

DIAGNOSIS, MANAGEMENT AND CLINICOPATHOLOGICAL FEATURES OF ACUTE APPENDICITIS IN PREGNANT WOMEN AND ITS IMPACT ON FETAL OUTCOMES

GEBE KADINLARDA GÖRÜLEN AKUT APANDİSİTİN TANI, TEDAVİ VE KLİNİKOPATOLOJİK ÖZELLİKLERİ VE FETAL SONUÇLAR ÜZERİNE ETKİSİ

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ABSTRACT

Objective: To evaluate the clinicopathological features and foeto-maternal outcomes of appendicitis during pregnancy.

Material and Method: This study involved comparisons of laboratory findings, preoperative ultrasonography (US), pathology and clinical outcomes of 17 pregnant and 59 age-matched non-pregnant women undergoing appendectomy.

Results: The total number of US scans, rates of non-visualized appendix on US, and length of hospital stay were higher in pregnant women than in non-pregnant subjects ($p<0.001$, $p=0.035$, and $p=0.014$; respectively). The rate of negative appendectomy was 1.5-times higher and the rate of complicated appendicitis was 7-times higher in pregnant compared with non-pregnant patients. The diagnostic accuracy of US was higher in the non-pregnant group (72.9% vs. 64.7%). In terms of the hematological parameters, no significant difference was found between the pregnant patients with and without appendicitis. There was one premature birth and one abortus in the second trimester, and one premature birth followed by a negative appendectomy in the third trimester.

Conclusion: The diagnosis of acute appendicitis in pregnancy may remain inconclusive despite comprehensive evaluation with clinical examination, laboratory studies, and US. We recommend that clinicians consider additional imaging scans when they suspect appendicitis during pregnancy to avoid unnecessary surgical interventions. Both complicated appendicitis and negative appendectomy can cause a non-negligible rate of fetal morbidity and mortality.

Keywords: Acute appendicitis, morbidity, pregnancy

ÖZET

Amaç: Çalışmanın amacı gebe kadınlarda görülen apandisit tanı ve tedavi stratejileri ile klinikopatolojik özellikleri ve feto-maternal sonuçlarını değerlendirmektir.

Gereç ve Yöntem: Bu çalışmada apendektomi yapılan 17 gebe kadın ve yaşları eşleştirilmiş 59 gebe olmayan kadın laboratuvar bulguları, preoperatif ultrasonografi (USG), patoloji ve klinik sonuçlar açısından karşılaştırıldı.

Bulgular: Toplam USG tarama sayısı, görüntülenemeyen apandisit oranları ve hastanede kalış süreleri gebe kadınlarda gebe olmayan kadınlara göre daha fazla idi (sırasıyla $p<0,001$, $p=0,035$ ve $p=0,014$). Gebe grupta negatif apendektomi oranı gebe olmayanlara göre 1,5 kat, komplike apandisit oranı ise 7 kat daha yüksekti. USG'nin tanılabilirliği ise gebe olmayan grupta daha yüksek bulundu (%72,9'a karşı %64,7). Hematolojik parametreler açısından apandisit olan ve olmayan gebe hastalar arasında anlamlı bir fark bulunmadı. İkinci trimesterde bir erken doğum ve bir abortus görülürken, üçüncü trimesterde bir hasta da negatif apendektomiyi takiben bir erken doğum gerçekleşti.

Sonuç: Gebelik sırasında laboratuvar parametreleri ve USG ile konulan apandisit tanısı hatalı olabilmektedir. Bu yüzden, gereksiz cerrahi müdahalelerden kaçınmak için, klinisyenlerin hamilelik sırasında apandisitten şüphelendikleri durumlarda ek görüntüleme tetkikleri yapmayı düşünmelerini öneririz. Çünkü hem negatif apendektomi hem de komplike apandisit, ihmal edilemez bir fetal morbidite ve mortalite oranıyla sonuçlanabilir.

Anahtar Kelimeler: Akut apandisit, gebelik, morbidite

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INTRODUCTION

During pregnancy, acute appendicitis is the most common condition occurring at a frequency of one in 500–1000 births, and it necessitates nonobstetric emergency surgery (1). It is usually difficult to diagnose acute appendicitis during pregnancy because non-specific symptoms such as nausea, vomiting, loss of appetite, and abdominal pain are often the case in appendicitis as well as pregnancy, and the classic signs of appendicitis can also be masked by physiologic leukocytosis, altered anatomical position of the appendix and increased abdominal wall laxity, especially during late pregnancy (2, 3). Also, due to the fact that diagnosing appendicitis in women is difficult, up to 50% of patients are misdiagnosed in the preoperative period (2, 4, 5).

Complicated appendicitis rates occurring during pregnancy may vary between 14.9% and 43% (6). Because non-complicated appendicitis may progress rapidly into perforation, and complicated appendicitis may be associated with premature birth, fetal loss, maternal and fetal morbidity, it is imperative to diagnose appendicitis in pregnant women correctly and quickly (7). Reduced efficiency of abdominal ultrasonography (US) due to anatomic reasons, avoidance of computed tomography (CT) typically due to sensitivity to radiation, and difficulties in obtaining magnetic resonance imaging (MRI) often contribute to delays in diagnosis (8-10). Traditionally, early surgery is performed to avoid complications such as potential perforations. However, it has been reported that this approach could result in a negative appendectomy in 11% to 50% of cases. While negative appendectomy is acceptable to a certain extent, it is also unclear whether negative appendectomy or complicated appendicitis may be associated with unfavorable fetal and pregnancy outcomes (11, 12).

It remains unclear what the optimal clinical and surgical approach to acute appendicitis during pregnancy is. Also unclear is whether or not negative appendectomy or complicated appendicitis may be associated with unfavorable fetal and pregnancy outcomes. In this study, the aim was to compare appendicitis in pregnant women to that in women of similar age, to determine its diagnostic, treatment and clinicopathological differences, to determine the accuracy of US, and to investigate the effect of appendicitis on maternal and fetal adverse outcomes.

MATERIAL AND METHOD

The Ethics Committee of Non-Interventional Clinical Research at the University of Health Sciences found no ethical issues in carrying out the present study as this study did not involve any prospective analysis of a new method but only research showing standard clinical practices or advancement of practices. This study was designed as a retrospective study. The participants were recruited

from among 466 female patients who underwent appendectomy between July 2016 and December 2019. The demographic characteristics and preoperative and postoperative findings of the pregnant women undergoing appendectomy were compared with those of their non-pregnant counterparts. The patients were matched by age at a ratio of 1:3 to eliminate age bias.

Initially, pregnant women with acute abdominal pain were investigated in a gynecology and obstetrics unit. If the origin of the pain was thought to be due to a non-obstetrical reason, the patients were identified for further investigation and a complete transabdominal US with sectorial and linear probes was performed. Before surgery, an obstetrician assessed the women to determine gestational age and to monitor fetal vitality. US was repeated both after the surgical procedure and before the patient's discharge.

Patient demographics, preoperative laboratory parameters, imaging results, details of the surgical intervention, pathological findings, and length of hospital stay were analyzed. Final pathologic diagnoses of appendix were grouped into the following categories: normal appendix, non-complicated appendicitis, and complicated appendicitis. The final diagnosis was accepted as a negative appendectomy if the resected appendix showed no histologically proven inflammation. Maternal and fetal outcomes were finalized by examining patient records and then conducting phone interviews. Fetal loss was defined as any loss after 20 weeks of gestation. Preterm delivery was defined as a birth before 37-weeks completed gestation.

All statistical analyses were performed using Statistical Package for the Social Sciences version 16.0 for Windows (IBM®, Chicago, USA). Descriptive statistics were reported as means \pm standard deviation in normally distributed numeric variables, as medians (minimum-maximum) in non-normally distributed data, and as frequency in categorical variables. The Shapiro-Wilk test was used to ensure the normality of the data. The Student's *t* test or Mann-Whitney *U* test were used to analyze continuous variables, where appropriate. Kruskal-Wallis test was used for comparisons of median values among more than two groups. Comparisons of categorical variables were compared using chi-square or Fisher's exact test. Propensity score analysis was used to make pregnant patients and non-pregnant patients homogeneous in terms of age and sex (1:3 ratio). The diagnostic performance of US for predicting acute appendicitis in the pregnant and non-pregnant women was also analyzed. All tests were two-sided, and a *p* value < 0.05 was considered statistically significant.

RESULTS

The baseline characteristics of 17 pregnant patients undergoing appendectomy were compared with 59 age-

matched non-pregnant controls also undergoing appendectomy between July 2016 and December 2019. A total of 4,511 pregnant women were monitored in the same hospital's obstetrics department during this time. Therefore, 0.38% of the pregnant women were calculated to have appendicitis.

The demographic and perioperative data of the patients are presented in Table 1 and Table 2. In the pregnant group, the median number of US scans done for diagnosis was significantly higher than in the non-pregnant group ($p<0.001$). There was a higher rate of non-visualized appendix vermiformis on US in the pregnant patients compared with that in the non-pregnant patients (41.2% vs. 16.9%, $p=0.035$). However, the median maximal diameter of the appendix was 8.5 mm (range, 6–14 mm) in the pregnant women and 9 mm (range, 5–17) in the non-pregnant women ($p=0.976$). While CT or MRI was not used as a secondary diagnostic imaging modality in the pregnant women, CT was performed on 28.8% of the non-pregnant patients.

No statistically significant difference was observed between the groups in terms of preoperative laboratory findings as well as the interval from admission to surgery. In 41.2% of the pregnant patients, the anesthesia meth-

od was spinal anesthesia, whereas this rate was 1.7% in the non-pregnant patients ($p<0.001$). There was no significant difference regarding surgical methods, surgical drain use, and the need for broad-spectrum antibiotics ($p=0.103$, $p=0.388$, and $p=0.151$, respectively). Preventive tocolytic therapy was administered in 35.3% of the pregnant patients. Length of hospital stay was statistically longer in pregnant patients (2 days vs. 1 day, $p=0.014$). In terms of pathological findings, the negative appendectomy rate was found to be 1.5 times higher (29.4% vs. 16.9%), and the complicated appendicitis rate was 7 times higher (23.5% vs. 3.4%) in the pregnant group than in the non-pregnant patients, respectively ($p<0.001$).

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of US for predicting appendicitis are presented in Table 3. When preoperative laboratory parameters and US findings were compared between the pregnant patients with and without appendicitis, no significant difference was found in laboratory findings (Table 4). However, median appendix diameter was significantly higher in the patients with acute appendicitis than those with negative appendectomy ($p=0.044$).

Table 5 shows the perioperative and fetomaternal out-

Table 1: Comparison of demographic characteristics of the pregnant and non-pregnant women.

	Pregnant women n=17	Non-pregnant women n=59	p
Age (year), median	27 (range, 19-40)	28 (range, 18-41)	0.713
Gestational age (week), median	17 (range, 6-36)		N/A
First trimester	7 (41.2)		
Second trimester	6 (35.3)		
Third trimester	4 (23.5)		
Preoperative ultrasound findings			
Total number of ultrasound scans, median	2 (range, 1-5)	1 (range, 0-2)	<0.001
Probable acute appendicitis, n (%)	10 (58.8)	49 (83.1)	0.035
Non-visualized/normal, n (%)	7 (41.2)	10 (16.9)	0.035
Appendix diameter, median	8.5 (range, 6-14)	9 (range, 5-17)	0.976
Definitive diagnosis with CT, n (%)	0	17 (28.8)	N/A
Preoperative laboratory parameters			
Leucocyte ($\times 10^9/L$), mean \pm SD	13.9 \pm 3.1	13.3 \pm 4.8	0.569
Neutrophil ($\times 10^9/L$), mean \pm SD	11.4 \pm 3.2	10.5 \pm 4.8	0.490
Lymphocyte ($\times 10^9/L$), mean \pm SD	1.9 \pm 0.7	1.9 \pm 0.8	0.587
NLR, mean \pm SD	7.2 \pm 4.1	8.5 \pm 9.4	0.572
PLR, mean \pm SD	153.5 \pm 86.5	180.6 \pm 104.5	0.331
C-reactive protein (mg/L), mean \pm SD	26.5 \pm 48.7	47.0 \pm 60.6	0.215

N/A; not applicable, CT; computed tomography, NLR; neutrophil-to-lymphocyte ratio, PLR; platelet-to-lymphocyte

Table 2: Comparison of perioperative findings and clinicopathological features of the pregnant and non-pregnant women.

	Pregnant women n=17	Non-pregnant women n=59	P
Interval between hospital admission and surgery (hour), median	10 (range, 2-45)	8 (range, 1.5-35)	0.428
Anesthesia procedure, n (%)			<0.001
Spinal	7 (41.2)	1 (1.7)	
General	10 (58.8)	58 (98.3)	
Surgical procedure, n (%)			0.103
Open	16 (94.1)	45 (76.3)	
Laparoscopic	1 (5.9)	14 (23.7)	
Surgical drain placement, n (%)	1 (5.9)	8 (13.6)	0.388
Broad spectrum antibiotic use, n (%)	4 (23.5)	6 (10.2)	0.151
Preventive tocolysis, n (%)	6 (35.3)		N/A
Hospital stay (day), median	2 (range, 1-18)	1 (range, 1-8)	0.014
Pathological findings, n (%)			<0.001
Normal	5 (29.4)	10 (16.9)	
Non-complicated appendicitis	8 (47.1)	47 (79.7)	
Complicated appendicitis	4 (23.5)	2 (3.4)	

N/A; not applicable

Table 3: Sensitivity, specificity, PPV, NPV, and diagnostic accuracy of sonography for predicting appendicitis in pregnant and non-pregnant women.

	Sensitivity (%95 CI)	Specificity (%95 CI)	PPV (%95 CI)	NPV (%95 CI)	Diagnostic accuracy (%95 CI)	Diagnostic odds ratio (%95 CI)
Pregnant	66.7 (34.9-80.0)	60.0 (14.7-94.7)	80.0 (56.0-92.6)	42.9 (20.4-68.7)	64.7 (38.3-85.8)	3.00 (0.23-45.23)
Non-pregnant	83.7 (70.3-92.7)	20.0 (2.5-55.6)	83.7 (78.6-87.8)	20.0 (5.85-50.15)	72.9 (59.8-83.6)	1.28 (0.15-8.72)

PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval

Table 4: The preoperative ultrasound findings and laboratory parameters of the pregnant women with acute appendicitis and those with a normal appendix.

	Pathological results		P
	Normal n=5	Appendicitis n=12	
Preoperative ultrasound findings			
Total number of ultrasound scans, median	3 (range, 1-5)	1.5 (range, 1-5)	0.130
Appendix diameter, median	6.3 (range, 5.5-7)	8.9 (range, 7.3-14)	0.044
Preoperative laboratory parameters			
Leucocyte (x10 ⁹ /L), mean±SD	15.4±1.1	13.3±3.4	0.264
Neutrophil (x10 ⁹ /L), mean±SD	12.8±2.1	10.8±3.4	0.237
Lymphocyte (x10 ⁹ /L), mean±SD	2.1±0.7	1.8±0.7	0.475
NLR, mean±SD	7.3±4.6	7.1±4.1	0.928
PLR, mean±SD	144.9±111.5	157.1±79.5	0.801
C-reactive protein (mg/L), mean±SD	11.1±11.3	32.5±56.9	0.478

NLR; neutrophil-to-lymphocyte ratio, PLR; platelet-to-lymphocyte

Table 5: Comparison of the preoperative and postoperative features of the pregnant women in terms of gestational age.

	First trimester n=7	Second trimester n=6	Third trimester n=4	P
Age (year), median	25 (range, 20-39)	25.5 (range, 19-40)	30 (27-35)	0.489
Interval between hospital admission and surgery (hour), median	12 (3-45)	7.5 (3-29)	5.5 (2-18)	0.186
Preoperative ultrasound findings				
Total number of ultrasound scans, median	2 (range, 1-5)	1.5 (range, 1-5)	1.5 (range, 1-3)	0.739
Probable acute appendicitis, n (%)	6 (85.7)	3 (50.0)	1 (25.0)	0.124
Non-visualized/normal, n (%)	1 (14.3)	3 (50.0)	3 (75.0)	0.124
Appendix diameter, median	7.9 (range, 5.5-11.5)	11 (range, 8.5-14)	8 (range, 8-8)	0.273
Preoperative laboratory parameters				
Leucocyte (x10 ⁹ /L), median	13.8 (range, 6.9-16.4)	13.2 (range, 9.7-19.9)	15.8 (range, 13.3-16.4)	0.555
Neutrophil (x10 ⁹ /L), median	9.6 (range, 4.7-15.1)	11.3 (range, 7.1-18.1)	12.7 (range, 11.2-14.1)	0.238
Lymphocyte (x10 ⁹ /L), median	1.8 (range, 1.0-3.2)	1.6 (range, 1.0-2.0)	2.4 (range, 0.9-2.6)	0.453
NLR, median	3.7 (range, 2.9-15.2)	7.8 (range, 3.6-14.6)	5.7 (range, 4.7-12.4)	0.472
PLR, median	111 (range, 70-339)	166 (range, 112-297)	110 (range, 61-315)	0.273
C-reactive protein (mg/L), median	5.9 (range, 4.5-12)	16.9 (range, 4.9-192)	17.1 (range, 5.3-32.5)	0.258
Surgical procedure, n (%)				
Open	6 (85.7)	6 (100)	4 (100)	0.468
Laparoscopic	1 (14.3)	0	0	
Hospital stay (day), median	2 (range, 1-18)	2 (range, 1-3)	2.5 (range, 1-5)	0.796
Preventive tocolysis, n (%)	3 (42.9)	1 (16.7)	2 (50.0)	0.481
Pathological findings, n (%)				
Normal	3 (42.9)	0	2 (50.0)*	0.033
Non-complicated appendicitis	4 (57.1)	2 (33.3)	2 (50.0)	
Complicated appendicitis	0	4 (66.7) [†]	0	
Pregnancy process				
Planned birth	7 (100)	4 (66.6)	3 (75.0)	0.427
Preterm birth	0	1 (16.7)	1 (25.0)	
Fetal loss	0	1 (16.7)	0	

NLR; neutrophil-to-lymphocyte ratio, PLR; platelet-to-lymphocyte, [†]One fetal loss and one preterm birth, *One preterm birth

comes according to gestational age. There was no significant difference between trimesters in terms of age, interval from admission to surgery, total US scans, appendix diameter, laboratory parameters, surgical procedures, hospital stays, and preventive tocolysis. While the rate of negative appendectomy and noncomplicated appendicitis was higher in the first and last trimesters, the rate of complicated appendicitis was higher in the second trimester ($p=0.033$). There was no premature birth in women on whom appendectomy had been performed in the first trimester; however, there was one premature birth and

one abortus (both had complicated appendicitis) in the second trimester, and one premature birth followed by negative appendectomy in the third trimester ($p=0.427$).

DISCUSSION

Given the unreliability of the clinical signs of appendicitis in pregnancy, an aggressive surgical approach has typically been recommended to prevent perforation, which leads to increased risk of adverse outcomes (5, 10, 13). However, in recent literature, negative appendectomy

rates have been reported to have risen when this strategy was introduced, resulting in fetal loss and early delivery (5, 12, 14). The need for early surgical management in case of appendiceal perforation and the need for enhancing preoperative diagnostic accuracy with additional imaging modality to avoid negative appendectomy have to be balanced. Currently, advances in the accuracy of diagnostic imaging methods and the efficacy of antibiotic treatment have made the traditional approach controversial. In the present study, we analyzed all pregnant women, who underwent appendectomy for acute appendicitis to demonstrate clinicopathologically different features of appendicitis in pregnancy and any potential adverse fetomaternal outcomes.

Appendicitis is the most prevalent cause of non-traumatic emergencies of the digestive tract necessitating surgical treatment in pregnant women, with a prevalence of 0.1-0.2% (6, 15). In this study, the appendicitis incidence during pregnancy was 1 in 265 births (0.38%) during the period between 2016 and 2019. In a study regarding acute appendicitis depending on trimesters, Zingone et al. (16) found the rates of acute appendicitis to be nearly same in the first and second trimesters (7.4 and 7.3 per 10,000 person-years) and to be lower in the last trimester (4.6 per 10,000 person-years). Some recent studies have reported that the incidence of appendicitis was higher during the second trimester of pregnancy than during the first or third trimesters (14, 17). In our study, appendicitis cases were observed most frequently in the first trimester (41.2%) and least frequently in the third trimester (23.5%).

It has been reported that the preoperative diagnosis of appendicitis can be difficult during pregnancy. Anatomical and physiological changes in pregnancy may make the diagnosis more uncertain and delay the treatment of appendicitis (3, 5, 10, 14, 18). While nausea and vomiting occur frequently during pregnancy, rebound tenderness and guarding are not often seen in pregnant women with appendicitis due to the shift of the appendix upward and laterally as the uterus grows, which results in diminished response to peritoneal irritation (9, 19). It was reported in previous literature that only less than half of patients with pathologically proven appendicitis had a classic history of abdominal pain (6, 9). Thus, the clinical diagnosis of appendicitis may pose a challenge for the physician.

Recently, in a large cohort study of pregnant women treated for appendicitis, Segev et al. (20) reported no significant difference between pregnant and non-pregnant women in terms of the time interval between the first symptoms and the visit to the emergency room, and from the emergency admission to surgical intervention; however an earlier study by Hirsch et al. (13) showed a significantly shorter period in pregnant patients from hospital admission to surgery. In our study, the time in-

terval between admission to emergency department and surgery was similar among the groups. However, in accordance with the previous studies (13, 20), it was observed that the median hospital stay was significantly longer for the pregnant women (2 days vs. 1 day). Additionally, in the pregnant group, the median number of US scans for diagnosis was higher than in the non-pregnant group. These findings suggest that the traditional aggressive approach was not preferred in appendicitis in pregnancy and that the patients were more closely monitored for potential complications in the postoperative period.

It has been shown that leukocytosis occurs due to an increased number of neutrophils in blood circulation during pregnancy and that neutrophils begin to increase in the second trimester, then remain constant with the total number ranging between 9 and 15000 (15, 17, 20). The differential diagnosis of appendicitis in pregnancy includes several inflammatory conditions, all of which are characterized by leukocytosis. It was suggested that the inflammatory markers seemed to have a less diagnostic value in pregnant women with suspected appendicitis compared to their healthy pregnant counterparts. Similarly, we did not find a significant difference between the pregnant women with appendicitis versus the non-pregnant women with appendicitis with regard to leucocyte and lymphocyte counts nor with regard to the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte, and CRP values on admission (13, 15). Although not statistically significant, the mean CRP level was found to be 3 times higher in the pregnant women with appendicitis than in the negative appendectomy group (11.1 mg/L vs. 32.5 mg/L, $p=0.478$). As reported in another study, the contributions of inflammation markers alone are limited, and thus their use must only be to contribute to diagnosis together with physical examination and imaging tests (18).

US is the main imaging modality for the diagnosis of acute appendicitis in both pregnant and nonpregnant patients (6, 14). Since ionizing radiation during pregnancy has some potential negative impacts on the fetus, we avoid using CT in pregnant women and women of reproductive age. In the current study, US was used preoperatively in all women to be sure of an accurate diagnosis of appendicitis and to avoid unnecessary surgery. It has been reported that US yields a high rate of non-visualization of the appendix during pregnancy in up to 75% of cases (9, 15) and a low sensitivity in 36%–71% of cases (3, 6, 13). These results can be explained by the fact that the use of US is limited due to its high operator dependence. We observed that the non-visualization of appendix on US was higher in the pregnant than in non-pregnant patients (41.2% vs. 16.9%; $p=0.035$). Previous studies showed that the rate of negative appendectomy in pregnant women reduced from 54% to 36% when US was used and to 8% when US was followed by CT (20, 21). The different rates of negative appendecto-

my among the studies can be explained by the differences in the rates of imaging assessment before the surgical intervention. Our negative appendectomy rate was 29.4% for the pregnant women and 16.9% for the non-pregnant women according to the pathological results. These rates are consistent with the 13%–50% range reported for negative appendectomy during pregnancy (22, 23) and the 15%–35% range for non-pregnant patients with appendicitis (5). This difference was due to the use of CT in 28.8% of the non-pregnant patients. When initial US findings are indeterminate, advanced imaging methods with improved preoperative diagnostic accuracy are required to decrease the number of negative appendectomies.

Currently, the main surgical technique in the management of acute appendicitis during pregnancy is yet to be established. The preferred surgical method is based upon the trimester of pregnancy and the surgeon's own preference (3, 9, 13, 24). Our findings indicated that the laparoscopic management of appendicitis was more frequently used in the non-pregnant women than in the pregnant women. Whereas both open and laparoscopic procedures were performed in the first trimester, only open appendectomies were performed in the second and third trimesters, showing that a majority of the pregnant women were subject to open appendectomy. However, a number of studies have indicated that there might be an increased risk of preterm delivery or fetal loss in those undergoing laparoscopic appendectomy compared with those undergoing open appendectomy (24, 25). Whether the choice of incision should be transverse or oblique or at or above McBurney's point in pregnant women is also a controversial issue (18, 26). Our study showed that oblique incisions at McBurney's point could be performed successfully in all pregnant patients. Moreover, in our study, the anesthesia method was primarily regional anesthesia in 41.2% of the pregnant patients, whereas this was only 1.7% in the non-pregnant patients. There is no conclusive evidence demonstrating superior safety for regional anesthesia. General anesthesia is still frequently required. Not surprisingly, the length of hospital stay was statistically longer in pregnant women who underwent appendectomy than among the non-pregnant women, which may be associated with the examination of pregnant women with additional imaging techniques, and thus, lengthened hospital stays. We also did not find any differences in terms of perioperative variables such as surgical procedures, drain use, and use of broad-spectrum antibiotics between the pregnant women with appendicitis and the non-pregnant women.

Different results have been reported in terms of whether complicated appendicitis in pregnancy occurs at a greater or similar rate than in non-pregnant patients (5, 17, 20). In our study, the rate of complicated appendicitis was 7 times higher in the pregnant compared to the non-preg-

nant patients. By contrast, non-complicated appendicitis was approximately 1.5 times less common. There was no statistically significant difference in the interval from admission to surgery. However, this lack of difference may also be attributed to the fact that a third of the pregnant patients were operated on after more than 24 hours, which therefore, resulted in a delay in diagnosis. While negative appendectomy rates were higher in the first and third trimesters, the rate of complicated appendicitis was higher in the second trimester. Tocolytics are indicated to preserve pregnancy if premature labor is the case. Although its efficacy during non-obstetric surgeries is debatable, prophylactic tocolytics may be considered during the third trimester in lower abdominal or pelvic surgeries with inflammatory conditions. In this study, a preventive tocolytic agent was administered especially in the last trimester.

In a study by McGory et al. (5), fetal loss rate was reported to be 6% in patients undergoing appendectomy for complicated appendicitis, 2% in patients with noncomplicated appendicitis and 4% in patients with a normal appendix. Other studies have also reported the rate of preterm delivery in pregnant women with acute appendicitis up to 11.4% (21). In the present study, the majority of the pregnant women (82.3%) gave birth to a full-term baby. While there was no premature delivery in any of the appendectomies performed in the first trimester despite the high negative appendectomy rate (42.9%), two premature deliveries and one fetal loss occurred in the second and third trimesters, respectively. One of the premature deliveries occurred following an appendectomy on a 36-week pregnant patient, and the other at the 32nd gestational week after surgery at the 17th week of another pregnant patient. The fetus was lost during the 24th gestational week following an appendectomy on a 21-week pregnant patient. In conclusion, it was agreed that one patient had a preterm birth (during the third trimester) and another had a fetal loss (during the first trimester) due to appendectomy. Based on these results, it is hard to determine whether complicated appendicitis or negative appendectomy has a fetal impact. However, it can be assumed that any interventions during late pregnancy are risky.

This study is subject to a number of limitations. Firstly, there are limitations inherent in any retrospective analysis. For instance, the variations in the timing of antibiotic treatment might have changed pathological progression, and the sample size may undermine the statistical interpretation of outcomes with relation to trimesters. Another limitation is that different radiologists evaluated the findings of the patients. Although they were all experienced radiologists, there may be some variations in the evaluations. The major strength of this study was to stratify the pregnant women with acute appendicitis according to gestation age, which had an impact on clinical outcomes and patient management.

In conclusion, we found some statistically significant differences in length of hospital stay, total numbers of US scans, types of anesthesia procedures, and the rates of complicated appendicitis and negative appendectomy between the pregnant and non-pregnant women. Accurate diagnosis of acute appendicitis in pregnancy remains uncertain based upon laboratory parameters and US scans. We recommend that clinicians consider additional imaging modalities when they suspect appendicitis in pregnancy to avoid unnecessary surgical interventions. Both a complicated appendicitis and negative appendectomy during pregnancy can cause a non-negligible rate of fetal morbidity and mortality.

Ethics Committee Approval: The research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects"

Informed Consent: Informed consent was not received due to the retrospective nature of the study.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- R.Ş.; Data Acquisition- R.Ş., S.U.Ç., Ş.K.; Data Analysis/ Interpretation- R.Ş., S.U.Ç.; Drafting Manuscript- R.Ş., S.U.Ç., Ş.K.; Critical Revision of Manuscript- R.Ş., S.U.Ç.; Final Approval and Accountability- R.Ş., S.U.Ç., Ş.K.; Technical or Material Support- R.Ş.; Supervision- R.Ş.

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Bilgilendirilmiş Onam: Retrospektif bir çalışma olduğundan bilgilendirilmiş onam alınmamıştır.

Hakem Değerlendirmesi: Dış bağımsız.

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