POST CONCUSSION SYNDROME FOLLOWING MILD TRAUMATIC BRAIN INJURY IN EMERGENCY DEPARTMENT HUSM

by

DR. CHUA SWEE HENG @ GOH SWEE HENG

A Dissertation Submitted In Partial Fulfillment Of The Requirements For The Degree Of Master Of Medicine (Emergency Medicine)

UNIVERSITI SAINS MALAYSIA

2016

POST CONCUSSION SYNDROME FOLLOWING MILD TRAUMATIC BRAIN INJURY IN EMERGENCY DEPARTMENT HUSM

by

DR. CHUA SWEE HENG @ GOH SWEE HENG

A Dissertation Submitted In Partial Fulfillment Of The Requirements For The Degree Of Master Of Medicine (Emergency Medicine)

UNIVERSITI SAINS MALAYSIA
May 2016

Supervisor: Dr Shaik Farid Abdull Wahab

POST-CONCUSSION SYNDROME FOLLOWING MILD TRAUMATIC BRAIN INJURY IN EMERGENCY DEPARTMENT HUSM

Dr Chua Swee Heng @ Goh Swee Heng

MMed (Emergency Medicine)

Department of Emergency Medicine,

School of Medical Sciences, Universiti Sains Malaysia

Health Campus, 16150 Kelantan, Malaysia

Introduction: Post-concussion syndrome is a treatable yet debilitating complication that is frequently seen in patients who sustained mild traumatic brain injury. Proper defining, evaluating and managing these patients and its associating factors can alter clinical course and severity of the illness. Various clinical tools were developed to aid proper diagnosis and management of these patients.

Objective: To determine the incidence of post-concussion syndrome and its association risk factors in patients presenting with a mild traumatic brain injury to the Emergency and Trauma Department Hospital USM.

Patients and methods: In this prospective cohort study, we recruited patients with mild traumatic brain injury, who fulfilled the inclusion and exclusion criteria, admitted directly or referral from local clinics to the Emergency and Trauma Department Hospital USM. Baseline interviews were conducted on those eligible consented patients to gather information on demographic data, type of injury and risk factors on the day of injury. Subsequent telephone interviews were carried out within 2 weeks after the initial presentation and post-concussion symptoms were documented using the Rivermead Post-Concussion Symptoms Questionnaires as the measurement tool. Present of three or more symptoms were considered as post-concussion syndrome. Statistical analyses were performed by using a simple and multiple logistic regressions. Adjusted OR and 95% CI were computed, and a p-value of less than 0.05 was set.

Results: A total of 113 patients with mild traumatic brain injury were included in this study, but only 80 patients have completed the study due to various reasons. 16.3% of the patients have three or more post-concussion symptoms at 2 weeks post mild TBI. The most common presenting symptoms were headache (30%), feeling of dizziness (28.7%), fatigue, tiring more easily (8.8%), nausea and/or vomiting (7.5%), and sleep disturbance (7.5%). Among the risk factors examined, previous history of concussion was statistically significant for post-concussion syndrome. Patients with previous history of concussion are 4 times more likely to experience Post-Concussion Syndrome as compared to those without a previous history of concussion.

Conclusions: Our study suggested that the incidences of post-concussion syndrome among patients with mild TBI are high, with previous history of concussion as the predictive risk factors for the patients with mild TBI to develop post-concussion syndrome.

Dr Shaik Farid Abdull Wahab: Supervisor

DEDICATION:

To my late grandfather,

Mr. Chua Geok Tong,

Who inspired me the journey of learning never ends until the day when you meet your creator.

To my Parents,

Mr. Chua Goh Kim & Mdm. Tan Guan Eng,

Their presences have turned every living minute into a spiritual experience of love, grace and gratitude. I am really thankful for them being in my life.

To my wife,

Dr. Ooi Tse Hun,

Her love and patience has helped to unlock the fullness in my life. Her perpetual support has helped to turn chaos to order, confusion to clarity and denial into acceptance. Without her, this dissertation would not have been completed.

And my children,

Goh Chen Ern** and **Goh Chen Xi,

You are the eagle beneath my wings that make me soar.

ACKNOWLEDGEMENTS

I would like to address special thanks to all the individuals for everything that they have done for me throughout the period of my dissertation project. Sincerest appreciation to my supervisor, Dr. Shaik Farid Abdull Wahab (Lecturer and Emergency Physician, Emergency and Trauma Department, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan) for his guidance and supervision. His exemplary knowledge and vast rich experience in the research field of emergency medicine has greatly enlightened me. The kindness and patience that he has shown to me during this whole period has been a pillar of support for me.

I would also like to take this opportunity to convey my deepest gratitude to the following individuals for their support of this dissertation project. Their patience, help and encouragement has helped to my dissertation into a fruitful reality. My sincerest thanks to:

- **Dr. Teo Aik Howe,** Consultant Emergency Physician, Emergency and Trauma Department, Hospital Pulau Pinang, Penang.
- **Dr. Kwanhathai Darin Wong,** Head of Department, Emergency and Trauma Department, Hospital Pulau Pinang, Penang.
- **Dr. Esther Rishma Sundram**, DrPH Student in Public Health, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan.
- **Dr. Wafaak Esa,** DrPH Student in Public Health, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan.

- **Dr. Siti Azrin Ab. Hamid,** Unit of Biostatistics and Research Methodology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan.
- **Professor Dr. Syed Hatim Noor@Nyi Nyi Naing**, Unit of Biostatistics and Research Methodology, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan.
- All lecturers, master students and staffs, Emergency and Trauma Department, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Kelantan.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMNS

AOR	Adjusted Odds Ratio
CI	Confident Interval
CT	Computed tomography
CDC	Center for Diseases Control
DSM	Diagnostic and Statistical Manual of Mental Diseases
GCS	Glasgow Coma Scale
GOS	Glasgow Outcome Scale
HUSM	Hospital Universiti Sains Malaysia
ICD	International Classification of Diseases
LOC	Loss of consciousness
MRI	Magnetic Resonance Imaging
NCAA	National Colligate of Athlete Association
NCD	Neurocognitive disorder
NICE	National Institute of Clinical Excellence
OR	Odds Ratio
PCS	Post-concussion Syndrome
PTS	Post Traumatic Amnesia
RPQ	Rivermead Post-concussion Symptoms Questionnaire
SD	Standard Deviation
TBI	Traumatic Brain Injury
USM	Universiti Sains Malaysia
WHO	World Health Organization

YLD	Years lived with disability

SINDROM GEJALA SELEPAS GEGARAN OTAK DALAM KES KECEDERAAN OTAK RINGAN DI JABATAN KECEMASAN DI HUSM.

ABSTRAK

Pengenalan: Sindrom Gejala selepas gegaran otak merupakan komplikasi yang serius tetapi ianya boleh dirawati, dan sering berlaku kepada pesakit yang mengalami kecederaan otak ringan. Definasi, penilaian dan pengurusan yang betul dalam pesakit ini dan faktor risikonya boleh mengubah halatuju klinikal dan keterukan gejala ini. Pelbagai jenis alat ukuran klinikal telah direka untuk membantu dalam penilaian dan pengurusan pesakit ini.

Tujuan: Untuk menentukan kadar insiden sindrom gejala selepas gegaran otak dan faktor risiko yang mempengaruhi dalam kalangan pesakit yang mengalami kecederaan otak ringan di Jabatan Kecemasan dan Trauma Hospital USM.

Bahan dan kaedah: Dalam kajian prospektif kohort ini, kami mengambil pesakit yang mengalami kecederaan otak ringan serta memenuhi kriteria, sama ada datang secara langsung atau dirujuk dari klinik tempatan ke Jabatan Kecemasan dan Trauma Hospital USM. Temubual asas dilakukan terhadap mereka yang layak dan telah memberi keizinan untuk mendapatkan maklumat tentang data demografi, jenis kecederaan dan faktor risiko pada hari kecederaan. Temubual berikutnya dilakukan melalui telefon dalam masa 2 minggu setelah hari kejadian dan gejala selepas gegaran otak didokumentasi menggunakan “the Rivermead Post-Concussion Symptoms Questionnaire” sebagai bahan ukuran. Kewujudan tiga atau lebih gejala dikenalpasti sebagai sindrom gejala selepas gegaran otak. Analisis statistik dijalankan dengan cara regresi logistik mudah dan pelbagai. Nisbah ganjil yang diselaraskan ‘Adjusted Odd Ratio’ (AOR) dan 95% selang keyakinan dikira dengan nilai-p kurang dari 0.05 yang ditetapkan.

Keputusan: Sejumlah 113 pesakit yang mengalami kecederaan otak ringan terlibat dalam kajian ini, tetapi hanya 80 pesakit yang berjaya menyudahkan kajian atas sebab-sebab tertentu. 16.3% pesakit mangalami tiga atau lebih gejala selepas gegaran otak dalam 2 minggu setelah kecederaan otak ringan. Gejala paling ketara adalah sakit kepala (30%), rasa pening (28.7%), lebih mudah letih (8.8%), loya dan/atau muntah (7.5%) dan gangguan tidur (7.5%). Di antara faktor risiko yang diuji, sejarah gegaran lampau adalah signifikan untuk sindrom gejala selepas gegaran otak. Pesakit yang mengalami sejarah gegaran yang lampau mempunyai 4 kali lebih risiko untuk mendapat sindrom gejala selepas gegaran otak.

Kesimpulan: Kajian kami mencadangkan bahawa kadar insiden sindrom gejala selepas gegaran otak dalam kalangan pesakit yang mengalami kecederaan otak ringan adalah tinggi. Sejarah gegaran lampau merupakan faktor risiko utama kepada pesakit yang mengalami kecederaan otak ringan untuk mendapat sindrom gejala selepas gegaran otak.

Post-Concussion Syndrome following mild traumatic brain injury in Emergency Department HUSM

ABSTRACT

Introduction: Post-concussion syndrome is a treatable yet debilitating complication that is frequently seen in patients who sustained mild traumatic brain injury. Proper defining, evaluating and managing these patients and its associating factors can alter clinical course and severity of the illness. Various clinical tools were developed to aid proper diagnosis and management of these patients.

Purpose: To determine the incidence of post-concussion syndrome and its association risk factors in patients presenting with a mild traumatic brain injury to the Emergency and Trauma Department Hospital USM.

Materials and methods: In this prospective cohort study, we recruited patients with mild traumatic brain injury, who fulfilled the inclusion and exclusion criteria, admitted directly or referral from local clinics to the Emergency and Trauma Department Hospital USM. Baseline interviews were conducted on those eligible consented patients to gather information on demographic data, type of injury and risk factors on the day of injury. Subsequent telephone interviews were carried out within 2 weeks after the initial presentation and post-concussion symptoms were documented using the Rivermead Post-Concussion Symptoms Questionnaires as the measurement tool. Present of three or more symptoms were considered as post-concussion syndrome. Statistical analyses were performed by using a simple and multiple logistic regressions. Adjusted OR and 95% CI were computed, and a p-value of less than 0.05 was set.

Results: A total of 113 patients with mild traumatic brain injury were included in this study, but only 80 patients have completed the study due to various reasons. 16.3% of the patients have three or more post-concussion symptoms at 2 weeks post mild TBI. The most common presenting symptoms were headache (30%), feeling of dizziness (28.7%), fatigue, tiring more easily (8.8%), nausea and/or vomiting (7.5%), and sleep disturbance (7.5%). Among the risk factors examined, previous history of concussion was statistically significant for post-concussion syndrome. Patients with previous history of concussion are 4 times more likely to experience Post-Concussion Syndrome as compared to those without a previous history of concussion.

Conclusions: Our study suggested that the incidences of post-concussion syndrome among patients with mild TBI are high, with previous history of concussion as the predictive risk factors for the patients with mild TBI to develop post-concussion syndrome.

CHAPTER 1

INTRODUCTION

1.1 Introduction.

Injuries are one of the top ten causes of death worldwide. According to World Health Organization report on May 2014, there were 1.3 million deaths due to injuries in 2012 which contributed to 2.2 percent of total deaths in that year (World Health Organization, 2014). Injuries also cause disabilities resulting in a significant burden to communities and their livelihood. It was reported that in the year 2013, a total of 10194.9 thousand years lived with disability (YLDs) were due to transport injuries alone in 188 countries surveyed in Global Burden of Disease Study 2013 (Vos *et al.*, 2013). In Malaysia, the similar patterns of injuries, deaths and disabilities were seen with a total of 166, 768 trauma patients being admitted into eight major hospitals across the country in 2009, in which 85.4 percent had injuries to the head and neck (Jamaluddin *et al.*, 2009).

Although we do not have any longitudinal study regarding the outcome of the patients following traumatic brain injury (TBI) in Malaysia, data from oversea had estimated that 43.3 percent of their patients have residual disability 1 year after injury. In United States, it was estimated that 3.2 million civilian residents living with disability following TBI in 2010 (Corrigan *et al.*, 2010). The study also reported that 3.8 percent of the population in northern Finland had at least 1 hospitalization due to TBI by 35 years of age, and 31.6 percent of the population in Christchurch New Zealand experienced at least 1 hospitalization due to TBI by 25 years of age.

The epidemiology of TBI is difficult to be described accurately. Problems in TBI cases collection, inconsistency in the definition and classification of TBI, differences in diagnostic tools and admission criteria were all contributed to it (Dawodu, 2014). Nevertheless, research in this field of injury also received “less funding than any other cause of human misery” (Roberts, 2001). A recent epidemiological study done in Europe faced the similar problems, in which an overall incidence rate of 262 per 100,000 for admission due to TBI was derived (Peeters *et al.*, 2015). Another study that comparing epidemiological parameters for Europe, United State, Australia, Asia and India revealed that Asia has the highest incidence rate of 344 per 100,000 population, with case fatality rate of 11 per 100 hospitalizations, and unfavorable Glasgow Outcome Scale of 27 percent out of all TBI cases (Tagliaferri *et al.*, 2006).

Common causes of injuries vary according to gender, age, race, and geographical location. Motor vehicle accident was the leading causes of TBI, accounted for approximately 50 percent of all TBIs in United State. This followed by falls, firearms and work-related traumatic brain injury (Dawodu, 2014). The epidemiological patterns were changing, data showed that the median age of individuals who experienced TBI is increasing, and falls have now surpassed motor vehicle accidents as the leading cause of injury (Roozenbeek *et al.*, 2013). However, their study unable to observe any decrease in traumatic brain injury-related mortality or improvement of overall outcome.

Long-term disability and survival in TBI was poorer of the general population, it depends on age, sex, and functional disability (Brooks *et al.*, 2013). They also noted that the survival prognosis for an individual, who suffers traumatic brain injury today, was about the same as it was for a person with comparable disabilities who suffered traumatic brain injury 20 years ago. Survivors of TBI often develop a TBI-related long-term disability, which are dependent on an instrument, social and financially, and are more likely to receive welfare or disability payments. In United State alone, it was estimated that the direct costs of TBI was $9.2 billion per year with additional $51.2 billion lost through missed work and lost productivity. The total medical costs estimated ranging from $48.3 billion to $76.5 billion (Ma *et al.*, 2014).

Most patients who sustained mild TBI may eventually recover. A significant proportion (15-30%) of mild TBI patients is a risk of developing post-concussional symptoms (King, 2003; Ruff and Jamora, 2009; Wood, 2004). It is a constellation of ongoing physical, cognitive, emotional, and sleep symptoms associated with mild TBI (Health and Services, 2015), which may last from several minutes to days, weeks, months or years. These have led to ongoing disability and distress for patients, and higher healthcare cost, in identifying and treating individuals who are at risk of developing long-term sequelae post-mild TBI (Carroll *et al.*, 2004).

There are two main diagnostic systems for post-concussion symptoms- ICD 10 (F07.2) and DSM-IV. The disagreement between two diagnostic systems renders the proper diagnosis, early intervention as well as difficulty in carrying out management (Marshall *et al.*, 2012; Marshall *et al.*, March 2011; McCauley *et al.*, 2008). Moreover, non-mild TBI patients were reported to have symptoms similar to post-concussion symptoms (Bazarian *et al.*, 1999; Iverson, 2006; Iverson and Lange, 2003). Although there is a lack of specificity to post-concussion symptoms, it does appear to have sufficient evidence of its sensitivity as a clinical measurement for this clinical phenomenal, by using various post-concussion symptoms checklists and questionnaires (Alla *et al.*, 2009).

In addition, there is sufficient evidence to recognize the interaction between biological, psychological and social factors in the development of post-concussion syndrome. Potential risk factors such as extreme age (Binder *et al.*, 1997), female gender (Elana Farace and Wayne M. Alves, 2000), post-traumatic amnesia (Collins *et al.*, 2003) and concussion history (Collins *et al.*, 1999) are among the highest predictive factors.

This study is attempted to determine the incidence rate of post-concussion syndrome in patients with TBI, in the hope to provide initial data for further study in this field. We also investigate on the association between predictive factors mentioned with the development of post-concussion syndrome in these patients. With this initial step on the research on post-concussion syndrome in patients with mild TBI, we hope to provide some data on this field, which can help in better early recognition, evaluation and management of patients with post-concussion syndrome, to provide better quality of life.

CHAPTER 2

LITERATURE REVIEW

2.1 Traumatic brain injury

The trauma to the head is a well-recognized cause of brain injury. The term "commotion cerebri" was used since sixteenth century by Berengarious de Capri and Ambroise Pare (Malgaigne, 1840) to describe the effects of injuries to the brain without fracture of the skull (Denny-Brown and Russell, 1941; Frowein and Firsching, 1990). It is a critical public health and socio-economic problem throughout the world. It is also the leading cause of death especially those young adults age below 45 years (Jennett, 1996; Kraus and McArthur, 1996) and lifelong disability is common in those who survive.

TBI is considered a "silent epidemic" because the society is largely unaware of its magnitude owning to its effects often not immediately visible and patients are not very vociferous. Although there has been significant evolution in the field of neurotrauma in the past 50 years especially in our understanding of the mechanism of injury, the progression of secondary brain injury, and improvements in therapy leading to better clinical outcomes. But due to the inconsistency in the definition and classification of the TBI, along with discrepancies in data collection, the epidemiology of TBI is difficult to be described accurately.

Confusion exists regarding head injury (HI) and traumatic brain injury (TBI). Head injury is a nonspecific entity, which describes clinically evident external injuries to the face, scalp, and calvarium, such as lacerations, contusions, abrasions, and fractures, which may or may not be associated with traumatic brain injury. Nevertheless, the terminology of the TBI has also become more comprehensive and at the same time, more complicated due to increasing awareness of the additional mechanisms that may contribute to TBI, and its impact on neurocognitive and neuroaffective deficits, and the previously unrecognized impact of undiagnosed TBI (Menon *et al.*, 2010).

To address this issue, The Demographics and Clinical Assessment Working Group of the International and Interagency Initiative towards Common Data Elements for Research on Traumatic Brain Injury and Psychological Health announced a position statement in 2010 (*NINDS Common Data Elements. 2010*):

TBI is defined *as an alteration in brain function, or other evidence of brain pathology, caused by an external force*. The definition further explanted as,

[A] Alteration in brain function is defined as 1 of the following clinical signs:

- *Any period of loss of or a decreased loss of consciousness (LOC)*
- *Any loss of memory for events immediately before (retrograde amnesia) or after the injury (PTA)*
- *Neurologic deficits: weakness, loss of balance, change in vision, dyspraxia paresis/plegia [paralysis], sensory loss, aphasia, etc*
- *Any alteration in mental state at the time of the injury: confusion, disorientation, slowed thinking, etc*

[B] Or other evidence of brain pathology, such evidence may include visual, neuroradiologic, or laboratory confirmation of damage to the brain.

[C] Caused by an external force may include any of the following events:

- *The head being struck by an object*
- *The head striking an object*

- *The brain undergoing an acceleration or deceleration movement without direct external trauma to the head*
- *A foreign body penetrating the brain*
- *Forces generated from events such as a blast or explosion*
- *Or other forces yet to be defined*

However, it remains difficult to accurately correlate the altered mental states at the time of injury with the traumatic brain injury. This is mainly due to the altered mental states which can be caused by pain, posttraumatic shock, medication, alcohol intoxication/abuse, and/or recreational drug use at the time of injury which may be responsible, but should not preclude a diagnosis of TBI. On the other hand, focal motor deficits caused by spinal, plexus or other peripheral nerves injury may present as a focal neurological sign and can be mistakenly attributed to the traumatic brain injury especially in patients with a reduced level of consciousness (Menon et al., 2010).

Clinical manifestations that are related to neuropsychiatric sequelae often present later. There are depression, impulsivity, apathy and others which may only be documented sometime after the insult, or may also be the consequence of non-TBI etiologies. Thus, diagnosis testing is needed for this context (Menon *et al.*, 2010).

Usually, TBI is classified as mild, moderate or severe using the Glasgow Coma Scale (GCS). It is the most widely used system to assess coma and impaired consciousness (Teasdale and Jennett, 1974). Unfortunately, it does not address the pathological and cellular/molecular features of this complex process. Till date, no any single classification of TBI exists that encompasses all these features.

In 2007, a comprehensive classification system was developed in a workshop convened by the National Institute of Neurological Disorders and Stroke, supported by the Brain Injury Association of America, the Defense and Veteran Brain Injury Center, and the National Institute of Disability and Rehabilitation Research. After reviewing the current status of the classification system, the workshop experts have arrived at recommendations for a classification system of TBI to support translational and targeted therapies (Saatman *et al.*, 2008). This classification system encompassed of pathological, clinical and mechanistic classifications.

However, this classification system only addresses the severity during the acute phase of an injury. It is no doubt that multiple acute injury indices are needed to make a diagnosis of the severity of TBI, which include GCS scale, the length of the posttraumatic amnesia, results of neuroimaging and focal signs (Friedland and Hutchinson, 2013). These issues were addressed by the development of The Mayo Classification System for Traumatic Brain Injury Severity (Malec *et al.*, 2007).

Table 2.1 Mayo Classification System for Traumatic Brain Injury Severity

Severity of TBI	**Criteria**
Moderate-severe (Definite)	A. Present of one or more of the following criteria: • Death due to this TBI • Loss of consciousness of 30 minutes or more • PTA of 24 hours or more • Worst GCS score in first 24 hours is <13 providing this is not invalidated by other factors such as intoxication or sedation

	• Evidence of neurological injury, eg hematoma, contusion, hemorrhage
Mild (Probable)	B. If none of the Criteria A apply, present of one or more of following criteria: • Loss of consciousness below 30 minutes • PTA less than 24 hours • Present of depressed, basilar, or linear skull fracture with intact dura
Symptomatic (Possible)	C. If none of the criteria A or B apply, Present of one or more following symptoms: • Blurred vision • Confusion • Feeling dazed • Dizziness • Headache • Nausea

The reason behind classifying TBI severity mainly is to address two important issues. First, the use of GCS scale can aid the acute management of the patient with TBI from a neurosurgical perspective which is an essential part of an assessment, and also one of the criteria to determine the need for CT scan as defined by the NICE guideline

(Fiona Lecky, January 2014; Yates *et al.*, 2007). Secondly, it can avoid misclassification of the patient by the treating clinician with the diagnosis of TBI but does not meet the criteria for such an injury, which can be due to other factors such as intoxication with drug or alcohol at the time of the injury that causes a memory gap which could be mistaken as posttraumatic amnesia (PTA) (Kemp *et al.*, 2010).

2.2 Mild Traumatic Brain Injury

More than 95% of all TBIs are mild in nature, with moderate and severe TBI together accounting for remaining 5% of the cases (Meerhoff *et al.*, 2000). The mortality rate is low, ranging between 0.04 and 0.29% and almost exclusively caused by intracranial bleed (Klauber *et al.*, 1989). It was also noted that intracranial bleed (extradural or subdural) that often requires neurosurgical intervention occurs only in 0.2 to 3.1% of all mild TBI patients, with 6.3 to 21% of them have other intracranial complications noted as computed tomography (CT) abnormalities (Borczuk, 1995; Culotta *et al.*, 1996; Dunham *et al.*, 1996; Haydel *et al.*, 2000; Hsiang *et al.*, 1997; Shackford *et al.*, 1992; Stein and Ross, 1992).

Again, the review of the literature on the topic of mild TBI is confounded by a variety of differing definition. Historically, the term concussion has been used since centuries (Denny-Brown and Russell, 1941) and is still used in clinical practice and also commonly used in the sports medicine literature. With the introduction of the Glasgow Coma Scale (Teasdale and Jennett, 1974), the term of mild TBI has been increasing in use. Till date, there is still ongoing debate over whether mild TBI is synonymous with "concussion" or not (McCrory *et al.*, 2009; McCrory *et al.*, 2013; Ruff and Jamora, 2009). The term mild TBI and concussion still being used interchangeably although the latter is more commonly used in sports medicine, and mild TBI in general medical contexts (Gerberding and Binder, 2003).

Mild TBI can be defined as "*an alteration in brain function or other evidence of brain pathology caused by an external force*" by Common Data Elements working group on demographics and clinical assessments (Menon *et al.*, 2010). The diagnostic criteria for mild TBI are available from the American Congress of Rehabilitation Medicine (Kay, 1993), the WHO Collaborating Centre for Neurotrauma Task Force on Mild Traumatic Brain Injury (Carroll *et al.*, 2004a) and Center for Disease Control and Prevention (Health and Services, 2010) .

Although the mortality rate is negligible, the post-traumatic sequel after mild TBI is appreciable. It is associated with substantial ongoing disability and distress for patients, and higher healthcare costs in identifying and treating individuals who are at risk for developing long-term sequelae post mild TBI (Carroll *et al.*, 2004b). In United State, healthcare cost alone was estimated about $12 billion annually (Health and Services, 2015).

Generally mild TBI results in a constellation of physical, cognitive, emotional and/or sleep-related symptoms which may or may not involve a loss of consciousness (LOC) (Health and Services, 2015). Immediate symptoms of mild TBI include headache, dizziness and nausea as well as physical signs which may include unsteady gait, slurred speech, poor concentration and slowness when answering questions (McCrory *et al.*, 2005). Typically the recovery following mild TBI is rapid, with most acute symptoms resolving within hours, and then symptoms free by around 10 days (McCrea *et al.*, 2003). Although the initial injury is mild, there are significant proportions of about 15-30% of mild TBI patients have a risk of developing ongoing physical, cognitive and emotional symptoms that are associated with this (King, 2003; Ruff and Jamora, 2009; Wood, 2004).

2.3 Post-concussion symptoms and syndrome

Most patients with mild TBI experience a favorable prognosis and outcome (Carroll *et al.*, 2004b). However, a significant proportion of mild TBI patients present with post-concussional symptoms months or years after the injury (Iverson, 2005a; Lundin *et al.*, 2006; Stålnacke *et al.*, 2007). Prevalence rate at three months post-injury is range from 24-84% (Ryan and Warden, 2003).

Post-concussion syndrome or persistent post-concussive symptoms is a constellation of symptoms in physical (e.g. fatigue, headaches), cognitive (e.g. difficulties with concentration and memory) and emotional (e.g. irritability, anxiety) domains that persist for weeks, months and even years after a mild TBI (Ruff *et al.*, 1996). The diagnostic criteria and other clinical determinants of such problem have been studied and debated over a long period of time and still subject to further debate (Iverson, 2005b; Meares *et al.*, 2011; Ruff, 2010; Ruff *et al.*, 1996).

Three inter-related issues were postulated that leading to the poor understanding of the true scale and scope of this problem. First, there is disagreement between diagnostic systems on key criteria; second, lack of specificity of symptoms; and third, a lack of clarity over pathogenesis (Williams *et al.*, 2010). Thus, it remains an area for further exploration not only to reach consensus on definitions but also in order to understand how to manage these patients in the health care system.

There are two main diagnostic systems for PCS – ICD 10 (F07.2) and as Postconcussional Disorder, (PCD) DSM-IV (research). The suggested criteria according to ICD – 10 (World Health Organization, 1992) are based on self-reported symptoms while the DSM-IV (American Psychaitic Association, 1994) for a post concussional condition also requires a demonstrable cognitive impairment by neuropsychological testing and persistent symptoms of at least 3 months (Boake *et al.*, 2004; Boake *et al.*, 2005; Kashluba *et al.*, 2006; McCauley *et al.*, 2008a). This has led to the difficulty in interpretation of such condition as noted by a comparison study of prevalence rates post TBI of PCS according to each criteria, which revealed a striking difference between them - with DSM-IV criteria being met by 11% and 64% by the ICD criteria (McCauley *et al.*, 2008b). This further complicated by the introduction of "neurocognitive disorder" in new DSM-5 (Association, 2013) owing to cognitive and behavioral impairments are more persistent and make a greater contribution to long-term disability in those who had mild TBI suffering post-concussion symptoms (Ganguli *et al.*, 2011).

In addition, in patients with a mild TBI, only about 5% of them have intracranial pathology as demonstrated by CT or MRI (Borg *et al.*, 2004; Stiell *et al.*, 2005) even with the mildest form of the mild TBI. However, the impact of such abnormalities on the long-term outcome has not been demonstrated. It is suggested that these symptoms are caused by a combination of brain injury and psychological, emotional and motivational factors (De Kruijk *et al.*, 2002).

Furthermore, post-concussion symptoms are not specific to PCS. It was reported that a high rate of similar symptoms were not only presented in patients of non-brain injured such as orthopedic patients (Bazarian *et al.*, 1999), they were also noted in those individuals with depression (Iverson and Lange, 2003), pain (Smith-Seemiller *et al.*, 2003) and whiplash (Haldorsen *et al.*, 2003) symptoms. However, it appear to be sensitive as measurement tools across a range of PCS checklists and questionnaires (Alla *et al.*, 2009), with considerably consistent structural of symptoms in cognitive, emotional and physical domains (Potter *et al.*, 2006).

2.4 Post-concussion symptoms measurement

In order to study the self-reported outcome after mild TBI, reliable measuring instruments are needed. There are various post-concussion symptoms scales developed to aid the measurement of post-concussion symptoms. In the attempt to make the diagnosis of post-concussion syndrome, clinicians must make a systematic evaluation to eliminate the possible contribution of many different diagnosis, co-morbidities, and risk factors that may cause or maintain self-reported symptoms long after a mild TBI. Some of the symptoms were found to be present in normal healthy adult (Iverson and Lange, 2003; Lange *et al.*, 2010).

Most widely used and cited post-concussion symptoms scales are the following:

- Post-concussion Syndrome Checklist (PCSC) (Gouvier *et al.*, 1992)
- The Rivermead Postconcussion Symptoms Questionnaire (RPQ)(King *et al.*, 1995)
- Post-Concussion Symptoms Interview(Mittenberg *et al.*, 1997)
- The Postconcussion Syndrome Scale (PCSSS)(J and JA, 2001)
- The British Columbia Postconcussion Symptom Inventory (BC-PSI)(Lovell *et al.*, 2006)
- Post Concussive Symptom-Revised (Naunheim *et al.*, 2008)

The most widely used measurement scales are The Rivermead Postconcussion symptoms Questionnaire, The Postconcussion Syndrome Scale, Post-concussion Syndrome Checklist, and the British Columbia Postconcussion Symptom Inventory. A study was performed to compare these tools and they were found to possess moderate to good reliability, with significant and positive correlation with each other (Sullivan and Garden, 2011).

Post-concussion symptoms interview is most widely utilized in the case of mild TBI in children and showed significant association (Taylor *et al.*, 2010).

2.5 The Rivermead Post-concussion Symptoms Questionnaire (RPQ)

The Rivermead Post Concussion Symptoms Questionnaire (RPQ) (King *et al.*, 1995) is a measurement tool designed to assess the severity of symptoms following mild or moderate traumatic brain injury. It lists 16 symptoms commonly experienced following a mild TBI. Using a 5 point Likert scale, 0 (*no more of a problem*) to 4 (*a severe problem*) to assess the severity of the symptoms that have been of a problem over the previous 24 hours than they were premorbidly. It does not include subscales and did not map onto either ICD- 10 or DSM-IV-TR diagnostic criteria.

Initial studies (King *et al.*, 1995; S Crawford *et al.*, 1996) were to sum all the items scores to yield a total score out of 64 and had been shown to measure post-concussion symptom severity reliably in terms of test-retest and interrater reliability for total and individual symptom scores. This questionnaire takes into account the high prevalence of background symptoms by asking the patients not only if symptoms are present, but also to rate the intensity of each of 16 symptoms as compared to the period preceding the mild TBI. However, it does not address the clinical implication of the total scores.

Subsequent studies (Eyres *et al.*, 2005; Potter *et al.*, 2006) had examined aspects of the structure of symptoms reported by patients after a mild TBI by use of RPQ. In a confirmatory factor analysis using structural equation modeling (SEM), Potter et al (Potter *et al.*, 2006) tested a single factor model that would reflect PCS as a unitary syndrome, in addition to a model of cognitive, somatic and emotional factors, as proposed by Smith-Seemiller et al (Smith-Seemiller *et al.*, 2003). While the one-factor solution was rejected by the factor analysis, there was some support for separable constellations of cognitive, emotional and somatic symptoms.

The other study by Eyres et al (Eyres *et al.*, 2005) examined the construct of the RPQ through Rasch-analysis of data from a sample with prior head injuries of varying severity. This analysis examines how data conform to the model, in contrast to the traditional approach whereby the model is used to explain the data (Linacre, 1998; Tennant and Conaghan, 2007). It is a probabilistic model specifying that a reasonable uniform level of randomness must exist throughout the data (Tennant and Conaghan, 2007). They found a significant deviation from the expectations of the Rasch Model, and that half of the 16 RPQ items displayed disordered thresholds. Removal of the first three items (headache, dizziness and nausea) did show an improvement of an overall fit, with resulting 13-item scale exhibits a unidimensionality as did the three removed items combined, indicating that the RPQ comprises two different constructs.

These two constructs did only partially correspond to the factors identified in the study by Potter et al (Potter *et al.*, 2006) and argued against summation of RPQ scores from items belonging to each of the two constructs. Thus, there is a need for further evaluation with regard to the interpretation of data provided by the RPQ.

2.6 Factors associated with post-concussion syndrome.

There is increasing recognition that post-concussion syndrome were the interaction between biological, psychological and social factors (Lishman, 1988; Macleod, 2010; Wood, 2004). Question regarding whether persistent symptoms are secondary to neurological and/or psychological factors and how premorbidity may influence these factors are yet to be answered (Carroll *et al.*, 2004a; Iverson, 2005b). Studies have been done to find prognostic indicators of the post-concussion symptoms and researches are continuing for this matter.

Increased age has been a well-known factor that strongly associated with poorer outcome in the patients with TBI (Binder, 1997; Hukkelhoven *et al.*, 2003; Jacobs *et al.*, 2010). A study comparing "pediatric population" which was age below 14 years old to normal "adult population" showed a tendency for the pediatric population to have a better outcome than the adult population (Luerssen *et al.*, 1988) gave some insights that increasing age associated with an increased risk of post-concussion symptoms. This was further supported by subsequent studies with consistent findings showing a significant association between the post-concussion symptoms and increased age (Bohnen *et al.*, 1995; Karzmark *et al.*, 1995), especially of age above 40 years old (Ryan and Warden, 2003). The recent systematic review did conclude that older age was a vulnerability factor in developing prolonged post-concussion symptoms (King, 2014).

Despite of evidence showing that the female sex hormone, particularly progesterone did offer some degree of neuroprotection in severe TBI (Niemeier *et al.*, 2013), studies had shown that the female gender were more associated with poorer initial outcome, particularly performed worse on neurocognitive (Colvin *et al.*, 2009a) and neuropsychological testing (Dick, 2009), with a poorer RPQ score (Preiss-Farzanegan *et al.*, 2009) in sport-related concussion.

In the studies looking at the effect of an impact to the head on the development of post-concussion symptoms, the results were rather mixed. Correlation between the mechanism of injury (direct acceleration/deceleration force direct strike on head versus those not direct strikes on head) and the type of injury, towards neuropsychological status and vocational outcome following a mild TBI had been demonstrated (Hanlon *et al.*, 1999), but the relationship between the head impacts biomechanics and acute clinical outcomes after concussions were yet to be established (Guskiewicz *et al.*, 2007).

The role of loss of consciousness (LOC) in predicting the severity of a mild TBI had been questioned (Lovell *et al.*, 1999). Although a study had shown some association to prolonged recovery post-concussion (Asplund *et al.*, 2004), but the presence of amnesia was reported to be more predictive than LOC, in developing post-concussion symptoms and neurocognitive deficits in a mild TBI (Collins *et al.*, 2003). However, it did not appear to be better or more sensitive in predicting the outcome of post-concussion than depth and duration of consciousness. It was the duration of posttraumatic amnesia that reported as the strongest predictor than all of these, as the best indicator of outcome post-TBI (Brown *et al.*, 2005; Cantu, 2001; Nakase-Richardson *et al.*, 2009).

Concussion history was another factor that was studied extensively and well reported to a prolonged recovery. Numerous studies shown not only it causes poor neuropsychological performance (Collins *et al.*, 1999; Colvin *et al.*, 2009b; Covassin *et al.*, 2008), history of multiple concussion and the cumulative effects of recurrent concussions did lead to prolonged recovery, likelihood of future concussive injury and more severe neurocognitive deficits (Guskiewicz *et al.*, 2003; Iverson *et al.*, 2004).

More researches are needed to look at the correlation between a headache and post-concussion symptoms. Debates are still ongoing as whether a pre-injury migraine leading to prolonged symptoms (Lau *et al.*, 2009) or a posttraumatic headache causes more severe symptoms regardless of a premorbid headache (Heyer *et al.*, 2015).

Similarly, further researches are needed to explore the developmental history leading to more severe post-concussion symptoms, although the child's anxiety level (Mittenberg *et al.*, 1997), learning difficulties (Collins *et al.*, 1999; Health and Services, 2015) and hyperactivity (Carroll *et al.*, 2004b) were reported as associated factors, but evidence is rather weak.

It is worth to mention that baseline mental and physical health status did play an important role on the recovery of post-concussion symptoms in mild TBI patients (McLean *et al.*, 2009). Psychiatry conditions such as depression, anxiety and conversion disorders were reported to be associated with prolonged recovery and persistent post-concussion symptoms (Carroll *et al.*, 2004b; Luis *et al.*, 2003; McCauley *et al.*, 2001; Mooney and Speed, 2001; Ponsford *et al.*, 2000). But studies were unable to correlate the premorbid medical conditions with prolonged and persistent post-concussion symptoms (Carroll *et al.*, 2004b; Karzmark *et al.*, 1995; Ponsford *et al.*, 2000; Reuben *et al.*, 2014; Savola and Hillbom, 2003). Thus, more researches are needed to look at this.

2.7 Conceptual Framework

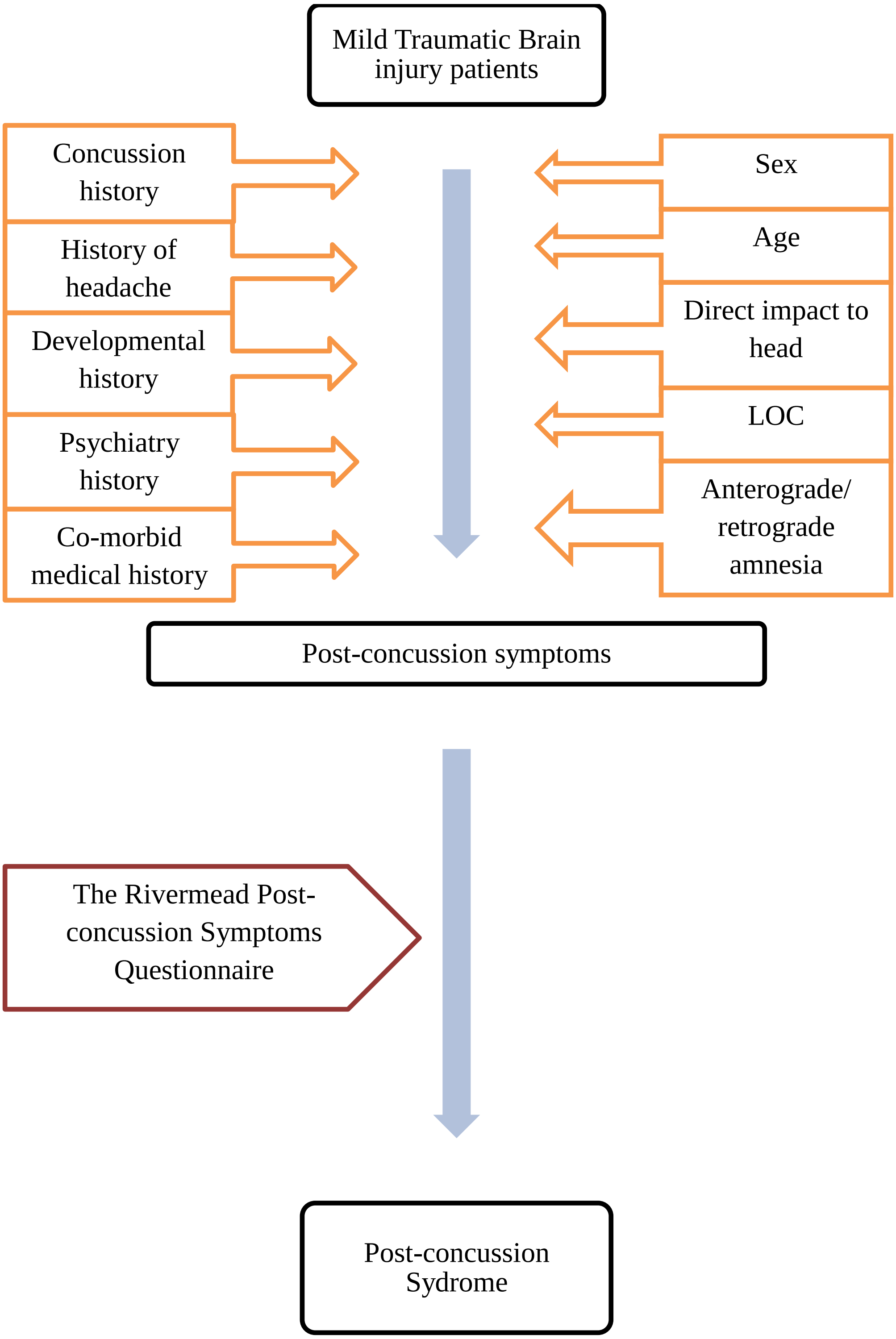

Figure 2.1: Conceptual Framework for Factors associated with Post-concussion Syndrome in Mild Traumatic Brain Injury Patients

2.8 Justification of Study

Not all the patients with mild TBI would have post-concussion symptoms and led to post-concussion syndrome. However, data from other countries have shown a wide difference in term of its prevalence and associated factors. So far, there is no study being done in Malaysia to look at post-concussion syndrome and its associated factors. This study will determine the proportion of patients with mild TBI presented with post-concussion syndrome and its associated factors in Hospital USM. It is essential to acquire at a minimum, the baseline data of post-concussion syndrome among mild traumatic brain injury patients.

Various factors that might predict the post-concussion syndrome derived from literature review were included into this study. Some of the factors may be preventable or modifiable which might help in creating awareness and attention towards prevention of morbidity and mortality secondary to this complication.

Data acquired may be used by clinicians, educators, nurses and other related units, in order to evaluate the post-concussion syndrome in patients sustained a mild traumatic brain injury and associated predictors. This might serve as wake up call to establish proper monitoring and education towards care in patients who suffered from post-concussion syndrome.

CHAPTER 3

OBJECTIVES & HYPOTHESES

3.1 General Objectives

To evaluate the post-concussion syndrome in patient with mild traumatic brain injury presented to Hospital USM within 24 hours of injury with GCS of 13-15 on presentation and brief loss of consciousness.

3.2 Specific Objectives

1. To determine the incidence of post-concussion syndrome in patients presenting with a mild TBI to emergency and trauma department Hospital USM.
2. To identify the risk factors predisposes to post-concussion syndrome in mild TBI patients presented to emergency and trauma department Hospital USM.

3.3. Research Questions

1. What are the incidences of the patients with mild TBI developed post-concussion syndrome?

2. What are the risk factors that predispose the patients with mild TBI to develop post-concussion syndrome?

3.4. Research hypotheses

1. There is a high incidence of post-concussion syndrome among patients with mild TBI presenting to emergency and trauma department HUSM.

2. There are several risk factors which may commonly predispose patients with mild TBI to develop post-concussion syndrome.

CHAPTER 4

RESEARCH METHODOLOGY

4.1 Study Design

Prospective cohort study researching post-concussion syndrome and its associated factors in patients with mild traumatic brain injury that presented to Emergency and Trauma Department Hospital USM.

4.2 Study period

- The research was carried out for 1 year duration started from 1st June 2014 till 31st May 2015.

4.3 Study location

- Emergency and Trauma Department, Hospital Universiti Sains Malaysia

4.4 Population and sampling

4.4.1 Reference population

- All the patients with mild TBI presented to the Emergency and Trauma Department in Kelantan state.

4.4.2 Source population

- All patients with mild TBI admitted directly or referred from local clinic to the Emergency and Trauma Department Hospital USM.