



Original study

## Use of laboratory parameters in the differential diagnosis of ovarian cyst rupture and acute appendicitis

### Over kist rüptürü ve akut apandisit ayırıcı tanısında laboratuvar parametrelerinin kullanımı

Süleyman Kardaş, Ecem Ermete Güler, Ahmet Kayalı, Umut Payza, Mehmet Göktuğ Efgan, Osman Sezer Çınaroğlu

Department of Emergency Medicine, Izmir Katip Celebi University, Atatürk Training and Research Hospital, Izmir, Türkiye

**Corresponding address:** Dr. Mehmet Göktuğ Efgan, [goktugefgan@gmail.com](mailto:goktugefgan@gmail.com)

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#### ABSTRACT

The study aimed to analyze the diagnostic power of laboratory parameters in the differential diagnosis of acute appendicitis and ovarian cyst rupture originating from the right lower quadrant in female patients presenting to the emergency department with right lower quadrant pain.

Between 2016 and 2021, 200 female patients who presented to the emergency department with acute right lower quadrant pain and were diagnosed with acute appendicitis or ovarian cyst rupture by abdominal tomography and post-operative pathology results were included in the study. Laboratory parameters of the patients were analyzed. The role of the obtained results in the differential diagnosis was investigated.

The diagnoses of acute appendicitis and ovarian cyst rupture were randomized 1:1 for the female patients included in the study. The groups were modeled to have similar demographic characteristics. Neutrophil, lymphocyte, leukocyte, leukocyte, MPV, platelet, and CRP values were analyzed. Neutrophil/lymphocyte and platelet/lymphocyte ratios were calculated. Inflammation parameters, N/L, and P/L ratios were significantly higher in patients with acute appendicitis. High inflammation findings shown by laboratory data support acute appendicitis.

Patients with acute appendicitis have a stronger inflammatory reaction. High inflammatory markers are interpreted in favor of appendicitis. Laboratory parameters facilitate clinical decision-making and support the preliminary diagnosis in the differential diagnosis of female patients presenting to the emergency department with right lower quadrant pain.

**Keywords:** Ovarian cyst rupture; appendicitis; laboratory parameters.

#### ÖZET

Çalışmanın amacı acil servise sağ alt kadranda ağrısı ile gelen kadın hastalarda sağ alt kadranda kaynaklı akut apandisit ve over kist rüptürünün ayırıcı tanısında laboratuvar parametreleri tanı koymadaki gücünü analiz etmek

2016-2021 yılları arası akut, sağ alt kadranda ağrısı ile acil servise başvuran, çekilen abdominal tomografi ve post-operatif patoloji sonuçları ile akut apandisit veya over kist rüptürü tanısı konulan 200 kadın hasta çalışmaya alındı. Hastaların laboratuvar parametreleri analiz edildi. Elde edilen sonuçların ayırıcı tanıdaki rolü araştırıldı.

Çalışmaya alınan kadın hastalar için akut apandisit ve over kist rüptürü tanıları 1:1 randomize edildi. Gruplar, demografik özellikler benzer olacak şekilde modellendi. Hastaların inflamasyonu gösteren parametreleri nötrofil, lenfosit, lökosit, mpv, platelet, crp değerleri analiz edildi. Nötrofil/lenfosit ve platelet/lenfosit oranları hesaplandı. Akut apandisit olan hastalarda inflamasyona ait parametreler, N/L ve P/L oranları anlamlı yüksek bulundu. Laboratuvar verileri ile gösterilen yüksek inflamasyon bulguları akut apandisit desteklemektedir.

Akut apandisit tanılı hastalarda daha güçlü bir inflamatuvar reaksiyon görülmektedir. Yüksek inflamatuvar markırlar apandisit lehine yorumlanır. Acil servise, sağ alt kadranda ağrısı ile gelen kadın hastaların ayırıcı tanısında laboratuvar parametreleri klinik karar vermeyi kolaylaştırır ve ön tanıyı destekler.

**Anahtar kelimeler:** Over kist rüptürü; apandisit; laboratuvar parametreleri.

## INTRODUCTION

Abdominal pain accounts for 4-8% of adult presentations to the emergency department (1). Although acute appendicitis is the first diagnosis that comes to mind in a patient presenting with right lower quadrant abdominal pain, ovarian pathologies are also among the differential diagnoses in women of reproductive age (WORA). Especially ovarian cyst rupture is one of the most common pathologies we encounter and mimics all findings of acute appendicitis. A detailed anamnesis and a complete physical examination are always valuable to differentiate these two similar clinics originating from different organ systems. Especially today, modern device technologies have made it easier to reach a definitive diagnosis. With ultrasonographic (USG) techniques, computed tomography (CT), and magnetic resonance imaging (MRI) devices, diagnosis has become almost dependent on device technologies. Physical examination, anamnesis, and laboratory tests have taken a back seat. However, the increased use of these devices has important consequences, such as radiation concerns, complications related to contrast agents, and high costs, especially in young female patients.

This study aims not to evaluate laboratory parameters as a definitive differential diagnostic tool. However, this study aims to ensure the utilization of laboratory markers in cases where radiation and contrast agents are avoided and to evaluate the usefulness of laboratory tests in differential diagnosis in cases where access to devices such as USG and tomography is limited or diagnostic difficulties are encountered for other reasons.

## MATERIAL and METHOD

All patients who presented to the emergency department with complaints such as abdominal pain, nausea, vomiting, diarrhea and constipation suggestive of acute abdomen were identified. Among this patient group, 1129 female patients with right lower quadrant pain were included in the study. The definitive diagnosis was based on the operated patients' computed tomography and post-operative pathology reports. We identified 422 female patients suspected of acute abdominal pain by an independent surgeon and diagnosed with acute appendicitis and ovarian cyst rupture on a CT scan or post-operative pathology findings. The archival records of these patients were analyzed. Demographic characteristics and laboratory parameters were evaluated. Neutrophil (NEU), lymphocyte (LYM), leukocyte ,

MPV, platelet (PLT), and CRP values were analyzed, and neutrophil/lymphocyte and platelet/lymphocyte ratios were calculated.

Female patients older than 18 years were included in the study. Patients whose data could not be reached, patients with a cancer diagnosis, patients with abnormal hematologic parameters, patients with positive  $\beta$ -HCG values, and pregnant women were excluded from the study.

Ethical approval for the study was obtained by the university ethics committee with the decision numbered and dated 15/08/21-0209.

## Statistical analysis

Statistical analyzes were performed in IBM SPSS Statistics Version 22 package program. Pearson Chi-Square, Fisher's Exact test and Chi-Square Trend statistical analyzes were used to compare the data between groups.  $p < 0.05$  was considered statistically significant. Proportions according to gender and age groups were evaluated according to Chi-Square trend analysis. Ratios according to laboratory values were calculated according to Fisher's Exact test and Chi-Square trend analysis.

## RESULTS

The mean age of the patients in our study was  $35.2 \pm 13.5$  years. The mean age of patients diagnosed with acute appendicitis was  $37.3 \pm 15.6$  years, while the mean age of patients diagnosed with ovarian cyst rupture was  $33.1 \pm 10.7$  years. There was no significant difference between the age values of both groups ( $p > 0.05$ ).

The laboratory data of the patients were analyzed in Table 1. Neutrophil/lymphocyte and platelet/lymphocyte ratios were calculated.

While the mean leukocyte ratio was  $14.4 \pm 5.2$  in patients with acute appendicitis, this ratio was  $9.5 \pm 4.3$  in ovarian cyst rupture cases and a significant difference was found ( $p = 0.001$ ). Similarly, the values of Neutrophil, CRP, Neutrophil/Lymphocyte, and Platelet/Lymphocyte were significantly higher in acute appendicitis cases ( $p < 0.05$ ).

Cut-off values were calculated as 10.8 for Leukocyte, 7.9 for Neutrophil, 3.8 for Neutrophil/Lymphocyte, 139.2 for Platelet/Lymphocyte, and 2.0 for Lymphocyte ( $p < 0.05$ ). ROC (Receiver Operating Curve) analysis was performed on the calculated laboratory parameters (Table 2).

<b>Table 1: Mean±Standard deviation values of laboratory data.</b>				
	<b>Laboratory data Mean±Sd</b>	<b>Acute Appendicitis Mean±Sd</b>	<b>Ovary Cyst Rupture Mean±Sd</b>	<b><i>p</i></b>
<b>Leukocyte</b>	11,9±5,4	14,4±5,2	9,5±4,3	<b>0,001</b>
<b>Neutrophils (N)</b>	9,1±5,3	11,7±5,1	6,5±4,1	<b>0,001</b>
<b>Lymphocyte (L)</b>	2,0±0,8	2,2±0,8	1,8±0,8	<b>0,002</b>
<b>Hemoglobin</b>	12,4±2,4	12,6±1,5	12,3±3,0	0,278
<b>Hematocrit</b>	38,5±6,7	39,1±4,2	37,9±8,5	0,207
<b>MPV</b>	10,2±1,1	10,1±1,1	10,3±1,1	0,342
<b>Platelet (P)</b>	285,6±73,1	292,9±77,8	278,3±67,7	0,158
<b>CRP</b>	3,6±6,4	5,3±7,6	1,9±4,4	<b>0,001</b>
<b>N/L</b>	5,9±5,5	8,2±6,4	3,5±3,2	<b>0,001</b>
<b>P/L</b>	170,6±107,9	200,5±136,0	140,7±55,7	<b>0,001</b>
MPV: mean platelet volume; CRP: C-reactive protein; N/L: neutrophil/lymphocyte ratio; P/L: platelet/lymphocyte ratio				

<b>Table 2: ROC analysis of laboratory parameters for acute appendicitis.</b>							
	Cutoff value	AUC*	Sensitivity 95%	Specificity 95%	<i>p</i>	Confidence interval %95	
						Lower Bound	Upper Bound
<b>Leukocyte</b>	10,8	0,798	73,0	73,0	<b>0,001</b>	0,736	0,861
<b>Neutrophil</b>	7,9	0,817	74,0	74,0	<b>0,001</b>	0,758	0,876
<b>CRP</b>	0,46	755	69,0	72,0	<b>0,001</b>	0,688	0,823
<b>N/L</b>	3,8	0,808	73,0	73,0	<b>0,001</b>	0,748	0,868
<b>P/L</b>	139,2	0,631	60,0	60,0	<b>0,001</b>	0,554	0,709
<b>Lymphocyte</b>	2,0	0,629	59,0	59,0	<b>0,002</b>	0,553	0,706

## DISCUSSION

Acute abdomen is one of the most common causes of admission to emergency departments. It is caused by pathologies of the intra-abdominal organs and mesentery or by non-abdominal causes such as radiating pain. Strong coordination between the emergency physician and general surgeons is essential to identify the underlying cause. This ensures that the correct diagnosis is made or complications due to delayed diagnosis are avoided.

One of the common causes of abdominal pain is the right lower quadrant pathologies. Acute appendicitis, diverticulitis, obstructions, perforation, and ovarian pathologies are the first diagnoses that come to mind in pain originating from this region. Only 5% to 40% of all abdominal pains require surgical intervention (2,3).

Appendicitis is a common cause of acute abdominal pain in women of reproductive age (WORA), and appendectomies are the most common of all emergency surgeries (4). Suspected appendicitis is the most common reason for surgical consultation in emergency departments. Even though clear diagnostic and therapeutic strategies have been es-

tablished for appendicitis for over a century, and despite the discovery of advanced laboratory panels and modern imaging methods, misdiagnosis rates are surprisingly high (5).

Usually, physicians blame the discrepancy between disease severity and physical findings for misdiagnosis, and this 'discrepancy' is most commonly seen in WORA. Diagnosing and treating pathologies that cause abdominal pain due to gynecologic pathologies mimicking acute appendicitis is still quite challenging for general surgeons and gynecologists. Surgeons may have to deal with gynecologic pathologies in women who undergo laparotomy with a diagnosis of acute appendicitis (6,7).

The most commonly used laboratory tests for diagnosing intra-abdominal pathologies are leukocyte and lymphocyte counts. Although they lack sensitivity and specificity, markers such as leukocytosis are used as a warning parameter (8-10). Similarly, relative neutrophilia is usually associated with the inflammatory process, and an altered neutrophil percentage is considered an early sign of infection (11). Akbulut wrote in his study that changes in the

values of these two laboratory parameters, lymphocytes, and neutrophils, are important findings in pathologies causing surgical abdomen.

In the same study, he emphasized the negative predictive value of these two markers and emphasized that surgical procedures should not be rushed without an increase (12). Yang et al. interpreted that elevated LYM and NEU values, especially in acute appendicitis, are significant for diagnoses requiring acute intra-abdominal surgery, although they are not specific findings (13). In addition to these parameters, Di Saverio pointed out in his study that the increase in LYM count changed significantly, especially in surgical pathologies (14). CRP value is one of the important indicators of inflammation. Mengüçük et al. emphasized that CRP was elevated in 97% of cases of acute appendicitis and CRP value was an important indicator of negative predictive value and argued that an emergency surgical procedure should not be performed in the absence of laboratory findings of inflammation (15). In the meta-analysis conducted by Hallan and Asberg, although variable results were shown, it was stated that increased CRP may be associated with intra-abdominal pathologies (16). Although sensitivity and specificity were low in our study, leukocyte, neutrophil, and CRP elevations confirmed the diagnosis of acute appendicitis. They suggested that surgical intervention may be necessary for these patients. The significantly elevated N/L P/L ratios we calculated also strongly correlated with the strong inflammation that had begun.

Pelvic pain during the menstrual cycle is observed due to a small amount of blood leaking from the ruptured follicle into the peritoneal cavity. Follicular pain is more common in patients undergoing ovulation therapy. The intensity of the pain is variable. It mimics symptoms of acute abdomen and is misleading (17). It has been reported that ovarian pathologies were found in approximately 20% of operations performed with suspicion of acute appendicitis in patients of fertile age (18). Surgical interventions performed without considering ovarian pathologies and without a definitive diagnosis may lead to unfavorable results, especially in female patients with pregnancy expectancy. In these patient groups, it is noted that surgical interventions, including surgical interventions resulting in negative appendectomy, may harm fertility (19). Therefore, it is recommended to establish as clear a diagnosis as possible for ovarian pathologies. Especially in ovarian cyst rupture, laboratory parameters are not a clear diagnostic tool. However, Ercan Ö et al. reported that lymphocyte and leukocyte biomarkers did not reach significant laboratory levels or were at borderline values, especially in ovarian cyst rupture (20). Similarly, Mitsuru reported that inflammatory biomarkers were observed within the range of normal laboratory values in patients diagnosed with ovarian cyst rupture (21). In our study, leukocyte, neutrophil, and

CRP markers for ovarian cyst rupture were within the normal range or just above these threshold values.

The most significant result of this study shows that although laboratory values cannot be used for direct diagnosis in patients presenting with right lower quadrant pain, they can help us in the differential diagnosis of acute appendicitis and ovarian cyst rupture. Elevated WBC, neutrophil, and CRP values can be interpreted in favor of acute appendicitis and encourage surgical procedures. At the same time, threshold laboratory measurements suggest ovarian pathologies and suggest reconsidering the decision to operate.

The study shows that inflammation markers can be used in the differential diagnosis of similar clinical findings, such as acute appendicitis and ovarian cyst rupture.

Limitations; The study was planned as a single center and should be supported by studies with more patients.

In conclusion; Advanced imaging technologies in diagnosing intra-abdominal pathologies have made differential diagnosis easier and faster. Physical examination and laboratory findings are rapidly losing their importance. However, especially in women of childbearing age, imaging methods used for diagnosis remain limited due to the increased use of medication and induction methods for pregnancy (22). This study has shown that biomarkers indicating inflammation should be utilized to avoid negative laparotomy in women of childbearing age.

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