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RESEARCH ARTICLE

Serum Albumin as Independent Predictor In Determining The Outcome Of Traumatic Brain Injury

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ABSTRACT

Context: Serum albumin is the major protein of the human plasma, accounting for about 60% of the total plasma protein. Serum albumin levels tend to decline in the plasma due to injury or infection independent of nutritional status. Serum albumin consumption increases in a state of stress. Reduction in serum albumin occurs with intracranial haemorrhages. In a patient with severe head injury, there is a significant decline in serum albumin leading to hypoalbuminemia. Serum albumin can be used as an outcome marker in various critical illnesses, including traumatic brain injury.

Aim: To determine that serum albumin is an independent predictor affecting the outcome of patients with severe traumatic brain injury over a 6-month duration

Settings and design: This was conducted as prospective cohort study in two neurosurgical centres in the East Coast of Malaysia from June 2020 to June 2021

Subjects and methods: A total of fifty-five patients were admitted to our emergency intensive care, or high dependency unit with varying degrees of severe head injuries. Forty patients fulfilled the inclusion criteria of our study and were recruited for data collection and further analysis. Their serum albumin levels were drawn, analysed, and recorded.

Statistical analysis used: Descriptive, univariate and multivariate analyses using Multiple Logistic Regression model were done using SPSS version 26.0.

Results: Average age for patients in this study was 42 years old. 87.5% of patients involved in this study were male, while the remaining 12.5% were female. The ethnicity of the majority of patients were Malays (77.5%) and the other ethnicities involved were Chinese, Indians and Bangladeshi, with a total of 22.5%. Multiple intracranial injuries were suffered by 57.5% of our study population, Subdural Hemorrhage, Extradural Hemorrhage, Contusional bleed, and Diffuse Axonal Injury were seen respectively in 20%, 10% 7.5% and 5% of the study population. At six months, the unfavourable outcome for serial serum albumin in patients with severe head injury patients was 62.5%, while the favourable outcome was 37.5%. Serum albumin of 30 g/L or less than 30g/L at day 1,3 and 5 post-trauma was noted to have unfavourable outcomes compared to serum albumin level of more than 30g/L.

Conclusion: Serum albumin is an independent predictor of outcome in severe TBI patients. However, larger prospective studies are required to verify these findings.

Keywords: Serum albumin, severe traumatic brain injury, Glasgow Coma Scale, Glasgow Outcome Scale Extended

Introduction

Traumatic brain injury (TBI) is a major problem that causes significant morbidity and mortality amongst the young population[1]. The incidence of TBI ranges from 108 to 332 new cases admitted to hospital per 100 000 population per year[2]. Approximately 39% of individuals with severe TBI die because of the injuries sustained and based on the Glasgow Outcome Scale (GOS), around 60% of severe TBI patients have poor outcomes[3]. According to the World Health Organization (WHO), TBI is the leading cause of death in those under the age of 40 in high-income nations. The risk of TBI patients has increased because of rapid urbanisation, particularly in Asian countries[4]. Based on the studies by the WHO, in two decades, head injury will be the third most frequent cause of death in the world[5]. Neurological examinations, mainly the Glasgow Coma Scale (GCS) and pupillary response are the most used tools for the assessment of severity of brain injury[6]. Neuroimaging examinations such as computed tomography (CT scan) and magnetic resonance imaging (MRI) are the preferred imaging modalities. However, they have drawbacks, namely low sensitivity, and the inability to detect secondary pathogenic events[7]. The Marshall CT Classification for head injury can also be used for the classification and severity of TBI[8]. The patency of the ambient cistern, displacement of midline structures and the presence of local lesions are all essential components of the Marshall CT Scan scale, which is then used to segregate patients into six groups[9,10].

The Rotterdam CT score is another tool for determining the severity of a brain injury[11,12]. Severe TBI initiates a complex cascade of metabolic disturbances with the primary injury triggering secondary events that evolve over many days, leading to deleterious pathophysiological and biochemical reactions[13,14]. A number of brain-specific biochemical markers are available like S-100B, neuron- specific enolase (NSE), glial fibrillary acidic protein, lactate dehydrogenase, myelin basic protein, and creatine kinase-B[15]. Albumin is one of the acute phase reactants which ideally can be used as biomarker for any brain injury as serum albumin tests are easily available and routinely done. Albumin is the major protein of the human plasma accounting to approximately 60% of the total plasma protein [6]. The liver produces on average 9 to 12 g of serum albumin daily. Albumin is the most abundant plasma protein, with normal serum levels between 35 g/L to 50 g/L[16]. Albumin acts as negative acute phase reactant whereby a decrease of 25% concentration is seen in response to inflammation[17].

Many studies have highlighted the role of albumin as a prognostic marker in life threatening illnesses, various types of cancer such as colorectal, lung and breast cancer[18]. Albumin level tend to fall in the plasma because of injury or infection independent of the nutritional status [14]. Serum albumin consumption is increased under a state of stress [16]. Haemorrhages of any kind can cause a decline in the albumin levels. In severe head injury patients, there is a significant loss of serum albumin that leads to hypoalbuminemia[19]. A significant increase of poor outcome states in severe TBI patients is seen as a direct result of hypoalbuminemia[20]. In this study, we conducted research in regard to the relationship between serum albumin levels

and the neurological outcome in severe head injury patients.

Subject and Methods:

ETHICAL APPROVAL AND CONSENT

This research has been approved by the International Islamic University Malaysia (IIUM)

Kulliyyah Research Ethics Committee with reference number: IIUM/504/14/11/12IREC 2020-072. All patients were provided with patient information sheets, and a written consent was obtained before participating in this research study. Confidential protection of all information obtained was protected as per Good Clinical Practice Guidelines Third Edition 2011.

OBJECTIVES OF STUDY

The primary objective of this study is to determine whether serum albumin is an independent predictor in determining the outcome of patient sustained traumatic brain injury. Other objectives include to analyse the demographic details of patients and other factors associated with the outcome of traumatic brain injury.

INCLUSION AND EXCLUSION CRITERIA

The inclusion criteria were as follows: (1) Severe head injury (Admission GCS of 3-8/15), (2) Male and female age >18 years old, (3) Patient with isolated brain injury, (4) Any types of injury that causes severe head injury. The exclusion criteria administered were as follows: (1) non-traumatic brain injury, (2) Patient with underlying Chronic Liver Disease or liver cirrhosis, (3) Major Polytrauma patient Clinical protocol.

SUBJECT

This study was a prospective observational study conducted at two neurosurgical centres over a period of 12 months from June 2020 to June 2021. A total of 55 patients were admitted to our emergency intensive care with varying degrees of severe head injuries. Out of 55 patients, only 40 patients fulfilled the criteria for data collection. The sample size was calculated using Fleiss method with the correction factor. The sample size was 36 patients. Considering the drop rate of 20%, the total sample size was 40.

STUDY PROTOCOL

Patients admitted to the intensive care unit with severe traumatic brain injury were approached within 24 hours of admission for enrolment in the study. Written informed consents were taken from the next of kins/patient relatives. The demographic, biochemical, and clinical data were collected, such as age, gender, race, comorbidities, and types of injury. CT scan images were collected, interpreted, and analyzed using Marshall CT Head Scan Score (Table 1).

Serial serum albumin levels were taken on day 1, day 3 and day 5. These specimens were taken and sent to the biochemistry laboratory for interpretation. The primary outcome was assessed using Glasgow Outcome Score (GOS) (Table 2). We assessed the patient's level of consciousness, functional status, and social interaction in 6 months after the severe traumatic brain injury. The questionnaire was assessed either by phone consultation or follow-up review at the clinic. Based on the GOS score, the patients were divided into Favorable Outcome (Score of 4 and 5) or Unfavorable Outcome (Score of 1 to 3).

Table 1: Marshall CT Head Scan Scoring

	MLS	Cisterns	High or Mixed-density lesion	Note
I	None	Present	None	No visible on CT scan
II	0-5mm	Present	None	
III	0-5mm	Compressed or absent	None	Swelling
IV	>5mm		None	
V	Any	Any	Any	Any lesion surgically evacuated
VI			>25cm^3	Not surgically evacuated

Reference: *Ahmed AJ et al*[21].

Table 2: Glasgow Outcome Score

Scale	Definition	Description
1	Death	Death
2	Persistent Vegetative State	Unable to interact with environment
3	Severe Disability	Unable to live independently. Conscious but disabled.
4	Moderate Disability	Capable of independent living but unable to return to work or school. Disabled but independent
5	Complete Recovery	Able to participate in work or school. Resumption of normal life even though may be minor neurological and psychological deficits.

Reference: *Wilson JT et al.*[22]

STATISTICAL ANALYSIS

The data was expressed as mean and standard deviation (SD). Chi-square test or Fisher's exact test was used to compare the proportions wherever appropriate. Multiple logistic regression analysis was conducted for adjusting well-known variables such as age, sex, and GCS. Two-sided significance tests were used throughout and the significance level was kept at p = 0.05. Statistical analysis was done using the SPSS version 26 software package.

Results:

BASELINE CHARACTERISTIC

The average age for patients in this study was 42 years. 87.5% of patients involved in this study were male while the remaining. 12.5% were female. The majority ,77.5% of the patients were Malays and the remaining 22.5% were Chinese, Indians and Bangladeshis. The average hospital stays, and ICU admission was 16 days and 7 days respectively. 60% of these patients had a GCS

score of 3-5 and 40% were admitted with GCS of 6-8. 67.5% of the patients scored 1-4 on the Marshall CT head score and 32.5% scored 5-6. 70% of the patients did not have any comorbidities while 30% had one or more of the following, Diabetes Mellitus, Hypertension, Hyperlipidemia, and chronic kidney diseases. A Glasgow Outcome Score (GOS) of 1-3 was seen in 62.5% of patients that had unfavourable outcome and 37.5% had favourable outcome with GOSE score of 4 –5 (Table 3).

Table 3: Demographic Profile of Patient with Traumatic Brain Injury

		Mean / Frequency	SD / Percentage
Age		41.95	15.22
Gender	Male	35	87.5
	Female	5	12.5
Ethnicity	Malay	31	77.5
	Others	9	22.5
Length of Stay in Hospital		15.5	7.69
Length of Stay in ICU		7.15	3.34
Glasgow Coma 3 – 5		24	60.0
Score (GCS) 6 – 8		16	40.0
Marshall CT Head	1 – 4	27	67.5
Score	5 – 6	13	32.5
GOSE	1	2	5.0
2		4	10.0
3		19	47.5
4		11	27.5
5		4	10.0
Premorbid	No	28	70.0
Yes		12	30.0
Outcome	Unfavourable	25	62.5
	Favourable	15	37.5

The demographic data that was analysed include site of injury, mechanism of injury and type of surgery. Multiple intracranial injuries (ICI) were seen in 57.5%, 20.0% of patients suffered Subdural Hemorrhage (SDH), 10% had Extradural Hemorrhage (EDH), 7.5% showed Contusional bleeds and the remaining 5% sustained Diffuse Axonal Injury (DAI). 80% of the Severe TBI was caused by Road Traffic Accidents (RTA), 17.5% by Alleged Falls and 2.5% was from Alleged Assaults. 82.5% of the patients required surgical treatment and 17.5% did not require surgery of any form. The types of surgery performed for patients included in this study were craniectomy, craniotomy, extended

burrhole followed by ICP Insertion and Monitoring. 50% of these patients were subjected to a Decompressive Craniectomy, 22.5% Craniotomy, 7.5% required ICP Insertion and Monitoring only while the remaining 2.5% required a Burrhole (Table 4).

Table 4: Distribution of traumatic brain injury according to sites, mechanism of Injury and type of surgery

		Frequency	Percent
Site of Injury	Contusion	3	7.5
	EDH	4	10.0
	Multiple ICI	23	57.5
	SDH	8	20.0
	Diffuse Axonal Injury	2	5.0
Mechanism of Injury	Alleged Assaulted	1	2.5
	Alleged Fall	7	17.5
	Road traffic Accident	32	80.0
Therapy	Non-Surgical	7	17.5
	Surgical	33	82.5
Type of Surgery	No	7	17.5
	Craniectomy	20	50.0
	Craniotomy	9	22.5
	Extended Burrhole	1	2.5
	ICP Insertion and Monitoring	3	7.5

EDH: Extradural Haemorrhage, SDH: Subdural haemorrhage , ICI: Intracranial injury

Referring to Table 5, only the length of stay in ICU and the length of stay in Hospital have significant result in terms of the outcomes (p-value <0.05). Patients that stayed longer in hospital (mean = 17.80 days) and ICU (mean = 7.96 days) have poorer GOSE outcome. Mean age for patients with poor outcome was 44 years and patients with good GOSE outcome was 38 years. Around 55.0% male and 7.5% female patients in this study had poor outcomes, while 32.5% male and 5.0% female patients had good outcome. According to ethnicity, 47.5% of Malays had poor outcomes and 30.0% had good outcomes after 6 months.

Table 5: Population Characteristic According to Neurological Outcome at 6 Months

Demographic		Unfavorable (n=25)		Favorable (n=15)		p-value
		Mean / Total	Std. Dev / Percentage (%)	Mean / Total	Std. Dev / Percentage (%)	
Age		44.52	16.62	37.67	11.87	0.171
Gender	Male	22	55.0	13	32.5	1.000
	Female	3	7.5	2	5.0	
Ethnicity	Malay	19	47.5	12	30.0	1.000
	Others	6	15.0	3	7.5	
Length of Stay in Hospital		17.80	8.06	11.67	5.29	**0.013***
Length of Stay in ICU		7.96	3.52	5.80	2.60	**0.006***
Site Injury	Contusion	0	0.0	3	7.5	
	EDH	3	7.5	1	2.5	
	Multiple ICI	17	42.5	6	15.0	
	SDH	4	10.0	4	10.0	
	Diffuse Axonal Injury	1	2.5	1	2.5	
Mechanism Injury	Alleged Assaulted	1	2.5	0	0	
	Alleged Fall	4	10.0	3	7.5	
	Road traffic Accident	20	50.0	12	30.0	
Therapy	Non-Surgical	2	5.0	5	12.5	0.081
	Surgical	23	57.5	10	25.0	
Type of Surgery	No	2	5.0	5	12.5	
	Craniectomy	16	40.0	4	10.0	
	Craniotomy	3	7.5	6	15.0	
	Burrhole*	1	2.5	0	0	
	ICP Insertion and Monitoring	3	7.5	0	0	
Comorbid	No	14	35.0	12	30.0	0.177
	Yes	11	27.5	3	7.5	
Marshall CT Head Score	1 – 4	14	35.0	13	32.5	
	5 – 6	11	27.5	2	5.0	

*Extended burr hole

In this study, serum albumin level was decreasing in trend from day 1, day 3 and day 5 following traumatic brain injury in both favourable and unfavourable groups. Our study showed that there was difference of serum albumin levels at presentation between the two groups. The highest mean of serum albumin levels at day 1 post trauma was 37g/L in the favourable group as opposed to serum albumin of 30g/L in the group with unfavourable outcome. Serum albumin levels of 30 g/L or less at day 1 post trauma carried a more unfavourable outcome as compared to serum albumin levels of more than 30g/L (Table 6)

Table 6: Comparison between Serial Serum Albumin with GOS Outcome

	Unfavorable				Favorable				p-value
	Mean	SD	95% CI		Mean	SD	95% CI		
			Lower	Upper			Lower	Upper	
Serum albumin day 1	30.80	4.43	34.92	39.34	37.13	3.87	29.09	32.51	P<0.001
Serum albumin day 3	28.60	3.45	32.19	35.41	33.80	2.27	27.36	29.84	P< 0.001
Serum albumin day 5	28.08	3.09	32.13	35.07	33.60	2.26	26.94	29.22	p<0.001

Using simple logistic regression, we discovered that the length of stay in Hospital, GCS, and type of surgery (craniectomy) were significant factors contributing to patient's outcome. A prolonged hospital stay lead to a decrease in the favourable outcome. GCS score of 6-8 was 3.857 times more likely to have a good outcome as compared to GCS score of 3-5. Patients that underwent decompressive craniectomy were 0.1 times more likely to have poorer outcomes as opposed to patients who underwent other types of surgery or patients who did not undergo any surgery. (Table 7)

Table 7: Factors associated with Outcome using Simple Logistic Regression

Variable	b	Wald	OR	95% CI		p-value
				Lower	Upper	
Gender - Female	-0.121	0.015	0.886	0.130	6.022	0.902
Age	-0.032	1.870	0.968	0.924	1.014	0.172
Length of Stay in Hospital	-0.147	5.400	0.863	0.762	0.977	**0.020***
GCS – (6-8)	1.350	3.827	3.857	0.997	14.916	**0.050***
Therapy - Surgical	-1.749	3.627	0.174	0.029	1.052	0.057
Type of Surgery - No		7.853				0.097
Craniectomy	-2.303	5.236	0.100	0.014	0.719	**0.022***
Craniotomy	-0.223	0.041	0.800	0.093	6.848	0.839
Burrhole	-22.119	0.000	0.000	0.000		1.000
ICP Insertion and Monitoring	-22.119	0.000	0.000	0.000		0.999
Comorbidities						
DM - Yes	-0.811	1.114	0.444	0.099	2.004	0.291
Marshall CT Head Score – (5-6)	-0.631	3.597	0.196	0.036	1.056	0.058
Length of Stay in ICU	-0.231	3.670	0.794	0.627	1.005	0.055

Based on multiple logistic regressions, the length of stay in hospital was the leading factor that contributed to the outcome, whereby a shorter length of hospital stay increased the favourable outcome (Table 8).

Table 8: Factors associated with Outcome using Multiple Logistic Regression

Variable	b	Wald	OR	95% CI		p-value
				Lower	Upper	
Age	-0.047	2.763	0.954	0.902	1.008	0.096
Length of Stay in Hospital	-0.191	5.823	0.827	0.708	0.965	**0.016***
Marshall CT Head Score	-1.813	3.273	0.163	0.023	1.163	**0.070**

Discussion:

Serum albumin is easily available, routinely measured and is not costly. Serum albumin is a major protein component, constituting 60% of protein in human plasma. Albumin is produced by the liver at a rate of 9-12g/day. Its hepatic synthesis is primarily affected by osmotic colloid pressure and inflammatory states, however to a lesser extent, by nutritional status and hormones[23,24]. It is one of the biochemical markers of visceral protein status. In addition, serum albumin is also one of the negative Acute Phase Reactants that is reported to decrease as a component of metabolic response to injury or infection, independent of the nutritional status of the patient[1,25]. It was reported that a state of hypoalbuminemia would last for at least 3 weeks following traumatic brain injury (TBI). This was likely to be due to the increase in vascular permeability as propounded by Fleck[26]. Acute post injury elevation of cytokines such as interleukin-1 (IL- 1), Tumour necrosis factor (TNF-á) and interleukin-6 (IL-6), will subsequently lead to endothelial dysfunction, increase in endothelial permeability properties and endothelial leak of albumin resulting in hypoalbuminemia following severe TBI[27]. Other mechanisms that cause hypoalbuminemia in TBI are haemodilution, decrease synthesis of albumin and increase protein catabolism[1,28].

Serum albumin concentration has been reported to be a good indicator of severity of injury as well as a prognosticator in variety of patient populations including patients admitted to the surgical intensive care unit, neurosurgical patients in high dependency unit, patients treated in the medial intensive care unit, critically ill patients and in any patients with a traumatic event. Patients with severe head injury are frequently in hypermetabolic and hypercatabolic state and demonstrate many aspects of acute-phase responses. The serum albumin consumption is increased under a state of stress[27]. Haemorrhages of any kind can lead to a decline in the levels of albumin in the body. In severe TBI, the serum albumin level was significantly lower than healthy individuals[29].

The blood brain barrier (BBB) is composed of vascular endothelium, basal lamina, pericytes and astrocytes foot processes anchored by tight junctions. The BBB prevents fluid,

macromolecules, and small molecules from exiting the microvasculature and entering the brain parenchyma. When the integrity of the BBB is compromised in patients with TBI, infiltration is one of the ways that result in albumin reduction that leads to hypoalbuminemia, eventually resulting in poor outcomes based on GOSE[2].

Our study demonstrated that the average age of patients in this study was 41.9 years. As a comparison to previous studies by Chen D *et al.* [2] and Pandey *et al.*[30], the mean age was 35.4 years and 38 years. In this study, 87.5% of patients were males while 12.5% were females.

This study has a unique set of respondents as Malaysia is a multiracial country consisting of 3 main ethnicities, namely the Malays, Chinese, and Indians and other smaller group of ethnicities from different parts of the country namely the indigenous populations and expatriates. It is acceptable that the majority of subjects recruited were Malays followed by Chinese, Indians or others, because by the race compositions, the Malays make up the majority of the Malaysian population.

Road traffic accidents was the main contributor of severe TBI in our study, accounting to 80% followed by alleged falls 17.7% and alleged assaults 2.5%. With regards to types of brain injury, 57.5 % of patients sustained multiple intracranial haemorrhages, followed by SDH (20%), EDH (10%), contusional haemorrhage (7.5%) and 5% sustained DAI. The percentage of patients sustained multiple intracranial haemorrhage is higher in this study as compared to 28% of patients recruited in a study by Pandey *et al* [30].

Out of 40 subjects, 17.5% (7 subjects) were treated with non-surgical therapy or conservative treatment, whereas 82.5% (33 subjects) were treated with surgical therapy. Decompressive craniectomy was the commonest type of surgery and 50% of the study population was subjected to it. The mean length of hospital stay was 15 days as compared to a study conducted by Chen D *et al.*[2] that reported the mean length of hospital stay of 10 days.

In this study, 40 patients with severe head injury were recruited for further analysis. The unfavourable outcome after 6 months of traumatic brain injury was 62.5% (25 subjects) while the favourable outcome was 37.5% (15 subjects). Out of 15 subjects from the unfavourable outcome group, 2 subjects died at 6 months post TBI. As a comparison, Bernard F *et al.*[31] found that the GOSE score of 70% of their subjects had favourable outcome and 30% had unfavourable outcome at 6 months post TBI and 22 (16%) of them died at 6 months post TBI.

Independent t-test was conducted to determine if any correlation is seen between serial serum albumin levels and GOS outcome. Based on Table 6, there was a significant correlation between outcome and serial serum albumin levels (p-value < 0.05). The mean serum albumin levels in the unfavourable outcome group are lower than the mean serum albumin levels in the group with favourable outcome. The results were consistently significant for all time points, similar with the previous study by Pandey *et al.*[30], due to the fact that the time points used are similar, highlighting importance of monitoring the albumin levels at day 1 to 5 to

allow more targeted management protocols to improve patient outcomes.

Our study showed that there was a difference in the serum albumin levels at presentation between two groups. The highest mean of serum albumin levels on day 1 post trauma was 37g/L in the group with the favourable outcome as opposed with a serum albumin level of 30g/L in the group with unfavourable outcome. Serum albumin levels of 30 g/L or lesser on post trauma day 1 were subject to a more unfavourable outcome compared to serum albumin levels of more than 30g/L on day 1 post trauma. These findings were consistent with studies by Nayak R *et al.* [32] and Dhandapani *et al.*[33]where patients with hypoalbuminemia demonstrated significantly poor neurological outcomes at follow-up. These serial measurements should be taken at standardized time points across all patients to reduce information bias and to allow a more precise estimate of the means, which can then be translated into neurosurgical policy action better.

In the present study, serum albumin levels were decreasing in trend from day 1, day 3 and day 5 following the traumatic brain injury in both the favourable and unfavourable groups. Our findings were similar with other studies by Pandey *et al.*[30] and Benard *et al.*[31] where serum albumin levels were higher in the first few days after head injury and subsequently decreased in trend. To improve on the current findings, further studies need to increase the frequency of albumin monitoring so that the reduction trend will become clearer. Since this is a univariate analysis, the results here might be confounded by other variables. Hence, this justifies the need to look at other risk factors of poor functional outcomes that may help in management of the patients by doing regression analysis. Another important aspect to improve on the current findings are to revisit the cutoff values of serum albumin to predict favourable outcomes through Receiver Operator Characteristics (ROC) curve analysis, looking at diagnostic accuracy parameters such as sensitivity. However, this was not done due to the limitation in sample size to obtain precise estimates.

Other risk factors associated with poor functional outcome:

Apart from the outcome and prevalence, we also investigate the risk factors associated with poor functional outcome in severe TBI patients. Among the studied variables were Glasgow Coma Scale (GCS), premorbid conditions, mechanism of injury, site of injuries, type of surgery, length of hospital stay, and Marshall Score from CT scan findings. In determining the other factors that affect the outcomes of GOS score, a simple logistic regression model was conducted as described in Table 7. Based on the result, it showed that length of stay in Hospital, GCS score and type of surgery were significant factors that contributed to GOS outcome.

Further analysis as depicted in Table 5 showed that the length of stay in ICU and length of stay in hospital have significant results in terms of outcome (p-value <0.05). Patients that endure a longer hospital stay (mean = 17.80 days) and ICU admission (mean = 7.96 days) have a poorer GOS outcome. Increasing duration of hospital stay, increases the unfavourable outcome compared to that of a favourable outcome. The shorter the

length of hospital stay, the better the outcomes in severe traumatic brain injury. The patients that are discharged home early showed better outcomes compared to those having stayed longer in the hospital. Rajendran *et al.* [4] in their study found that longer length of hospital stay leads to an unfavourable outcome with a mean hospital stay of 8 days, and a GCS score ranging from 6 – 8 were 3.857 times more likely to have a good outcome compared to those with a GCS score of 3 – 5($p < 0.05$). It showed that the higher the GCS in severe head injury patients the better the potential for a good outcome 6 months following TBI. It also explains that patients admitted with a low GCS score at initial presentation are prone to have poorer outcomes.

We found that patients who underwent Decompressive Craniectomy (DC) were 0.1 times more likely to have better outcomes compared to patients who underwent other types of surgery or patients who did not undergo any surgery. Aarabi B. *et al.*[31] describes in their study, decompressive craniectomy in patients with severe TBI was associated with a better functional outcome as opposed to other types of surgical therapy.

Upon removal of all confounding factors and analysis based on multiple logistic regression test (Table 8), prolonged hospital stay was a significant contributor to the poorer outcome states whereas a shorter in hospital stay increases the favourable outcome. Thus, apart from serum albumin, the length of hospital stay needs to be part of the outcome assessment. Further studies need to focus on the interaction between serum albumin and prolonged hospital stay, such as what day of admission that corresponds to lower serum albumin that leads to poorer outcome. This needs more time of follow up to better ascertain the interactions. Further improvement in future studies include recruitment of more samples at different sites to increase the generalizability of the findings.

Conclusion:

Serum albumin is as an independent predictor in the determination of poor outcomes in terms of recovery following severe TBI. Our results demonstrate that a low serum albumin level was an independent predictor of outcome in severe TBI, and the percentage of favourable outcome decreases with hypoalbuminemia. It would be better to maintain the level of serum albumin at more than 30 gm/L in traumatic brain injury patients, specifically in severe head injuries. Other factors which may affect the outcome was the duration of hospital stay. However, larger prospective studies are required to confirm these findings.

Conflict of Interest Statement:

I hereby declare that there are no conflicts of interest.

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