Abstracts

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

EVALUATION AND COMPARISON OF KNOWLEDGE AND ATTITUDE AMONG POSTGRADUATE DOCTORS IN HOSPITAL UNIVERSITI SAINS MALAYSIA TOWARDS RECOGNITION AND MANAGEMENT OF SEPSIS

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Introduction: Doctors' clinical knowledge and attitude of sepsis together with provision of sepsis-related care commands attention as its incidence increase. Despite improvements in recognition and management of sepsis, there is still limited literature available exploring the clinical knowledge of sepsis and attitude of doctors.

Methods: A sample of 190 doctors undergoing postgraduate training from six different departments namely, Anaesthesiology, Medical, Accident and Emergency, General Surgery, Neurosurgery and Orthopaedics at Hospital Universiti Sains Malaysia, Kelantan were surveyed on their clinical knowledge of sepsis. Results revealed gaps in sepsis knowledge related to time of last sepsis management education as well as year of service and specialisation.

Results: There were no significant differences in knowledge and attitude scores between genders and departments. Age, gender, years of service and specialisation in the respective departments did not correlate with both knowledge and attitude scores. However, the last education on sepsis management obtained showed significant associations with both knowledge (P = 0.002) and attitude scores (P = 0.005). The increase in the duration of last education correlated negatively with the knowledge and attitude scores. There were no significant differences between gender and department of specialisation with regards to high knowledge and attitude scores. However, years of service and year of specialisation in the respective departments showed significant correlations with higher knowledge score. An increase in years of service and year of specialisation in the respective departments associated with higher knowledge score. There is no significant factor associated with higher attitude score.

Conclusion: Educational interventions focused on these identified sepsis-related gaps are recommended as it has been shown that the lack of education was the main factor in lower knowledge and attitude scores.

Supervisor:

Professor Shamsul Kamalrujan Hassan

Co-supervisor: Professor Wan Mohd Nazaruddin Wan Hassan

PREVALENCE OF PAIN IN MECAHNICALLY VENTILATED CRITICALLY ILL PATIENT IN INTENSIVE CARE UNIT

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Introduction: Pain in intensive care unit (ICU) can be multifactorial, either from the disease process itself, routine nursing care or intervention done. Untreated pain in ICU is related with adverse outcomes. There are few pain assessment tools has been developed for sedated and mechanically ventilated patient, such as CPOT, BPS and ANVPS. Pain assessment in ICU is crucial in order to effectively treat pain in ICU.

Objective: The objective of this study was to assess presence of pain among sedated and mechanically ventilated patient at rest and during routine nursing care, eye care and suctioning.

Methods: This is a prospective observational study was conducted among 280 sedated and mechanically ventilated patients admitted to ICU, Hospital Sultanah Aminah and Hospital Universiti Sains Malaysia (HUSM) during rest and routine nursing care which is eye care and suctioning. Patients who received sedation and analgesia and on mechanically ventilated was included in this study. Pain assessment was done using three pain behavioural assessment: BPS, CPOT and adult NVPS.

Results: The findings revealed that low incidence of pain with prevalence 6.8% among sedated and mechanically

ventilated patient at rest with no marked difference with eye care. But, 58.2% of patient experienced pain during airway suction. The mean pain score during rest (mean 3.25, SD = 0.602) were lower than mean pain score during airway suctioning (mean = 5.04, SD = 1.358). The pain significantly correlates with age (r = -0.366, P < 0.001) and conscious state (r = 0.338, P < 0.001).

Conclusion: Sedated and mechanically ventilated patient experience pain at rest and during airway suctioning. Pain level was associated with age and conscious state.

Supervisor: Dr Laila Ab Mukmin

Co-supervisors: Professor Nik Abdullah Nik Mohammad Dr Salamah Azerai

DEVELOPMENT, VALIDATION AND EVALUATION OF THE EFFECTIVENESS OF A MENOPAUSE EDUCATIONAL INTERVENTION FOR SPOUSES OF MENOPAUSAL WOMEN IN KELANTAN

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Introduction: Although the spouse is recognised as the ideal person for providing comprehensive and sustainable support to menopausal women, such support is lacking.

Objectives: In order to facilitate this support, a study to develops, validates and evaluates an effective menopause educational intervention for spouses of menopausal women was carried out.

Methods: This study uses a multiphase-mixed methods design comprising three phases. Phases 1 and 2 implemented an explorative sequential mixed methods design and Phase 3 used a randomised control trial (RCT) intervention design. Phase 1 developed the menopausal spousal support questionnaire (MSSQ) based on a literature review, in-depth interviews with 13 menopausal women and discussions with the research team. This was followed by validation process with 146 couples to perform an exploratory factor analysis (EFA) and 431 couples for a confirmatory factor analysis (CFA). In Phase 2, the menopause educational module for spouses (MEMS) was developed based on the findings from Phase 1 and the modified Delphi technique was conducted with 10 expert panels. Phase 3 involved 59 couples for the intervention group and 50 couples for the control group. The MEMS was implemented as an educational tool for spouses in the intervention group while the control group were added to waiting list. The effectiveness of this intervention was evaluated using Kirkpatrick's four level evaluation models, with questionnaires administered at baseline, 2 weeks and 3 months following the intervention.

Results: The results showed that the validated MSSQ developed in Phase 1, which contained 17 items under four domains, demonstrated good model fit (RMSEA = 0.078, CFI = 0.934, TLI = 0.920, df = 3.641) and proved to be a reliable scale (CR > 0.6, AVE > 0.5, IR > 0.93). In Phase 2, the validated MEMS comprising seven units was highly satisfactory (CVI = 0.95). In Phase 3, repeated measures analysis of covariance (ANCOVA) demonstrated that the spouses in the intervention group had significantly higher menopause knowledge (P < .001) and provision of support (P < .001) scores than the control group which they sustained until month three, with a larger effect size for knowledge (ES knowledge = +1.16) and a smaller ES for provision of support (ES providing support = +0.22). Measurement of the spouses' attitudes and menopausal women's perceived support scores also showed moderate (ES attitude = +0.56) and small increments (ES perceived support = +0.22) following the intervention but no statistically significant difference was observed between the intervention and control group.

Conclusion: The MEMS intervention was effective at improving the spouses' menopause knowledge, attitudes and provision of support as well as the menopausal women's perceived support. However, since this is the first intervention study in Malaysia to focus on spouses of menopausal women, more evidence-based studies need to be conducted in the future to improve the outcomes of this promising intervention.

Supervisor: Professor Nik Hazlina Nik Hussain

Co-supervisors: Professor Azidah Abd Kadir Associate Professor Zaharah Sulaiman

RETROSPECTIVE STUDY ON THE FIRST CEREBROSPINAL FLUID ANALYSIS TAKEN FROM EXTERNAL VENTRICULAR DRAINAGE INSERTION IN MENINGITIS PATIENT WITH HYDROCEPHALUS

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Background: VP shunting is a permanent form of cerebrospinal fluid (CSF) diversion that can be performed for hydrocephalus. Sterility of the CSF is an important pre-requisite for permanent shunt placement. It has been hypothesised that in early stage of meningitis, ventricular CSF remains sterile. We are conducting a study on the first CSF sample taken from patient suspected to have meningitic hydrocephalus. We aim to evaluate the biochemical and cellular market to determine the sterility of the samples taken. It is hoped that this will proven evidence in support of early shunt placement in this group of meningitis.

Methods: A retrospective review case records of patients who had undergone external ventricular drainage (EVD) for suspected meningitic hydropcephalus in Hospital Sultanah Aminah, Johor Bahru was conducted from 2012 until 2016. The data of biochemical and culture parameters of CSF were identified and analysed.

Results: A total of 51 cases were analysed. The mean age of patients was 37.27 years old, with 64.7% of them were male. The values of parameters assessed in infected CSF samples were lesser compared to sterile CSF, which was positive for the hypothesis that CSF sample was sterile. The univariate analysis revealed that the main parameters to determine CSF sterility were CSF glucose (95% CI: 0.852, 10.290; P = 0.001), CSF protein (95% CI: 0.722, 14.898; P < 0.001), CSF gram stain (95% CI: 16.437, 0.877; *P* < 0.001) and CSF appearance (95% CI: 0.611, 6.362; P = 0.012). The multivariate analysis had proven that gram stain was the main parameter in the CSF analysis (95 % CI: 16.437, 0.029; P = 0.016). Of that, 45.1% of patients ended up with VP shunts. Sterile CSF was associated with VP shunt insertion. However, no significant difference on CSF parameters between CSF from EVD and lumbar puncture, was observed.

Conclusion: The first CSF sample analysis could help in determining further management of Meningitis patients. The most significant parameter in CSF to determine infection was gram stain. Most of the meningitis patients ultimately would need shunts in future.

Supervisor: Professor Zamzuri Idris

Co-supervisor: Dr Johari Adnan Siregar

ENDOCRINOLOGICAL OUTCOME OF ENDOSCOPIC TRANSSPHENOIDAL SURGERY FOR FUNCTIONING AND NON-FUNCTIONING PITUITARY ADENOMA

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Aim: This study is to analyse: i) remission and preservation of hormones; ii) endocrinological and anatomical complications and iii) visual improvement treated with endoscopic transsphenoidal surgery.

Methods: Retrospective observational study of all consecutive cases of pituitary adenoma treated with endoscopic trans-sphenoidal surgery in HKL between 2006 and 2015. Age, sex, pre- and post-operation hormone level, tumour size and complication were noted.

Results: Sixty-seven patients were diagnosed with non-functioning pituitary adenoma throughout this period with 16.4% (n = 11) patients had both visual and hormonal improvement post-operation. From the 27 patients who had tumour invaded into the cavernous sinus, 12.15% (n = 13) of

the patients vision improved. In terms of adenoma patients that had impaired hormonal function pre-surgery, 62.69% of the patients' hormone level normalised post-surgery.

Meanwhile, 39 patients were diagnosed with functioning pituitary adenoma. 31.25% of patients recovered from acromegaly and 57.14% patients recovered from Cushing disease within 7 days post-operation. 12.8% (n = 5) of the functioning adenoma patients suffered complications.

Conclusion: The outcome for preservation and hormone recovery in non-functioning pituitary adenoma group was very good, with only 1 (1.49%) patient's hormone worsening. There was no visual deterioration and mortality throughout this study. A dedicated team specialised in endoscopic transphenoidal pituitary surgery further improves the outcome of this surgery.

Supervisor: Dr Azmi Alias

Co-supervisors: Dr Abdul Rahman Izaini Ghani, Dr Mohammad Badrulnizam Long Bidin, Dr Azman Raffiq

CT PERFUSION IN DETECTING MALIGNANT MIDDLE CEREBRAL ARTERY INFARCT

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Introduction: Acute ischaemic stroke is a leading cause of adult disability worldwide. Neuroimaging plays a critical role in the assessment of acute stroke patients and often guides therapeutic interventions. CT perfusion (CTP) is an emerging modality that produces maps of time-topeak (TTP), cerebral blood flow (CBF) and cerebral blood volume (CBV), with a computerised automated map of the infarct and penumbra. This modality able to better evaluate the extent of an infarction making it a potential method for evaluating patients suffering from large middle cerebral artery (MCA) infarctions. This study is aimed at investigating the potential role of CT perfusion in the early identification of patients who develop malignant MCA infarct requiring surgical decompression. Early identification and prediction of malignant MCA infarction will aid in decision making and help to improve patient's outcome.

Methods: A prospective cohort study of all patients who presented with the clinical diagnosis of a large middle cerebral artery infarction within 48 h of onset was performed in Hospital Kuala Lumpur between August 2015 and March 2018. Patients were subjected to CT brain and CT perfusion scans on admission and were followed up to determine the development of malignant infarction requiring surgical decompression.

CT perfusion parameters such as CBF, CBV and timeto-peak (TTP) maps were determined. Optimum sensitivity, specificity, positive (PPV) and negative predictive values (NPV) were calculated for prediction of the development of malignant brain infarct by means of receiver operating characteristics (ROC). CTP parameters were also correlated with functional outcome in patients based on a 30-day mortality, Glasgow outcome scale (GOS) at discharge and modified ranking scale (MRS) at 6 months.

Results: A total of 95 patients were recruited in the duration of this study. Mean age were 56 in nonmalignant group and 63 in malignant group. Malays were the predominant race with 39 (72.7%) in non-malignant group and 16 (27.3%) in malignant group. Comorbidity such as hypertension, diabetes mellitus, hypercholesterolemia, obesity and smoking were not statistically significant. In this population 28 patients eventually developed malignant infarction that required surgical decompression. CT perfusion parameters were generally lower in patients with malignant brain infarct group compared to the non-malignant brain infarct group. The largest mean difference between the group was noted in the TTP values (P = 0.005). CT perfusion parameters had a very high and comparable PPV (83%-90%), high NPV (88%-93%) except for CBF parameter, NPV was 67.8%, a high sensitivity (71%-98%) and only a moderate specificity (50%-77 %). CBF with cut off value of > 32.85 of the hemisphere was able to accurately predict malignant infarctions in 81.4 % of cases. The National Institutes of Health Stroke Scale (NIHHS) score of more than 13.5 were also found to be able to accurately determine malignant infarct (97.6%). Functional outcome of the patients with malignant MCA infarct were compare based on a 30-day mortality, Glasgow outcome score (GOS) upon discharge and mRS (Modified Ranking Score) at 6 months. CT perfusion parameters for outcome base on a 30-day mortality showed almost similar results (P = 0.080). Functional outcome of patients based on GOS were similar upon discharge however showed improvement at 6 months during reviewed base on MRS (P < 0.001).

Conclusion: CT perfusion parameters have a role in predicting malignant brain infarction and should be included in the initial evaluation of patients in order to facilitate the early identification and surgical treatment of large middle cerebral artery infarctions. CT perfusion parameters may also help in the prediction of outcome following these types of stroke.

Supervisor: Dr Regunath Kandasamy

Co-supervisor: Dr Mohammed Azman Mohammad Raffiq

HYPERTENSIVE RETINOPATHY AND THE RISK OF HEMORRHAGIC STROKE

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Background: Haemorrhagic stroke and hypertensive retinopathy are known end organ damage, with hemorrhagic

stroke having deleterious consequence to the patients. This study is to correlate between hypertensive retinopathy and hemorrhagic stroke.

Methods: All patients with with hypertension with and without hemorrhagic stroke were recruited. Funduscopic examination was performed and then graded based on Wong and Mitchell hypertensive retinopathy classification. Clinical and radiological parameter included are demography, vital signs, Glasgow coma scale (GCS) on admission, clot volume, site of clot, intra-cerebral haemorrhage (ICH) score and Glasgow (GOS) score. Data were collected and correlated with the severity of hypertensive retinopathy.

Results: Fifty hypertensive patient without haemorrhagic stroke and 51 patients with haemorrhagic stroke were recruited. In the haemorrhagic stroke group, 21 had low severity (normal/mild retinopathy changes) accounting for 41.2% and 30 patients had high severity (moderate and severe retinopathy). In the non-haemorrhagic stroke patients, 49 had low severity and 1 had high severity (P-value = 0.001). Low severity showed better GCS score on admission as compared to high severity (P-value = 0.003). Low severity also showed a clot volume less than 30 mL, (P-value = 0.001) and also statistically significant with an ICH score of between 0-2 in most of the patients, (P-value = 0.006). Lastly, we compared the GOS score of patients and found a favourable outcome of GOS score 4-5 in low severity retinopathy for 17 patients with only 4 having unfavourable outcome (GOS score 1-3). As for high severity, 23 patients had unfavourable outcome with 7 having favourable outcome, this was statistically significant (P-value = 0.001).

Conclusion: Low severity retinopathy were found to have small clot volume and most likely treated by medical management and better outcome. With high severity retinopathy had larger clot volume and requiring surgical intervention and poorer outcome.

Supervisor: Dr Pulivendhan Sellamuthu

Co-supervisor: Dr Regunath Kandasamy

INTRACRANIAL VOLUME POST CRANIAL EXPANSION SURGERY USING 3D CT SCAN IMAGING IN CHILDREN WITH CRANIOSYNOSTOSIS

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Background: Craniosynostosis is a congenital defect that cause one or more suture to fuse prematurely. Cranial expansion surgery which consist of cranial vault reshaping with or without fronto-orbital advancement (FOA) is done to correct the skull to a more normal shape of the head as well as to increase the intracranial volume. Therefore, it is important to evaluate the changes of intracranial volume

(ICV) after the surgery and the effect of surgery, both clinically and radiologically.

Objectives: This study is to: i) evaluate the ICV in primary craniosynostosis patients after the cranial vault reshaping with or without fronto-orbital advancement and to compare between syndromic and non-syndromic synostosis group; ii) to determine factors that associated with significant changes in the ICV post-operative and iii) to evaluate the resolution of copper beaten sign and improvement in neurodevelopment after the surgery.

Methods: A prospective observational study of all primary craniosynostosis patients who underwent operation cranial vault reshaping with or without FOA in Hospital Kuala Lumpur from January 2017 until Jun 2018. The ICV pre-operative and post-operative was measured using the 3D CT imaging and analysed. The demographic data, clinical and radiological findings was identified and analysed.

Result: Fourteen cases (six males and eight females) with 28 3D CT scan were identified. The mean age of patients was 23 months. Seven patients were syndromic synostosis (4 Crouzon syndrome and 3 Apert syndrome) and 7 were non-syndromic synostosis. The mean pre-operative ICV was 880 mL (in ranges 641 mL-1234 mL) while the mean post-operative ICV was 1081 mL (in ranges 811 mL-1385 mL). The difference was 201 mL, which was statistically significant (P < 0.001). In comparison, the mean volume increment for syndromic synostosis and non-syndromic synostosis were 282 mL and 120 mL, respectively. The difference was statistically significant (P < 0.004). Mc Nemar's test was used to analyse pre- and post-operative changes within the same patients. At 3 months post-surgery, all 13 patients with copper beaten sign pre-operatively did not show complete resolution on 3D CT imaging. Therefore the P-value was insignificant (P > 1.0). While two patients with neurodevelopmental delay pre-operatively showed no improvement during assessment at 3 months post-surgery. Again the P-value was insignificant (P > 1.0). Hence, there were no significant resolutions in copper beaten sign and improvement in neurodevelopmental delay in this study.

Conclusion: Surgery in craniosynostosis patients increases the intracranial volume besides it improves the shape of the head. From this study, the syndromic synostosis had better increment of intracranial volume compared to non-syndromic synostosis

Supervisor: Dr Azmi Alias

Co-supervisor: Dr Badrishah Idris

RANDOMISED CONTROLLED TRIAL OF THE EFFECTIVENESS AND SAFETY OF TRANSCERVICAL BALLOON CATHETER AND PROSTAGLANDIN E2 FOR INDUCTION OF LABOUR IN WOMEN WITH ONE PREVIOUS CAESAREAN SECTION

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Introduction: Induction of labour (IOL) among women with one previous scar is one of important step for a success vaginal birth after caesarean section and this procedure carry increase risk to mother and baby. Transcervical balloon catheter and prostaglandin E2 are widely used. This study compared on the effectiveness and safety between both methods. This help the obstetrician to choose reasonable method.

Objectives: To evaluate the effectiveness and safety between transcervical balloon catheter and prostaglandin E2 as IOL agent among women with one previous caesarean section at term.

Methods: This is a randomised controlled study that was conducted at Obstetrics & Gynecology Department, Hospital Sultan Ismail, Johor Bahru on 129 pregnant women who admitted for induction of labor. Sixty-five women were randomised to receive prostaglandin E2 and 64 women to receive transcervical balloon catheter.

Results: The two groups were comparable for maternal age, gestational age, indication for IOL and indication of previous caesarean section. The mean age for balloon group was 30.41 (+/-4.18) compared to 32 (+/-4.8) from prostin group. Majority of patient in balloon and prostin groups were Malay (69%, 74%), Chinese (7.8%, 16.9%), Indian (9.4%, 6.2%) and others (4.7%, 1.5%), respectively. The prostin group with mean weight 76.11 (+/-14.56) kg were heavier than balloon group with mean weight 68.05 (+/-12.33) kg with significant difference (*P*-value = 0.001). The prostin group had more patients with previous vaginal delivery compared with balloon group, 27 (41.5%) versus 13 (20.3%) with *P*-value 0.009.

The success VBAC was not significant difference between the balloon group and prostin group, 40.7% versus 56.8% with *P*-value = 0.064. There was significantly higher prostin patient achieved favourable cervix compared to balloon patients within 12 h of IOL, 20 (30.5%) versus 9 (14.0%), respectively, with *P*-value = 0.023. However, if IOL continuous until 48 h, there was significantly higher balloon patients who achieved favourable cervix compared to prostin patients, 62 (97.0%) versus 55 (85%), respectively with *P*-value = 0.017. The duration of labour was shorter for prostin group compared to balloon group, 4.9 (+/-3.78) h versus 7.3 (+/-3.45) h, respectively with *P*-value = 0.001.

Regardless the method of IOL, previous vaginal delivery is important factor for success VBAC and it was statistically significant. In balloon group, patient with previous vaginal delivery had higher success VBAC compared patients who never had previous vaginal delivery, 9 (69%) versus 4 (31%) with *P*-value 0.042. Similar result in prostin group, where 20 (74%) versus 7 (26%) with *P*-value 0.019.

Previous vaginal delivery also a factor that significantly increase the chance for duration of IOL less than 12 h in both groups. In balloon group, 5 (38.5%) patients achieved favourable cervix within 12 h than 4 (7.8%) patients with P-value = 0.017. Similar result in prostin group where 13 (48.1%) patients compared to 7 (18.4%) patients with *P*-value = 0.01. Obesity was not significantly influence the success VBAC or duration of IOL in this study.

There were comparable complications between the group in incidence of uterine hyperstimulation and postpartum haemorrhage. There was no incidence of scar rupture in both groups. However there was higher indication caesarean section for moderate to thick meconium stained liquor in prostin group about 8 (28%) compared to 2 (5.0%) for balloon group with *P*-value = 0.009. None of the babies had meconium aspiration syndrome (MAS) complication. There were seven macrosomic babies who six of them delivered via caesarean section for poor progress and one of them delivered vaginally without complication.

Conclusion: Both balloon and prostin has comparable effectiveness as IOL agent in previous scar patients. Balloon catheter still offer better safety profile includes lesser case of moderate to thick meconium stained liquor incidence and cheaper than prostin. Previous vaginal delivery is an important factor for trial of scar with unfavourable cervix regardless of induction method.

Supervisor:

Professor Dr Nik Mohamed Zaki Nik Mahmood

THE ASSOCIATION BETWEEN LEVEL OF VITAMIN D AND THE OUTCOME OF TERM PREGNANCY

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Introduction: Vitamin D deficiency is an important nutritional problem in developing countries. In addition to immediate pregnancy concerns, the effect of low maternal vitamin D levels in pregnancy may have health effects in mothers and their children. This problem is prevalent even among pregnant women living in tropical countries despite abundance of sunlight.

Objectives: To purpose of this study is to determine the association between Vitamin D level and pregnancy outcome among pregnant women in Malaysia.

Methods: This was a prospective cohort study conducted at labour room HSAJB from October 2016 until September 2017. A total of 86 patients of more than 37 weeks of gestation with singleton, uncomplicated pregnancy were recruited for this study. After obtaining demographic information, convenience blood sampling of maternal venous blood and umbilical cord blood done to determine the circulating 25(OH) D level. Cord blood gas analysis was done as part of assessment of neonatal well being. Labour and neonatal outcome was documented. All results were tabulated and analysed using SPSS software and results were considered significant when P-value was < 0.05.

Results: Gestational age ranged from 37 to 41 weeks with mean maternal age of 26.8 years old. There were 79.1% women exhibited vitamin D deficiency (< 50 nmol/L) while only 20.9 % had sufficient level (> 50 nmol/L). Analysis showed higher prevalence of deficiency among Malay (64.7%) and Indian (20.6%) in comparison to Chinese (14.7%). Obesity leads to nearly two folds increment in the prevalence of deficiency among study population. Statistically no significant association between maternal vitamin D level and mode of delivery (P = 0.33). However the maternal vitamin D level (P < 0.005) and neonatal asphyxia (P = 0.01). Association between level of vitamin D level and birth weight was also significant (P = 0.001).

Conclusion: A high prevalence of vitamin D deficiency among Malaysian women is seen in this study. Overall a higher maternal and cord vitamin D level is associated with better neonatal outcomes. Thus, future studies should be conducted to assess the clinical benefits of routine vitamin D supplementation for pregnant women.

Supervisors: Professor Dr Nerminathan Dr J Ravichandran Professor Dr Nik Mohamed Zaki Nik Mahmood

EVALUATION OF INTRAOCULAR PRESSURE AND OCULAR PERFUSION PRESSURE PRE-AND POST-WHOLE BLOOD DONATION IN NORMAL HEALTHY BLOOD DONORS

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Introduction: Blood donors had loss about 10% of blood within 5 min to 7 min during each blood donation. This procedure is performed daily thousands of times worldwide, predominantly without complications. Even though the amount of blood loss during blood donation is relatively small and may mimic minimal acute blood loss, it was enough to cause a reduction in circulatory blood volume and subsequent alter or stimulate autonomic responses to maintain blood supply to the vital organ. Ocular structure perhaps could be influenced from a sudden decrease of blood supply after the blood donation. Ocular tissues are depending on the maintenance of ocular perfusion pressure (OPP) for adequate oxygenation via systemic regulation of blood pressure (BP) and local regulation of intraocular pressure (IOP). Auto-regulation plays a very important role in the control of blood flow in a tissue as well as optic nerve head, retina and choroid. Auto-regulation operates only within a certain critical range of perfusion pressure and it breaks

down when perfusion pressure goes below critical range. Numerous population-based epidemiologic studies have shown that low OPP is associated with open-angle glaucoma. Knowing this background, this study was conducted to measure IOP and OPP pre and immediately post blood donation whether IOP and OPP levels reached thresholds associated with optic nerve damage in normal healthy blood donors. It may further imply to the patient with ocular problem especially in glaucoma patient whether it is safe for them to donate blood.

Objectives: Objective in this study is to evaluate the IOP and MOPP pre- and immediately post-whole blood donation in healthy blood donors.

Methods: This is a prospective cohort study done in Transfusion Medicine Unit, Department of Hematology, Universiti Sains Malaysia, from October 2016 to December 2018. Total of 120 healthy blood donors that fulfilled the inclusion criteria were recruited with simple systematic sampling. The participant seated on donor's couch with semi recline position just before the blood donation procedure. IOP and systemic blood pressure (BP) were measured and proceed with withdrawal of the 450 mL of whole blood within 5 min to 7 min. IOP and systemic BP were measured immediately after the removal of needle without changing position. Formula was used to calculate mean arterial BP (MAP) = 1/3 systolic BP + 2/3 diastolic BP and MOPP = (0.84 × MAP) – IOP.

Results: There were 62 (51.7%) male and 58 (48.3%) female with age ranging from 20 to 45 years old. Mean (standard deviation) age of the blood donors was 27.6 (7.9) years old and majority were Malays (91.7%). IOP significantly reduced immediately after blood donation by 0.44 mmHg (95% confidence interval [CI]: 0.18–0.71) on right eye (P = 0.001) and 0.58 mmHg (95% CI: 0.28–0.89) on left eye (P < 0.001). MOPP also significantly decreased by 2.83 mmHg (95% CI: 1.78–3.87) on right eye (P < 0.001) and 2.68 mmHg (95% CI: 1.62–3.74) on left eye (P < 0.001).

Conclusion: This study showed significant reduction of IOP and MOPP after mild acute blood loss in healthy blood donors immediately after donation. The result suggest that it is safe to donate blood for healthy person as it reduced IOP and reduction of OPP are not exceeded the limit of autoregulation breakdown.

Supervisor: Associate Professor Dr Adil Hussein

Co-supervisor: Associate Professor Dr Rosnah Bahar

RETINAL NERVE FIBRE LAYER AND MACULAR THICKNESS IN PARKINSON'S DISEASE PATIENTS

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Introduction: Parkinson's disease (PD) is a neurodegenerative progressive, movement disorder characterised by the motor symptoms bradykinesia, tremor, rigidity and postural stability. It is caused the loss of dopaminergic neurons in the midbrain. Visual symptoms are common in PD including difficulty to read, double vision, feelings of presence and passage in the visual periphery and complex visual hallucinations. Human retina is considered part of the central nervous system in human body. Thus, we would expect anatomical changes of the retina if PD is affecting the patient. This study is to evaluate the changes in retinal nerve fibre layer (RNFL) thickness and macular thickness in patients with PD compared to normal populations.

Objective: To evaluate the RNFL thickness and macular thickness in patients with PD.

Methods: A comparative cross-sectional, hospitalbased study was conducted in Hospital Universiti Sains Malaysia. A total of 64 PD subjects and 64 controls were recruited. Candidates that fulfilled the criteria with normal ocular examinations were undergone optical coherent tomography (OCT) examinations of the right eye. RNFL thickness and macular thickness were evaluated. Independent t-test, Chi-square, ANCOVA and Pearson's correlation were used in the statistical analysis.

Results: There was statistically significant thinning of the RNFL in the PD group compared to control in average ($P \le 0.001$), superior (P = 0.010) and inferior ($P \le 0.001$) quadrants. There was also statistically significant macular thinning in PD group compared to control in average (P = 0.015), central (P = 0.001), outer superior (P = 0.014), outer inferior ($P \le 0.001$) and outer nasal (P = 0.001) quadrants. RNFL thickness in PD subjects showed significant correlations with visual acuity in the inferior (P = 0.020) and nasal ($P \le 0.001$) quadrant. Macular thickness in PD subjects showed significant correlations with visual acuity in inner temporal (P = 0.006), outer superior (P = 0.003) and outer temporal ($P \le 0.001$) quadrant.

Conclusion: The mean RNFL thickness was significantly lower in the PD group compared to control. The macular thickness also was significantly lower in the PD group compared to control. There were significant positive correlations between RNFL thickness and visual acuity, and between macular thickness and visual acuity in PD group.

Supervisor: Professor Dr Wan Hazabbah Wan Hitam

Co-supervisor: Dr Sanihah Abdul Halim



A STUDY ON LONG TERM EFFECT OF CHAIR BASED STRETCHING EXERCISE ON THE INTRAOCULAR PRESSURE AND QUALITY OF LIFE IN PRIMARY OPEN ANGLE GLAUCOMA PATIENTS

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Introduction: Thus far, intraocular pressure (IOP) is the only modifiable risk factor in glaucoma. Exercise has a potential modifiable risk factor in many chronic diseases especially on disease control and quality of life (QoL). Exercise may have a potential beneficial effect on glaucoma patients. However, the effect of exercise on IOP remains controversial. The challenge is to choose safe and effective exercise without causing elevation of IOP in glaucoma patients. Chair based stretching exercise (CBSE) seems to be safe and easy to practice among the elderly, especially those with advanced visual field defect. However, the effect of exercise on the IOP and QoL among primary open angle glaucoma (POAG) patients is not well studied.

Objective: To evaluate the long-term effects of CBSE on the IOP and QoL among POAG patients.

Methods: A randomised controlled trial was conducted in Hospital Universiti Sains Malaysia, Kelantan between August 2017 and January 2019. POAG patients who were 50 years old and older and who were known to be compliant to IOP lowering agents were recruited. Selected subjects were divided into two groups; group A with regular CBSE and group B without CBSE. Patients in group A performed CBSE at home five times a week, and their compliance was monitored using an exercise dairy. IOP monitoring was done once in every 3 months for a year for both groups. The QoL evaluation using the Bahasa Malaysia version of 36-item Glau-QoL© questionnaire was conducted at baseline and after a year of follow-ups.

Results: A total of 60 POAG patients were recruited (30 in group A and 30 in group B). There were no significant differences in age (P = 0.970) and sex (P = 0.184) between the groups. One patient in group A had been withdrawn or dropped out at a 3-month follow-up due to non-compliance. There was a reducing trend of IOP even though the baseline IOP was higher in group A. On the comparison between group A and group B, there was no significant statistical difference of IOP (P = 0.958). In general, there was no significant difference in QoL between the two groups at 12 months post-exercise (P = 0.739). There was an improvement of QoL domain for anxiety at 12 months post-CBSE in group A (P = 0.007). However, other domains had no significant improvements. There was no adverse event reported throughout this study.

Conclusion: Although there was no significant reduction of IOP, CBSE had a significant effect on the

reduction of anxiety. Besides, it is safe and practical in POAG patients.

Supervisor: Professor Dr Liza Sharmini Ahmad Tajudin

Co-supervisors: Associate Professor Dr Azhany Yaakub, Associate Professor Dr Ooi Foong Kiew

PROGNOSTIC SIGNIFICANCE OF HISTOPATHOLOGICAL PARAMETERS OF SOFT TISSUE SARCOMAS

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Introduction: Soft tissue sarcomas (STSs) is a rare malignancy, with only less than 1% from all adult malignancies. It comprised 60%-70% of orthopaedic related soft tissue malignancy and represents a heterogeneous group of rare malignant tumours with a wide spectrum in terms of histologic type and prognosis. Over the years the treatment evolved from limb amputation to limb salvage surgery with pre-and/or post-operative chemotherapy. With the emergence of multiple therapy for soft tissue sarcoma, several staging and grading systems recently have been proposed to correlate morphologic and clinical parameters with prognosis. However, there are still conflicting results regarding the value of these prognostic factors. We conduct this study to determine whether histopathological parameters have the prognostic significance in determining survival for soft tissue sarcomas patients

Objective: The aims of this study were to evaluate the prognostic significance of histopathological parameters of soft tissue sarcomas in Universiti Sains Malaysia (USM) Health Campus, Kelantan.

Methods: This is a retrospective cross-sectional study. Data was collected from 122 patients who were diagnosed and treated in Hospital USM (HUSM) as soft tissue sarcoma of the extremities from 1 January 2001 until 31 December 2010. All patients underwent surgeries; either limb salvage or amputation. Data were retrieved from the histopathological database in our pathology laboratory. From the histopathological reports, we analysed the presence of tumour necrosis, mitotic count, tumour differentiation score and the resected tumour margin with the survival of soft tissue sarcoma.

Results: The subject's mean age was 52.6 years old (SD = 18.59). Majority of the patients (59.0%, n = 72) were male while about 41.0% were female. 48.4% patients still survive after 5 years (n = 59). There were 107 patients with tumour free margin (n = 87.7%). Overall median survival time of soft tissue sarcomas were 88 months (95% CI: 53.73,

122.27). Analysis on Kaplan Meier Survival Analysis and Cox Proportional Hazard regression showed mitotic count, tumour necrosis, tumour differentiation score, and free margin resection did not show any prognostic significant for survival of soft tissue sarcoma with all (*P*-value > 0.05), respectively.

Conclusion: No single histological parameters in this study showed any prognostic significance for survival of soft tissue sarcoma. Prognostic significance of various histological parameters should base on each specific type of sarcoma. Histological grade is recommended to be included in each histopathological report.

Supervisor: Dr Wan Haiery Wan Nor

Co-supervisors: Dr Sahran Yahaya Dr Sharifah Emilia Tuan Sharif

DETECTION OF LARYNGOPHARYNGEAL REFLUX IN PATIENTS WITH CHRONIC SUPPURATIVE OTITIS MEDIA

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Introduction: Chronic suppurative otitis media is one of the most common chronic infectious diseases worldwide, affecting people in not only developing but also industrialised countries. This disorder is a major cause of acquired hearing loss, especially in developing countries and is a major disease entity in the field of otolaryngology. Many studies have proven the association of laryngopharyngeal reflux and otitis media with effusion. But there is no study on the association of laryngopharyngeal reflux and chronic suppurative otitis media.

Objective: This study aims to study on laryngopharyngeal reflux disease in patients with chronic suppurative otitis media.

Methods: This was a cross sectional study of 94 patients from otorhinolaryngology department, Hospital University Sains Malaysia, which were divided into two groups of 47 patients in each group of patients with chronic suppurative otitis media and patient without chronic suppurative otitis media. All patients were above 18 years of age. Diagnosis of laryngopharyngeal reflux is made based on reflux symptom index (RSI) questionnaires and reflux finding scores (RFS). The prevalence of laryngopharyngeal reflux is being determined and association of the laryngopharyneal reflux and chronic suppurative otitis media is being studied. Data were analysed using SPSS version 22.

Results: Prevalence of laryngopharyngeal reflux in patients with chronic suppurative otitis media is 17%, which is lower compare to control group, which is 25.5%. There was statistically proven no significant association between laryngopharyngeal disease and chronic suppurative otitis media (*P*-value = 0.4502). The reflux finding scores was proven no significant association with reflux symptom index in this study (*P*-value = 1).

Conclusion: Laryngopharyngeal reflux has no significant association proven in patients with chronic suppurative otitis media.

Supervisor: Professor Dr Mohd Khairi Md Daud

Co-supervisor: Dr Nik Fariza Husna Nik Hassan

PATTERNS OF ESCHERICHIA COLI AND KLEBSIELLA PNEUMONIAE URINARY TRACT INFECTION IN HOSPITAL USM PAEDIATRIC AGE GROUP: A 10-YEAR RETROSPECTIVE STUDY

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Introduction: Urinary tract infection (UTI) is common in children. Up to 8.4% of girls and 1.7% of boys have an episode of UTI before the age of 6 years old. The causative organisms vary with sex and age of the patients but Escherichia coli (E. coli) and Kleibsella pneumoniae (K. pneumonia) are the commonest. Diagnosis of UTI can be challenging and proper antibiotic usage is important to prevent antibiotic resistance in the future. Empirical antibiotics are started before the culture results becomes known, so knowledge of local resistance patterns of common uropathogens is important.

Objectives: This study aims to look at the local resistance trends towards frequently prescribed antibiotics against the commonest uropathogens encountered to cause urinary tract infection among children in Hospital Universiti Sains Malaysia (HUSM). At the same time, we would like to look at the possible associated risk factors to develop either E. coli or K. pneumoniae UTI and risk factors associated with the development of antibiotic resistance.

Methods: A retrospective record study was conducted from January 2009 till December 2018 involving children between the age of 2 months until 12 years old with positive urine cultures for *E. coli* or *K. pneumoniae* that were identified through an electronic database available in the Medical Microbiology Laboratory HUSM. A total of 182 children were included in the study and analysis were done using IBM SPSS Statistics version 24. The data were presented as descriptive analysis and Fisher's exact test or Pearson's Chi-square for univariate analysis.

Results: *E.* coli is the most frequent infection (72.0%; non-ESBL 91.0% & ESBL 9.0%) as compared to K. pneumoniae (28.0%; non-ESBL 78.0% and ESBL 22.0%). Girls (63.0%) are more prone to get UTI. K. pneumoniae is seen more in boys while *E.* coli is more common in girls (P = 0.001). Older children are more prone to develop UTI (42.9%). Children with neurogenic bladder are associated with higher risk of recurrent UTI. *E.* coli showed high resistance towards ampicillin (73.3%), cotrimoxazole (59.5%), cefepime (50.0%), cephalexin (41.0%) and amoxicillin-clavulanate (34.6%). *K. pneumoniae* showed high resistance towards ampicillin (89.0%), cefepime (80.0%), amoxicillin-clavulanate (48.0%) and cotrimoxazole (47.5%).

Conclusion: both organisms showed significant resistance towards antibiotics such as ampicillin, amoxicillinclavulanate and cotrimoxazole. Meanwhile, nitrofurantoin was shown to be very sensitive towards both organism followed by amikacin, gentamicin and cefuroxime.

Supervisor:

Professor Dr Hans Amin Van Rostenberghe

Co-supervisors: Professor Dr Zeehaida Mohamed Dr Mohamad Ikram Ilias

PROPORTION OF DIABETES MELLITUS AND FACTORS ASSOCIATED WITH POOR GLYCAEMIC CONTROL AMONG PAEDIATRIC PATIENTS IN HOSPITAL USM

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Introduction: Diabetes mellitus is a chronic disorder of childhood characterised by insulin deficiency or resistant resulting in chronic hyperglycaemia. The commonest types are Type 1 (T1DM) and Type 2 (T2DM). Incidence and proportion of both type are rapidly increasing every year. Chronic hyperglycaemia state is associated with long-term complications such as retinopathy, nephropathy, neuropathy and cardiovascular morbidity. The diabetes control and complications trial (DCCT) demonstrated that strict blood glucose control (HbA1c < 7.5%) was associated with 30% to 70% reduced risk of long term complications. There are various socio-demographic and factors associated with glycaemic control includes family history of diabetes, house whole income, parental supervision, duration of diabetes and body mass index.

Objectives: To study on proportion of diabetes mellitus and factors associated with poor glycemic control among pediatric patients with diabetes in Hospital USM.

Methods: Total of 111 patients were identified from five years retrospective data review from January 2014 until December 2018. The latest HbA1c from clinic follow-up was used as value of reference and traced via hospital online system. The inclusion criteria were all diabetes patients under follow-up at paediatric diabetic clinic, Hospital USM and syndromic or congenital malformation coexisting with diabetes mellitus patient will be excluded. All records retrieved were reviewed using data collection sheet containing patient's information and determinants.

Results: The proportion of Type 1 diabetes mellitus was 64.0% and 26.1% for Type 2. The mean age onset of diabetes was 9.4 years. The mean HbA1c was 10.3%. Univariate analysis showed that poor glycaemic control were associated with older age group, longer duration of diabetes, positive family history of diabetes and absence of parental supervision (P < 0.25). However multivariate analysis showed that duration of diabetes more than 5 years had statistically significant correlation with poor glycaemic control (P < 0.05).

Conclusion: The glycaemic control among young diabetes patients in Kelantan was still poor (HbA1c of 10.3%), but was comparable with other centres in Malaysia (HbA1c of 10.8%). The value was still above targeted level (HbA1c < 7.5%). The only significant association with poor glycaemic control was longer duration of diabetes (OR = 3.065, P < 0.05).

Supervisor: Dr Suhaimi Hussain

Co-supervisor: Dr Najib Majdi Yaacob

ULTRASONOGRAPHY MEAUREMENT OF COMMON CAROTID ARTERY BLOOD FLOW AND DIAMETER AMONG WHOLE BLOOD DONORS AS EARLY CHANGES IN BLOOD LOSS IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KELANTAN

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Introduction: The measurement of inferior vena cava (IVC) using ultrasound had been widely used in detecting early hypovolemic shock in Emergency Department. However, studies have shown IVC has several limitations. Currently, common carotid artery (CCA) ultrasound measurement has become more popular due to simple technique and anatomically friendly approach. Thus, this study aim is to compare the CCA blood flow and diameter with IVC among the whole blood donors at Hospital Universiti Sains Malaysia, Kelantan.

Methods: Cross-sectional study conducted on healthy blood donor presented to the blood bank. Ultrasound of CCA and IVC pre- and post-donation was scanned. Diameter and velocity time index measured before and after blood donation for CCA and diameter of IVC were measured.

Results: A total of 124 whole blood donor participated in this study. Study showed that the mean diameter of CCA increased by 0.10 from pre- to post- (95% CI: -1.76, -0.03) compared to the IVC. Whereas, CCA blood flow (VF) reported no significant changes in pre -and post-donation.

Conclusion: In conclusion, our study showed CCA ultrasound assessment is inconclusive compared to IVC assessment in detecting early simulated Type 1 haemorrhagic shock even though the measurement of CCA is accessible. Further studies are needed to confirm this finding on real patient with different volume blood loss.

Supervisor: Dr Mohd Hashairi Fauzi

A STUDY ON THE PROPORTION OF HIGH RISK OF MALNUTRITION AND ITS ASSOCIATED FACTORS AMONG ELDERLY PATIENTS ATTENDING KLINIK RAWATAN KELUARGA HOSPITAL UNIVERISTI SAINS MALAYSIA

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Introduction: Malnutrition is defined as imbalances and deficiencies of nutrients, characterised by changes in body composition and resulting in diminished function. Whereas at risk of malnutrition was identified via nutrition screening. Elderly at risk of malnutrition is widely known to have various adverse clinical outcomes.

Objective: The aim of our study was to determine the proportion of elderly at high risk of malnutrition and its associated factors in Klinik Rawatan Keluarga, Hospital Universiti Sains Malaysia (HUSM).

Methods: A cross-sectional study was conducted at Klinik Rawatan Keluarga, HUSM in 2017. Elderly aged 60 years and above were included and the exclusion criteria were elderly with known case of depression, dementia or inability to stand or having hand problem that limits the ability of holding dynamometer. Malnutrition risk screening tool-hospital (MRST-H), the modified Barthel index (MBI) and elderly cognitive assessment questionnaire (ECAQ) were used in this study. The data was analysed using descriptive statistic and multiple logistic regression.

Results: A total of 200 elderly participated in the study and the proportion of high risk of malnutrition was 27 (13.5%). Poor handgrip strength (OR = 3.56, 95% CI: 1.41, 8.98; P = 0.007) and living arrangement (OR = 4.6, 95% CI: 1.31, 16.1; P = 0.017) were found significantly associated with high risk of malnutrition in elderly.

Conclusion: The proportion of high risk of malnutrition among elderly was low, 13.5%. Poor handgrip strength and living arrangement are significant factors leading to high risk of malnutrition among elderly.

Supervisor: Dr Nani Draman

Co-supervisor: Dr Nur Suhaila Idris

SEXUALITY AND SEXUAL DYSFUNCTION AMONG WOMEN WITH BREAST CANCER: A QUALITATIVE STUDY AMONG HEALTHCARE PROVIDERS IN KELANTAN, MALAYSIA

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Introduction: In Malaysia, female sexual dysfunction (FSD) has been recognised as prevalent among breast cancer patients. It has been shown to cause negative impact on patients' emotion, the relationship with their spouses, which may leads to poor quality of life. However, little is known about the difficulties healthcare providers (HCPs) undergo when dealing with such patients.

Objective: To explore HCPs' experiences in managing FSD among women with breast cancer.

Methods: This qualitative study was conducted using face-to-face interview method on 15 healthcare providers from two tertiary hospitals in north-eastern state in Malaysia who involved in breast cancer management for at least 1 year. The interviews were recorded, transcribed verbatim and transferred to NVivo® for management of data. The transcriptions were analysed using thematic analysis.

We found overlapping themes with regards to HCPs' barriers in managing women with breast cancer with FSD.

Results: Three key barriers were identified: Scarcity of knowledge, sex and sociocultural influence and specialty-centric. Most of HCPs had very narrow meaning of sexuality, unfamiliar with FSD definition, and felt that their training on sexual health issues were very limited. Talking about sex was seen to embarrass both parties and not their priority. Their focused more on the breast cancer treatment, because it was more important for the patients in which it further limited their time to sit with patients discussing about sexual health and FSD.

The misconception about their role in managing sexual health issues and FSD among breast cancer patients occurs due to lack of knowledge and influence of the socioculture on their attitude, if left without appropriate training, the patients will be kept undiagnosed and untreated. The strength of this study includes phenomenological framework used to understand HCPs' working experiences and the variety of HCP' were interviewed. The limitations are only Malay, female, married HCPs were involved.

Conclusions: Our findings suggest lack of knowledge, low priority to sexual health and socio-cultural issues influence the conversation and discussion about sexual health hence most of healthcare providers had no experience in dealing with sexual disorders in breast cancer women. Due to the high prevalence of FSD and its negative consequences to breast cancer patients, the knowledge, training of FSD and ways for effective communication are essential for health care provider managing breast cancer women.

Supervisor: Dr Maryam Zulkifli

Co-supervisors: Professor Madya Dr Rosediani Muhamad, Dr Norhasmah binti Mohd Zain

OUTCOMES OF ASSISTED PERITONEAL DIALYSIS: A MULTICENTRE EXPERIENCE

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Introduction: Peritoneal dialysis (PD) is one of the options for renal replacement therapy in-patient with end stage renal disease (ESRD) apart from haemodialysis and renal transplant. Patients who are physically independent are capable of self-care PD while those with multiple comorbidities; peritoneal dialysis could be still performed with the aid of a trained assistant.

Objectives: The aim of this study is to compare the outcomes of patient's survival, peritonitis free survival and catheter outcomes between assisted PD and self-care PD and to model the prognostic factor for patient's survival among PD patients.

Methods: PD patients in Hospital Universiti Sains Malaysia, Hospital Raja Perempuan Zainab II and Hospital Tengku Ampuan Afzan were involved in this study. Patients were divided into assisted PD group and self-care PD group and the outcomes were observed among these groups.

Results: Peritonitis free survival in assisted PD versus self-care PD was 80%, 56% and 53% versus 90%, 67% and 65% at 12, 36 and 60 months, respectively (P = 0.1). Catheter survival in assisted PD versus self-care PD was 96%, 77% and 65% versus 98%, 83% and 79% at 12, 36 and 60 months, respectively (P = 0.1) and patient's survival in assisted PD versus self-care PD was 85%, 46% and 32% versus 94%, 79% and 48% at 12, 36 and 60 months, respectively (P = < 0.001). Multiple Cox proportional hazards regression model showed that assistance in peritoneal dialysis, male

gender and diabetes comorbidity were the significant variables in prognosticating death among PD patients.

Conclusion: Overall outcomes of peritonitis free survival and catheter survival were similar between patients on assisted PD and self-care PD. Assistance in peritoneal dialysis, male gender and diabetes comorbidity were risk factors for death among PD patients. Patients who need assistance may still receive PD treatment safely.

Supervisor:

Associate Professor Dr Wan Mohd Izani Wan Mohamed

Co-supervisors:

Associate Professor Dr Kamarul Imran bin Musa, Dr Fariz Safhan Mohamad Nor

INCIDENCE OF UPPER GASTROINTESTINAL BLEEDING AND ASSOCIATED FACTORS AMONG PATIENT WITH GOUT ON NONSTEROIDAL ANTI-INFLAMMATORY DRUG

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Introduction: Gout is a disease of global burden in which defective metabolism of uric acid causes arthritis. Gouty arthritis may lead to uric acid – associated complications such as renal stone, upper gastrointestinal bleeding (UGIB) and renal impairment. Gout may occur in patients with other comorbidities such as heart disease, hypertension and diabetes.

Objectives: Our goal was to determine the incidence of UGIB and its associated factors among patients with gout who were on regular nonsteroidal anti-inflammatory drugs (NSAIDs).

Methods: In this cross sectional study with retrospective record review, 403 established gouty arthritis patients from Hospital Raja Perempuan Zainab II (HRPZ II) were recruited from 1 Jan 2018 to 31 Dec 2018.

Results: Of the 403 gouty arthritis patients included in this study, mean age was 55.7 years old and majority (n = 359/403; 89.1%) was male. The incidence of UGIB among gouty arthritis patients who were on NSAIDs was 7.2 % (n = 29/403). There were significant association in older age (P < 0.001), smoking (P = 0.030), end-stage renal failure (ESRF) (4/29; P = 0.017) and diclofenac (P = 0.002) with UGIB among patients with gouty arthritis. Age (P = 0.001), ESRF (P = 0.012) and diclofenac (P < 0.001)were significantly associated with UGIB in multivariate analysis. There were significant association in age, ESRF and diclofenac with UGIB among patient with gouty arthritis.

Conclusion: Age, end-stage renal failure and diclofenac were significantly associated with upper gastrointestinal bleeding among patients with gouty arthritis indicating that patients with these factors were in higher risks to develope upper gastrointestinal bleeding (UGIB). Hence, it is important to monitor these high risks groups of gouty arthritis patients and aggressively address their disease as to avoid risks of UGIB.

Supervisor: Dr Wan Syamimie Wan Ghazali

Co-supervisor: Dr Najib Majdi

MANAGEMENT AND OUTCOMES OF LARGE MIDDLE CEREBRAL ARTERY INFARCT AMONG ISCHAEMIC STROKE PATIENTS TREATED IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Large middle cerebral artery (MCA) infarct is closely related to a significant morbidity and mortality. Effective and safe treatment methods are established to ensure adequate restoration of perfusion at the blocked vessels and therefore a good functional clinical outcome. However, not all centers are well-equipped with such treatment.

Objective: To look at the survival and functional outcome of ischemic stroke patients with large MCA infarct treated in Hospital Universiti Sains Malaysia (HUSM).

Methods: All patients with large MCA infarct admitted to HUSM from January 2014 until December 2018 were recruited. The demographic and clinical data from the patients' files were recorded and the survival outcome was analysed using the Kaplan Mayer survival analysis.

Results: A total of 160 patients were analysed. Most patients were treated conservatively with (35%, n = 57) or without anti-edema, 0.05% (n = 8) of patients were given medical thrombolysis, and 11% (n = 18) underwent decompressed craniotomy. The survival probability within the first week is 0.588 (0.51, 0.66) and the survival probability of a good functional outcome at three months is 0.188 (0.136, 0.259). Two prognostic factors affecting survival outcome identified using the multiple Cox proportional hazard were treatment with decompressive craniotomy and the presence of cardiac event during admission (P < 0.001).

Conclusion: The survival probability of patients presented with large MCA infarct in HUSM, measured by functional neurological outcome, without reperfusion therapy is low. More than 50% of patients died within the first 30 days of stroke onset. Risk factor contributing to poor survival probability is the presence of cardiac event during hospital admission. The prognostic factor protective against poor survival probability is decompression craniotomy.

Supervisor: Dr Sanihah Abd Halim

COMPARISON OF GFR DECLINE BETWEEN CHRONIC KIDNEY DISEASE PATIENTS WITH AND WITHOUT TYPE 2 DIABETES MELLITUS: A RETROSPECTIVE COHORT STUDY AMONG CKD STAGE 5 PATIENTS

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Background: Decline in glomerular filtration rate (GFR) can imply or lead to chronic kidney disease (CKD), a worldwide public health problem, with increasing prevalence, poor outcomes, and high treatment costs. However, the rate of GFR decline is described differently with wide variations in previous studies.

Objective: To compare the rate of GFR decline among CKD stage 5 patients 2 years before diagnosis, with or without diabetes mellitus (DM) and to identify the factors affecting the rate of GFR decline among CKD patients in Kelantan, Malaysia.

Methods: This retrospective cohort study was conducted in 2019 involving patients who had been diagnosed with CKD stage 5 in Hospital Raja Perempuan Zainab II and Hospital Universiti Sains Malaysia, Kelantan. Two groups of CKD patients were identified: i) CKD without DM and ii) CKD with DM. Medical records were retrospectively reviewed and the mean rate of GFR decline two years before the diagnosis of CKD stage 5 was calculated. Univariable and multivariable analysis by linear regression was conducted to identify factors associated with the rate of GFR decline for both groups.

Results: A total of 196 subjects were included, of which 138 (70.4%) participants were in DM group and the other 58 (29.6%) in non-DM group. The rate of GFR decline (mL/min/1.73 m2 per year) was significantly higher in diabetic patients (median = 9.00, IQR = 8.50) compared to non-diabetic patients (median = 6.00, IQR = 4.10) prior to CKD stage 5 (P < 0.001). For both groups, older age was found to be significantly associated with slower GFR decline (adjusted

 β = -0.19; 95% CI: -0.33, -0.04; *P* = 0.011 in DM group and adjusted β = -0.13; 95% CI: -0.22, -0.04, *P* = 0.006 in non-DM group). In DM group, significant proteinuria (3+) worsened rate of GFR decline (adjusted β = 6.64; 95% CI: 0.49, 12.78; *P* = 0.035) while in non-DM group, higher systolic blood pressure caused progressive GFR decline (adjusted β = 0.06; 95% CI: -0.01, -0.11; *P* = 0.023).

Conclusion: Rate of GFR decline in CKD patients with DM was higher than non-DM. GFR decline was higher in patients with diabetic nephropathy with overt proteinuria and in non-DM patients with uncontrolled hypertension. For both groups, older age was associated with a slower rate of GFR decline.

Supervisor: Dr Wan Mohd Izani Wan Mohamed

Co-supervisors: Dr Wan Hasnol Halimi, Dr Najib Majdi Yaacob

BODY COMPOSITION IN PATIENTS IN PATIENTS WITH THYROID DISEASE USING BIOELECTRICAL IMPEDANCE ANALYSIS

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Introduction: Thyroid hormone is an important hormone for body metabolism. Diseases affecting thyroid gland can cause either hyperthyroid or hypothyroid state. Both of these conditions can alter body metabolism and causing changes in body composition. This study will compare body composition in three different thyroid state, which were hyperthyroid, hypothyroid and euthyroid.

Objectives: The aim of this study were to study body composition (body fat, body water and lean weight) in patients with underlying thyroid disease in three differrent thyroid status (hyperthyroid, hypothyroid and euthyroid) using bioelectrical impedance analysis.

Methods: This was a cross sectional study involving 47 patients who have been diagnosed with thyroid disease such as Grave's disease, multinodular goitre (MNG), thyroiditis and congenital hypothyroid, age between 21–45 years old. Patients were divided into three groups which were hyperthyroid, hypothyroid and euthyroid group based on thyroid function test result. Body composition (body fat, body water and lean weight) was measured for each patients using Bioelectrical Impedance Analysis machine (Bodystat@Quadscan). Data was analysed to compare body composition in all three groups.

Results: A total number of 47 patients who had thyroid disease were analysed. Majority of the patients were female (85.1%) with mean age of $32.85 (\pm 7.43)$ years old. Eighteen (38.3%) patients were in hyperthyroid group, 11 (23.4%) patients were in hypothyroid groups and 18 (38.3%) patients

were in euthyroid groups. Body composition were measured and analysed between three groups. Total body fat was higher in hypothyroid group as compare to hyperthyroid group [F (2, 44) = 3.279, P = 0.047]. Total body water (TBW) was also higher in hypothyroid group compare to hyperthyroid group with statistically significant difference, P = 0.05. Lean weight was also higher in hypothyroid group compare to hyperthroid group with statistically significant difference, P = 0.03.

Conclusion: Thyroid hormone dysfunction cause significant changes in body composition in which hypothyroid state as compare to hyperthyroid patient cause higher total body fat, body water and lean weight.

Supervisor:

Professor Madya Dr Wan Mohd Izani Wan Mohamed

A RETROSPECTIVE STUDY ON THE SECONDARY ARTERIOVENOUS FISTULA FAILURE IN CHRONIC HEMODIALYSIS PATIENTS AND ITS PROGNOSTIC FACTORS

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Introduction: Morbidity and mortality related to vascular access failure in chronic hemodialysis patients has become the global burden since it was first introduced in 1966. The proportion for native arteriovenous fistula failure is between 20% and 50%. Functional arteriovenous fistula is a lifeline for those requiring long-term hemodialysis. A dysfunctional arteriovenous fistula leads to a devastating consequence to the patients and nephrologists with a substantial impact on health economic. Secondary arteriovenous fistula failure is not as common as primary fistula failure; therefore, the prognostic factors are not well understood.

Objectives: The aim of this study was to determine the patency of arteriovenous fistula after achieved hemodialysis suitability over 2 years of period and to determine the prognostic factors associated with secondary arteriovenous fistula failure among chronic hemodialysis patients in Hospital Universiti Sains Malaysia.

Methods: This was a retrospective study involved all patients age 18 years old and above who underwent AVF creation from January 2015 until December 2016. Those patients included in this study were already using AVF for at least 1 month. Data were obtained from medical record.

Results: A total of 151 patients were analysed. The proportion of patients with secondary AVF failure was 23.8%. Only brachiobasilic type of fistula was significantly associated with secondary AVF failure (HR: 4.49, 95% CI: 1.99 to 10.15, P < 0.001). Diabetes, age 65 years old and above, female sex, antiplatelet, statin and ACE-I/ARB were not significant prognostic factors.

Conclusion: Our secondary AVF failure was low in comparison to international centres. The decision to determine the optimal vascular access for long term haemodialysis should be made by looking through all aspects and tailored according to individual needs.

Supervisor:

Associate Professor Dr Wan Mohd Izani Wan Mohamed

Co-supervisor: Associate Professor Dr Azreen Syazril Adnan

CHARACTERISTICS AND OUTCOMES OF FIRST-EVER ACUTE STROKE AMONG YOUNGER ADULT IN TERENGGANU FROM 2010 TILL 2017: DATA FROM THE NATIONAL STROKE REGISTRY

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Introduction: Age has been associated with the incidence of stroke. Stroke is a major cause of disability and with more peoples are surviving from stroke nowadays it will have an immense economic effect. Recent studies have shown increasing incidence rates of ischemic stroke in young people while overall incidence has been declining. Worldwide, the number of individuals having strokes aged 20 to 64 years old has increased by 25% from 1980 to 2010. There are limited data regarding the incidence and prevalence of stroke, especially in working-age adult in Malaysia. More and more peoples are surviving stroke nowadays with disabilities, and this condition has a profound effect on patients and relatives and is associated with a vast economic burden. Those young adult who survived stroke event had a higher risk of recurrent stroke, and other consequences such as epilepsy and cognitive problems compare to the stroke-free people. The objective of this study is to describe the etiology, risk factor characteristic, and factor associated with poor outcome (mRS \geq 3) upon discharge among younger adult in Terengganu.

Methods: This is a retrospective cohort study. From National Stroke Registry (NSR) we include patients with first-ever stroke age from 18 to 60 years old from January 2010 until December 2017. Data were assessed using simple logistic regression to look for association with poor outcome upon discharge (mRS \geq 3). Any factor associated with P-value \leq 0.25 from simple logistic regression were included in the multiple logistic regression analysis, and P-value \leq 0.05 were considered to be significant.

Results: There were 2241 subjects with first-ever stroke age 18 to 60 years old from January 2010 until December 2017. The mean age (\pm SD) and the median age for these subjects were 50.78 (\pm 7.56) years old for mean and 52.44 years old for the median. The most common modifiable risk factor is hypertension, with 1520 (67.8%) subjects, followed by diabetes mellitus with 928 (41.4%) subject. For etiology 1736 (77.5%) subjects were an ischaemic stroke and 505 (22.5%) was haemorrhagic stroke. Atrial fibrillation was independently associated with the poor outcome (mRS \ge 3) with OR 2.178 (CI: 1.137, 4.172; P = 0.019). For dyslipidemia, there is a negative correlation for dyslipidemia history and poor outcome with odd ratio of 0.749 (CI: 0.619, 0.906; P = 0.003).

Conclusion: Atrial fibrillation was significantly associated with poor outcome in acute stroke among younger adult, and those with dyslipidemia history have a better stroke outcome. Optimal management of risk factor in a young adult is recommended to reduce the risk of stroke and to prevent significant morbidity and mortality in this group of patients.

Supervisor: Dr Abu Dzarr Abdullah

Co-supervisors: Dr Khairul Azmi Ibrahim, Dr Zariah Abdul Aziz

TREATMENT OUTCOMES OF PATIENTS WITH ACINETOBACTER INFECTION; COMPARISON BETWEEN POLYMYXIN VERSUS NON-POLYMYXIN BASED THERAPY

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Introduction: The growing resistance of Acinetobacter to almost all commercially available antibiotics is of major concern. Limited therapeutic options are currently available.

Objectives: The aim of the study was to compare the efficacy of sulbactam regime to that of polymyxin B in the treatment Acinetobacter infection.

Methods: This was a retrospective study of case records over one year period (1 January 2018 to 31 December 2018) at the Hospital Universiti Sains Malaysia. Patients of least 18 years old, with clinical and microbiological evidence of Acinetobacter infection, were enrolled in the study.

Results: Thirty-four patients received polymyxin and 38 received either ampicillin-sulbactam or cefoperazonesulbactam. Twenty-four (63.2%) from the non-polymyxin group achieved clinical success while 13 (38.2%) achieved clinical success in the polymyxin group. Twenty-six patients (68.4%) treated with non-polymyxin achieved microbiological success compared to 18 (52.9%) treated with polymyxin. Mortality was lower in the nonpolymyxin group with 17 deaths (44.7%) compared to 23 deaths (67.6%) in the polymyxin group. Multiple logistic regression showed that microbiological failure was significantly associated with 30 days in-patient mortality.

Abstracts Abstracts of theses approved for the PhD/MMed/MSc of School of Medical Sciences

Conclusion: The most important finding of our study is that sulbactam appears to have a better efficacy compared to polymyxin in treating Acinetobacter infection.

Supervisor: Dr Alwi Muhd Besari @ Hashim

Co-supervisors: Associate Professor Dr Zakuan Zainy Deris Associate Professor Dr Siti Suraiya Md Noor

TWENTY YEARS REVIEW ON COMPLICATED MICROVASCULAR FREE FLAPS IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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Introduction: Microvascular free flaps allow selection of the most appropriate tissue for the purpose of reconstruction, thus high quality reconstruction whilst minimising donor morbidity. It is a reliable method with high overall success rates. However, occasional failures still occur and are disastrous.

Methods: This is retrospective study conducted in our center over a period of 20 years, January 1997 to January 2017. Out of 587 microvascular free flaps performed, 75 were complicated and re-explored, out of which only 69 were included in this study. Seven were excluded as there were no proper documentation of information needed. The data were evaluated for all the predictors contributing to a complicated microvascular free flap and statistical analysis was performed using SPSS 23.0.

Results: Our overall microvascular free flaps success rate is 98.8%, where 12.8% was re-explored, with a salvage rate of 66.7%. Of all the 69 re-explored microvascular free flaps, 50 (72.5%) cases were total salvaged (TS), 12 (7.4%) cases had partial necrosis (PN) and 7 (10.1%) was not salvageable (NS). The educated patient had a higher salvage rate than those uneducated (33.3% versus 78.3%). The more intervention in re-exploring a compromised flap leads to a lower salvage rate. From the first to fourth re-exploration, there was a steady decrease in salvage rate, 76% to 20% to 4% to 0%, respectively. The use of vein graft and arterio-venous (AV) loop also causes higher failure rate; vein grafted versus non-vein grafted was 53.9% versus 21.5% and for AV loop versus non-AV loop was 62.5% versus 22.9%. There was no statistical significance in other demographic, pre-operative, intra-operative predictors including occurrence of vascular thrombosis, timing of re-exploration and their salvage rate.

Conclusion: Despite the excellent overall success rate of microvascular free flaps, complicated microvascular free flaps which were re-explored also yielded a good salvage rate. Therefore, this is a good study to highlight that close monitoring and an aggressive (early and low threshold) approach in surgical re-exploration is vital to salvage a compromised flap. Besides that, patient selection also plays an important role. Vein graft and AV loop should be cautiously used.

Supervisor: Associate Professor Dr Wan Azman Wan Sulaiman

Co-supervisor: Dr Arman Zaharil Mat Saad

PREDICTIVE FACTORS INFLUENCING THE RESULTS OF COMPUTED TOMOGRAPHY ANGIOGRAPHY MESENTERIC IN ACUTE NON-VARICEAL GASTROINTESTINAL BLEEDING: A COMPARISON STUDY OF ACTIVE VERSUS NON-ACTIVE CONTRAST EXTRAVASATION IN COMPUTED TOMOGRAPHY ANGIOGRAPHY MESENTERIC

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Introduction: An acute gastrointestinal bleed (GIB) is a common medical emergency that requires urgent intervention because of significant morbidity and mortality. The incidence of GIB in Malaysia is approximately 72 per 100000. Localisation of bleeding source particularly via computed tomography angiography (CTA) mesenteric is important to guide the subsequent therapeutic decision.

Objectives: The aims of this study are to elucidate the influential factors which may affect the outcome of CTA mesenteric. By comparing data regarding hemodynamic pattern, haematological profile and transfusion requirement between patients with active and non-active contrast extravasation, it is hoped that this finding can be used in the future as a general guideline for the evaluation of patient prior to CTA study in acute GIB patient.

Methods: Medical records of 68 patients in Hospital Sultanah Bahiyah (HSB), Alor Setar, Kedah who underwent CTA mesenteric with indication of acute non-variceal GIB based on inclusion and exclusion outlined was retrospectively reviewed. Parameters information regarding haemodynamic status (blood pressure, heart rate, mean arterial pressure, shock index and modified shock index), haematological profile (haemoglobin platelet and coagulation profile) and number of packed cell transfusion in 12 h and 24 h prior to CTA study were extracted and tabularised in group of positive and negative CTA mesenteric study.

Results: Total of 67 patients (male; n = 38) with mean age of 59.04 \pm 15.72 was identified. Active contrast extravasation in CTA mesenteric was detected in 19 patients (28.4%). Statistical result revealed that pre-transfusion haemoglobin level (P = 0.021), post-transfusion haemoglobin level (P = 0.022) and trend of haemoglobin level after transfusion (P = 0.001) were associated with active contrast extravasation of CTA. The likelihood of having active contrast extravasation outcome is found to be increased

by approximately two times for every addition of 1 unit of packed red blood cells transfused within 12 h prior to the CTA. The socio-demographic characteristic, haemodynamic status (BP, HR, MAP, SI and MSI) and other blood parameters (platelet and coagulation profile) showed no correlation with the outcome of CTA.

Conclusion: Haemoglobin level and its trend prior to CTA can be predictive factors for the outcome of the CTA study. The likelihood of active contrast extravasation was also increased with the number of packed red blood cells transfused.

Supervisor: Associate Professor Dr Mohd Shafie Abdullah

Co-supervisor: Dr Nik Fatimah Salwati Nik Malek

