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Effects of Hyperglycemia on Outcomes of Traumatic Brain Injury among Patients Admitted in Tertiary Level Hospital

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ABSTRACT

Various factors contribute to unfavorable outcomes of Traumatic Brain Injuries (TBI) and hyperglycemia is one of them. It occurs frequently at an early stage after having traumatic brain injuries and previous studies have identified that hyperglycemic patients encounter worse outcomes in terms of disability and death. **Objectives:** To determine the association of hyperglycemia to prognosis of traumatic brain injury patients with distinct blood glucose levels and co-morbidities. **Methods:** A cross-sectional study was conducted from June 2022 to October 2022 at Liaquat University Hospital, Hyderabad on 171 young to middle aged participants, admitted patients of TBI with GCS scores 3-13 selected through purposive sampling technique. Data were collected on a multi-sectioned questionnaire and analyzed by SPSS version 26.0. The results were analyzed by applying chi-square test at $p=\leq 0.05$ as the cut-off level of significance. **Results:** 44.4% of participants were hyperglycemic. Four times greater mortality rate was recorded in hyperglycemic patients as compared to normoglycemic patients. No patient could survive who had hyperglycemia at 72 hours of injury. Hyperglycemia at 24 hours as well as at 72 hours of TBI was significantly associated to poor prognosis ($p<0.01$). **Conclusions:** Hyperglycemia at 24 hours of injury resulted in four times greater mortality as compared to normoglycemic TBI victims, therefore blood glucose level should be maintained between 70-180 mg/dl for a favorable outcome of TBI. Moreover, patients with persistent hyperglycemia and comorbidities of hypertension, diabetes mellitus, and ischemic heart disease have shown more tragic outcomes of TBI so it should be investigated on a large scale sample size in different populations.

INTRODUCTION

Traumatic brain injuries (TBIs) are frequent cause of morbidity and mortality worldwide and a significant part of these injuries occur due to road traffic accidents [1]. TBIs are the major cause of mortality in general and particularly among young adults. In the United States of America over 64 thousand lives are lost every year because of TBIs [2, 3]. The situation is declining health status worldwide, specifically in low and middle-income countries (LMICs). Retrospective content analyses in Jakarta Indonesia reported 30.8% deaths among victims of road traffic accidents due to TBI [4, 5]. Like other LMICs, Pakistan is also suffering due to increasing burden of TBI. A tertiary care level hospital in Peshawar recorded an average of 13 hospitalizations per day due to TBIs. Another study by Uzair Yaqoob et al described that approximately 56 patients per day visit emergency department of Jinnah Postgraduate Medical Center Karachi owing to TBIs and almost 10% of these patients need hospitalization [6, 7]. There are various factors that contribute to unfavorable outcomes of TBI, and hyperglycemia is one of them. It is associated with poor prognosis of TBI and occurs frequently at early stage after having TBI [8]. A cross-sectional study at National Center of Neurological Sciences Sudan reported 66.6% deaths in traumatic brain injury patients presented with hyperglycemia [9]. Another retrospective study at a regional trauma center in Southern Taiwan recorded significantly high mortality ratio among hyperglycemic TBI patients as compared to patients with normal blood sugar

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levels [10]. In the same way Tseng *et al.*, identified that hyperglycemic traumatic brain injury patients encounter worse outcomes in terms of excessive hospital admissions, increased length of hospital stay, higher infection rates and deaths [11]. Previous studies have established hazardous role of hyperglycemia in worse clinical outcomes of TBI, hence some investigators controlled confounding factor of diabetes mellitus, while other factors contributing to poor prognosis due to hyperglycemia are not addressed [10]. No research data are available in Pakistan regarding association of hyperglycemia and its impact on outcome of TBI.

This study aims to determine association of hyperglycemia with the prognosis of traumatic brain injury and outcome among patients with distinct blood glucose levels and comorbidities. The main objective is to bridge the gap of epidemiological data concerning TBI in developing regions of the world which will ultimately help avert morbidity and mortality incurred due to hyperglycemia in TBI patients.

METHODS

A cross-sectional study was conducted during June 2022 to October 2022 at Liaquat University Hospital, Hyderabad. Research Ethics Committee and Advanced Studies and Research Board of Liaquat University of Medical and Health Sciences Jamshoro approved this study(Ref no: LUHMS/REC/-25). Informed consent was provided by patients' family members in the local language, with assurances that the study would not affect participants. Confidentiality was maintained, and all data were securely stored. The study followed standard research protocols set by the REC at LUMHS. The sample size was estimated 171 by using Raosoft calculator, based on a prevalence of poor prognosis of hyperglycemic traumatic brain injury patients (66.6%) [9], margin of error was taken as 5% and level of confidence 95%. An additional 10% was added to account for potential loss of follow-up cases. All admitted TBI patients with 3-13 GCS score in young and middle age group (15-50 years) whose family member gave permission were made part of the study. A non-probability consecutive sampling method was used to recruit participants. These individuals came from Hyderabad and nearby areas and exhibited a range of socio-demographic and clinical characteristics, including comorbidities such as type-II diabetes mellitus, cancer, liver disease, hypertension, kidney disease, and ischemic heart disease. Patients with poly trauma, associated spinal injuries, history of type-I diabetes mellitus, cerebrovascular accidents or who required cortisone or hyperglycemic medicine were excluded. A total of 171 patients of TBI were selected through purposive sampling technique. A self-developed questionnaire with information regarding socio-demographic status, physical examination findings laboratory results and outcome was administered. Blood sugar level was recorded after 24 and 72 hours of injury at minimum six to eight hours of fasting. Patients were followed till six weeks of admission or end outcome in hospital. Upon enrolment, the first two sections of the questionnaire (sections A and B) were completed by reviewing medical records and conducting interviews with the patient's family to collect socio-demographic information and the history of comorbidities. Physical examination findings were noted, including the patient's diagnosis and Glasgow Coma Scale (GCS) score which is widely regarded as a reliable and effective tool for assessing the severity of traumatic brain injuries and predicting patient outcomes. Data were recorded from the patient's file and were noted in section C of the questionnaire. The GCS score was assessed at admission and discharge by a neurosurgeon. Blood sugar levels were measured at two time points: first, after 24 hours of injury following a fasting period of 6-8 hours and then again after 72 hours. For section D of the questionnaire, patient outcomes were followed up to either discharge or death during hospitalization, or for up to six weeks after admission. The final outcome was recorded as declared by treating neurosurgeon. After data collection, all questionnaires were carefully reviewed to ensure completeness. The data were then entered into SPSS version 26.0. Descriptive statistics, including the mean and standard deviation for continuous variables such as blood glucose levels and age, were computed. For inferential analysis, chi-square tests and cross-tabulations were applied to sections B, C, and D of the questionnaire to compare the prognosis of traumatic brain injury (TBI) across different glycemic cut-offs and to identify associations. A p-value of ≤ 0.05 was considered statistically significant, ensuring robust analysis and valid conclusions drawn from the sample to infer findings for the population.

RESULTS

Mean age of the patients was 31.61 ± 9.40 SD. Young and middle-aged male encountered traumatic brain injury more frequently than female and teenagers. Peoples with good education and financial status experienced TBI regularly as compared to low income and poor literacy profile peoples as presented in table 1.

Table 1: Socio-Demographic Profile of Study Subjects

Gender Distribution	Frequency (%)
Male	138 (80.7)
Female	33 (19.3)
Other	-
Total	171 (100.0)
Age Distribution	
15-20 Years	31 (18.1)
21-35 Years	95 (55.6)
36-50 Years	45 (26.3)
Total	171 (100.0)

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Literacy Status	
Illiterate	55 (32.2)
Literate	86 (50.3)
Graduate and Above	30 (17.5)
Total	171 (100.0)
Monthly Income	
15000-25000	56 (32.7)
26000-40000	82 (48.0)
40000 and Above	33 (19.3)
Total	171 (100.0)

In general road traffic accidents at national highway and link roads caused TBIs but victims of assault and fall also got head injured as shown in figure 1.

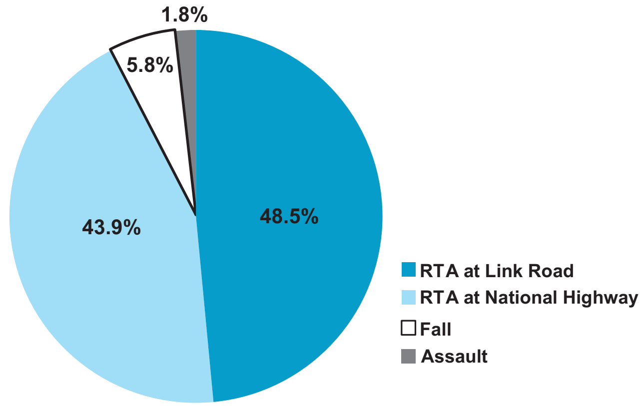

Figure 1: Mode of the Injury reported among the participants

Glycaemic status at 24 hours of injury and outcome of TBI had statistically significant association (p=0.001). Among 171 patients, hypoglycaemia detected only in 4(2.3%) patients, whereas 91(53.2%) were normoglycemic and 76(44.4%) had hyperglycaemia. Discharge from the hospital was the outcome of all hypoglycaemic patients and death occurred in 14.2% normoglycemic patients. While almost four times greater mortality rate (61%) was recorded in hyperglycaemic patients as compared to normoglycemic patients as shown in Table 2.

Table 2: Association of Distinct Blood Glucose Levels to Prognosis of Traumatic Brain Injury at 24 and 72 Hours of Injury

Category of Blood glucose level	Discharge Frequency (%)	Disability Frequency (%)	Vegetative Status Frequency (%)	Death Frequency (%)	Total Frequency (%)	p-Value
Blood Glucose Level at 24 Hours of Injury and Prognosis						
<70	4 (2.3)	0 (0)	0 (0)	0 (0)	4 (2.3)	0.001*
70-180	73 (80.2)	5 (5.4)	0 (0)	13 (14.2)	91 (53.2)	
>180	23 (30.2)	5 (6.5)	1 (1.3)	47 (61.8)	76 (44.4)	
Total	100 (58.4)	10 (5.8)	1 (0.58)	60 (35)	171 (100)	
*Significant Association df= 6 X2 value=48.5						
Blood Glucose Level at 72 Hours of Injury and Prognosis						
<70	4 (2.3)	0 (0)	0 (0)	0 (0)	4 (2.3)	0.00*
70-180	96 (67.6)	10 (7)	1 (0.7)	35 (24.6)	142 (83)	
>180	0 (0)	0 (0)	0 (0)	25 (100)	25 (14.6)	
Total	100 (58.4)	10 (5.8)	1 (0.58)	60 (35)	171 (100)	
*Significant Association df= 6 X2 value=55.9						

df=Degrees of Freedom; X2 =Chi-Square Value

Most of the patients (71.9%) had no comorbidity and experienced 31.7% death rate. Insignificant association of comorbidities to prognosis of traumatic brain injury (p=0.26) was observed. However high mortality rate was seen among patients who had hypertension (54.6%) and diabetic mellitus along with liver disease (66.6%). Most importantly, patients with diabetes mellitus and hypertension at the same time and patients with ischemic heart disease could not survive as presented in table 3.

Table 3: Association of Comorbidities to Prognosis of Traumatic Brain Injury

Comorbidity	Prognosis					p-Value
	Discharge Frequency (%)	Disability Frequency (%)	Vegetative Status Frequency (%)	DeathFrequency (%)	Total Frequency (%)	
None	73 (30)	10 (8.1)	1 (0.8)	39 (31.7)	123 (71.9)	0.26
Diabetes Mellitus	11 (68.7)	0 (0)	0 (0)	5 (31.3)	16 (9.3)	
Hypertension	5 (45.4)	0 (0)	0 (0)	6 (54.6)	11 (6.4)	
Ischemic Heart Disease	0 (0)	0 (0)	0 (0)	2 (100)	2 (1.1)	
Kidney Disease	3 (100)	0 (0)	0 (0)	0 (0)	3 (1.7)	
Liver Disease	7 (87.5)	0 (0)	0 (0)	1 (12.5)	8 (4.6)	
Cancer	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
DM+HTN	0 (0)	0 (0)	0 (0)	5 (100)	5 (2.9)	
DM+LD	1 (33.3)	0 (0)	0 (0)	2 (66.6)	3 (1.7)	
Total	100	10 (5.8)	1 (0.58)	60 (35)	(171) 100	
df=26 X^2 value=24.5						

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DISCUSSION

The results enhanced the evidential base of hyperglycaemia as an unfavourable factor that suppresses the TBI outcomes. In more detail, the identification of hyperglycaemia at 24 hours after the injury has proven that patients with blood glucose levels above 200 g/mL have four times higher mortality compared to patients with normoglycemia, which proves the significance of early glycaemic management. Moreover, sustained hyperglycaemia at 72 hours was found to predict poorer survival and no patient with hyperglycaemia was alive more than this duration. Like the results of this study Khan AA *et al.*, and Ali K *et al.*, pointed out high incidence rate of TBI among young and middle-aged male patients [12, 13]. Road traffic accidents at link roads and national highway were frequent mode of TBI but fall and assault also caused TBI in small number of patients. In the same way different studies in Kingdom of Saudi Arabia, China and Punjab were also reported road traffic incidents, falls and assault as principal reasons of TBI [13-15]. Statistically significant association (p=0.001) was witnessed between glycemic status at 24 hours of injury and outcome of the TBI. Hyperglycemic patients experienced four times greater mortality rate (61%) as compared to normoglycemic patients (14.2%). Similarly with a little difference a retrospective study in Taiwan reported six times high mortality ratio among TBI patients with raised blood sugar level [10]. Another study at National Centre of Neurological Sciences Sudan demonstrated 66.6% increase in death rate due to hyperglycemia in TBI [9]. Furthermore, 53% of the hyperglycaemic patients showed sever TBI as compared to those having normal blood glucose level [16]. Additionally significant association (p=0.00) between glycemic status at 72 hours of injury and outcome of TBI was noticed. Patients with hypertension and diabetes mellitus at the same time and patients with ischemic heart disease could not survive as shown in table 3. Similarly, Ahmadi N et al concluded greater mortality risk due to cardiovascular problems in patients with mild traumatic brain injury [17]. In addition, Shibahashi K *et al.*, described an upsurge in mortality graph among admitted congestive heart failure patients [18]. On the other hand, majority of the studies examining hypertension did not established significant association to mortality, even one study recorded a decrease in short-term mortality among hypertensive older adults with TBI, due to consumption of beta-blockers which is a commonly recommended antihypertensive medicine [18-19]. Concerning outcome of diabetic patients after having TBI this study found lower mortality rate. In contrast to our study findings, Tsai YU *et al.*, described statistically significant higher adverse outcomes in terms of mortality among TBI patients with diabetic hyperglycemia [20]. Nevertheless, the present study has limitations that should be considered even though it has supplied promising data for the link between hyperglycaemia and TBI outcomes. First, the study was a hospital-based study with few participants. Therefore, the study's findings cannot be generalized to other healthcare settings or populations. Moreover, the effects of other co-variables like pre-hospital care, treatment modalities, and the patient's nutritional status have not been otherwise controlled.

CONCLUSIONS

Generally young and middle-aged people get traumatic brain injury and experience adverse outcomes. Road traffic accidents at link roads and national highway predominantly remained principal reasons to TBIs and deaths. Hyperglycemia at 24 hours of injury resulted in four times greater mortality as compared to normoglycemia among TBI victims, therefore blood glucose level should be maintained between 70-180 mg/dl for favorable outcome. Following TBI, high mortality rate was seen in patients who had diabetes mellitus, hypertension and ischemic heart disease, hence TBI patients with comorbidities of hypertension, ischemic heart disease and diabetes mellitus should be investigated further. Furthermore, integrated management protocols should support the early identification of hyperglycemic patients with TBI in emergency and intensive care units.

Authors Contribution

Conceptualization: RA
Methodology: RA, IAS
Formal analysis: KNM
Writing, review and editing: FS, IAS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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