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Original Article / Özgün Araştırma

The role of triglyceride/high-density lipoprotein cholesterol ratio in the prediction of intensive care unit admission in the earthquake victims

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Abstract

Background: In the study of vascular and metabolic diseases, the ratio of triglycerides to high-density lipoprotein (HDL) cholesterol (TG/HDL) is crucial. Its significance for earthquake victims hasn't been fully investigated, though. This study investigates the relationship between the TG/HDL ratio and critical care unit admission in earthquake victims.

Methods: Sixty-four patients were enrolled. Both the laboratory results and the clinical features were documented. The TG/HDL ratio's prognostic value for intensive care unit (ICU) admission was then evaluated using ROC curve analysis. Spearman test was applied to analyze correlation between TG/HDL-c and inflammation markers. Logistic regression analysis was then used to elucidate the independent contribution of the TG/HDL-c ratio to the ICU admission risk.

Results: Median age of the cohort was 28 (IQR 17-40) and thirty-seven (57.8%) of the patients were female. 27 patients (42.2%) were admitted to ICU. In the multivariate model, the TG/HDL ratio was associated with higher risk of ICU admission (OR: 1.225, 95% CI: 1.003-1.496, p=0.047). The TG/HDL-c ratio may be a predictor of ICU admissions, according to the ROC curve (AUC: 0.737, 95% CI: 0.610-0.864, p=0.001). The TG/HDL ratio was positively correlated with procalcitonin (r = 0.620, p <0.001), white blood cells (r = 0.253, p = 0.044), and C-reactive protein (r = 0.410, p = 0.001).

Conclusion: The present study suggests a potential role for the TG/HDL ratio as a non-invasive and readily available biomarker for the prediction of ICU admission in the earthquake victims.

Keywords: earthquake, crush syndrome, triglyceride, high density lipoprotein cholesterol, inflammation

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Depremzedelerde Trigliserid/Yüksek yoğunluklu lipoprotein kolesterol oranının yoğun bakım ünitesine yatış öngörüsündeki rolü

Öz

Giriş ve Amaç: Trigliserid/yüksek yoğunluklu lipoprotein kolesterol oranı (TG/HDL) vasküler ve metabolik hastalıkların araştırılmasında önemli bir rol oynamaktadır ve depremzedelerdeki rolü üzerinde çalışmalar kısıtlıdır. Bu çalışmanın amacı depremzedelerde TG/HDL oranı ile yoğun bakım ünitesine yatış arasındaki inflamatuar ilişkiyi araştırmaktır.

Yöntemler: Altmış dört hasta çalışmaya dahil edildi. Hastaların klinik özellikleri ve başlangıç laboratuvar bulguları kaydedildi ve analiz edildi. ROC analizi TG/HDL'nin yoğun bakım ünitesine kabul için öngörücü rolünü değerlendirmek için kullanıldı. Spearman'ın sıra korelasyon katsayıları TG/HDL-c ve inflamatuar göstergeler arasındaki korelasyonu ölçmek için kullanıldı. TG/HDL-c oranının yoğun bakım ünitesine kabulündeki rolünü araştırmak için lojistik regresyon analizleri yapılmıştır.

Bulgular: Kohortun ortanca yaşı 28 (IQR 17-40) idi ve hastaların otuz yedisi (%57,8) kadındı. Hastaların 27'si (%42,2) YBÜ'ye kabul edilmiştir. Çok değişkenli modelde, TG/HDL oranı daha yüksek YBÜ'ye yatış riski ile ilişkilendirilmiştir (OR: 1.225, %95 GA: 1.003-1.496, p=0.047). ROC eğrisi (AUC: 0.737, %95 CI: 0.610-0.864, p=0.001) TG/HDL-c oranının YBÜ'ye kabulü öngörebileceğini göstermiştir. TG/HDL oranı beyaz kan hücreleri (r = 0.253, p=0.044), prokalsitonin (r = 0.620, p <0.001) ve CRP (r = 0.410, p =0.001) ile pozitif korelasyon gösterdi.

Sonuç: Çalışmamız, TG/HDL oranının depremzedelerde YBÜ'ye yatış için potansiyel olarak öngörücü bir belirteç olabileceğini göstermiştir.

Anahtar kelimeler: deprem, ezilme sendromu, trigliserid, yüksek yoğunluklu lipoprotein kolesterol, inflamasyon.

INTRODUCTION

On February 6, 2023, southern Turkey and northern Syria were struck by two powerful earthquakes. The initial 7.8 magnitude earthquake was followed by a 7.5 aftershock, causing widespread devastation[1]. These successive seismic events were accompanied by hundreds of aftershocks, with some reaching a magnitude exceeding 6. These earthquakes rank among the world's most destructive natural disasters since Haiti's 2010 earthquake[2]. The earthquakes had a major impact on the region, affecting ten cities and over 12 million people[3].

Natural disasters like earthquakes often bring several challenges for those affected[4]. A significant proportion of injured patients in disaster situations like this experience limb crush injuries of varying degrees, often due to being trapped under collapsed structures[5]. In crush syndrome, the prolonged pressure on muscles can lead to muscle damage, releasing myoglobin into the bloodstream, which can damage the kidneys[6]. As injured muscles and tissues release cellular contents into the bloodstream, the immune system becomes activated, leading to an inflammatory state[7]. Patients with crush syndrome often require admission to the care unit due to the high risk of developing serious complications. Moreover, the body's response to physical trauma and emotional stress can lead to an inflammatory response[8]. This response contributes to the development of various complications, including cardiovascular events and organ dysfunction[9]. In the aftermath of an earthquake, there is often a need to efficiently allocate limited resources, including intensive care unit (ICU) beds, to those who need them the most.

Lipids and their metabolites play active roles in numerous signaling pathways and cellular processes, many of which are closely linked to the body's immune and inflammatory responses[10,11]. Mounting evidence suggests lipid parameters have prognostic value in

diagnosis and progression of a wide spectrum of clinical conditions, encompassing inflammatory, metabolic, cardiovascular, infectious, and malignant diseases[12,13]. The triglyceride to high-density lipoprotein cholesterol (TG/HDL) ratio is a simple marker both insulin resistance and atherosclerotic dyslipidemia[14,15]. Furthermore, the TG/HDL ratio exhibits a robust association with both cardiovascular morbidity and mortality, demonstrating superior predictive power compared to individual assessments of HDL and TG in the context of atherosclerotic disturbances[16]. The TG/HDL ratio is a biomarker of the body's general inflammatory state in addition to endothelial dysfunction, which indicates an elevated risk of cardiovascular events[17]. However, the prognostic role of TG/HDL in the earthquake victims was not evaluated previously. Given these findings, we sought to investigate the relationship between the TG/HDL ratio and ICU hospitalization in earthquake victims.

METHODS

Study Population

The study involved earthquake victims who were affected by the February 6th earthquakes and hospitalized in a research and training hospital in the city of ***, located in Turkey's Southeastern Anatolia Region. A total of 161 patients were hospitalized with a diagnosis of earthquake victim (ICD-10 code X34). The 97 patients were excluded due to incomplete, or unattainable hospital records, due to missing lipid parameters, resulting in the inclusion of 64 patients for the study.

The following baseline clinical data were retrieved from the patient files and electronic hospital records: patient gender, age, types of injuries (abdominal, extremity, thoracic, and vertebral), baseline creatinine, creatinine kinase, C-reactive protein, complete blood count parameters, lipid parameters, need for renal replacement therapy, the presence of compartment syndrome and fasciotomies, ICU admissions, duration of hospitalization and last status (alive or exitus).

Statistical Analyses

Descriptive statistics for continuous variables with normal distributions were presented as mean and standard deviation, whereas those for non-normal distributions were presented as median with interquartile range. There were two ways to express categorical variables: frequency and percentage. Depending on whether they had an ICU admission or not, the patients were split into two groups. These groups were compared for continuous variables using independent sample t-tests and the Mann-Whitney U test, and for categorical variables using the Chi-squared test.

Spearman's correlation tests were used to determine the association between the TG/HDL ratio and other lab data. The predictive capacity of lipid parameters (triglyceride, HDL, and TG/HDL ratio) for ICU admission was assessed using ROC curve analysis, and the area under the curve (AUC) values were calculated. The risk factors for ICU admission were examined using multivariate logistic regression analyses, which included backward variable selection. In order to illustrate the relationships between the relevant variables and the result, odds ratios (OR) with 95% confidence intervals (CI) were used. SPSS 25.0 was used to conduct statistical analysis. P-values with two tails less than 0.05 were considered statistically significant.

RESULTS

64 patients in all were enrolled in the research consecutively. The cohort's median age was 28 (IQR 17–40), and 37 patients—or 57.8%—were female. The most common form of injury (81.3%) was spinal trauma, which was followed by extremity trauma (15.7%). Compartment syndrome affected 27 patients (42.2%) out of total. Fifteen (23.4%) patients underwent

fasciotomy, whereas four (6.3%) patients underwent amputation. The median stay in the critical care unit was 7 (5-14) days, with 42.2% of patients admitted. During the trial, there were no fatalities. Table 1 provides a summary of the study cohort's baseline characteristics.

Table I: Demographics and clinical characteristics of participants (n=64)

Characteristics	
Age (years), median (IQR)	29.50 (22-37)
Female gender, n (%)	37 (57.8)
Site of Injury	
Head and neck, n (%)	8 (12.5)
Thorax, n (%)	8 (12.5)
Abdomen, n (%)	2 (3.1)
Spinal, n (%)	10 (15.7)
Extremity, n (%)	52 (81.3)
Penetrating injury, n (%)	19 (29.7)
Number of traumatized extremities, median (IQR)	1 (1-2)
Treatment	
Debridement, n (%)	5 (7.8)
Fasciotomy, n (%)	15 (23.4)
Amputation, n (%)	4 (6.3)
Hemodialysis, n (%)	8 (12.5)
Hyperbaric Oxygen Treatment, n (%)	22 (34.4)
Clinical Outcome	
Presence of compartment syndrome,n (%)	27 (42.2)
Presence of sepsis, n (%)	2 (3.1)
ICU, n (%)	27 (42.2)
Death, n (%)	0 (0)
ICU length of stay (days), median (IQR)	7 (5-14)
Total hospital length of stay(days), median (IQR)	9.50 (4.25-16)

Abbreviations: ICU: Intensive care unit

There were similarities in the gender distribution (p=0.841) and median age (p=0.121) between the ICU and non-ICU patients. Compared to non-ICU patients, ICU patients exhibited higher rates of thorax trauma (p=0.045), limb trauma (p=0.008), higher potassium levels (p=0.018), higher CRP (p=0.005), higher triglycerides (p=0.017), and higher TG/HDL ratios (p=0.001). Additionally, ICU patients had lower levels of HDL (p=0.008) compared patients not admitted to ICU (Table 2). Median (interquartile range) TG/HDL ratio were 4.77 (2.61-8.06)in ICU patients and 2.37 (1.83-3.86) in non-ICU patients (p = 0.001). The graphical representation of TG/HDL ratio by groups is shown in Figure 1.

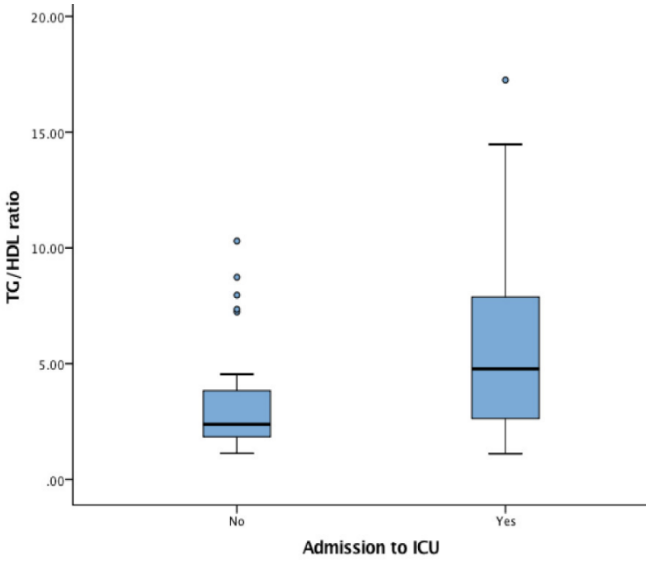

Figure 1. Triglyseride/HDL ratio according to the admission to Intensive Care Unit

Table II: Comparison of the baseline characteristics and laboratory findings of the two groups

	Admission to ICU (n=27), n (%)	**Non-admission to ICU (n=37), n (%)**	**p-value**
Age (years), median (IQR)	29 (17-33)	30 (23-41.50)	0.121
Female gender, n (%)	16 (59.3)	21 (56.8)	0.841
Site of Injury			
Head and neck, n (%)	4 (10.8)	4 (14.8)	0.632
Thorax, n (%)	6 (22.2)	2 (5.4)	0.045
Abdomen, n (%)	0 (0)	2 (5.4)	0.220
Spinal, n (%)	4 (14.8)	6 (22.2)	0.204
Extremity, n (%)	26 (96.3)	26 (70.3)	0.008
LOS-ICU time (day)	8 (4.5-14)	-	-
LOS-Hospital time (day)	16 (10-21)	5 (3-10)	<0.001
Laboratory results at admission,median (IQR)			
Creatinine (mg/dL)	0.65 (0.59-1.98)	0.69 (0.54-0.82)	0.568
CK	9630 (2000-69130)	5244 (2737-27498)	0.209
LDH	7.43 (3.71-22.14)	5.51 (4.14-13.90)	0.173
AST (U/L)	262 (66-883)	132 (59.50-539)	0.318
ALT (U/L)	105 (28-224)	76 (27-270)	0.729
Sodium (mmol/L)	137 (132-139)	137 (136-139)	0.370
Potassium (mmol/L)	4.50 (3.80-5.29)	3.96 (3.80-4.40)	0.018
Uric acid (mg/dL)	4.15 (3.07-6.50)	3.70 (2.70-5.22)	0.218
Haemoglobin (g/dl),	11.70 (9.90-16.60)	13.70 (12.00-16.05)	0.226
White cell count (10^3/ml)	16.20 (10.81-18.96)	13.25 (9.30-18.49)	0.240
Neutrophil count (10^3/ml)	12.62 (8.72-15.93)	10.98 (6.42-14.74)	0.140
Lymphocyte count (10^3/ml)	1.47 (1.17-1.94)	1.39 (1.08-1.98)	0.683
Platelet count (10^3/ml)	232 (173-298)	256 (199.50-322)	0.088
CRP (mg/dl)	1.13 (0.79-1.44)	0.61 (0.14-1.00)	0.005
Lipid profile, median (IQR)			
Triglyceride (mg/dL)	129 (86-171)	86 (68-124)	0.017
Total cholesterol (mg/dL)	100 (80-140)	111 (89-131)	0.644
HDL (mg/dL)	29 (20-35)	34 (28-39)	0.008
LDL (mg/dL)	56 (32-76)	59(42-69)	0.536
TG/HDL	4.77 (2.61-8.06)	2.37 (1.83-3.86)	0.001

Abbreviations: CRP: C-reactive protein; ICU: Intensive care unit; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; LOS: Length of stay; TG/HDL: Triglyceride/High-density lipoprotein cholesterol ratio.

A multivariate model was constructed with parameters that had a p value of <0.10 for ICU admission in the univariate analyses. The presence of thorax trauma (dichotomous), age (continuous), baseline C-reactive protein (continuous), platelet (continuous), baseline potassium level (continuous) and TG/HDL ratio (continuous) were included in the multivariate model. In the multivariate model, only TG/HDL ratio was associated with higher risk of ICU admission (OR: 1.225, 95% CI: 1.003-1.496, p=0.047) (Table 3).

Table III: Univariate and multivariate logistic regression analysis for admission to ICU

	Univariate analysis			Multivariate analysis		
Variable	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Age (continuous)	0.960	0.917-1.005	0.078	2.767	0.978-7.829	0.055
Presence of thorax trauma	5.00	0.923-27.078	0.062	3.138	0.491-20.042	0.227
Platelet	0.995	0.989-1.001	0.093	0.998	0.991-1.005	0.625
Baseline C-reactive protein	3.627	1.391-9.456	0.008	2.767	0.978-7.829	0.055
Baseline potassium level	3.049	1.341-6.929	0.008	1.320	0.462-3.774	0.604
TG/HDL	1.318	1.078-1.610	0.007	1.225	1.003-1.496	0.047

The ROC curve analysis was also used to find out the prediction in ICU admission by calculating the AUC. The triglyceride, HDL and TG/HDL ratio were all had significant predictive power for ICU admission prediction (Figure 2). The TG/HDL ratio had the highest AUC levels among all parameters (AUC: 0.737, 95% CI: 0.610-0.864, p=0.001). The TG/HDL ratio over 3.05 had 66.7% sensitivity and 73% specificity to predict the admission to ICU. The analysis of bivariate correlations showed a positive association between the TG/HDL ratio and WBC (r = 0.253, p=0.044), procalcitonin (r = 0.620, p <0.001), and CRP (r = 0.410, p =0.001). However, there were no significant correlations between the TG/HDL ratio and lymphocytes (r = 0.208, p= 0.099), as well as neutrophils (r = 0.161, p=0.203) (Table 4).

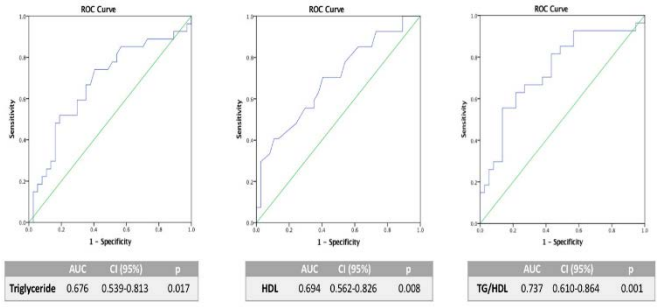

Figure 2. Evaluation of the ROC curve of the triglyceride level, HDL and the Tg/HDL ratio for the admission to ICU. Abbreviations: AUC, Area under the curve; CI, Confidence interval; HDL c, Highdensity lipoprotein cholesterol; ROC, Receiver-Operating Characteristic; Tg/HDL, Triglyceride/High-density lipoprotein cholesterol ratio.

Table IV: Correlation of TG/HDL ratio with the inflammatory indicators

Parameters	**r-values**	**p-value**
WBC	0.253	0.044
Neutrophils	0.161	0.203
Lymphocytes	0.208	0.099
CRP	0.410	0.001
Procalcitonin	0.620	<0.001

Abbreviations: CRP: C-reactive protein; WBC: White Blood Cells.

DISCUSSION

In our recent study, we discovered that patients admitted to the intensive care unit (ICU) had higher TG/HDL ratios than those who were not. We found that the TG/HDL ratio may be used to forecast if an ICU hospitalization is necessary. To our knowledge, this is the first study to report on the potential value of the TG/HDL ratio in predicting ICU admission in earthquake victims.

Crush syndrome is a significant and potentially life-threatening condition that that requires meticulous management in patients affected by earthquakes, as failing to address it promptly and effectively can result in a grim prognosis[18]. The pathogenesis of crush syndrome is very complex may involve factors such as renal ischemia-reperfusion injury, systemic inflammation, and the excessive deposition of myoglobin in renal tubules, which is released from damaged muscle tissue[19]. Recent studies in animal models of crush syndrome have demonstrated dysregulation of the inflammatory factors at both serum and tissue

levels. For instance, it has been shown that a significant elevation in the levels of IL-6 and IL-17 in the serum and kidney tissue of crush-induced rats, suggesting the promotion of a pro-inflammatory response primarily led by Th17 cells[20]. Additionally, Murata et al. also observed notable increases in serum TNF-α and IL-1β, within the initial 24 hours of reperfusion in crush syndrome model rats[21]. Inflammatory cells can also promote the release of various pro-inflammatory cytokines during the pathophysiological response following trauma, resulting in a cytokine storm that may potentially trigger multi-organ dysfunctions, and in some cases, even mortality[22]. Further research is needed for elaboration of precise mechanisms of inflammation on crush syndrome.

Triglyceride levels may increase during inflammation and infection[23]. Inflammatory cytokines may play a role in promoting TG synthesis and reduce TG hydrolysis during trauma[24]. Hypertriglyceridemia has been demonstrably linked to the induction of endothelial dysfunction, characterized by impaired vasodilation, pro-inflammatory and pro-thrombotic states, and enhanced oxidative stress. This dysfunction significantly elevates the susceptibility to a spectrum of cardiovascular diseases, including coronary artery disease, atherosclerosis, and thromboembolic events[25]. Conversely, lower HDL levels have been associated with worse clinical outcomes including need of ICU admission and mortality, particularly in infectious and inflammatory diseases[26,27]. Several hypotheses can be postulated, including an acute overconsumption of HDL particles and easier redistribution from the intravascular to the extravascular compartment following trauma[28]. Recently, the TG/HDL-C ratio, which is combination of HDL and TG, has garnered increasing attention due to its superior predictive capability for cardiovascular events and insulin resistance than the either parameter alone[29]. Moreover, the ratio of TG to HDL is a measure of the general level of inflammation. Notably, Jonas et al. demonstrated that an elevated TG/HDL ratio indicates systemic inflammation in individuals with idiopathic pulmonary arterial hypertension (IPAH)17. In the present investigation, we found that the TG/HDL ratio and procalcitonin, WBC, and CRP were positively correlated. These results aligned with a prior study that found higher levels of IL-6, IL-1β, and MCP-1 in IPAH patients with elevated TG/HDL17. Furthermore, Peng et al. discovered that a higher TG/HDL ratio was associated with an increased risk of COVID-19 death in instances of COVID-19 pneumonia[30].

There are several drawbacks to this study. First, no analysis of a causal association could be made because the study was retrospective in nature. Secondly, it was not feasible to assess the long-term outcomes and mortality rates of the patients involved in the study. Third, there were no sequential data or changes in the patients' lipid profiles during their hospital stay. Employing dynamic monitoring could offer a more comprehensive characterization of dyslipidemia. Fourth, this retrospective, single-center study involved a small sample size, potentially introducing selection bias. Finally, limitations of the current study include the potential for confounding by unmeasured variables, including dietary preferences, lifestyle habits, and medication use. These factors may have influenced the observed associations and should be considered in the interpretation of the results.

In conclusion, our study indicates that the TG/HDL ratio may be a valuable predictor of ICU admission in earthquake victims, highlighting its potential utility as an early risk assessment tool. The findings of this study can contribute to improving disaster response strategies, and mitigating the impact of such

catastrophic events on healthcare systems with limited ICU capacity.

Ethics Committee Approval: This study was approved by the Gazi Yaşargil Research and Training Hospital Ethics Committee on 04.08.2023 with the decision number 499. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Conflict of Interest: No conflicts of interest were disclosed by the authors.

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