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Evaluation of Serum Neuron Specific Enolase as a Prognostic Marker for Short Term Outcome in the Patients with Closed Traumatic Brain Injury

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ABSTRACT

Several studies have suggested increased Neuron-Specific Enolase (NSE) concentrations in blood following Traumatic Brain Injury (TBI), indicating a potential clinical role as a biomarker of the head injury. With this background, present study was done to estimate the levels of serum cleaved NSE as a diagnostic tool in patients with traumatic brain injury (TBI) and to correlate their outcome with other clinical parameters. In our study, twenty four patients of closed TBI were admitted in the Neurosurgery department at Trauma Centre and Surgical Superspeciality Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi, between August 2016 and July 2017 were enrolled. NSE levels of the patient's blood samples were determined and compared with those healthy controls. The data was statistically analyzed to determine their significance using SPSS software version 16.0. Majority of the patients in our study group i.e. 13 patients (54.17%) belonged to younger age group (up to 45 years) and were males (79.17%) The mean NSE levels of the study group was elevated in all three consecutive days with mean NSE level 50.96+19.59 mg L^{-1} on Day one (D1), 45.71+17.98 mg L^{-1} on Day three (D3) and 52.29+24.91mg L^{-1} on Day Five (D5). Mean NSE levels in patient's upto 45 years of age appeared to be higher compared to those with age above 45 years. Mean NSE levels in serum of females were lower than that of males on the all three days but the difference was statistically insignificant and only a matter of chance. Mean NSE levels in severe TBI patients were significantly elevated in comparison to the patients with mild TBI. The difference was statistically significant with $p<0.001$. When comparison of mean NSE levels in patients with different modality of treatment was done the NSE levels were higher in patients undergoing surgical treatment than those patients kept on conservative management but difference proved to be of no statistically significance. Neuron specific enolase can serve as a potential marker for diagnosis and prognosis in patients with mild to severe TBI. It may yield better prognostic information when combined with clinical examination and CT scan of the patients.

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Key Words

Serum neuron-specific enolase, prognostic marker, short term outcome, closed traumatic brain injury

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INTRODUCTION

Regardless of location, traumatic brain injury is a major cause of death and lifelong impairments globally, making it a public health, medical and socioeconomic concern. Common causes of traumatic brain injury (TBI) include violent incidents, falls from heights, industrial damage, and auto accidents[1,2].

After receiving neurosurgical intervention, patients with severe traumatic brain injuries are frequently sedated and treated in neuro-intensive care units, where their care is aimed at optimising intracranial conditions and promoting recovery. Changes in clinical indicators such elevated intracranial pressure (ICP), brain metabolism as measured by microdialysis monitoring and brain oxygen saturation may need adjustments to treatment plans. Sadly, a lot of TBI patients continue to have secondary insults, which can lead to chronic secondary injuries with high morbidity and mortality rates[3-6].

Even with significant advancements in clinical, radiographic and neuro-monitoring, it is still challenging to determine the full amount of initial brain injury as well as continuous secondary damage. As a result, effective therapeutic interventions and outcome prediction are not possible. Unfortunately, there aren't many resources available in an emergency room context for diagnosing and risk-stratifying intracranial injuries[7-9].

There are three different types of the glycolytic enzyme enolase alpha, beta and gamma. The gamma fraction, sometimes referred to as neuron specific enolase (NSE), is highly concentrated in neuroectodermal tissue. In serum, 5-12 ng mL^{-1} and in cerebrospinal fluid, 20 ng mL^{-1} are considered typical. NSE leaking into the extracellular compartment and circulation is caused by structural damage to the brain's neurons. After traumatic brain injury-related neuronal cell death, NSE can be found in serum[11-13].

NSE is a useful early predictor of neurocognitive and global function deficits following traumatic brain injuries and may allow early outcome prediction because it can be found in the serum within six hours of the event. Increased blood NSE concentrations after traumatic brain injury (TBI) have been reported in a number of investigations, suggesting that NSE may have a clinical role as a biomarker of the head injury[14-16]. Its relationship to the clinical result is still unknown, though.

Aims and objectives:

- To estimate the levels of serum cleaved NSE as a diagnostic tool in patients with traumatic brain injury (TBI)
- To correlate their outcome with other clinical parameters
- To assess the validity of outcome prediction with this serum marker in the patients with head injury

MATERIAL AND METHODS

Within 24 hrs of suffering a traumatic brain injury (TBI), patients with head injuries between the ages of 18-65 participated in this prospective pilot study. Initially, thirty patients were randomly selected for enrollment in the trial, however, six patients who passed away within three days of admission or were lost to follow-up were eventually removed from the analysis because it was not feasible to obtain three consecutive samples from them.

According to the study's inclusion criteria, twenty-four patients with closed traumatic brain injuries were admitted to the neurosurgery department of the Trauma Centre and Superspeciality Hospital of the Institute of Medical Sciences, Banaras Hindu University, Varanasi, between August 2016 and July 2017. First-degree relatives or patients themselves provided their informed permission. The investigator was given the authority to select any course of action that would be in the patient's best interests. Additionally, ten healthy controls were chosen.

Inclusion criteria:

Following were the inclusion criteria:

- Age between 18-65 years
- Closed head injury patients
- Isolated head injury patients
- Patients reporting within 24 hrs of TBI
- No patients with severe coagulopathy (which is defined as clinical evidence of excessive bleeding, platelet counts <1,00,000, INR>1.4, or a PTT>50)
- No patients with clinical indication for future anticoagulation (e.g. life-threatening deep vein thrombi, pulmonary embolism)
- Family or next-of-kin available to provide written informed consent
- Patients were selected randomly and prospectively and were included into the study on the day of admission and they were followed till the day of discharge or demise

Exclusion criteria:

Following were the exclusion criteria:

- Age <18 years
- Lack of informed consent
- Patients with prior neurologic disabilities (head injury, cerebral infarction and haemorrhage)
- Patients presenting at the emergency >24 hrs after injury
- Penetrating traumatic brain injury patients
- Traumatic brain injury associated with systemic injuries and polytrauma

- Non-availability of blood sample
- Pregnancy

Sample size: A total of twenty four patients were enrolled in the study from August 2016 to July 2017, along with ten healthy volunteers who served as the control group.

Clinical work up: The study covered patients who presented within 24 hrs of the injury. At the time of enrollment the demographic data of the patient was documented. Over the course of the hospital stay the GCS score was determined every 24 hrs. On a 3-15 point scale, the GCS assesses verbal performance, motor responsiveness and eye opening the highest score indicates normal performance. Records were kept of the injury's timing, any related injuries and the patient's arrival time at the hospital emergency room. Depending on the circumstances the mechanisms of harm were classified as falls, assaults, auto accidents, pedestrians hit by cars, or any other way.

The severity of TBI was graded according to the Glasgow Coma Scale (GCS) scores on admission as follow:

- Severe TBI = 3-8
- Moderate TBI = 9-12
- Mild TBI = 13-15

Investigation and management protocol: A radiologist who was blind to the study conducted a diagnostic CT scan at the time of admission and reported the results. Whenever clinically necessary, follow-up CT scans were carried out. Venous samples were taken from the patients as soon as feasible following admission on Day-1, Day-3 and Day-5. Additionally, ten healthy controls had their veins sampled. The same day these samples were centrifuged and the separated serum was kept between-200 and-400 degrees Celsius until it was time to use an enzyme immunoassay (EIA) kit for additional analysis to determine the NSE levels. The patients were treated properly in accordance with the protocols. Based on CT findings and clinical grounds, a surgical versus conservative course of treatment was chosen. As the primary endpoints for all predictive studies, or those conducted to evaluate the predictive capacity of a collection of patient and injury data, mortality and GOS were considered. The Glasgow Outcome Scale (GOS) was used to evaluate the clinical outcome. The person is rated on a five-point scale (from 1-5) according to their level of independence and function good recovery, moderate disability, severe disability, chronic vegetative state and death.

Outcome was determined at 3 months interval by using Glasgow Outcome Scale (GOS) using structured interview questionnaire. For statistical analysis of outcome, GOS was categorized into:

Favorable outcome:

GOS Category 4-5	GOSE Category 5-8

unfavorable outcome:

GOS Category 1-3	GOSE Category 1-4

Analysis of NSE: On Day 1, Day 3 and Day 5, 5 millilitres of venous blood samples were drawn from the patients in simple, non-pyrogenic vials upon admission. After allowing the blood to coagulate, centrifugation was performed for ten minutes at 3000 rpm. Before analysis the serum was separated and stored at-800C in a deep freezer. The solid-phase enzyme immunoassay (EIA) method was used to analyse the collected samples in order to qualitatively assess the presence of NSE in human blood serum or plasma. The pre-coated 12x8 strips and 96 wells of the XEMA Cat# K234 NSE EIA research kit were utilised for the analysis. According to XEMA's data the maximum amount of NSE in healthy donors is 13.0 g L^{-1}.

Statistical analysis: The patient's blood sample's NSE levels were calculated and contrasted with those of the healthy controls. Using SPSS software version 16.0, a statistical analysis was performed to ascertain the relevance of the data. $p>0.05$ indicated statistical significance of the calculated values.

OBSERVATION AND RESULTS

The study included twenty four patients between the age range of 18-65 years with the mean age of 44.25±11.18 years. Thirteen patients (13) were less than 45 year of age. In the present study, nineteen patients (19) were male and five patients (5) females. The male: female ratio was 3.8. (Table 1).

In the present study, eleven patients (45.83%) with mild TBI (GCS 13-15) had mean GCS of 13.09 and thirteen patients (54.17%) were with severe TBI (GCS 3-8) had mean GCS of 6.85. The most common mode of traumatic brain injury in the present study was Road traffic accidents (RTA) seen eighteen patients (75%) followed by fall from height in three patients (12.5 %) and physical assault in three patients (12.5%) (Table-2).

Most common CT scan finding was cerebral contusions in fourteen patients (58.33%) followed by diffuse axonal injury in four patients (16.67%). Other findings were extra-dural hematoma (EDH) and subarachnoid hemorrhage (SAH) in two patient (8.33%) each, subdural hematoma (SDH) and Intraventricular hemorrhage (IVH) in one case (4.17%)each (Table-2).

NSE levels were calculated in traumatic brain injury patients samples and healthy controls. Mean NSE level in control patients was 10.8+8.8mg L^{-1}. The mean NSE levels of the study group was elevated in all three consecutive days with mean NSE level 50.96+19.59 mg L^{-1} on Day one (D1), 45.71+17.98 mg L^{-1} on Day three (D3) and 52.29+24.91 mg L^{-1} on Day

Table 1: Age and gender distribution

	Case		Control	
Age	No.	Percentage	No.	Percentage
<45 years	13	54.17	5	50
>45 years	11	45.83	5	50
Mean age	44.25+11.18	43.70+13.21		
Age range	23-62	25-61		
Gender				
Males	19	79.17	7	70
Females	5	20.83	3	30
Total	24	100	10	100

Table 2: Mode of injury and CT findings

Mode of injury	No. of patients	Percentage
Road traffic accidents	18	75.00
Fall from height	3	12.50
Physical assault	3	12.50
Total	24	100
CT Findings		
Diffuse injury	4	16.67
Mass lesion	20	83.33
Extradural hematoma	2	8.33
Subdural Hematoma	1	4.17
Cerebral contusions	14	58.33
Subarachnoid hemorrhage	2	8.33
IVH	1	4.17

Table 3: Mean NSE levels in Total Cases and Controls

Admission day	Case Mean+SD (mg L^{-1}) n = 24	Control Mean+SD (mg L^{-1}) n = 10	T-value	p-value
NSE Day 1	50.96+19.59	10.8+8.8	6.1849	<0.0001
NSE Day 3	45.71+17.98	10.8+8.8	5.8181	<0.0001
NSE Day 5	52.29+24.91	10.8+8.8	5.0967	<0.0001

Table 4: Mean NSE levels in the age groups in TBI patients

Admission Day	Upto 45 years Mean+SD (mg L^{-1}) n = 13	More than 45 years Mean+SD (mg L^{-1}) n = 11	T-value	p-value
NSE Day 1	46.692+21.975	52.455+17.282	0.7039	0.4889
NSE Day 3	47.769+22.234	43.273+11.740	0.6027	0.5529
NSE Day 5	50.615+24.487	54.273+26.458	0.3517	0.7284
Mean NSE levels in the age groups in Mild TBI patients				
AdmissionDay	Upto 45 years Mean+SD (mg L^{-1}) n = 7	More than 45 yearsMean+SD(mg/L) n=4	t-value	p-value
NSE Day 1	32.429+5.062	32.750+6.702	0.0902	0.9301
NSE Day 3	31.571+9.289	37.750+3.686	1.2515	0.2423
NSE Day 5	37.143+10.839	42.250+4.856	0.8781	0.4027
Mean NSE levels in age groups in Severe TBI patients				
Admission Day	Upto 45 years Mean+SD(mg L^{-1}) n = 6	More than 45 years Mean+ SD (mg L^{-1}) n = 7	t-value	p-value
NSE Day 1	69.833+14.972	63.714+8.281	0.9322	0.3713
NSE Day 3	66.667+16.943	46.429+13.819	2.3986	0.0353
NSE Day 5	66.333+27.340	61.143+31.678	0.1323	0.7600

Table 5: Mean NSE level in gender group in TBI patients

Admission Day	Male Mean+ SD (mg L^{-1}) n = 19	Female Mean+SD (mg L^{-1}) n = 5	t-value	p-value
NSE Day 1	54.632+19.239	37.000+15.281	1.8790	0.0736
NSE Day 2	48.737+18.944	34.200+5.805	1.6712	0.1088
NSE Day 3	56.263+26.386	37.200+8.729	1.5696	0.1308
Mean NSE level in gender group in Mild TBI patients				
Admission Day	Male Mean+ SD (mg L^{-1}) n = 7	Female Mean+SD (mg L^{-1}) n = 4	t-value	p-value
NSE Day 1	33.714+5.376	30.500+5.447	0.0632	0.9510
NSE Day 2	33.714+9.322	34.000+6.683	0.0535	0.9585
NSE Day 3	40.571+9.199	36.250+9.777	0.7337	0.4818
Mean NSE level in gender group in Severe TBI patients				
Admission Day	Male Mean+SD (mg L) n = 12	Female Mean+SD (mg L^{-1}) n = 1	t-value	p-value
NSE Day 1	66.833+12.209	63	Small Female	Small Female
NSE Day 2	57.500+17.676	35	Sample	Sample
NSE Day 3	65.417+29.069	41	Small Sample	Small Sample

Table 6: Correlation of mean NSE levels with papillary reaction in all TBI patients

Admission day	Bilateral Reactive Mean+SD (mg L^{-1}) n = 19	UnilateralNon-reactiveMean+SD (mg L^{-1}) n = 5	t-value	p-value
NSE Day1	46.105+19.894	67.400+9.263	2.2997	0.0313
NSE Day3	43.105+15.726	55.600+24.296	1.4127	0.1717
NSE Day5	45.000+17.857	80.000+30.356	3.3642	0.0028

Five (D5). This elevation of NSE levels in cases compared to that of controlled found to be statistically significant with a p<0.001 (Table-3).

Mean NSE levels in patients upto 45 years of age appeared to be higher compared to those with age above 45 years. However the difference on all three

Table 7: Comparison of mean NSE levels at Day 1, Day 3 and Day 5

Admission Day	Mild TBI Mean+SD(mg L^{-1}) n = 11	p-value	Severe TBI Mean+SD(mg L^{-1})n = 13	p-value
NSE Day 1	32.545+5.373	0.0023	66.538+11.738	0.0134
NSE Day 3	33.818+8.097		55.769+18.038	
NSE Day 1	32.545+5.373	0.0018	66.538+11.738	0.0235
NSE Day 5	39.000+9.176		63.538+28.643	
NSE Day 3	33.818+8.097	0.0089	55.769+18.038	0.0336
NSE Day 5	39.000+9.176		63.538+28.643	

Table 8: Comparison of NSE levels between mild TBI patients, severe TBI patients and Controls

Admission Day	Mild TBI Mean+SD(mg L^{-1})n = 11	Severe TBI Mean+SD (mg L^{-1}) n = 13	Controls Mean+SD(mg L^{-1}) n = 10	t-value	p-value
NSE Day 1	32.545+5.373	66.538+11.738	10.800+8.804	8.8315	<0.0001
NSE Day 3	33.818+8.097	55.769+18.038	10.800+8.804	3.7217	0.0012
NSE Day 5	39.000+9.176	63.538+28.643	10.800+8.804	2.7176	0.0006

Table 9: Correlation of CT findings with mean NSE levels

CT Findings	Mean NSE (mg L^{-1})	t-value	p-value
Diffuse(n = 4)	57.500+18.065	0.7240	0.4767
Mass lesion(n = 20)	49.650+20.056		

Table 10:Treatment modality versus NSE levels total patients

Admission day	ConservativeTBIMean+SD((mg L^{-1}) n = 18	Operative TB Mean+SD (mg L^{-1}) n = 6	t-value	p-value
NSE Day 1	47.444+19.954	61.500+15.294	1.5697	0.1308
NSE Day 3	44.000+19.260	50.833+13.527	0.8001	0.4322
NSE Day 5	48.111+24.547	64.833+23.549	1.4584	0.1589
Treatment versus NSE levels in severe TBI patients				
Admission day	ConservativeTBI Mean+SD (mg L^{-1})n = 8	Operative TBI Mean+SD(mg L^{-1})n = 5	t-value	p-value
NSE Day 1	66.250+14.089	67.000+8.093	0.1074	0.9164
NSE Day 3	57.500+20.935	53.000+13.910	0.4224	0.6809
NSE Day 5	59.875+32.555	69.400+23.169	0.5666	0.5824

Table 11: Outcome versus NSE levels in TBI patients

Outcome versus NSE levels in total TBI patients

Admission day	Unfavorable outcome Mean+SD(mg L^{-1}) n=6	Favorable outcome Mean+SD(mg L^{-1}) n = 18	t-value	p-value
NSE Day 1	68.167+9.131	45.222+18.851	2.8409	0.0095
NSE Day 3	53.000+15.620	43.278+18.448	1.1557	0.2602
NSE Day 5	88.167+19.146	40.333+11.235	7.5454	<0.0001
Outcome versus NSE levels in severe TBI patients				
Admission day	Unfavorable outcome Mean+SD(mg L^{-1})n = 6	Favorable outcome Mean+SD(mg L^{-1})n = 7	t-value	p-value
NSE Day 1	68.167+9.131	65.143+14.182	0.4474	0.6633
NSE Day 3	53.000+15.620	58.143+20.812	0.4961	0.6296
NSE Day 5	88.167+19.146	42.429+14.455	4.9079	0.0005

days was not found to be statistically significant.No statistically significant relationship was found when mean NSE levels were compared in different age groups separately in the patients with mild TBI and severe TBI (Table- 4).

Mean NSE levels in serum of females were lower than that of males on the all three days but the difference was statistically insignificant and only a matter of chance .Mean NSE levels in males and females of severe TBI patients separately still showed no statistically significant relationship. Thus mean NSE levels showed no association with sex (Table-5).

All mild TBI patients demonstrated bilateral reactive pupils. When mean NSE levels were compared among all patients with TBI showing different papillary reaction pattern, it was found that mean NSE levels were highest in patients with unilateral non-reactive pupils and lowest in patients with bilateral reactive pupils. The difference was statistically significant on D1 and D5 with $p<0.05$ (Table-6). When mean NSE levels on any two days out of the three days were paired and p-value calculated, the decrease seen in NSE levels was found to be statistically significant (Table-7).

Mean NSE levels in severe TBI patients were significantly elevated in comparison to the patients with mild TBI (Table-8). The difference was statistically significant with $p<0.001$. Furthermore mean NSE levels were significantly elevated than controls which was statistically significant. When CT findings were broadly categorized into diffuse and mass lesions and mean NSE levels were calculated, no statistically important difference was seen between the two categories, as the $p>0.05$ (Table-9).

When comparison of mean NSE levels in patients with different modality of treatment was done, the NSE levels were higher in patients undergoing surgical treatment than those patients kept on conservative management but difference proved to be of no statistically significance. All the patients with mild TBI were kept on conservative management except one patient with large EDH with midline shift. Mean NSE levels in patients with severe TBI kept on different treatment modalities showed higher values in patients undergoing surgical management. The difference proved to be of no statistical significance. (Table-10).

On correlation of mean NSE levels of patients with outcome, those patients with unfavorable outcome showed higher values compared to the patients with more favorable outcome. Unfavorable outcome was seen in patients with higher mean NSE levels and favorable outcome in the lower values in severe TBI patients. The relationship was statistically significant. (Table-11).

DISCUSSIONS

India's rate of industrialization, urbanisation and vehicle population growth are all contributing factors to a dramatic increase in the prevalence of head injuries. Traumatic brain injury causes more than 1.5-2 million injuries and one million fatalities in India each year. The patients in the current study ranged in age from 23-62 years, with a mean age of 44.25+11.18 years. In this study, road traffic accidents accounted for the majority of traumatic brain injury cases (18 out of 75 patients). Falling from a height caused 3 cases (12.5%) and physical assault for 3 cases (12.5%). Road conditions that are in poor shape, reckless driving and traffic rule violations are the main causes of the high frequency of traffic accidents in this area.

The next leading cause of head injuries is falls from heights, which can be caused by kite flying on roofs, climbing on trees and exposed roof tops. In Wilberger *et al*.[17] study on traumatic brain injury (TBI), road traffic accidents accounted for 53% of injuries, with falls from height accounting for 37% of cases. In contrast to this study, Kiboiet *et al*.[18] discovered that physical assault accounted for 44.8% of head injuries, with falls and traffic accidents coming in second and third, respectively, at 24.7-30.5% of cases. Since the majority of working people are younger and frequently engage in outdoor activities, they are more likely to be involved in attacks and traffic accidents. Thirteen, or 54.17 percent of the patients in this study were younger in age.

Males (nineteen, 79.17%) had a higher frequency of traumatic brain damage than females (20.83%). It was 3.8 male to female. Males engage in a wider variety of activities and, as a result, are more likely to be injured in attacks and traffic accidents. This is why there is a higher male to female ratio. Females are restricted to their houses and are not employed. Patients with ages ranging from 23-62 years old, with a mean age of 44.25+11.18 years, were included in our study. A statistically significant association was not observed between serum NSE levels and age (t-value = 0.7039, 0.6027 and 0.3517 and p-value = 0.4889, 0.5529 and 0.7284 on the first, third and fifth day) when we compared NSE in different age groups.This is consistent with the findings of Casmiro *et al*.[19] who examined the connection between NSE and age and sex in 108 patients (68 males and 40 females) who did not have neurological illness. According to this study, there is no discernible age-related rise in serum NSE levels ($p = 0.15$ and $r = 0.5$). Additionally, Vos *et al*.[20] discovered that there is no significant correlation between age and blood NSE levels in their research of 85 individuals with severe brain injury (GCS<8).

There were 5(20.83%) girls and 19(79.17%) males in our study. Serum NSE levels in the two sexes were compared and we discovered that in all three serum samples on the first, third and fifth days, males had significantly higher NSE levels than females however, these differences were not statistically significant (t-value = 1.8790, 1.6712 and 1.5696 and p-value = 0.0736, 0.1088 and 0.1308 on the first, third and fifth day, respectively).We also examined the differences in NSE values between the sexes with mild and severe head injuries separately and statistical significance was seen. This was consistent with the findings of de Kruijk *et al*.[21] who examined the serum NSE levels of 91 controls, of whom 86% were male and 14% were female. The median NSE concentrations in serum of male controls was higher than female controls (9.7 versus 7.6 mg L^{-1} $p = 0.037$). However, both Casmiro *et al*.[19] and Vos *et al*.[20] found that NSE not significantly related to gender.

In relation to the level of brain injury severity, our research showed that, with a p-value of less than 0.0001, serum NSE levels upon admission were substantially greater in patients with severe head injury (66.538+11.738 g L^{-1}) than in those with moderate head injury (32.545+5.373 g L^{-1}). In comparison to patients with mild head injuries, those with severe head injuries had significantly higher serum NSE levels on the third day (mild TBI = 33.818+8.097g L^{-1}, severe TBI = 55.769+18.038 g L^{-1}, t-value = 3.7212 and $p = 0.0012$) and fifth day (mild TBI = 39.000+9.176 g L^{-1}, severe TBI = 63.538+28.643 g L^{-1}, t-value = 2.7126 and $p = 0.0006$). This is also consistent with research by Zahra *et al*.[22] on 45 patients, 14 of whom had moderate to severe head injuries (GCS<12) and the remaining patients had mild head injuries (GCS>12). The study's findings indicated that the serum level of NSE was significantly higher in those with moderate to severe head injuries (22.8+13.3 g L^{-1}) than in those with mild TBI (9.8+7.7 g L^{-1}) with a $p>0.01$. However, he discovered no statistically significant relationship ($p = 0.23$) between NSE levels and GCS. This is also consistent with the findings of Guezel *et al*.[23], Rothoeral *et al*.[24], and Herrmann *et al*.[25], who discovered a substantial negative connection between serum NSE levels and GCS and considerably higher NSE levels in patients with severe TBI (GCS<8). In contrast, Vos *et al*.[20] did not find a significant association between serum NSE levels and GCS in their investigation of individuals with serious head injuries.

We classified CT results in our study into two categories: diffuse lesions and mass lesions. Four patients (16.67%) had diffuse CT findings, while twenty patients (83.33%) had mass lesions. The mean NSE levels for each group were determined, however the p-value for the link between CT findings and NSE levels was not statistically significant.On the other hand, Manfred *et al*.[26] discovered a highly significant

association between the NSE and the lesion on the CT scan, which peaked at the second day of brain insult (r = 0.83, p = <0.0001). Additionally, they discovered that the magnitude of the lesion was more important than the kind of lesion hemorrhagic or ischemic stroke when determining serum NSE. There was also a statistically significant association (p<0.04) found between serum NSE levels and CT findings by Zahra *et al*.[22], Vos et al.[20] and Naeimi *et al*.[27] and Samit et al[28] discovered a significant association (p<0.001) between serum NSE levels and the advancement of head injury, which is again in opposition to our findings. The marker levels in the resolving group shown a trend of declining.

We separated the results of our investigation into two groups favourable (improved without any morbidity) and unfavourable (with morbidity and mortality). Six patients (or 25%) had a negative outcome, while eighteen patients (or 75%) had a positive outcome. Compared to patients who had a favourable outcome, those who had an unfavourable end had significantly higher NSE levels, particularly on the first day (p = 0.0095) and the fifth day (p<0.0001). Even in patients with severe traumatic brain injury, these values remained statistically significant. This is consistent with Samit *et al*.[28] findings from which showed that serum NSE was significantly lower in those who had a favourable outcome (17+5.1 g L^{-1}) than in those who had a poor outcome (25.4+5.1 g L^{-1}). There is a statistically significant correlation (p<0.001) between outcome evaluation and serum NSE levels. Additionally, serum NSE levels were observed to correlate with result by David et al.[29], Bandyopadhyay *et al*.[30] and Vos *et al*.[20]. The blood NSE levels of patients who did not have a favourable outcome were higher than those of patients who did R = 0.319, p<0.0001) and the enzyme levels 48 hrs after admission were more significant in predicting the outcome than the levels at admission. p-value for NSE2 was less than 0.001, while NSE1's was 0.065. This stands in contrast to the findings of Raabe *et al*.[31] who examined 82 patients who had suffered head injuries, of these, 49 had favourable outcomes (60%) and 33 had unfavourable outcomes (40%), with a mortality rate of 38% (31 patients) after 6 months. There was no discernible variation between the two result group's highest NSE levels. The positive outcome group's NSE was 26.7 mg L^{-1}, while the negative outcome group's NSE was 12 mg L^{-1}, with a p-value of 0.09.

The fact that NSE is found in erythrocytes in addition to neuronal tissue is one of the primary factors limiting its effectiveness as a marker in traumatic brain injury. Because of this, NSE results in hemolysis patients could be deceptive. The biological half-life of NSE is lengthy (>20 hrs), hence sample scheduling may potentially have an impact on NSE outcomes. By getting our first NSE sample within 24 hrs of the trauma, we tried to account for this.

CONCLUSION

Patients with mild to severe traumatic brain injury may benefit from using neuron specific enolase as a possible marker for diagnosis and prognosis. When paired with the patient's CT scan and clinical evaluation, it might produce more accurate prognostic data. To fully investigate all of its facets in TBI patients and to solve its limitations, carefully designed large-scale investigations are required. It is necessary to assess the NSE release pattern between patients who have been admitted with traumatic brain injury and those who have not. The effectiveness of neuron-specific enolase as a neurological outcome maker may be negated by the degree of hemolysis that results from severe blunt trauma. In order to lessen false positive results from serum containing traces of red blood cells, an attempt should be made to create a way to separate this isoenzymes form from its counterpart inside the red blood cells. Even though patients with worse neurological outcomes have significantly higher serum levels of NSE, more research is required to identify NSE cutoff values that may be linked to a poor prognosis.

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