ÖZGÜN ARAŞTIRMA ORIGINAL RESEARCH

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AN APPROACH TO ACUTE APPENDICITIS CASES DURING PREGNANCY: A PUBLIC HOSPITAL PRACTICE

GEBELİKTE AKUT APANDİSİT OLGULARINA YAKLAŞIM; BİR DEVLET HASTANESİ PRATİĞİ

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Öz

Amaç
Akut apandisit, gebelikte en sık yapılan non-obstetrik cerrahidir. Gebeliğin kendine özgü fizyolojik, anatomik değişiklikleri tanı ve tedavi sürecini güçleştirir. Literatürde bu konuyla ilgili çalışmaların çoğunlukla tersiyer merkezlerin deneyimlerini yansıttığı görülmektedir. Bu çalışmanın amacı gebelikte akut apandisit vakalarına ilişkin ikinci basamak bir hizmet hastanesindeki perioperatif deneyiminin sunulmasıdır.

Gereç ve Yöntem
Çalışma Ocak 2015- Kasım 2020 tarihleri arasında ikinci basamak bir devlet hastanesinde retrospektif olarak yapıldı. Gebelik döneminde akut apandisit tanısı alan, postoperatif takipleri ve doğumları hastanemizde gerçekleştirilen hastalar çalışmaya alındı.

Bulgular
Hastaların yaş aralığı 24 yaş (18-35), ortanca gestasyonel hafta 17 hafta (8-32) idi. Ortanca lökosit sayısı 11,6 x10^3 uL, nötrofil sayısı 8,6 x10^3 uL, lenfosit sayısı 2 x10^3 uL, trombosit sayısı 271 x10^3 uL, C-reaktif protein 4,5, nötrofil/lökosit oranı 4,3, trombosit/ lenfosit oranı 120,8, lökosit/ C-reaktif protein oranı 0,7 olarak saptandı. Spinal anestezi en çok tercih edilen yöntemdi ve hastaların tamamında açık cerrahinin uygulanmış olduğu görüldü. Ortanca doğum haftası 38 idi (36-40), sadece bir hastada preterm doğumun geliştiği saptandı. Ek maternal veya fetal komplikasyon gelişmediği görüldü.

Sonuç
Multidisipliner yaklaşım koşuluyla ikinci basamak hizmet hastanelerinde de gebe akut apandisit'li hastalar başarıyla tedavi edilebilir.

Anahtar Kelimeler: Akut apandisit, Appendektomi, Doğum, Gebelik, Devlet hastanesi.

Abstract

Objective
Acute appendicitis is the most common non-obstetric surgery performed during pregnancy. Physiological and anatomical changes specific to pregnancy complicate the diagnosis and treatment processes. It has been seen in the literature that the studies on this subject mostly reflect the experiences of tertiary centers. The present study aimed to present the perioperative experience of acute appendicitis cases in pregnancy in a secondary care hospital.

Materials and Methods
The present study was carried out retrospectively between January 2015 and November 2020 in a secondary state hospital. Patients diagnosed with

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acute appendicitis during pregnancy and whose postoperative follow-ups and labors were carried out in our hospital were included in the study.

Results
The median age of the patients was 24 years (18-35), the median gestational week was 17 weeks (8-32). The median leukocyte count was 11.6 x10^3 uL, neutrophil count was 8.6 x103 uL, lymphocyte count was 2 x10^3 uL, thrombocyte count was 271 x x10^3 uL, C-reaktif protein was 4.5, neutrophil/ leukocyte ratio was 4.3, thrombocyte/lymphocyte was ratio 120.8, and the leukocyte /C-reaktif protein ratio was 0.7. Spinal anesthesia was the most preferred method and it was observed that open surgery was performed in all patients. The median week of delivery was 38 (36-40) and preterm labor was seen in only one patient. It was observed that no additional maternal or fetal complications developed.

Conclusion
Pregnant acute appendicitis patients can also be successfully treated in secondary service hospitals on the condition of a multidisciplinary approach.

Keywords: Acute appendicitis, Appendectomy, Labor, Pregnancy, State hospital.

Introduction

The most common cause of non-obstructive emergency surgery in pregnant women is acute appendicitis (AA). Its incidence is 0.074% in the first trimester and 0.073.3% in the second trimester, and 0.046% in the trimester (1). Since the classical symptoms of AA such as abdominal pain, nausea, and vomiting are seen in the natural course of pregnancy, there may be delays in diagnosis (2). Also, as the uterus grows into the abdomen during pregnancy, the localization of the intraperitoneal appendix often changes. In addition to these reasons, physiological changes including leukocytosis during pregnancy and an increase in some acute phase reactants are other reasons that challenge the diagnostic process (3). The first and most preferred imaging method in diagnosis is ultrasonography. Magnetic resonance imaging (MRI) is applied as the second option. Computed tomography (CT) is used in exceptional cases due to ionizing radiation (2, 4, 5). Although the general approach in treatment is conventional open appendectomy, laparoscopic surgery is also applied safely today. However, it is also suggested that a non-operative approach (antibiotherapy) can be applied in some selected patients (6, 7). Delay in diagnosis and treatment of AA may lead to miscarriage, preterm labor, and even fetal/maternal losses (8). Similarly, negative appendectomy creates fetal/maternal risks related to anesthesia and surgery (8, 9). Therefore, the management of AA in pregnant patients requires a perioperative multi-disciplinary approach between anesthesiologists, obstetrics, radiology, and general surgery physicians.

There are a limited number of studies in the literature regarding the diagnosis and treatment of AA in pregnancy. Studies showing the experience of service hospitals are quite limited due to the low frequency of these cases in Turkey and the tendency of surgeons to direct patients to tertiary hospitals. In the present study, the perioperative approach and surgical experience related to the process were investigated in this patient group in a secondary service hospital; and the effects of AA on pregnancy, baby, and mother were evaluated.

Material and Methods

The study was conducted in line with the principles of the Helsinki Declaration. Ethical approval was obtained from Clinical Research Ethics Committee of Bozok University (2017-KAEK-189_2020.11.25_05). The present study was conducted retrospectively at the Yozgat City Hospital General Surgery Service between January 2015 and November 2020. A total of 9 patients over the age of 18 who were pregnant at the time of the diagnosis of AA, underwent appendectomy, and performed pregnancy follow-up and delivery in our hospital were included in the study. In the study, the demographic data, hemogram parameters, C-reactive protein (CRP) values, diagnostic imaging reports, surgical information, histopathological reports, morphological dimensions (width, length) of the appendix, the drugs used perioperatively, and the duration of hospital stay were recorded. Gestational week, birth data, infant APGAR score, infant birth weight data were recorded. The data were accessed through the hospital's electronic registration system. For the gestational age, 0-14 weeks were regarded as the first trimester, 14-28 weeks second trimester, and 28> week was taken as the third trimester. Fetal losses with a gestational age less than 20 weeks were considered as abortion, and births before 37 weeks as preterm labor. APGAR points n the 1st and 5th minutes below 7 were considered low. Leukocyte

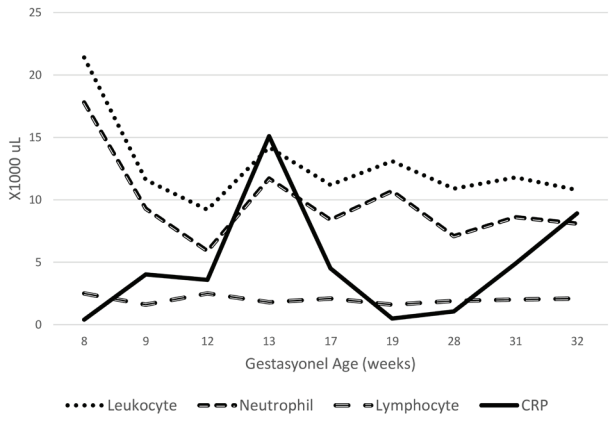
(WBC) reference range was 3.8-11.8 x10^3 uL, neutrophil count (percentage) range was 2.2-4.8x10^3 uL (43-65%), lymphocyte count (percentage) range was 1.3-2x10^3 uL (5.5-%) 20.5), thrombocyte count range was 130-400x10^3 µL, and the CRP reference range was 0-0.8 mg/dl. Neutrophil/lymphocyte ratio (NLR), thrombocyte/lymphocyte ratio (TLR), and lymphocyte/ CRP (LCR) ratio were obtained by dividing the numerical values found on the hemogram.

In abdominal USG imaging, appendix diameter greater than 7 mm with a blunt end, increased echogenicity in surrounding tissues, the presence of pericecal fluid were considered acute appendicitis. Abdominal USG failure, clinical or radiological suspicion was evaluated with MRI. In histopathological evaluations, lymphoid hyperplasia was accepted as a normal appendix, perforated appendicitis as complicated appendicitis, and other cases as simple acute appendicitis. The Clavien-Dindo classification was used as a reference in the evaluation of postoperative complications (10). Descriptive statistical analysis was performed using SPSS-22 (Statistical Package for the Social Sciences, Inc, Chicago, IL, USA) for statistical analysis. Categorical data were shown as number (N) and percentage (%), while the numerical values were shown as median (lower-upper values).

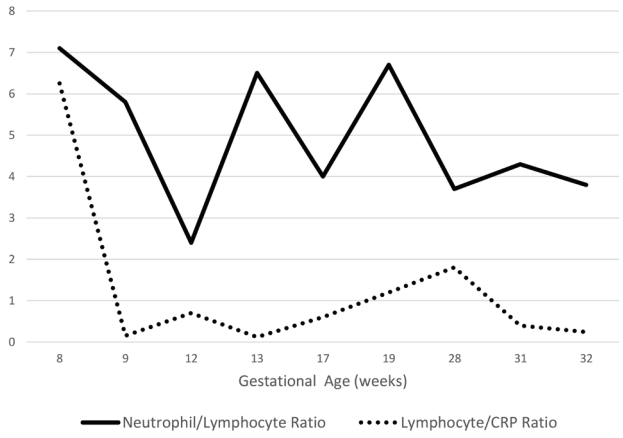
Results

A total of 14,174 live births (7904 vaginal (55.8%), 6270 cesareans (44.2%), and 1298 appendectomy operations were performed in our hospital during the study dates. Of the appendectomy operations, 499 (38.4%) were performed laparoscopically. Spinal anesthesia was adopted in 84 (6.5%) of the total patients. Of all the 1298 patients who underwent an appendectomy in our hospital, 557 (43%) were women, 211 of these 557 (37.9%) were treated laparoscopically. Spinal anesthesia was performed in 34 (6.1%) of the female patients and 7 of them were pregnant. The mean age range of the cases was 24 years (18-35), and the mean gestational fetal age was 17 weeks (8-32). Five patients, more than half of the pregnant women, were in the first trimester, two patients were in the second trimester, two patients were in the 3rd trimester. It was found that open surgery with Mc Burney incision was adopted in all patients. It was observed that no non-operative treatment was applied to any patient. The median and value range in hemogram parameters were, WBC 11.6 x10^3 uL (9.2x10^3 - 21.4x10^3 uL), neutrophil count 8.6 x10^3 uL (5.9 x10^3 uL-17.8 x10^3 uL), lymphocyte count 2 x10^3 uL (1.6 x10^3 uL) -2.5 x10^3 uL), thrombocyte count 271 x10^3 uL (169 x10^3 uL-583 x10^3 uL), CRP 4.5 (0.4-15.1), NLR 4.3 (2.4-7.1) TLR was determined to be 120.8 (84.8-306.8), and LCR to be 0.7 (0.12-6.25) (Table 1). The distribution of CRP and hemogram parameters by gestational week is shown in Graphs 1a, 1b, 1c. The median birth weight of the babies was 3100 grams (2100-3500) and very low birth weight, fetal anomaly, or fetal loss was not detected. The median delivery week was 38 (36-40). Only one patient had preterm labor at 36 weeks (Table 2). It was observed that tocolytic therapy was not given in this patient in the preoperative and postoperative periods.

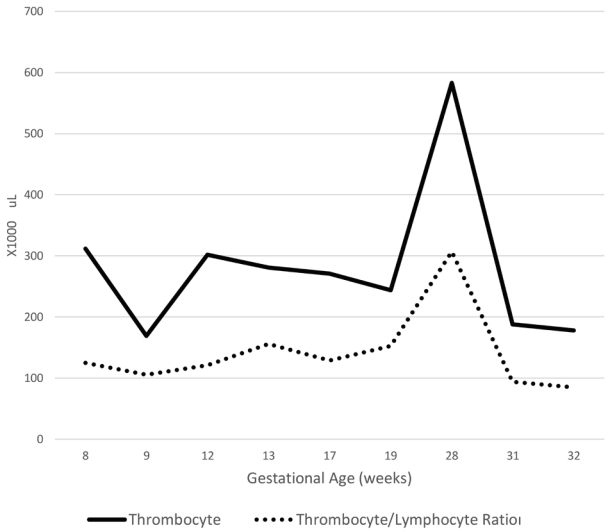
Two cases underwent MRI procedure since the appendix could not be visualized in one and due to clinical and radiological suspicions in the other. Retrocecal acute appendicitis was detected on MRI imaging of both patients. CT was not performed on



Graphic 1a:
Changes in leukocyte, neutrophil, lymphocyte, CRP according to gestational week



Graphic 1b:
Changes in neutrophil/lymphocyte ratio, lymphocyte/CRP ratio according to gestational week



any patient. In the pathological examination, normal appendix findings were detected in only one patient. The mean hospitalization period of the patients was 2 (range: 1-3) days and no postoperative complications were observed in the cases (Table 3). Penicillin, cephalosporins, and metronidazole as antibiotics, paracetamol as an analgesic and non-steroidal anti-inflammatory drug according to the week of gestation were used. Tocolytic therapy was applied to only one patient to prevent post-operative uterine contractions. Fetal heart rate was evaluated by the obstetrician in the pre-operative and post-operative periods.

Graphic 1c:
Changes in neutrophil/lymphocyte ratio, lymphocyte/CRP ratio according to gestational week

Table 1 Laboratory values according to gestational weeks

Gestational Age (weeks)	Leukocyte (uL)	Neutrophil (uL) (%)	Lymphocyte (uL) (%)	Thrombocyte (uL)	CRP (mg/dl)	NLR	TLR	LCR
8	21.4 x10^3	17.8 x10^3 (83.3)	2.5 x10^3 (11.5)	312x10^3	0.4	7.1	124.8	6.25
9	11.6 x10^3	9.3x10^3 (80.3)	1.6x10^3 (14.1)	169 x10^3	4.02	5.8	105.6	0.15
12	9.2 x10^3	5.9x10^3 (63.8)	2.5x10^3 (27.5)	302 x10^3	3.6	2.4	120.8	0.7
13	14.2 x10^3	11.7 x10^3 (82.8)	1.8 x10^3 (12.4)	281x10^3	15.1	6.5	156.1	0.12
17	11.2 x10^3	8.4 x10^3 (74.3)	2.1 x10^3 (18.5)	271x10^3	4.9	0.6	129	0.4
19	13.1 x10^3	10.7x10^3 (81.7%)	1.6x10^3 (12.2%)	244 x10^3	0.5	6.7	152.5	1.2
28	10.9 x10^3	7.1x10^3 (65.1)	1.9x10^3 (17)	583 x10^3	1.05	3.7	306.8	1.8
31	11.8 x10^3	8.6 x10^3 (72.6)	2 x10^3 (17)	188x10^3	4.5	4.3	94	0.4
32	10.8 x10^3	8.1 x10^3 (75)	2.1 x10^3 (20)	178x10^3	8.9	3.8	84.8	0.24

NLR neutrophil-lymphocyte ratio, TLR thrombocyte-lymphocyte ratio, LCR lymphocyte-CRP ratio, CRP C-reactive protein

Table 2 Obstetric data of patients

Patients	1#	2#	3#	4#	5#	6#	7#	8#	9#
Gravidity	5	1	1	3	2	3	1	1	1
Parity	2	1	1	1	2	2	1	1	1
Abortus	N/A	0	1	1	0	2	0	0	0
Labor Type	C/S	Vaginal	Vaginal	Vaginal	Vaginal	Vaginal	Vaginal	Vaginal	Vaginal
Labor Week	37	39	37	38	39	36	40	37	38
Baby weight	2800	3100	2100	3400	3500	2980	3300	2700	3160
APGAR	9-10	9-10	N/A	9-10	N/A	N/A	N/A	N/A	N/A

C/S Cesarean section, N/A Not available, APGAR Activity - Pulse - Grimace - Appearence - Respiration,

Table 3 Perioperative characteristics of the patients

Patients	Age (years)	GA (Weeks)	Surgery history	USG	MRI	Anesthesia Type	Pathological Diagnosis	Duration of Hospital Stay (days)
1#	29	32	+	Compatible with AA, 10-mm-diameter.	-	S	Compatible with AA, 10-mm-diameter.	2
2#	24	8	-	Compatible with AA, 7-mm-diameter.	-	G	AA, Length: 6 cm, Diameter: 8 mm	3
3#	28	31	-	Appendix diameter 7 mm, clinical correlation was recommended.	Retrocecal acute appendicitis, 10 mm in diameter	S	AA, Length: 10 cm, 12-mm-diameter	3
4#	35	17	-	The appendix could not be visualized.	Retrocecal acute appendicitis, 12-mm-diameter	S	Normal appendix (Lymphoid hyperplasia), Length: 7 cm, Diameter: 6 mm	1
5#	24	13	-	Compatible with AA, 7.6-mm-diameter.	-	G	AA, Length: 10 cm, Diameter: 8 mm	1
6#	24	9	-	Compatible with AA, Diameter: 14 mm	-	S	AA, Length: 8 cm, Diameter: 7mm	2
7#	19	12	-	Compatible with acute appendicitis, 8-mm-diameter	-	S	AA, Length: 7 cm Diameter: 10 mm	2
8#	18	28	-	Compatible with AA, Diameter: 9.2 mm	-	S	Perforated AA, Length: 6 cm, Diameter: 10 mm	2
9#	19	19	-	Compatible with AA, Diameter: 8.2 mm	-	S	AA, Length: 5.5 cm, Diameter 10 mm,	3

GA Gestational Age (weeks), USG Abdominal ultrasonography, MRI Magnetic resonance imaging,
AA Acute Appendicitis, (-) not present, (+) present, S Spinal, G General.

Discussion

Evaluating all the appendectomies performed in the hospital in the present study, it was seen that 0.7% of the cases were pregnant and open surgery was performed in all patients. Preterm labor (36 weeks) developed in only one of the 9 patients.

There were no specific inflammatory markers for AA. Considering the physiological changes observed during pregnancy, the proportional values of the inflammatory markers obtained from CRP and hemogram can complement each other with other auxiliary diagnostic methods and facilitate the diagnostic process. Yazar et al., in their retrospective study of pregnant women with AA, have reported 13.8 $x10^3$ uL for WBC, 1.54 $x10^3$ uL for lymphocyte, 234.4 $x10^3$ uL for thrombocyte, 1.01 mg/dl for CRP, 6.84 for NLR, and 0.13 for LCR values as the cut-off value for the diagnosis of acute appendicitis. In the present study, it was determined that, unlike WBC, CRP, and lymphocyte, NLR and PLR do not have diagnostic values alone, but when used with other markers, the accuracy rate of hematological tests will increase (11). Çınar et al. calculated 10.3 $x10^3$ uL for WBC, 7.9 $x10^3$ uL for neutrophil, 1.3 $x10^3$ uL for lymphocyte, 225 $x10^3$ uL for thrombocyte, 5.5 for NLR, 155.2 $x10^3$ uL for TLR as the cut-off values and suggested that each of these parameters had independent diagnostic significance (12). Pregnancy causes changes in hematological parameters due to its unique physiological interactions. Therefore, it may not be possible to accept the values belonging to the general population during pregnancy. In the present study, the median leukocyte was 11.6 $x10^3$ uL, neutrophil was 8.6 $x10^3$ uL, lymphocyte was 2 x $x10^3$ uL, thrombocyte was 271 x $x10^3$ uL, CRP was 4.5 mg/dl, NLR was 4.3, TLR was 120.8, and LCR was determined to be 0.7. Compared to the literature, NLR, LCR, and TLR values were low; whereas thrombocyte, CRP, lymphocyte values were high and leukocyte and neutrophil counts were similar. Examining the hemogram parameters and CRP values according to the week of gestation in the present study, as the gestational week advanced, it was observed that WBC and neutrophil count decreased, lymphocyte values remained constant, and CRP fluctuated. This situation can be explained by the hemoconcentration caused by pregnancy-related nausea and vomiting in the first trimester. In studies conducted with healthy pregnant women, it has been suggested that as the week of gestation increases, the number of CRP, leukocyte, and neutrophils increased, whereas the number of lymphocytes was variable (3, 13). Studies examining the relationship of inflammatory markers with the week of gestation in patients with AA are limited. The low number of patients in the present study made it difficult to make a healthy evaluation.

Imaging methods are an important auxiliary diagnostic tool. USG is an affordable, accessible, diagnostic tool that does not pose fetal and maternal risks. Its reliability varies according to the week of gestation, the weight of the patient, and the experience of the operator. Its sensitivity is 84%, specificity 96%, and positive and negative predictive values are 94% and 40%, respectively. In cases where abdominal USG is inconclusive or cannot be performed, the first option is MRI. Although our hospital is a secondary hospital, it has MRI facilities. Although the sensitivity of MRI varies in the range of 60-90%, specificity 92-100%, positive and negative predictive values are 92-100% and 94-100, respectively, these values decrease in the further weeks of gestational period (14, 15). AA was detected by abdominal USG in most of the patients in the present study (7/9) while MRI was used in two patients who could not be diagnosed. Acute appendicitis with retrocecal location was observed in both of these cases. It is known that the reliability of USG in retrocecal appendicitis is decreased due to colon gas. CT is rarely used in pregnant patients due to its ionizing radiation effect. An abdominopelvic CT scan can create up to an average of 50mGy radiation exposure. Exposure of the fetus to radiation above a certain threshold value may lead to congenital malformations, miscarriage, growth retardation, behavioral disorders, and mental retardation. The most sensitive period is the 1st trimester, the radiation threshold value is accepted as 100-150 mGy, this threshold value can go up to 500 mGy in the 3rd trimester (16). Therefore, CT can be applied in special cases by reducing the dose of the ionized substance, applying single-phase protocols, and considering the profit-loss ratio (16, 17).

Although laparoscopic surgery is performed safely during pregnancy, it differs from traditional laparoscopic techniques. Gestational age should be taken into account when inserting trocars, and it should be applied with an open method and under direct vision. The narrow operation area, lack of experience, and concerns about harming the fetus are the main reasons for preferring open surgery. Although laparoscopic surgery was performed in approximately 38% of women diagnosed with acute appendicitis between the study dates, especially in recent years, it was observed that open appendectomy was performed in all pregnant patients. Examining the literature, it was seen that similar results are given in small centers, in accordance with the data in the present study (9, 18,

19). Laparoscopic surgery is more commonly used in larger centers. However, it has been stated that as the comorbidity and the gestational week increased, the preference for open surgery increased in these centers (20). In comprehensive meta-analyses, it was shown that laparoscopic surgery did not increase the risk of fetal loss and preterm labor, however, decreased hospital stay and wound site infection rates (7, 21). Similarly, in the guidelines of the Society of American Gastrointestinal and Endoscopic Surgeons, it has been stated that laparoscopic appendectomy can be performed safely during all gestational weeks (22). Non-operative anti-biotherapy treatment of AA in the general population has become a new area of interest in recent years. Despite the 39% recurrence rate in 5 years, it has been suggested that an alternative treatment to surgical treatment can be used in simple non-pregnant AA patients (23). The data in the literature on nonoperative treatment in pregnant women are limited. Liu et al. treated 34 of 54 pregnant patients with AA non-operatively, and 20 surgically. The researchers have suggested that non-operative treatment is a safe and effective treatment with low recurrence rates (8.8%) in all trimesters (6). There is no study on these cases in Turkey. In the present study, surgery was applied to all cases and spinal anesthesia was the most preferred method.

It has been known that most of the drugs used in general anesthesia pass to the placenta. Some side effects found in animal experiments were not detected in human studies. However, it has been suggested that general anesthesia causes a slight increase in the risk of preterm labor and miscarriage (24). Since midazolam, propofol and some inhaler substances used in general anesthesia may have a negative effect on fetal brain development, it has been recommended that the fetal exposure should be kept at a minimum level and the surgical procedure should not exceed three hours (25). In the present study, it was seen that spinal anesthesia was preferred in 6.1% of non-pregnant patients, while 77.8% of pregnant patients. These rates were higher than those reported in the literature (9, 18, 19). This may be due to the defensive approach of anesthesiologists and surgeons.

The most important limitation of this study, which is important in terms of revealing the experience of a secondary hospital in Turkey, was the low number of cases and the fact that it was a retrospective study.

Conclusion

As a result, AA is a condition that can be difficult for general surgeons to diagnose and treat during pregnancy. One should be careful while approaching these cases, especially in diagnostic evaluations. Provided that a multidisciplinary approach was adopted in the management of cases, surgical treatment can be applied safely in public secondary hospitals.

Conflict of Interest Statement

The author has no conflicts of interest to declare.

Ethical Approval

The study was conducted in line with the principles of the Helsinki Declaration. Ethical approval was obtained from Clinical Research Ethics Committee of Bozok University (2017-KAEK-189_2020.11.25_05).

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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References

1. Zingone F, Sultan AA, Humes DJ, West J. Risk of acute appendicitis in and around pregnancy: a population-based cohort study from England. Ann Surg. 2015;261(2):332-7.
2. Franca Neto AHd, Amorim MMRd, Nóbrega BMSV. Apendicite aguda na gestação: revisão de literatura. Rev Assoc Med Bras. 2015;61(2):170-7.
3. Sanci M, Töz E, Ince O, Özcan A, Polater K, Inan AH, et al. Reference values for maternal total and differential leukocyte counts in different trimesters of pregnancy and the initial postpartum period in western Turkey. J Obstet Gynaecol. 2017;37(5):571-5.
4. Moreno CC, Mittal PK, Miller FH. Nonfetal Imaging During Pregnancy: Acute Abdomen/Pelvis. Radiol Clin North Am. 2020;58(2):363-80.
5. Masselli G, Derme M, Laghi F, Framarino-dei-Malatesta M, Gualdi G. Evaluating the acute abdomen in the pregnant patient. Radiol Clin North Am. 2015;53(6):1309-25.
6. Liu J, Ahmad M, Wu J, Tong XJ, Zeng HZ, Chan FSY, et al. Antibiotic is a safe and feasible option for uncomplicated appendicitis in pregnancy-A retrospective cohort study. Asian J Endosc Surg. 2020.
7. Lee SH, Lee JY, Choi YY, Lee JG. Laparoscopic appendectomy versus open appendectomy for suspected appendicitis during pregnancy: a systematic review and updated meta-analysis. BMC surg. 2019;19(1):41.
8. McGory ML, Zingmond DS, Tillou A, Hiatt JR, Ko CY, Cryer HM. Negative appendectomy in pregnant women is associated with a substantial risk of fetal loss. J Am Coll Surg. 2007;205(4):534-40.
9. Vujic J, Marsoner K, Lipp-Pump A, Klaritsch P, Mischinger H, Kornprat P. Non-obstetric surgery during pregnancy–an eleven-year retrospective analysis. BMC Pregnancy Childbirth. 2019;19(1):382.
10. Dindo D, Demartines N, Clavien P-A. Classification of sur-

gical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2):205.
11. Akbas A, Aydin Kasap Z, Hacim NA, Tokocin M, Altinel Y, Yigitbas H, et al. The value of inflammatory markers in diagnosing acute appendicitis in pregnant patients. Ulus Travma Acil Cerrahi Derg. 2020;26(5):769-76.
12. Çınar H, Aygün A, Derebey M, Tarım İA, Akalın Ç, Büyükakıncak S, et al. Significance of hemogram on diagnosis of acute appendicitis during pregnancy. Ulus Travma Acil Cerrahi Derg. 2018;24(5):423-8.
13. Mei Z, Li H, Serdula MK, Flores-Ayala RC, Wang L, Liu JM, et al. C-reactive protein increases with gestational age during pregnancy among Chinese women. Am J Hum Biol. 2016;28(4):574-9.
14. Patel D, Fingard J, Winters S, Low G. Clinical use of MRI for the evaluation of acute appendicitis during pregnancy. Abdom Radiol. 2017;42(7):1857-63.
15. Duke E, Kalb B, Arif-Tiwari H, Daye ZJ, Gilbertson-Dahdal D, Keim SM, et al. A systematic review and meta-analysis of diagnostic performance of MRI for evaluation of acute appendicitis. AJR Am J Roentgenol. 2016;206(3):508-17.
16. Yoon I, Slesinger TL. Radiation Exposure In Pregnancy. 2019.
17. Practice CoO. Committee opinion No. 723: guidelines for diagnostic imaging during pregnancy and lactation. Obstet Gynecol. 2017;130(4):e210.
18. Mantoglu B, Altintoprak F, Firat N, Gonullu E, Dikicier E, Akdeniz Y, et al. Reasons for Undesirable Pregnancy Outcomes among Women with Appendicitis: The Experience of a Tertiary Center. Emerg Med Int. 2020;2020:6039862
19. Şenocak R, Çelik Su, Kaymak Ş. Diagnosis, Management And Clinicopathological Features Of Acute Appendicitis In Pregnant Women And Its Impact On Fetal Outcomes. İstanbul Tıp Fakültesi Dergisi.135-40.
20. Ibiebele I, Schnitzler M, Nippita T, Ford JB. Appendicectomy during pregnancy and the risk of preterm birth: a population data linkage study. Aust N Z J Obstet Gynaecol. 2019;59(1):45-53.
21. Frountzas M, Nikolaou C, Stergios K, Kontzoglou K, Toutouzas K, Pergialiotis V. Is the laparoscopic approach a safe choice for the management of acute appendicitis in pregnant women? A meta-analysis of observational studies. Ann R Coll Surg Engl. 2019;101(4):235-48.
22. Yumi H. Guidelines for diagnosis, treatment, and use of laparoscopy for surgical problems during pregnancy. Surg Endosc. 2008;22(4):849-61.
23. Salminen P, Tuominen R, Paajanen H, Rautio T, Nordström P, Aarnio M, et al. Five-year follow-up of antibiotic therapy for uncomplicated acute appendicitis in the APPAC randomized clinical trial. JAMA. 2018;320(12):1259-65.
24. Kuczkowski KM. Nonobstetric surgery during pregnancy: what are the risks of anesthesia? Obstet Gynecol Surv. 2004;59(1):52-6.
25. Olutoye OA, Baker BW, Belfort MA. FDA Warning on Anesthesia and Brain Development: Am J Obstet Gynecol. 2018;218(1):98-102.