



## Blood Glucose Level as a Predictor of Abnormal Brain Computed Tomography Scan Findings in Patients with Mild Traumatic Brain Injury

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Received: December 22, 2022

Revised: March 09, 2023

Accepted: March 09, 2023

### ABSTRACT

**Objective:** This study aimed to investigate blood glucose levels in patients with brain injury caused by mild traumatic brain injury (TBI) as a foundation for determining whether these patients need a brain CT scan or not.

**Methods:** This cross-sectional study was conducted on patients with mild TBI, who were referred to the emergency department from March 1, 2022, to September 1, 2022. After the confirmation of mild TBI by an emergency medicine specialist, blood samples were taken from the patients to measure blood glucose levels. Then a brain CT scan was performed, and blood glucose levels were compared between patients with and without CT indications of brain injury. A checklist was used to collect data, and the data were analyzed using SPSS software (version 23).

**Results:** In the CT scans of the 157 patients included in the study, 30 patients (19.2%) had a brain injury in the CT scan. The mean blood glucose level was significantly higher in patients with brain injury, especially in the presence of vertigo and ataxia, than patients without brain injury in the CT scan ( $p < 0.0001$ ). There was a significant positive correlation between age and blood glucose level ( $r = 0.315$ ,  $p < 0.0001$ ).

**Conclusion:** Patients with mild TBI who had signs of brain injury in the CT scan had significantly higher blood glucose levels than patients with normal CT scan findings. Although indications for performing a brain CT scan are usually based on clinical criteria, blood glucose levels can be helpful in determining the requirement for a brain CT scan in patients with mild TBI.

**Keywords:** Blood glucose; Emergency department; Glasgow coma scale; Brain injury.

Please cite this paper as:

Torabi M, Amiri ZS, Mirzaee M. Blood Glucose Level as a Predictor of Abnormal Brain Computed Tomography Scan Findings in Patients with Mild Traumatic Brain Injury. *Bull Emerg Trauma*. 2023;11(2):83-89. doi: 10.30476/BEAT.2023.97582.1408.

## Introduction

Traumatic brain injury (TBI) is defined as brain functional or pathological changes caused by an external force. The prevalence of mild TBI (Glasgow Coma Scale; [GCS]=13-15) varies between 70% and 80% [1, 2]. Mild TBI was formerly assumed to be a benign and self-limiting condition, but it has now been proven that it can cause irreversible complications and persistent debilitating symptoms, highlighting the importance of paying attention to this condition [3].

The overuse of brain CT scanning can result in unnecessary radiation exposure and impose a great financial burden on healthcare systems [4]. Using a guideline for requesting brain CT scanning can thus eliminate unnecessary procedures and aid in the detection of patients with more severe injuries [5]. In patients with mild TBI, the decision for performing a brain CT scan is primarily based on clinical findings. The Canadian CT Head Rule, one of the seven clinical rules, provides a highly sensitive (98.4%) decision-making tool, according to which only 54% of patients with moderate TBI need to have CT scanning of the brain. Although the adoption of this rule greatly enhances the emergency management of patients with mild head injuries, its decision-making specificity is still moderate (49.6%), necessitating the use of other techniques to increase specificity [6].

In general, TBI-induced brain injury is classified into two types: primary and secondary. Primary injuries are triggered by physical traumas to the head, resulting in the compression and shearing of adjacent tissues, with or without loss of consciousness. Secondary injuries are complex and occur within hours to days following primary trauma, including cranial and systemic complications. TBI systemic complications include hypoxemia, hypotension, hypertension, hypoglycemia, and hyperglycemia, the latter of which can occur through different mechanisms, including stress-induced gluconeogenesis, hypermetabolism, and insulin resistance; systemic inflammatory response syndrome (SIRS), which causes the release of cytokines by inflammatory cells and the adrenocorticotrophic hormone by the pituitary gland, contributing to insulin resistance; pre-traumatic diabetes, and pituitary gland and hypothalamus dysfunction. The poor prognosis and clinical outcomes of patients who develop hyperglycemia after head traumas [7-9] may be attributed to post-traumatic pathological brain injuries. Consequently, in patients with mild head traumas, hyperglycemia may be a helpful predictor of the need for a brain CT scan [10].

The present study was conducted to determine blood glucose levels in patients with brain injury caused by mild TBI, who were referred to the emergency department, to decide whether a brain CT scan for these patients was necessary.

## Material and Methods

This cross-sectional study was conducted on patients with mild TBI who were referred to the emergency department of the Shahid Bahonar Hospital (Kerman, Iran), a level-two trauma center located in the southeast of Iran. The inclusion criteria were age over 16 years, being referred to the emergency department for mild TBI (GCS=13-15), and undergoing a brain CT scan. The exclusion criteria were the GCS less than 13, age<16 years, history of diabetes, requiring emergency surgery, suffering from penetrating head traumas, having multiple abdominal and chest traumas, developing shock, history of drug abuse, alcohol dependence, prior history of brain injury, and seizures.

The data were collected over six months from March 1, 2022, to September 1, 2022. After confirming the diagnosis of mild TBI by an emergency medicine specialist, blood samples were taken from the patients via a safe venous path. The samples were subsequently sent to the laboratory of the hospital for blood glucose level measurement. The patients underwent pulse oximetry, cardiac monitoring, and non-invasive blood pressure measurement. A brain CT scan was then performed, and the results were interpreted by a radiologist. Patients' data comprised demographic information, clinical symptoms, and brain CT scan findings, which were recorded on a checklist by a physician. Based on CT scan findings, the patients were divided into two groups: those with and those without brain injury. Finally, blood glucose level was measured in both groups. Based on neurosurgery consultation, if the patient required a second brain CT scan, the serum glucose level was measured again. Age, sex, clinical symptoms, CT scan findings, and blood glucose level were all recorded into a checklist.

### Statistical Analysis

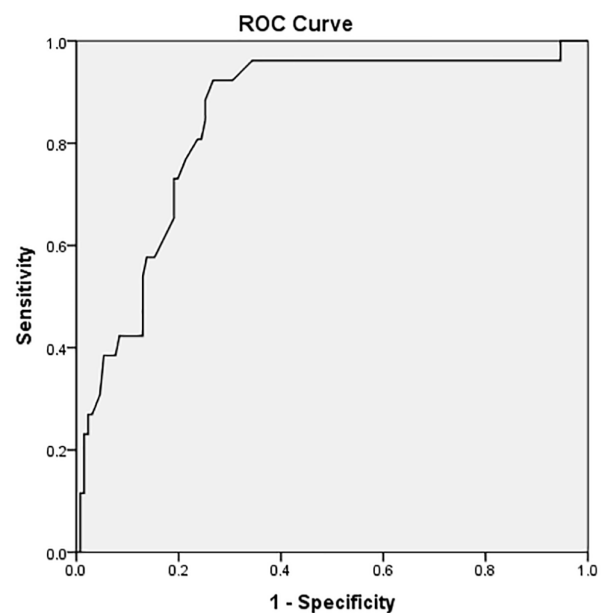
The data were analyzed using SPSS software, version 23.0 (SPSS Inc., Chicago, IL, USA). The quantitative variables were expressed as mean±SD, and qualitative variables were expressed as frequency (percentage). The Mann-Whitney non-parametric test was used to examine the associations between blood glucose level, clinical features, and brain CT scan findings. Moreover, Logistic regression was used to determine significant variables. Then, sensitivity, specificity, positive predictive value, and negative predictive value calculated based on significant variables. The area under the curve (AUC) was used to determine the applicability of blood glucose level as a predictor of brain injury in a CT scan. The blood glucose level cut-off was set at 120 mg/dL.  $P<0.05$  was considered statistically significant.

## Results

This study included 157 patients, with 111 (70.7%)

of them being men. The mean age of the patients was  $36.11 \pm 19.42$  years, and their mean blood glucose level was  $117.69 \pm 20.15$  mg/dL. Table 1 includes a summary of additional clinical features and brain injuries. According to the findings of the CT scan, 30 individuals (19.2%) were found to have a brain injury. In the CT scan, patients with brain injury had significantly higher mean blood glucose levels than those without brain injury ( $113.56 \pm 17.38$  vs.  $138.50 \pm 20.59$  mg/dL; OR=1.06; 95% CI=1.03-1.09;  $p < 0.0001$ ). Pearson's correlation revealed a significant relationship between age and blood glucose level ( $r = 0.315$ ,  $p < 0.0001$ ), but not between sex and blood glucose ( $p = 0.28$ ). As indicated in Table 2, patients with CT indications of brain injury, particularly those with vertigo and ataxia, had significantly higher blood glucose levels than patients without brain injury ( $p = 0.01$ ). However, blood glucose levels seemed to be independent of the presence or absence of skull fractures.

Based on the results of univariate logistic regression, there was a significant association between the presence of CT evidence of brain injury and glucose level ( $p < 0.0001$ , Table 3). In multivariate regression analysis with the backward method, the only variable that remained an independent predictor at the 5% level was blood glucose level. At the cut-off point of 120 mg/dL, the sensitivity, specificity, positive predictive values (PPV), and negative predictive value (NPV) of blood glucose levels were 92.33%, 73.34%, 40.73%, and 98%, respectively. According to the area under the Receiver operating characteristic (ROC) curve (AUC), the blood glucose level could most accurately predict the presence of CT signs of brain injury at the cutoff point of 120 mg/dL with an AUC of 0.83 (Figure 1).



**Fig. 1.** ROC curve for prediction of need to perform CT scan by blood glucose level in mild traumatic brain injury; Area Under Curve (AUC): 0.83

## Discussion

This study showed that patients with mild TBI who showed symptoms of brain injury on the CT scan had significantly higher blood glucose levels than patients with normal brain CT scan findings. This finding can assist specialists to determine whether or not to undertake a brain CT scan on patients who had mild TBI. Moreover, vertigo and ataxia can be considered alarming symptoms, indicating the need for CT scan imaging.

The majority of cases of traumatic brain injury are

**Table 1.** Basic Characteristics, Clinical Features, Brain CT Scan Findings and Blood Glucose Level in patients with Mild Traumatic Brain Injury

Variables	N (%)
Age (mean±SD)	36.11±19.42
Gender	
Male	111 (70.70)
Female	46 (29.30)
Clinical Features	
Headache	65 (41.40)
Nausea	34 (21.65)
Vomiting	18 (11.46)
Vertigo	17 (10.82)
Amnesia	2 (1.27)
Ataxia	1 (0.63)
Brain damages in CT scan	
SDH <sup>1</sup>	7 (4.45)
EDH <sup>2</sup>	6 (3.82)
SAH <sup>3</sup>	6 (3.82)
Pneumocephalus	7 (4.45)
ICH <sup>4</sup>	2 (1.27)
Contusion	2 (1.27)
Blood glucose (mean±SD)	117.69±20.15

<sup>1</sup>Subdural hematoma, <sup>2</sup>Epidural hematoma, <sup>3</sup>Subarachnoid hemorrhage, <sup>4</sup>Intracerebral hemorrhage

**Table 2.** The Association of Blood Glucose Level with Clinical Features and Brain Damage in CT Scan

Variables	Blood Glucose (mg/dl) (mean±SD)	p-value
Clinical Features		
Nausea		0.41
Yes	118.86±20.84	
No	120.51±25.28	
Vomiting		0.39
Yes	122.26±26.45	
No	119.93±24.21	
Vertigo		0.01
Yes	131.94±28.20	
No	115.96±18.34	
Headache		0.84
Yes	117.95±19.71	
No	121.50±26.79	
Ataxia		0.01
Yes	133.90±27.32	
No	117.13±18.96	
Brain damages in CT scan		
SDH <sup>1</sup>		0.001
Yes	138.14±27.71	
No	118.63±23.55	
EDH <sup>2</sup>		0.001
Yes	142.00±21.05	
No	118.87±24.01	
SAH <sup>3</sup>		0.008
Yes	143.28±30.16	
No	119.22±23.76	
Pneumocephalus		0.003
Yes	146.57±22.94	
No	119.09±23.90	
ICH <sup>4</sup>		0.009
Yes	170.75±45.65	
No	119.01±22.62	
Contusion		0.03
Yes	148.60±28.71	
No	119.35±23.85	

<sup>1</sup>Subdural hematoma, <sup>2</sup>Epidural hematoma, <sup>3</sup>Subarachnoid hemorrhage, <sup>4</sup>Intracerebral hemorrhage

**Table 3.** Univariate Logistic Regression for Predicting Brain Damage in CT Scan Using Blood Glucose Level

Variable	Odds ratio(CI95%)	p-value
Blood Glucose	0.94 (0.92-0.96)	0.001

classified as mild, and most patients are discharged from the emergency department within a few hours. Unnecessary CT scans not only harbor the risks associated with radiation exposure but also impose excessive costs on these patients [11, 12]. The six most important predictors pointing to the necessity of performing a brain CT scan in individuals presenting with mild TBI include abnormal mental function, scalp hematoma, loss of consciousness, severe traumatic injuries, the presence of palpable skull fracture, and acting normally per parent. It has been reported that machine learning could reliably and accurately predict the necessity for a head CT scan in patients with mild TBI. However, the final decision about whether a patient with mild

head trauma requires a CT scan or not is based on a specialist's discretion [13]. Although CT scanning is recommended in patients with moderate to severe TBI, the decision to perform this procedure in those with mild TBI is a challenging issue. Therefore, accurate guidelines are required to determine which patients need CT scanning and who can be confidently discharged from the emergency department without undergoing this procedure. Since mild TBI is the most common type of this condition, it is crucial to decide whether to perform a brain CT scan on patients who have mild TBI or not. On the other hand, head traumas are associated with considerable morbidity and mortality. In patients with mild TBI, there are several specific clinical criteria to



determine whether or not to perform a brain CT scan in patients with mild TBI, all of which are invariably based on clinical symptoms. The purpose of using these criteria is to make appropriate decisions to minimize the number of unnecessary brain CT scans in individuals who do not require such a procedure as well as prevent patients with brain injury from remaining undiagnosed [14-16].

These clinical-based criteria have high sensitivity but moderate specificity to determine the need for a brain CT scan. Meanwhile, there is currently no auxiliary criterion such as a laboratory test to assist decision-makers to employ these criteria effectively and confidently [17]. In order to predict CT indications of traumatic cerebral injuries, several blood biomarkers including C-terminal hydrolase-L1, glial fibrillary acidic protein, and S100B have been studied. However, these are expensive and not widely available [18, 19]. Blood glucose measurement is a low-cost laboratory test that is frequently performed in the emergency department and can be used to help determine whether it is necessary to undertake a CT scan for patients with minor head traumas.

Stress-induced hyperglycemia can occur after TBI as a result of insulin resistance and glucose metabolism deregulation [20], which aggravates the patient's prognosis [21, 22]. In addition, following head trauma, systemic inflammatory response syndrome can occur, contributing to hyperglycemia in these patients [23]. Peyton *et al.* conducted a study on a pediatric population and found that patients with brain injury had higher blood glucose levels than patients with normal findings in the brain CT scan [24]. Matovu *et al.* found that patients with severe TBI had significantly higher blood glucose levels at admission than those with mild-to-moderate TBI, which indicated a poor prognosis [25]. According to Kafakim *et al.*, hyperglycemia has also been shown to enhance the recovery of individuals suffering from severe head injuries [26]. Our findings also confirmed that individuals with mild TBI and signs of brain injury in the CT scan had relatively higher blood glucose levels.

Although no specific laboratory tests are regularly performed for monitoring the condition of patients with head traumas [27], blood glucose measurement may be helpful in determining to perform a brain CT scan in patients with mild TBI. Alexiou *et al.* demonstrated that blood glucose level at a cut-off of 120 mg/dL could be a useful complementary criterion for determining the necessity for a brain CT scan in patients with mild TBI, with a sensitivity of 74.4% and a specificity of 90.7%. In these patients, the level of blood glucose at admission was significantly associated with the presence of abnormal brain CT scan findings [10]. As a result, blood glucose levels can increase the specificity of clinical criteria in identifying mild TBI patients who require a brain CT scan, a procedure that currently relies primarily on clinical features. Overall, blood glucose level,

along with other clinical criteria, could be a useful complementary item for predicting the presence of CT signs of brain injury in patients with mild TBI, with a sensitivity and specificity of 92.3% and 73.3%, respectively, at the cut-off point of 120 mg/dL, as observed in the present study. Blood glucose measurement is a simple, low-cost diagnostic test that can be used with other clinical criteria to more reliably identify TBI patients who require further evaluation with brain CT scanning [28].

Following an acute TBI, both peripheral or central vestibular symptoms are prevalent, among which vertigo and ataxia suggest the existence of peripheral symptoms. Although routine treatment is not recommended for patients with acute TBI, a small group of these patients have a brain injury and are required to be screened by CT scanning [29-31]. According to the findings of the present study, patients with vertigo and ataxia had higher blood glucose levels, which could be a warning sign for brain injury.

Our study, however, had several limitations, including being a single-center study, the withdrawal of patients with moderate-severe TBI, the unwillingness of some patients to participate in the study, and the exclusion of patients under the age of 16 years, pregnant women, patients who refused to undergo a CT scan, as well as those who refused to undergo blood glucose level testing. Therefore, the findings cannot be generalized to a larger society.

## Conclusion

Patients with mild TBI who had CT signs of brain injury had significantly higher blood glucose levels than patients who had normal brain CT scan findings. This finding can assist physicians to determine whether or not to perform a brain CT scan. Although the indications for performing a brain CT scan are usually clinical-based, blood glucose level, as a laboratory criterion, can be helpful in selecting the TBI patients who may benefit most from brain CT scanning.

## Declaration

### Ethical approval and consent to participate:

Ethical guidelines and the principles of the Declaration of Helsinki were observed in this study. Ethical approval for this study was obtained from the Ethics Committee of the Kerman University of Medical Sciences (IR.KMU.AH.REC.1401.041).

**Consent for publication:** All authors read and approved the final manuscript to be published and agreed to be accountable for all aspects of the work in terms of the accuracy and integrity of any of its parts.

**Conflicts of Interest:** No potential conflict of

interest was reported by the authors.

**Funding:** The author(s) disclosed the receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by Kerman University of Medical Sciences.

**Authors' Contribution:** Study concept, study

design, and supervision: ZS.A., M.T.; acquisition of data: ZS.A.; analysis and interpretation of data: M.M.; drafting of the manuscript, technical and material support: M.T.

**Acknowledgment:** This study was supported by the Clinical Research Center of Shahid Bahonar Academic Hospital, Kerman University of Medical Science, Kerman, Iran.

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