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RESEARCH ARTICLE
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ROLE OF SERUM ZINC AND SERUM MAGNESIUM IN PROGNOSIS AND OUTCOME OF PATIENTS WITH TRAUMATIC BRAIN INJURY: A PROSPECTIVE STUDY

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Abstract:
Traumatic brain injury has been considered as global public health issues. Almost 1.7 million people with isolated or multiple organ damage suffers from traumatic brain injury each year. Severe traumatic brain injury caused secondary multiple organ dysfunction and death. Serum Zinc and serum magnesium level in acute stages after traumatic brain injury (TBI) may be capable of predicting clinical and functional prognosis.
Materials and Methods This prospective study was carried out on 461 TBI patients sample who met the inclusion and exclusion criteria. Sample was collected from clinically diagnosed TBI patients within 24 hrs. Serum zinc and serum magnesium were determined on CST 180 in the central. The association of the serum zinc and serum magnesium determined with severity and outcome post treatment of the TBI patients by chi-square test**.**
Results: The serum zinc level was found normal range(65-118)µg/dl and serum magnesium level observed normal (1.6-2.4)mgldl except in the age group (51-60) where it was noticed reduced(1.23±0.39)mg/dl .The the association of serum zinc level (p=0.00001) and serum magnesium (p=0.00515) level with the outcome after six month(GOS based) were found significantly associated. Similarly, the association of severity (GCS Based) and Serum level of zinc (0.00001) and serum level of magnesium (0.0515) was also studied and observed significantly associated.
Conclusion: The serum zinc level of zinc and serum level of magnesium were found both found significantly associated with both severity and outcomes of the TBI patients. The serum zinc and serum magnesium may play the role in prognosis of the diseases.

Keywords: Traumatic Brain Injury, GCS, GOS, prognosis

INTRODUCTION

Traumatic brain injury has been considered as global public health issues. The figure of the people with permanently disables or death is considerably high. Almost 1.7 million people with isolated or multiple organ damage suffers from traumatic brain injury each year [1]. In Indian population, proper and accurate record of TBI patients is lacking. Total accidental death of was 413457 according to the crime record bureau of India in year 2015. [2] A large medical and economic burden over a long period of time also has large social impact.[3, 4]

Injuries are the ignored epidemic of modern society. Head injuries are the most serious and preventable major public health problem and a frequent cause of morbidity and mortality in young people and children. There is an astounding range of different forms of head trauma, each with unique care needs and prognosis consequences. Traumatic brain injury (TBI) is regarded as a "silent epidemic" since the extent of the issue is mainly unknown to the general public. [5]

Despite many studies on traumatic brain injury, few markers have been applicable to diagnose trauma at tissue concentration. Some of the neuronal damage in TBI is caused by primary or mechanical injury occurring at the time of the traumatic event. However, much of the damage also appears to involve secondary or delayed processes that are activated in the hours, days, or weeks following the injury. Several factors have been implicated in the occurrence of this progressive secondary injury cascade, including alterations in ion homeostasis. [6,7,8,9] Accurate predictive models for the diagnosis and prognosis of traumatic brain injury have been necessary for an effective therapeutic strategy to improve clinical outcomes and decrease disease burden of TBI.[10] There have been many approaches to know the finding of cellular and biochemical biomarkers predicting prognosis of TBI.[11,12]

Zinc is a trace metal that is essential for normal development of the central nervous system in the early neonatal periods and the maintenance of brain function in adults.[13] It is an important element present in the hippocampus, neo-cortex, amygdala, olfactory bulbs, and hypothalamus.[14, 15] Zinc is to be known that play an important role in neurological recovery through the regulation of oxidative stress that causes secondary injury.[16] The changes in brain and neuronal zinc level have declared to trauma, stroke and seizures associated with neuronal damage and death.[17] The induction of zinc progenitor cell proliferation and neurogenesis is essential in the modulation of hippocampus neurogenesis after TBI.[18] The In vivo study of experimental animal showed evidence of a reduced and protective effect on the injured neurons while chelation of free zinc to the brain in animal TBI models.[19,20] It has been suggested that zinc deficiency should be prevented to optimize the neurological recovery potential in acute care after TBI.[21]

Magnesium is considered to be a crucial diagnostic marker of neurotrauma with important implications in cytotoxic and reperfusion pathways of secondary brain damage.[22] Numerous studies showed that there is a profound decline in total tissues and intracellular magnesium levels of brain or spinal cord after trauma and magnesium supplementation have influenced the degree of post traumatic cellular damage.[22,23,24] A comprehensive analysis of neurometabolic cascade after brain injury also revealed that intracellular magnesium levels reduce immediately after TBI and remain low for up to 4 days. Hypomagnesemia may lead to neuronal dysfunction as both glycolytic and oxidative generation of ATP is impaired when magnesium levels are below normal. [25] In addition, low magnesium effectively unblocks the NMDA receptor channel more easily, leading to greater Ca^{2+} influx which has been shown to disrupt neurofilaments and microtubules impairing post - traumatic neural connectivity.[24]

In this study, we attempted the relationship between serum zinc and serum magnesium levels with the neurological outcome in severe and moderate traumatic brain injury patients.

MATERIAL AND METHODS

This was a prospective study conducted over a period of 2 year from May 2022 to April 2024 in NIMS Hospital at NIMS University, Rajasthan, Jaipur, India. This study was approved by the Institutional Ethical committee. The sample size of the study was 461TBI Patients admitted in the NIMS hospital

to who met the inclusion criteria and written informed consent. The selected patients sample was collected under aseptic precaution in plain vial and holds it 10 minutes at room temperature for clotting then centrifuged it at 2500 rpm for 5 minutes to separate the serum sample, which was further used to analyse the level of zinc and magnesium with calorimetric end point method. The calculation of serum zinc level and serum magnesium level was based on measuring at 560 nm in green filter on semi automated machine.[26]

Examination of severity:
Glasgow coma scale (GCS) were used to assess and calculate the patient conscious level. The following course of action which were analyzed during the examination which is suggested approach based on own clinical experiences. The examination was performed at neurosurgery ICU.[27]

	Maximum Scores
● Eye opening:	1-4
● Verbal responses:	1-5
● Motor response :	1-6

Measurement of outcome:
The outcomes of patients were measured with Glasgow outcome scale (GOS). It is one of the highly accurate scales for indexing. It has 5-point score given to the victims of TBI measures during their recovery period of the person who suffered with TBI.[28]

Statistical analysis: Mean± SD were calculated for all the parameters. The association between the variables were analysed by chi- square test. The value $p<0.05$ were significant and $P<0.001$ were highly significant.

RESULT AND DISCUSSION
In our study, the level of Zinc(Zn) were found in µg/dl , 86.69±26.45, 91.06±38.9, 86.79±30.80, 92.46±27.48, 81.41±28.54 and 80.08±28.84 in moderate traumatic brain injury Whereas 97.77±18.6, 90.25±37.71, 74.86±33.75, 96.81±30.18, 85.18±31.21 and 73.39±28.549 in severe traumatic brain injury patients of age group in year 18-20,21-30,31-40,41-50,51-60 and 61-70 respectively. The finding of serum zinc level was in normal range (65-110) µg/dl in both severe and moderate traumatic brain injury patients.
.The result of our study was similar to the study carried out by Kim Hong et. al.[26], Isaev et. al. [16], Choi et. al., [17], Gower winter et. al.[13], Leveson et.al.[29], solati et. al [30] in the patients of traumatic brain injury with intracranial haemorrhage.
The serum zinc level was found significantly associated with moderate and severe TBI patients (p= 0.00001). Serum concentration interval (65-118) µg/dl was found in the maximum number of the patient moderate (144) & severe (124).The finding of the study was consistently resemble with the result of the previous study carried out by Al-Adham et .al.[31]Mohammad Rashid et.al.[32],p-value<0.046.which was observed significantly associated with GCS based severity in TBI patients. The serum zinc was found highly significant with the outcomes (p=0.00001). At Serum zinc level (65-118) µg/dl was found in maximum good recovered (144) TBI patients and death (62) patients. Death patients were also maximum at serum Zinc level (>65 µg/dl.). The finding of the study was validated similar to the study conducted by Mohammad et. Al.[32],Kim et.al. [26] p-value=0.046, which was significantly associated with six month out come after hospital discharge.
The serum level of magnesium were found in **mg/dl** , 1.8±0.23, 1.85±0.54, 1.89±0.41, 2.05±0.84, 1.88±0.38 & 2.08±0.32 in moderate Traumatic brain injury patients and 1.92±0.24, 1.81±0.4, 1.86±0.48, 1.96±0.38, 1.23±0.39 and 1.95±0.21 in Severe Traumatic brain injury patients of age group in year 18-20,21-30,31-40,41-50,51-60 and 61-70 respectively. It was observed level of magnesium in normal range (1.6-2.4)mg/dl in both moderate and severe traumatic brain injury

patients of all the categorized age group except the severe TBI patients of age group of (51-60) years where low magnesium level were observed.

The result of our study was similar the study conducted by Nayak, et. al [33] (2018), Dhandapani et al. [22], Polderman et.,al., [34]. The serum magnesium was found significantly associated with the severity i.e. moderate and severe patient (p=0.00515).The serum magnesium interval (1.6-2.4)mg/dl observed in moderate (179) & severe (153).The result of the study was similar to observation reported by Ghasemi et. al..[35]2010, Mohammad Rashid et. al.[32] which was reported significantly associated with severity in TBI patients

The serum magnesium was found highly significant with the outcomes (p=0.000001).At serum magnesium interval (1.6-2.4)mg/dl, good recovered was maximum (168) and death was (90). The result of the study were consistently resemble with finding reported by (Mohmmad et. al..[32], Nayak, et. al., [33] p-value=0.01.which was significantly associated with of outcome of six month follow up study.

In the analysis, zinc and magnesium both found significantly associated with GCS based severity of the patients. Overviews of research, association of zinc &magnesium with outcome in patients with TBI were also observed. The result was found significantly associated.

CONCLUSION

In the study of trace elements, serum zinc level (70-100)µg/dl was observed in maximum 33.4% of TBI patients. In 39.7% of TBI patients were noticed, where as in maximum 46.4% TBI patient serum magnesium level were noticed (1.51-2) mg/d. serum zinc (p=00001) and magnesium (p=0.00515) were significantly associated with severity based on GCS. The association also observed signicant With GOS based outcomes between serum zinc (p=0.00001) and magnesium (p=0.03051).

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CONFLICT OF INTEREST

The author declares that they have no any conflict of interest

Table 1: Serum level of Zinc and magnesium in severe & moderate TBI patients

Age interval Year	Zinc		magnesium	
	Moderate	Severe	Moderate	severe
18-20	86.69±26.45	97.77±18.6	1.8±0.23	1.92±0.24
21-30	91.06±38.9	90.25±37.71	1.85±0.54	1.81±0.4
31-40	86.79±30.80	74.86±33.75	1.89±0.41	1.86±0.48
41-50	92.46±27.48	96.81±30.18	2.05±0.84	1.96±0.38
51-60	81.41±28.54	85.18±31.21	1.88±0.38	1.23±0.39
61-65	80.08±28.84	73.39±28.549	2.08±0.32	1.95±0.21

Table 2: Association of severity of GCS and trance element

Variable		Moderate	Severe	Chi-square test	P-Value	Significance
Zinc	< 65 Mg/dl	30	84	35.66	0.00001	All are significant
	65-118 Mg/dl	144	124			
	> 118 Mg/dl	20	59			
Magnesium	< 1.6 mg/dl	9	94	10.537	0.00515	
	1.6-2.4 mg/dl	179	153			
	> 2.4 mg/dl	6	20			

Table 3: Association of post operative outcomes and trance

Variable		Good Recovery	Moderate Recovery	Poor Recovery	Death	Chi-square test	P-Value	Significance
Zinc	**< 65 Mg/dl**	32	7	10	65	66.66	0.00001	All are Significant
	65-118 Mg/dl	140	52	14	62			
	> 118 Mg/dl	19	9	12	39			
	90-190 Mg/dl	125	51	16	140			
Magnesium	**< 1.6 mg/dl**	16	17	6	64	58.3	0.00001	
	1.6-2.4 mg/dl	168	49	25	90			
	> 2.4 mg/dl	7	2	5	12			

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