

Acute appendicitis in pregnant women

A Tunisian center experience

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Abstract

Acute appendicitis is the most common surgical pathology during pregnancy. It occurs in about 1 in 500 to 1 in 635 pregnancies per year.^[1] and appendectomy is the gold standard in the treatment approach.^[2] However, its diagnosis represents a challenge to both surgeons and obstetrician-gynecologists. In addition, the role of laparoscopy remains controversial.

This study discusses the diagnostic approach and reviews the appropriate surgical approach while evaluating the part of laparoscopy.

This is a retrospective descriptive analysis reviewing 36 patients who underwent surgery for acute appendicitis during pregnancy at the “Surgery Department of Jendouba Hospital from January 1, 2005 to December 31, 2019. Data include age, comorbidities, previous abdominal surgery, symptoms, physical examination findings, complementary exams results, operative treatment details, the emergency status of the procedure, associated medical treatment, antibiotics and tocolysis, the pathology reports, and follow-up.

The mean age of patients was 27 years. Twenty-one patients (58, 33%) were in the second trimester of pregnancy, 6 patients (16, 66 %) were in the first trimester, and 9 (25%) in the third one. The physical examination reported a right iliac fossa tenderness in 27 patients (75%). The abdominal ultrasound was performed in all cases and guided the diagnosis in 24 cases (66, 66%). 18 patients (50%) underwent laparoscopy, 12 patients (33, 33%) underwent laparotomy. The remaining 6 patients (16, 66%) required a conversion from laparoscopic to open surgery.

The clinical presentation of appendicitis in pregnancy is often misleading. Therefore, an abdominal ultrasound should be performed for all pregnant patients having abdominal pain. The difficulty of operating under laparoscopy increases with the pregnancy term, leading to a higher risk of conversion, which increases the operating time and the doses of anesthetics, causing a maternal and fetal risk.

Abbreviations: CRP = C reactive protein, CT = computed tomography, MRI = Magnetic resonance imaging, NLR = neutrophil-to-lymphocyte ratio, NPV = Negative predictive value, PPV = positive predictive value, SPSS = Statistical Package for the Social Sciences, US = ultrasonography, WBC = White blood cells.

Keywords: abdominal ultrasound, appendicitis, emergency, laparoscopy, pregnancy, tocolysis

1. Background

Acute appendicitis is the most common surgical pathology during pregnancy.^[3] It represents 65.6% of nontraumatic surgical emergencies in pregnancy.^[3] Acute appendicitis can occur at any time during pregnancy, but it is more common in the second trimester.^[1] Its diagnosis represents a challenge, as its classic clinical presentation is not always present; its common symptoms are nonspecific and often associated with normal pregnancy.^[4,5] Therefore, a high index of diagnostic suspicion is required to lead to an emergency appendectomy.

This study discusses the diagnostic approach when appendicitis is suspected and reviews the appropriate surgical approach while evaluating laparoscopy.

2. Methods

The study was based on a retrospective descriptive analysis. It included patients who underwent surgery for acute appendicitis during pregnancy at the “Surgery Department of Jendouba Hospital, located in north-western Tunisia, from January 1, 2005 to December 31, 2019. The “Surgery Department of Jendouba Hospital” is a tertiary care and teaching department

Consent to participate: A written informed consent to participate was obtained from all subjects.

Consent for publication: A written informed consent for the publication of personal/clinical data has been obtained from each patient.

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Availability of Data and materials: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate: An ethical approval was obtained from the Jendouba Regional Hospital Medical Ethics Committee No. JG13Y21. We confirm that all methods were performed in accordance with the ethical guidelines of the 1975 Declaration of Helsinki.

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affiliated with the Faculty of Medicine of Tunis. It is the general surgery department of reference in the region, a unit with a capacity of 35 beds serving more than 500,000 people. The files of all pregnant patients hospitalized at the “Gynecology department of Jendouba Hospital” for acute abdominal pain were reviewed. Only files of patients with a definitive diagnosis of appendicitis based upon radiological findings or surgery were included. Data of these patients were obtained from the surgical ward, patient charts, and operation registry books. Data were collected using a data collection tool, and it included demographic and clinical details, results of biological and radiological examinations, and therapeutic procedures used, as well as morbidity, mortality, hospital stay, the pathology reports and follow up visits clinical findings. All patients underwent routine blood tests, abdominal ultrasonography and obstetric ultrasonography. The treatment protocol included necessary intensive care measures (rehydration therapy, monitoring, intravenous analgesics) combined with an emergency surgery. Tocolysis therapy was indicated to 15 patients post operatively. A standard follow up period until delivery was assigned to all patients. A follow up visit was scheduled twice a month the first month after surgery, followed by a visit every month thereafter. During these visits, details about medical history, physical examination (searching for fever, abdominal pain, vomiting, wound dehiscence, etc) and abdominal ultrasonography findings.

An ethical approval was obtained from the Jendouba Regional Hospital Medical Ethics Committee on March 9, 2021 under number JG13Y21. Statistical analyses were performed using the SPSS statistical package for Windows version 20. The study is reported in line with the STROBE guidelines.^[6]

3. Results

During the study, 1645 pregnant patients presented to the Gynecology department of Jendouba Hospital for abdominal pain. Among them, 36 patients had acute appendicitis and were managed at our surgical department. All these patients were included in this study. The mean age of patients was 27 years and ranged from 18 to 41 years. The highest incidence was in 21–30 years with several 15 (41.66%) patients. In our series, the incidence of appendicitis in pregnancy was estimated

to 2,18%. Only 9 primiparous patients were reported (25%) versus 27 multiparous patients (75%). 21 patients (58, 34%) were in the second trimester of pregnancy, 6 patients (16, 66%) were in the first, and 9 (25%) in the third one (Fig. 1). Only 4 patients had gestational diabetes, and the remaining 31 had no comorbidities. All patients had no history of abdominal surgery. 27 patients presented fever, and 9 patients presented nausea or vomiting. 27 patients presented right iliac fossa pain, 6 patients presented epigastric or upper right quadrant pain, and 3 patients presented right flank pain. The physical examination reported a right iliac fossa tenderness in 27 cases (75%), a right iliac fossa guarding in 9 cases (25%), and digital rectal pain in 12 cases (33,33%). The average of the inflammatory markers, white blood cells (WBC) count and C-reactive protein (CRP) level were respectively $16,729 \times 10^9/L$ and 29,41 mg/L. The abdominal ultrasound, performed on all patients, showed uncomplicated appendicitis in 15 patients (41, 66% of cases), appendicular abscess in 6 patients (16, 66%), a widespread peritoneal fluid in 3 cases (8, 33%), and the appendix were nonvisualized in 12 cases (33, 33%). An abdominal CT scan was not performed on any of the patients. The obstetric ultrasonography was normal in 26 patients (72, 22%), and threatened preterm labor was suspected in 16, 66% of patients with a shortened cervix (10). Table 1 summarizes the different clinical and radiological findings in the current series. The average symptoms-surgery duration was 2,33 days. Only 12 patients (11, 11%) received antibiotic treatment. None of our patients was managed nonoperatively. 14 patients (38, 38%) underwent laparoscopy, 16 patients (33, 33%) underwent laparotomy and 6 patients (16, 66%) underwent a conversion from laparoscopic to open surgery (Fig. 2). The laparoscopic approach was opted for in all the 6 patients in their first trimester, in 11 out of the 21 patients in the second semester, and 3 of the 9 patients in their third trimester. Conversion from laparoscopy to open surgery was necessary for 3 of the patients in the second trimester and 3 patients in the third trimester. Table 2 details the intraoperative findings and surgical procedures performed. The diagnosis of acute appendicitis was confirmed in all cases: The pathology reports pointed out catarrhal appendicitis in 18 cases, phlegmonous appendicitis in 12 cases, and gangrenous perforated appendicitis in 6

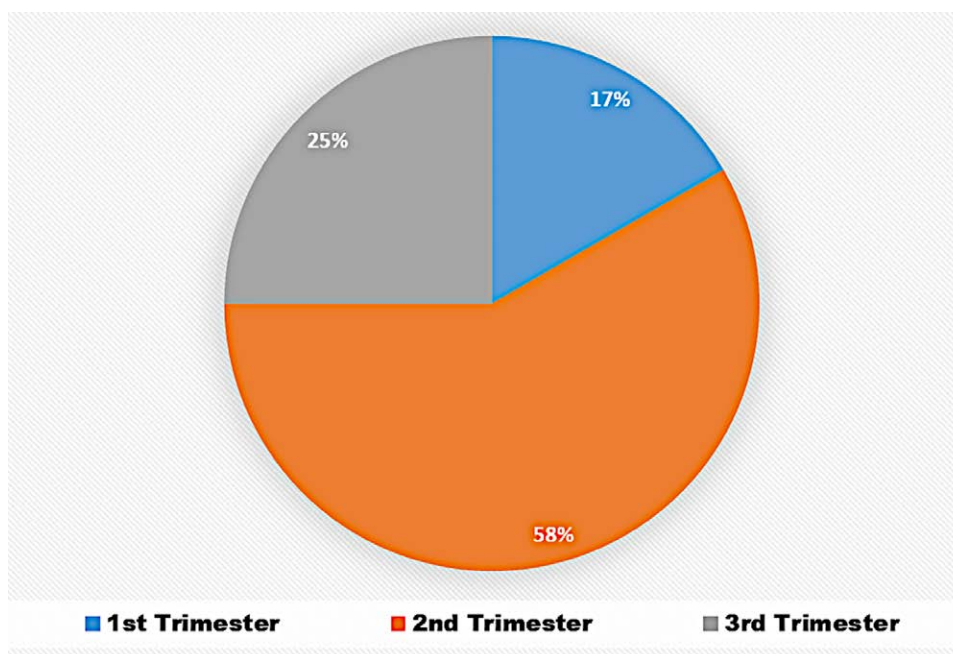


Figure 1. Distribution of appendicitis by trimester of pregnancy.

Table 1
Clinical and radiological findings.

Trimester of pregnancy	Patients	Localization of abdominal pain	Abdominal ultrasonography	Obstetrical ultrasonography
1 st trimester	6 (16, 66%)	Right iliac fossa	6 -Appendix with thickened wall and appendicolith -Appendicular abscess -Widespread peritoneal fluid -Non-visualized	5 -Normal pregnancy 0 -Arrested pregnancy 0 -Threatened preterm labor
2 nd trimester	21 (58, 34%)	Right iliac fossa	21 -Appendix with thickened wall and appendicolith -Appendicular abscess -Widespread peritoneal fluid -Non-visualized	7 -Normal pregnancy 4 -Arrested pregnancy 1 -Threatened preterm labor
3 rd Trimester	9 (25%)	Right flank upper right quadrant	3 -Appendix with thickened wall and appendicolith -Appendicular abscess 6 -Widespread peritoneal fluid -Non-visualized	3 -Normal pregnancy 2 -Arrested pregnancy 2 -Threatened preterm labor

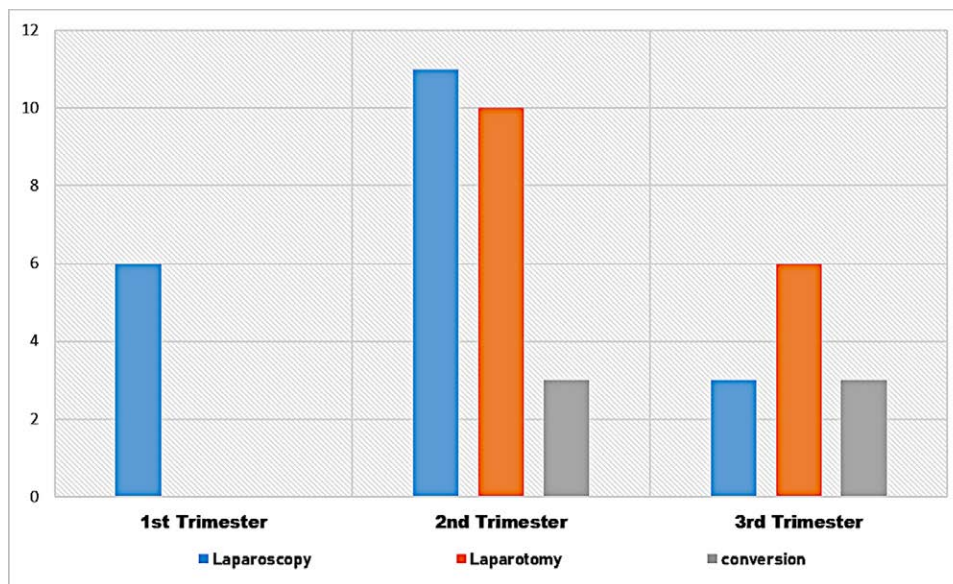


Figure 2. Surgical approach for each trimester of pregnancy.

Table 2
Operative findings.

	Number of patients by trimester	Number of patients by operative findings	Procedure performed
Laparoscopy	1 st trimester	6 Uncomplicated acute appendicitis	6 Appendectomy
	2 nd trimester	8 Uncomplicated acute appendicitis Appendicular abscess	6 Appendectomy 2 Appendectomy + wide drainage of abscess
Laparotomy	1 st trimester	0	—
	2 nd trimester	10 Uncomplicated acute appendicitis Appendicular abscess Appendicular peritonitis	8 Appendectomy 1 Appendectomy + wide drainage of abscess 1 Appendectomy + peritoneal toilet
	3 rd trimester	6 Uncomplicated acute appendicitis Appendicular abscess Appendicular peritonitis	3 Appendectomy 2 Appendectomy + wide drainage of abscess 1 Appendectomy + peritoneal toilet
Conversion from laparoscopy to laparotomy	1 st trimester	0	—
	2 nd trimester	3 Uncomplicated acute appendicitis Appendicular abscess	2 Appendectomy 1 Appendectomy + wide drainage of abscess
	3 rd trimester	3 Uncomplicated acute appendicitis Appendicular peritonitis	2 Appendectomy 1 Appendectomy + peritoneal toilet

cases. Table 3 summarizes further operative details such as the mean operative time, the amount of bleeding and the hospital duration according to the operative method used. 15 patients received tocolysis. All pregnancies were followed until delivery: 30 full-term deliveries, 2 miscarriages, 4 preterm births.

4. Discussion

Acute appendicitis in pregnancy is the most frequent nonobstetric surgical pathology that occurs during pregnancy.^[7] It is challenging for both the surgeon and obstetrician-gynecologists since the clinical manifestations are vague.^[8] Moreover, some features may be misconstrued due to anatomical and physiological changes secondary to pregnancy. The usual location of appendicitis during pregnancy is high-situated and more lateralized.^[9] In our studies, 23 patients out of 36 suffered from right upper quadrant pain. The gravid uterus progressively modifies the appendix's anatomical disposition, which remains in the right iliac fossa during the first trimester, moves to the pelvic brim during the second trimester, and reaches the right upper quadrant in the third one. Therefore, acute appendicitis should always be suspected in pregnant women, even if the pain is not located in the right iliac fossa.

Due to anatomical changes in pregnant women, clinical signs of acute appendicitis are variable, and complementary biological and radiological examinations are of great interest. Indeed, despite the reputed unreliability of the inflammatory markers during pregnancy due to physiological hyperleukocytosis and the lack of specificity of the C reactive protein level,^[10] the studies done by Mellenick et al^[4] show the meaningful contribution of WBC count on admission. A WBC count > 18,000 is highly predictive of appendicitis in these women. Besides, Quinn et al demonstrate that a neutrophil percentage of <70% in the pregnant patient provided a 100% negative predictive value of acute appendicitis in these patients.^[11] A recent systematic review and meta-analysis found that neutrophil-to-lymphocyte ratio (NLR) of 4.7 conferred a sensitivity of 88.9% and specificity of 90.9% for acute appendicitis, and higher NLR values were predictive of complicated appendicitis.^[12] Also, abdominal ultrasounds have a tremendous diagnostic value, with a sensitivity estimated at 70% and a specificity of 83%.^[9] The US diagnosis of acute appendicitis is confirmed by objectifying direct signs: an increase in the thickness of the appendix and an inflamed immobile and incompressible appendix, or indirect features; the presence of effusion in the right iliac fossa or Douglas or a heterogeneous collection in the right iliac fossa.^[7] The abdominal CT-scan may be indicated when the ultrasound examination is inconclusive. It should be performed without injection of a contrast agent and at a late gestational age after organogenesis.^[13] However, abdominal MRI remains the most reliable and accurate diagnostic method, with NPV 99.5% and PPV of 90.4%.^[14] Moreover, a study conducted in 2018 showed that a positive MRI result has a high precision rate with a 100% positive predictive value.^[15] Since delayed treatment of appendicitis carries a risk for both the fetus and mother,^[15] an early diagnosis through all available biological and radiological examinations is recommended.^[16]

Acute appendicitis treatment is based on surgery and should not be delayed as the fetal and maternal prognosis is engaged,^[15,17] and according to Abbasi et al, in a study conducted in America of over 7000 cases treated with antibiotic

therapy: Conservative treatment is relied on to a high risk of septic shock.^[18,19] Surgical techniques depend on factors such as gestational age, clinical features, patient obesity, preexisting incisions, radiological data, and surgeon preferences and skills. When a laparotomy approach is chosen, a transverse incision should be made at the point of maximal pain and not necessarily next to Mac Burney point. If the diagnosis is uncertain, a lower midline vertical incision in the lower midline is recommended. This allows better surgical exposure and treatment of other surgical conditions that may mimic acute appendicitis.^[20] According to recent studies, the laparoscopic approach is recommended for Grade 2B,^[16] for maternal and fetal safety, better abdominal exploration, especially when the diagnosis is doubtful, and better identifying the appendix's anatomical variants.^[19] Furthermore, studies showed that laparoscopy could be safely performed for surgical indications in pregnancy's second and third trimesters^{21,14}. However, the laparoscopic approach should be avoided after the 20th week of pregnancy, considering the risk of uterine injury in connection with small operational space and the fetal risk related to abdominal hyper-pressure and carbon dioxide pneumoperitoneum reduced uteroplacental blood flow.^[2] Furthermore, some precautions must be taken, such as limit insufflation pressure to 12 mm Hg and an open-access approach to avoid uterine trauma.^[21] In addition, operating time must be shortened, and hypotension associated with anesthesia must be corrected to account for the risk of uteroplacental hypoperfusion.^[19]

Appendicitis in a pregnant woman is combined with a high morbidity fetal rate and is correlated with the stage of appendicitis.^[14] Fetal mortality is around 35% for appendicular peritonitis, while it is around 1.5% for uncomplicated forms.^[9,14] This underlines the importance of using all additional resources to ensure an early diagnosis. Besides, appendicitis in a pregnant woman leads to 20% of preterm birth,^[14] and a meta-analysis conducted in 2019^[17] showed that a fetal loss was significantly higher among those who underwent laparoscopic appendectomy compared with those who underwent an open approach. Therefore, an abdominal and pelvic ultrasound must be performed without exception when suspecting acute appendicitis in a pregnant woman. Its safe nature for both patient and fetus without the need to use ionizing radiation and intravenous contrast agent make it an excellent and ideal diagnostic modality in the context of pregnancy. Also, since we are based in the developing world, we advocate the first-line ultrasonography use at the slightest doubt of acute appendicitis in pregnant women especially in developing countries with resource-limited settings as it is the most affordable and available diagnostic tool. Inconclusive trans-abdominal US should be followed by MRI to help establish the diagnosis. It is the second-line proven safe and accurate diagnostic modality. It also helps reduce the rate of unnecessary surgery in pregnant women with acute appendicitis clinical suspicion as demonstrated in a recent study conducted by Lukenaitė et al.^[22]

Furthermore, according to Lebeau et al, tocolytic agents should be systematically prescribed in all patients to prevent uterine contractions, which allows delaying the delivery and therefore reducing cases of abortion or threatened preterm can be reported.^[8]

Table 3

Operative details and mean hospital stay according to operative procedure used.

	Laparoscopic group (n = 14)	Laparotomy group (n = 16)	Conversion group (n = 6)	Study population (n = 36)
Mean operative time (min)	32.8	40.3	62.5	41
Amount of bleeding estimation (mL)	32.1	56.8	116.6	57.1
Duration of hospital stay (d)	2.28	3.18	3.33	2.85

The major limitations of this study are the small number of patients included and the retrospective single centered design. We also acknowledge our limitation of not being able to comment on pharmaceutical therapies administered during sedation as well as some preoperative parameters such as detailed past medical drugs and tobacco use, and BMI as they were not mentioned in every medical record. Further multicenter prospective studies including larger pregnant patients population with acute appendicitis compared to control groups of pregnant woman without acute appendicitis are needed to be able to comment on the outcome of pregnancies complicated with acute appendicitis.

5. Conclusions

Since diagnostic delay and treatment deficiencies for pregnant women in the context of suspected acute appendicitis may lead to disastrous complications and fetal loss, a clear diagnostic approach and therapeutic protocol should be established. The abdominal ultrasound remains the best first-line radiological examination especially in the developing world. Even though it may highly increase the medical costs, additional abdominal MRI is a valuable diagnostic tool in inconclusive cases.

Despite all debates concerning the safety of Laparoscopic appendectomy in pregnancy, the satisfying results of our study encourage us to pursue the careful use of this technique in selected patients before the 20th week of pregnancy. Tocolytic drugs should always be prescribed to avoid fetal mortality, miscarriage, and preterm delivery.

Author contributions

Conceptualization: Atef Mejri

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Supervision: Atef Mejri

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