Clinical and laboratory features and treatment approaches of pregnant woman with acute appendicitis

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Abstract

Aim: Since it is difficult to diagnose acute appendicitis (AA) in pregnant women, the negative appendectomy and complicated appendectomy rates are higher than the normal population. However, both negative appendectomies and complicated appendicitis have negative effects on the fetus and mother. This study aims to evaluate the patients who underwent appendectomy during pregnancy according to clinical, laboratory and imaging findings. In addition, the Neutrophil-Lymphocyte ratio (NLR) and Platelet-Lymphocyte ratio (PLR) parameters, which are used in the evaluation of pregnant AA patients in the literature, will be evaluated.

Material and Methods: Between January 2013 and January 2020, pregnant patients operated for AA were retrospectively analyzed. The patients were evaluated in terms of age, gestational age, clinical, laboratory and imaging findings, operation information, length of hospitalization, pathology results and complications.

Results: Twelve patients were included in the study. The mean age of the patients was 29.3 ± 7.38 (min-max 17-41). Three patients were in the 1st trimester (two intrauterin and one extrauterin tubal pregnancy), seven were in the 2nd trimester, and two were in the 3rd trimester. All patients applied with abdominal pain and no appendix could be visualized in any patient on ultrasound imaging. In our study, the average of WBC (White Blood Cell), PDW (Platellet-Distribution Widht), NLR and PLR values were found to be as 13.2 (mcL), 16.9 (%), 3.4 and 79.2, respectively.

Conclusion: In our study, a clear distinctive finding to be used in detecting pregnant appendicitis could not be reached. Although imaging and laboratory findings play a role in assisting the diagnosis of AA, our study has revealed that the most important criterion in the diagnosis of AA in pregnant patients is that the general surgery and gynecology team evaluate the patient together.

Keywords: Appendicitis; pregnancy; neutrophil lymphocyte ratio; platelet lymphocyte ratio

INTRODUCTION

Acute appendicitis (AA) is the most common pathology in pregnant women due to acute abdomen (1,2). In non-pregnant patients, the AA clinic typically begins with a pain in the periumbilical region that cannot be well localized, and as the inflammation progresses, the pain progresses to the right lower quadrant (3). These findings may be accompanied by anorexia, vomiting, and an increase in serum white blood cell values. In addition, imaging findings supporting AA in these patients are often detected. As a result, AA is diagnosed with these clinical, laboratory and imaging findings, and surgery is performed with low negative appendectomy rates (4,5). However, depending on the enlargement of the uterus during pregnancy, the appendix can be displaced, and the reduced appendix contact with the anterior abdominal wall may hinder peritoneal signs during abdominal examination. In

addition: serum white blood cell (WBC). C-reactive protein (CRP) increases due to physiological changes due to the natural course of pregnancy, and nausea, vomiting and anorexia may also be seen (6,8). All these limiting factors hardens to establish a diagnosis of AA during pregnancy. Moreover, considering the limitation in imaging studies involving radiation and the limited success of ultrasound (US) in showing appendix during pregnancy, it can be understood how difficult it is to diagnose AA in pregnant women. This may cause delays in diagnosis and treatment or result in negative appendectomies (9). However, in order to reduce negative appendectomy rates, appendicitis may become complicated if pregnant patients with AA suspicion are monitored for a long time and surgery decision is made after significant symptoms and signs appear (10). Unfortunately, negative appendectomies and appendectomies performed in complicated AAs have higher fetal loss rates than appendectomies applied to

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uncomplicated AA patients (9). For this reason, it is vital to evaluate pregnant patients and to make the correct diagnosis and treatment quickly.

This study aims to evaluate patients who underwent appendectomy during pregnancy according to clinical, laboratory and imaging findings. In addition, the patients have been evaluated in terms of inflammatory parameters such as Neutrophil-Lymphocyte ratio (NLR) and Platelet-Lymphocyte ratio (PLR), which are used in the evaluation of pregnant AA patients in the literature.

MATERIAL and METHODS

The clinical and laboratory parameters of 12 pregnant patients who underwent appendectomy between January 2013 and January 2020 at University of Health Sciences, Tepecik Education and Research Hospital were retrospectively analyzed. The patients were examined in terms of age, symptoms and findings, gestational age, physical examination findings, routine blood tests, Neutrophil-Lymphocyte ratio (NLR) and Platelet-Lymphocyte ratio (PLR) obtained from blood tests, complete urine analysis, imaging findings, surgical technique, complications and pathology results.

All of the patients included in the study applied to the emergency department and the patients were evaluated together with the general surgery and gynecology team. After anamnesis and background information were obtained from the patients, a physical examination was performed. For all patients routine blood tests, complete urine analysis, and US were requested. In the preoperative and postoperative period, fetal viability and heart beats were evaluated with US. All appendectomies were performed under general anesthesia with laparatomy. Preoperative antibiotic prophylaxis was applied to all patients. In case of appendix perforation or periapendicular abscess in the operation, the postoperative antibiotic was continued. Although the McBurney incision is generally used as a surgical incision, different incision sites are used when the gestational week or differential diagnosis of other pathologies have necessitated. Tocolytic treatment was given to the patients who were in the third trimester and whose pregnancy continued.

The patients' age, physical examination findings, imaging findings, pathology results, presence of postoperative complications and gestational week were extracted from the electronic files. All patients were evaluated by the gynecology team during the preoperative and postoperative period. Patient characteristics were determined as numbers and percentages.

SPSS V.17 software was used for analysis. Compatibility with normal distribution was analyzed with the Kolmogorov-Smirnov and Shapiro-Wilks test. Descriptive statistics are given as median and min-max. Mann-Whitney U test was used for non-parametric distrubition in variables (age and blood parameters). p<0.05 was considered significant.

RESULTS

Twelve pregnant patients operated for acute appendicitis were included in the study. The mean age of the patients was 29.3 ± 7.38 (min-max 17-41). Three patients were in the 1st trimester (two intrauterin and 1 extrauterin tubal pregnancy), seven were in the 2nd trimester, and two were in the 3rd trimester. All of the patients applied to the emergency department with abdominal pain, and 5 (41.6%) patients had nausea and 4 patients (33.3%) had vomiting. In physical examination tenderness was present in all patients, defense was present in 7 (58.3%) and rebound was present in 5 (33.3%) patients. The symptoms and findings of the patients at the time of admission are summarized in Table 1.

When the biochemical parameters of the patients were evaluated, it was observed that the serum calcium values were just below the normal limit in 2 patients, and other than that the biochemical parameters were within normal limits. In full urine examination, microscopic hematuria was detected in 2 patients, while 3 positive leukocytes were detected in one patient. In our study, the average of WBC, PDW (Platellet-Distribution Widht), NLR and PLR values were found to be as 13.2 (mcL), 16.9 (%), 3.4 and 79.2, respectively. Laboratory parameters, NLR and PLR values of all patients are summarized in Table 2. In Table 3 are given laboratory values, NLR and PLR parameters of 10 patients with acute appendicitis. When compared age and laboratory parameters of patients with negative appendectomy and those with proven appendicitis we found that there was no statistical difference (Table 4).

Abdominal US was used in all patients as an imaging method. During ultrasonographic examination; appendix could not be visualized in any of the patients however a simple ovarian cyst and periappendiculary heterogenicity have been detected in two patients separately. No computed tomography (CT) or magnetic resonance imaging (MRI) was used as further investigation.

In the postoperative period, incisional cellulitis was seen in the wound of a patient and seroma was observed in another. In addition, a patient had abdominal pain in the postoperative period but regressed with medical treatment. Since one patient had term pregnancy during AA clinical course; appendectomy, cesarean section and tubal ligation (at the request of the patient) were performed together. Curettage was applied to a patient with ectopic pregnancy after appendectomy and salpingectomy. Postoperative maternal and fetal mortality was not observed in our study.

In the pathological examination of two patients, no acute appendicitis findings were detected and these patients were defined as negative appendectomy. While one of these patients had ectopic pregnancy, an etiology that could explain the acute abdomen was not found in the other patient.

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Table 1. Demographic data of patients								
Patient	Age	Gestational week	Comorbidity	Time to Intervention (h)	Treatment	Hospital LOS (day)	Operation finding	Complication
1	29	25	CHF	24	Арр	2	Acute appendicitis	-
2	33	26	Morbid obesity	36	App +Z plasti	5	Acute appendicitis + hematoma in right tuba	Abdominal pain
3	37	24	-	24	Арр	2	Acute appendicitis	-
4	17	22	-	48	Арр	2	Normal appendix	-
5	26	17 (Twin Pregnancy)	-	48	Арр	2	Acute appendicitis +hematoma in right ovary	-
6	26	27	-	48	Арр	3	Perforated appendicitis	-
7	20	14	-	24	Арр	2	Acute appendicitis	-
8	36	25	-	48	Арр	3	Perforated appendicitis	-
9	23	Ectopic pregnancy	-	24	App+ salpingectomy	4	Minimal hyperemic appendix + simple cyst in the left ovary	-
10	41	38	-	48	App +tubal ligation+C/S	5	Acute appendicitis	Cellulite in the wound
11	36	24	-	72	Арр	5	Perforated appendicitis	-
12	28	11	-	24	Арр	2	Acute appendicitis	-
7 8 9 10 11 12	20 36 23 41 36 28	14 25 Ectopic pregnancy 38 24 11	-	24 48 24 48 72 24	App App App+ salpingectomy App +tubal ligation+C/S App App	2 3 4 5 5 2	Acute appendicitis Perforated appendicitis Minimal hyperemic appendix + simple cyst in the left ovary Acute appendicitis Perforated appendicitis Acute appendicitis	- - Cellulite in th wound - -

CHF: congestive heart failure, App: appendectomy, C/S: Cesarean section, LOS: length of stay

Table 2. Laboratory values NLR, and PLR parameters of 12 pregnant patients undergoing an appendectomy								
Patient	WBC	Neutrophil count	Lymphocyte count	Platellet count	PDW (%)	NLR	PLR	Negative appendectomy
1	13.2	9.2	2.7	214	16.9	3.4	79.25	No
2	17.2	13.5	2.8	318	16	4.82	113.5	No
3	18	13.2	3.5	296	16.3	3.77	84.5	No
4	11	6.9	2.8	272	17.2	2.46	97.1	Yes
5	15.9	14	1.5	354	16.9	9.33	236	No
6	17.1	12.5	1.4	199	15.9	8.92	142.1	No
7	14.6	12.6	1.6	201	17	7.87	125.6	No
8	15.6	13.6	1.4	227	17	9.71	162.1	No
9	14	11.5	1.5	304	16.6	7.66	202.6	Yes
10	10.6	8.3	1.7	211	17.6	4.88	124.1	No
11	20.8	18.1	1	296	17.8	18.1	296	No
12	15.3	12.8	2	259	16.4	6.4	129.5	No

AA: Acute Appendicitis, WBC: White blood cell count, PDW: Platellet-Distribution Widht, NLR: Neutrophil-tolymphocyte ratio, PLR: Platelet-tolymphocyte ratio

Table 3. Laboratory values, NLR and PLR parameters of 10 patients with acute appendicitis proven with pathology						
Laboratory values	(n)	Mean±std. Deviation (min-max)				
WBC	10	15.83±2.76 (10.6-20.8)				
Neutrophil counts	10	12.78±2.66 (8.3-18.1)				
Lymphocyte counts	10	1.96±0.78 (1-3.5)				
Platellet counts	10	257.5±55.31 (199-354)				
PDW (%)	10	16.78±0.63 (15.9-17.8)				
NLR	10	7.72±4.32 (3.4-18.1)				
PLR	10	149.2±67.68 (79.2-296)				

WBC: White blood cell count, PDW: Platellet-Distribution Widht, NLR: Neutrophil lymphocyte ratio, and PLR: Platelet lymphocyte ratio

Table 4. Comparison of age and laboratory parameters of patients with negative appendectomy and those with proven appendicitis

Parameters	Proven appendicitis (n=10)	Negative appendectomy (n=2)	p-Value	Z Score
	median (min-max)	median (min-max)		
Age	31 (20-41)	20 (17-23)	0.052	-1.940
WBC	15.8 (10.6-20.8)	12.5 (11.0-14.0)	0.133	-1.504
Neutrophil counts	13.0 (8.3-18.1)	9.2 (6.9-11.5)	0.086	-1.719
Lymphocyte counts	1.7 (1.0-3.5)	2.2 (1.5-2.8)	0.666	-0.432
Platellet counts	243.0 (199.0-354.0)	288.0 (272.0-304.0)	0.389	-0.860
PDW(%)	16.9 (15.9-17.8)	16.9 (16.6-17.2)	0.666	-0.431
NLR	7.1 (3.4-18.1)	5.1 (2.5-7.7)	0.283	-1.074
PLR	127.6 (79.3-296.0)	149.9 (97.1-202.6)	1.000	0.000
Platellet counts	243.0 (199.0-354.0)	288.0 (272.0-304.0)	0.389	-0.860
PDW(%)	16.9 (15.9-17.8)	16.9 (16.6-17.2)	0.666	-0.431
NLR	7.1 (3.4-18.1)	5.1 (2.5-7.7)	0.283	-1.074
PLR	127.6 (79.3-296.0)	149.9 (97.1-202.6)	1.000	0.000

WBC: White blood cell count. PDW: Platellet-Distribution Widht. NLR: Neutrophil lymphocyte ratio, and PLR: Platelet lymphocyte ratio

DISCUSSION

It is difficult to differentiate AA symptoms and signs from other abdominal pain causes in pregnant patients. In addition, there is no reliable scoring system that will allow the recognition of pregnant AA patients in the studies conducted (2). The physician evaluating the pregnant patients, who are currently suspected of AA, faces the risk of unnecessary overtreatment by rapid intervention, or being late in treatment only by following and not intervening on time. Difficulties in the recognition of abdominal pain in this group of patients can be explained by physiological and anatomical changes in pregnant women in general (11,12). In addition, the lack of routine use of computed tomography (13), which is an important imaging method in non-pregnant female patients, is another reason that makes it difficult for both general surgeons and gynecologists to recognize acute

abdominal pathologies developing in this patient group. However, approximately 0.39-2% of pregnant women undergo surgical interventions due to non-obstetric pathologies (14,15). Most of these surgical interventions are performed for acute appendicitis and it is reported to be approximately 1 in 766-1500 pregnancies (1,2). Although AA can be seen in every trimester during pregnancy, it is frequently detected in the 2nd or 3rd trimester (2,16). In our study, most of the pregnant appendicitis applied in the 2nd and 3rd trimesters. However, with the progression of pregnancy, physiological and anatomical changes increase. This may cause the diagnosis of AA to be delayed and the appendicitis to become complicated and perforated (17,18). While appendectomies normally performed in uncomplicated pregnant appendicitis cases constitute low risk for the fetus, on the other hand when the appendicitis becomes complicated, the risk of fetal and maternal loss increases (10). In our study, all of our

patients with perforated appendicitis were identified in the 3rd trimester in accordance with the literature, and their application times varied between 48-72 hours. This makes us think that not only the physicians evaluating the patients but also the patients have difficulties in interpreting the symptoms and signs of progressing pregnancy (19).

Various imaging methods can be used to support diagnosis in cases of acute appendicitis with suspected clinical and laboratory findings. Among them, US is used as the first choice in pregnant patients because it is free of radiation and fast and cheap (10). However, the most important disadvantages are the fact that US is operator dependent, it has a limited use in differential diagnosis, and the appendix cannot be visualized at high rates (12). In the study of Yagci et al. (19), ultrasound findings of all patients were found compatible with acute appendicitis, while this rate was 62.5% in the study of Tiryaki et al. (20). However, in the studies of Cobben et al. (21) and Pedrosa et al. (22), a high rate of appendix could not be visualized as in our study (92-96%, respectively). In our current study, appendix could not be visualized in any patient, and inflammation in the surrounding tissues due to appendicitis was mentioned in only one patient. Although advanced gestational week, morbid obesity or the presence of intestinal gas decreases the success of US (23), the fact that appendix could not be visualized in any patient in our study is one of the most important evidence that US is operator dependent (12).

The literature suggests the use of MRI with high sensitivity and specificity when the appendix cannot be detected by US (10,24). In addition, computed tomography can be used as an alternative imaging method in pregnant women when MRI is not possible (25). Although MRI is performed in our hospital, MRI and interpretation of these images cannot be done immediately under emergency conditions. For this reason, in order to avoid loss of time, MRI is not used in our routine practice. However, in our hospital, CT is used in non-pregnant patients, where differential diagnosis of acute abdomen cannot be made and can be interpreted quickly. However, our pregnant patients believe that depending on the radiation they will be exposed to during CT, there will be a problem in the fetus during or after pregnancy (26). American College of Radiology (ACR) does not recommend CT as the first imaging in the diagnosis of suspected AA in pregnant patients with right lower quadrant pain, fever, and leukocytosis, and states that imaging quality decreases in modified CT images by reducing the radiation dose (24). However, for the suspicion of AA, it is stated that in the CTs taken at modified doses, although the mother and fetus are exposed to a reduced radiation dose, there is a 2-fold overall risk of life-long childhood cancer in the fetus (27,28). For this reason, we do not use CT in our routine practice unless there is an absolute cause in the differential diagnosis of acute abdomen in pregnant patients (25).

Although negative appendectomy rates in pregnant

patients vary between 23% - 25% in publications (1,9), it is known that negative appendectomy rates decrease with the help of imaging methods such as MRI and CT (29). In our study, our negative appendectomy rate was 16.6% and was generally lower than the the literature. However, as we mentioned above, appendix could not be visualized in any of our patients using US and no MRI or CT was taken in our patients. Despite this, the fact that we obtained a lower negative appendectomy rate than the literature may be attributed to the fact that an experienced general surgery and gynecology team evaluates patients together since the hospital is the reference center in the region. However, the low rate of negative appendectomy can be interpreted as suspicious cases sent to their homes and that patients may have been operated at another center later on. Finally, pathologists evaluating the appendix material may have a role in this. Although there is no information in the literature about whether the pathologist is blind or not in appendectomies performed in pregnant women, it is thought that this will not affect the negative appendectomy rates (2). However, we think that a specimen whose clinical and surgical information is reported as AA by the general surgeon will make the pathologist more prone to diagnose AA in the pathological diagnosis, especially in ambiguous situations.

In the literature, laboratory findings have been studied in the recognition of pregnant appendicitis, but generally WBC and CRP could not be helpful enough in the diagnosis of AA since it increases in the later trimesters of pregnancy (7,8). Nevertheless, Baskıran (30) et al. reported that other parameters studied in routine blood count may help to diagnose AA in pregnant patients. According to this study, when AA cases detected in 1st trimester versus 2nd and 3rd trimesters were examined in terms of Lymphocyte count, NLR and PLR, it was stated that there was a significant difference between this laboratory parameters. This study compared pregnant appendicitis only within itself (1. trimester vs 2. and 3. trimester). Yazar et al. (31) compared pregnant AA cases with pregnant women who were considered AA but not detected AA, healthy pregnant women and healthy women who were not pregnant. In the aforementioned study; mean WBC counts and CRP levels, median NLR and PLR values were significantly higher in women with proven AA. Also when NLR, PLR, WBC count, CRP level and lymphocyte count were combined, an accurate diagnosis of AA could be established with 90.5% accuracy. The fact that the average of WBC, lymphocyte count, NLR and PLR values of 10 pregnant patients with AA in our study was higher than the cut-off values determined by Yazar et al. (31), supports that these parameters can be used in the diagnosis of pregnant AA.

Limitations; The retrospective nature and the small number of patients are the major limitations of our study.

CONCLUSION

As a result, in our study, a clear distinctive finding that could be used to predict pregnant appendicitis was not detected. Although imaging and laboratory findings play

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a role in determining the diagnosis of AA, our study has revealed that the most important criterion in the diagnosis of AA in pregnant patients is that the general surgery and gynecology should evaluate the patients together as a multidiciplinary team.

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