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Original Research

Acute Appendicitis in Pregnancy: How to Manage?

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Abstract

Objectives: Acute appendicitis during pregnancy may be associated with severe maternal and fetal complications. The clinical, laboratory and radiological parameters used in diagnosis and the effects of the surgical method and timing on the results are controversial. The present study aims to reveal the relationship between clinical approach, surgical treatment methods and complications in pregnant women with suspected acute appendicitis.

Methods: Between December 2007 and August 2019, 21 pregnant women who underwent appendectomy were included in this study. Age, gestational age, complaints at admission, leukocyte count, radiological examination results, type of surgery (conventional or laparoscopic), histopathology results, time from admission to operation, maternal and fetal complications were retrospectively evaluated.

Results: The number of patients who developed complications was six (28.6%). Three (14.3%) of these patients had preterm birth and three (14.3%) had an abortion. There was no statistically significant relationship between trimester and complication (p=0.747). Fourteen patients (66.7%) underwent laparoscopic surgery and seven patients (33.3%) underwent conventional surgery. Although the complication rate was higher in the laparoscopic group, there was no statistically significant difference (p=0.306). The fetal loss rate in the series was 14.3% and all were in the laparoscopic group. However, there was no statistically significant difference between the groups (p=0.158).

Conclusion: Pregnancy-related limiting factors may complicate the diagnosis of acute appendicitis. These patients definitely need a more skeptical assessment and additional diagnostic tools beyond the standard clinical approach. Although laparoscopic appendectomy appears to be a safe option in treatment, its relationship with a higher risk of fetal loss should be kept in mind.

Keywords: Appendicitis; appendectomy; pregnancy; complication; laparoscopy.

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Acute appendicitis during pregnancy is one of the most frequent non-gynecological and non-obstetric pathology requiring emergent intervention.[1, 2] Its incidence rate during pregnancy has been reported between 1:1000 and 1:1500.[1-3] Moreover, it is a condition that may complicate the pregnancy period. Acute appendicitis in pregnancy has a variable and non-specific clinical presentation. Pregnancy-related localization change of appendix vermiformis according to the gestational age may mask or change the symptoms and physical examination findings with a remarkable risk of delay in diagnosis.[4, 5] Besides the ordinary complications of appendicitis, additional comorbidities for mother and fetus in these patients should also be kept in mind.[1-5]

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Perforation and other forms of complicated acute appendicitis are more frequently seen in pregnant women than those in the normal population.[6, 7] While the fetal loss rate is 1.5% in uncomplicated patients, this may rise up to 36% in cases with perforation.[1, 8] Therefore, early diagnosis and treatment are quite important in terms of avoiding both maternal and fetal morbidity and mortality. The present study aims to investigate the diagnosis, treatment and outcomes of acute appendicitis in pregnant patients to show its impact on both the mother and the fetus, which may help clinicians determine a diagnostic and surgical strategy.

Methods

Data were collected from the hospital data management system and patients' archives for the records of 21 pregnant women who were operated on with the diagnosis of acute appendicitis between December 2007 and August 2019. All patients underwent a thorough workup by the gynecology and obstetrics department before and after surgery. Age, gestational age, duration of symptoms, leukocyte count, radiological workup, type of surgery, histopathologic results and comorbid diseases were recorded, as well as maternal and fetal complications. Gestational age was divided into three terms: 0-13 weeks, 14-27 weeks and 28 weeks and later. The relationship between trimester and complication development was questioned. The patients who were operated on with conventional and laparoscopic surgery were compared. Complicated cases were examined in more detail. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the participants. This study was approved by the Local Ethical Committee of Gazi University Faculty of Medicine (Date:13.01.2020-No:12).

Statistical Analysis

All the statistical analyses were performed using SPSS software, version 20 (SPSS Inc., Chicago, IL, USA). Data were expressed as mean±standard deviation and range. Relevant variables were analyzed using descriptive statistics. For comparison of the patients operated either with conventional or laparoscopic surgery, the Chi-square test was used. The significance level for all analysis was considered as 0.05.

Results

The mean age of 21 patients was 29.05 ± 3.23 years (range 21-36) and the mean gestational age was 141 ± 51.02 days (range 64-267 days). Three patients (14.3%) were operated in the first trimester; 16 patients (76.2%) at the second and two patients (9.5%) at the third. Laparoscopic surgery was performed in 14 patients (66.7%) and conventional surgery in seven patients (33.3%). On admission to the hospital, 10 patients (47.6%) had generalized abdominal pain, seven patients (33.3%) had right lower quadrant pain, three patients (14.3%) had epigastric pain and one patient (4.8%) had abdominal pain and fever. None of the patients had a comorbid disease (Table 1).

Mean leukocyte count was 13.926/mm^3 ± 4.857 (range 4.740-24.790/mm^3). Ultrasonography (US) was performed on all patients, but a positive ultrasonographic assessment was performed in only eight of 21 patients (38.1%). The mean time from admission to surgery was 18.76 ± 30.48 hours (range 3-144 hours) (Table 1).

As for the histopathologic results, 13 patients (61.9%) had acute appendicitis, three patients (14.3%) had lymphoid hyperplasia, two patients (9.5%) had a normal appendix, one patient (4.8%) had a focal perforation, one patient (4.8%) had lymphoid hyperplasia and intraluminal parasite, one patient (4.8%) had a lymphoid obliteration and fibrosis hyperplasia. No other attributable cause was identified in the two patients with a histopathologically normal appendix. One of them lost the fetus due to spontaneous abortus at the postoperative sixth hour.

Table 1. Demographic, clinical and surgical characteristics of patients

Characteristics (n=21)	Results
Age (years)	Mean: 29.05±3.23 (SD) (range 21-36)
Gestational age (days)	Mean: 141±51.02 (SD) (range 64-267)
Leukocyte (/mm^3)	Mean: 13.926±4.857 (SD) (range 4.740-24.790)
Admission-surgery gap (hours)	Mean: 18.76±30.48 (SD) (range 3-144 hours)
Main complaint, n (%)	
Generalized abdominal pain	10 (47.6)
Right lower quadrant pain	7 (33.3)
Epigastric pain	3 (14.3)
Fever	1 (4.8)
Trimester, n (%)	
First	3 (14.3)
Second	16 (76.2)
Third	2 (9.5)
Ultrasonography, n (%)	
Positive	8 (38.1)
Negative	13 (61.9)
Surgery type, n (%)	
Laparoscopy	14 (66.7)
Conventional	7 (33.3)

SD: Standard deviation.

Some type of complication developed in six patients (28.6%). Of these patients, three (14.3%) had a preterm delivery and three (14.3%) had abortus. Out of these complicated six patients, four (66.7%) were operated in the first trimester, and two (33.3%) in the second and third trimester. No statistically significant relationship was found between the trimester and complication development (p=0.747).

As for the relationship between the US reports and pathology results, of the patients who were radiologically diagnosed to have appendicitis, seven (87.5%) patients had a pathological proof of acute appendicitis, one (12.5%) had lymphoid hyperplasia and intraluminal parasite. Of 13 patients (61.9%) for whom the US was negative, histopathological examination revealed acute appendicitis-related pathologies in 11 patients (84.6%) (Table 2).

Concerning the surgical approach, the rate of complication was 35.7% in the laparoscopic group (5 patients) and 14.3% in the open surgery group (1 patient). Although the rate of complications was higher in the laparoscopic group, no statistically significant difference was found (p=0.306). The fetal loss rate in the series was 14.3%, all in the laparoscopic group. However, there was no statistically significant difference between the groups (p=0.186).

Discussion

The clinical approach to pregnant patients with suspicion of acute appendicitis is still controversial and variable. The incidence is presented as similar to or less than that of the usual population. Acute appendicitis in pregnant women is more frequently seen between the ages of 20 and 30.[4, 9, 10] The mean age in our series was 29.05 years, ranging between 21 and 36. It may occur at any trimester during pregnancy. Studies argue that it is seen the most frequently in the different trimesters.[2, 4, 7] In the present study, 76.2% of the cases were operated in the second trimester, but it is not true to generalize the dominancy of one of the three trimesters.[4]

The most important problem for pregnant patients who admitted to the emergency department is the wide spectrum of differential diagnosis. Non-specific symptoms, such as nausea, vomiting, lower abdominal or inguinal pain, which can be seen in the nature of pregnancy consist of the large part of the patients at the time of admission.[4, 5, 10, 11] The anatomical changes caused by the pregnancy play a role both in masking the clinical picture and decreasing the diagnostic sensitivity of the physical examination. The growth of uterus, by pushing the appendix, may cause a deviation in its normal axis.[2, 4, 7, 12, 13] The distance between the appendix and anterior abdominal wall grows bigger ending up with a reduction in abdominal wall sensitivity and defense.[4, 7] Thus, it becomes challenging to make the diagnosis over the symptoms and clinical picture in pregnant patients.

Table 2. The relationship between ultrasonography and pathology

Pathologhy	Ultrasonography (+) (n=8)	Ultrasonography (-) (n=13)
Abnormal pathology	8 (100)	11 (84.6)
Normal appendix	0 (0)	2 (15.4)

It has been reported that the rate of admission to the emergency department with fever is more than twice higher in non-pregnant patients.[14] In this study, only one patient had fever with accompanying abdominal pain. This patient was the one who had the longest admission-operation time gap, 144 hours. She developed perforation and a periappendicular abscess and her pregnancy ended up with preterm birth. Excessive intraoperative pelvic manipulations increased the risk of preterm birth and unnoticed appendicitis causes early maternal and fetal complications.[7] A pregnant patient who was admitted to the hospital with abdominal pain and fever without any other source of infection should be inspected for complicated appendicitis.

Besides nonspecific symptoms, the physiological leukocytosis in pregnancy also makes the laboratory findings undependable.[11, 14] Although the perforation risk rises when the leukocyte count in the pregnant with acute appendicitis reaches over 16.000/mm^3,[4] the normal leukocyte count does not eliminate the possibility of acute appendicitis. Although the mean leukocyte count was 13.926/mm^3 in our study, five patients (19%) had normal leukocyte counts. Leukocytosis was observed in 81% of the patients, while 83% in complicated patients, which was also similar to that of the general patient population. This result supports the opinion that leukocytosis is common in acute appendicitis in pregnancy but unable to detect complications alone. Other parameters, such as neutrophil count, neutrophil-to-lymphocyte or platelet-to-lymphocyte rates, seem to have more diagnostic efficiency.[11, 13] In a recent study, as a screening test, a left shift with neutrophils >70% provided a sensitivity and negative predictive value of 100%. It was suggested to consider neutrophil count and percentage in the diagnostic evaluation.[15] It is possible to interpret the routine hemogram test concerning multiple inflammatory parameters in each patient.

In a pregnant patient with suspected appendicitis, the US should be the first radiological diagnostic test.[1, 4, 16] For these patients, the sensitivity of the US varies between 20-77%.[1, 10] We performed US imaging for all patients. The number of radiologically confirmed patients in our

series was eight (38.1%) and the pathological examination for all these patients confirmed the diagnosis. For 13 patients (61.9%), the US failed to make a diagnosis of the acute appendicitis of which the pathological results had no appendicitis in only two patients (15.4%). The sensitivity of the US was 63.3% and specificity 100%. The approach suggested by the American College of Radiology (ACR) is to move on to magnetic resonance imaging (MRI) in patients whose initial US is negative, given that MRI has no fetal side effects and has 91.8% sensitivity and 97.7% specificity rates.[3, 10] The ACR suggests that MR contrast agents should not routinely be used in pregnant patients. Risk-benefit ratio should be evaluated for each patient individually. The ACR does not recommend the administration of gadolinium contrast material to pregnant women, as gadolinium-based contrast agents have been shown to cross the placental barrier.[17] In the differential diagnosis of pregnant patients with US negative, having a suspected acute abdominal pain, the use of MRI should be highly suggested.[18] The reason for the absence of MRI studies in our series is the lack of coordination in performing and interpreting MRI in emergency settings, which is one of the major defects of our center.

The standard treatment of acute appendicitis during pregnancy is surgery. Although there are studies suggesting non-operative treatment, this approach has no wide acceptance for possible catastrophic results.[19-21] Studies comparing conventional and laparoscopic surgery obtained different results. It was shown in several studies that laparoscopic surgery during pregnancy is safe for both the mother and fetus.[2, 5, 11, 21, 22] Laparoscopic appendectomy is suggested as a standard approach for pregnant patients.[22, 23] Despite this, there are also studies showing that the fetal loss rate in laparoscopy is higher.[24] In a recent meta-analysis of 21 studies, including 6276 patients, the laparoscopic approach caused a slight increase in the risk of fetal loss during delivery. However, it has not been shown to cause any other poor postoperative or obstetric outcomes.[25] There was no maternal mortality in our study. In the laparoscopic surgery group, both the rate of complications and the fetal loss rate were higher. Preterm birth rate was also the same with 14.3% in both groups. However, while there were no abortus or fetal loss in the conventional surgery group, the rate of abortus and fetal loss was 21.4% in the laparoscopic surgery. Our results were similar to studies reporting that the laparoscopic approach increases fetal loss.

As a result of the limited number of patients in our series, the complicated cases deserve to be questioned in detail (Table 3). One striking point was that the patient with perforation and a peri-appendicular abscess had admitted

Table 3. Demographic distribution of the complicated cases and their results

Age (year)	Gestational age (week/day)	Trimester	Main complaint	Leukocyte (/mm³)	US	Admission-surgery gap (hour)	Type of surgery	Pathology	Complication
31	24 w 3 d	2	CAP and fever	17.639	(-)	144	L	Acute appendicitis	Perforation, peri-appendicular abscess, preterm delivery
31	18 w 2 d	2	RLAP	13.380	(+)	4	L	Acute appendicitis	Incomplete abortus, fetal loss on the 6th day
31	32 w 6 d	3	RLAP	24.790	(+)	22	L	Acute appendicitis	Preterm delivery, urgent caesarean at 11th hour
30	9 w 3d	1	RLAP	16.960	(-)	18	L	Normal appendix	Spontaneous abortus, fetal loss at 6th hour
21	18 w	2	CAP	10.950	(-)	9	L	Lymphoid hyperplasia	Chorioamnionitis induced abortion, fetal loss at 5th day
26	26 w	2	CAP	6.150	(-)	5	O	Focal perforation	Perforation, peritonitis, preterm delivery

US: Ultrasonography; CAP: Common abdominal pain; RLAP: Right lower abdominal pain; L: Laparoscopy; O: Open.

to the emergency department 144 hours before surgical consultation demand. She was operated on within an extra eight hours after consultation. For other patients, the time gap between admission and surgery was between 4-22 hours. The proposed timing for appendectomy in the general population is between 24 and 36 hours from the onset of symptoms or between 10 and 24 hours after accepting the patient.[6, 26] It was reported that appendectomy performed in the first 24 hours had no increased risk of perforation or other side effects.[27] Surprisingly, in our series, there was also a case that was operated five hours after admission to the hospital but still having perforation. This suggests that the only reason for the higher incidence of complicated appendicitis during pregnancy is not the delay in diagnosis or treatment. Some pathophysiological changes caused by pregnancy also contribute to this. Pregnancy puts the woman in a state of relative immune suppression that alters the normal inflammatory response.[7]

The main limitation of this study is the number of patients. Although most of the studies on this subject contain a limited number of patients, it is clear that studies with more patients may be more valuable. It is also a limitation in this study that only the number of leukocytes was examined concerning laboratory parameters. It may be useful to evaluate the sensitivity of acute phase reactants and other inflammatory parameters in diagnosis and complications. Another disadvantage due to this retrospective study is that the factors affecting the choice of the surgical method are unknown. The absence of MRI in this series is an important limitation.

Conclusion

In conclusion, that the deficiencies in the diagnosis and treatment for pregnant patients with a suspicion of acute appendicitis will result in severe complications and fetal loss should force surgeons to develop an efficient diagnosis and treatment strategy for this particular group of patients. An addition of MRI for US negative patients on the agenda will probably provide benefits. Although the obvious advantages of laparoscopic and conventional methods cannot be demonstrated, the relationship between laparoscopy and increased risk of fetal loss should be considered.

Disclosures

Ethics Committee Approval: This study was approved by The Local Ethical Committee of Gazi University Faculty of Medicine (Number: 13.01.2020/12).

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Conflict of Interest: None declared.

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