Vilnius University Press

Contents lists available at Vilnius University Press

Lietuvos chirurgija
2022, vol. 21(2), pp. 109–115

ISSN 1392–0995 eISSN 1648–9942
DOI: https://doi.org/10.15388/LietChirur.2022.21.62

Does Acute Appendicitis in Pregnancy a Clinical Challenge in Surgery Practice? Our Experience

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Abstract. *Objective.* This study was designed to compare the diagnosis, treatment, and results of acute appendicitis in pregnant and non-pregnant women. *Material and Methods.* Women between the ages of 18 and 40 who were operated for acute appendicitis between 2015 and 2020 were included in the study. *Results.* There were 27 (3.8%) patients in Group Pregnant, and 679 (96.2%) patients in Group non-Pregnant. The mean WBC values in Group P and Group non-P was 16.53±2.91 and 13.99±4.31 (x103), and there was a significant difference between the groups.Mean pain symptom duration time was 3.40±1.90 in Group P and 1.91±1.34 day in Group non-P, while it was significantly longer in Group P . When the preoperative USG reports were evaluated, no significant difference was found between the groups.The diagnosis was made by MRI in 2 (7.4%) pregnant patients who non-visualized according to the USG report. In Group P, 10 patients were laparoscopic, 17 patients open; In group non-P, 153 patients laparoscopic and 526 patients were operated using open surgery technique. While the mean operation time did not differ significantly between the groups. Length of hospital stay was significantly higher in Group P with 3.48±4.26 days to 1.95±1.45 days. *Conclusion.* Diagnosis and treatment of acute appendicitis during pregnancy may be difficult, but with advanced radiological examinations and experienced surgeons, these difficulties can be easily overcome.

Keywords: Acute appendicitis, appendectomy, pregnant women.

Introduction

Acute appendicitis (AA) is the most common non-obstetric surgery during pregnancy, with an incidence of 1 in 1 400 to 1 500 births similar to the non-pregnant population [1, 2]. It should be kept in mind that symptoms such as nausea, vomiting and nonspsific pain can be seen during pregnancy and this may be mis-

Received: 2022/02/237. **Accepted:** 2022 04 05.

leading in the history and physical examination, also physiological leukocytosis of pregnancy, enlargement of the uterus and anatomical displacement of the appendix can decrease the accuracy rates of complementary diagnostic tools such as laboratory and ultrasonographic evaluation [3, 4]. Therefore diagnosis of AA is complex due to physiological and anatomical changes that occur during pregnancy and can lead to delayed or misdiagnosis. Negative appendectomy with misdiagnosis increases the risk of preterm labor, while perforation secondary to delay in treatment increases the rates of premature birth and fetal loss [2]. Despite the tendency to diagnose AA late in pregnancy, negative appendectomy rates of up to 23% have been reported [5]. At the same time higher perforation rates have been reported in pregnant women [6]. The treatment of acute appendicitis is appendectomy. It is reported that laparoscopic appendectomy is as safe as open appendectomy under appropriate conditions [7]. In any case, rapid diagnosis and treatment of AA patients is important to avoid negative maternal and neonatal consequences during pregnancy [4, 8].

The aim of this study is to compare the diagnosis, management and outcomes of AA with age-matched nonpregnant women.

Materials and Methods

A comparative retrospective study was designed in a tertiary training and research hospital. The study was carried out in accordance with the laws and guidelines in the Helsinki Declaration, after the approval of the local ethics committee. Informed consent was obtained from all patients included in the study. Patient data were obtained by scanning the hospital electronic record system. Pregnant women over 18 years of age who were operated with the diagnosis of acute appendicitis between 2015–2020 were included in the study (Group P), and non-pregnant women under 40 years of age (Group non-P) were included in the study as a control group to be agematched. Patients <18 and >40 years of age and patients who underwent appendectomy during intraabdominal surgery for any reason were excluded from the study.

For diagnosis, history, physical examination wbc and ultrasonography (USG) was performed as a and imaging method. USG results was evaluated as normal, not visualized, appendicitis, perforated appendicitis, and suspicious findings. The pregnant patients who failed to be diagnosed with USG and clinical findings were diagnosed by magnetic resonance imaging (MRI). Prior to surgery, pregnant patients were evaluated by an obstetrician to rule out the presence of other pregnancy-related complications. Obstetric ultrasonography was performed on pregnant patients to determine the viability of the fetus. Then, USG was repeated after the operation and before the patient was discharged. Preoperative data were determined as: age, white blood cell count (WBC), American Society of Anesthesiologists (ASA) scores, duration of syptoms (pain) and USG findings. Operative data as: surgical technique and operation time. Length of hospital stay, postoperative complications and pathology results were also recorded. Pathology results were categorized as: negative appendectomy; with no pathological findings, appendicitis; inflammation of the appendix, complicated appendicitis; perforated appendicitis and appendicular abscess, including gangrenous appendicitis, carcinoma and mucocele. Then the groups were compared in terms of variables.

Statistical Method

Frequency and percentage values were given for categorical variables, median, mean and standard deviation values were given for continuous variables. The normality of continuous variables was checked with the Shapiro-Wilk test. Mann Whitney U test was used to compare continuous variables that are not normally distributed. Chi-Square test was used for comparison of categorical variables. All analyzes were performed with the Social Sciences Statistics Package for Windows 22.0 (SPSS Inc., Chicago, Illinois, USA) and results with $p < 0.05$ were considered significant.

Results

A total of 706 patients were included in the study. There were 27 (3.8%) patients in Group P, and 679 (96.2%) patients in Group non-P. The median age was 28.0 (range: 18–40) in Group P and 27 (range 21–40) (years) in Group non-P. There was no significant difference between the groups in terms of age (p = 0.629). The mean WBC values in Group P and Group non-P was 16.53±2.91 and 13.99±4.31 (x103), and there was a significant difference between the groups (p < 0.001). Mean pain symptom duration time was 3.40±1.90 in Group P and 1.91±1.34 (days) in Group non-P, while it was significantly longer in Group P (p < 0.001). When the preoperative USG reports were evaluated, no significant difference was found between the groups (p = 0.062) (Table 1). The diagnosis was made by MRI in 2 (7.4%) pregnant patients who non-visualized according to the USG report.

Table 1. Demographic and diagnostic variables

	Group P (n = 27/3.8%)	**Group non–P (n = 679/96.2%)**	***P* value**
Age (years)	28.0 (18–40)	27.0 (21–40)	0.629
WBC (x10^3)	16.53±2.91	13.99±4.31	**<0.001***
Symptom (pain) duration (days)	3.40±1.90	1.91±1.34	**<0.001***
ASA scores			
1	604 (89.0%)	26 (96.3%)	0.346**
2	75 (11.0%)	1 (3.7%)	
USG findings			0.062**
Normal	0 (0%)	101 (14.9%)	
Non-visualized	2 (7.4%)	49 (7.2%)	
Appendicitis	25 (92.6%)	462 (68.0%)	
Perforated appendicitis	0 (0%)	14 (2.1%)	
Suspicious	0 (0%)	53 (7.8%)	

Continuous variables are expressed as median (min-max) and mean±SD (standart deviation); categorical variables are expressed as (n/%).
* Mann Whitney U test; ** Chi-square test was used for statistical analysis; p < 0.005 was considered significant.

In Group P, 10 (37.0%) patients were laparoscopic, 17 (63.0%) open. In group non-P, 153 (22.5%) laparoscopic and 526 (77.5%) patients were operated using open surgery technique. There was no significant difference between the groups in terms of surgical technique (p = 0.101). While the mean operation time did not differ significantly between the groups (p = 0.573). It was 48.62±15.12 in Group P and 45.80±11.86 (minutes) in Group non-P (Table 2).

Length of hospital stay was significantly higher in Group P with 3.48±4.26 days to 1.95±1.45 days (p = 0.002). When postoperative pathology results and complications were evaluated, no significant difference was found between the groups (p = 0.130, p = 0.066) (Table 3). Maternal and fetal death did not occur during the perioperative period.

Table 2. Operative characteristics of the groups

	Group P (n = 27/3.8%)	Group non–P (n = 679/96.2%)	*P* value
Surgical technique			
Laparoscopic	10 (37.0%)	153 (22.5%)	0.101**
Open	17 (63.0%)	526 (77.5%)	
Conversion to open	2 (20.0%)	10 (6.5%)	0.161**
Operation time (minutes)	48.62±15.12	45.80±11.86	0.573*

Continuous variables are expressed as mean±SD (standart deviation); categorical variables are expressed as (n/%).
* Mann Whitney U test; ** Chi-square test was used for statistical analysis; p < 0.005 was considered significant.

Table 3. Postoperative outcomes of groups

	Group P (n = 27/3.8%)	**Group non–P (n = 679/96.2%)**	***P* value**
Length of hospital stay (day)	3.48±4.26	1.95±1.45	0.002*
Pathology			
Negative appendectomy	1 (3.7%)	32 (4.7%)	0.130**
Appendicitis	22 (81.5%)	599 (88.2%)	
Complicated appendicitis	3 (11.1%)	43 (6.3%)	
Carcinoma	1 (3.7%)	4 (0.6%)	
Mucocele	0 (0%)	1 (0.6%)	
Complications			
No	23 (85.2%)	626 (92.2%)	0.066**
Wound infection	2 (7.4%)	35 (5.2%)	
Intra-abdominal abscess	0 (0%)	5 (0.7%)	
Ileus	2 (7.4%)	13 (1.9%)	

Continuous variables are expressed as mean±SD (standart deviation); categorical variables are expressed as (n/%).
* Mann Whitney U test; ** Chi-square test was used for statistical analysis; p < 0.005 was considered significant.

Discussion

Correct diagnosis of AA during pregnancy is challenging. Associated physiological and anatomical changes may prevent the diagnosis of appendicitis in pregnancy [9]. Symptoms such as nausea, vomiting and loss of appetite, which are common in both cases of AA diagnosis during pregnancy, the typical right lower quadrant pain in appendicitis varies due to the upward and lateral displacement of the appendix due to uterine enlargement during pregnancy, and leukocytosis, which is an important finding of AA, may cause delays in diagnosis.

Pregnancy in healthy women is associated with leukocytosis, this predominantly related to the increasing number of neutrophils [10]. Therefore, inflammatory markers have lower diagnostic accuracy in pregnant women. L. Hiersch et al. showed that there was no significant difference in WBC counts in AA in pregnant and non-pregnant patients. In our study, WBC values were found to be significantly higher in the pregnant group. This can already be explained by the increased WBC numbers triggered by pregnancy leukocytosis and AA-related inflammation.

In most pregnant women, pain in the lower quadrants can occur regardless of the stage of pregnancy. Pregnant women are less likely to give a classic presentation in AA, although the most common symptom is pain in the right lower quadrant [11]. At the same time, the appendix moves upwards by a few centimeters in position with the increase in uterine volume in the third trimester, and pain can be seen in the flank area or in the right upper quadrant [12]. Although the sensitivity of the pain symptom is less pronounced during pregnancy, still the most common finding in the diagnosis of AA is pain. In our study, the duration of pain was significantly longer in the pregnant group. This reflects the fact that pregnant patients have a longer symptom duration in AA due to the ambiguous presentation of abdominal pain.

The data indicate that the use of preoperative imaging has increased due to the increasing rates of negative appendectomy, which improves the diagnostic accuracy of clinicians. The American College of Radiologists (ACR) has adopted abdominal USG as the first preferred imaging for pregnant women in the face of any suspected AA [13]. USG will also assist in determining gestational age and fetal viability, in eliminating an associated adnexal or obstetric pathology. In our study, USG was used successfully as the first diagnostic method. When clinical examination and USG are inconclusive, MRI is an excellent method of excluding acute appendicitis in pregnant women [5, 14, 15]. Similarly, the diagnosis was made by MRI in two patients who could not be diagnosed by USG in our study.

Surgical appendectomy is the gold standard treatment for acute appendicitis in pregnant women. An aggressive surgical approach is accepted in pregnant women to prevent delayed diagnosis and the associated increased risk of perforation and adverse pregnancy outcomes [5]. There are controversial results in the literature regarding the surgical technique. C. A. Walsh et al. [16] was reported that laparoscopic appendectomy in pregnancy is associated with increased incidence of preterm labor and fetal loss. A. Westerband et al. [17] concluded since increased intra-abdominal pressure during pneumoperitoneum in pregnant women may cause a decrease in venous return and this may result in a simultaneous decrease in cardiac output, therefore laparoscopy is not safe. J. D. Amos et al. [18] and M. L. McGory et al. [5] reported that the rate of fetal loss is higher in laparoscopic appendectomy compared to open technique. Conversely, M. B. Reedy et al. [19] was reported that laparoscopic appendectomy during pregnancy caused a decrease in hospital stay, cost, fetal loss and post-operative complication rates compared to open surgery. U. Guller et al. [20] showed a significant decrease in postoperative morbidity, S. Lyass et al. [7] laparoscopic appendectomy does not cause any complications on mother and fetus. Cheng at al. [21] and B. Kirshtein et al. [22] emphasized that laparoscopic appendectomy can be performed successfully in all trimesters with low complication rates. Ultimately, the choice of treatment approach should be considered based on skill, surgeon's experience in laparoscopy, and the size of the gravid uterus. Although not statistically significant, the high rate of open surgery in our study reflects the uncertainty in terms of the preferred approach to pregnancy.

Considering the difficulties in the clinical diagnosis of appendicitis and the significant risk of fetal death in perforated appendicitis; higher rates of negative laparotomy (from 20% to 35%) compared to non-pregnant women are acceptable in pregnant women [5, 23]. M. L. McGory et al. [5] reported that negative appendectomy was more common in pregnant women compared to nonpregnant women (23% versus 18%), but in our study, no significant difference was found with 3.7% vs 4.7%.

Overall morbidity rates associated with appendicitis are higher in pregnant women [2, 24]. Similarly, the incidence of perforation is believed to be higher in those who are pregnant than those who are not [24]. On the contrary, there are also publications arguing that complicated appendicitis is not different in pregnant and non-pregnant women [5, 25]. In recent years, a decrease in perforation rates in AA has been observed in pregnant patients, this decrease can be accepted as a result of more aggressive surgical treatment to minimize maternal and fetal complications. However, high negative rates should also be accepted. Our study found much less negative appendectomy rate than the literature. In our study, no significant difference was found

between pregnant and non-pregnant patients in terms of complicated appendicitis. This contrasts with studies reporting higher rates of complicated appendicitis in pregnant women. However, according to our results, the natural course of acute appendicitis was not different from non-pregnant women of reproductive age and pregnant women. Fetal loss after appendectomy has been previously reported between 3% and 15%. In addition, the rate of fetal loss has been reported to be higher (20% to 37%), especially in the first trimester of pregnancy and in patients with complicated appendicitis [26]. No maternal or fetal loss was observed in our study. This may be attributed to the small number of patients.

Contrary to the studies reporting that the operation time was faster in the pregnant group [10], no significant difference was found in our study in terms of operation time in pregnant and non-pregnant AA patients.

There are studies reporting that the length of hospital stay is not different between pregnant women and non-pregnant women [10], on the contrary, some studies report that the duration of hospitalization is more than 3 days in pregnant women compared to non-pregnant women [2]. Not surprisingly, the length of hospital stay in pregnant women was statistically longer compared to non-pregnant women in our study. This may be related with obstetric evaluation of pregnant women and prolonged hospital stay due to additional medical treatments.

Data from a single center and the limited number of patients can be considered among the limitations of our study. Information about the patients was also limited as it was a retrospective study. Since we did not know which trimester the pregnant women were in, we could not evaluate the clinical presentation, management and results for different trimesters separately. Perhaps another limitation is that different radiologists evaluate patients, even if they are all experienced and different pathologists to examine samples.

Conclusion

Diagnosis and treatment of acute appendicitis during pregnancy may be difficult, but with advanced radiological examinations and experienced surgeons, these difficulties can be easily overcome.

Conflict of Interest. Authors did not declare any.
Funding. The authors received no specific funding for this work.
Ethical approvel number: KAEK/2021.01.234. Ethical committee of University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, General Surgery, Istanbul, Turkey.
Authors Contribution. Hakan Bolukbasi, Serhan Yilmaz, Engin Okan Yıldırım and Aziz Ocakoğlu are responsible for the design of manuscript. Hakan Bolukbasi, Aziz Ocakoğlu and Engin Okan Yıldırım collected the data, Serhan Yilmaz analyzed the data. All the authors discuss the results and writing-review and editing the manuscript. Approval of final manuscript: Hakan Bolukbasi, Serhan Yilmaz, Engin Okan Yıldırım, Aziz Ocakoğlu.

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