

Abstract

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

DISTINCT MICRORNA AND GENE EXPRESSION-PATHWAY BASED ANALYSIS IN ASSOCIATION WITH CLINICAL AND LABORATORY FEATURES OF ACUTE PROMYELOCYTIC LEUKAEMIA

Imilia Ismail
PhD (Human Genetics)

Department of Haematology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: According to the French American British (FAB) classification, acute promyelocytic leukaemia (APL) is an M3 subtype of acute myeloid leukaemia (AML). The classification is based on the blast cell morphology. Although APL treatment is successfully treated via all trans retinoic acid (ATRA), the molecular mechanism of APL pathogenesis is still unclear. Analysis of new markers such as microRNA (miRNA) and gene expression as well as DNA mutation suggests more areas to be further explored.

Objectives: Hence, this study aims to examine the expression profiles of miRNA and messenger RNA (mRNA) in APL patients in association with the clinical and laboratory features of APL and molecular pathways involved in the profiling.

Methods: MiRNA and mRNA analysis were performed by using the nCounter[®] Human v2 MicroRNA Expression Assay Kit (NanoString Technologies, USA) and the nCounter[®] Pan Cancer Pathways Panel (NanoString Technologies, USA), respectively on NanoString nCounter[®] system (NanoString Technologies, USA). MiRWalk software was used to identify putative target genes for differentially expressed miRNA in APL patients. Meanwhile, direct DNA sequencing was performed to detect *FLT3/ITD* and *NPM1* mutations in APL patients. Chi-squared and Mann Whitney tests were used to perform the association between miR-100 and *FLT3* expression with clinical and laboratory features of APL patients.

Results: From the miRNA analyses, 11 miRNA that differentially expressed in newly diagnosed APL patients were identified in which six miRNA (miR-100, miR-125b, miR-34a, miR-181b, miR-181c and miR-154) are up-regulated while the remaining five (miR-185, miR-194, miR-28, miR-342 and miR-363) are down-regulated. Therefore, it was suggested that these miRNA have potential roles in APL pathogenesis. In silico analysis revealed that some genes identified were experimentally validated in other cancers.

The proposed miRNA-mRNA interaction model of APL pathogenesis was also developed based on in silico target genes. Gene expression pathway-based analysis showed 90 differentially deregulated genes, in which 30 are up-regulated and the remaining 60 are down-regulated in the newly diagnosed APL patients. Differential pathway expression revealed that transcriptional misregulation, MAPK, RAS and Notch signalling pathways significantly influence APL pathogenesis. Furthermore, mutation analysis of *FLT3/ITD* and *NPM1* genes were also performed on the newly diagnosed APL patients. The results demonstrated that seven patients were having mutation within exon 14 of *FLT3/ITD*, while no *NPM1* mutation was detected in all patients' samples. From all parameters evaluated, there is no significant ($P > 0.05$) correlation between miR-100 and *FLT3* expression with clinical and laboratory features of newly diagnosed APL patients.

Conclusion: The current findings in fact provide new insight into the role of miRNA and mRNA in APL pathogenesis and could help to discover the de novo prognostic biomarkers, thus enabling better stratification for APL patients.

Supervisor:
Professor Dr Rosline Hassan

Co-supervisor:
Associate Professor Dr Sarina Sulong

THE EFFECTS OF TRICHOSTATIN A AND 5-AZACYTIDINE ON THE DIFFERENTIALLY EXPRESSED GENES AND EPIGENETIC PROFILING IN ACUTE MYELOID LEUKEMIA

Dr Siti Asmaa Mat Jusoh
PhD (Human Genetics)

Department of Hematology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Acute myeloid leukemia (AML) is a clonal hematological malignancy, which involved a multistep process of genetic and epigenetic events. Studies have shown an interactive collaboration of both events in tumor onset and progression. Aberrant histone deacetylation and DNA hypermethylation are two common epigenetic events leading to leukemogenesis which are interrelated. Targeting

epigenetic in complement to genetic profiles serve as a promising prognostic indicator in AML.

Objectives: The aim of the study was to identify the differentially expressed genes in leukemic cell lines after treatment with epigenetic modulating agents; trichostatin A (TSA), a histone deacetylase (HDAC) inhibitor and 5-Azacytidine (5-Aza), a DNA methyltransferase (DNMT) inhibitor and their association with various mutational state in AML patients.

Methods: Two types of AML cell lines; MV4-11 (harbouring a *FLT3-ITD* mutation) and Kasumi 1 (harbouring a *t(8;21)/AML1-ETO*), were treated with TSA and 5-Aza and subjected to gene expression profiling by microarray. Gene ontology and pathway of the up and down-regulated genes were studied by DAVID software analysis. Validation and identification of genes of interest in AML patients were performed by quantitative real-time polymerase chain reaction (qRT-PCR). Protein of the genes of interest was analysed by Western blot. For the epigenetic analyses, detection of histone H3 and H4 proteins was performed by 'Western blot' and methylation profile of genes of interest was conducted by Bisulfite sequencing. Next, *FLT3-ITD/NPM1* mutation analysis of 52 AML patients was performed by conformation sensitive gel electrophoresis (CSGE). Finally, association study of the expression pattern of genes of interest with positive *FLT3-ITD/NPM1* patients was studied by bivariate correlation analysis, and survival analysis was performed by Kaplan Meier.

Results: The IC_{50} of MV4-11 and Kasumi 1 treated TSA were 2.20 μ M & 6.25 μ M and in 5-Aza were 2.30 μ M and 6.95 μ M, respectively. There were 8194 (55.4%) and 5270 (41.8%) genes in TSA treated, and 4792 (74.6%) and 4860 (55.1%) in 5-Aza treated were up-regulated in both cell lines. Whereas, 6584 (44.6%) and 7328 (58.2%) genes in TSA treated, and 1634 (25.4%) and 3968 (44.9%) in 5-Aza treated were down-regulated in both cell lines, respectively (Genespring, $P < 0.05$). Gene ontologies with associated signaling pathways identified drugs response signatures enriched for genes implicated in cancer; JAK-STAT, Cell cycle, Gap junction and PPAR pathways (EASE score = 0.1). A representative gene of each pathway; *SOCS3*, *CCNA1*, *TUBB2A*, and *ANGPTL4* were highly re-expressed at mRNA (> 100 folds), analysed by qRT-PCR with up-regulated protein level analysed by 'Western blot'. Their expressions in 52 AML patients showed a distinct expression pattern in different cytogenetic groups of AML ($P < 0.05$). *FLT3-ITD* and *NPM1* mutational status was evaluated in these AML patients by CSGE which showed 9 (17.3%) and 8 (15.4%) harbouring the mutations, respectively. DNA methylation analysed using bisulfite sequencing PCR observed DNA hypermethylation in *TUBB2A* and *ANGPTL4* promoter regions, which are in accordance with their lower gene expression pattern. However, hypermethylation shown in *CCNA1* was not in accordance with its higher expression pattern. *SOCS3* gene analysed in exonic region revealed patient-specific methylation profile compare to promoter region. *CCNA1*, *TUBB2A*, and *ANGPTL4* methylation profiles have a significant correlation with AML patient with *FLT3-ITD* and *NPM1* mutations ($P < 0.05$), associated

with poor overall survival (OS) by Kaplan-Meier analysis. The acetylating effect of TSA treatment shown by the up-regulation of histone H3 and H4 proteins indicative of transcriptional activation, was assessed by 'Western blot'.

Conclusion: In conclusion, *SOCS3*, *CCNA1*, *TUBB2A* and *ANGPTL4* are the putative epigenetic biomarker of tumor suppressor gene, and a possible correlation with the genetic alteration could be appraised, which could serve as a prognosticator for the future prospect in the treatment management of AML.

Supervisor:

Associate Professor Dr Muhammad Farid Johan

Co-supervisors:

Professor Dr Shaharum Shamsuddin

Dr Faezahtul Arbaeayah Hussain

THE EFFECTIVENESS OF POST OPERATIVE ANALGESIA IN POST RENAL TRANSPLANT PATIENTS IN SELAYANG HOSPITAL: A RETROSPECTIVE REVIEW

Dr Bavani Naidu a/p Ragupathy Naidu
MMed (Anaesthesiology)

Department of Anaesthesiology and Intensive Care,
School of Medical Sciences, Universiti Sains Malaysia,
Kubang Kerian, Kelantan, Malaysia

Background: Patients who have undergone renal transplants pose a challenge in terms of pain relief post operatively. The objective of this study was to review the effectiveness of the acute pain service in terms of patient controlled analgesia morphine (PCAM) versus patient controlled analgesia fentanyl (PCAF), length of hospital stay and side effects of both modalities in post renal transplant patients in Hospital Selayang.

Methods: This was a retrospective cross-sectional study over a period of 5 years (1 January 2011 till 31 December 2015) in Hospital Selayang. Data was obtained from the computerised patient data system, operation theatre census as well as reviewing the medical records in pertinent cases. Patients' demographics, perioperative details, post-operative analgesia and length of stay were recorded.

Results: Descriptive methods and multiple logistic regression techniques were applied to answer the objectives of the study. A total of 85 patients were involved. PCAF was 100% effective at rest, P -value = 0.056. For pain score (PS) upon movement between both groups, approximately 50% demonstrated effective good analgesia with a PS of less than 4. There was no significant difference between PCAM and PCAF in terms of side effects and length of hospital stay.

Conclusion: The acute pain service was effective in post renal transplant patients across both groups. There was no significance difference between PCAM and PCAF. Side effects across both groups were negligible.

Supervisor:
Dr Mohamad Hasyizan Hassan

Co-supervisors:
Associate Professor Dr Wan Mohd Nazaruddin Wan Hassan
Dr Ng Kim Swan

COMPARISON OF BASKA MASK® AND THE I-GEL™ SUPRAGLOTTIC AIRWAY DEVICES IN PATIENTS UNDERGOING ELECTIVE SURGERY

Dr Thanesh Kumar a/l Sinasamy
MMed (Anaesthesiology)

*Department of Anaesthesiology and Intensive Care,
School of Medical Sciences, Universiti Sains Malaysia,
Kubang Kerian, Kelantan, Malaysia*

Background: The Baska Mask® and the i-Gel™ are two types of new supraglottic airway devices (SGAD) which are classified as second generation of SGAD. The aims of this study were to compare these two devices in terms of quality of insertion, quality of ventilation and post insertion complications.

Methods: A total of 80 patients, aged between 18–60 years, ASA I-II, scheduled for elective surgery under general anaesthesia using SGAD, were randomised into two groups: i) Group B: Baska Mask® ($n = 40$); and ii) Group I: i-Gel™ ($n = 40$). The assessment was on ease of insertion, number of attempts, success rate at first attempt, insertion time, number of corrective maneuvers, oropharyngeal leak pressure, inspired and expired tidal volume (VT), peak airway pressure (PAP) and post-operative complications.

Results: Group I showed significantly shorter median insertion time [13.3 (IQR 7.8) versus 17.0 (IQR 9.6) sec; $P < 0.001$], higher percentage in 'very easy' category of ease of insertion assessment [62.5% versus 10.0%; $P < 0.001$], lower in generated PAP [11.5 (2.2) versus 12.7(1.8) cmH₂O; $P = 0.010$] and higher percentage in no post-operative throat pain [67.5% versus 32.5%; $P = 0.011$] than Group B. There were no significant differences in number of attempts, number of corrective manoeuvres, inspired and expired VT, oropharyngeal leak pressure and other post insertion complications such as post-operative nausea and vomiting, blood-stained devices, or injury to tooth, gum or tongue.

Conclusion: The i-Gel™ was better than the Baska Mask® in terms of easier insertion, faster insertion time, lower PAP and reduced post-operative throat pain.

Supervisor:
Associate Professor Dr Wan Mohd Nazaruddin Wan Hassan

Co-supervisor:
Dr Rhendra Hardy Mohd Zaini

THE EFFECT OF ORAL CARBOHYDRATE DRINK VERSUS ORAL PLAIN WATER PREOPERATIVELY TO GASTRIC VOLUME, pH AND GLUCOSE LEVEL IN ELECTIVE NON-ABDOMINAL SURGERY

Dr Maryam Jameelah Haji Nawawi
MMed (Anaesthesiology)

*Department of Anaesthesiology and Intensive Care,
School of Medical Sciences, Universiti Sains Malaysia,
Kubang Kerian, Kelantan, Malaysia*

Introduction: Overnight fasting pre-operatively has been a routine practice to reduce residual gastric volume (RGV). With the introduction of the enhanced recovery after surgery (ERAS) concept, there has been a major change in established practice whereby patients are able to continue with solid food up to six hours and clear fluids up to two hours prior to surgery. Instead of plain water, taking carbohydrate (CHO) drink has become new alternative concept of allowing some amount of drink preoperatively which could improve patient's satisfaction. Nevertheless, barriers to the introduction of routine evidence-based clinical care and changing dogmas still exist.

Objectives: To compare the RGV, gastric pH and random blood sugar (RBS) of patients given CHO drink to oral plain water three hours preoperatively.

Methods: Eighty-eight American Society of Anesthesiologists (ASA) physical status I–II patients for elective non-abdominal surgery under general anesthesia (GA) were randomised into two groups; (CHO)-rich (Resource TM) drink group (Group A, $n = 44$) received 200 mL of oral CHO solution 3 h before anesthesia. The other group (Group B, $n = 44$) received plain water in the same protocol as Group A. Both groups were tested for RGV using Ryle's tube aspiration and pH using pH-indicator strips (MColorpHast™). The Independent t-test was used to analyze RGV, pH and RBS level.

Results: The RGV were significantly lower for group A [7.50 (8.69) versus 13.59 (10.45); $P = 0.004$] while pH level and glucose level were comparable for both groups ($P = 0.672$, $P = 0.235$, respectively).

Conclusion: Pre-operative CHO drink up to 3 h before surgery reduced RGV but did not differ in term of pH and RBS if compared to conventional plain water practice.

Supervisor:
Dr Sanihah Che Omar

Co-supervisor:
Dr Laila Ab Mukmin

INTRODUCTION OF A NEWLY CREATED AW STEREOTACTIC FRAME: A PHANTOM-BASED ACCURACY EVALUATION AND AN INITIAL EXPERIENCE IN CLINICAL USAGE

Dr Lau Bik Liang
MSurg (Neurosurgery)

Department of Neurosciences, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Objective: A new stereotactic frame was created by Albert Wong, based on a linear algorithm. It is called AW (Albert Wong) frame. A simple AW stereo-calculator was also designed based on Microsoft Excel® programme for the frame. The aim of this study is to test the accuracy of the AW frame by a direct head to head comparison with Cosman-Roberts-Wells (CRW®) frame on a phantom.

Methods: This is a pilot prospective cross-sectional phantom study with a total of 42 (21 for AW and 21 for CRW®) laboratory testings performed in 2017 at the Sarawak General Hospital to compare the accuracies of both frames in a consecutive manner. A phantom (BL) was created by Bik Liang (BL) Lau, where targets can be placed at different heights and positions on a platform attached under the frame for accuracy testing comparing between the AW and CRW® frames.

Results: A comparable accuracy testings were observed between the AW and CRW® frames of 0.6483 mm versus 1.0707 mm, respectively. With this, we had obtained approval from Medical Research Ethic Committee (MREC), Malaysia for a clinical trial. We reported on three case illustrations who had the AW frame-based biopsies with definitive diagnoses and without any post-biopsy related complication.

Conclusion: AW frame successfully demonstrated a good accuracy of 0.6483 mm in phantom testings using the BL phantom through a linear algorithm calculation. The clinical trial with three patients demonstrated definitive diagnoses and safety with its use.

Supervisors:
Professor Dr Zamzuri Idris
Dr Albert Wong Sii Hieng

CORTICOMOTOR EXCITABILITY AFTER TWO DIFFERENT REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION PROTOCOLS IN HAEMORRHAGIC STROKE PATIENTS

Dr Asrarul Fikri bin Abu Hassan
MMed (Neurosurgery)

Department of Neuroscience, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Intracerebral haemorrhage (ICH) or haemorrhagic stroke is the most disabling type of stroke

and associated with high mortality and morbidity. Stroke is listed as one of the top five leading cause of mortality and hospital admission in Malaysia. Latest studies reported there was no significant different comparing medical treatment and surgical treatment in haemorrhagic stroke patient. Transcranial magnetic stimulation (TMS) is non-invasive tool and utilisation of TMS has shown promising result in stroke patient and promote better motor neurological recovery. Therefore, this study intended to investigate the corticomotor excitability between the two repetitive transcranial magnetic stimulation (rTMS) settings in haemorrhagic stroke patients. Finding from this study will produce informative and communicating evidence on how TMS can help haemorrhagic stroke patient in the rehabilitation process. It can also provide an alternative means to the pharmacological treatment by promoting recovery of motor function and improve quality of life.

Objectives: The aims of this study to investigate the changes in corticomotor excitability after two different rTMS therapy regimes in haemorrhagic stroke patient.

Methods: A randomised control trial was performed in Hospital Universiti Sains Malaysia (HUSM). Twenty-nine patients were recruited in this study and randomised into three groups: i) facilitatory group; ii) inhibitory group; and iii) Sham group. Patient underwent two weeks TMS Stimulation protocol for total of 10 sessions. Motor evoked potential (MEP) reading was taken pre and post TMS stimulation for each different protocol and analysed.

Results: The mean age of patients was 52.86 years old, with 16 (55.2%) of them were male and 13 (44.8%) were females. The mean ICH clot size was 22.95 cm³ and mean for intervention time was 5.76 months. It was found that MEP score after TMS facilitatory protocol was significantly higher compared to the Sham protocol group ($P = 0.02$) but no significant improvement in MEP score after TMS inhibitory protocol ($P = 0.175$). There was no significant different with correlating the MEP score with age, ICH clot size and intervention time.

Conclusion: TMS is safe non-invasive tool which can be used for ICH stroke patient. Patient who underwent facilitatory rTMS protocol has significantly improved MEP post intervention. Patient with stable ICH will have better motor function recovery post rTMS facilitatory protocol regardless of their age, clot size and time for the intervention.

Supervisor:
Dr Muhammad Hafiz Hanafi

Co-supervisors:
Professor Zamzuri Idris
Professor Dato' Dr Jafri Malin Abdullah

A 5-YEAR REVIEW OF SINGLETON PREGNANCIES WITH SMALL-FOR-GESTATIONAL AGE/FOETAL GROWTH RESTRICTION, MATERNAL RISK FACTORS AND DELIVERY OUTCOMES: HOSPITAL UNIVERSITI SAINS MALAYSIA EXPERIENCES

Dr Nurul Ashikin Abu Bakar
MMed (Obstetrics and Gynaecology)

Department of Obstetrics and Gynaecology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Small for gestational age (SGA) and foetal growth restriction (FGR) are common diagnosis in obstetrics in this part of the world and they carry a significant perinatal morbidity and mortality. Due to the potential adverse outcomes of these two conditions, identifying pregnancies with SGA/FGR is important. Early identification with a proper evaluation followed by an accurate management can lead to favourable outcomes.

Objectives: To determine the prevalence of SGA/FGR, the maternal risk factors for developing SGA/FGR, the perinatal outcome of these infants and to evaluate the association of preterm/term SGA/FGR to delivery outcome.

Methods: A retrospective study conducted in Maternity unit in Hospital Universiti Sains Malaysia for a period of 5 years from January 2012 until December 2016 involving 275 mothers with singleton pregnancy who delivered a foetus with birthweight < 10th centile and fulfilled the inclusion and exclusion criteria.

Results: The prevalence of SGA/FGR in Hospital Universiti Sains Malaysia is 7.6%. The mean age of patient is 27.96 years old (SD 5.88). They were at the age group of 20–34 years old (79.6%) followed by 13.8% from age 35 years and above and 6.5% from less than 19 years of age group. Half of them were nullipara (53.1%), 20.4% of parity 1, 21.7% of parity 2–4 and 4.7% of parity 5 or more. The mean BMI is 23.1 (SD 5.39) and about 121 patients (44.0%) were of normal BMI followed by 22.2% were from low BMI group. Passive maternal smoking was seen in 52.4% of the cases. Majority of mothers with SGA/FGR were not anaemic (83.3%). Only 26 out of 275 cases were complicated by preeclampsia. 16% of these cases had gestational hypertension, 3.6% of chronic hypertension and majority were normotensive mothers (80.4%).

Predominantly there were 98.9% live births at delivery. 73.5% were born at term and 26.5% were preterm with mean gestational age of 37.6 (SD 5.67) weeks and 28.99 (SD 6.48) weeks, respectively. The mean birth weight is 2.09 kg (SD 0.44). The mean birth weight for preterm SGA/FGR is 1.59 kg (SD 0.45) and for term is 2.27 kg (SD 0.26). About 1/3 of cases required induction of labour and most of them were from the term SGA/FGR group (41.6%). In the induction group, 32.7% ended up with emergency caesarean section but majority (62.5%) achieved spontaneous vertex delivery. Pregnancies with SGA/FGR required induction of labour ($P = 0.001$), and the foetuses were born with poor Apgar score ($P < 0.001$) and required NICU admission ($P < 0.001$).

Among all maternal risk factors, preeclampsia is the only factor associated with increased risk of preterm delivery by calculation using simple logistic regression. Women with preeclampsia have 5.39 times odds of experiencing preterm delivery compared to those without preeclampsia (OR = 5.39, 95% CI: 2.31, 12.53). Patients with preterm delivery have 90% lower odds to experience good Apgar score compared to patients with term delivery (OR = 0.10, 95% CI: 0.03, 0.36). In this study, there was significant association between induction of labour and successful vaginal delivery ($P < 0.001$). For mothers whose labour is induced, there are 5.92 higher odds of achieving vaginal delivery rather than caesarean section.

Conclusion: Out of all the maternal risk factors, only pre-eclampsia is shown to have statistically significant association with SGA/FGR foetus. Other strong factors such as anaemia and passive smoking failed to demonstrate any causal relationship with the diagnosis of SGA/FGR. Pregnancies complicated with SGA/FGR required induction of labour and most had successful vaginal delivery. Future prospective studies using our own customised centiles are needed to distinguish true SGA/FGR from the constitutionally small foetus in our population.

Supervisor:
Dr Hoo Pek Sung

Co-supervisor:
Professor Mohd Pazudin Ismail

THE PREDICTORS FOR THE SUCCESS OF IN VITRO FERTILISATION/INTRACYTOPLASMIC SPERM INJECTION AMONG ADVANCED AGE WOMEN IN SPECIALISED HOSPITAL USM FERTILITY UNIT

Dr Nurul Izza Mohamed Rusdi
MMed (Obstetrics and Gynaecology)

Department of Obstetrics and Gynaecology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: As a woman become older, her ovarian function will start to decline, thus making woman's age as an important factor to determine her ability to conceive. Women start to experience a decline in natural fertility in their mid-30's, and they will often reach sterility many years before the complete cessation of menses. Therefore, the number of women facing fertility problem at advance age and seek medical attention is increasing. Assisted Reproductive Techniques (ART) is one of the solutions for this issue.

Objective: To evaluate the factors that could predict the success of IVF/ICSI treatment among elderly women, aged between 35 and 45 years by determine the ovarian response, the number of good quality oocytes retrieved, endometrial thickness and endometrial morphology.

Methods: This prospective study involved 85 patients at the age of 35–45 years old that are going to receive IVF/

ICSI treatment at infertility unit HUSM over the period of 24 months. The patients who had undergone controlled ovarian hyperstimulation until matured follicles were observed, followed by oocytes retrieval and embryo fertilisation by IVF/ICSI. Embryo transferred was done at blastocyst stage. Serum beta hCG was taken after 14 days embryo transferred. Data was analysed to look for association between successful pregnancy with ovarian response and endometrium receptivity.

Results: Pregnancy was achieved in 9 out of 85 patients (10.6%). The mean age of pregnant patient was 36.89 years. The mean numbers of oocytes retrieved and fertilized embryo in pregnant patient were 11.44 oocytes and 8.0 embryos, respectively. The number of fertilised embryo showed statistically significant with successful IVF/ICSI with P -value 0.014. The mean of endometrial thickness in pregnant patient was 9.81mm whereas in non-pregnant patient was 10.05mm. Seven patients out of 9 patients who got pregnant had trilaminar endometrial pattern. This endometrial receptivity was not statistically significant.

Conclusion: The pregnancy rate among advanced age group that undergone IVF/ICSI was low only 10.6%. The fertilised embryo as a predictor of ovarian respond was statistically significant with successful IVF/ICSI, however neither endometrial thickness nor morphology is associated with higher pregnancy rate. This result was guarded by the small sample size.

Supervisor:

Associate Professor Dr Adibah Ibrahim

EVALUATION OF 2015 REVISED FIGO CARDIOTOCOGRAPH CLASSIFICATION FOR INTRAPARTUM FOETAL HYPOXIA/ACIDOSIS IN HOSPITAL RAJA PERMAISURI BAINUN IPOH

Dr Kaamini Planisamy
MMed (Obstetrics and Gynaecology)

Department of Obstetrics and Gynaecology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Cardiotocography (CTG) is the primary means of intrapartum foetal monitoring. However, it has resulted in an increased incidence of operative delivery for presumed foetal compromise, with an extra 11 CS being performed to prevent one case of neonatal seizure. A major limitation of CTG is the subjective nature of its interpretation with significant intra and inter-observer disagreement. Hence, there is a need to assess the efficacy of CTG interpretation.

Objectives: To determine sensitivity and specificity of the International Federation of Gynaecology and Obstetrics (FIGO) 2015 cardiotocograph (CTG) guidelines. To determine risk factors leading to foetal distress. To ascertain neonatal outcomes in cases of foetal hypoxia/acidosis.

Methods: This was a observational cross sectional study, which involved 539 women that delivered in Hospital

Raja Permaisuri Bainun Ipoh between 11 May 2017 and 10 June 2017. These women's period of gestation was > 37 weeks and delivered either via Caesarean section or vaginal delivery. CTG tracings prior to delivery were collected and interpreted by independent observers. Following delivery, all these women had the arterial cord blood taken and sent for analysis of cord blood gases.

Results: The sensitivity of FIGO 2015 CTG classification is 46%, higher compared to NICE 2017 CTG guidelines which is 29.6%. Specificity of FIGO 2015 fared worse at 66.9% compared to NICE 2017 at 87.7%. Intrapartum risk factors that lead to abnormal CTG tracings and foetal hypoxia include, advanced maternal age, primigravida, prolonged rupture of membranes and nuchal cord. Of the 539 babies born, only 14 had an Apgar score < 7. Of these 14, only 2 babies required intubation and ended up with seizures and HIE and both of these babies had cord ABG pH < 7.

Conclusion: There is still a lot of room for improvement of CTG classification in order to achieve better sensitivity and specificity. Further studies need to be done to evaluate the role of assessing risk factors and its complications to be incorporated into any future new amendments of CTG classification. Babies born with moderate and mild hypoxia/acidosis usually don't experience severe morbidity.

Supervisor:

Dr Wan Rosilawati Rosli

EVALUATION OF MACULAR THICKNESS, RETINAL NERVE FIBRE LAYER THICKNESS AND OPTIC NERVE HEAD PARAMETERS WITH BODY MASS INDEX AMONG NONPROLIFERATIVE DIABETIC RETINOPATHY PATIENTS

Dr Nur Afiah Kamaluddin
MMed (Ophthalmology)

Department of Ophthalmology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Overweight or obesity is a well-known major public health problem worldwide including our country, Malaysia. It is an established risk factor for many modern health diseases such as diabetes mellitus (DM), hypertension and ischemic heart disease. Diabetic patients also were found to be at high risk getting other comorbidities including overweight or obesity. Therefore, these accelerate the potential ocular effects for the patients.

Objective: To compare the mean macular thickness, retinal nerve fiber layer (RNFL) thickness and optic nerve head (ONH) parameters among diabetic patients with non-proliferative diabetic retinopathy (NPDR) in normal body mass index (BMI) and overweight groups.

Methods: This is a cross-sectional study conducted in Hospital Universiti Sains Malaysia (HUSM), Kelantan from February 2017 until February 2019. Patients with

confirmed to have NPDR were selected based on the inclusion and exclusion criteria and were divided into normal and overweight groups. Macular thickness, RNFL thickness and ONH parameters were measured by using Optical Coherence Tomography.

Results: A total of 136 NPDR patients were recruited into this study, comprised of 68 patients of normal BMI group and 68 patients of overweight group. The global, superior and temporal outer macular thickness in the overweight group were significantly thinner than the normal BMI group (274.20 μm versus 278.91 μm , $P = 0.047$, 273.86 versus 282.56, $P = 0.001$ and 253.85 μm versus 2261.59 μm , $P = 0.001$, respectively) after adjusted for the duration of diabetes, level of HbA1c, CKD and HPL status. The inferior quadrant of RNFL thickness was significantly thinner 120.61 μm ($P = 0.025$) in the overweight group than normal BMI group after adjusted for the duration of diabetes, level of HbA1c, CKD and HPL status. However, there was no significant difference in the ONH parameters between the two groups after adjusted for the age, duration of diabetes and level of HbA1c.

Conclusion: Diabetic patient with NPDR among overweight patients showed significant thinning effect in the mean macular thickness and mean RNFL thickness. This showed that higher BMI may affect the retinal layers among NPDR patients thus raise the alarm that our population need to implement a better and healthier lifestyles. However, further extensive and comprehensive studies are needed to prove the strong relationship.

Supervisor:
Professor Dr Mohtar Ibrahim

Co-supervisor:
Associate Professor Dr Datin Zunaina Embong:

EXPRESSION OF OSTEOCLAST- SPECIFIC MARKER NUCLEAR FACTOR OF ACTIVATED T- CELLS (NFATC1) IN OSTEOSARCOMA TISSUE

Dr Jufithri bin Abd Halim
MMed (Orthopaedic)

Department of Orthopaedics, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Osteosarcoma is a primary malignant bone tumour derived from primitive bone-forming mesenchymal tissue characterised by the production of osteoid or immature bone by malignant, proliferating spindle cells. It is highly malignant and has a tendency to metastasize to the lung. The survival rate has increased exponentially in the 1970s and has since plateaued at around 60%–70% for the past decade. It is therefore paramount for us to understand the basic molecular pathology of osteosarcoma tissue to shed light into possible new therapeutic strategies to further improve the survival rate of osteosarcoma patients. Osteosarcomas secrete osteoclast-stimulating cytokines that

stimulate bone resorption, while tumour growth is supported by factors that are released during osteolysis. Two key factors that are required for osteoclast differentiation are RANKL, a tumour necrosis factor (TNF) receptor family member, and macrophage colony-stimulating factor (M-CSF). RANKL is required for osteoclast formation and function. However the use of RANKL inhibitors in treatment of osteosarcoma is still contradicting. NFATc1 is a member of NFAT (nuclear factor of activated T cells) family of transcription factor genes. It was proven to be vital for regulating terminal differentiation of osteoclasts. It is important to study the function of NFATc1 in osteosarcoma as the relationship between osteoclast and osteosarcoma has been established before.

Methods: This was a cross sectional study using available osteosarcoma tissue in Pathology Tissue Bank, HUSM. We evaluated the immunohistochemical staining for expression of NFATc1 in 31 osteosarcoma tissue samples at protein level. These tissue samples were taken from patients who have completed treatment of osteosarcoma in Hospital Universiti Sains Malaysia (HUSM) from January 1998–December 2010. Thirty-one patients were included and randomised between disease free survival and early failure of treatment with distant metastases.

Expression of NFATc1 was assessed by immuno-histochemical staining in all representative archive tumor sections from each patient. Serial sections size 5 μm thick were cut and immuno-histochemical techniques were carried out. NFATc1 expression over nuclear area of tumor cells were examined using immunohistochemistry. Immunostainings were evaluated in three randomly chosen microscopic fields using a standard light microscope at 40 \times 100 magnification by two-blinded independent observers. Positivity for NFATc1 expression was accepted as stained cells within the said slides. Two captured images of stained or unstained cells were then examined for positivity and was taken for statistical analysis using SPSS version 24. Statistical analysis was determined using Pierson chi square test for different group and considered statistically significant when the P -values were less than 0.05.

Results: A total of 31 osteosarcoma patients that received treatment in HUSM since January 1998 to December 2010 were recruited for this study. The data obtained was expressed as mean (SD = standard deviation) for numerical and n = frequency (%) for categorical variables. Fifteen patients had disease free survival and another 16 patients succumbed to early metastases. The result of the data showed that the mean age of the participants is 20.00, and the SD is 11.74. Meanwhile, there were more than half male participants included in the study ($n = 19$, 61.3%). Predominantly, there were 87.1% ($n = 27$) Malay patients compared to other races. 74.2% ($n = 23$) patients with negative NFATc1 reported in the present study. There were no statistically significant association between survival status and NFATc1 expression (P -value = 0.433) and also no statistically significant association between different types of osteosarcoma and NFATc1 expression (P -value = 0.614).

Conclusion: Our study has shown that NFATc1 is poorly expressed in osteosarcoma tissue. There is also no statistically significant association between survival, different types of osteosarcoma in relation to NFATc1 expression.

Supervisor:

Professor Dr Wan Faisham Nu'man Wan Ismail

Co-supervisors:

Dr Muhammad Syahrul Fitri Zawawi

Dr Sharifah Emilia Tuan Sharif

INTRAOPERATIVE MORPHOMETRIC MEASUREMENT OF DISTAL FEMUR DIMENSIONS AND CORRELATION WITH IMPLANT SIZING IN FEMALE TOTAL KNEE ARTHROPLASTY PATIENTS

Dr Sanjeevan Radhakrishnan
MMed (Orthopaedics)

Department of Orthopaedics and Traumatology,
School of Medical Sciences, University Sains Malaysia,
Kubang Kerian, Kelantan, Malaysia

Introduction: An accurate implant sizing is one of the major determinants in defining the success of total knee arthroplasty. Total knee arthroplasty (TKA) implants currently in use are based on Caucasian knee morphometry which is well documented to be larger than Asian knees. The significant clinical implication of implant mismatch has led researchers to greatly delve into this field of study worldwide. With regards to sizing, implant mismatch tends to be more evident in the female population.

Objectives: This study was designed to evaluate the distal femur dimensions of female patients who underwent TKA in our institution and to compare them with the current single prosthetic system in use.

Methods: Total of 101 female patients (105 knees) who underwent TKA were recruited in this study. Intraoperatively, the anteroposterior (AP) dimensions of the medial and lateral condyles and mediolateral (ML) width were measured. Known dimension of the femoral component of the prosthetic knee system currently in use were obtained from the implant manufacturer. Correlation between the AP and ML dimensions of the morphological data were determined. The mean difference in the ML dimension between the implant and patient's knee were statistically analysed to ascertain the amount of femoral component ML mismatch. In addition, a characterisation of the aspect ratio (ML divided by AP) was made; this aspect ratio was compared with that of the currently used prosthetic system.

Results: The average femoral component overhang was 2.11 mm (SD 3.94 mm). There was significant difference between the ML width of the resected femur and the femoral component ($P < 0.01$). As in our population of study, the femoral components used were predominantly from the lower half of the available sizes. Thus, we could get away with lower magnitude of implant overhang. If we were to encounter larger knees, we expect to deal with a wider margin of overhang and its associated complications.

Correlation analysis also revealed a significant positive and weak relationship between both, AP (medial and lateral) and ML dimension. The aspect ratio for the morphological data showed a larger ratio for smaller knees and inversely

a smaller ratio for larger knees. Although the aspect ratio of the morphological data were generally smaller than the implant aspect ratio, the trend of change in the aspect ratios of the initial five sizes of implant were seen to follow the morphological data. However, the larger implant sizes showed little change in its aspect ratio. In other words, the implant ML overhang is expected to be more pronounced in the larger knees.

Conclusion: The currently used implant is suboptimal in its sizing for our population as depicted by the disparity in the aspect ratio and ML length for a given AP dimension, notably in the larger sizes. The results of this study could provide a guide to implant manufacturers to tailor implants which suit the morphometric measurements of Malaysian population especially female patients hence maximizing the outcome of TKA and reducing its complications.

Supervisor:

Dr Shaifuzain Abdul Rahman

Co-supervisor:

Professor Dr Amran Ahmed Shokri

TREATING ACETABULAR FRACTURES BY USING MODIFIED STOPPA APPROACH AND ITS CLINICAL OUTCOMES

Dr Noor Azmi bin Mohamad Nor
MMed (Orthopaedics)

Department of Orthopedics, School of Medical Sciences,
Universiti Sains Malaysia, Kubang Kerian, Kelantan,
Malaysia

Introduction: Acetabular fracture require an accurate anatomical reduction, stable fixation and early rehabilitation to obtain the best outcome. Surgical intervention has become the gold standard for this fracture. This study presents the experience of treating acetabular and pelvic fractures using modified Stoppa approach in Hospital Tuanku Ja'afar Seremban (HTJS).

Objectives: The aims of this study were to identify the demographic types of fracture, intra-operative and post-operative outcome and complications among patients with acetabular fractures treated with modified Stoppa approach in HTJS.

Methods: This is a cross sectional retrospective study and were done among 33 patient that presented with acetabular and pelvic fractures following trauma and treated surgically using modified Stoppa approach in HTJS from 1 January 2015 to 31 December 2016. The data of this study was collected from the patient's folder and X-ray obtained from Unit Rekod Perubatan, HTJS and Orthopedic Clinic, HTJS.

Results: Mean of blood loss intraoperatively is 1,150 mL which are ranging from 200 mL to 3,300 mL. Total surgical time intraoperatively also measured showed range from 60 min to 592 min (means 136.9 min). A number of 18 patients (54.5%) were able to achieve anatomic reduction, 12 patients (36.4%) were imperfect reduction and only

3 patients (9.1%) were poor reduction. For rate of union, all patient (100%) was achieved union less than 6 months. The related complication of this approach was surgical site infection (6 patients, 18.2%), heterotopic ossifications (7 patients, 21.2%) and 6 patients (18.2%) developed avascular necrosis of femoral head. All of the patients with AVN of femoral head was found in group of imperfect and poor reduction. This study also showed there was an association between fracture reduction of acetabular fracture with AVN of femoral head ($P = 0.008$).

Conclusion: This study shows that using modified Stoppa approach in treating acetabular fractures only achieve anatomical reduction in half of the patient (54.5%). However, it is still can be considered as an alternative approach because its advantages such as small incision, less soft tissue dissection and has minimal risk in order to get anatomic reduction and fixation of the acetabular fractures.

Supervisor:
Dr Norazman Mat Zin

Co-supervisor:
Dato Dr Abdul Rauf Ahmad

THE STUDY OF THE ORBITAL FLOOR AS A SURGICAL LANDMARK FOR ANTERIOR SKULL BASE IN HOSPITAL USM

Dr Chew Shiun Chuen
MMed (Otorhinolaryngology)

Department of Otorhinolaryngology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Background: Revision endoscopic surgery for recurrent chronic rhinosinusitis and destructive lesions might distort the normal anatomical landmark in endoscopic sinus surgery (ESS). The aim of this study was to evaluate the use of the orbital floor (OF) as a surgical landmark for ESS and to use its position to develop a new classification to assess the risk of skull base injury.

Methods: A cross-sectional study of previously performed computed tomography of paranasal sinuses (CT PNS) from 1 January 2010 to 31 December 2015 was performed. The distance from the nasal floor to five structures; the OF, cribriform, ethmoid roof, sphenoid roof and the sphenoid floor was measured. The relation of anterior skull base to the OF was also assessed. The ratio of the nasal floor-orbital floor (NF-OF) to the orbital floor-ethmoid roof (OF-ER) was calculated.

Results: A total of 150 CT PNS (300 sides) was evaluated. The orbital floor was found below the skull base on all sides. The distance of the nasal floor to the OF was 35.4 ± 3.1 mm, cribriform was 46.2 ± 3.9 mm, ethmoid roof was 49.5 ± 4.4 mm, sphenoid roof was 45.9 ± 3.7 mm and sphenoid floor was 29.6 ± 3.5 mm, respectively. The distance of the cribriform plate, ethmoid roof and the sphenoid roof to OF was 10.7 ± 2.1 mm, 14.1 ± 2.9 mm and 10.5 ± 1.8 mm,

respectively. The mean ratio of the NF-OF to the OF-ER (NF-OF: OF-ER) was 2.65 ± 0.77 .

Conclusion: The orbital floor is a useful landmark and its distance to nearby structures serves as reference points in ESS. The use of TMS classification allows surgeon to assess the risk of skull base surgery in patients undergoing ESS.

Supervisor:
Professor Dr Baharudin Abdullah

Co-supervisors:
Associate Professor Dr Mohd Ezane Aziz
Dr Norasnieda Md Shukri

COMPARATIVE STUDY ON EFFECT OF TUALANG HONEY AND TRIAMCINOLONE IMPREGNATED NASAL PACKING IN PATIENTS POST-ENDOSCOPIC SINUS SURGERY

Dr Guhan Kumarasamy
MMed (Otorhinolaryngology, Head and Neck Surgery)

Department of Otorhinolaryngology – Head and Neck Surgery, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: To evaluate the effects of Tualang honey impregnated absorbable nasal pack versus Triamcinolone impregnated nasal pack on post-operative outcome after endoscopic sinus surgery (ESS). Post-operative healing assessments of edema, crusting, secretions, scarring and symptoms were done at post-operative days 7, 14, 28 and at 3 months using validated Modified Lund-Kennedy Scoring System, SNOT-22 Questionnaire and Perioperative Sinus Endoscopy (POSE) scores.

Objective: To compare the effects of Tualang honey and Triamcinolone soaked absorbable nasal packing in patients post-ESS.

Methods: Design: Prospective, randomised, single blinded, positive-controlled trial; Setting: Two tertiary care government hospitals; Participants: Thirty-two patients aged 18 years old and above, diagnosed with chronic rhinosinusitis, who underwent endoscopic sinus surgery from March 2017 to April 2018.

Results: Both the Tualang honey group and Triamcinolone group responded to the medications post-surgery (P -value < 0.05). However, no statistically significant differences were noted in the scores of SNOT 22, POSE and Modified Lund-McKay at day 7, 14 and 28 (P -value > 0.05). At third month, patients in the Triamcinolone group had better endoscopic findings and lesser symptoms (P -value < 0.05).

Conclusion: Tualang honey is not an adequate replacement to Triamcinolone when it comes to preventing recurrences of chronic rhinosinusitis in the long run.

Supervisor:
Professor Dr Baharudin Abdullah

Co-supervisors:
Associate Professor Ramiza Ramza Ramli
Dr Harvinder Singh

PARTIAL THICKNESS STERNOMASTOID ROTATIONAL FLAP IN PAROTID SURGERY — THE FUNCTIONAL AND AESTHETIC OUTCOME

Dr Nurul Farahiyah Abdullah
MMed (Otorhinolaryngology, Head & Neck
Surgery)

Department of Otorhinolaryngology, Head & Neck Surgery,
School of Medical Sciences, Universiti Sains Malaysia,
Kubang Kerian, Kelantan, Malaysia

Introduction: Most salivary glands tumour are benign and occur in parotid gland which account about 80%. The most common type is a pleomorphic adenoma. Most tumours require parotid surgery and complications following parotidectomy are facial palsy, Frey's syndrome, cosmetic defect and hypoaesthesia of greater auricular nerve. Multiple surgical techniques were conducted in preventing parotidectomy sequelae particularly cosmetic defect and Frey's syndrome. Parotidectomy with sternomastoid flap (SCM) is one of the methods used in preventing Frey's syndrome and correcting contour deformity at parotid bed. In this study, we compare the occurrence of Frey's syndrome, aesthetic outcome, facial nerve palsy and cervical/ear lobe paraesthesia between two groups of patients (parotidectomy with sternomastoid flap and parotidectomy without sternomastoid flap).

Objectives: The aims of this study were to investigate the operative outcomes of using sternomastoid rotational flap during parotid surgery, to compare the occurrence of Frey Syndrome in post-parotidectomy patient who undergoes sternomastoid rotational flap and without flap, to assess the aesthetic outcomes of post-parotidectomy patient using the sternomastoid flap and those without the flap, to assess the occurrence of the facial nerve palsy in post parotidectomy with flap and without flap. And to assess cervical/ear lobule paraesthesia in post-parotidectomy patient who undergoes sternomastoid rotational flap and without flap.

Methods: This was a comparative cross sectional study done at Hospital Universiti Sains Malaysia from June 2016 until October 2018. All patients that underwent superficial or total parotidectomy with sternomastoid flap and without sternomastoid flap that met inclusion or exclusion criteria were recruited. Evaluation of Frey's syndrome was evaluated subjectively and objectively by minor starch iodine test while evaluation of aesthetic outcome was by using visual analog score. Assessment of facial nerve was using House-Brackmann grading. Evaluation of hypoaesthesia of greater auricular nerve via enquiring symptoms of cervical/ear lobe numbness.

Results: The occurrence of Frey's syndrome in parotidectomy without SCM flap group was higher than parotidectomy with SCM flap group. It stated that 13 patients (72.2%) in nonSCM flap group had Frey's syndrome whereas only 2 patients (11.8%) in SCM flap group. The aesthetic result showed that patients underwent parotidectomy with SCM flap had lower mean score of 1.21 (SD = 0.36) at day 14, 0.06 (SD = 0.24) at day 30 and 0.03 (SD = 0.12) at day 60, respectively. Both outcomes were statistically significant ($P < 0.05$). While incidence of facial nerve palsy and cervical/ear lobe numbness disclosed the same outcome.

Conclusion: There was a difference in functional and aesthetic outcomes between parotidectomy with SCM flap and without SCM flap for Frey's syndrome and aesthetic outcome.

Supervisor:
Dr Norhafiza Mat Lazim

Co-supervisors:
Professor Dr Baharudin Abdullah
Dr Zulkifli Yusof

THE EFFECTIVENESS OF ENDOSCOPIC DIAGNOSIS OF UPPER AERODIGESTIVE TRACT TUMOURS BY IMAGES/SPIES (STORZ PROFESSIONAL IMAGE ENHANCEMENT SYSTEM)

Dr Nurul Syeha Abdull Rasid
MMed (Otorhinolaryngology, Head & Neck
Surgery)

Department of ORL-HNS, School of Medical Sciences,
Universiti Sains Malaysia, Kubang Kerian, Kelantan,
Malaysia

Introduction: The standard diagnostic procedure in the assessment of upper aerodigestive tract (UADT) tumours is by white light endoscopy (WLE) combined with biopsy. However, WLE has difficulty identifying minute epithelial changes and cannot directly differentiate benign from malignant tumours. Storz Professional Image Enhancement System (SPIES) is designed to enhance the visualisation of microvasculature on the mucosal surface and detect any epithelial changes.

Objectives: In this study, we aimed to evaluate the use of Ni endoscopic classification with SPIES endoscopy system in the detection of UADT tumours.

Methods: Fifty-nine patients with suspected UADT tumours underwent WLE followed by SPIES endoscopy examination. All the masses were biopsied and sent for histopathological examination (HPE) for comparison. The sensitivity, specificity, and positive and negative predictive values for WLE and SPIES endoscopy were calculated.

Results: The sensitivity and specificity in the differentiation between WLE and HPE were 77.5% and 84.2%, respectively with positive predictive value of 91.2% and negative predictive value of 64%. The differentiation

between SPIES endoscopy using Ni classification and HPE demonstrated a sensitivity of 97.5% and specificity of 94.7% with positive predictive value of 97.5% and negative predictive value of 94.7%.

Conclusion: SPIES endoscopy using Ni classification offers a high sensitivity and specificity rate in the distinction between benign and malignant lesion and appears as a reliable diagnostic tool for earlier UADT tumours recognition.

Supervisor:

Professor Dr Baharuddin Abdullah

Co-supervisors:

Dr Norhafiza Mat Lazim

Dr Nik Fariza Husna Nik Hassan

CLINICAL CHARACTERISTICS AND OUTCOMES OF PAEDIATRIC PATIENTS ON LONG TERM OXYGEN THERAPY

Dr Siti Sarah Ismail
MMed (Paediatrics)

Department of Pediatric, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Home oxygen therapy or long-term oxygen therapy (LTOT) refer to provision of oxygen therapy for continuous use at home for patient with chronic hypoxemia of various aetiologies in order to maintain good oxygen saturation above 93% or arterial oxygen tension above 8 kPa (60 mmHg). It may be required 24 h/day or during period of sleep only. LTOT facilitate earlier discharge from hospital to home environment and this environment is important for better neurodevelopment of these children

Objectives: To study clinical characteristics and outcomes of children who require LTOT under Pediatric Respiratory Unit, Hospital Raja Perempuan Zainab II (HRPZ II), Kota Bharu, Kelantan and to compare median time to discontinue oxygen using different oxygen dosages of LTOT (very low flow LTOT < 1 L/min versus low flow LTOT ≥ 1 L/min–3 L/min). We also wanted to identify prognostic factors for discontinuation of LTOT.

Methods: A retrospective cohort study was conducted between 1 May 2018 till 31 January 2019 on patients receiving current or LTOT. Database of patients started on LTOT via oxygen concentrator from 1 January 2010 till 31 January 2017 by pediatric respiratory unit at HRPZ II were reviewed. LTOT were started if the children were proven hypoxic breathing in room air (defined as spending 5% of time with saturation less than 94% by continuous oximetry).

Results: Mean age of starting LTOT 15.8 (SD 30.54) months and mean duration on LTOT 16.9 months (SD 16.45). Infant who required higher oxygen flow at initiation of LTOT required a longer duration before able to be off. The indications for LTOT were mainly for other chronic neonatal lung condition of various aetiologies followed by bronchopulmonary dysplasia and bronchiolitis obliterans. Overall median time for discontinuation of LTOT were 9

months and it was shorter if the children were on a very low oxygen flow < 1 L/min (8 months) compared to low oxygen flow ≥ 1 L/min–3 L/min (13 months). The only independent risk factor for discontinuation of LTOT was birth weight at birth.

Conclusion: The clinical characteristics and outcomes of pediatric patients on LTOT under Pediatric Respiratory Unit, HRPZ II were similar with other studies done in Malaysia, United States, Chile and Brazil. This study cohort over 7 years duration likely represent children on LTOT and give an insight of quality of care in pediatric patients on LTOT in Kelantan.

Supervisor:

Dr Mariana Daud

Co-supervisors:

Associate Professor Ariffin Nasir

Dr Mohamad Ikram

THE ASSOCIATION OF CT BRAIN FINDINGS WITH NEUROLOGICAL OUTCOME AT 1-YEAR-OLD IN TERM NEONATES WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY (HIE): A RETROSPECTIVE STUDY

Dr Yap Chu Gek
MMed (Paediatrics)

Department of Paediatrics, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Perinatal asphyxia is the commonest cause of hypoxic ischemic encephalopathy (HIE) in newborns. Published data had showed that majority of patient survived from severe HIE suffered from live long detrimental neurological sequela later in life. Clinical assessment of severity of HIE is often difficult and insufficient to predict prognosis and outcome. Many studies correlate Apgar score, electroencephalography (EEG) and many modalities of cranial imaging but these only limited to Western country. Even though, magnetic resonance imaging (MRI) brain is the recommended choice of cranial imaging but long waiting list and difficulty to perform may hinder its usefulness. In our study, some of patients with moderate severe HIE had done computerised tomography (CT) brain scans during initial admission due to other specific reasons besides to assess for severity of HIE brain insult.

Objectives: The aims of this study were to study relationship between CT brain findings and outcomes in term neonates with hypoxic ischemic encephalopathy and to study prevalence of HIE in Hospital Raja Perempuan Zainab II (HRPZ II).

Methods: This was a retrospective cross-sectional review of patients medical notes at HRPZ II, Kota Bharu, Kelantan, from June 2015 to December 2017. Term neonates diagnosed with HIE and fulfilled inclusion and exclusion criteria were enrolled in this study. The purpose of the study

is to correlate CT brain scan findings with neurological outcome at 1-year-old.

Results: Total of 28 patients participated in this study. Prevalence of moderate to severe HIE was 8.3%. Sixteen patients (57%) were moderate HIE and 12 (42.9%) were severe HIE. In HIE group with abnormal CT brain findings ($n = 21$), 14 (66.7%) had abnormal neurological outcome including 4 died (19%) due to complications related to neurological sequela and 7 (33%) had normal neurological outcome at 1-year-old (P -value = 0.38). Seven patient (25%) had evidence of basal ganglia/thalamus involvement in their CT scan and all of them had abnormal neurological outcome including one death (P -value = 0.03). Four patients (14%) had both intracranial haemorrhage and basal ganglia thalamus involvement with all of them had abnormal neurological outcome (P -value = 0.13). Twelve patients (42.9%) had intracranial haemorrhage only, 83.3% ($n = 10$) had abnormal neurological outcome ($P = 0.05$). Severe HIE patients had poorer neurological outcome at 1-year-old ($P = 0.01$). The sensitivity of CT scan was 82%, specificity 36%. Presence of basal ganglia thalamus involvement on CT brain either alone or in combination with intracranial haemorrhage had specificity and positive predictive value (PPV) of 100%.

Conclusion: In this study involving moderate to severe HIE patients who had done CT brain due to other reasons, that overall abnormal CT brain report did not showed statistically significant association with abnormal neurological outcome at 1-year-old. However, presence of basal ganglia and thalamus abnormalities on CT had strong association with abnormal outcome, of which findings were similar to many other reported studies.

Supervisor:
Dr Nor Azni Yahaya

Co-supervisors:
Dr Nor Rosidah Ibrahim
Dr Surini Yusuff

THE UTILITY OF H3K27 TRIMETHYLATION IMMUNOHISTOCHEMISTRY IN DIFFERENTIATING MALIGNANT PERIPHERAL NERVE SHEATH TUMOUR AND ITS HISTOLOGIC MIMICKERS

Dr Nurulhasanah Mustapar
MMed (Pathology)

Department of Pathology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Diagnosis of malignant peripheral nerve sheath tumor (MPNST) is rather challenging due to its divergent morphologic heterogeneity and lack of specific ancillary test. The emergence of H3K27 trimethylation (H3K27me3) as a new immunohistochemistry (IHC) marker for MPNST have recently offered as a diagnostic strategy to

pathologists in differentiating MPNST from other histologic mimics.

Objectives: The aims of this study were to determine the expression of H3K27me3 between MPNST, its histologic mimickers and the association with the histologic grade.

Methods: This was a case control study involving 59 benign and malignant spindle cell tumours were tested for the protein expression of this marker by IHC. Of the 59 cases, 18 (30.5%) were MPNST and 41 of its histologic mimickers (10 schwannoma, 13 neurofibroma, 4 synovial sarcoma, 3 fibrosarcoma, 2 gastrointestinal stromal tumour (GIST), 4 leiomyosarcoma, 1 spindle cell liposarcoma, 1 solitary fibrous tumour, 2 low grade fibromyxoid sarcoma and 1 unclassified spindle cell sarcoma), which were diagnosed in HUSM from January 1998 to April 2018. The MPNST histological grade was assessed based on the French Fe'de'ration Nationale des Centres de LutteContre le Cancer (FNCLCC) for 3 tiers system (low grade, intermediate grade and high grade).

Results: Loss of H3K27me3 expression was statistically significant in MPNST as compared to its histologic mimics ($P < 0.001$). Similar findings were also observed in 9 out of 14 (81.8%) of high grade MPNST and none of the low grade MPNST ($P = 0.026$).

Conclusion: H3K27me3 is a useful marker as a diagnostic aid in diagnosing MPNST and distinguishable from its histological mimickers.

Supervisor:
Dr Sharifah Emilia Tuan Sharif

Co-supervisor:
Dr Muhamad Syahrul Fitri Zawawi

COMPARISON OF CLINICAL OUTCOME AND IN VITRO BACTERICIDAL ACTIVITY BETWEEN β -LACTAM/ β -LACTAMASE INHIBITOR AND CARBAPENEM FOR TREATMENT OF URINARY TRACT INFECTION CAUSED BY EXTENDED SPECTRUM BETA-LACTAMASES-PRODUCING ORGANISMS

Dr Nur Hafiza Muharam
MPath (Microbiology)

Department of Medical Microbiology and Parasitology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Overused of carbapenem is one of the contributing factor for development of carbapenem resistant organism. Based on previous studies, some authors recommended the use of β -lactam/ β -lactamase inhibitor (BLBLI) for treating mild to moderate extended spectrum beta-lactamases (ESBL) infection, such as urinary tract infection (UTI) but the available data are scarce. This study aimed to compare the clinical outcome between BLBLI and carbapenem in cases of ESBL UTI as well as the in vitro bactericidal activity of these antibiotics.

Methods: Clinical outcomes were evaluated in a retrospective study of patients with ESBL UTI in Hospital Raja Perempuan Zainab II (HRPZ II) from January 2015 till December 2017. Demographic data, clinical and microbiological characteristic, and outcome in patients received definitive therapy with BLBLI and carbapenem were compared in two cohorts. Further analysis was done by controlling the confounders using multiple logistic regression. Time kill analysis was performed for two ESBL-producing strains (*K. pneumoniae*, *E. coli*) in triplicate for ertapenem (at final concentration 1 µg/mL), piperacillin/tazobactam (32 µg/mL) and ceftolozane/tazobactam (4 µg/mL) by using ~10⁶ CFU/mL inoculum.

Results: The clinical failure for those treated with BLBLI versus carbapenem were 18.8% (6/32) versus 23.4% (11/47), respectively. After adjusting for the confounders, the only significant risk factors for clinical failure were severe sepsis or septic shock at presentation (OR = 21.812; 95% CI: 3.735, 127.373; *P* = 0.001), presence of external catheter (OR = 9.741; 95% CI: 1.720, 55.162; *P* = 0.010), and presence of other concomitant infection (OR = 5.168; 95% CI: 1.272, 20.990; *P* = 0.022). Empirical and definitive treatment with BLBLI were not associated with increased risk of clinical failure. In time kill study, ertapenem exhibited rapid and sustained bactericidal effect against both strains. Piperacillin/tazobactam was initially bactericidal against both strains, however regrowth was demonstrated after 8 h. Ceftolozane/tazobactam was initially bactericidal against *E. coli*, however regrowth occurred after 4 h. No activity was observed against *K. pneumoniae*.

Conclusion: In conclusion, BLBLI was non-inferior to carbapenem for treatment of ESBL UTI. Though ertapenem showed the most potent and stable activity against ESBL-producing organism, the use of carbapenem should be limited to moderate to severe ESBL infection to avoid the increase of carbapenem-resistant strain. Piperacillin/tazobactam still can be an acceptable alternative for treatment of ESBL infection but must be limited to mild cases of UTI. On the other hand, more studies are needed to evaluate the activity of ceftolozane/tazobactam in treatment of ESBL infection.

Supervisor:
Associate Professor Dr Zakuan Zainy Deris

PREVALENCE OF DEPRESSION AND ITS ASSOCIATED FACTORS AMONG CURRENT ADULT SMOKERS ATTENDING OUTPATIENT CLINIC, HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr Adam Firdaus Dahlan
MMed (Family Medicine)

Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Smoking behaviour is associated with nicotine dependence resulting in various health issues worldwide including Malaysia. It is a known factor that

eventually will lead to spectrum of chronic diseases for example heart diseases, respiratory diseases, cancers and highly correlated with mental health illnesses. There are many factors contributing to smokers to continue smoking despite knowing its harmful consequences. Depression is usually taken lightly for which its complications can be devastating to a person.

Objective: To study on prevalence of depression and its associated factors among current adult smokers attending outpatient clinic, Hospital Universiti Sains Malaysia.

Methods: This cross-sectional study was done in Hospital Universiti Sains Malaysia involving patients presented to outpatient clinic. The Malay version Patient Health Questionnaire-9 (PHQ-9) was applied in this study. Patients were also screened for biosocial aspect, comorbidities and nicotine dependence score using Malay version of Fagerstrom Test for Nicotine Dependence (FTND).

Results: There were 194 adult smokers who participated and completed the questionnaire in this study. The prevalence of depression among current adult smokers was 29.9%. For each one-unit increment of FTND score, there will be 1.39 higher odds of developing depression through series of simple and multiple logistic regression. Other factors including sociodemographic and comorbidities were not associated with depression among current adult smokers.

Conclusion: Throughout this cross-sectional study, depression was seen among current adult smokers in a ratio of 1:3. Reduction in nicotine addiction thus quit smoking are two most sensible reasons to halt depression and other chronic diseases. Prevention from smoking will avoid nicotine dependence and depressive symptoms. This responsibility is not solely lay on smoker's shoulder, in fact health care workers, family members, friends and co-workers should have the initiative and express their concern of smoking behavior which is a current dilemma.

Supervisor:
Dr Imran Ahmad

Co-supervisor:
Professor Dr Shaiful Bahari Ismail

KNOWLEDGE ON PRE-PREGNANCY CARE AMONG MEN IN HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr Siti Hartini Ishak
MMed (Family Medicine)

Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Pre-pregnancy care has been proposed for improving pregnancy outcomes by encouraging behavioural change or allowing early identification of risk factors. However mostly it was directly to women and study on men's knowledge on pre-pregnancy care was scarce. Men's involvement in pre-pregnancy care are important in sharing

responsibilities for future health of the mother, child and his family. This study focused on knowledge of men on pre-pregnancy care as they can participate in maternal health care by being involved in safe motherhood programmes such as family planning and birth spacing.

Objectives: To determine the level of knowledge on pre-pregnancy care among men in Kota Bharu and associated factor for poor knowledge.

Methods: This was a cross sectional study conducted at outpatient clinics in Hospital Universiti Sains Malaysia (HUSM) involving 235 married men. A self-administered questionnaire was administered and consisted of four domains, assessing sociodemographic data, reproductive characteristics of couples, clinical characteristics and knowledge on pre-pregnancy care.

Result: More than half of men 122 (51.9%) had poor knowledge on pre-pregnancy care mostly regarding high risks pregnancy, consequences of poor birth spacing and effect of maternal anemia to baby. The mean (SD) knowledge was 11.86 (3.85). The poor knowledge on pre-pregnancy care was associated with age and education level of respondents.

Conclusion: Men in our study still have poor knowledge on pre-pregnancy care. Further health promotion and education is needed to be focused on men to increase their knowledge and sharing their responsibilities in maternal health.

Supervisor:

Dr Lili Husniati Yaacob

Co-supervisor:

Dr Azlina Ishak

OUTCOME OF CEREBRAL VENOUS SINUS THROMBOSIS IN HOSPITAL UNIVERSITI SAINS MALAYSIA: A RETROSPECTIVE STUDY

Dr Norhashimah Che Mohamood
MMed (Internal Medicine)

Department of Internal Medicine, School of Medical Science, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Data regarding cerebral venous sinus thrombosis (CVST) in Asian countries are limited. This study aims to describe the clinical presentation, risk factors, radiological findings, treatment and outcome of CVST in Hospital Universiti Sains Malaysia (HUSM.)

Objectives: The aims of this study were to look at the clinical presentations, predisposing risk factors, neuroimaging findings, methods of treatments and outcome of cerebral venous sinus thrombosis (CVST) in HUSM.

Methods: This was retrospective study of patients with radiologically confirmed CVST admitted in HUSM between January 2007 and December 2016. The demographic, clinical, radiological, treatment and outcome data were retrospectively recorded and analysed. Primary outcome was

death or dependency as assessed by Modified Rankin Score (MRS) > 2 at the end of follow up.

Results: Forty-seven patients were included. Mean age at diagnosis was 38.7 years (range 16–68) and predominantly women (63.8%). Mean duration of hospital stay was 12.7 days (SD 11.2–14.4). Median follow up duration was 12 months (IQR = 33). Headache was the most common symptom occurred in 36 patients (76%), followed by vomiting, seizure, paresis and others. The most common sites of CVST were the superior sagittal sinus in 28 patients (60%), right lateral sinus in 22 (46%), and left lateral sinus in 16 (34%) and less common in other sinuses. Multiple sinuses were involved in 31 patients (66%). Major risk factors were OCP (43%), and infections (23.6%). Forty patients (85%) received anticoagulant with median duration of anticoagulation was 3 months, 8 (17%) received antiplatelet and 5 (10.6%) received surgical intervention. Mortality rate at discharge was 6.4%. The proportion of patient with good neurological outcome (MRS ≤ 2) was 75.1% at 12 months. At end of follow up, 31 patients (66.0%) had good neurological outcome (MRS ≤ 2), 16 (34.0%) were either dependent (11 [23.4%]) or dead (5 [10.6%]). One patient (2.1%) had recurrent CVST and 7 patients (14.9%) developed other thrombotic events.

Independent predictors of death and dependency were Glasgow coma scale (GCS) 3–8 ($P = 0.006$), GCS 9–12 ($P = 0.005$), no repeat imaging ($P = 0.003$), unfractionated heparin (UFH) ($P = 0.005$), and duration of anticoagulant 0–6 month ($P = 0.02$). Male, haemorrhage, deep CVST and infection were not significant predictors in our study.

Conclusion: Clinical presentation, neuroimaging, treatment and outcome of CVST in HUSM were comparable to western countries. The ova, cysts and parasite (OCP) and infection were most common risk factors. Mortality rate in acute phase was 6.4% and 10.6% at the end of follow up. Sixty-six percent had favourable neurological outcome at the end of follow up. Recurrence rate was 2.1%. We identified GCS ≤ 12, no repeat imaging, UFH and duration of anticoagulant 0–6 month as significant predictors of poor outcome.

Supervisor:

Dr Sanisah Abdul Halim

THE PROPORTION OF HIGH FOOT PLANTAR PRESSURE IN DIABETIC PATIENTS AND IT ASSOCIATED FACTORS

Dr Siti Badariah Zakaria
MMed (Internal Medicine)

Department of Internal Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: High foot pressure is one of key factor to predict foot ulceration in diabetes patients. However, there was no local study assessing proportion and factors associated with high foot pressure in Malaysia.

Objectives: The aim of this study was to obtain proportion of diabetes patients with high plantar foot

pressure, socio demographic of the patients with high foot pressure and assess the associated factors that lead to high foot plantar pressure.

Methods: This cross-sectional study was conducted in November 2018 till August 2019 involving patients who had been diagnosed with diabetes mellitus in Hospital Universiti Sains Malaysia. A total of 378 established diabetes patients were selected. All patients' information such as age, weight, height, and body mass index, diabetes duration, smoking status, HbA1c level and history of previous foot ulcer were obtained and they had been assessed for peak plantar pressure using MatScan system (Tekscan), Diabetes Neuropathy Symptom Score and Vibration Perception Threshold (VPT) using biothesiometer. The patients were divided into normal and high foot pressure group based on peak plantar pressure finding.

Results: A total of 378 diabetic patients were included. Fifteen (4%) of them had high foot plantar pressure and 363 (96%) had normal foot pressure. High foot pressure group consisted of 8 (53.3%) female and 7 (46.7%) male, respectively. The mean (SD) HbA1c for high foot pressure group was 11.0 (\pm 2.06) compared to 9.1 (\pm 2.23) in normal foot pressure group. Both groups were overweight with mean (SD) BMI of 27.8 (\pm 5.42) in high foot pressure group and 28.6 (\pm 2.76) in normal foot pressure group. Mean (SD) duration of diabetes in high foot pressure and normal foot pressure group were 15.9 (\pm 37.59) and 15.7 (\pm 8.91), respectively. In high foot pressure group, 2 (26.7%) were smoker, 4 (26.7%) had previous history of foot ulcer and 9 (60%) had diabetic neuropathy. There was significant association of HbA1c with high foot pressure have found by multivariate analysis.

Conclusion: The proportion of high foot pressure among diabetic patients in HUSM was 4% and lower compared to other previous study done. In addition, high HbA1c is a significant associated with high foot pressure. Hence improvement of diabetic control by reducing HbA1c can prevent future development high foot pressure and combat foot ulceration.

Supervisor:

Associate Prof Dr Wan Mohd Izani Wan Mohamed

RELAPSED/PROGRESSIVE DISEASE AND ITS PROGNOSTIC FACTORS AMONG MULTIPLE MYELOMA PATIENTS RECEIVING NOVEL AGENT TREATMENT

Dr Hany Haqimi Wan Hanafi
MMed (Internal Medicine)

Department of Internal Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Background: Since the era of novel agent in Multiple Myeloma therapy, there has been significant prolongation of survival in patients with Multiple Myeloma, leading to a paradigm shift from an incurable disease to chronic disease. Nonetheless, a proportion of patients does relapse

or progress ultimately, needing salvage or subsequent line of therapy. Thus, the knowledge of relapse/progression in multiple myeloma is a vital area of ongoing research in this era of novel treatment.

Objectives: This retrospective cohort study aimed to evaluate the time to relapse/progression among multiple myeloma patients who received novel agent therapy in our local setting as well as to determine its associated prognostic factors.

Methods: A total of 89 patients with multiple myeloma treated in HUSM from 1 January 2006 until 30 April 2018 were included in this study with an additional follow up one year between 1 May 2018 and 30 April 2019. We analysed the type of relapse/progression (asymptomatic versus symptomatic) and the time to relapse/progression. A stepwise regression analysis, according to the Cox proportional hazard model, was used to identify the variables with the most significant prognostic factors.

Results: Sixty-four percent of patients had biochemical (asymptomatic) relapse/progression, while 36% of patients had clinical (symptomatic) relapse/progression. The overall median time to relapse/progression among multiple myeloma patients who received the novel agent(s) was 29.33 months. Type of paraprotein ($P = 0.026$, $P = 0.228$), International Staging System (ISS) ($P = 0.036$, $P = 0.067$) and autologous stem cell transplant (ASCT) ($P = 0.002$), were prognostic factors for relapse/progression by simple cox proportional hazard model, but ultimately ASCT was the only significant predictor detected by multiple cox proportional hazard model ($P = 0.002$).

Conclusion: Our study reflected the critical aspect of serum paraprotein and serum free light chain monitoring at regular interval to detect the initial feature of biochemical relapse/progression. ASCT is the only significant prognostic factor that may lengthen the time to relapse/progression, and there was no substantial evidence to suggest one novel agent is more superior to another in treating newly diagnosed and untreated Multiple Myeloma.

Supervisor:

Associated Professor Dr Azlan Husin

Co-supervisor:

Dr Najib Majdi Yaacob

PHOTOGRAMMETRIC ANALYSIS OF FACIAL ATTRACTIVENESS IN MALAY MALAYSIAN WOMEN

Dr Akmal Hisham Miswan
MSurg (Plastic Surgery)

Department of Reconstructive Sciences Unit, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Background: Asians are a heterogeneous group with different average and attractive facial features between individual ethnicities. This study aimed to establish normative anthropometric measurements of the Malay

Malaysian Women's (MMW) face, compare results with the standard for North American White Women (NAWW), the neoclassical canons of facial proportions and other Asian ethnicities, and quantitatively defined aesthetic facial features in the MMW.

Methods: This is a cross-sectional photogrammetric study. In part 1 of this study, we obtained standardised frontal and lateral facial photographs of 103 MMW volunteers between the ages of 18–35. For each face, we measured 24 standard anthropometric parameters. We compared our results with the published NAWW norms and the facial canons proportions. In part 2 of the study, ten raters evaluated the photographs for aesthetics using a 10-point Likert's scale. Attractive MMW (top 15%) were compared with the average MMW (remaining 85%), NAWW and other ethnicities.

Results: The neoclassical facial canons were not found to apply to most of the MMW. We found significant differences between MMW and NAWW in 20 of 24 measurements ($P < 0.05$). Attractive face in the MMW had a smaller total face height, smaller lower face height and narrower mandible width compared to the average MMW. Comparing the normative and attractive MMW with other ethnicities indicated various interracial differences.

Conclusion: Grouping this patient into a single Asian category or using analysis standards used for whites are impractical. This study detailed comprehensive facial anthropometric data and aesthetic criteria for this population. The values presented here could be used as a standard for facial analysis in women of Malay descent.

Supervisor:

Associate Professor Dr Wan Azman Wan Sulaiman

MUSCLE FIBRE TRACK OF ROTATOR CUFF MUSCLE OF SHOULDER BETWEEN TWO DIFFERENT DIFFUSION DIRECTION IN 3 TESLA MRI

Dr Nur Falahiah Fauzi
MMed (Radiology)

Department of Radiology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Diffusion tensor imaging (DTI) has been widely used to study microstructured and anisotropy in brain, spinal cord, kidney and heart. It gives benefit to musculoskeletal imaging at microstructured level through 3D fibre tractography analysis and potentially use in diagnosis of muscle injuries. This study determined the difference of fractional anisotropy (FA) and fibre density index (FDI) of rotator cuff muscle of shoulder in different diffusion direction. Till this date there was no specific study to determine effect of different diffusion direction to the muscle fibre track parameter in musculoskeletal imaging.

Objectives: The aim of this study were to determine the optimum diffusion direction for DT tractography of rotator cuff muscles in healthy subjects and to compare FA

and fibre density index of rotator cuff muscles with different diffusion direction of 16 and 32 at b -value of 400.

Methods: A thirty-seven DTI MRI of shoulder were performed with MR (Philips 3 Tesla Achieva MR scanner, Best, the Netherlands) using standard shoulder coil in b -value of 400 s/mm² was selected. Diffusion direction of 16 and 32 were selected as its provide the highest signal to noise ratio (SNR). Range of interest (ROI) was manually drawn following the muscle bulk of three rotator cuff muscle in sagittal oblique view (in scapular Y-view) using FiberTrack tool in Philips Extended MR Workspace 2.6.3.5. Fibre tracking was set at a fractional anisotropy (FA) threshold more than 0.15 and cut off turning angle of 35°. FA, apparent diffusion coefficient (ADC), muscle fibre line and voxel were automatically generated by software. Fibre density index was determined by the number of fibre path passing through the ROI divided by area of ROI in pixels. Measurement was taken 2 times to reduced biased. Statistical analysis was using paired T-test.

Results: The mean and standard deviation of FA for supraspinatus, infraspinatus and subscapularis muscle with diffusion direction of 16 was 0.53 (± 0.05), 0.10 (± 0.02) and 0.56 (± 0.05) and with diffusion direction of 32 was 0.45 (± 0.04), 0.09 (± 0.02) and 0.46 (± 0.05). The difference was significance, $P < 0.001$.

Mean and standard deviation of fibre density index for supraspinatus, infraspinatus and subscapularis muscle with diffusion direction of 16 was 0.11 (± 0.02), 0.10 (± 0.02) and 0.14 (± 0.02) and with diffusion direction of 32 was 0.09 (± 0.02), 0.07 (± 0.02) and 0.12 (± 0.02). The difference is significance, $P < 0.001$. The confidence interval was good to excellent.

Conclusion: This study had shown the significant difference of FA and FDI with different diffusion direction. The optimal diffusion direction for DT tractography for rotator cuff muscle was 16 on 3 Tesla system.

Supervisor:

Associate Professor Mohd Ezane Aziz

A COMPARISON BETWEEN ADULT AND PAEDIATRIC LATERAL LAMELLA CRIBRIFORM PLATE (LLCP) HEIGHT IN HOSPITAL UNIVERSITI SAINS MALAYSIA (HUSM)

Dr Gilbert Sakandar
MMed (Radiology)

Department of Radiology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Objectives: Lateral lamella cribriform plate (LLCP) is the thinnest and most vulnerable bone of the skull base which is closely related to the anterior ethmoidal artery. By knowing the height of the LLCP, it will provide surgical-mapping to the operator during endoscopic sinus surgery (ESS) and reduce risk of LLCP injury. The purpose of this study was to determine whether there is any difference in mean LLCP

height between adult and paediatric, based on the fact that there is difference in body and skull size of an adult and paediatric, with ethmoidal expansion occurring from birth till late puberty and upon reaching compact bone.

Methods: Thin-sliced (1 mm) image of computed tomography (CT) brain were constructed into 3-dimensional (3D) high kernel algorithm using multi-detector CT. The coronal view that clearly showed cribriform plate was chosen. The measurement of LLC height was performed using facial bone review of 3D application (GE PACS Universal Viewer Version 5.0 SP6). Paired and unpaired T-test was used to compare mean of LLC height between group, gender and sides.

Results: A total of 76 adults and 76 paediatrics with equal number of male and female in each group were analysed. The mean LLC height for adults was 4.821 mm (SD: 1.415) and mean LLC height for paediatrics was 4.686 mm (SD: 1.543). There was no significant difference in LLC height between adults and paediatrics; $P = 0.573$, (95% CI: -0.339 to 0.610). No significant difference also noted between genders among both groups. However, significant difference was noted between sides among adults and paediatrics. The left LLC height was significantly higher than the right in both groups. The mean LLC height for adults was 5.086 mm (SD: 1.702) on the left and 4.487 mm (SD: 1.459) on the right ($P \leq 0.001$, 95% CI: 0.292–0.906). The mean LLC height for paediatric was 5.050 mm (SD: 1.859) on the left and 4.279 mm (SD: 1.508) on the right ($P \leq 0.001$ (95% CI: 0.439–1.104).

Conclusion: There was no difference in adult and paediatric LLC height. However, the left LLC height was higher than the right LLC in both adult and paediatrics. A careful pre-operative assessment of LLC height by the surgeon is of essence to provide surgical-mapping and avoid iatrogenic complication to the LLC and closely related anterior ethmoidal artery.

Supervisor:
Dr Juhara Haron

Co-supervisors:
Associate Professor Dr Irfan Mohamad
Associate Professor Dr Ramiza Ramza Ramli

CORRELATION OF ENLARGED PERIVASCULAR SPACE AND WHITE MATTER LESION ON MRI WITH AGE USING TWO DIFFERENT VISUAL SCORING METHODS IN ASYMPTOMATIC INDIVIDUALS

Dr Saraswathy a/p Subramaniam
Mmed (Radiology)

Department of Radiology, School of Medical Sciences,
Universiti Sains Malaysia, Kubang Kerian, Kelantan,
Malaysia

Introduction: Enlarged perivascular space (EPVS) and white matter lesions (WML) are considered reliable magnetic resonance imaging (MRI) markers for cerebral

small vessel disease (CSVD). Although the associations of these markers with age and cardiovascular risk have been established in the stroke and elderly population, their correlation with age and cardiovascular risk in younger asymptomatic individuals remains unclear.

Objectives: The purpose of this study is to correlate EPVS (centrum semiovale [CS], basal ganglia [BG]) using MacLulich visual rating score and white matter lesion (WML) (periventricular hyperintensity [PVH], deep white matter hyperintensity [DWMH]) using Fazekas score with age in asymptomatic individuals in Hospital Universiti Sains Malaysia and to find their correlation with cardiovascular risk using QRISK2-2016 score.

Methods: A total of 49 selected subjects from 'Klinik Rawatan Keluarga (KRK)', Hospital Universiti Sains Malaysia (HUSM) were included in this cross-sectional study. Subjects underwent MRI brain from September 2016 to August 2018. T1-weighted, T2-weighted and fluid-attenuated inversion recovery (FLAIR) images were retrieved from the picture archive communication system (PACS). These images were analysed using two different visual rating scoring methods, MacLulich Visual Rating Score for EPVS (CS, BG) and Fazekas score for WML (PVH, DWMH) by the researcher. Spearman correlation test was used to determine correlations of MacLulich score and Fazekas score with age and QRISK2-2016 score of the selected subjects. Level of significance was determined ($P < 0.05$).

Results: Good positive correlation was seen between EPVS score (BG) and age ($P = 0.000$, $r = 0.536$). Fair positive correlations were seen between EPVS score (CS) and WML score (PVH and DWMH) and age ($P = 0.004$, $P = 0.404$; $P = 0.042$, $r = 0.291$; and $P = 0.035$, $r = 0.301$), respectively. Fair positive correlations were also present between EPVS scores (CS and BG) and QRISK2-2016 score ($P = 0.035$, $r = 0.300$; $P = 0.001$, $r = 0.467$), respectively. The WML scores (PVH and DWMH) showed fair positive correlations with QRISK2-2016 score ($P = 0.019$, $r = 0.333$ and $P = 0.005$, $r = 0.392$), respectively.

Conclusion: Age and QRISK2-2016 score are two significant associated factors that contribute to the development of EPVS and WML in asymptomatic individuals.

Supervisor:
Associate Professor Dr Mohd Ezane Aziz

Co-supervisors:
Associate Professor Dr Muzaimi Mustapha:
Associate Professor Dr Win Mar @ Salmah Jalaluddin

A MRI STUDY ON MYOCARDIAL VIABILITY AND WALL MOTION IN PATIENTS WITH CHRONIC TOTAL OCCLUSION AND SEVERE STENOSIS OF CORONARY ARTERY

Dr Thilagah Chenasammy
MMed (Radiology)

Department of Radiology, School of Medical Sciences,
Universiti Sains Malaysia, Kubang Kerian, Kelantan,
Malaysia

Introduction: Coronary artery disease is the leading cause of death in the world. Decision on optimal management of patients diagnosed with coronary artery disease remains a challenge until now. It is important that patients selected for revascularisation have viable myocardium and thus good outcome is expected post successful procedure. This can improve rate of mortality and morbidity among these patients. The aim of this study is to assess the myocardial viability by magnetic resonance imaging (MRI) in patients with different category of stenosis before revascularisation.

Objectives: The aim of this study is to determine the association between chronic total occlusion (CTO) and severe stenosis with myocardial viability and wall motion in MRI.

Methods: A cross sectional study on patients with two categories of coronary artery stenosis (CTO and severe stenosis) diagnosed at conventional coronary angiography. Patients underwent cardiovascular MRI with intravenous gadolinium. The total volume and the proportion of myocardium with late gadolinium enhancement in each segment supplied by the stenotic vessel were measured using Philips MR Extended Workspace. The myocardial segment was grouped as either viable or non-viable. The wall motion of the corresponding segment with stenotic coronary artery was also evaluated. Correlations were determined between the category of stenosis of the coronary artery and viability of myocardial segments as well as the myocardial wall motion.

Results: A total of 33 patients (32 men and 1 woman, age range 43–79 years) that had CTO and severe stenosis of more than 70% were included in this study. A total of 417 myocardial segments were studied, 214 segments supplied by severely stenotic artery and 203 segments supplied by CTO. CTO lesion showed two times higher odds of having non-viable myocardium than viable myocardium ($P = 0.007$). CTO segments had 24.6% of non-viable myocardium wherein severe stenotic segments had 14% of non-viable myocardial segments. Of 337 viable myocardial segments, only 100 segments had normal myocardial wall motion. In terms of wall motion, normal wall motion is more associated to CTO compared to severe stenosis ($P = 0.006$).

Conclusion: Contrast enhanced-MRI is a useful tool to study the myocardial viability in chronic total occlusion and severe stenosis of coronary arteries. The CTO group was more associated with non-viable than viable myocardial segments. The non-viable segments are more in CTO group than severe stenosis. Normal myocardial wall motion is more associated with CTO group compared to abnormal wall motion. CTO also has higher association with normal wall motion than severe stenosis.

Supervisor:
Dr Khairil Amir Sayuti

Co-supervisor:
Dr Wan Yus Haniff Wan Isa

LAPAROSCOPIC CHOLECYSTECTOMY; INTRAOPERATIVE CHOLANGIOGRAPHY VERSUS NO INTRAOPERATIVE CHOLANGIOGRAPHY: A MULTICENTRE RANDOMISED CONTROL TRIAL

Dr Nur Zawani Zainudin
MMed (Surgery)

Department of Surgery, School of Medical Sciences,
Universiti Sains Malaysia, Kubang Kerian, Kelantan,
Malaysia

Introduction: Intraoperative cholangiogram (IOC) is not something new in the world of laparoscopic cholecystectomy (LC). However it is still not a favourite method to use as a routine procedure in LC.

Objectives: To determine the feasibility and safety of performing IOC during LC, to detect the incidence of undiagnosed pre-operative bile duct stone and to identify if IOC can prevent bile duct injury.

Methods: Multicentre, double blinded randomised controlled trial done from 2016–2018. Total of 308 patients recruited and divided into two arms; with IOC and without IOC. Exclusion criteria includes in situ biliary stent placement, history of multiple laparotomies, pregnant and in acute pancreatitis. Demographic analysis, independence T -test and univariate analysis was performed.

Results: There was a highly significant difference of mean operation time between the group with IOC and non-IOC [t -statistics ($df = 306$) (6.78), P -value < 0.001]. In the IOC group, the mean operation time was analysed according to surgeon's status and noted that the consultant took more time to perform IOC compared to trainee [(SD) 70.0 (30.20) versus 57.6 (24.06), respectively; P -value < 0.001] and also it was higher in patient with previous history of ERCP, P -value = 0.001. From 12 IOC with presence of filling defects, two cases were confirmed with endoscopic retrograde cholangiopancreatography (ERCP) performed the next day and other two cases were converted to common bile duct exploration (CBDE) intra-operatively. Eight cases was noted negative of stone after ERCP performed the next day. There was only one case of bile duct injury noted during IOC. No patients developed allergic reaction to the dye and the post op complications are similar in both groups.

Conclusion: IOC is a useful tool to identify silent stone and also to detect early bile duct injury. Therefore it is important to learn the procedure and to be able to interpret it better.

Supervisor:
Dr Ikhwani Sani Mohamad

Co-supervisor:
Dr Leow Voon Meng

ASSOCIATION OF BODY MASS INDEX AND GASTROESOPHAGEAL REFLUX DISEASE AND ITS COMPLICATIONS

Dr Sarmukh Singh a/l Charanjit Singh
MMed (Surgery)

Department of Surgery, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Obesity is a fast-emerging epidemic in the Asia-Pacific region especially in Malaysia. According to National Health and Morbidity Survey of 2015, obesity in Malaysians make up 17.7% of the population while those who are categorised as overweight make up 30%. The landscape of gut diseases in Asia has been drastically changed by obesity, especially the gastroesophageal reflux disease (GERD) and its complication such as hiatus hernia, reflux esophagitis and Barrett's esophagus. The objectives of this study are to determine the association between GERDs complications such as hiatus hernia, reflux esophagitis and Barrett's esophagus with body mass index via esophagogastroduodenoscopy (OGDS) in Hospital Universiti Sains Malaysia (HUSM).

Methods: GERD patients with GerdQ questionnaire scoring system who had underwent OGDS in Hospital Universiti Sains Malaysia from January 2014 to Mei 2017 were reviewed retrospectively. The patients were divided into two groups according to their body mass index (BMI) based on WHO (ASIAN population classification): i) Normal BMI group with BMI less than 22.9 kg/(m²) (54 patients); and ii) Obese group with the BMI more than 23 kg/(m²) (73 patients). The clinical factors (age, gender, ethnicity, weight, height, BMI and GerdQ questionnaire scoring) and OGDS findings (hiatus hernia, reflux esophagitis and Barrett's esophagus) were analysed. We used a gastroenterologist to be the interobserver to analyse the OGDS films. He graded the findings based to its severity. Hiatus hernia by using Hill's Grading, reflux esophagitis according to Los Angeles classification and Barrett's esophagus according to Prague Classification (C and M).

Results: A total sample of 127 patients were included in this study where male population predominantly conquered with 57.48% compared to female population which is 42.52%. The mean age of the samples were 43.91 years old. Obesity as in BMI > 30 kg/m² were statistically significant association ($P = 0.028$) with Hiatus hernia based on Hill's grading and statistically significant association ($P = 0.015$) with reflux esophagitis based on LA classification. However, obesity was statistically insignificant association ($P = 0.704$) with Barrett's esophagus histologically. Obese patient also showed statistically insignificant association with Barrett's esophagus endoscopically based on Prague classification of circumferential of metaplasia (C) ($P = 0.660$) and maximum extend of metaplasia (M) ($P = 0.524$). The risk prediction shows statistically significant association ($P = 0.002$) between body mass index (BMI) with reflux esophagitis based (LA classification). Those in obese group have 3.6 times higher odds to get reflux esophagitis symptoms compared to those in normal BMI group.

Conclusion: Obese patient has association with hiatus hernia and reflux esophagitis but not for the Barrett's esophagus. The risk prediction association between BMI is with reflux esophagitis based (LA classification) in obese group have 3.6 times symptoms compared to those in normal BMI group. In obese patient with severe and persistent GERD symptoms such as regurgitation and heartburn despite on medical treatment (Proton pump inhibitor) should undergo bariatric surgical correction. We suggest that, Laparoscopic Roux En Y Gastric bypass procedure have shown to be more effective procedure for alleviating the symptoms of GERD as it plays a role in significant weight loss compare with laparoscopic sleeve gastrectomy patient.

Supervisor:
Associate Professor Zaidi Zakaria

Co-supervisor:
Professor Dr Lee Yeong Yeh

PHASE 2 TRIAL OF CHEWING LIGNOCAINE SOAKED GAUZE: A NOVEL METHOD TO REDUCE GAG REFLEX

Dr Asraf Haslam Jasmani
MMed (General Surgery)

Department of Surgery, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: The gag reflex has been identified as a factor that reduces patient tolerance towards the procedure that involves stimulation of pharyngeal area, hence a better method to reduce the gag reflex is investigated.

Objectives: This study aimed to look at the feasibility of chewing lignocaine soaked gauze to reduce gag reflex besides identifying the optimum dosage of lignocaine.

Methods: This is phase two, three arms, double-blinded, randomised control trial. Participants were divided into three groups: i) group A received gauze soaked with 160 mg lignocaine; ii) group B received gauze soaked with 320 mg lignocaine; and iii) group C received gauze soaked with water. Allocation of participants was determined by computer-generated block randomisation. Baseline information, vital signs, gag reflex score and gag reflex location, were recorded. Participants were assessed by two designated individuals at the end of 3 min, and gag reflex score is given. Vital signs were monitored and adverse effect recorded. Results were analysed using one-way ANOVA and post hoc test.

Results: Thirty participants were recruited and divided into three groups with 1:1:1 ratio according to block randomisation. Baseline information, vital signs and gag reflex score between groups were compared and were homogenous except age. Gag reflex reduction was seen highest in group B ($M = 2.3$, $SD = 0.67$, $P = 0.000$, $t = 10.776$, 95% CI = 1.817, 2.813) and no statistically significant changes in the control group ($M = 0.1$, $SD 0.316$, $P = 0.343$, $t = 1.000$, 95% CI = -0.126, 0.326). There was statistically significant difference in gag reflex severity score between

the groups ($P = 0.00$, $F = 27.271$). No differences were seen in systolic pressure, diastolic pressure, pulse rate and oxygen saturation between pretest and posttest for all group. Significant difference in gag reflex score were seen between group A and group C ($P = 0.000$, 95% CI = -2.90 , 1.30) and between group B and group C ($P = 0.000$, 95% CI = -2.70 , -1.10). There was no significant difference between group A and group B ($P = 1.00$, 95% CI = -1.00 , 0.60).

Conclusion: Chewing lignocaine soaked gauze is a feasible method to reduce gag reflex and 320 mg lignocaine is not superior to 160 mg of lignocaine in gag reflex reduction.

Supervisor:

Dr Wan Muhamad Mokhzani Wan Muhamad Mokhter

Co-supervisors:

Dr Mohd. Ridzuan Abd. Samad

Associate Professor Dr Mohd Faisal Jabar

Puan Nur Amalina binti Che Rahim

ENDOSCOPIC CLEARANCE OF LARGE BILE DUCT STONE AND ITS ASSOCIATED FACTORS: 5 YEARS REVIEW

Dr Siti Nurul Hidayah Mat Safien
MMed (Surgery)

Department of Surgery, School of Medical Sciences,
Universiti Sains Malaysia, Kubang Kerian, Kelantan,
Malaysia

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) is considered a gold standard treatment in the current management of bile duct stone. A vast number of endoscopic techniques and devices have been developed in order to facilitate rapid, safe and effective bile duct stones extraction.

One major problem that needs to be dealt with is extraction of stone larger than the orifice of the access point. This can be achieved by either enlarging the ampulla or reducing the size of stones.

However, even by using advanced endoscopic techniques, there are some limitation when dealing with large bile duct stones. Some author refer to this entity as 'difficult stone'. In general practice, large bile stone is defined as stone of 1.5 cm in diameter and larger.

Objectives: The aim of this study is to investigate the percentage of endoscopic clearance of large bile duct stone, and its associated factors.

Methods: This is a retrospective observational study involving all patients who were diagnosed with 1.5 cm bile duct stones or larger in Hospital Raja Perempuan Zainab II (HRPZ II) from January 2013 until December 2017.

All bile duct stones of 1.5cm or larger are included in this study. This includes both primary and secondary stones. The associated factors that may influence the endoscopic clearance of large bile duct stones are investigated.

Patient's clinico-pathological data and details of follow up were studied. The data was collected in a structured proforma. The result of data collection was subsequently analysed.

Result: Endoscopic clearance of large bile duct stone in HRPZ II from January 2013, until December 2017 is 28.9% (33 out of 114 cases). The rate of incomplete or failed clearance by endoscopic means is 71.1% (81 out of 114 cases).

The significant factors for complete endoscopic clearance are the location of stones (P -value = 0.01823), size of stones (P -value = 0.001) and type of stones (P -value < 0.001).

Conclusion: In conclusion, the successful rate of endoscopic clearance of large bile duct stone in HRPZ II using conventional techniques is 28.9%. This is comparable with other studies in the literature. Recent introduction of electrohydraulic lithotripsy (EHL) and laser lithotripsy (LL), under guidance of mother-baby cholangioscope, can facilitate clearance of larger and more difficult bile duct stones.

Supervisor:

Mr Wan Muhamad Mokhzani Wan Muhamad Mokhter

Co-supervisors:

Mr Ikhwan Sani Mohamed

Mr Ahmad Zuraimi Zulkifli

VALIDATION OF SINGAPORE ACUTE KIDNEY INJURY SCORE IN PREDICTING ACUTE KIDNEY INJURY AFTER CORONARY ARTERY BYPASS GRAFT SURGERY IN HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr Ooi Cheng Tian
MMed (General Surgery)

Department of General Surgery, School of Medicine
Sciences, Universiti Sains Malaysia, Kubang Kerian,
Kelantan, Malaysia

Background: Acute kidney injury after coronary artery bypass surgery is a common complication which increase length of hospital stay. A clinical score which can accurately predict the post-cardiac surgery acute kidney injury is very important for the early detection of acute kidney injury. Our study is to validate the Singapore Acute Kidney Injury Score.

Methods: This is a retrospective review of patient clinical data at Hospital Universiti Sains Malaysia from January 2012 until July 2017. Total cases of 183 patients who met the inclusion criteria during the period were included. The following 6 clinical variables (age > 60 years old, diabetes requiring insulin, estimated glomerular filtration rate < 60 mL/min/1.73 m², ejection fraction < 40%, cardiopulmonary bypass time > 140 min and aortic cross clamping time > 100 min) were reviewed. Acute Kidney Injury Network criteria was used to define the acute kidney injury. Patients who had an increase in serum creatinine of > 0.3 mg/dL, a 50% increase in the serum creatinine from the baseline value or the need for hemodialysis indicates acute kidney injury.

Results: Frequency of acute kidney injury after the cardiac surgery is 26.8%. Singapore Acute Kidney Injury Score had better prediction value with the area under the

receiver operating curve for the test cohort 0.66 (95% CI: 0.57–0.75) compare to the Acute Kidney Injury prediction following elective cardiac surgery score 0.55 (95% CI: 0.46–0.64).

Conclusion: The Singapore Acute Kidney Injury Score is more accurate in predicting the post cardiac surgery acute kidney injury when apply on the Asian population.

Supervisor:
Dr Ahmad Zuhdi Mamat

COMPARATIVE OF BISAP AND RANSON SCORES IN PREDICTING THE SEVERITY OF ACUTE PANCREATITIS SUBJECTS: A RETROSPECTIVE STUDY OF FIVE YEARS (2012–2017) IN HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr Maathichsudhaar Muniandy
MMed (General Surgery)

Department of General Surgery, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Background: Acute pancreatitis (AP) is an inflammatory disorder of the pancreas in along with its complications is one of the most common causes of morbidity and mortality in hospitalised patients. Several multifactorial scoring systems such as Ranson, Glasgow and APACHE II which has its own limitations with its low sensitivity and specificity based on clinical and biochemical data have been used over the past few decades. To date, there is a lack of information about the predictive value of bedside index of severity in acute pancreatitis (BISAP) scoring in comparison to Ranson score among AP subjects particularly in tertiary referral hospital in Malaysia

Objective: To compare the BISAP and Ranson score in predicting the severity of AP (severe acute pancreatitis (SAP), pancreatitis necrosis (PN) and mortality).

Methods: Hence, this study was conducted among 154 subjects from Hospital Universiti Sains Malaysia (HUSM) by retrospective method between the period of 2012–2017 to compare the BISAP and Ranson score for predicting the severity of AP.

Results: Out of 154 patients, 69 (44.8%) were males and 85 (55.2%) were females. The mean age was 48.2 ± 16.2 years. Of all patients, 24 patients (15.6%) were classified as severe AP and 6 patients (3.9%) had evidence of pancreatic necrosis on CT scan and 1 (0.6%) on mortality. The number of patients with a BISAP score of ≥ 3 was 1 and Ransons score ≥ 3 was 37. There were significant, substantial and positive correlation between Ransons with BISAP in disease severity ($P < 0.05$).

Conclusion: BISAP can be considered as a simple and accurate tool for severity stratification and equally effective as Ranson score in predicting the severity of acute pancreatitis.

Supervisor:
Prof Zaidi Zakaria

Co-supervisor:
Dr Ikhwan Sani Mohamad

A RETROSPECTIVE STUDY OF LAPAROSCOPIC APPENDICECTOMY CONVERSION RATE TO OPEN APPENDICECTOMY AND ASSOCIATED RISK FACTORS FOR CONVERSION IN HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr Nelson Rao Pushpanathan
Mmed (General Surgery)

Department of General Surgery, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

Introduction: Introduced by Semm in 1983, laparoscopic appendicectomy (LA) has widely been accepted over the last few years as a standard approach to acute appendicitis. About 5%–10% of LA patients still need to be converted to open surgery for multiple reasons. Conversion from LA to open appendicectomy (OA) negates all the beneficial attributes of laparoscopic approach as, it also increases cost and operating time. Hence this study is aimed to determine the conversion rate of LA to OA and to identify its associated risk factors in Hospital Universiti Sains Malaysia (HUSM), Kelantan, Malaysia.

Objectives: To determine rate of LAs conversion rate to open and its associated risk factors for conversion by retrospective analysis from the period of December 2015 to January 2017 in HUSM, Kelantan, Malaysia.

Methods: A retrospective study was conducted by obtaining the medical records of patients with acute appendicitis who were referred/treated or diagnosed and underwent LA at HUSM, Kelantan, Malaysia from the period of December 2015 till January 2017.

Results: A total of 120 subjects were recruited between this retrospective study. Of the 120 patients who underwent initial LA from December 2015 to January 2017, 33 cases were converted to OP, which the conversion rate is 27.5%. Associated factors of conversion of LA to OA were identified, which were age, gender, ethnicity, histopathology, and temperature on presentation, duration of symptoms on presentation and total white blood cells. Patients presented with perforated appendix has 8.55 higher odds to convert to OA if compared to others histopathology.

Conclusion: Histopathology of the appendix was strongly associated with conversion of LA to OA. Conversion rate in HUSM can be improved with better investigations and diagnosis confirmation as the rates are higher than in other population.

Supervisor:
Dr Mohd. Nizam Mohd Hashim

A RETROSPECTIVE STUDY TO COMPARE BETWEEN RIPASA SCORE AND ALVARADO SCORE IN DIAGNOSIS OF ACUTE APPENDICITIS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

Dr Hasmali Mohamad
MMed (Surgery)

Department of Surgery, School of Medical Sciences,
Universiti Sains Malaysia, Kubang Kerian, Kelantan,
Malaysia

Introduction: Acute appendicitis is one of the most common surgical emergencies. The Alvarado score was developed to aid in diagnosis of acute appendicitis. However, this score has poor sensitivity and specificity when applied to Asian populations. RIPASA score was then developed to help to diagnose acute appendicitis in Asian populations. The aim of this study was to compare between Alvarado score and RIPASA score in diagnosis of acute appendicitis in local population.

Methods: Clinical data obtained retrospectively from 188 files of patients who were diagnosed as acute appendicitis and undergone appendectomy in Hospital Universiti Sains Malaysia from 2016 to 2017. All clinical data pertaining to Alvarado score and RIPASA score parameters were obtained from the files and written in performa. All patients diagnosed with acute appendicitis and undergone appendectomy were included into the study except patients with pregnancy, age less than 5 years old and operation for other indications. Both data were analysed using SPSS version 24 and sensitivity and specificity each scoring system compared.

Results: Total 188 patients were included into the study with mean age 27.62 ± 12.722 years old and mostly female. Negative appendectomy for the patient in this study was 13.8%. RIPASA score with cut of point 7.5 is more sensitive 84.6% compared to Alvarado score with score > 7 78.4% and specificity of the RIPASA score 57.7% is more than Alvarado score 42.3%.

Conclusion: RIPASA score is better scoring system compare to Alvarado score in diagnosis of acute appendicitis in Kelantan population.

Supervisor:
Associate Professor Dr Zaidi Zakaria

ELUCIDATION OF TOLL-LIKE RECEPTOR 4 ANTAGONIST ON LEARNING AND MEMORY FUNCTIONS OF MICE FOLLOWING CHRONIC STRESS

Khairiah Razali
Master of Cognitive Neurosciences

Department of Neuroscience, School of Medical Sciences,
Universiti Sains Malaysia, Kubang Kerian, Kelantan,
Malaysia

Introduction: Learning and memory functions are severely impacted by chronic stress due to Toll-like receptor 4 (TLR4)-mediated microglial upregulation and dopaminergic (DA) neuronal imbalance. Although Lipopolysaccharide-*Rhodobacter sphaeroides* (LPS-Rs), a TLR4 antagonist, can inhibit TLR4 activation pathway, its role in alleviating chronic stress-induced learning and memory impairments is still elusive.

Objective: This study primarily aimed to elucidate the potential role of LPS-Rs in preserving learning and memory functions of mice following chronic stress.

Methods: Learning and memory performances of Swiss albino male mice underwent 21 days of chronic stress paradigm (restraint stress with social isolation) were assessed using Morris water maze (MWM) test. Immunohistochemistry (IHC) analysis was done to measure the expression levels of TLR4 protein, microglia and DA neurons in the dentate gyrus (DG) of hippocampus, prefrontal cortex (PFC) and ventral tegmental area (VTA).

Results: Twenty-one mice were included in this study. Stressed mice treated with LPS-Rs performed better than untreated mice in MWM test (latency: 9.30 s versus 16.79 s, P -value = 0.041; pathlength: 217.40 cm versus 396.80 cm, P -value = 0.045). IHC analysis showed significantly lower expression level of TLR4 protein in LPS-Rs treated compared to untreated groups in all the three brain regions (mean OD DG: 0.10 versus 0.24, P -value = 0.022; PFC: 0.09 versus 0.20, P -value < 0.001; VTA: 0.17 versus 0.27, P -value = 0.003). Similar findings were observed on microglial expression level (mean OD DG: 0.14 versus 0.33, P -value < 0.001; PFC: 0.10 versus 0.31, P -value < 0.001; VTA: 0.15 versus 0.31, P -value < 0.001). For DA neuronal expression level, both LPS-Rs treated and untreated groups exhibited significantly higher expression than control in the VTA (mean OD LPS-Rs treated: 0.14 versus 0.07, P -value = 0.016; untreated: 0.17 versus 0.07, P -value = 0.001) while no differences on DA neuronal expression were observed in hippocampal DG and PFC.

Conclusion: LPS-Rs improved MWM performance as well as reduced TLR4 and microglial activation in the hippocampal DG, PFC and VTA of stressed mice. Nevertheless, lack of effect of LPS-Rs was observed on DA neuronal expression. This study concluded that LPS-Rs has the potential to intercept chronic stress-induced TLR4-dependent neuroinflammation pathways.

Supervisor:
Dr Mohd Zulkifli Mustafa

Co-supervisors:
Professor Dato' Dr Jafri Malin Abdullah
Dr Sangu Muthuraju