

ORIGINAL ARTICLE

Yield of leukocytosis in predicting brain computed tomography pathological findings in pediatric patients with head traumatic injuries

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ABSTRACT

Background: Head trauma is an urgent medical condition that is prevalent in pediatric patients. The association between white blood cell (WBC) counts and their prognostic value in pediatric traumatic brain injury (TBI) has been proposed in multiple studies. Hence, WBC count can be used to determine the presence of TBI. Thus, we aimed to address this gap by assessing the value of WBC count in predicting pathological computed tomography (CT) findings in pediatric patients with traumatic head injuries.

Methods: This retrospective cohort study included 108 patients with isolated head trauma aged 0-14 years who underwent brain CT examination and had available data on WBC count upon presentation to the emergency room. Chi-square and Fisher's exact tests were used to determine the statistical significance. Logistic regression analysis was performed to further explore the relationships between the variables.

Results: Falls were the most common cause of head trauma [88 (81.48%) patients]. Leukocytosis was reported in 35 (32.41%) patients and non-leukocytosis in 73 (67.59%) patients. Sixty-four patients (59.26%) had pathological brain CT findings, whereas 44 (40.74 %) had non-pathological findings. The leukocytosis status differed [odds ratio (OR) = 0.99, 95% confidence interval (CI) = 2.55-0.38; p = 0.9839] according to the pathological CT findings, but the difference was not significant. Age (0-2 years) and Glasgow Coma Scale score (≤14) were significant predictors of pathological brain CT findings (OR = 3.79, 95% CI = 9.24-1.55, p = 0.0033 and OR = 14.04, 95% CI = 127.59-1.54, p = 0.0189, respectively).

Conclusion: The presence of leukocytosis might be a useful and limited predictive factor for pathological brain scan findings in patients with decreased GCS. Therefore, further multi-center studies with a larger sample size are warranted to determine the benefits of WBC count in patients with head trauma.

Keywords: Head trauma, fall, road traffic accident, white blood cells, injury.

Introduction

Head trauma is one of the most common causes of emergency visits in pediatric patients. It has a major impact on pediatric age groups, predisposing them to a higher risk of mortality and disability [1-3]. In the United States, the incidence of head trauma was 73.5/100,000. However, this may vary among countries [4]. One-third of hospital pediatric trauma admissions are related to head injuries [4]. Furthermore, riding bicycles, playing combat games, and engaging in other outdoor activities can increase the risk of head injury. Falls and road traffic

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accidents are the main causes of head trauma in pediatric patients [1,3]. In a previous study conducted in Saudi Arabia, head trauma related to falls occurred in 45.9% of children aged <6 years, while head trauma related to motor accidents commonly occurred in patients aged 16-18 years [4]. In addition, boys had a higher rate of head trauma than girls, which can be explained by the girls' tendency to stay indoors most of the time [1,3].

Despite the current advances in managing head trauma, the outcomes in half of the patients are still considered unfavorable. Thus, patients with traumatic brain injury (TBI) should be carefully assessed. The clinical value of brain injury can be assessed using the Glasgow Coma Scale (GCS), which helps clinicians classify patients with mild, moderate, or severe TBI [5]. Computed tomography (CT) imaging is a beneficial diagnostic tool in cases of head trauma as it is more sensitive than magnetic resonance imaging for visualizing skull and cervical spine fractures and hematomas [6]. Nevertheless, it is not routinely performed in all patients with head trauma owing to its high cost, the risk of radiation exposure to children, the differences in CT protocols for various patients, the absence of intracranial pathology, and the patients' clinical status [1,4,7-9]. In addition, the Pediatric Emergency Care Applied Research Network rules were used for identifying children with a low risk of TBI, while the Canadian Assessment of Tomography for Childhood Head Injury 2 (CATCH-2) rules were used for identifying children with a high risk of TBI [10]. Since a low GCS score is an indication of performing CT (CATCH-2), it would be helpful to determine whether white blood cell (WBC) count be useful in predicting CT abnormalities among children with mild head injury in the setting of trauma (since PECARN is used for identifying low-risk children and CATCH only applies to those with a GCS score of <15).

Certain studies have been conducted to determine the association between biomarkers such as WBC and neutrophil counts and their assistive prognostic value in pediatric TBI [1,2]. Several theories may explain the increase in the levels of these biomarkers. Disruption of the blood-brain barrier can lead to microglial cell activation, resulting in the release of pro-inflammatory cytokines and other neurotoxic products. Consequently, free radicals damage tissues and propagate injury. In addition, an acute increase in cortisol levels can lead to neutrophil storage and release and extend their lifespan in the circulation. Finally, the entry of marginalized Neutrophils into the circulation can be driven by an acute increase in catecholamine levels [1,2,5]. A significant association was observed between abnormal brain CT findings and leukocytosis. However, normal brain CT did not show leukocytosis. In addition, a low GCS score is significantly associated with a high WBC count [1].

Hence, WBC count can be valuable in determining the presence of TBI. Therefore, an in-depth study of this topic should be conducted in other medical centers and countries. In addition to the lack of relevant studies, no local studies have examined this subject. Therefore, this study aimed to assess the value of leukocytosis at presentation for predicting pathological brain CT findings in pediatric patients presenting to the emergency room (ER) with a history of isolated acute traumatic head injuries.

Materials and Methods

Study settings and design

This retrospective study was conducted at a tertiary care center in King Abdulaziz Medical City, Jeddah, Saudi Arabia.

Identification of study participants

Patients aged 0-14 years with isolated head trauma on CT scan and with data on WBC counts upon presentation to the ER were included in this study. Those who did not undergo a CT scan had no data on WBC count, or had other injuries with head trauma were excluded from the study. Patients' data from July 2016 to December 2022 were obtained from the medical electronic records and used in this study. A non-probability consecutive sampling technique was used; thus, all patients who met the inclusion criteria were included in the specified period.

Study measures

The patient's age, sex, causes of trauma, road traffic accidents, and abuse have been reported. In addition, the symptomatic presentations, GCS scores, WBC values, and CT findings were classified as non-pathological or pathological. Finally, data on whether patients were admitted and hospitalized, the duration of intensive care unit (ICU) admission, or whether the patients were discharged from the ER without the need to be admitted were obtained.

In our study, the presence of leukocytosis was determined based on the reported values from the hospital's electronic medical records. In addition, the brain CT findings reported in this study included cranial bone fracture, epidural subdural hemorrhage, contusion hemorrhage, traumatic subarachnoid hemorrhage, ventricular hemorrhage, parenchymal hematoma, and/or pneumocephalus.

Statistical analysis

The collected data were cleaned, assessed for completeness, and analyzed using the JMP Statistical Software version 15.2.0 (SAS Institute, Cary, NC; a subsidiary of the SAS Institute). Categorical variables were expressed as frequencies (%). Chi-square and Fisher's exact tests were used to assess the association between the demographic characteristics, the presence of leukocytosis, and CT findings. A subgroup analysis was performed for those with GCS scores of ≤14 and 15. Logistic regression was performed to predict the pathological findings on CT based on the presence of leukocytosis, age at incidence, sex, and GCS score. A p-value of <0.05 was considered significant, and the corresponding 95% confidence interval (CI) was set.

Table 1. Demographics and characteristics of patients.

Item	GCS 15 *N* (%)	GCS ≤ 14 *N* (%)	*N* (%)	*p*-value
Gender				0.6064
- Female	34 (35.05%)	3 (27.27%)	37 (34.26%)	
- Male	63 (64.95%)	8 (72.73%)	71 (65.74%)	
Age				0.0085*
- 0-2 age	39 (40.21%)	0	39 (36.11%)	
- 2-14 age	58 (59.79%)	11 (100%)	69 (63.89%)	
Trauma				
- Fall	79 (89.77%)	9 (10.23%)	88 (81.48%)	0.9758
- RTA	13 (81.25%)	3 (18.75%)	16 (14.81%)	0.2197
- Abuse	3 (100%)	0	3 (2.778%)	0.5542
Presentation				
- Non-symptomatic	28 (28.87%)	1 (9.09%)	29 (26.85%)	0.1608
- Symptomatic	69 (71.13%)	10 (90.91%)	79 (73.15%)	
Presentations				
- Loss of consciousness	29 (29.90%)	9 (81.82%)	38 (35.19%)	0.0006*
- Vomiting	33 (34.02%)	5 (45.45%)	38 (35.19%)	0.4517
- Dizziness	11 (11.34%)	2 (18.18%)	13 (12.04%)	0.5087
- Headache	11 (11.34%)	0	11 (10.19%)	0.2386
- Seizure	8 (8.25%)	1 (9.09%)	9 (8.33%)	0.9236
- Nausea	6 (19%)	2 (18.18%)	8 (7.407%)	0.1499
- Decreased activity	5 (5.15%)	0	5 (4.630%)	0.4407
- Nasal bleeding	2 (2.06%)	1 (9.09%)	3 (2.778%)	0.3853
- Pain	3 (3.09%)	0	3 (2.778%)	0.8395
- Agitation	2 (2.06%)	0	2 (1.852%)	0.6307
- Ear bleeding	1 (1.03%)	0	1 (0.926%)	0.3853
- Swelling	1 (1.03%)	0	1 (0.926%)	0.7351
- Sweating	1 (1.03%)	0	1 (0.926%)	0.7351
CT findings				
- Non-pathological	43 (40.74%)	1 (9.09%)	44 (40.74%)	0.0242*
- Pathological	54 (55.67%)	10 (90.91%)	64 (59.26%)	
Presence of leukocytosis				
- No	72 (74.23%)	1 (9.09%)	73 (67.59%)	<0.0001*
- Yes	25 (25.77%)	10 (90.91%)	35 (32.41%)	

*Statistical significant difference.

Results

A total of 108 patients were included in this study, 71 (65.74%) of whom were men. Approximately 63.89% (69) of the children were aged 2-14 years. Falls were the most common cause of head trauma in the included patients [88 (81.48%) patients]. Head trauma due to road traffic accidents occurred in 16 (14.81%) patients. Moreover, 79 (73.15%) patients experienced symptoms after the incident, while 29 (26.85%) remained asymptomatic. Leukocytosis was reported in 35 (32.41%) patients and non-leukocytosis in 73 (67.59%) patients. Only 11 patients (10.19 %) had a GCS score of ≤14. Nevertheless, significant differences were observed in the GCS scores based on age, CT findings, and the presence or absence of leukocytosis ($p = 0.0085$, $p = 0.0242$, and $p < 0.0001$, respectively). For example, 10 patients (90.91%) with a GCS score of 14 showed pathological CT findings. Similarly, 10 (90.91%) patients with a GCS score of ≤14 had leukocytosis, while only 25 (25.77%) with a GCS score of 15 had leukocytosis.

In the brain CT scan reports, 64 (59.26%) patients had pathological brain CT findings, whereas 44 (40.74%) patients had non-pathological findings. Cranial bone fractures were found in 50 (68.49%), subdural hemorrhage in 17 (23.29%), epidural hemorrhage in 8 (10.96%), contusion hemorrhage in 6 (8.219%), and traumatic subarachnoid hemorrhage in 3 (4.11%) patients (Table 2).

Table 2. Brain CT results.

Item	*N* (%)
Normal	44 (40.74%)
Cranial bone fractures	50 (68.49%)
Subdural hemorrhage	17 (23.29%)
Epidural hemorrhage	8 (10.96%)
Contusion hemorrhage	6 (8.219%)
Traumatic subarachnoid hemorrhage	3 (4.11%)
Pneumocephalus	3 (4.11%)
Parenchymal hematoma	1 (1.37%)
Ventricular hemorrhage	1 (1.37%)

Furthermore, significant differences were observed in age and GCS based on WBC counts ($p = 0.0471$, $p < 0.0001$). In addition, significant differences were found between the WBC count and the type of trauma, specifically RTA ($p = 0.0273$). Sex, CT pathology, symptomatic presentation, and isolated head injury were not significantly associated with leukocytosis (Table 3). Similarly, significant differences were observed in brain CT findings in terms of age and GCS score ($p = 0.0163$ and $p = 0.0242$, respectively). Significant differences were also observed in the presence or absence of symptoms based on the brain CT findings ($p = 0.0334$). Other parameters did not differ significantly (Table 3).

Logistic regression analysis was performed to predict the pathological brain CT findings based on gender,

Table 3. Relationship of leukocytosis and CT findings with other characteristics.

Item *N* (%)	Leukocytosis		*p*-value	CT results		*p*-value
	No 73 (67.59%)	Yes 35 (32.41%)		Non-pathological 44 (40.74%)	Pathological 64 (59.26%)	
Gender Female Male	 23 (31.51%) 50 (68.49%)	 14 (40%) 21 (60%)	0.3841	 15 (34.09%) 29 (65.91%)	 22 (34.38%) 42 (65.63%)	0.9756
Age 0-2 years 2-14 years	 31 (42.47%) 42 (57.53%)	 8 (22.86%) 27 (77.14%)	0.0471*	 10 (22.73%) 34 (77.27%)	 29 (45.31%) 35 (54.69%)	0.0163*
GCS score 15 ≤14	 72 (98.63%) 1 (1.37%)	 25 (71.43%) 10 (28.57%)	<0.0001*	 43 (97.73%) 1 (2.27%)	 54 (84.38%) 10 (15.63%)	0.0242*
Trauma Fall RTA Abuse	 63 (86.30%) 7 (9.59%) 2 (2.74%)	 25 (71.43%) 9 (25.71%) 1 (2.86%)	 0.0626 0.0273* 0.9723	 36 (81.82%) 5 (11.36%) 2 (4.55%)	 52 (81.25%) 11 (17.19%) 1 (1.56%)	 0.9404 0.4025 0.3540
Symptoms No Yes	 22 (30.14%) 51 (69.86%)	 7 (20%) 28 (80%)	0.2659	 7 (15.91%) 37 (84.09%)	 22 (34.38%) 42 (65.63%)	0.0334*
CT findings Non-pathological Pathological	 31 (42.47%) 42 (57.53%)	 13 (37.14%) 22 (62.86%)	0.5983			

*Statistical significant difference.

Table 4. Logistic regression analysis of pathological CT findings.

Item	Odds ratio	Upper 95% CI	Lower 95% CI	*p*-value
Gender Male Female	 0.94 1.05	 2.26 2.53	 0.39 0.44	 0.8981
Age 0-2 years 2-14 years	 3.79 0.26	 9.24 0.64	 1.55 0.10	0.0033*
Leukocytosis	0.91	2.37	0.34	0.8481
GCS score ≤14 15	 14.04 0.07	 127.59 0.64	 1.54 0.01	0.0189*

*Statistical significant difference.

age, absence or presence of leukocytosis, and GCS. The contributing factors were examined using regression analysis to determine the possibility of obtaining pathological findings on CT. The leukocytosis status differed according to (OR = 0.91, 95% CI = 2.37-0.34; $p = 0.8481$) the presence or absence of pathological CT findings, but the difference was not significant. Age (0-2 years) and GCS (score: 14) were significant predictors of pathological brain CT findings (OR = 3.79, 95% CI = 9.24-1.55, $p = 0.0033$) and (OR = 14.04, 95% CI = 127.59-1.54, $p = 0.0189$). Moreover, regression analysis showed that female patients had a higher risk of having a pathological CT finding (OR = 1.05, 95% CI = 2.53-0.44, $p = 0.8981$); however, no significant difference was found between the two gender groups (Table 4).

Furthermore, all patients who had a GCS score of 14 were hospitalized, and 6 (54.55%) were admitted to the neonatal ICU (NICU)/pediatric ICU (PICU) ($p = 0.0085$, $p<0.0001$). Finally, 39 (36.11%) of the total patients were discharged from the ER without being admitted for hospitalization (Table 5).

Discussion

The frequency of physicians ordering brain CT scans in the pediatric age group has recently increased owing to the possibility of pathological brain CT findings in trauma patients. Nevertheless, CT increases the risk of exposure to ionizing radiation and malignancy in children than in adults [11-13]. Thus, biomarkers such as WBC count and clinical examination have been used to predict the possibility of brain pathology resulting from trauma [1]. Therefore, this study aimed to assess the value of leukocytosis at presentation for predicting pathological brain CT findings in pediatric patients presenting to the ER with a history of isolated acute traumatic head injuries.

The results of this study showed no statistical difference in patients with leukocytosis at ER presentation in terms of CT findings. Several studies have examined the association between leukocytosis and different aspects of the pathological brain scan findings in patients with acute pediatric traumatic injuries. In contrast to our results, Sahin et al. [1]. found a significant association between leukocytosis at ER presentation and pathological brain scan findings . One possible reason for this is the existence of several major differences between the study samples in

Table 5. Outcomes of head trauma patients.

Item	GCS 15 *N* (%)	GCS ≤ 14 *N* (%)	N (%)	*p*-value
Hospitalization - No - Yes	 39 (40.21%) 58 (59.79%)	 0 11 (100%)	 39 (36.11%) 69 (63.89%)	**0.0085***
Length of hospitalization - 1-2 days - 3-5 days - ≥ 6 days	 47 (81.03%) 5 (8.62%) 6 (10.34%)	 5 (45.45%) 2 (18.18%) 4 (36.36%)	 52 (75.36%) 7 (10.14%) 10 (14.49%)	0.0350
NICU/PICU admission - No - Yes	 93 (95.88%) 4 (4.12%)	 5 (45.45%) 6 (54.55%)	 98 (90.74%) 10 (9.259%)	**<0.0001***
Outcome - Discharged from the ER - Discharged home after hospitalization	 39 (40.21%) 58 (59.79%)	 0 11 (11%)	 39 (36.11%) 69 (63.89%)	**0.0085***

*Statistical significant difference.

Sahin et al.'s [1] study and the current study . More than half of the sample had pathological brain scan findings in the current study, while almost one-fifth had pathological brain scan findings in Sahin et al.'s [1] study. The most common CT finding in our study was cranial bone fracture, whereas the least common was ventricular hemorrhage, which is consistent with the report published by Khadiga. In contrast to the findings of Sahin et al. [1], Assiry et al. [3] mostly reported normal CT findings . In addition, the current study included patients aged 14 years or younger, while Assiry et al.'s [3] study included patients aged 2-18 years. However, they found that patients with a GCS score of 14 or 15 were less likely to have leukocytosis than those with a GCS score of 13 or lower. In our study, a significant difference was found in the GCS scores and leukocytosis status.

Notably, nearly 10% of the patients in the current study had a GCS score of ≤14, while approximately 30% of the patients in Assiry et al.'s [3] study had a GCS score of 13. We can infer that pediatric patients with acute isolated traumatic injuries who demonstrated a slight decrease in GCS scores upon presentation are more likely to have normal WBC counts than those with moderately/severely decreased GCS scores; therefore, it can be more difficult to use WBCs in this group of patients to predict pathological brain scan findings. These major differences between the two studies may have contributed to the contradictory results [1].

The focus of other studies was different from that of our study; a prospective study by Mukherjee et al. [2] investigated the prognostic value of leukocytosis in 201 pediatric patients with isolated traumatic head injuries . Results showed that a cut-off WBC count of more than $16.1 \times 10^9/l$ is a predictive factor for longer hospital stays and poor cognitive outcomes. In addition, most of their patients had a GCS of 13 or less upon presentation, and they found that leukocytosis was associated with an increased intracranial mass effect on brain scans. The authors also suggested that incorporating initial WBC count into the traumatic head injury prediction models may improve prognostication. Enforcing the inferred observations mentioned earlier, they also found that patients with a GCS score of 14 or 15 had significantly lower WBC counts compared with those who presented with severely decreased GCS scores [2].

In our study, children aged 0-2 years were more likely to have pathological CT findings than children aged 2-14 years; however, the majority of children with leukocytosis were aged 2-14 years. Nevertheless, the results reported by Sahin et al. [1] and Al-Gahtany [5] showed no significant relationship . Similar to the findings of our study, boys accounted for more than half of the patients with head trauma [1,14-17]. In addition, the most common etiology of head trauma in our patient was falls, which is similar to the results reported by Sahin et al. [1], Mukherjee et al. [2], and Ciurea et al. [18]. By contrast, several studies have reported that motor vehicle accidents are the most common cause of head trauma in their patients [3-4,19].

With regard to patient outcomes, our study showed that the majority of patients required hospitalization, and only 15% required admission to the PICU/NICU. Alhabdan et al. [4] reported that 33.6% of the patients required PICU/NICU admission. However, death did not occur in 4.7% of the aforementioned patients .

This study has some limitations. It has a small sample size and a low proportion of patients with a GCS score of 14 or less. Despite the high proportion of patients with a GCS score of 15 in our study, the proportion of those with pathological CT findings was significantly higher. In addition, only patients with isolated head injuries were included to authenticate and support our findings. The results of this study can contribute to the literature by addressing this gap, and multicenter studies with larger sample sizes are needed to draw a conclusion on the benefit of utilizing WBC counts as predictors for pathological brain CT findings in pediatric head trauma patients.

Compared with other studies, our results showed that the presence of leukocytosis might not be a useful predictive factor for pathological brain scan findings in general, but it might be limited and applied to those patients with low GCS. Such an observation can be enforced by the high percentage of patients with a GCS score of 15 compared to Low GCS patients in our study and the significantly lower WBC counts among patients with GCS scores in other similar studies.

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List of Abbreviations

CT	Computed tomography
ER	Emergency room
GCS	Glasgow Coma Scale
ICU	Intensive care unit
TBI	Traumatic brain injury
WBC	White blood cells

Conflict of interest

The authors declare that they have no conflict of interests.

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Consent to participate

A waiver of informed consent by KAIMRC was considered for this study due to the retrospective study design.

Consent for publication

Not applicable.

Ethics approval

The study was approved by the Institutional Review Board (IRB) of King Abdullah International Medical Research Center (study number: NRJ22J/154/05, IRB approval number IRB/1282/22, IRB approval date: July 19, 2022).

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