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Akut Kolesistit-Kolelitiazis Ayırıcı Tanısında Nötrofil/Lenfosit Oranının Klinik Önemi

Clinical Importance of Neutrophil/Lymphocyte Ratio in Differential Diagnosis of Acute Cholecystitis and Cholelithiasis

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ÖZET

GİRİŞ ve AMAÇ: *Akut kolesistit (AK), acil servise karın ağrısı başvurularının önemli nedenlerinden biridir. Nötrofil sayısındaki artış ve lökosit sayısındaki azalma inflamasyonun fizyolojik bir sonucudur nötrofil lenfosit oranı (NLO) diğer inflamatura markırlar gibi bu süreçte kullanılabilir..Bu çalışmamızda AC tanızında NLO'nın tanısal değeri araştırıldı.*

GEREÇ ve YÖNTEM: *Bu çalışmaya sağ üst kadran ağrısı ile başvuran 318 yetişkin hasta dahil edildi. Bu hastalar 1 Temmuz- 31 Aralık 2013 tarihleri arasında medikal kayıtları olan sağ üst kadran ultrasonografisi yapılan hastalardı. Hastalar AC, kolelitiazis ve patology olmayan grup olmak üzere 3 gruba ayrıldı. Ultrasonografik bulguları ve hastanın tam kan sayımı parametreleri kaydedildi. Grupların NLO skorları hastanın kan parametrelerinden hesaplandı.*

BULGULAR: *Çalışmamızda 382 hasta dosyası incelenmiş olup dışlama kriterlerine uyan 64 hasta çalışma dışı bırakılmıştır. Çalışmaya 318 hasta dahil edilmiştir. Hastaların 221 tanesi (%69,5) kadın, 97 tanesi (%30,5) erkektir. Hastaların 58 tanesinde (% 18,2) akut kolesistit, 70 tanesinde (% 22) kolelitiazis saptanmıştır. 190 hastada (% 59,8) ise her hangi bir patoloji saptanmamıştır.*

Hastaların yaş ortalaması 47,12±17,30'tir. Akut kolesistit saptanan hastaların yaş ortalaması 55,87±18,48, kolelitiazis saptananan hastaların yaş ortalaması 46,41±16,27, herhangi bir patoloji saptanmayan yaş ortalaması 44,71±16,52'dir

Gruplar arasında karşılaştırma yapıldığında NLO'ı akut kolesistit saptanan hastalarda 8,78±6,30, kolelitiazis saptananan hastalarda 2,93±1,69, herhangi bir patoloji saptanmayan hastalarda 3,72±4,02'dir. (p=<0.001)

TARTIŞMA ve SONUÇ: *NLO kolesistit tanısı alan hastalarda diğer 2 gruba göre anlamlı olarak yüksek bulunmuştur. Akut kolesistit tanısında diğer inflamasyon belirteçleri ile birlikte kullanılabilecek değerli bir veri olduğu düşünülmüştür.*

Anahtar Kelimeler: *Akut kolesistit, nötrofil/lenfosit oranı, acil servis*

ABSTRACT

INTRODUCTION: *Acute cholecystitis (AC) is one of the major causes of abdominal pain in emergency department admissions. Since the number of neutrophils increase and the lymphocytes decrease as a result of a physiological response of circulating leukocytes to inflammation, the neutrophil-to-lymphocyte ratio (NLR) can be used as an inflammatory marker with other inflammatory markers. In this study we investigated the diagnostic value of the NLR in the diagnosis of AC*

METHODS: *Included in this study were 318 adults with complaints of right upper quadrant pain. These patients were evaluated with ultrasonography and other data from their medical records between 1 July 2013 and 31 December 2013. The patients were divided into three groups: AC, cholelithiasis, and no pathology. The ultrasonographic findings and complete blood count parameters of the patients were recorded. After the patients were divided into groups, the NLR scores were calculated from patients' blood parameters.*

RESULTS: *A total of 382 patient files were examined and 318 patients were included in the study. Fifty-eight patients (18.2%) had AC, 70 patients (22%) had cholelithiasis, and in 190 patients (59.8%) no pathology was detected. The average NLR scores were 8.78 ± 6.3 in the AC group, 2.93 ± 1.69 in the cholelithiasis group, and 3.72 ± 4.02 in the "no pathology" group (p < 0.001).*

DISCUSSION AND CONCLUSION: *The NLR was significantly higher in AC patients when compared to the other two groups. NLR is a valuable piece of data that can be used with other inflammation markers in the diagnosis of AC*

Keywords: *Acute cholecystitis, neutrophil/lymphocyte ratio, emergency departmen*

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INTRODUCTION

Abdominal pain is most common cause in admission to the emergency department. Since there are many causes of this pain and high mortality-morbidity increases the importance of early diagnosis. Acute cholecystitis (AC) is one of the major causes of abdominal pain on admission to an emergency department. An early AC diagnosis and good treatment responses are crucial for reducing mortality and morbidity from this condition (1). Emergency doctors have a great responsibility for this process. Seperation of acute cholecystitis and cholelithiasis is important for differential diagnosis of the patients applied to the hospital with right upper quadrant pain for emergency surgery and hospitalization.

An accurate AC diagnosis requires specific diagnostic criteria. The Tokyo Guidelines (TG 13) are commonly used criteria for this diagnosis. (2) These criteria were classified as clinical markers and ultrasonography findings of inflammation. USG is utilized as a gold standard for diagnosis of acute cholecystitis. However, USG may not be achievable immediately. For that reason, we need helpfull diagnostic bedside tests before USG.

Given that the number of neutrophils increase, and the lymphocyte numbers decrease due to the physiological response of the circulating leukocytes to inflammation, the neutrophil to lymphocyte ratio (NLR) is used as an inflammatory marker together with other inflammatory markers. (3)

The limited study with NLR shows the increase of NLR may be the evidence acute cholecystitis. However there is a need for further study. In addition to this, acute appendicitis and pancreatitis with inflammation be in the front the similar studies showed the increase of NLR.(6,8,9) For acute cholecystitis with the same inflamation process the increas of NLR will be usefull for the differential diagnosis.

In this study, we investigated the diagnostic value of the NLR in the diagnosis of AC in patients who were admitted to the emergency department with the complaint of right upper quadrant pain.

The purpose of our study was to investigate the diagnostic value of the NLR in AC patients by comparing NLR values of patients presenting with right upper quadrant pain and diagnosed with cholelithiasis, cholecystitis, or having no other pathology.

MATERIAL and METHOD

This retrospective, single-center, observational study has been performed in third stage Education And Research Hospital

This study included 318 adult patients who were admitted to the emergency department between 1 July 2013 and 31 December 2013 with complaints of right upper quadrant pain. These patients were evaluated with ultrasonography with an initial diagnosis of a gallbladder pathology. This diagnosis and data from available medical records were included in this study. The data were examined retrospectively through the patients' files.

Patients with a history of infectious, autoimmune, or neoplastic diseases were excluded from this study. Additional exclusion criteria included patients with severe liver failure, renal failure, previous surgery or trauma, use of immune suppressive medicines or steroids, and those with missing file information.

The demographic characteristics, ultrasonographic findings, and complete blood count parameters of the patients were recorded.

The patients were grouped into three subgroups that included AC, cholelithiasis, and no pathology. Diagnosis of AC was made according to the criteria of the Tokyo Guidelines (TG13). After the subgroups were formed, the NLR values of patients were calculated from complete blood count parameters and comparisons were made.

Statistical Analysis

The statistical analyses were performed using IBM SPSS software package for Windows Version 21.0. Quantitative variables were summarized as mean ± standard deviation and median values. Categorical variables were expressed by number and percentage. Differences between the groups in terms of categorical variables were evaluated with the chi-square test. Normality of the quantitative variables was examined with the Shapiro-Wilk test and homogeneity of variance was examined with the Levene test. Differences between the groups independently in terms of numeric variables were examined by a one-way analysis of variance when parametric test assumptions were provided, and

when there was a difference, pairwise comparisons were performed with the Tukey HSD test. If the assumptions of the parametric tests were not provided, the Kruskal-Wallis test was used for group comparisons. The group making the difference was determined by the Siegel-Castell test. The difference between two groups in terms of numeric variables was examined by the Mann Whitney U test, since the assumptions of the parametric tests were not provided. The cut-off point for the best value of the NLR to estimate cholecystitis was determined by a receiver operating characteristic (ROC) curve analysis. The sensitivity and specificity values of this cut off point were calculated. A p-value of < 0.05 was considered significant.

RESULTS

A total of 382 patient files were examined and 318 patient files, which fullfilled the inclusion criteria, were included in the study. Of the 318 patients, 221 (69.5%) were females and 97 (30.5%) were males.

The AC subgroup included 58 patients (18.2%; 21 males and 37 females), the cholelithiasis subgroup included 70 patients (22%; 16 males and 54 females), and the no pathology subgroup included 190 patients (59.8%; 60 males and 130 females).

The mean age of all patients was 47.12 ± 17.30 years. The mean age of the AC patients was 55.87 ± 18.48 years, the mean age of the cholelithiasis patients was 46.41 ± 16.27 years, and the mean age in the no pathology subgroup was 44.71 ± 16.52 years. There was no statistically significant difference between the mean ages of the cholelithiasis and no pathology subgroups ($p = 0.751$); however, the mean age of the AC group was significantly higher than that of the cholelithiasis and no pathology subgroups ($p = 0.005$ and $p < 0.001$, respectively).

The distribution of pain characteristics and examination findings are given in Table 1. In AC patients, sludge in the gallbladder was detected in 12 (20.7%) patients, hydrops in 9 (15.5%) patients, Murphy's sign in ultrasonography (USG) in 33 (56.9%) patients, gallbladder wall thickness over 5 mm in 12 (20.7%) patients, pericholecystic liquid in 21 (36.2%) patients, and pancreatitis in 1 (1.7%) patient.

Gallbladder stones were detected in 46 of the 58 AC patients (79.3%), however, no stones were detected in 12 patients (20.7%). Multiple stones were detected in 19 of the 46 patients (41.3%) who were diagnosed with cholecystitis with stones and a single stone was detected in 27 patients (58.7%).

The number of neutrophils was increased and the number of lymphocytes was decreased significantly in the AC subgroup when compared to the other two groups. Accordingly, NLR was significantly higher in the AC subgroup (Table 2). According to the ROC curve analysis, the optimal cut-off value of NLR being able to predict AC was > 4.115 with 75.9% sensitivity and 77.7% specificity (area under the curve [AUC] = 0.822; asymptotic 95%; confidence interval [95% CI]: 0.769–0.888) (Figure 1).

DISCUSSION

In the observational retrospective study old age, high WBC, high neutrophil, low lymphocyte and NLR increase has been found statistically more significant compared to the cases with acute cholecystitis and cholelithiasis of no pathology group.

Abdominal USG holds an important place in determining the etiology of abdominal pain. In cases of right upper quadrant pain, the sensitivity and specificity of USG in defining cholelithiasis and cholecystitis are 92–96% and 95–99%. Since severe cholecystitis is associated with more adverse clinical features than simple cholecystitis, prompt detection of the severe cholecystitis and surgical intervention before its further advancement is essential to avoid complications related to advanced histology spectively (4).

Mills et al. (5) examined 177 patients admitted with right upper quadrant pain and detected AC in 42.4%, cholelithiasis in 27.1%, and normal biliary tracts in 30.5% of patients with ultrasound. In our study, we detected AC in 18%, cholelithiasis in 22%, and normal biliary tracts in 59.8% of the patients. These differences may depend on the patient population and the individuals who performed the USG. AC constitutes 3–10% of patients with abdominal pain.

Table 1: The Distribution of Pain Characteristics and Examination Findings of The Patients

		Acute cholecystitis		Cholelithiasis		No Pathology		
		(N)	(%)	(N)	(%)	(N)	(%)	p
Pain characteristics	Blunt	36	62.1	25	35.7	127	66.8	<0.001
	Colic	22	37.9	45	64.3	63	33.2	
Epigastric pain	Yes	32	55.2	32	45.7	68	35.8	0.023
	No	26	44.8	38	54.3	122	64.2	
Right upper quadrant	Yes	18	31	22	31.4	126	66.3	<0.001
	No	40	69	48	68.6	64	33.7	
Non-localized pain	Yes	51	87.9	61	87.1	159	83.7	0.687
	No	7	12.1	9	12.9	31	16.3	
Duration of pain (hours)	0-6	1	1.7	5	7.1	102	53.7	<0.001
	6-12	14	24.1	37	52.9	53	27.9	
	>12	43	74.2	28	40	35	18.4	
Right upper quadrant sensitivity	Yes	8	13.8	8	11.4	23	12.1	0.916
	No	50	86.2	61	86.6	167	87.9	
Murphy's sign	Yes	22	37.9	50	71.4	171	90	<0.001
	No	36	62.1	20	28.6	19	10	
Diffuse sensitivity	Yes	52	89.7	59	84.3	157	82.6	0.406
	No	6	10.3	11	15.7	33	17.4	

Table 2: Comparison of Complete Blood Count Parameters Between The Three Subgroups

	AC mean ±SD	Cholelithiasis mean±SD	No pathology mean±SD	p
Wbc	12129±4099	8990±2355	9372±3030	<0.001 <0.001 0.827
Neutrophils	9587±3941	5812±1901	6193±2868	<0.001 <0.001 1.000
Lymphocytes	1632±1171	2354±990	2273±983	<0.001 <0.001 1.000
NLR	8,78±6,30	2,93±1,69	3,72±4,02	<0.001 <0.001 1.000

AC:Acute cholecystitis, NLR: Neutrophil-to-lymphocyte ratio

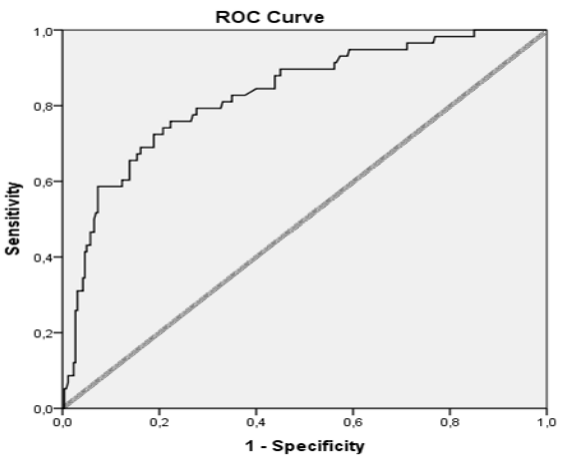

Figure 1: According to the receiver operating characteristic (ROC) curve analysis for simple and severe cholecystitis (The area under ROC curve:0.822- [95% CI]: 0.769–0.888) p<0.01)

It is often associated with gallstones, but ischemia, motility disorders, chemical injury, infections, collagen diseases, and allergic reactions may also be involved. Cholecystitis with stones constitutes 90–95% of the cases, and 5–10% of the cases are acalculous cholecystitis (1). In our study, we did not detect any stones in the gallbladder in 20.7% (n=12) of the AC patients. This ratio is greater than the ratios reported in other studies. The average age of our patients was 47 years. The mean age of the AC patients was 55 years and the female-to-male ratio (F:M) was 2:1. The average age of our study population of patients with cholecystitis and female dominance is similar with studies found in the literature (6).

Lee at al. found that increas of NLR was more in acute severe cholecystitis than chronic simple cholecystitis and in addition to this NLR>3 is related with mortality and high risk. (7) Three years observational study of Basol et al. showed that high values of WBC,CRP and NLR are the signature of diagnosis of acute cholecystitis. (8)

NLR is a marker for infection and inflammation that can easily be calculated from a complete blood count. Because of this, it has been used in the diagnosis of infectious diseases such as acute appendicitis, ulcerative colitis, pneumonia, and acute pancreatitis. It has also been used as a prognostic factor in inflammatory mechanisms such as cerebrovascular disease, acute coronary syndrome, and pulmonary thromboembolic diseases (9-13). Ishizuka et al. evaluated 314 patients who underwent appendectomy with the diagnosis of acute appendicitis and found that NLR of the patients with gangrenous appendicitis was significantly higher than that of the patients with phlegmonous appendicitis and cataral appendicitis (9). Çelikbilek et al. (10) found that NLR was significantly higher in patients with ulcerative colitis (UC) compared with the control group. They also found that NLR was increased in the activation period of UC (10). Jager et al. (11) compared NLR of patients with community-acquired pneumonia and found that the duration of the hospital stay was longer and the rates of both the intensive care hospitalization and mortality were higher. Gökhan et al. (12) investigated the relationship between NLR and a short-term prognosis and mortality in stroke patients and the subtypes found that NLR is significantly higher in the group with higher mortality. Zazula et al. (13) examined acute coronary syndrome patients and found that between NLR and a short-term prognosis and mortality in stroke patients and found that NLR is significantly higher in the higher mortality group (12). Çavuş et al. (14) compared NLR values of patients with pulmonary thromboembolism with a healthy control group and found that NLR was significantly higher in patients with pulmonary thromboembolism. Suppiah et al. (15) found that NLR increases in patients with acute pancreatitis in proportion to the severity of the disease and this rate increases in the first 24 hours in severe pancreatitis cases.

In our study, in the population of patients who presented with right upper quadrant pain, NLR was significantly higher in AC patients when compared with cholelithiasis patients and the no pathology patients.

CONCLUSION

As a result of our findings, AC can be diagnosed earlier upon admission to the emergency department and mortality and morbidity can be reduced with an early diagnosis and treatment. Various inflammatory markers can be employed for this diagnosis. NLR may be used in the diagnosis of AC along with other inflammation markers due it being inexpensive and easy calculated.

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