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Akut Pankreatit Hastalarında Nötrofil/Lenfosit ve Trombosit/Lenfosit Oranlarının Tanısal ve Prognostik Değeri

Diagnostic and Prognostic Value of Neutrophil/Lymphocyte Ratio and Platelet/Lymphocyte Ratios on Acute Pancreatitis Patients

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ÖZ

Amaç: Bu çalışmada, pankreatit hastalarının hastalık şiddetinin izlenmesinde nötrofil-lenfosit oranı (NLO) ve trombosit-lenfosit oranlarının (TLO) bir parametre olarak kullanılıp kullanılamayacağını göstermeyi amaçladık.

Materyal ve Metot: Akut pankreatit tanısı ile gastroenteroloji servisinde yatan ve takip edilen, dosyaları retrospektif olarak incelenen toplam 200 hasta çalışmaya dahil edildi. Akut pankreatitin şiddeti ve prognozu Atlanta sınıflaması ile değerlendirildi.

Bulgular: NLO ortalaması hasta grubunda 9,84±9,60, kontrol grubunda ise 2,00±0,86 idi. Hasta grubunda NLO düzeyi yüksek saptandı ve cut-off değeri 2,85 olarak bulundu (Duyarlılık: %86 ve özgüllük: %81). Hastalık şiddetine göre NLO ortalamasında anlamlı bir değişiklik bulunmamakla birlikte, gruplar arasında NLO ortalamasındaki düşüş 48 saatte anlamlı bulundu.

Sonuç: Sadece ilk 48 saatteki NLO düzeyindeki değişikliğin hastalık şiddeti ile ilişkili olabileceğini bulduk. NLO'nun kullanılabilecek, uygulanabilecek ve kolay ulaşılabilecek bir parametre olduğunu gördük

Anahtar Kelimeler: Akut pankreatit, platelet, prognostik faktörler, NLO ve TLO

ABSTRACT

Objective: In this study, we aim at demonstrating whether we can use neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratios (PLR) as a parameter in monitoring the disease severity of Pancreatitis Patients.

Materials and Methods: A total of 200 patients diagnosed with acute pancreatitis, hospitalized and monitored in gastroenterology service, whose files had retrospectively been studied, were included in the study. The severity and prognosis of acute pancreatitis were evaluated with the Atlanta classification.

Results: The average of NLR was 9.84±9.60 in the patient group but 2.00±0.86 in the control group. The NLR level was found higher in the patient group. The cut-off value was found as 2.85 (Sensitivity: 86% and specificity: 81%). Although no significant change was found in terms of the average of NLR concerning the disease severity, the decrease in the average of NLR among the groups was found significant in 48 hours.

Conclusion: We have found that only the change in NLR level in the first 48th-hour could be associated with the disease severity. We found NLR as a parameter that can be used, applied, and accessed easily.

Keywords: Acute pancreatitis, platelet, prognostic factors, NLR and PLR

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INTRODUCTION

Acute pancreatitis is characterized by the activation of pancreatic enzymes, amylase, and lipase, in the pancreas for various reasons and the digestion of pancreatic tissue itself.[1] It is an inflammatory disease characterized by abdominal pain and elevated serum pancreatic enzyme levels. Gallbladder and bile duct stones, alcohol, drugs, infections, trauma, ischemia, and genetic factors are the leading causes of acute pancreatitis etiology. In 80% of cases, gallstones and alcohol are the most common etiologic agents.[2]

Complete inhibition of pancreatic cathepsin B in an in vitro environment inhibits the activation of trypsinogen. Trypsin catalyzes the conversion of proenzymes and activates quinine and complement systems. These activated enzymes cause autodigestion in the pancreas, releasing more active enzymes.[3] Trypsinogen is typically activated in the pancreas in a small amount spontaneously, but by intrapancreatic mechanisms, this active trypsin is removed. Pancreatic secretory trypsin inhibitor inactivates by binding 20% of the active trypsin.[4] The pancreas also includes nonspecific antiproteases such as alpha-1-antitrypsin, alpha-2-macroglobulin.[5]

In literature, there have been researches on diagnostic values of neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte (PLR) ratios in some clinical diseases and health problems. According to these researches, NLR and PLR ratios may give clinicians an idea of potential disease and health conditions.[6]

Although there has been some research on NLR, PLR, and pancreatitis individually, there have not been enough studies on NLR and PLR on acute pancreatitis. Thus, it was aimed to evaluate diagnostic values of NLR and PLR ratios for acute pancreatitis.

MATERIALS AND METHODS

Ethical Status of the Study: Our study was approved by the Sakarya University Ethics Committee (Date: 17.07.2014, decision no: 71522473/050.01.04/64). The study was carried out in accordance with the international declaration and guidelines.

Study Group: The present study was conducted with 200 patients, who were admitted to the RT Ministry of Health, Sakarya University, Faculty of Medicine, Education and Research Hospital Gastroenterology Clinic between 15.09.14-15.01.15, who met the inclusion criteria, and who were diagnosed with acute pancreatitis clinically and radiologically (the Patient Group). A total of 35 healthy individuals matched by gender and age were included in the study as the Control Group. The standard study form was prepared previously for clinically diagnosed with acute pancreatitis, and the laboratory was filled. The patients' age, gender, medical history (diabetes, hypertension, ischemic heart disease, arrhythmias, hyperlipidemia), and the hemogram and biochemistry parameters were recorded on this form.

Diagnosis and evaluating of the severity of Acute Pancreatitis: The diagnosis of acute pancreatitis is made by the criteria of abdominal pain and serum amylase or three times the normal lipase level, determined with Atlanta classification. Many different terminologies have been defined in the definition of acute pancreatitis and its complications. In order to avoid these confusions, a consensus statement was written and published at a meeting held in Atlanta, the USA, in 1992. [2] According to this classification, our patients were divided into mild and severe pancreatitis. The number of patients in the severe group was 41, and the number in the mild group was 159.

Hemogram and extensive biochemistry tests were performed at admission and 48th hour for hospitalized patients. Especially hemoglobin (Hgb), neutrophil, lymphocyte, platelet, C-reactive protein (CRP), sedimentation, calcium, triglyceride (TG), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and glucose values of the patients also were recorded. Each patient was evaluated with abdominal ultrasonography imaging (USI) regarding biliary/nonbiliary distinction after hospitalization.

Statistical analysis: The statistical package for social sciences for Windows 18.0' (SPSS 18 Inc.) program was used for statistical analysis in evaluating the data obtained in the study. Descriptive statistical methods (i.e., mean, standard deviation, frequency distribution, and %) were used to evaluate the study data, and ANOVA and Fischer's Test were used to compare the categorical data. Before the quantitative data were analyzed, it was tested whether the data showed normal distribution with the help of the Kolmogorov Smirnov Test. The data with normal distribution were evaluated using the ANOVA test to compare two independent groups, and the data that did not show normal distribution were evaluated using the Mann-Whitney U Test. The Kruskal Wallis Test was used to compare more than two groups. The Non-Parametric Spearman Test was used for correlation analyses, and the results were evaluated at a 95% Confidence Interval and the significance level was taken as $p<0.05$.

RESULTS

A total of 200 patients who had acute pancreatitis and 35 healthy volunteers who met inclusion criteria were included in the present study, and 72 (36%) of

these 200 patients were male, 128 (64%) were female, 18 (51%) of 35 healthy volunteers were male, and 17 (49%) were female. No statistically significant differences were detected between the two groups in terms of gender (p>0.05) (Table 1). The mean age of the Patient Group was 60.17±17.19, and the mean age of the Control Group was found to be 46.68±16.96. Statistically significant differences were detected between the two groups in terms of age (p<0.05) (Table 1).

The patient and control groups were compared with each other regarding the admission lymphocyte levels, neutrophil levels, platelet levels, 48th-hour lymphocyte levels, 48th-hour neutrophil levels, and 48th-hour platelet levels. The lymphocyte, platelet, 48th-hour lymphocyte, and 48th-hour platelet levels were lower in the Patient Group at statistically significant levels when compared to the Control Group (p<0.05). The neutrophil and 48th-hour neutrophil levels were higher in the patient group at statistically significant levels when compared to the control group (p<0.05) (Table 1).

The mean NLR was found to be 9.84±9.60 in the Patient Group and 2.00±0.86 in the Control Group, and the NLR level was higher in the Patient Group at a statistically significant level compared to the Control Group (p<0.05). The mean PLR was found to be 0.23±0.18 in the Patient Group and 0.12±0.04 in the Control Group, and the PLR level was higher in the patient group at a statistically significant level when compared to the Control Group (p<0.05) (Table 2).

The mean arrival NLR was 9.18 in the mild group, the mean 48th-hour NLR was 5.42, and a statistically significant difference was detected between the two mean values (p=0.00). The mean NLR was 11.99 at the end of the 48th-hour in the severe group, the mean NLR at the 48th-hour was 11.82, and no statistically significant differences were detected between the two mean values (p=0.15) (Table 3).

In the present study, when the cut-off value was taken as 2.85 for the admission NLR parameter, the diagnostic value of the test was found to be 86% sensitive and 88% specific in terms of disease severity (Figure 1) (p=0.02, R2:0.61).

In the mild group, the mean PLR was 0.23 at admission and 0.17 at 48th-hour. No significant difference was found between groups (p=0.13). The mean PLR was 0.24 at admission in the severe group and 0.20 at the 48th-hour. No statistically significant difference was detected between the mean PLR at 48th-hour and the mean PLR at admission (p=0.15) (Table 4).

Table 1. Some demographic and biochemical characteristics of the patient and control group.

Variable	Patient (mean±sd)	Control (mean±sd)	P-value
Male gender n (%)	72 (36%)	18(51%)	0.08***
Female gender n (%)	128(64%)	17(49%)	0.06***
Age (years)	60.17±17.19	46.68±16.96	0.01*
Lymphocyte (K/uL)(admission)	1420.58±813.34	2869.37±3183.09	0.01**
Neutrophil (K/uL)(admission)	9410.15±4883.12	4532.86±1402.27	0.01**
Platelet (K/uL)(admission)	240.76±80.03	285.71±69.08	0.01*
Lymphocyte (K/uL)(48th-hour)	1705.61±1155.63	2869.37±3183.09	0.01*
Neutrophil (K/uL)(48th-hour)	7898.22±4970.14	4532.86±1402.27	0.01**
Platelet (K/uL)(48th-hour)	212.92±72.38	285.71±69.08	0.01*

*: ANOVA; **: Mann-Whitney U; ***: Chi-Square.

Table 2. Relation between NLR and PLR levels of the patient and control group at admission.

Variables (mean±sd)	Patient	Control	P-value
NLR	9.84±9.60	2.00±0.86	0.01*
PLR	0.23±0.18	0.12±0.04	0.01*

*: Mann Whitney U.

Table 3. The relation between admission and 48th-hour values of NLR mean in the mild and severe group.

NLR (mean)	Admission	48th-hour	P-value
Mild n:159	9.18	5.42	0.01*
Severe n:41	11.99	11.82	0.15*

*: Wilcoxon.

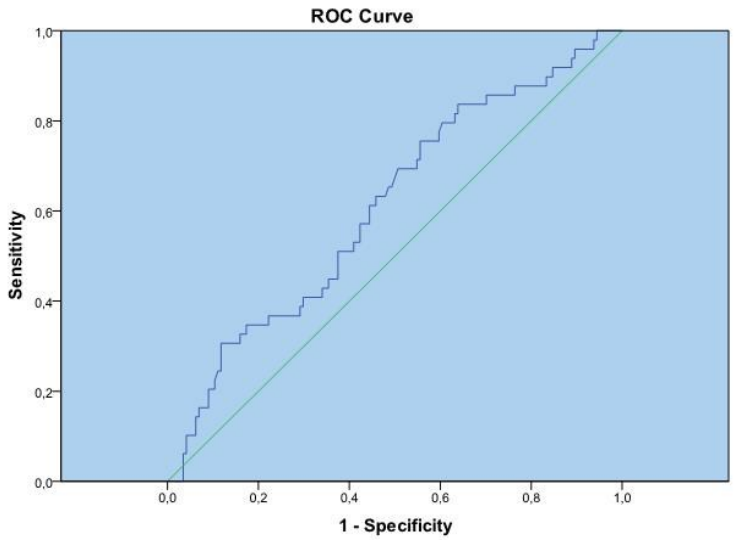

Figure 1. Admission NLR ROC Curve according to disease severity.

Table 4. Relation between PLR mean admission and 48th-hour values in the mild and severe group.

PLR (mean)	Admission	48th-hour	P-value
Mild	0.23	0.17	0.13*
Severe	0.24	0.20	0.15*

*: Wilcoxon.

DISCUSSION AND CONCLUSION

Acute pancreatitis is a significant disease of the pancreas drawing attention with high mortality and morbidity rates, its incidence varying between 4.9-35/100.000.[7,8] The fact that the disease is sometimes very mild and very severe clinically makes it challenging to diagnose, which may cause avoidable causes to be missed and mortality with second attacks that may develop. A total of 80% of the cases are mild and without serious morbidity, and 20% are severe. A decrease has not been observed over the years in the frequency of severe pancreatitis.[9,10]

Its pathophysiology consists of acute inflammation causing changes in regional tissues and other organs. The inflammation cascade was explained in previous clinical and experimental studies. According to the degree of inflammation, the histopathology of the disease exhibits a broad spectrum that ranges from mild interstitial edema to severe hemorrhagic gangrene and necrosis.[8,11,12]

Gallbladder stones and alcohol make up 70-80% of the etiology. Etiology differs among countries. For example, although alcohol ranks first in western countries, biliary causes are the first.[13,14] Other causes include abdominal trauma, hypertriglyceridemia, ampulla of Vater, pancreatic tumor, infectious causes, drugs, ERCP, or surgical interventions. Also, the etiologic cause cannot be detected in 10% of the cases called "idiopathic pancreatitis".[15,16] When the literature was reviewed, many studies on the etiology of acute pancreatitis in our country came to the forefront. Especially in a study with 129 patients, biliary (64.3%) and idiopathic (26.4%) causes made up the first two lines.[17-19] Similarly, in a study with 84 patients, biliary causes accounted for 66% of the cases and idiopathic causes 31%.[20-22]

The severity of acute pancreatitis occurs in different degrees, and the main reasons for determining the severity are usually multifactorial. In general, it is thought that tissue damage is triggered by the activation of digestive zymogens in acinar cells as the mechanism of emergence of the clinic and causes acute pancreatitis.[23-26] On the other hand, there is no sufficient and definite information about the exact mechanism of pancreatitis.

Even if the severity and complications vary widely, the causes of acute pancreatitis are similar to clinical and laboratory findings. It can be argued that all causes of acute pancreatitis meet at a common point.[27-29] However, this idea needs to be proven by clinical and scientific research.

From this point of view, the idea of looking at the diagnostic value in diseases by making easy access to the values obtained in the routine tests and the results of the clinical tests has made significant

contributions to clinical applications. Although there is not enough literature base for diagnosis based on NLR and PLR rates and only based on these data, such studies may be important sources for further research and meta-analysis.

Early diagnosis is essential in pancreatitis and in evaluating the underlying ideas and findings. Therefore, any clinical practice that may express diagnostic value may be considered valuable. Although the findings obtained in the study are not sufficient for the diagnosis of pancreatitis, NLR and PLR ratios are essential in providing a basis for clinical studies and meta-analyzes and guiding clinical applications. In the study, applying a high sample according to the studies in the field may contribute to the NLR and PLR studies in diagnosing pancreatitis.

In conclusion, there is a need for an easily accessible and inexpensive biomarker to indicate the diagnosis and clinical progression of acute pancreatitis, which may have different clinical manifestations. In our study, the purpose was to show the relations between NLR and PLR, which were shown in previous studies to increase inflammatory diseases and have prognostic importance, and acute pancreatitis. A significant increase was detected in NLR and PLR levels in the diagnosis of acute pancreatitis. However, it was found that only the change in NLR levels in the first 48 hours was associated with disease severity. Based on this finding, in our study, we would like to draw attention to NLR as an easily applicable and accessible parameter, which can be used similarly to the Atlanta classification. One of the limitations of this study is the small number of samples and the single center of the data. It is suggested that future studies be conducted with a larger number of samples from several medical centers.

Ethics Committee Approval: Our study was approved by the Sakarya University Ethics Committee (Date: 17.07.2014, decision no: 71522473/050.01.04/64).

Conflict of Interest: No conflict of interest was declared by the authors.

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