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Leuko-Glycemic Index as a Predictor of Mortality and Morbidity in Trauma Patients

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ABSTRACT:

Background: The accurate prediction of outcomes in critically injured trauma patients remains challenging. Simple, affordable biomarkers that indicate inflammatory and metabolic response to injury could help improve early risk prediction. This study aimed to evaluate the prognostic value of the leuko-glycemic index (LGI)—a composite of admission white blood cell count and blood glucose level—for predicting mortality and morbidity in multiple trauma patients admitted to the intensive care unit (ICU).

Methods: This analytical cross-sectional study included 407 consecutive multiple trauma patients (ISS ≥ 16) admitted to the ICU of a major trauma center in Yazd, Iran, between 2019 and 2021. LGI was calculated as (WBC count × blood glucose level) / 1000. The primary outcome was in-hospital mortality. Secondary outcomes included length of ICU stay, need for emergency interventions, and occurrence of infection. The optimal LGI cut-off for predicting mortality was determined using receiver operating characteristic (ROC) curve analysis with Youden's index.

Results: The mean LGI was significantly higher in non-survivors than in survivors (4,173.91 vs. 1,447.25 mg/dL·mm³, P < 0.001). ROC analysis demonstrated excellent predictive ability for in-hospital mortality (AUC = 0.905, 95% CI: 0.85-0.96). The optimal cut-off was 1,706.55 mg/dL·mm³, yielding a sensitivity of 91.7% and specificity of 76.7%. Based on this threshold, 145 patients (35.6%) were categorized as high LGI. High LGI was significantly associated with increased rates of intubation (28.2% vs. 6.9%), chest tube insertion (19.4% vs. 2.6%), blood product transfusions, ICU stay >10 days (25.7% vs. 5.9%), and in-hospital mortality (10.7% vs. 0.3%) (all P < 0.001). The high LGI group also had significantly longer mean ICU stays (7.4 vs. 3.6 days, P < 0.001).

Conclusion: The leuko-glycemic index is a simple, cost-effective and reliable predictor for in-hospital mortality and morbidity in multiple trauma patients. With a high sensitivity and specificity, LGI can serve as a valuable tool for early risk stratification upon ICU admission, independent of age and sex. Further multicentric studies are needed to establish the these findings and their application in various trauma patient populations.

INTRODUCTION

Trauma continues to be an important cause of death and disability around the world, imposing enormous economic and social burdens on communities. Even with advancements in emergency and intensive care, correct prediction of outcomes for critically injured trauma patients remains challenging for clinicians [1, 2]. The development of simple and affordable indicators that would serve as markers for determining the seriousness of inflammatory and metabolic reactions of patients upon arrival at the hospital could help make triage easier and more effective.

2. METHODS

2.1. Study Design and Setting

This analytical cross-sectional study was done at Shahid Rahnemoon Hospital (the major trauma referral facility in Yazd, Iran). The study had received ethical clearance from the Ethics Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.MEDICINE.REC.1400.XXX) and was executed in accordance with the Declaration of Helsinki.

2.2. Participants

This study included 407 consecutive patients with multiple traumas who were admitted to the ICU from 2019 to 2021. Multiple trauma was defined as injuries to two or more regions of the body with an Injury Severity Score (ISS) of 16 or above. The inclusion criterion was admission to the ICU for multiple traumas. Exclusion criteria included: age less than 18 years, incomplete laboratory data at admission, missing outcome data, and concomitant infections (for example, pneumonia, diabetic foot, and sepsis).

2.3. Data Collection

Demographic and clinical data of the years 2019-2021 were obtained from the trauma registry database of Shahid Rahnemoon Hospital, which is maintained by the Trauma Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran. Age, sex, laboratory values upon admission, clinical results, and treatment in the emergency room were among the variables gathered. The laboratory findings, including the number of white blood cells (WBC) and blood sugar level, were derived from peripheral venous blood taken when admitted and were tested at the hospital's laboratory. The leuko-glycemic index (LGI) was calculated with the following formula:

$$LGI = (\text{WBC count} \times \text{Blood glucose level}) / 1000$$

and reported as mg/dL·mm^3 [20].

2.4. Outcomes

The primary outcome of this study was in-hospital mortality. Secondary outcomes included:

1. Length of ICU stay (days)
2. Need for emergency therapeutic interventions (intubation, chest tube insertion, blood product transfusion including packed red blood cells, platelets, and plasma)
3. Occurrence of infection during ICU stay
4. Duration of mechanical ventilation (days)
5. ICU stay exceeding 10 days

2.5. Statistical Analysis

The statistical analyses were carried out using SPSS version 25 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD) or median (interquartile range) while categorical variables are presented as frequency and percentage. Normality of the continuous variables was verified using Q-Q plots and the Kolmogorov-Smirnov test. The best cut-off for LGI to predict in-hospital mortality was determined by means of the receiver operating characteristic curve analysis with Youden's index (sensitivity + specificity - 1). Based on this cut-off, the patients were divided in two groups, the high-LGI group and the low-LGI group. Comparisons between groups were assessed based on the independent samples t-test or Mann-Whitney U test for continuous variables, and chi-square test or Fisher's exact test for categorical variables. A P-value < 0.05 was considered to be statistically significant.

3. RESULTS

3.1. Patient Characteristics

A total of 407 multiple trauma patients were included in this study. The study population was predominantly male (331 patients, 81.3%), with a mean age of 37.8 ± 18.0 years (range: 18-93 years). The mean ICU length of stay was 4.57 ± 6.5 days (range: 1-69 days). Mean WBC count was 10,981 ± 4,966 cells/mm³ (range: 1,600-38,000), and mean blood glucose level was 131.6 ± 59.3 mg/dl (range: 64-516 mg/dl). The mean LGI was 1,527 ± 1,199 mg/dL·mm³ (range: 171-8,494). Emergency interventions included intubation in 50 patients (12.3%), chest tube insertion in 28 patients (6.9%), packed red blood cell transfusion in 83 patients (20.6%), platelet transfusion in 5 patients (1.5%), and plasma transfusion in 23 patients (5.9%). Forty-four patients (10.8%) had ICU stays exceeding 10 days. In-hospital mortality occurred in 12 patients (2.9%).

3.2. Determination of Optimal LGI Cut-off

The mean LGI in the deceased group was 4,173.91 mg/dL·mm³, significantly higher than 1,447.25 mg/dL·mm³ in the discharged group ($P < 0.001$). ROC curve analysis revealed an area under the curve (AUC) of 0.905 (95% CI: 0.85-0.96) for LGI in predicting in-hospital mortality (Figure 1).

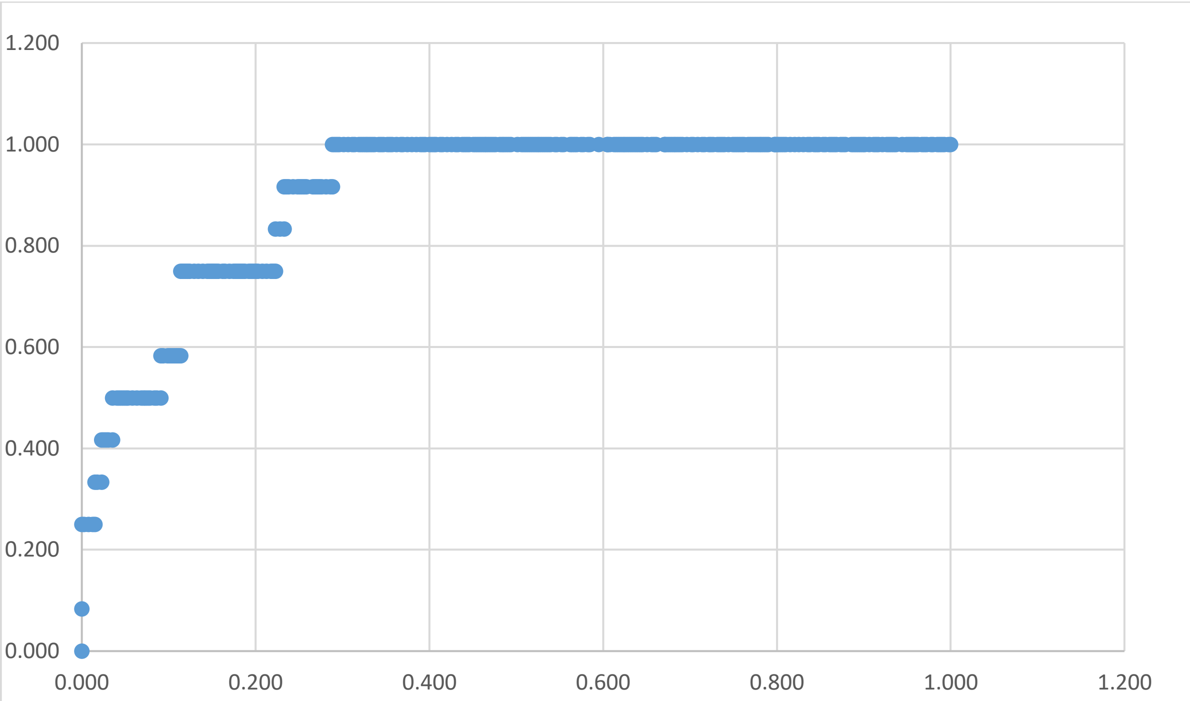

Figure 1. Receiver operating characteristic (ROC) curve of leuko-glycemic index (LGI) for predicting in-hospital mortality in trauma patients. AUC = 0.905.

According to Youden's index, the best LGI threshold was found to be 1,706.55 mg/dL·mm³, with a sensitivity of 91.7% and specificity of 76.7%. High LGI patients were defined as those whose LGI exceeded the threshold, while low LGI patients had an LGI of this value or lower.

3.3. Association of LGI with Clinical Outcomes

Based on the determined cut-off, 145 patients (35.6%) were categorized as high LGI (>1,706.55) and 262 patients (64.4%) as low LGI (≤1,706.55). The associations between LGI and clinical variables are presented in Tables 1 and 2.

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Table 1. Qualitative characteristics of patients and their Association with LGI.

variable	High LGI Group N (%)	Low LGI Group N (%)	Total N (%)	P value
Sex				
Male	84 (81.6)	247 (81.3)	331 (81.3)	0.98
Female	19 (18.4)	57 (18.8)	76 (18.7)	
Intubation				
Yes	29 (28.2)	21 (6.9)	50 (12.3)	<0.001
No	74 (71.8)	283 (93.1)	357(87.7)	
Chest tube				
Yes	20 (19.4)	8 (2.6)	28 (6.9)	<0.001
No	83 (80.6)	296 (97.4)	379 (93.1)	
Packed cell transfusion				
Yes	39 (37.9)	44 (14.5)	83 (20.6)	<0.001
No	64 (62.1)	259 (85.5)	324 (79.4)	
Platelet transfusion				
Yes	3 (2.1)	2 (0.8)	5 (1.5)	0.35
No	142 (97.9)	259 (99.2)	402 (98.5)	
Plasma transfusion				
Yes	17 (11.7)	6 (2.3)	23 (5.9)	<0.001
No	128 (88.3)	255 (97.7)	384 (94.1)	
ICU stay >10 days				
Yes	26 (25.7)	18 (5.9)	44 (10.8)	<0.001
No	74 (74.3)	286 (94.1)	361 (88.7)	
Mortality				
Yes	11 (10.7)	1 (0.3)	12 (2.9)	<0.001
No	92 (89.3)	303 (99.7)	395 (97.1)	
Total	145 (100)	262 (100)	407 (100)	

No significant difference was observed between high and low LGI groups regarding sex (P = 0.98) or age (P = 0.23). However, high LGI was significantly associated with all other clinical outcomes:

- **Intubation:** 28.2% of high LGI patients required intubation compared to 6.9% of low LGI patients (P < 0.001)
- **Chest tube insertion:** 19.4% vs. 2.6% (P < 0.001)
- **Packed red blood cell transfusion:** 37.9% vs. 14.5% (P < 0.001)
- **Plasma transfusion:** 11.7% vs. 2.3% (P < 0.001)

- **ICU stay >10 days:** 25.7% vs. 5.9% ($P < 0.001$)
- **Mortality:** 10.7% vs. 0.3% ($P < 0.001$)

Platelet transfusion showed no significant association with LGI ($P = 0.35$). Mean ICU length of stay was significantly longer in the high LGI group (7.4 ± 7.9 days) compared to the low LGI group (3.6 ± 5.9 days, $P < 0.001$).

Table 2. Quantitative characteristics of patients and their Association with LGI.

variable	High LGI Group mean (SD)	Low LGI Group mean (SD)	Total mean (SD)	P value
Age (years)	35.7 (22.7)	38.5 (20.3)	37.8 (21.0)	0.23
ICU stay (days)	7.4 (7.9)	3.6 (5.9)	4.57 (6.5)	<0.001

4. DISCUSSION

4.1. Summary of Key Findings

This research highlights that leuko-glycemic index (LGI) is an effective prognostic factor with regard to morbidity and mortality among multiple trauma patients who have been hospitalized in the intensive care unit. The best cut-off of LGI was found to be 1,706.55 mg/dL·mm³, having a good area under curve (AUC=0.905), sensitivity of 91.7%, and specificity of 76.7%. high LGI was strongly correlated with increased need for emergency procedures (intubation, chest tube insertion), number of blood transfusions, length of stay at ICU, and mortality rate. Importantly, LGI was independent of age and sex, suggesting its utility across diverse patient populations.

4.2. Comparison with Previous Studies

The predictive role of LGI is well studied in cardiovascular disease populations. Sadeghi et al. [22] studied 296 subjects having acute myocardial infarction (AMI) and presented LGI cut-offs as 2,970.4 mg/dL·mm³ in the population of diabetic subjects and 2,249.4 mg/dL·mm³ in the non-diabetic population which possessed AUCs listed as 0.93 and 0.92 when predicting in-hospital mortality. Qi et al. [21] presented cut-off values of 3,593 for diabetic AMI patients and 1,402 for non-diabetic AMI patients. Our values of 1,706.55 mg/dL·mm³ cut-off are closer to the cut-off values for non-diabetic AMI patients in these studies, which may reflect the predominantly non-diabetic nature of our trauma population or differences in the acute metabolic response between trauma and ischemic heart disease.

The reason behind the elevated LGI cut-off in trauma patients as opposed to non-diabetic AMI patients may be attributed to more pronounced acute stress response in trauma with the release of more catecholamines and more systemic inflammation [25, 26].

Recent research has expanded LGI's applicability across fields apart from heart-related ailments. Shen et al. [23] examined 1,125 patients with severe illnesses suffering from non-traumatic subarachnoid bleeding from the MIMIC-IV database and established that a significant connection existed between LGI and mortality after extending the timeline to 30 days, six months, and one year after diagnosis, with the threshold of 1,269.71 mg/dL·mm³ set for the estimation of the 30-day mortality. Ye et al. [24] examined 112,235 patients suffering from the acute kidney damage from the MIMIC-IV and eICU-CRD databases and established that more elevated levels of LGI were strongly associated with higher mortality rates 30 days and 90 days after hospital admission, since the patients in the highest quartile of LGI were 22% more likely to die than those within the lowest quartile. These findings, along with our results, suggest that LGI has prognostic value across a wide spectrum of critically ill populations beyond cardiovascular disease.

The correlation between high LGI and higher demand for emergency treatments in our study coincides with the results from prior trauma studies. Kreutziger et al. [29] proved that the blood glucose level upon admission predicts hemorrhagic shock in multiple traumas, while Kassum et al. [30] found out that higher blood glucose and leukocyte levels correlate with mortality in blunt trauma. The combination of these two indicators in LGI can reveal additional prognostic information according to our findings.

The high-LGI group had a significantly longer ICU stay (7.4 days vs. 3.6 days), which is consistent with the results of Kreutziger et al. [31]. The authors investigated 555 multiple trauma patients and concluded that there is a high association between hyperglycemia upon admission and length of stay in both the ICU and the hospital regardless of the severity of injuries, age, and gender. Madgon et al. [32] also showed that LGI correlated well with both mechanical ventilation time and time spent in the ICU in cardiac surgery patients.

4.3. Biological Plausibility

The prognostic importance of LGI in trauma patients can be understood through the interplay between the pathophysiological processes of glucose metabolism and inflammation. Trauma induces a complex neuroendocrine stress response that is manifested in elevation of catecholamines, cortisol, and glucagon which lead to stress hyperglycemia [33]. At the same time, tissue damage activates the immune response, evoking leukocytosis and secretion of pro-inflammatory cytokines. The two processes are interrelated: hyperglycemia fosters inflammation through a number of pathways, including increased formation of reactive oxygen species, activation of NF-κB, and creation of glycation end products [16, 35]. In addition, pro-inflammatory cytokines, such as TNF-α and IL-6, result in insulin resistance, thus creating a cycle where hyperglycemia is perpetuated [18].

Patients who have a considerably high level of the LGI might often face greater disturbances in both metabolism as well as inflammatory pathways, thereby exposing them to a greater chance of developing complications like sepsis, multiple organ failure, and death. The close relationship between a high LGI and an increased probability of blood product transfusions might be indicative of the fact that patients who have experienced higher severity of hemorrhagic shock [27]. In fact, some studies have indicated that hyperglycemia, a prominent feature of LGI, serves as an independent risk factor of coagulopathy [36].

4.4. Comparison with LGI Studies in Other Conditions

The prognostic abilities of LGI have been studied in many clinical circumstances outside the realms of trauma and heart diseases. Cañas et al. [37] studied 178 subjects with Guillain-Barré syndrome, wherein they stated that LGI was useful in predicting ventilator assistance. In another research done by Mureşan et al. [38] involving 158 dialysis patients, it was found that high pre-operative LGI resulted in increased chances of failure of the arteriovenous fistula at a cutting score of 0.95 and 72% validity. When it comes to infectious diseases, the leukocyte glucose index has been studied for its added value as a novel marker of COVID-19 severity, regarding studies that showed the role of LGI in predicting the disease progression needed for intensive therapy [39]. The various applications of this marker demonstrate that LGI can be a possible universal marker of metabolic-inflammation dysregulation in different disease conditions.

4.5. Comparison with Other Trauma Prognostic Markers

Various other markers and scoring systems were checked for prognosis in patients with trauma. Lam and co-authors [40] studied people who suffered from trauma and found out that indicators of blood count do not show good predictability regarding the possibility of death in 7 days. However, the parameters of LGI that is a combination of one composite number, demonstrate good predictive quality (AUC = 0.905) in terms of the prognosis of death. Thus, it can be concluded that by using some inflammatory markers, one will get much more accurate prognostic parameters than separately. Esme and co-authors [41] discovered that the increase in WBC count, strong injury of lungs, rib fractures in combination with head injuries are the indicators of prognosis for the condition of the patients with chest injuries. Heffernan and co-authors [42] state that one of the prognostic factors is the failure of recovery from the state of lymphopenia after the injury. Thus, the results of the studies show the importance of the use of indicators of inflammation for prognostication, however, LGI combines both indicators of inflammation and metabolism thus, giving better measures. According to Guo et al. [43], an elevated level of HbA1c was identified as an independent risk factor for sepsis and death in patients sustaining trauma. This indicates that chronic hyperglycemia might be as significant as acute stress hyperglycemia. Since this study focused on acute admission parameters, future research should be done to determine whether the combination of LGI with chronic glycemic control parameters (e.g., HbA1c) can augment prognostic value.

4.6. Limitations

This research has a number of considered limitations. First, the cross-sectional design does not allow determining causation and findings should therefore be regarded as associations, not definitive prognostic relationships. Second the single-center design may limit generalizability to other trauma populations, which may in some ways differ from other trauma populations in aspects of injury characteristics and demographic profile. Third data on important confounding factors such as presence of diabetes mellitus, chronic inflammatory states, and medications that might affect both glucose and leukocyte count was not available. fourth, the number of events (n=12) prevented us from doing multivariable analysis that could correct for injury severity and other confounding variables. Fifth, we did not have serial measurements of LGI during ICU stay and could therefore not check if there were any changes over time. Lastly, the absence of standardized injury scores in our calculations does not allow for comparison with trauma scoring systems.

4.7. Strengths

Despite these limitations, our study has a number of important strengths. To begin with, it represents one of the first studies to address the prognostic significance of LGI in trauma patients, which broadens the scope of application of this marker outside cardiovascular diseases. Secondly, the relatively large sample size (407 patients) and various clinical outcomes (mortality, length of stay, emergency interventions, need for transfusions) allow for an extended examination of LGI's prognostic value. Thirdly, the establishment of the optimal LGI cut-off point through standardized methods (ROC curve and Youden's index) adds to its clinical significance. Fourthly, the fact that routine laboratory parameters are employed makes it possible to apply this method without any additional expenses in practice.

5. CONCLUSION

According to this study, the leuko-glycemic index (LGI) is an independent risk factor for morbidity and mortality in patients with trauma who are admitted in the ICU. The optimum cut-off point of LGI calculated to be 1706.55 mg/dl•mm³ showed high sensitivity and specificity values of 91.7% and 76.7%, respectively. This means that LGI provides high predictive values for in-hospital death based on the AUC value of 0.905. High values of LGI are correlated with higher rates of the required emergency interventions, increased need for blood transfusion, longer stay in the ICU, and higher mortality rates. The independence of LGI from age and sex along with the low cost of its components can make LGI a feasible and practical method for early risk stratification for patients with trauma and further studies in this regard are warranted.

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