methodology : In this concurrent control study, female rats with

regular estrous cycle were selected and randomly divided into five groups. The normal and diabetic control groups were given carboxyl methyl cellulose (CMC) 2% as vehicle. Other three diabetic groups were treated orally with 95% AP ethanol extracts at doses 50, 100 and 200 mg/kg/day respectively for 42 days. The rats body weight, fasting blood glucose and fasting serum insulin level were measured and daily estrous cycle evaluations were performed. At the end of experiment, rats were fasted overnight and sacrificed after anaesthetised. Then, blood sample were taken for serum insulin level determination and their pancreases were removed for histological examination.

Results : The survival percentages of AP-treated diabetic groups were seen to increased dose dependently. The fasting blood glucose level were not significantly difference (p>0.05) in AP-treated diabetic group compared to diabetic control group after treatment with 95% AP ethanol extract for six weeks. Diabetic rats treated with 100 mg/kg 95% AP ethanol extract, showed significant decreased (p<0.05) in the fasting serum insulin level compared to diabetic control group. Endocrine cells densities were significantly increased (p<0.05) in 50 mg/kg AP-treated diabetic rats compared to both diabetic and normal control groups. Histological examination of diabetic rats pancreas, showed recovered from hydropic degeneration in the islet cells of Langerhans after treatment with 100 mg/kg 95% AP ethanol extract compared to diabetic control group. Meanwhile, normal female SD rats which were given 95% AP ethanol extract at doses 10, 100 and 1000 mg/kg/day for 21 days, showed no significant difference (p>0.05) in the percentage of weight gain, wet weight of reproductive organs, estrous cycle, serum insulin and serum progesterone levels compared to normal control group (CMC 2%). However, serum FSH and serum LH levels were significantly decreased (p<0.05) in all three doses of 95% AP ethanol extract compared to normal control group. Only, 95% AP ethanol extract at dose 1000 mg/kg showed significant decreased (p<0.05) in serum 17p-estradiol level compared to normal control group.

Conclusions : Based on experimental findings and available data it is suppose that 95% AP ethanol extract have no antihyperglycemic effect in STZ-induced diabetic rats and not to disturb estrous cycle in normal female SD rats. However, 95% AP ethanol extract show some abilities of increasing the survival percentage of diabetic rats, repaired hydropic degeneration of endocrine cells due to STZ action and increasing endocrine cells densities in the islet of Langerhans of STZ induced diabetic rats.

Prof. Syed Mohsin Sahil Jamalullail : Supervisor
Assoc. Prof. Dr. Siti Amrah Sulaiman : Co-Supervisor

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PSYCHOLOGICAL PREDICTORS OF INJURY AMONG MALAYSIAN PROFESSIONAL FOOTBALL PLAYERS

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Doctor of Philosophy

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Introduction : Injury is common occurrence in many sports and games. Sportsmen get injured either by accident or intentionally by other players. There are many factors responsible for injuries in sports, of which psychological factors are one, and an important one. Many studies have shown the impact and influence of psychological characteristics of athletes in determining risk of injuries and rehabilitation.

Objectives : The objectives of this study was to determine psychological profiles of footballers, to document injury profiles, and to identify psychological predictors of injury occurrence among footballers involved in the Malaysian Professional Football League.

Methodology : A prospective research design was used in this study.

Psychological profiles of the subjects were determined using a validated questionnaire. In addition, a pilot study was carried out to test the validity and reliability of the questionnaire. A cluster sampling method was used, in which all teams were grouped into five clusters; North, South, East and West of Malaysia and East Malaysia (Sabah and Sarawak). Two teams from each cluster were randomly selected and all 25 registered players in each team were taken as the study samples. A total of 250 players were selected. The subjects were then instructed to answer the questionnaire. This procedure was repeated for all subjects throughout. In addition, an interview was conducted with players who were injured during or after the game. Data were entered and analysed using Statistical Package for Social Science version 11.0. Significant differences in the mean score between injured and non-injured subjects were determined by logistic regression. Psychological predictors were derived by performing multivariate logistic regression.

Results & Conclusions : Univariate analysis, significant differences in the mean score of psychological profiles between the injured and non-injured players were observed in self-esteem, reboundability, ability to handle pressure, level of confidence, and motivation. However, after multivariate analysis, only self-esteem, level of confidence, and motivation were found to be predictors of injury among Malaysian football players involved in Malaysian Professional Football League.

Assoc. Prof. Dr. N. Kumaraswamy : Supervisor
Assoc. Prof. Dr. Mohamed Rusli bin Abdullah : Co-Supervisor

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A STUDY OF THE CONTRACEPTIVE PROFILE OF TRADITIONAL HERBAL PREPARATIONS OF THE ORANG ASLI TEMIER GROUP

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Doctor of Philosophy

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Introduction : Research and development to seek for new contraceptives are necessary to fulfill the requirement of the population at large. Studies to authenticate and evaluate three herbal contraceptives belonging to Orang Asli Temier Group were performed. The herbs were *Lepidagathis longifolia* (P1), *Palaquium sp.* (P2) dan *Phyllagathis rotundifolia* (P3). Traditionally, a combination decoction of the three plant species was consumed monthly for three to five consecutive days before the commencement of each anticipated menstrual period or the individual plant species could be consumed daily.

Objectives & Methodology : The water-based extract of the combined herbal formulation (EP123) and the individual plants (EP1, EP2 and EPS) were given to pregnant, pseudo-pregnant and non-pregnant rats.

Results : The combined herbal extract (EP123) caused reduction in maternal body weight, fetal resorption, fetal death, prolongation of duration of pregnancy and failure of delivery. No teratogenic effects were observed. EP123 significantly reduced plasma estradiol concentration and inhibited decidual formation in pseudo-pregnant rats. EP1, EP2 and EPS did show a similar effect, however they were less potent compared to EP123. The herbal extracts caused anovulatory and prolongation of estrus cycle. EP123 reduced the estradiol, progesterone, FSH and LH concentrations. EP1 and EP2 reduced the estradiol while maintaining progesterone concentrations. EP3 reduced estradiol concentration but increased the progesterone concentration. The ratios of estradiol : progesterone concentration were reversed, mimicking a pseudo-pregnancy state. Histological examination of the uterus revealed the presence of corpora lutea and atretic ova. The ratios of uterine endometrial : muscular thickness were increased and peaked

in animals that received EPS. The cell density and mean cell area of the folliculotroph were reduced in herbal treated animals.

Conclusions : The anovulatory cycle was a reversible phenomena upon cessation of treatment, however the recovery was slow. Administration of eCG followed by hCG stimulated ovulation in all EP123 treated animals. These findings supported the use of the three herbs as contraceptive and the possible mode of action was through the mimicking of a pseudo-pregnancy state in non-pregnant rats. Current findings suggested that P3 was the best candidate for contraceptive development. P3 has a strong antiestrogenic and progestogenic effects. EP123 was a potent antiestrogenic and a weak progestogenic agent. The administration of EP123 before each menses can reveal its abortifacient properties.

Prof. Amar Chatterjee : Supervisor
Prof. Syed Mohsin Sahil Jamalullail : Co-Supervisor

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STUDIES TO INVESTIGATE REPRODUCIBILITY OF MEASUREMENT PARAMETERS AND FACTORS INFLUENCING MEASUREMENT OF POSTOCCLUSIVE REACTIVE HYPEREMIA IN FOREARM SKIN MICROCIRCULATION

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Introduction : A standardized technique to noninvasively assess skin microvascular function *in vivo* has not been fully developed, so is the analysis of the response it produced.

Objectives : The aim of this thesis was to establish an optimized and reproducible method and analysis of responses from postocclusive reactive hyperemia (PORH) in forearm skin measured using laser Doppler fluximetry monitoring (LDF). The objectives were: [1] to investigate the influence of occlusion duration on PORH+LDF measurement model (optimization study); [2] to determine the reproducibility of several different laser-Doppler-derived PORH parameters (reproducibility study); [3] to characterize the "effective" occlusion duration in subjects with differing age, gender and menstrual phases (characterization study).

Methodology : In the optimization study, 20 healthy male volunteers aged 21-30 years old were studied on 3 separate days in a randomized study manner. The volunteers were then randomized to receive 1, 2 or 3 min occlusion on 3 different days. Skin perfusion was measured before, during and after occlusion using LDF. The magnitude and temporal courses of PORH were expressed as $PORH_{max}$ (absolute maximal increase in hyperemia perfusion) and T_p (time-to-peak), respectively. Eighteen males were recruited in the reproducibility study. Forearm blood flow was occluded for 3 min. Parameters studied were $PORH_{max}$, T_p , $PORH_{peak}$ (amplitude of peak perfusion), $PORH\%$ (percentage of hyperemic response) and $PORH_{max/tp}$ (mean velocity of hyperemia increase). Measurement was performed twice within each study day for 2 study days. Coefficient of variation (CV) and intraclass correlation coefficient (ICC) were calculated for each parameter. In the characterization study, 120 subjects were studied (20 subjects each in the age ranges of 21-30 years, 31-40 years, 41-50 years for both genders). Similar study protocol as in the optimization study was applied. Males were studied for 3 study days. Female came for 6 study days: the first 3 days was performed during low estrogenic phase (days 2-5 of menstrual cycle) and subsequent 3 visits were done during high estrogenic (days 10-13).

Results : In the optimization study, significant difference ($p < 0.001$) in PORH changes were shown between 1 min ($PORH_{max} 15.39 \pm 1.27$ AU; $T_p 9.16 \pm 0.43$ s), 2 min ($PORH_{max} 24.84 \pm 1.62$ AU; $T_p 12.56 \pm 0.56$

s) and 3 min occlusion duration ($PORH_{max} = 32.14 \pm 1.73$ AU. $T_p = 14.17 \pm 0.61$ s). Three min occlusion produced significantly greater $PORH_{max}$ and T_p changes. Analysis using ICC showed that all studied parameters, except for $PORH\%$, demonstrated excellent reproducibility for within- and between-day measurements. Satisfactory intraday and interday CVs were obtained for these parameters (intraday, interday CVs for each parameter: $PORH_{max}$ 4.77, 6.50; T_p 8.89, 6.87; $PORH_{peak}$ 6.50, 8.70; $PORH_{max/tp}$ 10.64, 10.65, respectively). The $PORH_{max}$ and T_p values were the most reproducible magnitude- and temporal-based parameters, respectively. The characterization study showed that for the $PORH_{max}$ analysis, the occlusion duration should be applied based on age, gender and menstrual phase. $PORH$ response was more homogenous during high estrogenic phase with 2 min found as the "effective" occlusion duration in all female groups. Three min occlusion produced the most significant change in all age ranges in both genders in T_p analysis and it was irrespective of menstrual phase.

Conclusion : These studies revealed a dependence of $PORH+LDF$ response on occlusion duration. $PORH_{max}$ and T_p were the most reproducible $PORH$ indices. The occlusion duration applied during the measurement of $PORH_{max}$ was influenced by age, gender and menstrual phase factors. The measurement based on T_p was however independent of these factors.

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THE ROLE OF THE CELL SURFACE PROTEINS OF BURKHOLDERIA PSEUDOMALLEI IN THE SERODIAGNOSIS OF MELIOIDOSIS AND COMPARATIVE SEROLOGICAL PROTEOMIC ANALYSIS OF THE HUMORAL IMMUNE RESPONSE IN MELIOIDOSIS

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Introduction : Melioidosis refers to an infection by the bacterium, *B. pseudomallei*, affecting man and animals. Clinical manifestations are protean, ranging from mild and self-limited diseases to progressive multi-organ infection with fatal consequences, if untreated. Treatment with prolonged course of antibiotics is required for the acute infection and the prevention of development of persistence of infection and relapse. The diagnosis based on clinical evidence is a challenging task, as the presenting symptoms mimic many other common infectious diseases. Direct isolation remains the mainstay in the laboratory diagnosis for melioidosis although it is less sensitive and time consuming. Over the last two decades, many experimental approaches towards the development of a reliable serological assay for rapid serodiagnosis of melioidosis have been reported. However, these attempts were often met with limited success.

Methodology : In the present study, a standardized protocol of dot enzyme immunoassay (dot EIA test) with two optimized concentrations of the cell surface proteins (CSP) antigens from *B. pseudomallei* was established for serological diagnosis of melioidosis by detecting the IgM, IgG and IgA antibody isotypes as markers for current infection.

Results : The sensitivity of the dot EIA test for the detection of IgM, IgG and IgA antibody isotypes individually were 47.7%, 89.2% and 60% respectively. However, the overall combined detection of the IgM, IgG and IgA antibody isotypes improved the sensitivity and specificity of the dot EIA test to 95.5% and 92.5%, respectively. In addition, the dot EIA performed satisfactorily in the prospective study for the diagnosis of melioidosis by detecting the IgM, IgG and IgA antibody

isotypes in the sera tested from clinically suspected cases of melioidosis. The preliminary finding from this study demonstrated for the first time the potential use of the CSP of the *B. pseudomallei* as a source of antigens in the dot EIA test for early and accurate diagnosis of melioidosis by detecting the IgM, IgG and IgA antibody isotypes in the patient's serum. Characterization of the SDS-PAGE separated CSP antigens by conventional Western blot (WB) analysis revealed 25 antigenic bands recognized by melioidosis sera with variable frequency and intensity. When the patterns of the antigenic bands were compared between the 55 sera from melioidosis patients, no single pattern was found to be diagnostically adequate. Great diversity in the humoral immune response against the CSP antigens was observed in each of the melioidosis patient during the time course of the infection. The heterogeneous antigenic protein profiles observed in the WB assay were categorized into three clusters of antigens. These included broadly diffused antigenic bands with the molecular weights ranging from 43 kDa to 36.8 kDa (cluster 1), regularly spaced antigenic bands with molecular weights ranging from 35.6 kDa to 25 kDa (cluster 2), and low molecular weights antigenic bands with molecular weights ranging from 22 kDa to 13.2 kDa (cluster 3). Some degree of comparable cross-reaction was observed between normal sera and non-melioidosis patients sera from endemic regions against the antigens in cluster 1. However, the endemic sera showed very limited cross-reactions with the antigens in the clusters 2 and 3.

Discussions : These data suggested that healthy individuals and non-melioidosis patients in endemic regions possessed antibodies specific to the CSP reflecting significant degree of background immunity to melioidosis. Although the reactivity of the non-melioidosis and melioidosis sera were not distinguishable in the WB analysis especially against the antigens in the cluster 1, whether the non-melioidosis and melioidosis sera recognized similar and different epitopes present in the same antigens remains to be elucidated. In serological proteomic study, the CSP was fractionated based on molecular charge in preparative Rotofor isoelectric focusing (IEF) and polyacrylamide gel IEF (PAGE IEF). Fractionation in the preparative Rotofor IEF produced 20 rotofor fractions. A new protocol to perform immunoblotting of the proteins separated by PAGE IEF gel was developed. The IEF immunoblot analysis of the 20 rotofor fractions with pooled melioidosis sera demonstrated presence of several strongly reacting bands located at the pi values approximately 4 to 6.5. Preliminary analysis was performed to determine the antigenic composition in the selected reactive rotofor fractions number F16 and F7 by PAGE IEF method. The fractionated proteins in the gel matrix were extracted in adequate quantity by sonication for subsequent analysis. Preliminary analysis by SDS-PAGE of the extracted proteins revealed the existence of the isoforms protein antigens and successful enrichment of the hidden low abundance antigenic proteins present in the CSP that otherwise may not be possible to detect by the conventional WB analysis. The purified proteins extracted from the selected fractions from IEF study showed strong and specific reaction with pooled melioidosis sera. These antigens can be used along with the antigens identified by the conventional WB assay of the CSP separated by SDS-PAGE to develop an improved multi-antigens based diagnostic assay for melioidosis.

Conclusions : This work would clearly be relevant for the development of newer serologic tests for diagnosis for melioidosis. Elucidation of the pathological mechanism in melioidosis disease progression and recovery, exposition of more antigenic components for diagnostic application and development of vaccine for melioidosis would be other spin offs.

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EXPRESSION OF RETINOID X RECEPTORS (AND) IN AUTOIMMUNE DIABETES

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Introduction : The non-obese diabetic (NOD) mouse is an animal model of autoimmune diabetes. type 1 diabetes mellitus (T1DM) that spontaneously develops autoimmune diabetes between the ages of 9 to 30 weeks of life. The major pathological event in these mice is mononuclear cell infiltration into the islets of Langerhans, known as insulinitis. mainly by macrophages, T lymphocytes and B lymphocytes. Retinoid X receptor (RXR) plays an important role in regulating the morphogenesis, development, growth and differentiation of cell and may be involved in the regulation of immune response. It also acts as a major heterodimer partner with other nuclear receptors such as PPARs, RAR and VDR.

Objectives : The aim of this study was to analyze the mRNA expression of two RXR isoforms in splenic T lymphocyte CD4⁺ and CD8⁺ of NOD mice using quantitative real time polymerase chain reaction.

Methodology : Splenic CD4⁺ and CD8⁺ T cells were isolated from three groups of NOD mice. specifically five week old (NOD5), nine week old (NOD9) and diabetic group (dNOD). Total RNA was isolated and cDNA was synthesized from each cell subset. The same procedures were also carried out on groups of the non-obese resistance (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 RXR isoforms in each subset of T lymphocytes were quantified by real time PCR using specifically developed homologous internal standards for each RXR isoform. In addition, the levels of RXR proteins in the pancreas of both NOD and NOR mice were also studied using immunohistochemistry.

Results : This research demonstrated that RXR_α and RXR_β were differentially expressed in the splenic CD4⁺ and CD8⁺ T cells. RXR_α mRNA expression was found to be significantly decreased in both CD4⁺ and CD8⁺ T cells of NOD mice compared to NOR mice at pre diabetic stage but decreased at diabetic stage. These findings suggest that alterations of mRNA expression of both RXR subtypes may be important in the development and progression of T1DM. Meanwhile, only RXR_β protein was observed in both NOD and NOR mice at pre diabetic and diabetic stages, whereas RXR_α was not detected.

Conclusions : The expression of RXR_α protein was observed only in the islets of Langerhan and not in the acinus cells in the pancreas, suggesting that only this type of RXR receptor isoform plays a significant role in the physiology of the pancreas.

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