Abstracts

Abstracts of Theses Approved for the PhD/ MSc at the School of Medical Sciences, Universiti Sains Malaysia Health Campus, Kubang Kerian, Kelantan, Malaysia

ANALYSIS OF GENETIC POLYMORPHISME IN TYPE II DIABETES MELLITUS AMONG MALAYS: RISK FACTORS AND PHARMACOGENETIC STUDY

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Introduction: Type 2 diabetes mellitus (T2DM) is the most common type of diabetes disorder. T2DM arises from a combination of environmental and genetic factors. Genome wide association studies have found several single nucleotide polymorphisms in different genes such as SLC30A8, TCF7L2, FTO, KCNQ1, HHEX, and CDKN2A/2B associated with risk factors of T2DM. Although sitagliptin is known as an effective oral antidiabetic agent, some patients do not respond to it and fail to achieve a desirable glucose level.

Objectives: This study attempted to investigate the association of genetic polymorphisms in SLC30A8, TCF7L2, FTO, KCNQ1, HHEX, and CDKN2A/2B with T2DM and the response to sitagliptin among Malaysia's Malay population.

Methods: T2DM patients (n = 180) aged 18 years and above as well as healthy subjects (n = 180) were recruited following institutional ethical approval. All patients signed written informed consents. Out of 180 T2DM patients, 113 patients with uncontrolled glucose level were enrolled for 6 months to sitagliptin in addition to their previous medication (metformin and sulphonylureas). Lipid profiles, liver and renal function tests, fasting plasma glucose, and HbA1c at baseline and after 6 months of sitagliptin therapy were determined using commercially available kits. Response to sitagliptin was defined as HbA1c reduction of more than 0.5% from baseline following sitagliptin therapy.

Results: Genomic DNA was extracted from whole blood using a commercial kit. A total of 18 single nucleotide polymorphisms in SLC30A8, TCF7L2, FTO, KCNQ1, HHEX, and CDKN2A/2B were screened using the minisequencing method. The risk association of 18 single nucleotide polymorphisms with T2DM and association of these SNPs with response to sitagliptin were analyzed using the logistic regression test. Significant differences in the frequencies of CT genotype of rs7901695, AC genotype of rs8050136, and GG genotype of rs7923837 between T2DM and control groups were observed. Findings from this study show that people with GG genotype of HHEX (rs7923837) showed 2.32 odds or chances to get type 2 diabetes compared to AA genotype (OR: 2.32 (95% CI 1.07–5.03), P = 0.033). The other 17 single nucleotide polymorphisms were found to be not associated with T2DM risk in this population. Out of 113 T2DM patients, only 93 patients finished the sitagliptin therapy for 6 months. After 6 months of sitagliptin therapy, 47 (50.53%) of the patients achieved a reduction of HbA1c by more than 0.5% and were considered as responders. T2DM patients with AG genotype of HHEX, rs1111875 and CT genotype of rs7903146 showed lower odds or chance to respond to sitagliptin compared to the reference genotype (OR = 0.33 (95% CI 0.11–0.99), P = 0.045) and (OR = 0.15 (95% CI 0.03–0.72), P = 0.018), respectively. In addition to that, the eGFR level was found to be significantly associated in response to sitagliptin (OR = 0.93 (95% CI 0.89–0.98), P = 0.012).

Conclusion: This study supports the hypothesis that SNPs in HHEX (rs7923837) is associated with susceptibility of risk to T2DM among Malaysia's Malay population. The eGFR level, SNPs rs1111875 (HHEX), and rs7903146 (TCF7L2) were found to be a predictive factor for response to sitagliptin.

Supervisor:
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THE NEURAL CORRELATES AS PREDICTORS OF MENTAL TOUGHNESS IN UNIVERSITY TEAM GAME ATHLETES DURING VIRTUAL PENALTY SHOTS

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Introduction: Currently, no comprehensively valid and reliable measure of mental toughness (MT) exists and this demands further work in order to develop a conceptually sound and multifaceted MT measure. The athletic performances exhibited by the mentally tough athletes in terms of increased precisions in executing superior performance are known to reflect their level of perception, anticipation and decision making.

Objective: This study aimed to develop a novel approach to the assessment of MT for penalty shots sports from amongst university student athletes by coherence analysis using event related potentials (ERPs) for neural correlates as the predictors of MT status and participants' performances for the tasks. To the best of our knowledge, this study is the first to use ERPs as an MT assessment measure.

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Methods: The study design was divided into two phases. Phase 1 consisted a MT questionnaire 48 (MTQ48) completion (n = 310 participants) for validity and reliability; and Phase 2 consisted of ERPs visual paradigm that featured penalty shots as knock out stressor to correlate high and low (HMT and LMT) scores with the latency and amplitude of selected ERP components (P100, N100, P200, N200, and P300) in university students' athletes (n = 24 participants who competed in four sports, namely soccer, basketball, netball and futsal).

Results: We found a significant relationship between MT and gender, and age (P < 0.05). However, there were no significant differences among athletes who participated in different sport types (P < 0.05). Vital signs and anxiety scores after the stress induction by the stimulus were higher than before the stimulus presentation, confirmed that the task elicited the expected emotions. In predicting the outcome of stimulus, athletes group exhibited a faster and more accurate response rate compared to control. ERPs results indicated that the amplitude and latencies of selected components were different between groups (P < 0.05), and that the ERPs components correlated with the differential processing of information processing during stressful situation. These results provided evidence for the existence of a strategy regarding cognitive processing for HMT individuals that differs from that among LMT. Source localisation results also revealed that HMT individuals were characterised by a reduced cortical activation by visual stimuli and there were also moderate to strong significant relationships between ERPs components and MT subscales. These correlations can serve to further explore MT concept.

Conclusion: Our findings potentially expand the current traditional models of MT towards an empirically guided, objective measurement as featured by the emerging neuro-technological advances.

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MOLECULAR GENETICS ANALYSIS OF MYH3 GENE AND CHROMOSOME 22Q11.2 DELETION AMONG ATRIAL SEPTAL DEFECT PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Congenital heart defects (CHDs) occur in approximately 8/1000 live births worldwide. Atrial septal defect (ASD) is the most common form of CHD affecting about 1/1500 live birth. Myosin heavy chain 3 (MYH3) is a skeletal myosin heavy chain protein expressed in human foetal and adult skeletal muscle and it has been implicated to play a crucial role in atrial septal development and it was hypothesized that MYH3 could influence the risk of ASD. Chromosome 22q11.2 deletion syndrome (22q11.2DS) is the most common human deletion syndrome. CHD present in 74% of individuals with 22q11.2DS and is the major cause of mortality.

Objectives: This study was conducted to determine the plausible role of MYH3 and 22q11.2DS among patients with ASD.

Patients and methods: This case-control study involved 150 study subjects consisted 77 non-syndromic ASD patients and 73 healthy controls matched for gender and ethnicity. Peripheral blood or saliva samples were collected from the study subjects. Screening of MYH3 was carried out by employing targeted next-generation sequencing coupled with long range-PCR (LR-PCR) using MiSeq, Illumina platform.

Results and discussions: A total of 12 variants were identified from the sequencing analysis, of which seven were exonic variants: two non-synonymous variants (c.3574G>A [rs2285477] and (c.5254G>A[rs34393601]) and five synonymous variants (c.6T>C[rs17817203], c.2916A>G[rs2285472], c.2952T>C[rs2285474], c.4731C>T [rs2285479] and c.4957-16 G>C [rs2239936]) and four intronic variants (c.349-36A>G[rs2285467], c.2926-12A>G[rs2285473], c.3857-925A>C [rs55980976] dan c.4648-134A>G[rs1981514]) and one intronic insertion (c.5457+9_5457+10insA [rs3216886]). Statistical analysis showed that the IQ domain variants: c.2916A>G (P = 0.0002, OR: 2.65 [1.52–4.66]), c.2952T>C (P = 0.003, OR = 2.57 [1.48–4.50]) and c.2926-12A>G (P = 0.00003, OR = 3.10 [1.75–5.51]) and two tail domain variants c.3574G>A (P = 0.001, OR: 2.36 [1.36–4.11]) and c.4648-134A>G [P = 0.02, OR: 1.88[1.06–3.34]) displayed risk association towards ASD. In-silico analysis showed that the c.2916A>G variant will affect splicing mechanism, thus reducing the SC35 binding motif to a SRp40 binding motif. This study also revealed that the rs2285477 c.3574G>A (rs2285477), c.2952T>C (rs2285474) and c.2926-12A>G (rs2285473) variants are in complete linkage disequilibrium (LD) with each other. The 22q11.2DS was investigated using Multiplex Ligation-dependent Probe Amplification (MLPA) and Fluorescent in-situ Hybridisation (FISH) assay. Microdeletions and/or microduplications were not detected within the 22q11.2 chromosomal region with both techniques, indicating that the microdeletion/microduplication within this locus is not common among the recruited ASD patients.

Conclusion: Hence, this study concludes the identification of MYH3 genetic variants and chromosome 22q11.2 microdeletion among ASD patients in Kelantan, thus providing new perspectives on the causation of ASD.

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EFFECTS OF CESSATION OF EXERCISE AND HONEY SUPPLEMENTATION ON BONE PROPERTIES AND ANTIOXIDANT STATUS IN YOUNG FEMALE RATS AND HUMANS

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Introduction: Research findings on the effects of detraining and termination honey supplementation on bone properties and antioxidant status is lacking in the literature.

Objectives: This study aims to investigate effects of cessation of exercise and honey supplementation on bone properties and antioxidant status in young female rats and humans.

Methods: At phase 1, 84 12-week-old Sprague-Dawley female rats were divided into seven groups: 16S, 16J, 16H, 16JH, 8J8S, 8H8S, and 8JH8S (8 = 8 weeks, 16 = 16 weeks, S = sedentary, H = honey supplementation and J = jumping exercise). Jumping exercise consisted of 40 jumps/day for five days/week. Honey was given to the rats at a daily dosage of 1 g/kg body weight/rat/day via force feeding. Jumping exercise and honey supplementation were terminated for 8 weeks in 8J8S, 8H8S, and 8JH8S groups. Tibial and femoral mass, bone mineral density (BMD), mid-shaft cortical area and moment of inertia (MOI), mechanical properties, dimensions, bone metabolism markers and related hormones, antioxidant status and oxidative stress markers were measured after 16 weeks of study period. At phase 2, 48 young female college students aged between 19–25 years old were recruited and assigned into four groups: 16S, 8Ex8S, 8H8S and 8ExH8S (8 = 8 weeks, 16 = 16 weeks, S = sedentary, H = honey supplementation and Ex = aerobic dance exercise). Aerobic dance exercise sessions consisted of 1 h of aerobic dance exercise per session, three sessions per week for 8 weeks. Honey was consumed at a daily dosage of 20g/day for eight weeks. Aerobic dance exercise and honey supplementation were terminated for another 8 weeks in 8Ex8S, 8H8S, and 8ExH8S groups. Parameters measured at pre-, mid- and post-tests included body mass, body mass index (BMI), percentage of body fat, bone speed of sound (SOS) (indicator of bone mineral density), muscular strength and power, bone metabolism markers, antioxidant status and oxidative stress markers.

Results: In phase 1, after 8 weeks of cessation of jumping exercise and honey supplementation, tibial and femoral wet weight, fat free dry weight, proximal total BMD, energy, minimum diameter, serum total calcium, osteocalcin, calcitonin and TAS were significantly higher and serum 1CTP was significantly lower in 8JH8S as compared to 16S. Meanwhile mid-shaft cortical MOI and cortical area, as well as maximal load were significantly higher in tibia of 8JH8S, and mid-shaft cortical BMD and maximum diameter were significantly higher in femur of 8JH8S as compared to 16S. It was also found that continuous 16 weeks of combined jumping and honey (16JH) resulted in significant greater tibial and femoral wet weight, fat free dry weight, proximal total BMD, trabecular BMD, mid-shaft cortical BMD, maximal load, maximum force, energy, minimum diameter, serum total calcium, ALP, osteocalcin, calcitonin, TAS, blood SOD, GSH and GSH/GSSG ratio, as well as lower serum 1CTP and PTH when compared to 16S. Meanwhile mid-shaft cortical MOI and cortical area were significantly higher only in tibial of 16JH and maximum diameter was significantly higher in femur of 16JH as compared to 16S. In phase 2, comparisons between groups showed that after 8 weeks of combined aerobic dance exercise and honey supplementation (8ExH8S), bone speed of sound, serum ALP, osteocalcin, right knee extension and flexion peak torque at 60°.s^{-1} and right knee extension and left knee flexion average power at 300°.s^{-1} were significantly higher in 8ExH8S as compared to 16S at mid test. After 8 weeks of cessation of aerobic dance exercise and honey supplementation, bone SOS, right knee flexion peak torque at 60°.s^{-1}, and left knee flexion average power at 300°.s^{-1} were significantly greater in 8ExH8S as compared to 16S at post-test. Furthermore, comparison over time revealed that after 8 weeks of cessation of aerobic dance exercise and honey supplementation, serum total calcium, ALP, osteocalcin, TAS, GSH, right knee extension and right and left knee flexion average power at 300°.s^{-1} were significantly higher, and percentage of body fat as well as serum 1CTP was significantly lower in 8ExH8S at post-test as compared to pre-test. These discernable beneficial effects were less obvious in 8Ex8S and 8H8S groups.

Conclusion: The results of the phase one of the present study demonstrated that after 8 weeks of cessation, greater preservation of bone properties and antioxidant status were observed when jumping exercise was combined with honey supplementation for 8 weeks. Similarly, discernable positive effects on the measured parameters were observed after 16 weeks of continuous combined jumping exercise and honey supplementation. The findings of the phase 2 of the present study demonstrated that there was greater maintenance of the beneficial effects induced by 8 weeks of combined aerobic dance exercise and honey supplementation on body composition, bone properties, muscular strength and power, and antioxidant status after 8 weeks of the cessation of exercise and honey supplementation as compared to exercise alone and honey supplementation alone. Therefore, the combination of exercise and honey supplementation can be recommended for enhancing and maintenance of bone health and antioxidant status of an individual.

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EFFECTS OF *TUALANG* HONEY ON PARAQUAT INTOXICATION IN RATS

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Introduction: Paraquat (PQ) is an herbicide widely used in the world and has been postulated to exert its toxic effects via the production of various reactive oxygen species causing subsequent oxidative damage at key cellular components. *Tualang* honey (TH) has been reported to possess good anti-oxidant properties and may help ameliorate the oxidative damages in case of PQ poisoning.

Objectives: The main objectives of this study were to evaluate the possible protective effect of TH in acute (study 1) and subacute (study 2) PQ toxicities in rats. In study 1, the effects of single and multiple TH treatments (based on survival rate at 28 days and histological changes of major organs) on PQ-intoxicated rats were investigated. In study 2, the protective effect of TH on PQ-induced oxidative stress in rats' midbrain and lung regions were investigated.

Methods: Male Sprague-Dawley rats aged eight weeks old were used. In study 1, selected oral doses of PQ and TH were 225 mg/kg and 0.2 g/kg, respectively. Single TH treatment groups received TH at 0.5 (PQ + TH0.5h), 2 (PQ + TH2h) or 6 (PQ + TH6h) h following PQ administration while multiple TH treatment groups received TH at 0.5, 2 and 6 h (PQ + THtrp) or further daily treatment for next six days (PQ + TH7d) following PQ administration, respectively (n = 6 per group). The survival time of each rat was recorded until day 28 before sacrifice. In study 2, the rats were orally treated with distilled water (Groups N & PQ, 2 mL/kg/day), TH (Groups TH & PQ + TH, 1.0 g/kg/day) or ubiquinol (Group PQ + QH, 0.2 g/kg/day) throughout the experimental period (n = 15 per group). Two weeks after the respective treatments, the rats were administered with saline (Groups N & TH; 1 mL/kg/week, i.p) or PQ (10 mg/kg/week, i.p.; Groups PQ, PQ + TH and PQ + QH) once a week for four consecutive weeks. The animals were then sacrificed a week following the final injection of saline or PQ.

Results: In study 1, treatment with TH did not improve the survival rate of PQ-intoxicated rats. However, the median survival time of rats which received multiple TH treatments was significantly longer when compared to group PQ + TH6h. Furthermore, TH treatment improved the histological outcome of PQ-intoxicated rats particularly in the lungs. In study 2, serum urea was significantly lower in groups which received TH (TH and PQ + TH) or ubiquinol (PQ + QH). Serum creatinine was markedly reduced in group PQ + TH as well, when compared to controls (N and TH). Significantly lower levels of ALT were observed in groups TH and PQ + TH when compared to group PQ. These findings suggest that TH treatment may have some beneficial effects on the kidney and liver's function. Following four-weekly PQ-administration, the midbrain GPx activity was significantly reduced when compared to healthy control (N). PQ-induced dopaminergic neuronal damage was demonstrated by a significant reduction in the number of tyrosine hydroxylase-immunopositive neurons in the midbrain substantia nigra pars compacta while in the lungs, marked reduction in the activities of SOD and GST were observed in group PQ when compared to the control group. Treatment with TH ameliorates the toxic effects seen in the midbrain and lungs with comparable effects to ubiquinol, the control drug used in study 2.

Conclusions: Treatment with TH did not improve the survival rate in acute PQ-intoxication in rats. However, it may reduce or delay the toxic effects of PQ as evidenced by the post-mortem histological analyses of the major organs. As for the subacute PQ toxicity study, our study is the first to show the possible prophylactic effects of TH against PQ-induced oxidative stress related damage particularly in the SNpc dopaminergic neurons.

Supervisor:
Professor Dr Siti Amrah Sulaiman

THE KNOWLEDGE OF PAEDIATRIC POST OPERATIVE PAIN MANAGEMENT AMONG TRAINEES IN ANAESTHESIOLOGY IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Hospital Sains Universiti Malaysia is one of the few accredited institutions for anesthesiology training program. Anaesthetist play an important role as part of multidisciplinary team in managing pain post-operatively. Lack of knowledge and insufficient emphasis on paediatric pain management during specialty training has been attributed as one of the main factor of under recognised and undertreated pain in children.

Objectives: This study aims to assess the level of knowledge of paediatric post-operative pain management among trainees in this centre and to determine if sociodemographic factor (such as gender, level of qualification, prior pain or paediatric posting) have an independent association with level of knowledge

Methods: The questionnaire was adapted from previous studies. The questionnaire has 35 questions consisted of 17 multiple choice questions and 18 true or false questions to cover two domains: 1) use of age-appropriate pediatric pain assessment (10 questions) and 2) pediatric pain treatment (25 questions). Performance levels defined based on total score in percentage; Poor (< 50%), Average (50%–69%), Above average (70%–79%) and Excellent (≥ 80%). Frequency of each items answered correctly will reflects; 1) area of strength–if ≥ 70% of participants answered correctly for each item analysed; 2) area of weakness–if ≤ 30% of participants answered correctly for each item analysed. All 46 participants were mainly anaesthesiology master students and specialists working in HUSM. Data were analysed by descriptive and inferential statistics.

Result: The response rate was 83.6%. Half of the study population regarded their level of knowledge as low based on self-assessment. For the total of 35 questions, the mean correct score was 20.4 ± 3.34 (58.2%). The highest score was 26 and the lowest score was 13. For pain assessment domain; the mean proportion of correct score was 53% (range 20% to 90%). For pain treatment domain; the mean proportion of correct score was 60.4% (range 36% to 80%). There was no significant association between having done pain and/or paediatric posting and mean score, *P*-value = 0.698, X^2(df) = 1.43).

Conclusion: Knowledge among trainees in HUSM still have a lot of room for improvement. Encouraging more trainees to go for paediatric rotation and providing more time for trainees to rotate in the paediatric area, could potentially improve the quality of knowledge about paediatric postoperative pain management

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ASSESSING THE KNOWLEDGE AND PRACTICE OF THE VENTILATOR ASSOCIATED PNEUMONIA BUNDLE AMONG THE INTENSIVE CARE NURSES IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Ventilator associated pneumonia (VAP) is a major contributor to the morbidity and mortality among patients in the intensive care unit (ICU). It also contributes to a significant increase in the cost of healthcare. As it is a cause of concern among the healthcare personnel worldwide, the VAP bundle was established as a step in the prevention of the development of VAP.

Objective: This study aims to determine the level of knowledge and practice of the VAP bundle among the ICU nurses in Hospital Universiti Sains Malaysia.

Methods: This was a two part study. The first part was an interviewer rated questionnaire study which comprised of 12 single best answer questions conducted on 106 general ICU, neurosurgical ICU and surgical ICU staff nurses regarding VAP and the practices of the VAP bundle, and the second part of the study was the observation of the compliance of the VAP bundle practices among the ICU nurses.

Results: There was a significant mean difference of Total Knowledge Score between the ICUs (*F*-stat (df) = 39.17 (2), *P*-value < 0.001). The highest score was among staff nurse in general ICU (mean (SD) = 9.7 (1.27)). When comparing the association between the three ICUs and compliance, there was significant difference between ICU and compliance for head of bed elevation 30°–45° (χ^2(df) = 25.45 (2), *P*-value < 0.001) with general ICU being the most compliant to head of bed elevation 30°–45°.

Conclusion: Although general ICU fared better than the other ICUs when it came to knowledge and compliance to the practices of VAP prevention, it is shown that the protocols available are not consistently and uniformly applied in all three ICUs.

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STOP-BANG SCORE AND MANDIBULOHYOID DISTANCE IN PREDICTION OF DIFFICULT AIRWAY IN PATIENT WHO COME FOR ELECTIVE SURGERY REQUIRING ENDOTRACHEAL INTUBATION IN HOSPITAL USM

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Introduction: Incidence of difficult laryngoscopy and difficult intubation are higher among patients with obstructive sleep apnoea (OSA). Precision in making the diagnosis and predicting difficult laryngoscopy preoperatively may help to reduce anaesthetic complications. This study was designed to evaluate the diagnostic performance of combined and non-combined radiological parameter (mandibulohyoid distance) and STOP-BANG questionnaire as screening tool.

Methodology: Total of 41 subjects who score > 3 using STOP-BANG questionnaire screening were recruited during admission (STOP BANG score > 3 indicate the subject at risk for OSA). Lateral cephalometry (lateral head and neck X-ray) was done to measure for mandibulohyoid distance and other radiological parameters. Evaluation for difficult laryngoscopy was carried out during general anaesthesia. Cormarch Lehance view of grade 3 and 4 were considered as difficult intubation, grade 1 and grade 2 were considering not difficult intubation. Result analysed using multiple logistic regression to look for association between STOP-BANG score and mandibulohyoid distance with difficult intubation in OSA patients.

Results: STOP-BANG score, mandibulohyoid distance (mm), were higher in the OSA group. OSA patients had a higher incidence of difficult laryngoscopy and intubation. There was association between STOP-BANG score and mandibulohyoid distance with difficult intubation in OSA patients. AUC (95% CI), 0.86 (0.74, 0.97). In prediction of airway difficulty, for STOP BANG alone, sensitivity and

specificity (85.71%, 66.7%, respectively), for mandibulohyoid alone, sensitivity and specificity(77.8%, 69.6%, respectively). Combination of STOP-BANG score and mandibulohyoid distance had improved the specificity and sensitivity of the screening tool to predict difficult airway (77.3% and 84.2%, respectively).

Conclusion: The STOP-BANG score and mandibulohyoid distance proved to be useful in the preoperative diagnosis of difficult laryngoscopy and intubation. The performance of the diagnostic tool improved when combined both STOP-BANG score and mandibulohyoid distance (mm). OSA patients were more prone to difficult laryngoscopy.

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COMPARISON ON INCIDENCE, RADIOLOGICAL FEATURES AND OUTCOME OF SKULL BASE VERSUS NON-SKULL BASE MENINGIOMAS IN GENERAL HOSPITAL KUALA LUMPUR: A 5-YEAR RETROSPECTIVE STUDY

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Introduction: Meningiomas are the most common intracranial tumours, accounting for 13%–26% of all the primary intracranial tumours. In the United States, an estimated 2%–3% of the population has an incidental asymptomatic meningioma, and annual incidence of symptomatic meningioma is two cases per 100,000 individuals. Skull base meningiomas comprise 30% of meningiomas and are one of the most difficult intracranial tumours to be managed surgically because of the difficulty in approaching the lesions and their proximity to vital structures such as cranial nerves and major blood vessels. Meningiomas are commonly seen in Malaysia, however there is minimal local data published. The main purpose of our study was to identify the demographic data, tumours characteristic and surgical outcome of patients with meningiomas operated in General Hospital Kuala Lumpur (GHKL).

Methods: A total of 199 patients with histologically proven meningiomas were operated from January 2010 till December 2014 in GHKL. They were categorised into skull base and non-skull base groups. Demographical data, tumour characteristics and patients' outcome were studied. Kaplan-Meier overall survival curve and Cox hazard univariable and multivariable regression for possible predictors of survival were analysed.

Results: There was 199 patients included in the study, 97.5% of the patients (n = 194) had WHO grade I meningioma. Only five patients had WHO grade II meningiomas. However, no new WHO grade III meningiomas diagnosed throughout the study period. Majority of our patients were female (n = 134; 67.3%) with only 65 patients were male (32.7%). Malay ethnicity has the highest incidence (n = 138; 69.3%). Skull base meningioma (n = 54) comprised 27.1 % of all the intracranial meningioma. Majority of the skull base meningiomas were histopathologically WHO grade I (n = 52, 96.3%). Seventy percent of the skull base meningioma group was female (n = 38) with mean age at diagnosis was 51.7 (SD 11.01), as compared to non-skull base group with mean age of diagnosis at 54.1 (SD 9.4). Both categories showed highest prevalence in age group 40–60 with skull base group (n = 33; 61.1%) and non-skull base group (n = 91; 62.8%). Majority of the patients in both skull base and non-skull base group presented with clinical feature of headache, with 94.4% (n = 51) and 91% (n = 132) respectively. Radiologically, 94% of the patients with skull base meningioma (n = 51) had radiological evidence of oedema; 30 cases (55.6%) had hyperotosis and 16 patients (29.6%) had calcification as reported by radiologists.

Skull base meningioma was related to poorer outcome with poor discharge condition (n = 23; 42.6% P-value < 0.01) and higher possibility of incomplete resection (n = 34; 63% P-value < 0.01). In contrast, 88% (n = 128) patients in non-skull base meningiomas group were discharged well and only 11 cases out of the total 145 patients were incompletely resected. Our study showed a shorter median survival of 37.6 months (SD 20.94) for skull base group as compared to 47.8 months (SD 18.2) in the non-skull base group with P-value 0.187.

Multivariate cox hazard regression test showed skull base meningioma group had four times the chance to succumb to death as compared to non-skull base group (adjusted HR 4.22; 95% CI 1.53–11.66; P-value 0.005), adjusted with gender, comorbidities, WHO grading and extends of meningioma.

Conclusion: The primary treatment for symptomatic meningioma is surgery, which can be curative if the tumour is completely removed. Skull base meningiomas are widely accepted as more technically challenging for gross total resection. Our study has showed skull base meningiomas operated locally had higher rate of incomplete resection and poorer surgical outcome as compared to non-skull base group. Patients with skull base meningioma had four times higher risk to succumb to death as compare to non-skull base group. More studies need to be carried out locally to look into skull base meningioma seriously for the improvement of surgical outcome.

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FACTORS ASSOCIATED WITH OUTCOMES IN SURGICALLY MANAGED RUPTURED CEREBRAL ANEURYSMS

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Background: Ruptured cerebral aneurysm is a life-threatening condition that requires urgent medical attention. In Malaysia, a prospective study by Hospital Sarawak Neurosurgical centre in year 2000–2002 revealed an average of two cases of intracranial aneurysm per month with an operative mortality of 20% and management mortality of 25%. Failure to recognise, delay in admission to neurosurgical center and lack of facilities may lead to poor surgical outcome of these patients. The purpose of the study is to review the epidemiology of the ruptured cerebral aneurysm who underwent surgical clipping in this region and to identify the predicting factors that influence the prognosis and outcome of these patients.

Material and methods: A single centre retrospective study with review of medical records was performed involving 105 patients who were surgically treated for ruptured intracranial aneurysm in Hospital Sultanah Aminah, Johor Bahru from July 2011 until January 2016. Information collected including the patient's demographics data, Glasgow Coma Scale (GCS) prior to surgery, World Federation of Neurosurgical Societies Scale (WFNS) of the patients and timing between SAH ictus and surgery. Good clinical grade is defined as WFNS grade I–III while poor grade as WFNS grade IV and V. The outcomes at discharge and after six months of surgery were assessed using modified Rankin's Scale (mRS). mRS scores of 0 to 2 were grouped into "favourable" and mRS scores of 3 to 6 were grouped into "unfavourable". Only cases of proven ruptured aneurysmal SAH involving anterior circulation and underwent surgical clipping were included in the study. Data collected were analysed using SPSS. Univariate and multivariate analysis were performed and *P*-value of < 0.05 was taken as statistical significance.

Result: A total of 105 patients were included which consisted of 42.9% male and 57.1% of female patients. The mean GCS of the patient subjected for surgical clipping was 13 with majority fall into the good clinical grade (78.1%). Mean timing of surgery after SAH was 5.3 days and was further categorised into early (day 1 to day 3, 45.3%), intermediate (day 4–day 10, 56.2%) and late (after day 10, 9.5%). Total favourable outcome achieved at discharge was 59.0% as compare to 41.0% of unfavourable outcome with an overall mortality rate of 10.5%. At sixth month of review (n = 94), the patient with favourable outcome constituted 71.3% as compared to 28.7% with unfavourable outcome. The mortality at sixth month was 3.2%. On univariate analysis, early surgical clipping, patient with better GCS and good clinical grade had significant better outcome at discharge. Timing of surgery and clinical grade remained significant predictors for outcome at sixth month base on univariate study. On multivariate analysis, younger age male patient with good clinical grade is associated with favourable outcome at discharge when other factors were adjusted. Multivariate analysis done for outcome at 6th month showed only male patient and good clinical grade was associated with favourable outcome.

Conclusion: In our study, we conclude that younger male patient with good clinical grade are associated with favourable outcome at discharge and at sixth month post-surgery. We do not find timing of surgery, size of aneurysm and duration of surgery to be associated with the outcome of the patient post-clipping. Increasing age is not associated with surgical outcome in longer term of patient's follow up.

Supervisor:
Datuk Dr Johari Siregar Adnan

Co-supervisor:
Dato' Dr Abdul Rahman Izani Ghani

A SHUNT DEPENDENCY OUTCOME OF ENDOSCOPIC THIRD VENTRICULOSTOMY IN THE MANAGEMENT OF OBSTRUCTIVE HYDROCEPHALUS

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Introduction: Endoscopic third ventriculostomy (ETV) is an accepted alternative to cerebro-spinal fluid (CSF) shunting in cases of obstructive hydrocephalus. Success rates have been attributed to various variables including age, aetiology of hydrocephalus, complications and also expertise. Reported success rates ranging from 30%–90%.

Objectives: The aim of this study is to evaluate the shunt dependency following ETV in obstructive hydrocephalus patients and factors influencing it. This was a cross-sectional study of which a total of 206 patients presenting with obstructive hydrocephalus that underwent ETV from three major centres; Kuala Lumpur General Hospital, Hospital Universiti Sains Malaysia and Sarawak General Hospital were studied. Successful ETV is taken as clinically no symptoms of raised intracranial pressure and imaging evidence of resolution of hydrocephalus.

Results: Mean age of patients was 21.1 ± 22.6 years with 98 (47.6%) being paediatrics (< 12 years) and 108 (52.4%) adults (≥ 12 years). 63 (30.6%) were of congenital causes, 90 (43.7%) tumoral related, 40 (19.4%) due to hemorrhage and 13 (6.3%) post-infective. Shunt free outcome at one month was 179 (86.9%) and 177 (85.9%) at six months. Chi-square test showed no statistical significance in outcome with age groups (*P*-value = 0.629) or outcome with diagnosis (*P*-value = 0.057). Univariate analysis via logistic regression

showed significance of Liliequist membrane with odds ratio 4.375; 95% CI (1.188–16.115), *P*-value 0.027; of which patients with Liliequist membrane present are 4-fold risk of failure and ending up with a shunt after 1 month following ETV. Also noted the nature of fenestration with the outcome where at 1 month odds ratio 17.969; 95% CI (2.077–5.957), *P*-value 0.009 and at 6 months odds ratio 19.154; 95% CI (2.11, 173.868), *P*-value 0.009 signifies a large fenestra with well flapping floor of the third ventricle has a 17-fold chance of being shunt free at 1 month and 19-fold chance at 6 months. Multivariate logistic regression analysis showed significance of nature of fenestration with the outcome where at 1 month adjusted ratio 0.231; 95% CI (0.091–0.518), *P*-value 0.005 and at 6 months adjusted ratio 0.241; 95% CI (0.092–0.535), *P*-value 0.006 signifies a large fenestra with well flapping floor of the third ventricle has a 0.2-fold chance of being shunt free at 1 month and 6 months, respectively. Also noted was 6 months outcome based on age group with adjusted ratio 0.202; 95% CI (0.109–0.206), *P*-value 0.006; of which adult patients have 0.2-fold chance of being shunt free at 6 month following endoscopic third ventriculostomy.

Survival analysis using Cox regression to generate Hazard ratio showed ETV failure at any point of time in this study for tumoral causes are 0.322 times less likely to fail compared to congenital causes (HR 0.322; 95% CI 0.122–0.847; *P*-value 0.022).

Conclusion: ETV is a safe and effective procedure in patients with obstructive hydrocephalus. Patients with presence of Liliequist membrane has a higher chance of ETV failure and nature of the fenestra plays a vital role in outcome of ETV. Paediatric age group has a slightly higher chance of ETV failure. Patients with tumors predominantly pineal and posterior fossa tumors has a higher chance of success compared to congenital cases.

Supervisor:
Professor Dr Zamzuri Idris

Co-supervisor:
Dr Azmi Alias

TELENEUROSURGERY: OUTCOME OF MILD HEAD INJURY PATIENTS MANAGED IN NON-NEUROSURGICAL CENTER IN THE STATE OF JOHOR

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Background: Technological advancement has influenced the way health care professions in managing cases. The implementation of teleneurosurgey been proven to reduce the rate of unnecessary transfer of patient from primary hospital to hospitals with neurosurgical services. Head injury patients are among those who were managed in the primary hospital under the care of general surgical unit (GSU), with the help of teleneurosurgery. As more head injury patients are managed utilising this model of management, there are growing concerns regarding the safety and outcome of the patients with no immediate neurosurgical services. This study is to evaluate the outcome of patients with mild head injury which is managed in a non-neurosurgical centers with the help of teleneurosurgery.

Methods: This study was conducted in the period of 16 months from the month of June 2015 through September 2016, by recruiting samples from five primary hospitals utilising teleneurosurgery for neurosurgical consultations in managing mild head injury cases in Johor state. Low risk mild head injury patients that undergone CT brain were referred to neurosurgical unit HSAJB and was managed remotely in the GSU. Two main outcomes were noted; favourable and unfavourable, with the unfavourable outcome was considered when the patient needs a delay transfer to NSU, death or discharge with a lower Glasgow Coma Scale (GCS) from admission. A follow up review of the Glasgow Outcome Scale (GOS) at 3 and 6 months was noted in the study.

Results: A total number of three 359 samples were recruited in this study with a total of 36 exclusion. Mean age of the patients were of 45.39 years old, with 77.2% of them were male. Malay ethnicity constitutes a majority of 60.45% of all the subjects. A total of 11 (3.06%) patients had an unfavourable outcome with 10 (2.79%) needing a delay transfer to NSU. There was no significant difference in GOS at 3 and 6 months for patient in the unfavourable group (P = 0.368) on McNemar test. Unvariate analysis reveals Malay ethnicity (P = 0.021) and referral GCS (P = 0.024) are two important factors in determining patient's outcome. This finding was however not reproducible when using multivariate analysis.

Conclusion: Despite absence of identified factor on multivariate analysis that determines patient's outcome, Malay ethnicity and referral GCS are two possible important factors if larger sample was studied. The percentage of failure in utilising this model of practice is relatively low, 3.06%. A prospective and multicentric model study with a bigger sample size is proposed in order to address the limitation encountered in this study.

Supervisor:
Datuk Dr Johari Siregar Adnan

Co-supervisor:
Dato' Dr Abdul Rahman Izani Ghani

FACTORS AFFECTING VISUAL FIELD OUTCOME POST SURGERY IN SELLAR REGION TUMORS: RETROSPECTIVE STUDY

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Background: Despite the broad category of differentials for sellar region, most of them present with similar clinical signs and symptoms. Headache and visual disturbance are among the frequently seen as presenting symptom. Visual field (VF) assessment is one of the crucial component of neuroophtalmologic assessment and Mean Deviation (MD) value from automated perimetry allows quantification of the visual field defect. We formulated a study to look into the factors that affect the visual field outcome after surgery.

Methods: All patients with sellar region tumor who has underwent surgery in Queen Elizabeth Hospital from July 2010 to July 2016 were retrospectively analysed through hospital notes. VF assessment via Humphrey visual assessment for these patient pre and post-surgery were reviewed for MD value.

Results: Eighty four patients were recruited and out of them, 151 eyes were taken into analysis after excluding eyes with missing data. Mean age of patients were 45.4 years with 70.2% of them were male. Visual disturbance is the commonest presenting symptom with mean duration of symptom prior to surgery is 9.7 months. Majority of them were pituitary adenomas (75%) followed by sellar meningioma (19%), craniopharyngioma (4.8%), and rathke cleft cyst (1.2%). 70.9% of patients showed improvement in VF based on MD outcome. Mean MD for pre-surgery and post-surgery were –14.0dB and –12.4dB, respectively. Univariate analysis reveals younger age, female sex, shorter duration of symptom, pituitary adenoma, transsphenoidal approach, and transcranial approach favours improvement in VF. Multivariate analysis shows only shorter symptom duration, transphenoidal approach, and transcranial approach are significant for favourable VF outcome when other factors adjusted.

Conclusion: Symptom duration and surgical approach were independent factors that affects the visual field after surgery in patients with sellar region tumors.

Supervisor:
Dr Pulivendhan Sellamuthu

Co-supervisor:
Associate Professor Dr Abdul Rahman Izani Ghani

FECUNDITY RATE AND PREGNANCY OUTCOME AFTER SURGICAL TREATMENT OF ECTOPIC PREGNANCY IN HOSPITAL KUALA LUMPUR

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Introduction: Ectopic pregnancy is a gynaecological emergency and is an important cause of morbidity and mortality in developing countries. Although the risk factors of ectopic pregnancy have been determined in previous studies, the main risk factors of ectopic pregnancy are different in various countries due to different cultural and social characteristics. Early diagnosis and referral may reduced the morbidity and mortality associated with this life threatening condition. With earlier diagnosis, medical therapy with methotrexate can be offered and surgical management may be avoided. However, this will need a protocol for patient follow up for medical or expectant management of ectopic pregnancy. In the surgical management of ectopic pregnancy, the benefits of salphingectomy over salphingostomy in predicting the future fertility are uncertained. Laparoscopy procedure is generally more favoured over laparotomy. However, it depends on the stability of the patient's haemodynamic status. However, whether these surgical factors and surgeon's expertise will affect the subsequent pregnancy and its outcome is questionable.

Objectives: To determine the fertility rate and pregnancy outcome after ectopic pregnancy that has been managed surgically in Hospital Kuala Lumpur.

Patients and methods: A retrospective study was carried out in the Department of Obstetrics and Gynaecology in Hospital Kuala Lumpur, utilising the data from the year 2006 to 2010. This comprised of randomly 120 patients that presented for ectopic pregnancy managed surgically and also confirmed histology. The surgical approach and the level of surgeon data were determined from patient's case notes and analysed for the associations and significance. Statistical significance was taken as *P*-value of less than 0.05 ($P < 0.05$).

Results: From 120 patients of ectopic pregnancy during the study period, 41 patients were able to conceive within five years after the ectopic pregnancy. Out of this subsequent pregnancy, there were 29 (70.7%) intrauterine pregnancies and 12 (29.3%) recurrent ectopic pregnancies. Out of the intrauterine pregnancies, 24 (82.8%) had live birth babies and another 5 (17.2%) had miscarriages. The mean time to next pregnancy for patient to get pregnant was 18.73 ± 11.267 months. The maternal characteristics (age, parity and smoking status) do not contributed to the risk of recurrent ectopic pregnancy. The surgical approach and the surgeon's level also do not have any statistically significant for the fecundity rate and the subsequent pregnancy outcome.

Conclusion: In view that any surgical approach and type of surgery done for the ectopic pregnancy does not influence the fecundity rate in subsequent pregnancy, the

choice for surgical management in a stable patient should be the one that has less surgical complications, therefore laparoscopy procedure should be encouraged.

Supervisor:
Associate Professor Dr Adibah Ibrahim

Co-supervisor:
Dr Noor Haliza Yusoff

THE EFFECT OF SYMPHYSIOFUNDAL HEIGHT MEASUREMENT IN DETECTING MACROSOMIA AND PREDICTING SHOULDER DYSTOCIA IN HOSPITAL SULTAN ISMAIL, JOHOR BAHRU

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Objective: To assess the diagnostic valutracte of Symphysiofundal height measurement in detecting macrosomia and predicting shoulder dystocia at term. To determine the incidence, risks factors and complications associated with shoulder dystocia.

Methods: A prospective cross sectional study in Hospital Sultan Ismail was conducted from 1 June 2015 until 30 September 2015 (four months). The study included 961 pregnant women with singleton fetus completed 37 weeks. Symphysiofundal height measurement was done and the details regarding the antenatal review, intrapartum events, immediate postpartum event and neonatal outcome were recorded. The incidence of shoulder dystocia was assessed and risk factors for shoulder dystocia were examined by multiple logistic regression analysis.

Results: A total of 961 patients were recruited in this study. Incidence of shoulder dystocia was 0.04% (n = 42). The SFH measurement of 40 cm cut-off value for macrosomic babies (birth weight of 4,000 g and above) proved to be useful with sensitivity of 78.2% and specificity of 97.9%. While the positive predictive value was poor at 48.6%, the negative predictive value of 99.4% provided a useful indicator. The incidence of shoulder dystocia rose with increasing SFH measurement (2 to 6 fold) and birth weight (3 to 7 fold). When the SFH (≥ 40 cm), the incidence of shoulder dystocia was 13.5% (5/37) as compared to 2.3% (17/735) when SFH (< 39 cm) and 16% (20/126) with SFH (> 39 cm but < 40 cm), respectively. When the birth weight ≥ 4,000 g, the incidence of shoulder dystocia was 21.7% (5/23) and the association was also noted when birth weight ≥ 3,800 g to 3,990 g group (29.3%). The incidence noted to be increased from the universal (4.0%) starting with the birth weight ≥ 3,600 g. A total of 21 babies admitted to NICU with five of them with incomplete Moro Reflex and two with low Apgar score. There was one case of maternal third degree perineal tear.

Conclusion: The 40 cm cut-off for macrosomic babies (birth weight of 4,000 g and above) proved to be useful with sensitivity of 78.2% and specificity of 97.9%. Although the overall incidences of macrosomia and shoulder dystocia were low, the risk of shoulder dystocia was strongly linked to increasing birth weight and SFH measurement.

The only reliable risks factors associated with shoulder dystocia in this study were symphysio fundal height measurement more than 40 cm (n = 5, 11.9%) and birth weight more than 4,000 gram. (n = 5, 11.9%). However shoulder dystocia can occur at SFH measurement ≥ 37 cm and birth weight of ≥ 3,600 g. International guidelines for elective caesarean delivery in suspected cases of macrosomia may not, therefore, apply to Malaysian population.

Supervisor:
Dato' Dr Ghazali Ismail

Co-supervisor:
Dr Ahmad Amir Ismail

A COMPARISON OF THE CLINICAL AND ANTIBACTERIAL EFFECTS BETWEEN TUALANG HONEY AND MANUKA HONEY AS ADJUNCTIVE TREATMENT IN PSEUDOMONAS KERATITIS IN RABBIT EYES

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Introduction: Honey is a known alternative therapy for varies diseases. Manuka honey antibacterial eye drop is established marketed honey for eye infection. We aim to explore the potential of *Tualang* honey to be commercialised in ophthalmic usage. Thus, we conducted an experimental study to compare the clinical and antibacterial effects of *Tualang* and Manuka honey as adjunctive treatment in *Pseudomonas keratitis*.

Objectives: Several in vitro studies documented that *Tualang* and Manuka honey had antibacterial effect towards *Pseudomonas aeruginosa*. This study is done to compare the mean Slit Lamp Examination (SLE) score and mean Colony Forming Unit (CFU) count of Pseudomonas-induced keratitis in rabbit eyes.

Methods: This experimental animal study consisted of 20 rabbits induced with *Pseudomonas keratitis* that were randomly and equally divided into two groups. Group A was treated with a combination of *Tualang* honey 30% and gentamycin 0.3% eight times per day, while Group B was treated with a combination of Manuka honey and gentamycin 0.3% eight times per day. At the same time, a parallel study with similar methodology was conducted on ten rabbits which were treated with gentamycin 0.3% as a control group. Serial clinical examination using Slit Lamp Examination (SLE) score was done at 24, 48, 72 h, day 5 and day 7.

All rabbits were euthanised at day 7 and their corneas harvested. The harvested corneas were processed and CFU counts were performed on the next day. Repeated measure ANOVA and Mann-Whitney test were used for the data analysis.

Results: There was no statistically significant difference of clinical outcome (P = 0.434) and antibacterial effect (P = 0.198) between *Tualang* honey and Manuka honey as adjunctive treatment in *Pseudomonas keratitis*.

Conclusion: *Tualang* honey is comparable to Manuka honey as adjunctive treatment in *Pseudomonas keratitis* in rabbit eyes.

Supervisor:
Professor Dr Shatriah Ismail

Co-supervisors:
Professor Dr Siti Amrah Sulaiman,
Professor Dr Habsah Hasan

A COMPARATIVE STUDY ON OPTIC NERVE FUNCTION, RETINAL NERVE FIBRE LAYER THICKNESS AND VEP PRE AND THREE MONTHS POST-TREATMENT WITH ETHAMBUTOL IN TUBERCULOSIS PATIENTS

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Introduction: Ethambutol is a first line drug for the treatment of tuberculosis. However this drug has caused incidences of irreversible ocular toxicity. This study is to compare the anatomical and visual function using conventional optic nerve function tests, measurement of retinal nerve fibre layer and pattern visual evoked potential changes in patients with tuberculosis treated with a regime containing ethambutol.

Methods: This is a prospective study involving 72 eyes of 36 patients treated with ethambutol according to the Directly Observed Treatment Short Course (DOTS) strategy in Hospital Universiti Sains Malaysia, Kelantan, Malaysia. The optic nerve function, retinal nerve fibre layer (RNFL) on optical coherence topography (OCT) and pattern visual evoked potential (PVEP) were assessed. The examination was performed before the start of therapy and 3 months after.

Results: Visual field analysis of mean deviation (md) showed significant statistical change (P = 0.010). There were also significant changes on OCT and PVEP. Comparison of RNFL thickness showed an increased thickness in all quadrants (P < 0.05) and a delayed P100 peak latency and decreased amplitude on PVEP assessment (P < 0.001).

There was no change in visual acuity, colour vision, light brightness, red saturation and fundus findings pre and post ethambutol.

Conclusion: The use of OCT to detect RNFL thickness and PVEP to assess P100 latency and amplitude can assist in the detection of subclinical anatomical and visual function changes prior to conventional optic nerve function tests. These changes may represent early ethambutol related optic neuropathy, making OCT and PVEP important tools in monitoring tuberculosis patients.

Supervisor:
Professor Raja Azmi Mohd Noor

Co-supervisor:
Professor Wan Hazabbah Wan Hitam

EVALUATION OF VISUAL ELECTROPHYSIOLOGICAL TEST IN OBSTRUCTIVE SLEEP APNOEA

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Introduction: Obstructive sleep apnea (OSA) is a life-threatening, sleep-related breathing disorder characterised by partial (hypopneas) and complete pauses (apneas) in breathing that last at least 10 s during sleep. As a consequence, the blood oxygen saturation may fall, with resulting in a hypoxia state. OSA has been associated with ocular conditions such as non-arteritic anterior ischemic optic neuropathy (NAION), papilloedema, glaucoma and central retinal vein occlusion. Visual electrophysiological tests like pattern visual evoked potential (PVEP) and pattern electroretinogram (PERG) may be able to detect functional impairment of the retina and visual pathway in OSA patients.

Objective: To compare the PVEP & PERG changes in patients with OSA and control group. We also analysed the relationship between visual electrophysiological tests with the severity of OSA.

Material and methods: A comparative cross-sectional study was conducted in Hospital Universiti Sains Malaysia involving 40 samples of OSA patients and 31 control subjects. A complete ocular examination was performed which include visual acuity, anterior and posterior segment. PERG (0.8° checks size) and PVEP (0.25° checks size) were conducted by a single technician. Independent *t*-test, Mann-Whitney, Kruskal-Wallis Test, Pearson and Spearman's correlation test were used in statistical analysis.

Results: There were statistically significant reduction of the PVEP P100 wave amplitude (P < 0.001) and delay in PVEP P100 and N75 latency (P < 0.001) in the OSA group. Among OSA patients, we also observed a significant reduction of the P50 wave amplitude (P < 0.001) in PERG, compared to the control group. However, there is no finding on association of PVEP and PERG according to severity of OSA. There was no significant differences of PERG latency were observed in either group. There was no significant correlation in PVEP or PERG between OSA patients with different disease severity except PVEP latency N75 which is statistically significant but fair negative correlation.

Conclusion: OSA patients have significant abnormalities in VEP amplitude and latency, and ERG amplitude, suggesting that hypoxia may be a pathophysiology in these conditions. There were no significant relationships between PVEP and PERG in AHI of OSA patients.

Supervisor:
Associate Professor Dr Raja Azmi Mohd. Noor

Co-Supervisors:
Professor Dr Wan Hazabbah Wan Hitam,
Associate Professor Dr Baharudin Abdullah

ANTIFUNGAL EFFECT OF KAFFIR LIME LEAF EXTRACT ON SELECTED FUNGAL SPECIES OF PATHOGENIC OTOMYCOSIS IN IN-VITRO CULTURE MEDIUM

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Introduction: Kaffir lime (*Citrus hystrix* D.C) has been used for a long time in agricultural and alternative medicine. Kaffir lime leaf (KLL) had been proved effective against certain fungi that could infect human body. This study aims to demonstrate the antifungal effect of KLL extract on pathogenic otomycosis species, particularly *Aspergillus niger* and *Candida albicans*.

Methods: This is a laboratory-controlled prospective study conducted in Universiti Sains Malaysia. KLL was extracted via Soxhlet extraction method by using 70% ethanol and aqueous, then evaporated using rotary evaporator to a thicker compound. The concentrated extract then freeze dried to obtain powdered form which was diluted to establish five different concentrations of 50 g/mL, 25 g/mL, 12.5 g/mL, 6.25 g/mL and 3.125 g/mL. Sabouraud Dextrose agar (SDA) lawned with tested fungal isolates were inoculated with the extracts using well-diffusion method. Zone of inhibition was measured followed by minimum inhibitory concentration (MIC).

Results: There were zone of inhibition for both aqueous and alcohol KLL extracts on *Aspergillus niger* and *Candida albicans* growth. *Candida albicans* has anti-fungal activities in concentrations of 50 g/mL, 25 g/mL and 12.5 g/mL for both aqueous and alcohol KLL extracts. However, zone of inhibition for *Aspergillus niger* was obtained only in 50 g/mL concentration for both aqueous and alcohol KLL extracts. Statistically antifungal activity of *Aspergillus niger* is better by aqueous KLL extracts as compared to alcohol KLL extract with significance difference $P < 0.001$. In contrast, antifungal activity of *Candida albicans* is better in alcohol extracts as compared to aqueous extract with significance $P < 0.001$. The MIC of KLL aqueous extract against *Candida albicans* was 12.02 g/mL, KLL alcohol extract against Candida albicans was 10.23 g/mL, KLL aqueous extract against *Aspergillus niger* was 47.86 g/mL and KLL alcohol extract against *Aspergillus niger* was 48.97 g/mL.

Conclusion: KLL has significant antifungal effect towards pathogenic fungi species causing otomycosis, particularly *Aspergillus niger* and *Candida albicans*. The antifungal effect of both aqueous and alcohol KLL are seen more on Candida albicans as compared to *Aspergillus niger*.

Supervisor:
Professor Madya Dr Irfan Mohamad

Co-supervisors:
Professor Madya Dr. Rosdan Salim
Professor Dr Zeehaida Mohamed

SIGNIFICANCE OF ZONE 2 PEAK ON CAPILLARY ELECTROPHORESIS FOR THE DETECTION OF HAEMOGLOBIN CONSTANT SPRING

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MPath Haematology

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Introduction: Haemoglobin Constant Spring (Hb CS) is a point mutational defect of α thalassaemia at the termination codon and leads to α chain extension and reduced mRNA stability. It is a prevalent and common non deletional α thalassemia in most Southeast Asian countries. This abnormal haemoglobin has clinical heterogeneity and can interact with α^{o} and cause non deletional Hb H CS.

Screening for this abnormal haemoglobin is performed by capillary electrophoresis (CE). It is one of the analytical separation techniques and can be used to separate and quantitate Hb A2, Hb F and other abnormal haemoglobins. CE gives peak at the Zone 2 for Hb CS and it is a sensitive method to detect Hb CS.

Objectives: The aims of this study were to determine the significance of presence of Zone 2 peak on CE in diagnosing Hb CS, to compare the haematological profiles between different Hb CS genotypes and to estimate range for Zone 2 peak by CE with different Hb CS genotypes.

Methods: A cross sectional study was done from July 2015 to July 2016 by collecting 137 samples randomly which showed positive peak on Zone 2 of CE. The samples were tested for red cell indices (Hb, RBC, MCV, MCH, and RDW) by using Sysmex XN 3000 analyser, Sysmex Corporation, USA. Haemoglobin analyses were performed using CAPILLARYS2 Flex-Piercing System Sebia, PN 1227, France and DNA analyses using Multiplex PCR and ARMS were done for non deletional and deletional α thalassaemia.

Results: One hundred and eighteen (86.1%) out of 137 samples that showed positive peak in Zone 2 of CE, were positive for termination codon Hb CS mutation, confirmed by molecular analysis. The most common types of Hb CS found

was Heterozygotes Hb CS which was 92 samples (67.2%), followed by compound heterozygotes which was 22 samples (16%) and homozygotes group which was 4 samples (2.9%).

There were significant number of samples that had positive peak at Zone 2 which confirmed for termination codon CS mutation. The range of Hb CS level for Hb CS trait can be estimated to lie within mean of 0.67 ± 0.27%. Meanwhile, the range of Hb CS level for compound heterozygotes Hb CS and homozygotes Hb CS were from 0.3% to 2.2 % and 4.5% to 5.5%, respectively. This might aid in making the diagnosis if the molecular technique is not available. Significant haematological differences which include Hb level, MCV, MCH, RDW, RBC count and Hb CS level were observed between heterozygotes, homozygotes and compound heterozygotes Hb CS.

Conclusion: Consequently, we will able to predict these groups from the haematological indices and Hb CS level/ quantification on Zone 2 peak if the molecular technology is not available.

Supervisor:
Dr Marini Ramli

Co-supervisor:
Associate Professor Dr Rosnah Bahar

TRAUMATIC BRAIN INJURY IN PAEDIATRIC MILD BLUNT HEAD TRAUMA IN HOPSITAL UNIVERSITI SAINS MALAYSIA

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Background: Paediatric minor head injury is a common presentation in emergency department worldwide. There is controversy about which patients should undergo computed tomography (CT) of the brain. The purpose of our study was to identify the predictors for paediatric traumatic brain injury on CT scan in our population. We also aimed to determine the association between isolated versus non-isolated vomiting with traumatic brain injury on CT brain.

Methods: Children with minor head injury (GCS 13-15) presented to Hospital Universiti Sains Malaysia (HUSM) during the period from 2009 to 2013 were retrospectively reviewed. We evaluated clinical variables such as the mechanism of injury, presenting symptoms and physical signs on the examination for positive traumatic brain injury as determined by CT brain. The data was analysed by chi-square test, simple and multiple logistic regression analyses.

Results: A total of 274 patients were enrolled into our study. The mean and standard deviation age of study group was 11.2 (5.39) years old. Traumatic brain injury on CT scan occurred in 49.3% of patients. On multivariable analysis, we identified the following three predictors which were statistically significant: headache (adjusted OR 2.24, 95% CI 1.24, 4.05, $P = 0.008$), giddiness (adjusted OR 3.08, 95% CI 1.27, 7.51, $P = 0.013$) and presence of scalp hematoma (adjusted OR 2.93, 95% CI 1.60, 5.34, $P < 0.001$). TBI on CT scan occurred in 2 of 24 patients in the isolated vomiting group versus 71 of 123 in the non-isolated vomiting group. We found significant association between isolated versus non-isolated vomiting with traumatic brain injury on CT brain ($P < 0.001$).

Conclusion: Headache, giddiness and presence of scalp hematoma are independent predictors for minor blunt head injury in our pediatric population. CT brain should be seriously considered in children presenting with vomiting accompanied by other symptoms and signs suggestive of traumatic brain injury.

Supervisor:
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PREMATURE EJACULATION AMONG MEN ATTENDING OUTPATIENT CLINIC IN UNIVERSITI SAINS MALAYSIA HOSPITAL AND ITS ASSOCIATED FACTORS

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Background: Premature ejaculation (PE) is a common male sexual disorder. Several factors have been proven to be associated with PE namely erectile dysfunction, general medical condition and psychological illness. However, there is little data on prevalence of PE according to its four subtypes; lifelong PE, acquired PE, natural variable PE and premature-like ejaculatory dysfunction.

Objectives: To determine the prevalence of PE and its associated factors among men attending outpatient clinic in USM hospital.

Methods: A cross sectional study among men aged 18 to 60 years old was conducted from January 2014 to January 2015. Premature Ejaculation Diagnostic Tool (PEDT) and 5-item International Index of Erectile Function (IIEF-5) questionnaire were distributed. Participants who were identified as having PE were further assessed with 21-item Depression, Anxiety and Stress Scale. PE was defined as PEDT score of 9 and above.

Results: A total of 294 men recruited in this study with the mean (SD) age of 46.3 (10.1) years. The prevalence of PE was 21.4% ($n = 63$). Among those with PE, 7.9% ($n = 5$), 15.9% ($n = 10$), 58.7% ($n = 37$), 17.5% ($n = 11$) were identified as lifelong PE, acquired PE, natural variable PE and premature-like ejaculatory dysfunction, respectively. Multiple logistic regression showed that only mild erectile dysfunction (ED) [adj. OR (95% CI): 5.65 (1.89, 16.91)], $P = 0.002$)

mild-moderate ED [adj. OR (95% CI): 8.2 (2.72, 24.46), $P < 0.001$] and moderate-severe ED [adj. OR (95% CI): 6.0 (1.15, 31.23), $P = 0.03$] were significantly associated with PE. The proportion of depression, anxiety and stress among men with PE in this study were 20.6%, 33.3% and 14.3%, respectively. More than two third of them discussed their ejaculatory problem with others.

Conclusion: The prevalence of PE in this study was comparable with other regions. Erectile dysfunction was the only factor that significantly associated with PE but no association were seen between age, ethnicity, educational and occupational status, frequency of sexual intercourse, smoking status or underlying comorbidities. Men who were detected as having PE in this study also reported certain degree of anxiety, depression and stress.

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QUALITY OF LIFE AND ITS ASSOCIATED FACTORS AMONG KNEE OSTEOARTHRITIS PATIENTS

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***Introduction*:** Osteoarthritis is the most common form of arthritis around the globe. The aim of knee osteoarthritis treatment is to alleviate pain, delay progression of osteoarthritis, improvement in mobility, walking as well as improvement in the quality of life. Despite the clear goal of treatment mentioned, quality of life is the least considered or often neglected aspect in the overall management of patients with knee osteoarthritis.

Objectives: To determine the quality of life and its associated factors among knee osteoarthritis patients.

Patients and method: A cross-sectional study was conducted from 1 June 2014 until 30 October 2014 at the orthopaedic clinic in Hospital Universiti Sains Malaysia (HUSM). Systematic random sampling was applied based on attendance list in orthopaedic clinic, HUSM. A set of questionnaires which includes case report form and the Malay version of Osteoarthritis Knee and Hip Quality of Life (OAKHQOL) questionnaire was given to patients before determining their body mass index (BMI) and reviewing their latest knee radiograph. Data analysis was done using SPSS Version 22. The overall quality of life among knee osteoarthritis were expressed by using mean OAKHQOL score for each domain while the associated factors that affecting the quality of life were analysed by using general linear regression analysis.

Results: The mean quality of life among patient with knee osteoarthritis were average. The worse domain was a social functioning domain with a mean score of 59.1 (SD 26.31) and the least affected domain was mental health domain with the mean score of 35.7 (SD 22.42). Increasing BMI was consistently associated with worsening of almost all domains of OAKHQOL which include physical activity (CI 0.50, 1.68), mental health (CI 0.17, 1.49), pain (CI 0.24, 1.58) and professional activity (CI 0.34, 1.94) except for social support which showed an improvement with increasing BMI (CI −2.39, −0.63). Social functioning was not associated with any studied variables. An ever-used glucosamine associated with worsening score on physical activity (CI 1.51, 14.99), mental health (CI 1.79, 17.17) and pain (CI 2.98, 18.68) domains. Longer duration of knee osteoarthritis and bilateral involvement of knee were both associated with worse sexual activity (CI 0.42, 2.59); (CI 3.68, 20.37) and relationship item score (CI 0.28, 2.48); (CI 2.83, 19.79). Higher education status appears to have a better score in mental health (CI −33.24, −7.42) and pain (CI −32.11, −5.75). domain. An ever used NSAIDs was associated with poorer score in sexual activity item (CI 0.20, 17.11). Higher grade of knee osteoarthritis by Kellgren Lawrence grading of knee osteoarthritis have worse professional activity item score (CI 0.03, 24.49).

Conclusion: The quality of life among patients with knee osteoarthritis in this study was average. Increasing BMI was consistently associated with worsening of almost all domains of OAKHQOL, except for social functioning. Social functioning was not associated with any studied variables. Variables that had an association with at least one domain of OAKHQOL were education status, grade of knee osteoarthritis, medication usage (glucosamine or NSAIDs), duration of knee pain and knee involvement (unilateral or bilateral).

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