Diagnostic and predictive value of white blood cell count, erythrocyte sedimentation rate, and coagulation tests in patients with blunt head trauma

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Introduction
Traumatic brain injuries are one of the leading causes of death and trauma-related disability.1 The incidence of these injuries is about 200 per 100 000 people in developed countries and more than 500 per 100 000 people in the United States.2 An estimated 5.3 million Americans live with disabilities due to traumatic brain injuries.4 These include a diverse range of mild, reversible to severe, and permanent or even life-threatening disabilities. Mild brain injuries are without any structural changes and sufferers typically have a level of consciousness between 13 and 15 based on the Glasgow Coma Scale.5 Head injury is one of the biggest causes of death and disability in low- and middle-income countries. The World Health Organization (WHO) estimates that approximately 90% of all deaths from injury occur in these areas.6 Low- and medium-income countries with risk factors are more likely to suffer head injuries. However, they do not have adequate health care capacity to deal with the associated complications.6 Significant head injury-related disabilities impose a significant burden on the health care system of those countries. Therefore, the epidemiologic knowledge of head injury and the development of preventive measures are critical to reducing this burden.1 Head injury is the important cause of disability in people under 40 and severely disabling 200-150 people per million annually.7,8 Most cases are caused by road injuries (60%), followed by falls (20%-25%), and violence (10%), and the young men

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are the most affected population. In children under 15 years of age, head injury is the important cause of death. In the elderly, the most important cause of head injury is falls. In medical science, trauma refers to any type of trauma, injury, shock, and incident to the human body that enters the body externally and causes injury or disease within the body. The importance of the difference between these two topics lies in the emergency and medical emergencies. For example, in dealing with a patient with syncope or shock, the rescuer can easily move the patient if the cause is a condition. But, in traumatic conditions due to the possibility of severe injuries such as spinal cord dislocation, any movement of the patient without support and fixation of moving organs is prohibited by untrained persons. Head trauma, especially its severe form may require emergency treatment.

Trauma is the first leading cause of death and one of the leading causes of disability of active population in developing countries. Unfortunately, the importance of this issue in these countries has received little attention. The situation is deteriorating and according to WHO forecasts by 2020, accidents alone will be the second leading cause of lost lives worldwide. Trauma is the sixth and third leading cause of death worldwide and in the United States, respectively and the leading cause of death in people under the age of 40. Head trauma is known to be the leading cause of death in the first 4 decades of life. Thus, the severity of these patients’ diagnosis are increasing day by day. Therefore, studies have biased the search for easier indices to decide on the necessary diagnostic and therapeutic measures and to predict patients. Nowadays, blood indices are among the most convenient and accessible indices that are routinely asked for all trauma patients and can be examined in all centers. One of these indices is leukocytosis. Leukocytosis is an increase in the number of white blood cell (WBC) in the bloodstream. The normal WBC count is 1 to 4 WBC per microliter (LCM). An increase in the number of WBC is called leukocytosis. Leukocytosis is generally present in: infectious diseases, inflammatory diseases (such as rheumatoid arthritis and allergies), some neoplasms such as leukemia, severe mental or physical stress, and tissue damage (severe burns). These cases are often accompanied by the presence of immature WBC (left shift). WBC types can increase individually for different reasons, so neutrophils, monocytes, eosinophils, lymphocytes, and basophils can be found in blood. On the other hand, other studies have shown that serum glucose levels, erythrocyte sedimentation rate (ESR) status, and blood oxygen saturation are other predictors of head trauma. Given the time and speed of decision making for trauma patients which determine mortality and morbidity thereafter, having an index that is easy to measure and that does not depend on the technician performance, is cheaper and more accessible. It is becoming increasingly important, so we decided to design a study to evaluate the diagnostic and predictive value of leukocytosis in patients with blunt head trauma.

**Methods**
This was a cross-sectional study of a prospectively collected database of trauma patients used to evaluate the utility of initial WBC count, base deficit (BD), lactate (LAC) to detect major injury. Tabriz University of Medical Sciences (TUOMS) with the cooperation of committee approved this study. Requirement for informed consent was waived by the Tabriz University of Medical Science. All patients referred to the Emergency Department of Tabriz Imam Reza hospital from March to August 2017 with complaining of blunt head trauma of type DAI were enrolled in a complete and sequential study. A checklist containing research variables was completed for all patients. Research variables included: age, sex, vital signs, patient outcome (Including emergency discharge, inpatient ward), severity of injury, trauma mechanics, WBC count, laboratory results including arterial blood gas analysis, complete blood cell count, and sodium and potassium levels, urea and creatinine and urinary analysis, coagulation factors and ESR were the factors studied. After completion of the checklist, WBC values including total numbers, lymphocytes, neutrophils, eosinophils and basophils were recorded. Positive and negative diagnostic value and sensitivity and specificity of this variable were evaluated in predicting long-term (GOS) and short-term (good or bad prognosis) outcomes.

**Sample size**
According to the 6-month interval approved for this study, the sample size was selected as a whole. All patients admitted to the emergency department were enrolled in this study based on the inclusion and exclusion criteria. Inclusion criteria was patients with blunt trauma to the head, DAI, patients with GCS less than 8 without radiologic findings, over 14 years old, CT scan, confirmation of DAI, or presence of DAI symptoms with normal radiologic findings. Exclusion criteria was unwillingness to cooperate at any point in the study, history of previous head trauma, previous history of head surgery, people over 14 years of age with ISS criteria of 12 or lower, patients with shock (systolic pressure less than 90 mm Hg) and those without primary CT scan during the study.

Patient status was assessed by direct patient observation or by telephone contact with the patient’s family. The record for all patients was recorded by a research assistant. Patients were divided into two groups with good and poor prognosis and its association with leukocytosis status and other paraclinical factors was evaluated at the time of referral.

**Statistical analysis**
The data were entered into SPSS version 15.0 and analyzed. Chi-square test for qualitative data and t test...
for quantitative data were used. Pearson correlation coefficient test was used to examine the relationship between the data. Both intention to treat and pre protocol were used for statistical analysis, and it was possible to perform a sensitivity analysis at the end of the task, and in this way, the Miss to follow up cases also came into the test. Mean ± SD indices in case of normality and IQR in case of non-normality of distribution and preliminary tables were used to determine the frequency (percentage) of different levels of qualitative variables. We also used ROC (Receiver operator characteristics and sensitivity) to evaluate the predictors of leukocytosis in patient outcomes. Kolmogorov-Smirnov test was used to check the normality of the distribution of the scores.

Results
In this study, 91 patients were enrolled, that (44.59%) 49 ) of them were male and 42 (38.22%) were female. The mean age of the patients was 51.92 ± 19.15 years. Among patients, 42 (38.22%) patients had high consciousness and 49 (44.59%) patients had low consciousness. The mean of WBC, ESR and International Normalized Ratio (INR) were 5510.531 ± 14.102, 31.18 ± 22.54 and 1.5 ± 3.5, respectively. The incidence of intubation, surgery, and death, as well as the absence of treatment, were 13 patients, 22 patients, 30 patients, and 26 patients, respectively. In the high consciousness group of 42, 51.6% were male and 42.85% were female. In the low consciousness group, 49 patients were 51.02% male and 36.73% female. Significance level of chi-square test was equal to 0.674, indicating that there is no significant difference between the two groups in terms of gender.

Frequency distribution of final outcome of patients
The final outcome in high consciousness group was 11.9% need for intubation, 26.19% need for surgery, 52.38% no complications and 9.52% mortality. In the low consciousness group, 19.32% required intubation, 22.44% required surgery, 8.16% no complications and 53.61% experienced mortality. The significance level of the chi-square test was 0.001, indicating a significant difference between the two groups in terms of final outcome. In the high alert group, there was no improvement; and in the low alert group, mortality was higher. Table 1 shows the result of the outcome of patients.

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<th>High Consciousness=11.9%</th>
<th>Low Consciousness=19.32%</th>
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<tr>
<td>Intubation</td>
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<td>Surgery</td>
<td>52.38%</td>
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<td>Mortality</td>
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Table 1. Frequency distribution of final outcome of patients

Descriptive indices of variables studied
Mean, standard deviation, minimum and maximum were calculated for studying the variables and their histogram were plotted. Independent t test was used. The results of the independent t test showed that the WBC and ESR values in the low consciousness group were significantly higher than the high consciousness group. But the INR in the high consciousness group was significantly higher than the low consciousness group (P<0.05).

Predictive value of leukocytosis with severity of injury in patients with blunt head trauma
Logistic regression was used because the dependent variable is two-level and the independent variable is the distance scale. Chi-square statistic is used to determine the effect of independent variables on the dependent variable and overall fit of the whole model. The chi-square value was 18.84 and the chi-square significant was 0.001. Since the significance level is less than 0.05, the regression model is significant. Nigel’s crack R2 represents the percentage of changes in the dependent variable that is explained by the independent variables. This value was 0.36. That means 36% of the variation in injury severity was related to the WBC variable. The percentage of detection sensitivity also indicated that approximately 67% of the substitution in the dependent variable was correctly recognized by the model. The parental test also examined the significance of the variables entered in the regression equation. The results showed that WBC had a significant direct effect on injury severity (positive coefficient B and significance level of parental test was 0.001).

Predictive value of coagulation factors in patients with blunt head trauma
The level of chi-square was 34.17 and the significance level of chi-square was 0.001. Since the significance level was less than 0.05, the regression model was significant. Nigel's crack R2 represents the percentage of changes in the dependent variable that is explained by the independent variables. This value was 0.58. That means 58% of the variation in injury severity was related to the INR variable. The percentage of detection sensitivity also indicated that approximately 77% of the substitution in the dependent variable was correctly recognized by the model. The results showed that INR had a significant direct effect on injury severity (positive coefficient B and significance level of parental test was 0.001).

Predictive value of ESR in patients with blunt head trauma
Chi-square was 75.28, since the significance level was less than 0.05, the regression model was significant. Nigel's crack R2 represents the percentage of changes in the dependent variable that is explained by the independent variables. This value was 0.95. That means 95% of the variation in injury severity was related to the ESR variable.
The percentage of detection sensitivity also indicated that approximately 97% of the substitution in the dependent variable was correctly recognized by the model. The results showed that ESR had a significant direct effect on injury severity (positive coefficient B and significance level of parental test was 0.001).

Discussion
There are many debates about impaired WBC levels and their association with the severity of trauma and the prognosis and prognosis of related complications. However, it can be understood that catecholamine can cause shifts during major traumatic injuries. The shifting of the WBC to left, increasing number of white globules,

According to the study of Malone et al21 which included 9500 patients, all patients were enrolled in the first level of head trauma and the prognostic criterion was SIRS. WBC above 12000, hypothermia below 36 and above 38 Celsius, heart rate per minute above 90, and respiratory rate per minute above 20, which is ultimately the strongest predictor of hypothermia mortality and the strongest criterion for increasing the length of hospitalization in head trauma patients. WBC was considered.

Evaluation of the association between the likelihood of leukocytosis in persons with higher severity of head trauma has been described in various sources and most studies of the level of consciousness based on the Glasgow criterion below 8 have been considered as cut-offs to better assess the severity of injury in different individuals. There is also a good distinction between these assumptions.

According to a study by Rovlias and Kotsou22 in 2001 a significant association was found between severity of head trauma in terms of level of consciousness, pupil response, presence or absence of cerebral arachnoid hemorrhage, which was significant in its kind. Also based on the study by Souter et al23 who first assessed leukocytosis on admission to head trauma patients and then assessed the descending or ascending trend of leukocytosis with concurrent evaluation of the level of consciousness and extent of injury or related cerebral hemorrhage. Both of the above studies like this study justified the strong and significant relationship between leukocytosis and severity of trauma and its relation with level of consciousness.

According to a study by Paladino et al24 of 810 patients, leukocytosis was significantly different between the two groups with major trauma and minor trauma, but unlike the present study, leukocytosis was still an independent evaluation factor. There was no mention of prognosis and need for surgery, but in our study there was a significant relationship between the level of leukocytosis and the prognosis and final survival of patients.

Unlike the study of Paladino et al25 based on the study of Rovlias and Kotsou26 who examined the precise relationship between patients' consciousness level and leukocytosis from hospitalization to discharge day, there was a significant relationship between individuals with a level of consciousness based on the Glasgow criteria below 8 and its relationship with the severity of leukocytosis and ESR was found to be consistent with the present study.

In a 2001 study by Rovlias and Kotsou,27 624 patients with minor, moderate, and severe head trauma were enrolled. WBC was obtained and all factors that could elevate WBC false-positive as a sub-factor were excluded. In people with severe trauma, there was a significant relationship between high WBC level and low Glasgow score, the presence of bleeding. Cerebral subarachnoid and pupillary response to low light have been reported and this relationship has been confirmed.

In 2010, Paladino and colleagues28 studied a diagnostic value of leukocytosis in determining prognosis in major injuries. In this study, 806 patients were studied. The demographic data, injury mechanism, WBC count, BD, LAC and severity of injury were recorded. The mean age of patients was 38.6 years. Major trauma patients had a statistically significant higher heart rate but were not clinically significant. Patients with major trauma had higher WBC counts, but both were in normal range. This study showed that the number of WBC counts is not an auxiliary finding in major trauma.

In 2008, Chang et al29 investigating the predictive value of WBC counts in determining the severity of injury in blunt trauma patients. In this study, two groups of patients with blunt trauma with clear trauma and the other group with no obvious trauma were compared for primary WBC in the emergency department. The number of WBCs with injury severity score was also evaluated. They indicated that the number of WBCs in the two groups was different. There was a significant positive relationship between WBC count and injury severity score. Although WBC is effective in differentiating injury, it is not very reliable in individual cases. However, WBC counting can be used as an aid in decision making. This study showed that secretive aphids should be taken into account in significant increases in WBC even with poor signs of injury.

Conclusion
In the present study, a significant relationship between the initial assumptions of leukocytosis, ESR, and coagulopathy was found with the INR study. Leukocytosis as an important factor in determining the prognosis of patients with head trauma can be identified. Considering the importance of the relevant assumptions, it is possible to evaluate these factors in head trauma patients at the first admission in the emergency department and take further measures based on probable prognosis and survivalship. Although it cannot definitely confirm the necessity of operation but it can be used as a predictor for transferring patients to the operating room.

Conflict of Interest
Authors declare no conflict of interest in this study.
Ethical Approval
The study protocol was approved by the ethical committee of TUOMS (IR.TBZMED.AC.IR.1397.898).

Authors contribution:
Study design, A.Gh.; Study conduct, M.P.; writing, Z.P.; Analysis, N.Gh.; Critique and article search, M.C.; data gathering, F.S.Kh

Acknowledgments
The authors gratefully acknowledge TUOMS for financial support, staff of emergency medicine department, TUOMS for their kind cooperation. Besides, the authors appreciate the patients and their families.

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