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RESEARCH ARTICLE

The Clinical Course of Acute Appendicitis During Pregnancy: Comparison of Reproductive Age Patients and Pregnant Patients

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ABSTRACT

Aim: The differential diagnosis of acute abdominal pain in women of reproductive age is challenging. Acute appendicitis is the most common cause of acute abdomen during pregnancy. This study aimed to compare pregnant women with nonpregnant women of reproductive age in terms of diagnostic approach, clinical management, and surgical outcomes in acute appendicitis and to identify any differences occurring in pregnant patients.

Method: Female patients aged between 18-45 years, who underwent appendectomy between January 2015 and December 2018 were included in this retrospective study. Pregnant and non-pregnant patients were compared in terms of clinical presentation, management, and outcomes.

Results: A total of 277 patients (28 pregnant and 249 non-pregnant) were included. In terms of diagnostic imaging, ultrasound was used in all pregnant patients, and 57.1% also underwent magnetic resonance imaging. In the non-pregnant group, computed tomography (CT) was used in 87.9%. There was a higher negative appendectomy rate in the pregnant group (21.4 vs 8.8%; p=0.038). Laparoscopic surgery was performed significantly more often in the non-pregnant group (21.4 vs 59.8%; p=0.001). Duration of diagnosis and length of stay was longer in the pregnant group. Both groups had similar rates of complicated appendicitis (7.1 vs 10.8%; p=0.416) and overall postoperative complications (14.2 vs 8.8%; p=0.316).

Conclusion: The use of CT in the diagnosis of acute appendicitis was common in women of reproductive age. In pregnant women, negative appendectomy rates were higher. Clinical management and surgical outcomes were similar in pregnant women and non-pregnant women of reproductive age.

Keywords: Acute appendicitis, pregnancy, surgical outcomes

Introduction

Acute appendicitis is the leading abdominal surgical emergency in the world.[1] The diagnosis can usually be made with clinical and laboratory findings.[2] However, a diagnosis may be challenging in women of reproductive age due to possible additional intra-abdominal pathologies.[3,4] In women of reproductive age, diagnosis based on history, clinical findings, and laboratory results are often difficult. Reliable clinical features may be absent in up to 70% of patients with suspected appendicitis.[5] Over the past decades, computed tomography (CT) has been increasingly used for the assessment of patients with possible appendicitis. CT can reduce both unnecessary surgery and delay of surgery.[6] Today, especially in adult female patients, diagnostic difficulties are largely eliminated with routine use of CT.[7,8]

Another subgroup that creates diagnostic difficulties for the clinician is pregnant patients. During pregnancy, acute appendicitis is the most common non-obstetric pathology that requires surgical intervention.[9] The diagnosis is more challenging due to anatomical and physiological changes during pregnancy.[10] It is known that both delayed cases and unnecessary operations increase maternal and fetal morbidity.[11] Therefore, it is important to make an accurate diagnosis in pregnant women. Traditional teaching states that there is an increased risk of complications in pregnant patients with acute appendicitis.[12,13] Recent studies indicate

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similar clinical presentation and outcomes in pregnant patients with acute appendicitis[14,15].

This study aimed to compare pregnant patients with non-pregnant, reproductive age patients to reveal whether the clinical course of appendicitis is affected by pregnancy.

Materials and Methods

This was a retrospective analysis of a tertiary referral university hospital database. The study protocol was approved by the Ege University Faculty of Medicine Local Ethics Committee (approval number: 20-4.1T/35). This study was conducted in accordance with the ethical standards of Helsinki Declaration. All female patients aged between 18-45 years, who underwent appendectomy for acute appendicitis between January 2015 and December 2018 were included in the study. Patients, all of whom were of reproductive age, were divided into two groups; pregnant and non-pregnant. The two groups were compared in terms of preoperative, operative, and postoperative clinical results.

Emergency department medical records, radiological data, surgical operation reports, follow-up records, and pathology reports of the patients were evaluated retrospectively. Included parameters were: fever; leukocyte count; C-reactive protein (CRP) level; imaging method used which included ultrasound [USG], CT, and/or magnetic resonance imaging (MRI); preoperative hospital interval; pregnancy gestation week; operation type (open/laparoscopic); perforation; duration of hospitalization complications; re-attendance at hospital within 30 days; fetal loss or preterm birth; and histopathological results. Hospital admission time was defined as the time from onset of abdominal pain to admission to the hospital. Preoperative hospital interval was defined as the time from hospital admission to surgery. Before surgery, all pregnant patients were evaluated by a gynecologist and obstetrician for confirmation of fetal well-being and gestational age. Fetal USG was performed on all pregnant patients before they were discharged from the hospital, and postoperative fetal well-being was checked. Complications were classified according to Clavien-Dindo classification. Negative appendectomy was defined as no signs of acute or chronic inflammation, no tumor or infection on histopathological examination.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, N.Y., USA). Continuous variables are presented as mean ± standard deviation and data were compared using an unpaired t-test. Categorical variables are expressed as numbers and percentages and analyzed for comparisons using a chi-square test. For all hypothesis tests, $p \leq 0.050$ was considered statistically significant.

Results

A total of 277 patients, 28 (10.1%) in the pregnant group and 249 (89.9%) in the non-pregnant group, were included in the study. The mean age was 29.2±7.4 years. Table 1 summarizes the information about the demographics, clinical data, laboratory data, and imaging differences between the groups.

At time of diagnosis, 5 (18%) women in the pregnant group were in the first trimester, 18 (64%) were in the second trimester and 5 (18%) were in the third trimester. There were no significant difference between the groups in terms of hospital admission time (p=0.185), total leukocyte count (p=0.343), lymphocyte count (p=0.310), or body temperature (p=0.748). CRP values were higher in non-pregnant patients (p=0.005). When the physical examination

Table 1. Comparison of pregnant women and non-pregnant women of reproductive age

	Pregnant group (n=28)	Non-pregnant group (n=249)	p
Age (year)	28.3±5.7	29.3±7.6	0.390
Body temperature (^{0}C)	36.6±0.4	36.8±2.2	0.748
Leukocyte (10^3/μL)	14.6±4.0	13.9±4.0	0.343
Neutrophil (%)	80.2%	77.2%	0.237
C-reactive protein (mg/dL)	2.1±4.0	4.7±6.9	**0.005**
Hospital admission time (days)	1.6±0.9	2.1±1.8	0.185
Pre-op hospital interval (hours)	14.0±8.4	7.2±4.3	0,001
Diagnostic US	28 (100%)	173 (69.4%)	-
Diagnostic CT	0	219 (87.9%)	-
Diagnostic MRI	16 (57.1%)	0	-
Laparoscopic surgery	6 (21.4%)	149 (59.8%)	**<0.001**
Complicated appendicitis	2 (7.1%)	27 (10.8%)	0.416
Thirty-day readmission	3 (11%)	17 (7%)	0.328
Negative appendectomy	6 (21.4%)	22 (8.8%)	**0.038**
Overall complication	4 (14.2%)	22(8.8%)	0.316
Length of hospital stay (days)	2.9	2.0	**0.001**

US: Ultrasonography, CT: Computed tomography, MRI: Magnetic resonance imaging, normal C-reactive protein value: <0.5 mg/dL

findings were evaluated, in the pregnant appendicitis group isolated abdominal tenderness was found in 15 (53.5%) patients and tenderness and rebound in 13 (46.4%) patients. In the control group, isolated tenderness was found in 96 (38.5%), tenderness and rebound in 136 (54.6%), and tenderness and defence in 17 (6.8%) patients.

In terms of cross-sectional imaging methods, no diagnostic CT was used in the pregnant group, while diagnostic MRI was used in 16 (57.1%) pregnant patients. In the control group, the main imaging method was CT and was used in 219 patients (87.9%). Comparison of CT and MRI findings with histopathological results can be seen in Table 2, 3. When histopathalogical results were evaluated, the negative appendectomy rate was significantly higher in the pregnant group compared to the control group (21.4% vs 8.8%, respectively; p=0.038).

Laparoscopic surgery was performed at a significantly higher rate in the non-pregnant group compared to the pregnant group (59.8% vs 21.4%, respectively; p=0.001). Complicated appendicitis (perforation or abscess) rates were similar (7.1 and 8.8%). There were no significant differences between the pregnant and non-pregnant groups in terms of complications (p=0.316) and thirty-day readmission rates (p=0.328) (Table 4). Length of stay was longer in pregnant patients (p=0.001). Preterm labor occurred only in one pregnant patient at the 29th week of pregnancy. No fetal losses occurred in association with acute appendicitis.

Table 2. CT and histopathological findings of non-pregnant women of reproductive age

CT findings	Histopathological findings	n
Consistent with acute appendicitis (n=200)	Acute appendicitis	182
	Appendix vermiformis	14
	Other appendiceal pathologies	5
Suspicious for acute appendicitis (n=12)	Acute appendicitis	5
	Appendix vermiformis	6
	Other appendiceal pathologies	1
Normal appendix (n=2)	Acute appendicitis	2
	Appendix vermiformis	0
	Other appendiceal pathologies	0
Non diagnostic (n=1)	Acute appendicitis	1
	Appendix vermiformis	0
	Other appendiceal pathologies	0
CT was not taken (n=34)	Acute appendicitis	32
	Appendix vermiformis	2
	Other appendiceal pathologies	0

CT: Computed tomography

Table 3. MRI and histopathological findings of pregnant women

MRI findings	Histopathological findings	n
Consistent with acute appendicitis (n=9)	Acute appendicitis	6
	Appendix vermiformis	3
Suspicious for acute appendicitis (n=2)	Acute appendicitis	1
	Appendix vermiformis	1
Normal appendix (n=1)	Acute appendicitis	0
	Appendix vermiformis	1
Non diagnostic (n=4)	Acute appendicitis	3
	Appendix vermiformis	1
MRI was not taken (n=12)	Acute appendicitis	12
	Appendix vermiformis	0

MRI: Magnetic resonance imaging

Table 4. Clavien-Dindo classification grades of complications

Clavien-Dindo grade	Pregnant group (n=28)	Non-pregnant group (n=249)	p
I	4	19	
II	0	1	
III	0	2	
IV	0	0	
V	0	0	
Overall complication	4 (14.2%)	22 (8.8%)	0.316

Discussion

The diagnosis of acute abdominal pain has distinctive difficulties in women of reproductive age. Gynecological pathologies may have clinical findings similar to acute appendicitis. Therefore, a diagnostic approach to acute abdominal pain is a challenging process, especially in women of reproductive age. According to accepted knowledge, pregnant women are thought to be less likely to have a classical clinic course of appendicitis than non-pregnant women[10,13]. Recently, increased use of cross-sectional diagnostic imaging modalities and improvement in minimally invasive surgical techniques have called this belief into question. In this study, the selection of the imaging method used was the foremost difference between groups. CT was used for diagnostic purposes in 87.9% of non-pregnant patients, and the negative appendectomy rate was found to be 8.8% in these patients. In comparison, the rate of negative appendectomy was higher in pregnant women in which USG was used as the primary imaging modality,

with a rate of 21.4%. Negative appendectomy rates have decreased in recent decades, which is likely attributable to the increased use of CT[16]. Today, CT has become the preferred method in the imaging of suspected appendicitis in adults[7]. Women are more than twice as likely as men to have a nontherapeutic appendectomy for suspected acute appendicitis. Liberal use of CT scan dramatically decreases the negative appendectomy rate, especially in adult female patients[17].

The recommendation of the American College of Radiology is that ultrasonography should be the first-line imaging method in diagnosis. However, the use of MRI has increased in pregnant women due to technical difficulties in localizing the appendix and compressing the appendix sufficiently. It is important to make an accurate diagnosis before surgery to eliminate unnecessary surgeries and potentially negative fetal effects[11]. In this study, USG was used in all pregnant women, and half of the pregnant women also underwent MRI. Despite this, the negative appendectomy rate was high in the pregnant group. Although this rate was compatible with many previous studies, it was significantly higher than the control group where CT was routinely used[6,15,18]. Since late diagnosis in pregnant women may increase fetal morbidity, the decision for surgical intervention is made easier. Therefore, higher negative appendectomy rates are expected in pregnant women[14].

A delay in diagnosis of acute appendicitis has been associated with higher complications and fetal mortality rate[19]. Therefore, accurate and fast diagnosis is crucial during pregnancy[15]. In this study, the hospital interval was longer in the pregnant group. Although it remained within acceptable limits, the difference between the means of "time from admission to the operation" was about seven hours[20]. In previous studies, there were conflicting results in terms of hospitalization time and hospital intervals in pregnant patients[14,15,21]. A few factors may cause long hospital waiting time in pregnant patients. Firstly, all pregnant patients were evaluated by the gynecologist in the preoperative period. Another factor was the delay between USG and any subsequent MRI in those who are not diagnosed with initial USG. Both these procedures may cause long preoperative waiting time in pregnant patients.

Pregnancy is characterized by low-grade systemic inflammation and therefore the use of leukocytosis to aid the diagnosis of acute appendicitis is of less utility[22]. Leukocyte counts increase from the first to the third trimester and the increase is mainly due to neutrophilia[23]. In the present study, at the time of presentation, many parameters, including leukocyte count, lymphocyte count and body temperature were similar, whereas CRP values were higher in the non-pregnant group. Inflammatory markers such as CRP and complete blood cell count (CBC) parameters play an essential role in the diagnosis of acute appendicitis[24]. We found that CBC parameters were similar between groups and these parameters had a diagnostic value. The difference in CRP levels between the groups could be explained by the low rate of negative appendectomy in non-pregnant patients.

In this study, the use of laparoscopic surgery was rare in pregnant patients. Laparoscopy may be thought to be contraindicated in pregnancy. However, it has been shown repeatedly that the maternal and fetal results following laparoscopy during pregnancy are acceptable. In general, laparoscopy is the first choice for pregnant women in the first and second trimesters, while open surgery is preferred in the third trimester due to the size of the uterus and technical difficulties[9,25,26]. In our study, all laparoscopic procedures were performed in the second trimester. The surgeon's experience, gestational condition, the patient's structure, and the patient's desire are factors that influence the surgeon's decision to perform laparoscopic or open surgery[26].

In this cohort, perioperative and postopertive outcomes were similar between groups. There was no difference between groups in terms of perforated or complicated appendicitis. It is well known that complicated appendicitis increase maternal and fetal morbidity[13]. The complicated appendicitis rate was similar in our study. Probably as a result of this, no difference in morbidity was detected between groups. Pregnancy alone does not significantly increase the risk of major surgical morbidity[21,27]. Length of stay was longer in pregnant patients. A reason for having a longer length of stay in the pregnant group could be a result of higher open surgery rates, as well as postoperative obstetric assessment.

Study Limitations

The present study has certain limitations. This was a single-institution experience with retrospective nature and small size. Our study comprised only those who had undergone surgery with suspicion of acute appendicitis. Despite these limitations, an evaluation was made on objective criteria by using the data of a well-documented electronic database.

Conclusion

In pregnant women with acute appendicitis the most obvious difference is limited use of cross-sectional imaging methods and pregnant women have higher negative appendectomy rates than non-pregnant women. Nevertheless, there is no difference between pregnant and non-pregnant women in terms of clinical course and postoperative outcomes of acute appendicitis.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ege University Faculty of Medicine Local Ethics Committee (approval number: 20-4.1T/35).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: O.B., C.U., Design: O.B., T.Y., C.Ç., Supervision: M.A.K., E.A., C.Ç., Data Collection or Processing: C.U., O.B., Analysis or Interpretation: O.B., T.Y., E.A., M.A.K., Literature Search: C.U., T.Y., C.Ç., Writing: O.B., C.U., Critical Review: C.C.

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References

1. Ferris M, Quan S, Kaplan BS, Molodecky N, Ball CG, Chernoff GW, Bhala N, Ghosh S, Dixon E, Ng S, Kaplan G. The global incidence of appendicitis. Ann Surg 2017;266:237-241.
2. Yu YR, Shah SR. Can the Diagnosis of Appendicitis Be Made Without a Computed Tomography Scan? Adv Surg 2017;51:11-28.
3. Tatli F, Yucel Y, Gozeneli O, Dirican A, Uzunkoy A, Yalçın HC, Ozgonul A, Bardakci O, Uyanikoglu H, İncebiyik A. The Alvarado Score is accurate in pregnancy: a retrospective case-control study. Eur J Trauma Emerg Surg 2019;45:411-416.
4. Hatipoglu S, Hatipoglu F, Abdullayev R. Acute right lower abdominal pain in women of reproductive age: clinical clues. World J Gastroenterol 2014;20:4043-4049.
5. Laméris W, van Randen A, Go PM, Bouma WH, Donkervoort SC, Bossuyt PM, Stoker J, Boermeester MA. Single and combined diagnostic value of clinical features and laboratory tests in acute appendicitis. Acad Emerg Med 2009;16:835-842.
6. Krajewski S, Brown J, Phang PT, Raval M, Brown CJ. Impact of computed tomography of the abdomen on clinical outcomes in patients with acute right lower quadrant pain: a meta-analysis. Can J Surg 2011;54:43-53.
7. Expert Panel on Gastrointestinal Imaging:, Garcia EM, Camacho MA, Karolyi DR, Kim DH, Cash BD, Chang KJ, Feig BW, Fowler KJ, Kambadakone AR, Lambert DL, Levy AD, Marin D, Moreno C, Peterson CM, Scheirey CD, Siegel A, Smith MP, Weinstein S, Carucci LR. ACR Appropriateness Criteria® Right Lower Quadrant Pain-Suspected Appendicitis. J Am Coll Radio 2018;15:S373-S387.
8. Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet 2015;386:1278-1287.
9. 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;261:332-337.
10. Erkek A, Anik Ilhan G, Yildizhan B, Aktan AO. Location of the appendix at the third trimester of pregnancy: A new approach to old dilemma. J Obstet Gynaecol 2015;35:688-690.
11. 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;205:534-540.
12. Atila K, Uçar AD, Unek T, Sevinç A, Cevik AA, Sökmen S. Acute appendicitis in pregnancy. J Ulus Travma 2002;8:98-101.
13. Sharp HT. The acute abdomen during pregnancy. Clin Obstet Gynecol 2002;45:405-413.
14. Segev L, Segev Y, Rayman S, Nissan A, Sadot E. Acute Appendicitis During Pregnancy: Different from the Nonpregnant State World J Surg 2017;41:75-81.
15. Hiersch L, Yogev Y, Ashwal E, From A, Ben-haroush A, Peled Y. The impact of pregnancy on the accuracy and delay in diagnosis of acute appendicitis. J Matern Fetal Neonatal Med 2014;27:1357-1360.
16. Lu Y, Friedlander S, Lee SL. Negative Appendectomy: Clinical and Economic Implications. Am Surg 2016;82:1018-1022.
17. Wagner PL, Eachempati SR, Soe K, Pieracci FM, Shou J, Barie PS. Defining the current negative appendectomy rate: for whom is preoperative computed tomography making an impact? Surgery 2008;144:276-282.
18. Tatli F, Yucel Y, Gozeneli O, Dirican A, Uzunkoy A, Yalçın HC, Ozgonul A, Bardakci O, Uyanikoglu H, İncebiyik A. The Alvarado Score is accurate in pregnancy: a retrospective case-control study. Eur J Trauma Emerg Surg 2019;45:411-416.
19. Abbasi N, Patenaude V, Abenhaim HA. Management and outcomes of acute appendicitis in pregnancy-population-based study of over 7000 cases BJOG 2014;121:1509-1514.
20. Kim JY, Kim JW, Park JH, Kim BC, Yoon SN. Early versus late surgical management for complicated appendicitis in adults: a multicenter propensity score matching study. Ann Surg Treat Res 2019;97:103-111.
21. Vasileiou G, Eid AI, Qian S, Pust GD, Rattan R, Namias N, Larentzakis A, Kaafarani HMA, Yeh DD; EAST Appendicitis Study Group. Appendicitis in Pregnancy: A Post-Hoc Analysis of an EAST Multicenter Study. Surg Infect (Larchmt) 2020;21:205-211.
22. Wagner M, Tubre DJ, Asensio JA. Evolution and Current Trends in the Management of Acute Appendicitis. Surg Clin North Am 2018;98:1005-1023.
23. Sanci M, Töz E, Ince O, Özcan A, Polater K, Inan AH, Beyan E, Akkaya E. 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;37:571-575.
24. Çınar H, Aygün A, Derebey M, Tarım İA, Akalın Ç, Büyükakıncak S, Erzurumlu K. Significance of hemogram on diagnosis of acute appendicitis during pregnancy. Turk J Trauma Emerg Surg 2018;24:423-428.
25. Gök AFK, Soytaş Y, Bayraktar A, Emirikçi S, İlhan M, Koltka AK, Günay MK. Laparoscopic versus open appendectomy in pregnancy: A single center experience. Turk J Trauma Emerg Surg 2018;24:552-556.
26. Ball E, Waters N, Cooper N, Talati C, Mallick R, Rabas S, Mukherjee A, Sri Ranjan Y, Thaha M, Doodia R, Keedwell R, Madhra M, Kuruba N, Malhas R, Gaughan E, Tompsett K, Gibson H, Wright H, Gnanachandran C, Hookaway T, Baker C, Murali K, Jurkovic D, Amso N, Clark J, Thangaratinam S, Chalhoub T, Kaloo P, Saridogan E. Evidence-Based Guideline on Laparoscopy in Pregnancy: Commissioned by the British Society for Gynaecological Endoscopy (BSGE) Endorsed by the Royal College of Obstetricians & Gynaecologists (RCOG). Facts Views Vis Obgyn 2019;11:5-25. Erratum in: Facts Views Vis Obgyn 2020;11:261.
27. Silvestri MT, Pettker CM, Brousseau EC, Dick MA, Ciarleglio MM, Erekson EA. Morbidity of appendectomy and cholecystectomy in pregnant and nonpregnant women. Obstet Gynecol 2011;118:1261-1270.