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Hyperglycemia as Prognostic Factor in Pediatric Traumatic Brain Injury in Emergency Hospital Mansoura University

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ABSTRACT

Background: Blood glucose possesses all properties of an ideal serum marker of systemic injury. It is highly sensitive for cerebral cellular injury secondary to head trauma. Although the pathophysiology of hyperglycemia's neuropathic effect is not entirely clear, it has been reported that it aggravates ischemic acidosis, which in turn worsens brain edema.

Objective: To determine the relationship of blood glucose elevation to outcome in pediatric traumatic brain injury to improve the management of polytrauma patients.

Patients and methods: This was a prospective study conducted over 100 pediatric patients with traumatic brain injury admitted to Emergency Hospital Mansoura University over a year from December 2020 to December 2021.

Results: There were statistically significant correlations between ICU length of stay (LOS) and Glasgow Coma Scale (GCS) score (either on admission or on discharge) and random blood glucose (RBG) and fasting blood glucose (FBG). However, there were statistically significant correlations between hospital LOS and GCS (on discharge only) and RBG and FBG. Random blood sugar (RBS) could be considered as positive significant predictor, while GCS on admission could be used as negative significant predictor of death among studied cases. RBG and FBG could be used as significant predictors of death among studied cases with high sensitivity, specificity, and accuracy of RBS and moderate sensitivity, specificity, and accuracy of FBS.

Conclusion: In the context of pediatric populations, the current study suggested that hyperglycemia at an early stage could be used as a reliable predictor of the outcome of head trauma and its prognosis. A higher blood glucose level may be a threatening sign that predicts a poor prognosis and an increased risk of death.

Keywords: FBG, GCS, Hyperglycemia, Pediatric Traumatic Brain Injury, RBG.

INTRODUCTION

Traumatic brain injury (TBI) affects approximately 500 000 children under 14 years of age annually, resulting in approximately 35 000 hospitalizations and over 2000 deaths. The majority of moderate and severe cases are admitted to the hospital and require intensive care unit (ICU) level care [(1)]. Pediatric TBI is complicated by the fact that this population is dynamically changing as a part of normal maturation with unique cerebral developmental milestones in infancy, as toddlers, young children, and as adolescents [(2)]. There are significant developmental changes in skull properties, head size, neck musculature, brain water content, myelination, hormones, and synaptic connectivity throughout the pediatric time period [(3)]. TBI introduced during each of these different cerebral developmental phases will produce differential pathologies, impairments, and recoveries. Pediatric TBI is further complicated by the fact that the types of TBI injuries sustained varies with age, and this will influence, severity/pathology, response to injury, and recovery profiles [(4)].

The care of hospitalized children with traumatic brain injury requires a multidisciplinary team, including emergency physicians, critical care physicians, trauma and/or neurosurgeons, and child neurologists. There is increasing recognition that a cooperative program which implements best practices for the management of these patients can have a significant effect on outcomes [(5)].

In recent years, efforts have been made to search for predictors of poor prognosis in children with moderate to severe TBI to allow for early intervention and treatment so as to reduce morbidity and mortality [(6)]. This is especially relevant in pediatrics, due to the varied and nonspecific complaints among head-injured children. Age, Glasgow Coma Scale (GCS), accidental hypothermia, hyperglycemia, and coagulation disorders are reported to be independent prognostic factors for mortality[(7)]. Hyperglycemia occurs frequently in the pediatric traumatic brain injury (TBI) population [(7)]. It has been reported to be present within the first 12 hours of trauma in up to 44% of patients with moderate to severe TBI [(8)]. Hyperglycemia has been demonstrated to be associated with increased mortality, prolonged mechanical ventilation and length of stay (LOS) in the pediatric intensive care unit (PICU) in children with moderate to severe TBI [(7)]. In addition, hyperglycemia within the first 48 hours of admission was reported as an independent risk factor for mortality in children with severe TBI [Glasgow Coma Scale (GCS) score ≤8] [(9)].

The aim of this study was to determine the relationship between blood glucose elevation and outcome in pediatric traumatic brain injury to improve the management of polytrauma patients at Emergency Hospital Mansoura University.

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PATIENTS AND METHODS

This was a prospective study conducted over a total of 100 pediatric patients with traumatic brain injury and were admitted to Emergency Hospital Mansoura University over a year from December 2020 to December 2021. Emergency Hospital Mansoura University is a level one trauma center with about 250,000 visit and 25,000 trauma cases per year.

Inclusion criteria: Patients with traumatic brain injuries younger than 18 years old, and moderate to severe TBI (GCS ≤13).

Exclusion criteria: Recognized pre-injury diagnosis of diabetes mellitus.

All patients were subjected to:

1. **Resuscitation of the patient to prevent secondary brain injury:**
   - **Airway maintenance and cervical spine immobilization:** The head-tilt/chin-lift and jaw-thrust were used in unconscious individuals for preventing the tongue from obstructing the upper airway.
   - **Breathing and ventilation:** Look, listen and feel for the general signs of respiratory distress: sweating, central cyanosis, use of the accessory muscles of respiration, and abdominal breathing.
   - **Circulation and control of hemorrhage:** Assessment of hypovolemia and capillary refill time were performed followed by establishment of venous line and replacement of fluids and blood transfusion if needed.
   - **Disability:** All the pervious maneuvers were re-assessed again-neurological status and Glasgow coma scale (GCS) were performed. Assessment of pupillary size and check for history of ingestion of depressant drugs were also carried out.
   - **Exposure / environmental control:** Full exposure of the body was also performed to examine the patient in a proper manner.
2. **History taking by AMPLE history:** A = Allergies, M = Medication currently used, P = Past illnesses / Pregnancy, L = Last meal, and E = Events / Environment related to injury.
3. **Clinical Examination and 2ry survey:** Vital signs (Arterial blood pressure, Temperature, pulse, respiratory rate), Glasgow coma scale (GCS), and complete general examination.
4. **Assessment of glycemic state:** Admission serum glucose (in milligrams per deciliter). Follow up fasting blood glucose and postprandial blood glucose on 3rd day of hospital stay, and fasting blood glucose on discharge.
5. **Laboratory investigations:** Complete blood count (CBC), international normalized ratio (INR), ABO grouping, and serum creatinine.
6. **Radiological investigations:**
   - FAST (Focused Assessment with Sonography for Trauma): The machine used was LOGIQ P5 model to identify the presence of hemoperitoneum in a patient with suspected intraabdominal injury.
   - X-ray (chest, pelvis, lumbosacral spine and cervical spine).
   - Multi-slice CT brain:
     a) By using Toshiba scanner Aquilion Prime TSX-303A (164-MCCT scanner) with reconstruction at 0.5 mm slice thickness.
     b) To identify any of the following lesions: Fissure fractures of the skull. Depressed fracture of the skull. Brain edema. Diffuse axonal injury (DAI). Subarachnoid hemorrhage (SAH). Extradural hematoma (EDH). Intra-ventricular hemorrhage (IVH). Intracerebral hematoma (ICH), and brain contusion and laceration.

Ethical consideration:

An approval of the study was obtained from Mansoura University Academic and Ethical Committee. The research objectives were explained to the participants' care givers individually and in groups. Informed written consent was obtained from each participant's care giver sharing in the study. Confidentiality and personal privacy were respected in all levels of the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data were fed to the computer and analyzed using IBM SPSS Corp. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Qualitative data were described using number and percent. Quantitative data were described using median (Range) and mean ± standard deviation (SD) for parametric data after testing normality using Kolmogorov-Smirnov test. Significance of the obtained results was judged at the (0.05) level. Monte Carlo test was used for comparison of qualitative data. Independent Student t-test was used to compare parametric quantitative data. Mann-Whitney U test was used to compare nonparametric quantitative data. The Spearman's rank-order correlation was used to determine the strength and direction of a linear relationship between two non-normally distributed continuous variables and/or ordinal variables. The accuracy of a test to discriminate diseased cases from non-diseased cases was evaluated using Receiver Operating Characteristic (ROC) curve analysis. Adjusted odds ratios and their 95% confidence interval were calculated.

RESULTS

Demographic characteristics of the studied cases are demonstrated in table 1.

Table (1): Demographic characteristics of the studied cases

	N=100	%
Age/years mean±SD	8.24±5.53	
Sex Male Female	 75 25	 75.0 25.0

Mode of trauma could be used as prognostic factor of long ICU stay duration among pediatric cases with traumatic brain injury, while associated fracture are not, as demonstrated in table 2.

Table (2): Relation between both mode of trauma and associated Injuries and long ICU stay duration among pediatric cases with traumatic brain injury

	Total number	ICU LOS <4 days N=60	ICU LOS ≥4 days N=40	P
Mode of trauma N (%) RTA FTG FFH FDS Direct head trauma	 45 10 22 8 15	 21 (46.7) 10 (100) 14 (63.6) 4 (50) 11 (73.3)	 24 (53.3) 0 8 (36.4) 4 (50) 4 (26.7)	 P=0.021*
Associated Injuries N (%) None Orthopedic fracture Lung contusion Abdominal hemorrhage	 63 15 8 14	 41 (65.1) 8 (53.3) 4 (50.0) 7 (50.0)	 22 (34.9) 7 (46.7) 4 (50) 7 (50)	 P=0.599

RTA: Road traffic accident. RTA: Road traffic accidents. FFH: Fall from height. FDS: Falling Stairs. FTG: Falling to ground, *: Statistically significant

Mode of trauma and associated injuries could not be used as prognostic factors of long hospital stay duration among pediatric cases with traumatic brain injury as demonstrated in table 3.

Table (3): Relation between both mode of trauma and associated injuries and long hospital stay duration among pediatric cases with traumatic brain injury

	Total number	Hospital LOS <10 days N=53	Hospital LOS ≥10 days N=47	P
Mode of trauma N (%) RTA FTG FFH FDS Direct head trauma	 45 10 22 8 15	 22 (48.9) 6 (60.0) 10 (45.5) 5 (62.5) 10 (66.7)	 23 (51.1) 4 (40) 12 (54.5) 3 (37.5) 5 (33.3)	 0.659
Associated Injuries N(%) None Orthopedic fracture Lung contusion Abdominal hemorrhage	 63 15 8 14	 38 (60.3) 4 (26.7) 4 (50) 7 (50)	 25 (39.7) 11 (73.3) 4 (50) 7 (50)	 0.132

The mean RBG and FBG were are demonstrated in table 4.

Table (4): Laboratory findings among studied cases

	N=100
RBG mean±SD Median	213.97±7.37 180
FBG mean±SD Median	 134.15±8.52 119

Twenty one out of the studied cases have developed sepsis of which 16 cases died. The mean ICU LOS, hospital LOS, GCS on admission and GCS on discharge are demonstrated in table 5.

Table (5): Outcome among studied cases

	N=100	%
Sepsis	21	21.0
Died	16	16.0
ICU LOS /days mean±SD Median (range)	6.66±7.51 4 (1-30)	
Hospital LOS/days mean±SD Median (range)	15.24±13.75 10 (3-60)	
GCS on admission mean±SD Median (range)	9.59±2.79 10 (4-13)	
GCS on discharge mean±SD Median (range)	14.17±1.55 15 (10-15)	

RBG, FBG, GCS on admission and GCS on discharge could be used as significant prognostic factors of sepsis among pediatric cases with traumatic brain injury as demonstrated in table 6.

Table (6): Correlation between RBS, FBS, GCS on admission and GCS on discharge and sepsis among pediatric cases with traumatic brain injury

	Total number	No sepsis N=79	Sepsis N=21	P
RBG	100	207.61±80.77	237.90±58.58	0.111
FBG	100	128.89±49.53	153.90±39.59	0.035*
GCS on admission	100	9.95±2.61	8.24±3.06	0.012*
GCS on discharge	100	14.61±1.21	12.41±1.54	<0.001*

Data are presented as mean±SD, *: Statistically significant

RBG, FBG and GCS on admission could be used as significant prognostic factors of death, while GCS on discharge not as demonstrated in table 7.

Table (7): Correlation between RBS, FBS, GCS on admission and GCS on discharge and death among pediatric cases with traumatic brain injury

	Total number	Alive N=64	Dead N=16	P
RBG	100	196.20±65.54	307.25±58.55	<0.001*
FBG	100	128.56±7.39	13.50±3.95	0.008*
GCS on admission	100	10.37±2.21	5.50±1.71	<0.001*
GCS on discharge	100	14.17±1.55	NA	….

Data are presented as mean±SD, *: Statistically significant

RBG, FBG and GCS on admission and could be used as significant prognostic factors for long ICU stay duration as demonstrated in table 8.

Table (8): Correlation between RBS, FBS, GCS on admission and GCS on discharge and long ICU stay duration among pediatric cases with traumatic brain injury

	Total number	ICU LOS <4 days N=60	ICU LOS ≥4 days N=40	P
RBG	100	189.10±37.83	251.28±103.21	<0.001*
FBG	100	117.28±29.95	159.45±9.37	0.008*
GCS on admission	100	10.12±2.34	8.80±3.21	0.02*
GCS on discharge	100	14.88±0.32	13.0±2.0	<0.001*

Data are presented as mean±SD, *: Statistically significant

RBG, FBG and could be used as significant prognostic factors for long hospital stay duration, while GCS on admission not as demonstrated in table 9.

Table (9): Relation between RBS, FBS, GCS on admission and GCS on discharge and long hospital stay duration among pediatric cases with traumatic brain injury

	Total number	Hospital LOS <10 days N=53	Hospital LOS ≥10 days N=47	P
RBG	100	189.09±51.59	242.02±91.43	<0.001*
FBG	100	114.04±3.89	156.83±5.74	<0.001*
GCS on admission	100	9.75±2.99	9.40±2.56	0.533
GCS on discharge	100	14.83±0.54	13.53±1.91	<0.001*

Data are presented as mean±SD, *: Statistically significant

There were statistically significant correlations between ICU LOS and GCS (either on admission or on discharge) and RBG and FBG. However, there were statistically significant correlations between Hospital LOS and GCS (on discharge only) and RBG and FBG as demonstrated in table 10.

Table (10): Correlation between ICU and hospital stay duration and GCS and RBG and FBG

	ICU LOS		Hospital LOS	
	r	P	r	P
GCS on admission	-0.355	<0.001*	-0.022	0.828
GCS on discharge	-0.646	<0.001	-0.419	<0.001*
RBG	0.304	0.002*	0.288	0.004*
FBG	0.453	<0.001*	0.397	<0.001*

RBG and FBG could be used as significant predictors of death among studied cases (cut off =252.5 and 130 respectively). Sensitivity, specificity, PPV, NPV and accuracy of RBS are demonstrated in table 11.

Table (11): Validity of RBG and FBG in predicting death among studied cases

	AUC (95%CI)	P value	Cut off point	Sensitivity %	Specificity %	PPV %	NPV%	Accuracy %
RBG	0.923 (0.869-0.976)	<0.001*	252.50	75.0	89.3	57.1	94.9	87.0
FBG	0.726 (0.607-0.845)	0.004*	130	75.0	63.1	27.9	93.0	65.0

AUC: Area under curve, PPV: Positive predictive value NPV: Negative predictive value

RBS could be considered as positive significant predictor, while GCS on admission could be used as negative significant predictor of death among studied cases as demonstrated in table 12.

Table (12): Predictors of death among studied cases

	β	P value	AOR (95%CI)
RBG	0.02	0.049*	1.45(1.04-1.98)
FBG	-0.028	0.09	0.972(0.941-1.004)
GCS on admission	-0.579	0.001*	0.561(0.398-0.789)
Overall % predicted= 85.0			

AOR: Adjusted odds ratio

DISCUSSION

As regards the demographic features the current study demonstrates that; the mean age of the studied cases was 8.24, while male to female ratio was 75/25.

The present study reported that RTA was the most common mode of trauma, followed by FFH and direct head trauma then FTG and lastly FDS. In addition, the majority of the studied cases had no associated injuries (63%), while orthopedic fracture, lung contusion and abdominal hemorrhage were recorded in 15%, 8% and 14% of cases respectively. In agreement, **Danisman *et al.*** [10] have reported that; the most common causes of isolated head trauma were out-of-vehicle traffic accident (37%) and falls (30%).

The current study demonstrated that the mean GCS on admission was 10 ranging from 4 to 13 and the mean±SD was 9.59±2.79. This came in accordance with several studies who have reported that the mean GCS on admission was 11 [10- 12]. On the contrary, **Chong *et al.*** [7] conducted a retrospective cohort study in a tertiary pediatric hospital between 2003 and 2013. They have reported a lower GCS in which median GCS and pediatric trauma scores were 7 and 4, respectively[7].

With regard to laboratory findings the current study demonstrated that the mean±SD RBG and FBG were 213.97±77.37 and 134.15±48.52 respectively. Concerning outcomes, the current study reported that 21 out of the studied cases have developed sepsis of which 16 cases died. The mean±SD ICU LOS, hospital LOS, GCS on admission and GCS on discharge were 6.66±7.51 15.24±13.75, 10 and 15 respectively.

Mortality and morbidity of head trauma may be due to the direct injury produced by the trauma itself on one side, and due to ischemia and hypoxia secondary to head trauma on the other [13]. These effects include traumatic ischemia, infarction, cardiorespiratory dysfunction, secondary hemorrhages, diffuse cerebral edema, and hypoxic ischemia mediated by neuromediators released by body in response to trauma [14]. In addition, it should also be kept in mind that brain injury secondary to head trauma may lead to impaired systemic hemostasis and organ dysfunction [10].

Essentially, the current study demonstrated that, age and sex could not be significant prognostic factors for sepsis, death as well as long hospital or ICU stay duration. In addition, mode of trauma as well as associated injuries could be used as significant prognostic factors for sepsis as well as death. In addition, mode of trauma could be used as significant prognostic factor for long ICU stay duration only.

In the context of correlation between ICU and hospital stay duration and GCS and RBG and FBG, the current study reported that; there were statistically significant correlations between ICU LOS and GCS (either on admission or on discharge) and RBG and FBG. However, there were statistically significant correlation between hospital LOS and GCS (on discharge only) and RBG and FBG (OR for ICU LOS were -0.355, -0.646, 0.304 and 0.453 as regards GCS on admission, GCS on discharge, RBG and FBG respectively) (OR for hospital LOS were -0.022, -0.419, 0.288 and 0.397 as regards GCS on admission, GCS on discharge, RBG and FBG respectively).

In the same line, **Danisman *et al.*** [10] have displayed that; there was a significant negative correlation between blood glucose level and GCS ($p < 0.05$). A significant correlation in the negative direction was observed between GCS and blood glucose level ($r = -0.658$, $p < 0.05$).

Similarly, **Cochran *et al.*** [15] conducted their study on trauma patients admitted during a single year to their regional pediatric referral center with head regional Abbreviated Injury Scale scores ≥ 3. They have illustrated that patients who died had significantly higher admission serum glucose values than those patients who survived (267 mg/dL vs. 135 mg/dL; $p < 0.001$). Admission serum glucose ≥ 300 mg/dL was uniformly associated with death. Admission Glasgow Coma Scale score (Odds ratio, 0.560; 95% confidence interval, 0.358-0.877) and serum glucose (Odds ratio, 1.013; 95% confidence interval, 1.003-1.023) are independent predictors of mortality in children with traumatic head injuries.

Likewise, **Chong *et al.*** [7] have displayed that; initial hyperglycemia was associated with death (37% in the hyperglycemia group versus 8% in the normoglycemia group), reduced median PICU-free days (6 days versus 11 days), and reduced median ventilation-free days (8 days versus 12 days). This association was however not significant in the stratified analysis of patients with GCS ≤ 8. Thus, they concluded that early hyperglycemia is associated with increased mortality, prolonged duration of mechanical ventilation, and PICU stay in children with TBI.

Similarly, **Rovlias *et al.*** [16], in a study with 267 patients with head trauma and a GCS of 3–13, demonstrated that clinical course was worse in patients with a blood glucose level greater than 200 mg/dl. **Chiaretti *et al.*** [17] reported that 87.5% of cases with

head trauma and a GCS below 8 had a high blood glucose level.

Moreover, **Babbitt *et al.*** [18] showed that hyperglycemia was related to intracranial injury in younger children. The study results revealed that the median glucose level was 177 mg/dl in the severe head trauma group and 233 mg/dl in the patients who died. In addition, there was a negative correlation between blood glucose level and GCS. That is, GCS dropped as blood glucose level increased. The blood glucose levels have been lower than those reported in previous studies since we drew blood samples within three hours of admission. In agreement with the literature, the study demonstrated a parallel worsening in brain injury with elevating blood glucose level. Hyperglycemia may increase mortality by augmenting brain edema and hypoxia.

This came in accordance with a study on a total of 50 children with head injury who were evaluated in an attempt to establish a correlation between post-traumatic hyperglycemia and long-term outcome. In all the patients, the blood glucose level was measured on admission and on the days following the trauma (threshold of normal value set at 150 mg/dl). Hyperglycemia was seen more frequently in children with severe head injury than in those with mild and moderate head injury. It was present in 87.5% of the patients with a Glasgow Coma Score (GCS) ≤ 8 (the average blood glucose level on admission was 237.8±92 mg/dl), in 60% of the patients with a GCS of 9-12 (178±78.7 mg/dl) and only in 25% of those with a GCS of 13-15 (131.5±39 mg/dl). A close correlation was also seen between the outcome and the blood glucose level. Finally, hyperglycemia persisted beyond the first 24 hours after trauma in all the children who died or who survived with a poor outcome. Hyperglycemia, and especially its persistence over time, appears to be an important negative prognostic factor in children with head injury[17].

The current study reported that; RBS could be considered as positive significant predictor, while GCS on admission could be used as negative significant predictor of death among studied cases. In addition, RBG and FBG could be used as significant predictors of death among studied cases (cut off =252.5 and 130 respectively). Sensitivity, specificity, PPV, NPV and accuracy of RBS were 75%, 89.3%, 57.1%, 94.9% and 87% respectively, while sensitivity, specificity, PPV, NPV and accuracy of FBS were 75%, 63.1%, 27.9%, 93% and 65% respectively.

Likewise, **Melo *et al.*** [19] conducted a retrospective cross-sectional study on children with severe TBI (GCS ≤8) whose mean age was 7 years. They have demonstrated that; hyperglycemia ≥200 mg/dL is an independent predictor for mortality—OR 6.14 (95% CI 2.25–16.73). In the same line, **Cochran *et al.*** [15] have illustrated that; admission glucose had adjusted OR for head-injury related death of 1.01 (95% CI 1.003–10.23). Also, **Smith *et al.*** [20] have displayed that; mean glucose concentrations in the early period (<48 hours) were similar in children with favorable and unfavorable outcomes. Hyperglycemia in the late period (49–168 hours) was associated with unfavorable outcome at 6 months. In addition, **Elkon *et al.*** [21] have found that; severe blood glucose elevation (blood glucose >200 mg/dL) had increased adjusted OR of 3.5, compared with mild glucose elevation (glucose 110–160 mg/dL). Similarly, **Seyed Saadat *et al.*** [22] have illustrated that persistent hyperglycemia during the first 2 and first 3 days had adjusted ORs for mortality of 2.84 (95% CI 0.89–9.06) and 11.11 (95% CI 2.95–41.71), respectively.

CONCLUSION

In the context of pediatric populations, the current study suggested that hyperglycemia at an early stage could be used as a reliable predictor of the outcome of head trauma and its prognosis. A higher blood glucose level may be a threatening sign that predicts a poor prognosis and an increased risk of death. In addition, low GCS could be used as a reliable predictor of the severity of head trauma and its prognosis.

RECOMMENDATIONS

Utilization of hyperglycemia as a reliable predictor of the outcome of head trauma as well as its prognosis. Measuring RBG routinely in the emergency department in head trauma patients.

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REFERENCES

1. **Guilliams K, Wainwright M (2016):** Pathophysiology and management of moderate and severe traumatic brain injury in children. Journal of Child Neurology, 31(1): 35-45.
2. **Ryan N, Catroppa C, Godfrey C *et al.* (2016):** Social dysfunction after pediatric traumatic brain injury: a translational perspective. Neuroscience & Biobehavioral Reviews, 64: 196-214.
3. **Vasung L, Turk E, Ferradal S *et al.* (2019):** Exploring early human brain development with structural and physiological neuroimaging. Neuroimage, 187: 226-254.
4. **Prins M (2017):** Glucose metabolism in pediatric traumatic brain injury. Child's Nervous System, 33(10): 1711-1718.
5. **Hussain E (2018):** Traumatic brain injury in the pediatric intensive care unit. Pediatric Annals, 47(7): 274-279.
6. **Araki T, Yokota H, Morita A (2016):** Pediatric traumatic brain injury: characteristic features, diagnosis, and management. Neurologia Medico-Chirurgica RA., 57: 82-93.

7. **Chong S, Harjanto S, Testoni D *et al.* (2015):** Early hyperglycemia in pediatric traumatic brain injury predicts for mortality, prolonged duration of mechanical ventilation, and intensive care stay. International Journal of Endocrinology, 4: 1-4.
8. **Fu Y, Chong S, Lee J *et al.* (2017):** The impact of early hyperglycaemia on children with traumatic brain injury. Brain Injury, 31(3): 396-400.
9. **Khajavikhan J, Vasigh A, Kokhazade T *et al.* (2016):** Association between hyperglycaemia with neurological outcomes following severe head trauma. Journal of Clinical and Diagnostic Research, 10(4): 11-15.
10. **Danisman B, Yilmaz M, Isik B *et al.* (2015):** Analysis of the correlation between blood glucose level and prognosis in patients younger than 18 years of age who had head trauma. World Journal of Emergency Surgery, 10(1): 1-4.
11. **Işık H, Bostancı U, Yıldız Ö *et al.* (2011):** Retrospective analysis of 954 adult patients with head injury: an epidemiological study. Turkish Journal of Trauma and Emergency Surgery, 17(1): 46-50.
12. **Kavalci C, Aksel G, Salt O *et al.* (2014):** Comparison of the Canadian CT head rule and the New Orleans criteria in patients with minor head injury. World Journal of Emergency Surgery, 9(1): 1-5.
13. **Şahin S, Doğan Ş, Aksoy K (2002):** Childhood head traumas. Journal of Uludag University Faculty of Medicine, 28(2): 45-51.
14. **Kihtir T, Kihtir S (2005):** Trauma Treatment Systems. In: Ertekin C, Taviloglu K, Guloglu R, Kurtoglu M (eds). Trauma. Istanbul: Istanbul Medical Publishing. Pp. 65-71. https://www.tgcd.org.tr/wp-content/uploads/dosyalar/toraks-travmasi.pdf
15. **Cochran A, Scaife E, Hansen K *et al.* (2003):** Hyperglycemia and outcomes from pediatric traumatic brain injury. Journal of Trauma and Acute Care Surgery, 55(6): 1035-1038.
16. **Rovlias A, Kotsou S (2000):** The influence of hyperglycemia on neurological outcome in patients with severe head injury. Neurosurgery, 46(2): 335-342.
17. **Chiaretti A, De Benedictis R, Langer A *et al.* (1998):** Prognostic implications of hyperglycaemia in paediatric head injury. Child's Nervous System, 14(9): 455-459.
18. **Babbitt C, Halpern R, Liao E *et al.* (2013):** Hyperglycemia is associated with intracranial injury in children younger than 3 years of age. Pediatric Emergency Care, 29(3): 279-282.
19. **Melo J, Di Rocco F, Blanot S *et al.* (2010a):** Acute hyperglycemia is a reliable outcome predictor in children with severe traumatic brain injury. Acta Neurochirurgica, 152(9): 1559-1565.
20. **Smith R, Lin J, Adelson P *et al.* (2012):** Relationship between hyperglycemia and outcome in children with severe traumatic brain injury. Pediatric Critical Care Medicine,13(1): 85-89.
21. **Elkon B, Cambrin J, Hirshberg E *et al.* (2014):** Hyperglycemia: an independent risk factor for poor outcome in children with traumatic brain injury. Pediatric Critical Care Medicine, 15(7): 623-631.
22. **Seyed Saadat S, Bidabadi E, Seyed Saadat S *et al.* (2012):** Association of persistent hyperglycemia with outcome of severe traumatic brain injury in pediatric population. Child's Nervous System, 28(10): 1773-1777.