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PARAMETERS ASSOCIATED WITH ACUTE APPENDICITIS IN PREGNANCY

GEBELIKTE AKUT APANDISITLE İLIŞKILI PARAMETRELER

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Öz

Amaç

Akut apandisit, gebelerde obstetrik olmayan akut batının en sık nedenidir. Gebe hastalarda sempatomatolojinin akla ilk olarak obstetrik nedenleri getirmesi, fizyolojik lökositozun gebelik boyunca görülmesi ve görüntüleme yöntemlerindeki kısıtlılıklar tanıda kafa karışıklığına neden olmaktadır. Bu durum laboratuvar parametrelerinde ayrıntılı değerlendirme ihtiyacını kaçınılmaz kılmaktadır. Çalışmanın amacı nötrofil lenfosit oranı (NLR), trombosit lenfosit oranı (PLR), lenfopeni gibi laboratuvar parametrelerinin apandisit tanısı ile ilişkisini ve tanısal gücünü ortaya koymaktır.

Gereç ve Yöntem

Değerlendirmede Ocak 2017-Şubat 2021 tarihleri arasında gebelikte akut apandisit tanısı ile opere edilen 31 hasta değerlendirildi. Hastaların demografik verileri, laboratuvar sonuçları, ultrasonografi veya manyetik rezonans görüntüleme raporları ve intraoperatif bulguları değerlendirilerek korelasyon ve roc analizi yapıldı.

Bulgular

Eksplorasyonda apandisit saptanması ile nötrofil, lökositoz ve NLR artışı arasında anlamlı bir ilişki bulundu (sırasıyla p: 0,014, p: 0,015, p: 0,020). Yine lenfopeni varlığı, yüksek NLR ve artmış palet/lenfosit oranı (PLR) uzamış yatış ile ilişkili bulundu (sırasıyla, p:0,037, p:0,008, p:0,024). Roc analizi ayrıca lökositoz [AUC: 0,938 (%95 CI: 0-1,00, p:0,019)], nötrofil yüksekliği [AUC: 0,938 (%95 CI: 0-1,00, p:0,019)] ve NLR [AUC: 0,917 (0-1,00 p: 0,025)] anlamlı akut apandisit varlığını ortaya koyma gücüne sahip olduğu bulundu.

Sonuç

Gebelerde akut apandisit tanısında hemogram parametrelerinin ve görüntüleme yöntemlerinin etkin bir şekilde kullanılması önerilmektedir.

Anahtar Kelimeler: Akut apandisit, Appendektomi, Gebelik

Abstract

Objective

Acute appendicitis is the most common cause of non-obstetric acute abdomen in pregnant women. The fact that sympathomatology brings to mind primarily obstetric causes in pregnant patients, physiological leukocytosis is observed throughout pregnancy, and limitations in imaging methods cause confusion in the

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diagnosis. This makes the need for detailed evaluation in laboratory parameters inevitable. The aim of the study is to reveal the relationship of laboratory parameters such as neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), lymphopenia with the diagnosis of appendicitis and its diagnostic power.

Material and Method
In the evaluation of 31 patients who were operated on with the diagnosis of acute appendicitis during pregnancy between January 2017 and February 2021 were evaluated. Correlation and roc analysis were performed by evaluating patients' demographic data, laboratory results, ultrasonography or magnetic resonance imaging reports and intraoperative findings.

Results
A significant correlation was found between detection of appendicitis in exploration and increased neutrophils, leukocytosis, and NLR (p: 0.014, p: 0.015, p: 0.020, respectively). Again, the presence of lymphopenia, high NLR and increased palletelet / lymphocyte ratio (PLR) were found to be associated with prolonged hospitalization (p:0.037, p:0.008, and p:0.024, respectively). Roc analysis also showed that leukocytosis [AUC: 0.938 (95%CI: 0-1.00, p:0.019)], neutrophil elevation [AUC: 0.938 (95%CI: 0-1.00, p:0.019)] and NLR [AUC: 0.917 (0-1.00 p: 0.025)] was found to have the power to reveal the presence of significant acute appendicitis.

Conclusion
It is recommended to use hemogram parameters and imaging methods effectively in the diagnosis of acute appendicitis in pregnants.

Keywords: Acute appendicitis, appendectomy, Pregnancy

Introduction

Acute appendicitis (AA) is the most seen reason of non-gynecological acute abdomen in gravid patients (1). Even though the incidence is similar in gravid and non-gravid populations, trying to associate symptomatology with the current pregnancy status in pregnant patients may lead to delays in the diagnosis of AA. Concerns about the health of the fetus, changes in the definition and localization of pain due to physiological reasons during pregnancy, and the inability to use imaging methods such as computed tomography can be shown among the reasons leading to this situation (2). Among the imaging methods, ultrasonography (US) is the most used and first choice method in pregnant women. Although the incidence is higher especially in the 2nd trimester, compared to other trimesters, there is a risk of AA during the whole pregnancy. In addition, increase in the area occupied by the fetus and uterus in the abdomen during pregnancy may lead to delays in diagnosis, especially in the 3rd trimester, when the fetal volume is the highest. The risks of anesthesia and surgery in cases of AA in gravid women require timely diagnosis and timely administration of appropriate treatment, and continuation of gynecological follow-up in the preoperative, perioperative, and postoperative periods. Therefore, effective use of clinical findings, laboratory parameters and imaging methods can both prevent delays in diagnosis and prevent unnecessary surgical decisions that may cause fetal and maternal complications (3).

Laboratory hemogram findings, especially leukocytosis and increased c-reactive protein (CRP) in AA cases support the diagnosis. Neutrophils are among the most abundant white blood cells and take an important role in immunity. In addition, it helps to regulate the role of many other cells in the immune system, especially mast cells, macrophages and platelets. Again, platelets are among the cells that play a regulatory role in inflammation. Therefore, changes in the neutrophil / lymphocyte (NLR) or platelet / lymphocyte ratio (PLR) can be used as a marker in the AA diagnosis in pregnant women with physiological leukocytosis (4).

It was aimed to evaluate the preoperative data leading to the diagnosis in pregnants, operated for AA, and to discuss the diagnostic effect of the mentioned laboratory findings of the patients.

Material and Method

Pregnants, operated on with the diagnosis of AA between 2016 and 2021 were evaluated retrospectively. For the ethical compliance of the study, the approval of the Aydın Adnan Menderes University, School of Medicine, Non- Interventional Clinical Research Committee (protocol no:2021/35,

decision no:6) was obtained.

Belonging to patients; demographic and clinical findings, laboratory findings of leukocytes, neutrophils, lymphocytes, platelets, albumin, NLR, PLR values, imaging method, parameters of appendix diameter detected on imaging, presence of appendicitis in exploration, postoperative hospital stay and presence of postoperative complications were evaluated.

Statistical analyzes were conducted using SPSS version 24, (SPSS, Inc., IBM, Armonk, NY, USA). After the descriptive analyses were performed, spearman correlation test was performed to evaluate the relationship between laboratory parameters and parameters showing the severity of appendicitis and pregnancy trimester. ROC analysis was performed to evaluate the power of patients to predict appendicitis protrusion during exploration. P<0.05 was accepted as significance value.

Results

The mean age of 31 patients was 27.87 (±5.6). It was observed that 10 (32.63%) of the participants were in the trimester I, 18 (58.1%) patients were in the trimester II, and 3 (9.7%) patients were in the trimester III. Information on the preoperative clinical, laboratory, imaging methods, intraoperative and postoperative findings were shown in table 1.

Correlation analysis was performed between the laboratory findings of the preoperative period and the parameters showing the severity of the appendicitis clinic. Accordingly, when the correlation between appendix diameter, the detection of appendicitis in the intraoperative exploration, the parameters of the postoperative hospital stayof the patients and the pregnancy trimester were evaluated, it was seen that the increase in the diameter of the appendix was associated with increase in the NLR and PLR (p: 0.006 and p:0.022 respectively). Also there was a significant correlation between appendicitis as an exploration finding and leukocyt, neutropil values and NLR (p:0.001, p<0.001 and p:0.001 respectively). Again, high NLR was found to be associated with prolonged hospitalization (p:0.013). In the evaluation of pregnancy trimester and laboratory findings, leukocytosis, neutrophil elevation and NLR elevation were found to be associated with the trimester (p: 0.001, p: 0.001 and p:0.013 respectively) (Table 2).

In the ROC analysis, leukocytosis [AUC: 0.893 (95%CI: 0.717-1.00, p:0.002)], neutrophil elevation [AUC: 0.929 (95%CI: 0.793-1.00) p:0.001)] and NLR [AUC: 0.899 (95%CI: 0.757-1.00) p: 0.025)] were found to have significant power to detect the presence of AA (Table 3).

Discussion

Although AA is the most common non-gynecologic surgical pathology in pregnancy, its incidence is very low; our study covers a period of five years, the fact that the number of participants is limited to 31 patients supports this data. In our study, the gestational week of our patients diagnosed with AA was 18.90 ±7.63 weeks, and 18 (58.1%) of the patients were diagnosed in the trimester II. This finding was evaluated in accordance with the literature (5). In the presence of AA in gravid women, abdominal pain is a very common symptom and the patient's most common complaint during the emergency admission. In our study, when the location of the pain was questioned inthe patients, the pain could not be localized in 19 (61.3%) of the patients. When looking at the normal course of AA, visceral and non-localized pain is seen at the beginning, while localized pain occurs when the inflammation reaches beyond the serosa and affects the parietal peritoneum. In the literature, there are opposing views about the movement pattern of the appendix and cecum during pregnancy, while many studies argue that the cecum shifts superiorly as the trimester progresses, some studies show that the cecum does not move as much as thought during pregnancy (6, 7). As a result, considering that the abdominal wall, that is, the parietal peritoneum, also moves away because of the increase in the uterine diameter in pregnant women, the removal of the appendix from the parietal peritoneum independent of the superior mobilization of the cecum may have prevented the localization of pain in the patients. In fact, the fact that Rutherford-Morrison expansion was needed more than normal in the patient group in our study was evaluated due to the difficulty in visualizing the deeply located appendix. In pregnant women who develop abdominal pain, this pain primarily brings to mind obstetric reasons and because of the concern about fetal mortality, applications are faster than the normal population. Again, the period from the first application to the operation in pregnant women was reported to be shorter than in non-pregnant patients (8). In addition, the patients were young women of childbearing age may have provided an advantagein revealing the appendicitis clinic. Because, in the literature, the diagnosis of appendicitis is made later in elderly patients than in younger patients, and accordingly, the possibility of encountering

Table 1 Data on preoperative clinical, laboratory, imaging methods, intraoperative and postoperative findings of the patients

Parameters		**n= 31**
Age (±SD)		27,87 (5,6)
Gestational Week (±SD)		18,90 (7,63)
Trimester (%)		
	1.	10 (32,63)
	2.	18 (58,1)
	3.	3 (9,7)
Location of pain (%)		
	Not localizable	19 (61,3)
	Right lower quadrant	4 (12,9)
	Flank pain	2 (6,5)
	Groin pain	6 (19,4)
Anorexia (%)		
	(-)	10 (32,3)
	(+)	21 (67,7)
Nausea and vomiting (%)		
	(-)	23 (74,2)
	(+)	8 (25,8)
Leukocyte (x10^3/McL) (±SD)		11,77 (3,83)
Neutrophil (x10^3/McL) (±SD)		9,84 (3,58)
Lymphocyte (x10^3/McL) (±SD)		1,45 (0,82)
PLT (x10^6/McL) (±SD)		225,6(51,45)
Albumin (g/dl) (±SD)		3,23 (0,52)
NLR (ıqr)		7,15 (5,14-12,13)
PLR (ıqr)		169,73 (114-244,62)
Appendix diameter (mm) (iqr)		8 (7-9)
Imaging technique (%)		
	US	26 (83,9)
	MR	5 (16,1)
Surgical method (%)		
	Open technique	27 (87,1)
	Laparoscopic	4 (12,9)
Intraoperative diagnosis (%)		
	Acute appendicitis	24 (77,4)
	Normal appendix	7 (22,6)
Length of stay / day (iqr)		2 (1-4)

Mcl: microliter, PLT: Platelet, PLR: platelet / lymphocyte ratio, NLR: Neutrophil / lymphocyte ratio, iqr: interquartile range, n: number of patients

Table 2 Correlation analysis of laboratory parameters performed in the preoperative period and parameters for the severity of appendicitis clinic

	Leukocyte	Neutrophil	Lymphocyte	NLR	PLT	PLR	Albumin
Appendix diameter							
Rho	0,192	0,287	-0,258*	0,478**	0,138	0,410*	-0,271
p	0,300	0,117	0,161	**0,006**	0,460	**0,022**	0,141
Appendicitis in Exploration							
Rho	0,570**	0,622*	-0,039	0,579**	-0,199	0,121	-0,061
p	**0,001**	**<0,001**	0,835	**0,001**	0,282	0,517	0,746
Length of stay							
Rho	0,181	0,183	-0,275*	0,423*	0,093	0,329	-0,109
p	0,329	0,324	0,134	**0,018**	0,619	0,070	0,560
Pregnancy trimester							
Rho	0,547**	0,564**	-0,130	0,442*	-0,341	-0,067	-0,469*
p	**0,001**	**0,001**	0,485	**0,013**	0,060	0,718	**0,008**

NLR: Neutrophil/ Lymphocyte ratio, PLR: Platelet/ Lymphocyte ratio, PLT: Platelet, Rho: Spearman correlation (*:Correlation is significant at the 0.05 level (2-tailed).**: Correlation is significant at the 0.01 level (2 -tailed)).

Table 3 ROC analysis to evaluate the predictive power of diagnosing appendicitis with preoperative laboratory findings

	Cut off	AUC (%95 CI)	p value	Sensitivity	Spesifity
Leukocyte	9400	0,893 (0,717-1,00)	**0,002**	0,917	0,857
Neutrophil	7000	0,929 (0,793-1,00)	**0,001**	1,00	0,857
Lymphocyte	1290	0,473 (0,242-0,705)	0,832	0,583	0,714
Platelet	197500	0,363 (0,086-0,640)	0,277	0,750	0,286
NLR	4,76	0,899 (0,757-1.00)	**0,002**	0,958	0,857
PLR	104,13	0,583 (0,327-0,840)	0,502	0,917	0,429

NLR: Neutrophil/Lymphocyte Ratio, Mcl: mikrolitre, AUC: Area under the curve

complications such as perforation, abscess development, and surgical site infection increases (8). It was seen that the patient group had an admission time of 8-36 hours in our study. Anorexia, nausea, and vomiting, which are common in AA, are shown in a wide range for pregnant patients (9). In our study, anorexia is more common than nausea and vomiting and is in accordance with the literature.

It has been shown that laparoscopic appendectomy does not increase both maternal and infant mortality, especially in the 1st and 2nd trimesters in the literature (10). The use of the laparoscopic method in pregnancy appendicitis, which has started to be used in pregnant appendicitis patients, is more suitable for fetal acidosis, premature birth, decrease in uterine blood flow due to pressure and possible harms, and it is more suitable for first trimesterpatients (10). We also operated laparoscopically on 4 of our patients in the first trimester of their pregnancy and we did not encounter any fetal or maternal complications.

The rate of negative appendectomy in pregnancy has been reported 30% (11). This rate was seen as 22.6% and was consistent with the literature.

Despite the fact that there is no specific laboratory finding for AA, leukocytosis and C-Reactive Protein (CRP) level are widely used in the diagnosis of AA (12). Early and accurate diagnosis of AA in pregnant patients is very important in terms of preventing both fetal and maternal complications, which makes laboratory parameters even more important considering our limitations in the imaging process in pregnant women. Looking at the laboratory parameters; Up to 80% leukocyte elevation is detected in non- pregnant appendicitis patients, but leukocyte and CRP values are already physiologically high in pregnant women in all three trimesters (13). Therefore, high wbc alone is insufficient to support AA in pregnancy. It was inevitable to evaluate other ratios such as neutrophil count, NLR, PLR belonging to laboratory parameters and laboratory parameters. We found that both NLR and PLR were associated with both the increase inappendix diameter and the length of stay. Again, in the Roc analysis, the power of NLR in predicting AA was found to be significant. In a study evaluating the relationship between laboratory parameters and pregnant appendicitis cases, it was found that WBC and neutrophil counts, NLR and PLR were significantly higher, and lymphocyte counts were lower in pregnant women diagnosed with AA (14). In particular, the fact that NLR is unrelated to the trimester of pregnancy supports its importance in diagnosing AA in gravid patients in all three trimeters.

In addition, the presence of lymphopenia was found to be associated with the postoperative hospital stay, but the predictive power of AA was found to be insufficient in the ROC analysis. When we look at the literature, lymphopenia is found to be significantly higher in pregnant appendicitis (15).

The most used imaging method in pregnant AA is ultrasonography. MRI without known fetal and maternal risk can also be used as an aid in diagnosis and provides benefits in patients who cannot be diagnosed with ultrasound (16). In our study, the majority of the patient group could be diagnosed with ultrasound, but 2 patients needed MRI as an advanced imaging method. In addition to these, there are publications showing that low-dose CT is used in the 2nd and 3rd trimesters and does not cause fetal mortality or morbidity (17). As mentioned at the beginning, cases of pregnant appendicitis are rarely encountered, which supports the fact that only 19 patients were identified in the 4-year clinical data. However, the small number of patients can be cited as a limitation of the study.

Conclusion

Although AA is a rare acute surgical disease in pregnant women, it requires not only general surgery but also a multidisciplinary evaluation jointly with obstetrics clinics in the diagnosis and effective treatment of the disease. This multidisciplinary approach becomes even more important in preventing both fetal and maternal morbidity and mortality. For this reason, it is recommended to use hemogram parameters and imaging methods effectively, which can be done in emergency conditions. Because of the limited number of patients in our study and similar studies, multicenter studies with larger patient groups are needed.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Ethical Approval
Ethical approval of the Aydın Adnan Menderes University, School of Medicine, Non- Interventional Clinical Research Commite (protocol no:2021/35, decision no:6) was obtained. The study was conducted in line with the principles of the "Helsinki Declaration".

Consent to Participate and Publish
Written informed consent to participate and publish was obtained from all individual participants included in the study.

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Availability of Data and Materials
Data are available on request due to privacy or other restrictions.

Authors Contributions
S.Ş: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Validation; Visualization; Writing-original draft.

E.M.Y: Conceptualization; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Validation; Writing-review & editing.

M.K: Investigation; Validation; Writing-original draft.
E.B: Formal analysis; Investigation; Visualization; Writing-original draft.

A.E.D: Funding acquisition; Resources; Supervision; Writing-review & editing.

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