Validity of S100B protein as a prognostic tool in isolated severe head injuries in emergency patients

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Introduction
Trauma results in 10% of all deaths or five million died annually. In spite of the progress in monitoring and imaging studies, definite, correct prediction of brain death after brain trauma is not possible until now, and brain injury is the third most common cause of mortality in the world.
Aim
The aim of the study is to identify the validity of S100B protein as a predictor of mortality in isolated severe head trauma patients.
Patients and methods
Th study was a cross-sectional one that was carried out among 44 patients who presented with isolated severe head trauma to the emergency room. All the patients fulfilled our inclusion and exclusion criteria of this study. The initial level of S100B protein was obtained from each patient on admission, 48 h later, and every patient was followed up for 28 days.
Results
This study demonstrates that the mean of S100B dimer levels within the first 2 h was 0.12 mg/l, while after 48 h the mean was elevated to 1.09 mg/l. In addition, the S100B protein to roll in as a prognostic marker in severe head trauma is 76 and 100%, respectively (sensitivity), while the ability of the test to roll out is 75 and 86% (specificity) and the overall accuracy is 76 and 90%.
Conclusion
The results of this study confirm the value of quick prognosis for the S100B protein to inform the relatives about the most expected outcome for the patient as this is the most common question asked to the physician and he his answer should have a scientific basis.

Keywords:
outcome, S100B protein, traumatic head injuries

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Introduction

Trauma is an injury to the body when an uncontrolled force or acute source of energy comes in direct contact with the body and the body cannot tolerate it. In Egypt, trauma accounted for 8% and is considered the eighth leading cause of death in 2010. Injury in Egypt is several times higher due to underreporting and misclassification [1].

Many studies have tried to make definite predictions of brain death after trauma; prediction of brain death is useful in that it will enable us to save body organs if transplantation is considered [2].

Although several scoring systems, for example, Glasgow coma scale (GCS) score, revised trauma score, and injury severity score (TRISS) have developed for the assessment of injuries, they are not useful in the prediction of outcome in traumatic brain injury (TBI) [3].

There are many systems for classifying TBI; systems include classifying TBI by severity, which is generally based on clinical indexes at presentation. TBI may be classified by pathoanatomic, for example, relating to the type of injuries as diffuse axonal injury, hemorrhages, and hematomas. There are new systems for classification of TBI by outcome and prognosis [4].

The classification of TBI by severity was classified as mild, moderate, or severe by using the GCS. which is used to assess impaired consciousness or level of coma. GCS is divided into three components – eye opening, verbal response, and motor responses. These are usually added to produce a total score [5].

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A GCS score of 13–15 is defined as mild, 9–12 as moderate, and 3–8 as severe [5].

Newly developed severity TBI by the Mayo Classification System is aimed to assess the unreliability of severity parameters and the frequency of missed injuries in medical records. This classification has three main items including definite moderate–severe TBI, probable TBI, and possible TBI [6].

The clinical criteria in TBI are used for the diagnosis including the low level of conscious, skull fracture, posttraumatic amnesia, and evidence of neuroradiological abnormalities, for example, cerebral contusion, subdural hematoma, and hemorrhage contusion [7].

The Mayo System classified TBI into definite, moderate, and severe. If one or more of the following criteria apply: death due to TBI, posttraumatic amnesia of 24 h or more, loss of conscious of 30 min or more, and worst GCS less than 13 in first 24 h and this is not by other factors such as intoxication or sedation. In addition, if there is evidence of neurological injury such as contusion, hematoma, and hemorrhage all these criteria of TBI would be in the definite moderate–severe category [7].

There are different scales in the classification of TBI according to the outcome such as neuropsychological functioning, the Glasgow outcome scale, and mood. Also, TBI dimension scales are measured by community participation, challenging behavior, and neuropsychiatric difficulties [8].

To avoid brain death misdiagnoses which is based on the clinical criteria, the role of biomarkers in predicting brain death attracted the researchers' attention [6]. These markers may be used in the monitoring of brain damage, for example, creatinine kinase isoenzyme BB, neuron-specific enolase, 14–3–3 protein, polyamines, and S100B protein [7].

S100B protein is one of the brain-specific biomarkers used in the past decades and are produced by astrocytes in vertebrate brains [9].

S100B protein is highly soluble molecule with calcium-binding proteins in characters, which includes 21 members with cell-specific expression. In the gray matter of the central nervous system, astrocytes are the major cells producing S100B protein and oligodendrocytes in the white matter are the predominant S100B protein-producing cells [10].

S100B protein is produced by other cells such as lymphocytes, adipocytes, bone marrow, chondrocytes, and melanoma cells [11].

Our study aimed to assess the validity of S100B protein as a predictor of mortality in isolated severe head trauma patients. The changes in S100B protein, especially the levels of this dimer 48 h after trauma can be used as a marker to predict brain death and if there is correlation between GCS and the level of S100B protein. In addition, we can use this dimer in cases of contraindications for Computed Tomography (CT) scanning in critical patients until resuscitation tools finished.

Therefore, this study aims to evaluate the short-term prognostic value of S100B protein in isolated severe head injury patients in Suez Canal University Hospitals and it may help in improving the management processes.

Patients and methods

Research design

This is a prospective study on isolated severe head trauma patients attending to the emergency room (ER) of Suez Canal University Hospital on the basis of the following criteria:

Inclusion criteria

(1) All patients.
(2) Both sexes.
(3) Isolated severe head trauma (GCS<8).

Exclusion criteria

(1) Polytrauma patients.
(2) Patients with underlying medical conditions affecting the results of the study.
(3) Patients transferred from other hospitals after performing medical or surgical procedures.
(4) Patients discharged on his demand, transferred to other hospitals. or escaped.

Sample size

The sample size is calculated using the following formula [12]:.

$$n = \left[\frac{Z_{\beta/2} + Z_{\beta}}{\frac{1}{2}\log\frac{1+r}{1-r}}\right]^2 + 3$$

where:

n=sample size.

$Z_{\alpha/2}$=1.96 (the critical value that divides the central 95% of the Z distribution from the 5% in the tail).

r=correlation coefficient (−0.803).

Therefore, by calculation, the sample size is equal to 44 cases.

Study objectives

Aim of the study

The aim of the study is to improve the management process in patients with isolated severe head trauma by predictions of their outcome at the Emergency Department of Suez Canal University Hospital.

Primary objective

(1) Assessment of the sensitivity and specificity of S100B protein as an indicator of mortality in isolated severe head injury patients.

Secondary objectives

(1) To evaluate the short-term prognostic value of S100B protein in isolated severe head injury patients in Suez Canal University Hospitals.
(2) To assess short-term morbidity and mortality in isolated severe head injury patients in Suez Canal University Hospitals.

Study question

What is the role of the use of S100B protein in isolated severe head injury patients?

Data collection

Methods

Patients attended to the Emergency Department of the University Hospital of Suez Canal (Ismailia, Egypt) with isolated severe head trauma were prospectively screened for inclusion in the study. The patients were evaluated for vital signs, clinical history, and physical examination.

Initial sample level of S100B protein was obtained as a single 5 ml blood sample via an intravenous catheter from each patient on admission (first blood sample was taken 2±0.5 h after admission), 48 h later (our emergency protocol allowed for patient stay at the ER for 48 h), and for close follow up of the patients for a time frame of 28 days for major events, for example death, ICU stay, inpatient stay, surgical intervention, and discharge with improving, to determine the level of S100B protein in Emergency Department at Suez Canal University Hospital.

S100B protein normal levels were 0.02–0.15 μg/l and it is considered to be elevated if more than 0.15 μg/l [11].

Data were collected in a preorganized datasheet by the researcher from patients fulfilling the inclusion and exclusion criteria. The patients were clinically assessed and managed according to the ABCDE protocol; after stabilizing the patient, a questionnaire was filled by the researcher of the patient presenting as isolated severe head trauma by the medical team.

The questionnaire contains the following data:

All the injured patients in ER subjected to:

(1) Full history (from patient or relative) including:
    (a) Patient's file number.
    (b) Personal data: age, name, and sex.
    (c) Mechanism and type of injury.
    (d) Associated comorbidities, for example, hypertension, diabetes, infection.
(2) Clinical examination:
    (a) Patient's assessment according to the ABCDE approach.
    (b) Vital signs: pulse, blood pressure, and respiratory rate.
    (c) Patent's mental status (central nervous system assessment using the GCS).
    (d) Presence of fractures, wound.
(3) Laboratory measurements and imaging:
    (1) All laboratory data and imaging were done in the Suez Canal University Laboratory except for measurement of S100B protein, which was not one of the routine laboratory tests and will be afforded by the researcher.
        (1) Complete blood picture and cross-matching.
        (2) Blood samples: an initial blood sample of 5 ml was taken within 2 h after arrival to the ER and another one was taken 48 h after admission.
        (3) Chest radiograph: pelvis–abdominal ultrasound (FAST scan).
        (4) CT scan done for all patients with the inclusion criteria.
(5) Type of management (operative or conservative).
(6) Following up patients after admission to discharge or mortality.

Time frame: a 28-day follow-up for short outcome

After initial level of S100B protein was obtained from each patient on admission (first blood sample taken 2 ±0.5 h after admission), 48 h later, every patient was followed up for 28 days and was classified according to:

(a) The type of management: operative and conservative.

(b) ICU stay time: less than 2 days, more than 2 days.

(c) Outcome after admission: discharge – improved or with deficit; death.

Data management and statistical analysis

(1) Data were collected and coded then entered as spreadsheets using Microsoft Excel for Windows Office 2013 (SPSS Inc., Chicago, IL, USA).
(2) Data analysis using the Statistical Package for the Social Sciences software program (SPSS Inc., Chicago, IL, USA), version 10.0 for analysis
(3) Data were presented as tables and graphs; we used the *t* test to compare between quantitative data expressed as mean and SD.
(4) Receiver operating characteristic (ROC) curves were used to evaluate the cutoff point for both sensitivity and specificity of given S100B dimer values.
(5) χ^2 test was used to compare between the qualitative data expressed as number and percent.
(6) *P* value is considered as significant when the *P* value is less than 0.05.

Ethical considerations

The researcher himself took an informed consent from each patient or from his relatives before taking any data or sample.

The consent contained:

(1) Aim of the research and brief scientific background.
(2) Explanation of the aim in a simple manner to understood by the common people.
(3) No harmful maneuvers has been used (safety precautions considered while taking the sample).
(4) Right of the patient to refuse involving in the research and he had his usual treatment.
(5) All data are confidential and are used in this research only.
(6) Right of the patient or his relatives to withdraw from the study at any time without giving any reason.
(7) An identified person to whom the patient or his relative returned to any time for any explanations.
(8) Right of the patient to have a copy from the informed consent.
(9) All participants announced by the results of the study.

The Ethics committee (reference number 1245/2017) approved this consent.

Budget

The researcher will afford the main budget of the study:

As measurement of S100B protein is not one of the routine laboratory tests, other laboratory investigations and interventions' budget was covered as part of the health service provided in the Emergency Department in Suez Canal University Hospital. The candidate afforded the cost of any extra investigations.

Results

This study was conducted on 44 patients in two sets (one after 2 h and the second was 48 h after trauma) with severe head trauma in the Emergency Department of Suez Canal University Hospital.

Our aim was to assess the validity of S100B protein as a prognostic tool in isolated severe head injury patients at the Suez Canal University Hospital for improving the management process in patients with isolated severe head trauma by predictions of their outcome.

To take a step in the validity of S100B protein as a predictor of mortality in isolated severe head trauma patients, especially to know if we can use the levels of this dimer after the occurrence of trauma as a marker to predict brain death and if there is correlation between GCS and the level of S100B protein.

This study demonstrates that the mean age group of the patients affected by head trauma is 31 years and motor car accidents is the most common cause (47.7%) and the percentage of trauma in rural areas were more than urban (73%) and also shows that men represent about 73% of the studied patients.

Our study showed that the mean GCS among patients with severe head trauma was six, which is associated with tachypnea and tachycardia; and 25% of patients with hypoxia were the most prominent abnormal signs between the patients. In addition, the study showed that the mean of S100B dimer levels within the first 2 h were 0.12 mg/l, while after 48 h the mean was elevated to 1.09 mg/l.

Our study (Table 1) shows that the overall result indicates that the use of operative intervention in patients with head trauma was accompanied with low levels of S100B protein as a rapid intervention,

Table 1 Comparison between serum level of S100B (2 h from trauma) according to the patient way of management (*N*=44)

	Mean±SD	Independent sample *t* test (*P* value)
Operative	0.1100±0.024	*t*=3.518
Conservative	0.13133±0.01569	*P*=0.001*

*Statistically significant difference (*P*? 0.05).

Table 2 Comparison between serum level of S100B (48 h from trauma) according to the patient way of management (*N*=44)

	Mean±SD	Independent sample *t* test (*P* value)
Operative	0.7364±0.8	*t*=2.88
Conservative	1.267±0.89	*P*=0.05 (NS)*

*Statistically significant difference (*P*>0.05).

Table 3 Comparison between serum level of S100B (48 h from trauma) according to fate after a 28-day follow-up (*N*=44)

	Fate after follow up 28 day	*N*	Mean±SD	Independent sample *t* test (*P* value)
48 h S100B	Discharged	20	0.205000 ±0.0848	*t*=15.5
	Mortality	24	1.842500 ±0.4648	*P*=0.00*

*Statistically significant difference (*P*? 0.05).

while the patients who were following conservative protocols had higher levels of S100B protein.

Our study (Table 2) showed that comparing the mean levels of S100B protein after 48 h, we find that the levels became higher when following the conservative treatment, which is a statistically significant difference which means urgent interventions had better outcomes.

As shown in Table 3 the overall result indicates that there is significant difference of S100B protein levels to predict the occurrence of mortality in severe head trauma after a follow-up time frame of 28 days (24 mortality vs. 20 discharged).

Table 4 shows that the ability of the test to clarify the performance characteristics of patients prognostic marker in severe head trauma S100B protein to roll in is 76% (sensitivity), while the ability of the test to roll out is 75% (specificity) and the overall accuracy is 76%. In addition, the ROC curve analysis of the accuracy of 2 h S100B in the prediction of conservative way of management (*N*=44) shows that the area under the curve (AUC) is 0.76 (fair accuracy) with statistically significant *P* value of 0.002 (Graph 1).

Table 5 shows that the ability of the test to clarify the performance characteristics of patient prognostic

Table 4 Analysis of the accuracy of 2 h S100B in the prediction of conservative way of management (*N*=44)

	2 h S100B			
	Positive		Negative	
Positive		20		6
Negative		6		12
Sensitivity	Specificity	PPV	NPV	Accuracy
76%	75%	76%	75%	76%

NPV, negative predictive value; PPV, positive predictive value.

markers in severe head trauma S100B protein to roll in is 100% (sensitivity), while the ability of the test to roll out is 86% (specificity) and the overall accuracy is 90%. In addition, Graph 2 the ROC curve analysis of the accuracy of 48 h S100B in the prediction of conservative way of management (*N*=44) shows that the AUC is 0.94 (excellent accuracy) with statistically significant *P* value of 0.00*.

Table 6 shows that the ability of 48 h S100B titer in thee prediction of length of ICU stay is 58% (sensitivity), while the ability of the test to roll out is 100% (specificity) and the overall accuracy is 80%. In addition, Graph 3 the ROC curve analysis of the accuracy of 2 h S100B in the prediction of length of ICU stay (*N*=44) shows that the AUC is 0.8 (good accuracy) with statistically significant *P* value of 0.000.

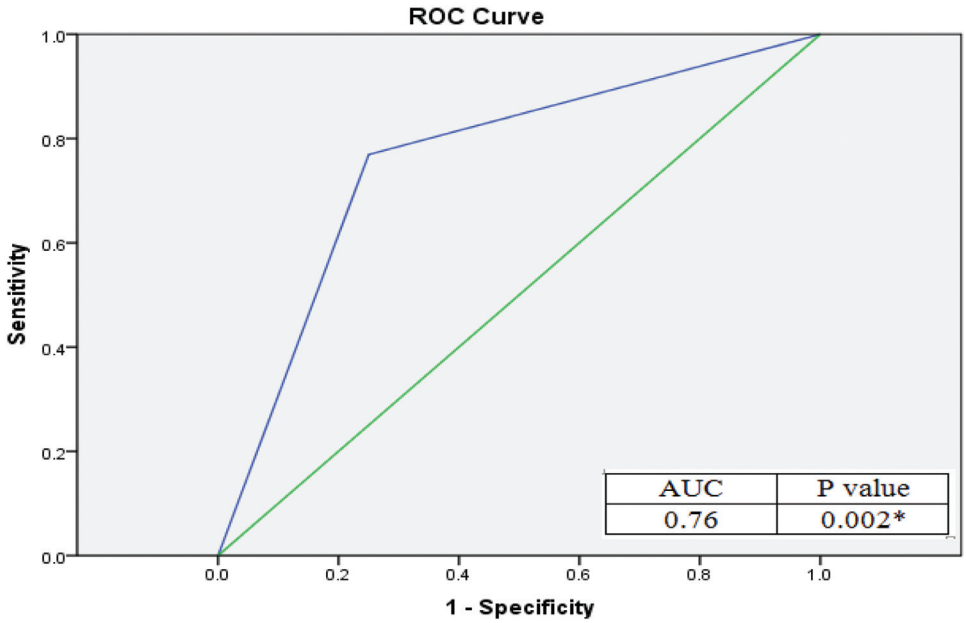
Table 7 shows that the ability of S100B titer in the prediction of survival and death of patients is sensitive (57% after 2 h and 72% after 48 h), while the ability of the test to roll out (specificity) is 88% after 2 h and 67% after 48 h and the overall accuracy is 70.4% after 2 h and 75.7% after 48 h. In addition, Graph 4 the ROC curve illustrates the accuracy of S100B protein to differentiate between survival and death of patients (fate of 28-day follow-up) (*N*=44). Graph 4 shows that the AUC is 0.71 (fair accuracy).

Our study showed that 68% of patients go under conservative treatment and with prolongation of the ICU stay for more than 2 days, 75%) of patients had an increase in the rate of mortality (up to 54%). Therefore, it gives us a correlation between the patients who were treated with conservative protocol and their ICU stay length with the high mortality rate after a 28-day period follow-up.

This study showed that 30 patients out of the 44 (68%) had followed conservative treatment and the same group showed prolonged ICU stay (26 from 30 patients, 79%) and with a mortality of 20 from 26 patients (83%).

Graph 5: the scattered plot curve represents the correlation between the level of GCS

Graph 1



ROC curve analysis of the accuracy of 2 h S100B in the prediction of conservative way of management (N=44). ROC, receiver operating characteristic.

Table 5 Analysis of the accuracy of 48 h S100B in the prediction of conservative way of management (*N*=44)

		48 h S100B				
		Positive			Negative	
Positive		32			2	
Negative		0			10	
Sensitivity	Specificity	PPV	NPV	LR+	LR–	Accuracy
100%	86%	90%	100%	9	0	90%

LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

and S100B protein after 2 h of head trauma, which gives us a weak negative correlation.

Graph 6: the scattered plot curve represents the correlation between the level of GCS and S100B protein after 48 h of head trauma, which gives us a weak negative correlation.

Discussion

Our aim is to assess the validity of S100B protein as a prognostic tool in isolated severe head injury patients for improving the management process in these patients by predictions of their outcome and if there is a correlation between GCS and the level of S100B protein.

Our study population included patients of all age groups, of both sexes with a GCS of less than or equal to 8.

The mean age was 31±8.35 years and ranged from 12 to 44 years and these results match the results of a study performed by Abbasi *et al.* [13], in which the mean age of the study participants was 33.1±10.3 years and ranged from 18 to 50 years.

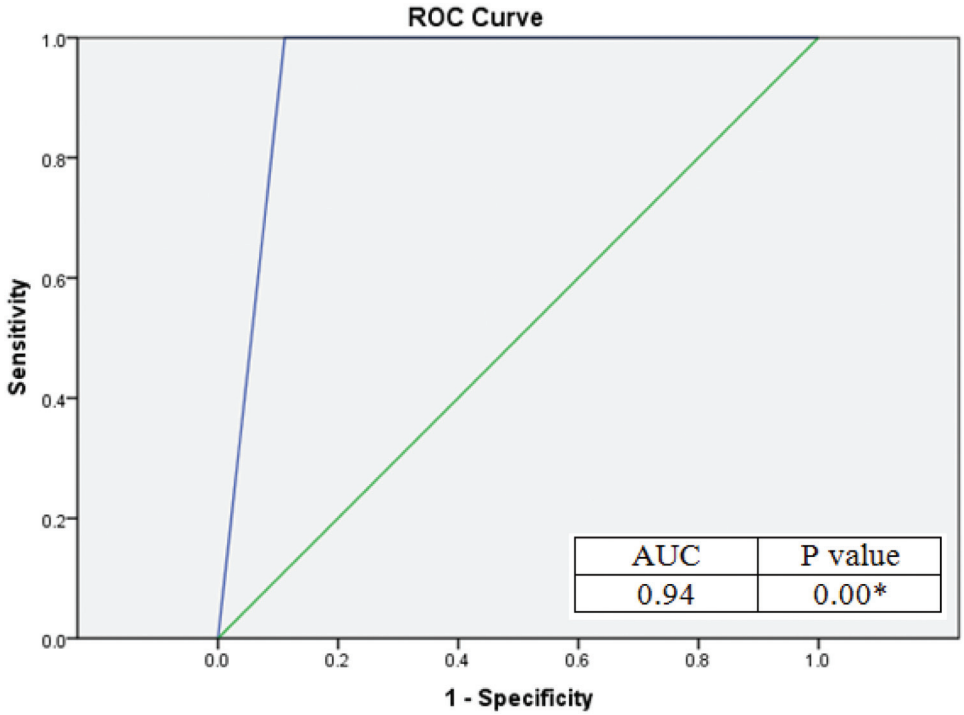
This study showed that 73% of the studied patients were men while 27% of them were women. These results were similar to the study by Fan *et al.* [14], in which 70% of the patients were men and 30% of them were women.

Injury mechanism

Regarding the mechanism of trauma the study showed that direct trauma was the most common cause of head truama (47.7%), followed by motor car accident (MCA) (31.8%). These results were not similar to the results by Egea-Guerrero *et al.* [15], in which MCA was the most common cause of head trauma (60%) in the patients. This may be due to the inclusion criteria of patients in both studies as they selected severe head trauma in polytrauma patients, while in our study the selected patients had only isolated severe head trauma not associated with extracranial injuries.

This study showed that the mean GCS among patients with severe head trauma was 6.59±1.49 which was associated with tachypnea and tachycardia. This was similar to the results of a study performed by Shakeri *et al.* [16], in which the average of primary GCS score of patients was 5±2.

Graph 2



ROC curve analysis of the accuracy of 48 h S100B in the prediction of conservative way of management (N=44). ROC, receiver operating characteristic.

Table 6 Measurement of the accuracy of 48 h S100B in the prediction of length of ICU stay (*N*=44)

		48 h S100B		
		Positive	Negative	
Positive		0		10
Negative		24		10
Sensitivity	Specificity	PPV	NPV	Accuracy
58%	100%	100%	72%	80%

NPV, negative predictive value; PPV, positive predictive value.

Diagnostic and prognostic tools

This study showed that the mean of S100B dimer levels within the first 2 h was 0.124±0.021 µg/l, while after 48 h the mean was elevated to 1.098±0.89 µg/l.

These results were similar to the results of a study conducted by Shakeri *et al.* [16], in which the mean of S100B protein within the first 2 h was 1.13±0.6 µg/l, while after 48 h the mean was elevated to 1.42±0.81 µg/l.

In this study, the results indicated that the operative intervention in head trauma patients was accompanied with low levels of S100B protein (0.1100±0.024), while the patients who underwent conservative protocols had higher levels of S100B protein (0.13133±0.01569) with statistically significant difference between both types of management.

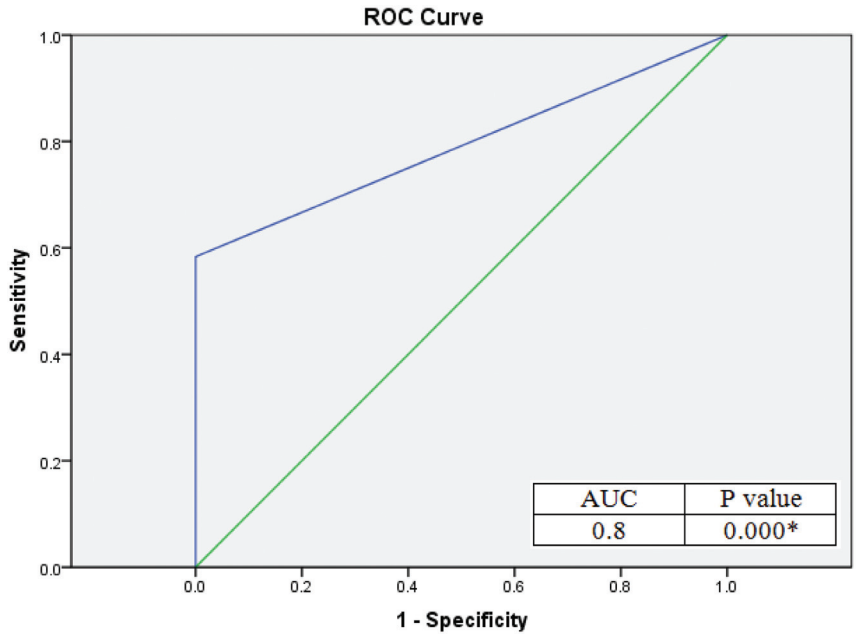
This study showed that comparing the mean levels of S100B protein after 48 h, the level became higher when following the conservative treatment (1.267±0.89) while after operative management the mean level was 0.7364±0.8 which showed statistically significant difference and shows that urgent intervention had better outcomes.

This study showed that there was no significant difference of S100B protein levels to determine the length of ICU stay for patients with head trauma as the mean of S100B was 0.131±0.0194 in patients admitted in the ICU for less than 48 h, while the S100B level was 0.122±0.0213 in patients admitted in the ICU for more than 48 h.

We did not find any studies that had a relationship between the type of management and S100B concentrations or relationship between the length of ICU admission and level of S100B.

This study showed that there was significant difference in S100B protein levels in 48 h to predict the occurrence of mortality in severe head trauma after a 28-day follow-up (24 died vs. 20 discharged) as the mean level of the S100B in the mortality group was 1.8425±0.4648, while the mean level of S100B in the discharged group was 0.2050±0.0848.

Graph 3



ROC curve analysis of the accuracy of 2 h S100B in the prediction of length of ICU stay (N=44). ROC, receiver operating characteristic.

Table 7 The accuracy of S100B protein to differentiate between survival and death of patients (fate of 28 day) (*N*=44)

Variables	AUC	Cut off	Sensitivity	Specificity	PPV	NPV
S100B protein 2 h	0.711	0.99 µg/l	56.76 (39.5–72.9)	88.37 (74.9–96.1)	80.8 (60.6–93.4)	70.4 (56.4–82.0)
S100 protein 48 h	0.710	1.127 µg/l	72.73 (54.5–86.7)	66.67 (50.5–80.4)	63.2 (46.0–78.2)	75.7 (58.8–88.2)

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value.

These results were similar to the results of a study conducted by Egea-Guerrero *et al.* [15], in which the median of the S100B level after 24 h follow-up was 0.213 mg/l in the survived group, while it was 0.474 m g/l in the brain death group with statistically significant difference.

In this study, the ROC analysis showed that the 2 h S100B could predict the conservative way of management with AUC (0.76, *P*=0.002) with a sensitivity of 76% and specificity of 75% with fair accuracy (76%), while the ROC analysis of the 48 h S100B showed better AUC (0.94, *P*=0.00) with a sensitivity of 100% and specificity of 86% with excellent accuracy (90%).

Also in this study, the ROC analysis showed that the 2 h S100B had the ability to predict the length of stay in the ICU with AUC (0.8, *P*=0.000) with a sensitivity of 58% and specificity of 100% with good accuracy (80%).

We did not find any studies that had a relationship between the type of management and S100B concentrations or relationship between the length of ICU admission and level of S100B.

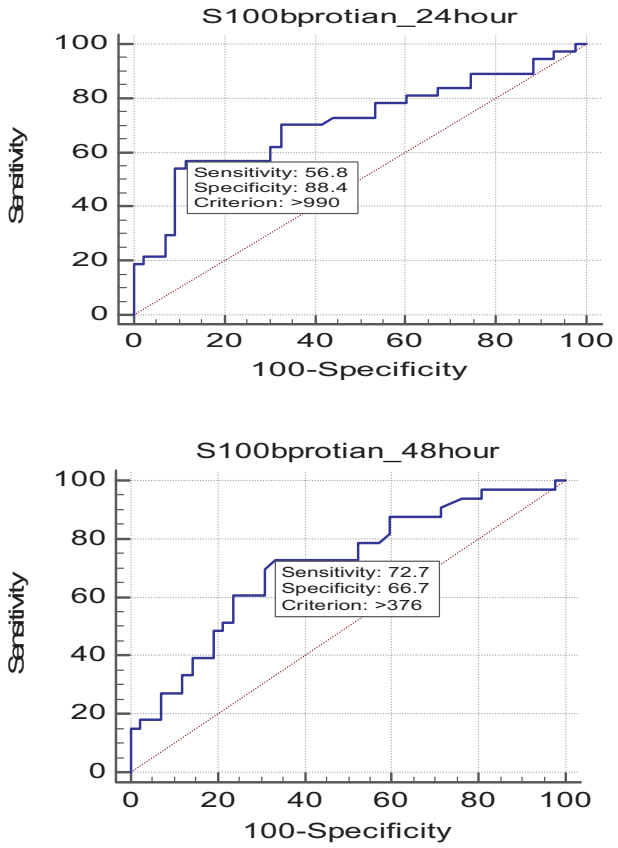
In this study, the ROC analysis showed the ability of S100B in the prediction of mortality of patients at 2 h with AUC (0.711) and the optimal cutoff value was 0.99 µg/l with a sensitivity of 57% and specificity of 88% and its ability after 48 h with AUC (0.710) and the optimal cutoff point was more than 1.127 µg/l and its sensitivity was 72.73% and specificity was 67%.

These results were not similar to the results by Egea-Guerrero *et al.* [15], in which the ROC curve showed that S100B had AUC 0.80 at admission and 0.86 at 24 h later and in their study in order to maximize the relationship between sensitivity and specificity, they used the highest AUC plot (24 h) to assign a cutoff value for serum S100B (0.372 µg/l) with 85.7% sensitivity, 79.3% specificity, 18.7% positive predictive value, and 98.9% negative predictive value.These dissimilarities may be due to the difference in the time of sample collection and the variance in the cutoff value as they collected the samples at admission and after 24 h, while in our study, the samples had been collected at 2 h after admission and 48 h after head trauma.

In addition, they selected a cutoff value (0.372 µg/l) to predict mortality, while in our study the cutoff value

was 0.99 µg/l after 2 h of head trauma and >1.127 µg/l after 48 h of head trauma.

Graph 4



ROC curve illustrates the accuracy of S100B protein to differentiate between survived and death of patients (fate of 28 day) (N=44). ROC, receiver operating characteristic.

Outcomes

This study showed that regarding the outcome of the patients 68% of them had conservative treatment with 75% of them admitted in the ICU for more than 2 days and the mortality rate was 54%.

These results agreed with the results of the study conducted by Shakeri *et al.* [16], in which 73.7% of the studied patients had conservative treatment (TTT) and the mortality rate was 41.7%.

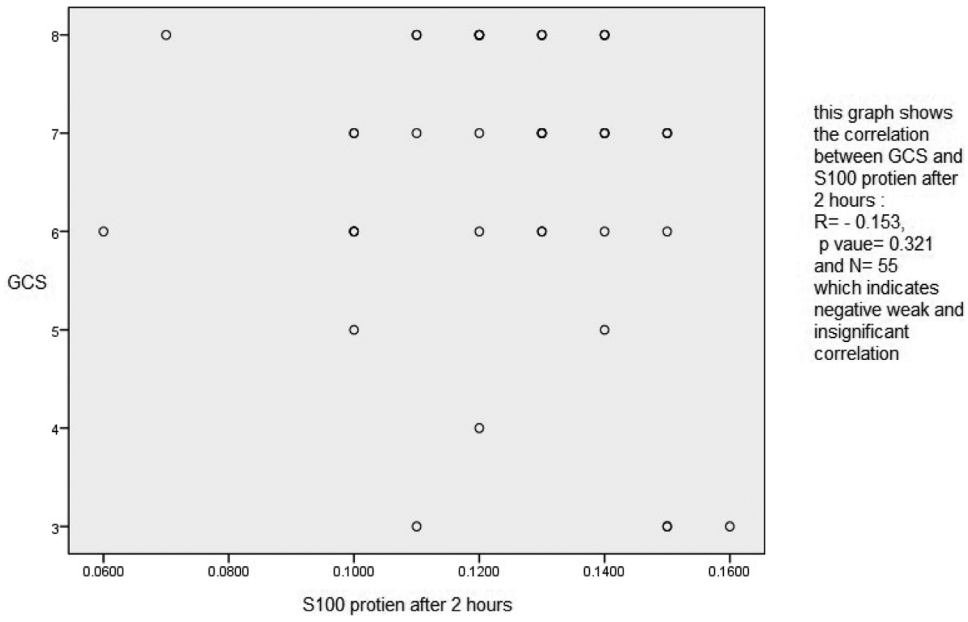
These results disagree with the results of a study performed by Pfortmueller *et al.* [17], in which 76.3% of the patients were admitted to the ICU and the mortality rate was 19.5%.

These differences may be due to the selection of patients in their study as they selected polytrauma patients with head trauma and the sample size was 266, while in our study the sample size was 44 patients and the patients selected were those with isolated severe head trauma.

This study regarding the relationship between the level of 2 h serum S100B and GCS showed that there was weak negative correlation with a *P* value of 0.321 and also showed weak negative correlation between the level of 48 h serum S100B and GCS with a value of 0.138.

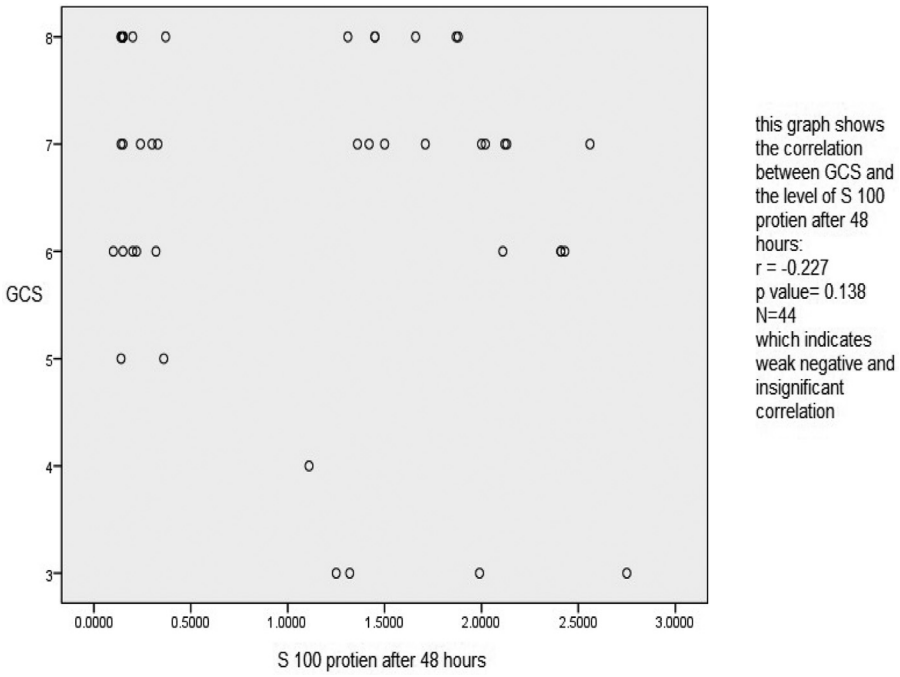
These results disagree with the results of a study by Shakeri *et al.* [16], in which there was association

Graph 5



Scattered plot curve represents the correlation between the level of GCS and S100B protein after 2 h of head trauma. GCS, Glasgow coma scale.

Graph 6



Scattered plot curve represents the correlation between the level of GCS and S100B protein after 48 h of head trauma. GCS, Glasgow coma scale.

between primary GCS and S100B protein levels at the first hour, 48 h later and at the final measurement, which showed a significant correlation, with *P*=0.02, *P*=0.007, *P*=0.006, respectively, which represented a negative association between GCS and protein S100B.

These differences may be due to the selection of patients in their study as they selected polytrauma patients with head trauma and the sample size was 72 patients, while in our study the sample size was 44 patients and the patients selected were those with isolated severe head trauma.

Another difference may be significant in their study, which is the third set of S100B protein levels after 1 week while our study was done for two sets only, one after arrival and the other one was after 48 h.

We can see that there are some ideas that may be of benefit about our study starting with a small sample size that could not be blind which may give us bias into the results, so we have to enlarge the sample size in our further studies and try to use a blind study design to be more accurate.

There are also some limitations in funding our study as the S100B dimer kits are too expensive (90% of our expense) and should be available in our hospital laboratory to enlarge our sample size or it should be totally funded by our university.

We used our selected S100B dimer in expecting the prognosis of our patients, while we can use it also in the diagnosis, management, and follow-up of these patients.

In addition, we used S100B protein in severe head injury only while it can be applied to minor and moderate head injuries, especially in hospitals not equipped with CT scanning and will be of benefit to reduce CT radiation hazards.

Limitations

Although we used an average sample size, the sample size was still small and the study could not be blind which might have introduced some bias into the results.

Additionally, the accuracy of S100B dimer as a diagnostic and prognostic tool is still debatable and could not be precisely detected from other causes that lead to chronic S100B dimer rise, which may lead to its rise in the initial evaluation, so it should be scanned and rolled out from the start.

Few studies were done for S100B dimer in relation to GCS, way of management, and its sensitivity as a prognostic tool in predicting the outcomes in isolated severe head injuries, which made the comparison is limited.

Fund limitation for further sets of the protein which made us to limit to two sets of S100B dimer only, while the majority of studies in this field were at least three sets of S100B dimer.

Conclusions

To overcome the possibility of misdiagnoses of brain death on the basis of clinical criteria, biomarkers have attracted the researchers' attention. One of the brain-specific biomarkers found in the past decades is S100B, expressed and produced by astrocytes in vertebrate brains.

The use of S100B protein from the beginning in ER (after 2 h level of S100B dimer) is to inform the relatives about the most expected outcome for the patient as this will be the most common question asked to the physician and he should have a scientific basis to his answer.

Recommendations

The best way to reduce rates of death or disability from life-threatening injuries is to prevent them. However, it is often possible to minimize the consequences of serious injuries, including long-term morbidity or mortality, by promptly providing effective expected prognosis and management plan.

Therefore, we recommend the following:

(1) The potential correlation of trauma biomarkers with injury and outcome measures in severe isolated head trauma is promising. In our study, S100B levels can be used as a predictive and prognostic value for severe head trauma mortality.
(2) S100B concentrations were weak and were significantly associated with injury severity and GCS, so we recommend depending on GCS for clinical evaluation of the patients and also on injury severity score to evaluate injury severity.
(3) The use of operative intervention in head trauma patients were accompanied with low levels of S100B protein as a rapid intervention, while the patients who were following conservative protocols had higher levels of S100B protein, so we advise to select surgical intervention whenever possible because of better outcomes in comparison with conservative treatment.
(4) We advise to use S100B dimer as a predictor for follow-up for patients with isolated severe head injuries after admission for patients who follow the conservative way of management or surgical intervention as it shows high sensitivity and specificity with an overall accuracy of 90%.
(5) The levels of 2 h S100B and 48 h S100B with a cutoff of more than 0.99 μg/l and more than 1.127 μg/l, respectively, exhibited the highest sensitivity, specificity, and negative predictive value for head trauma patient mortality.
(6) We used our selected S100B dimer in expecting the prognosis of our patients while we recommend its use in the diagnosis and management follow-up of these patients.
(7) In addition, we used S100B protein in severe head injuries only while it can be applied to minor and moderate head injuries especially in hospitals not equipped with CT scanning and will be of benefit to reduce CT radiation hazards.
(8) Our follow-up for the patients was short term (28 days). which leads to find weak or insignificant relationship between the levels of S100B protein with patient's length of ICU stay or in relation to patients GCS levels, so we recommend further studies with long-term follow-up with a large sample size to confirm more results.

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Conflicts of interest

There are no conflicts of interest.

References

1 Elbaih AH. Resuscitation of polytrauma patients: an overview. Narayana Med J 2016; 5:126–140. DOI: https://doi.org/10.5455/nmj/00000111

2 Elbaih AH, El-sayed DA, Abou-Zeid AE, Elhadary GK. Patterns of brain injuries associated with maxillofacial fractures and its fate in emergency Egyptian polytrauma patients. Chin J Traumatol (2018), https://doi.org/10.1016/j.cjtee.2017.12.005

3 Wijdicks EF. The diagnosis of brain death. N Engl J Med 2001; 344:1215–1221.

4 Saatman KE, Duhaime AC, Bullock R, Maas AI, Valadka A, Manley GT, *et al.* Classification of traumatic brain injury for targeted therapies. J Neurotrauma 2008; 25:719–738.

5 Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1999; 2:81–84.

6 Nakase-Richardson R, Sherer M, Seel RT, Hart T, Hanks R, Arango-Lasprilla JC, *et al.* Utility of post-traumatic amnesia in predicting 1-year productivity following traumatic brain injury: comparison of the Russell and Mississippi PTA classification intervals. J Neurol Neurosurg Psychiatry 2011; 82:494–499.

7 Mild Traumatic Brain Injury Committee, A.C.o.R.M, Head Injury Interdisciplinary Special Interest Group. Definition of mild traumatic brain injury. J Head Trauma Rehabil 1998; 8:86–87.

8 Boyd CR, Tolson MA, Copes WS. Evaluating trauma care: the TRISS method. Trauma score and the injury severity score. J Trauma 2006; 27:370–378.

9 Ingebrigtsen T, Romner B. Biochemical serum markers of traumatic brain injury. J Trauma 2012; 52:798–808.

10 Lima JE, Takayanagui OM, Garcia LV, Leite JP. Use of neuron-specific enolase for assessing the severity and outcome in patients with neurological disorders. Braz J Med Biol Res 2004; 37:19–26.

11 Marenholz I, Heizmann CW, Fritz G. S100 proteins in mouse and man: from evolution to function and pathology (including an update of the nomenclature). Biochem Biophys Res Commun 2004; 322:1111–1122.

12 Dawson B, Trapp RG. Basic & clinical biostatistics (LANGE Basic Science). (4th ed). New York: The McGraw-Hill Companies, Inc.; 2004.

13 Abbasi M, Sajjadi M, Fathi M. Serum S100B protein as an outcome prediction tool in emergency department patients with traumatic brain injury. Turk J Emerg Med 2014; 14:147–152.

14 Fan W, Wang H, Yin J. Increase of plasma S100B level in patients with moderate and severe traumatic brain injury. Int J Clin Exp Pathol 2016; 9:12130–12135.

15 Egea-Guerrero JJ, Murillo-Cabezas F, Gordillo-Escobar E, Rodríguez-Rodríguez A, Enamorado-Enamorado J, Revuelto-Rey J, *et al.* S100B protein may detect brain death development after severe traumatic brain injury. J Neurotrauma 2013; 30:1762–1769.

16 Shakeri M, Mahdkhah A, Panahi F. S100B protein as a post traumatic biomarker for prediction of brain death in association with patient outcomes. Arch Trauma Res 2013; 2:76–80.

17 Pfortmueller CA, Drexel C, Krähenmann-Müller S, Leichtle AB, Fiedler GM, Lindner G, Exadaktylos AK. S-100 B concentrations are a predictor of decreased survival in patients with major trauma, independently of head injury. PLoS One 2016; 11:e0152822.