

Acute Appendicitis and Pregnancy; Difficult Diagnosis and Specific Features of care

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Abstract: Acute appendicitis is an infrequent surgical emergency in pregnancy occurring in about 1:1500 pregnancies. The classical abdominal pain in the right lower quadrant of the abdomen is the only reliable clinical sign. Delay in diagnosis is attributed to presence of symptoms commonly seen in pregnancy like nausea and vomiting and difficulty in localizing abdominal pain due to displacement of the appendix with advancing gestation. Its frequency is not altered by pregnancy. This is a serious association that involves the maternal and fetal prognosis. This association is characterized by clinical polymorphism, resulting in a diagnosis difficult and often delayed treatment. Perforated appendix and generalized peritonitis impacts adversely on pregnancy contributing to increases in miscarriage, pre-term delivery, fetal loss and even maternal mortality. Imaging studies like abdominal ultrasonogram, and computerized tomography have been utilized to complement clinical suspicion and decrease 'negative appendectomies. Although the laparoscopic approach is a useful diagnostic and therapeutic tool in early pregnancy, its use as the primary approach for appendectomy in pregnancy requires further evaluation as increases in the incidence of fetal loss. The aim of our study is to evaluate therapeutic modalities of the non-gynecological abdominal emergencies of the pregnant woman

Keywords: acute appendicitis–pregnancy–generalized peritonitis– diagnosis difficulties-laparoscopic surgery

I. Background

Appendicitis in pregnancy is relatively rare, but it has significant morbidity and is a cause of maternal and infant mortality. Abdominal pain is the most common presenting symptom, and the consideration of multiple pathologic disorders should be entertained. Accurate diagnosis of appendicitis in pregnancy is the largest challenge since the signs and symptoms may vary depending on the trimester in which the patient presents.

Materials and Methods

31 patients were admitted for suspicion of acute appendicitis during pregnancy in our hospital over a period of 11 years [2004-2015]. Two patients had perforated appendicitis with generalized peritonitis. The average age was 31.5 years [24-43 years]. The average term was 20 weeks and 2 days of amenorrhea. Seven patients were operated in the first trimester, 14 in the second and ten in the third trimester. The Mac Burney incision was performed for twenty nine patients, and two patients were operated by midline incision.

Results

All the patients were operated and the postoperative period was uneventful for 29 patients but one patient had an abortion and another a premature delivery. Some clinical signs are wrongly blamed on sympathetic signs of pregnancy. The mother and the fetal prognosis depends on the therapeutic delay and severity of the acute appendicitis. The time between onset of symptoms and response is an important prognostic factor.

Conclusion

Acute appendicitis may involve the maternal & fetal prognosis. The management should be fast and provided by a multidisciplinary team. The treatment is surgical consisting of an appendectomy either by laparoscopy or open surgery approaches. Morbidity and mortality is not negligible.

II. Introduction

Acute appendicitis is the most common non-gynecological abdominal emergency during pregnancy [1, 2]. Its frequency is not altered by pregnancy. Occurs in approximately one in 500 to one in 635 pregnancies per year. [3, 4]. Appendicitis occurs most often in the second trimester of pregnancy. [3, 5]. Abdominal surgery during pregnancy, particularly an appendectomy, can increase the risk of unfavorable outcomes. [6]. This is a serious

association that involves the fetal maternal prognosis. This association is characterized by clinical polymorphism, resulting in a diagnosis difficult and often delayed treatment [7, 8]. Clinical diagnosis should be strongly suspected in pregnant women with classic findings such as abdominal pain that migrates to the right lower quadrant. The main purpose of imaging is to reduce delays in surgical intervention due to diagnostic uncertainty. Differential diagnosis of suspected acute appendicitis usually includes pathologies considered in non-pregnant people. Diagnosis is particularly difficult during pregnancy, because of the relatively high prevalence of abdominal discomfort and gastrointestinal complaints, as well as anatomical changes related to the increase in uterine volume and the physiological leukocytosis that occurs during this period. A ruptured appendix is more common in pregnant women, especially in the third trimester, possibly due to these difficulties and the reluctance to operate on pregnant women, which ultimately delays diagnosis and treatment [4].

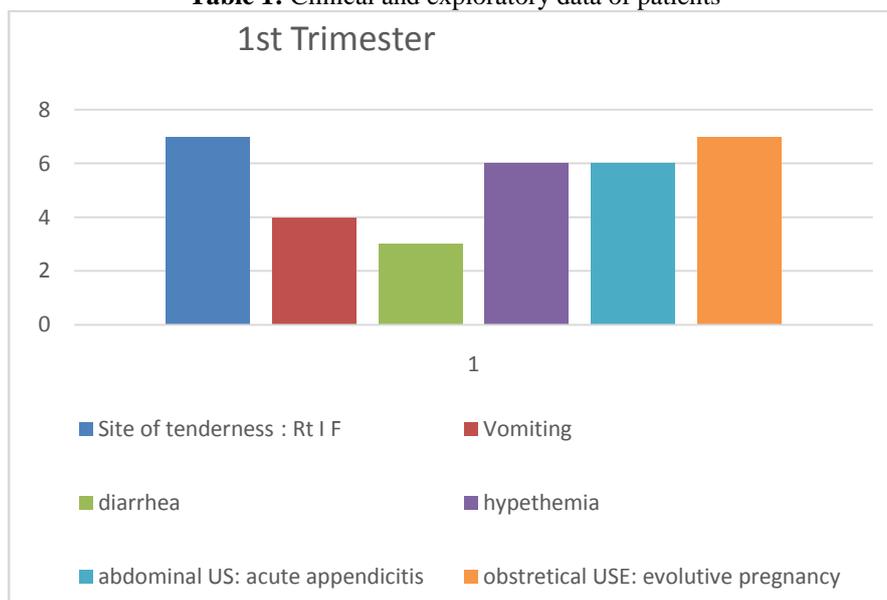
III. Materials and Methods

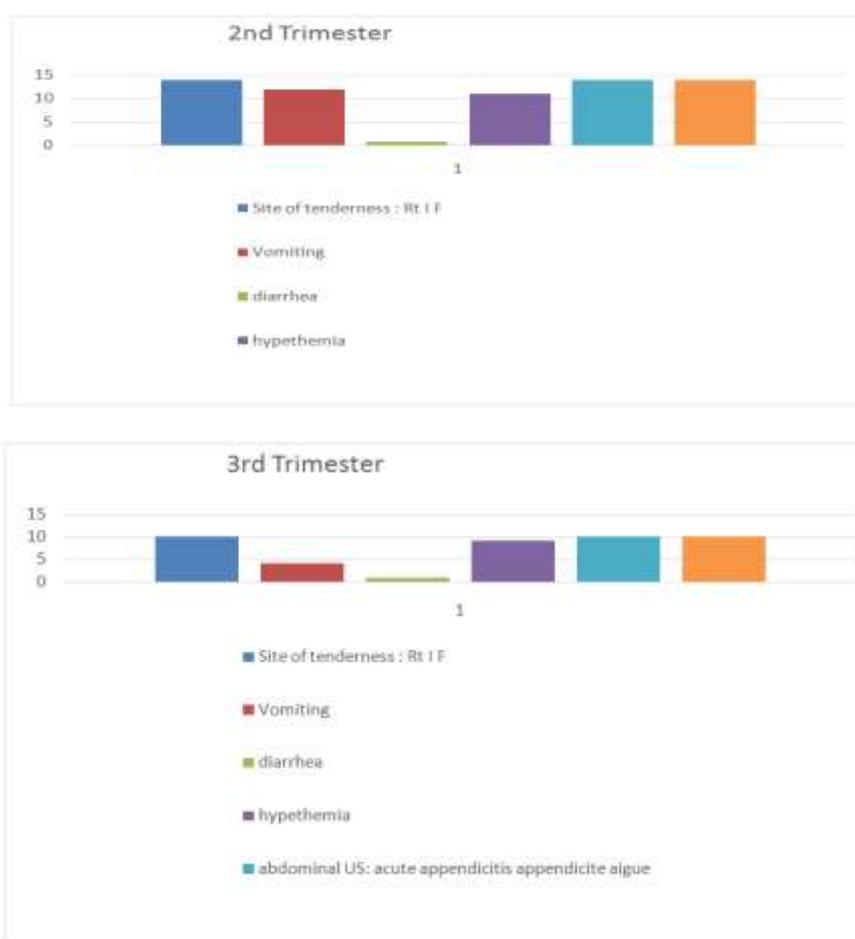
Between January 2004 and December 2015, thirty-one pregnant patients with non-gynecological abdominal emergency were collected to emergency and general surgery department. The average age of patients was 31.5 years [24-43 years]. Twenty-nine of our patients had acute appendicitis and two patients had perforated appendicitis with generalized peritonitis. The medium-term pregnancy was 20 weeks and 3 days of gestation. All patients were symptomatic. The observation period ranged from 10 hours to 8 days. The clinical picture was dominated by abdominal pain and fever. Abdominal ultrasonography was performed in all our patients. It had shown an aspect of acute appendicitis in 19 patients, it was inconclusive in 7 patients and had found a diffuse peritoneal effusion in 5 cases. All patients were operated by laparotomy; twenty-nine through Mac Burney and two by midline incision. Seven patients were operated in the first trimester, fourteen in the second and ten in the third trimester.

IV. Résultats

All patients received antibiotic therapy a type of amoxicillin (3 g / 24h) intravenously during the first 48 hours, followed by oral take of the same antibiotic (3 g / 24 h) for a week. The patients in the second and third trimesters of pregnancy were tocolysed by salbutamol. All patients were operated with a delay of 6 hours to 6 days. Twenty-nine through Mac Burney incision and two by midline incision. The intraoperative exploration had found in all our patients an acute appendicitis appearance. They had an appendectomy, drainage was performed in two patients with perforated appendicitis. It was shown macroscopically an appendix ranked in twenty three patients, a catarrhal appendix in four cases, a gangrenous appendix in two cases, and a perforated appendix in two other cases. Histologically, there was an acute appendicitis without signs of malignancy in all our patients. The average of hospital stay for patients was three days [1 to 4 days] otherwise it was 8 days [6 to 12 days] for women in labor with generalized peritonitis. The postoperative period was uneventful for 29 patients. One patient had an abortion at seventh postoperative day "operated for appendicular abscess" (17 weeks of gestation) and another a premature delivery at the fourth postoperative day (35 weeks of gestation). Both of the two cases were operated for perforated appendicitis.

Table 1: Clinical and exploratory data of patients





V. Discussion

Although a rare presentation acute appendicitis is the most common non-obstetrical and non-traumatic surgical emergency during pregnancy with a frequency of 62% [11, 12, 13]. Most of the authors have made the same observation and report same frequencies from 33, 3% to 66, 5% [14, 15, 13]. Its incidence is ranging between 0.02 to 0.05% in western series [9, 10, 11, 13]. It is of the order of 0.2% in our series. Pregnancy does not change the overall incidence of appendicitis, but the severity of the surgical affection can be increased in pregnancy. Appendicitis is one of the most common causes of an acute abdomen in pregnancy, occurring in approximately 1 in 1500 pregnancies. [16, 17]. This represents an overall incidence of 0.05% to 0.07% and does not appear to be any difference in the non-gravid population. [18, 19]. One report of a reduced incidence of appendicitis during pregnancy suggested a possible protective effect, and the mean age is 28 years. [20]. Incidence rates in the first trimester range from 19% to as high as 36%. [17, 18, 21, 22]. There is a higher incidence of appendicitis in the second trimester, ranging from 27% to 60%. [17, 18, 21]. Although incidence decreases from 15% to 33% in the third trimester; some studies reported a 59% incidence in the third trimester. [17, 18, 21, 22]. Perforation rates for pregnant patients have been reported as high as 55% of cases, compared with 4% to 19% of the general population. [18, 23, 24]. Due to the lack of specificity of the preoperative evaluation; the pathologic diagnosis of appendicitis is confirmed in only 30% to 50% of cases. [17, 21, 22]. The first trimester yields a greater accuracy, but more than 40% of patients in the second and third trimester will have a normal appendix. [25]. Overall, normal histology was reported to be 11% to 50%. [26, 27]. Appendicitis was correctly diagnosed 50% to 86% of the time. [18, 21, 22, 26]. The risk of delay in diagnosis is associated with a greater risk of complications such as perforation, infection, preterm labor, and risks of fetal or maternal loss. [21, 23]. Maternal mortality has been reported from none to 2%. [17, 18, 21, 22]. An unruptured appendix carries a fetal loss of 1.5% to 9%, while this rate increases up to 36% with perforation. [17, 21, 28]. The risk of perforation increases with gestational age, and perforation in the third trimester often results in preterm labor. Delay in surgical intervention carries increased fetal loss [18]. The risk for premature delivery is the greatest during the first week after surgery. However, maternal mortality is very low. [17, 21, 22]. This may be due to rapid administration of antibiotics, close perioperative monitoring, improved cooperation between general surgeons, obstetricians, and anesthesiologists and improved

perioperative care. Abdominal pain is the most constant sign. It was found in all patients in this group is located at the right iliac fossa. Nausea and vomiting are common at this age of pregnancy and are not useful elements for diagnosis. [11] This pain can lead to discuss the risk of early abortion or a urinary tract infection, where the interest of the obstetrical examination and a urine culture [7, 30].

In the second and third trimesters, the diagnosis is more difficult, firstly, because of the high position of the cecum and, secondly, because of the existence of uterine contractions evoking a birthing threat premature and may delay or mislead the diagnosis [31, 32]. A belatedly diagnosed appendicitis can lead to maternal and fetal severe complications [33,34]. Both obstetrical and gynecological conditions can present with abdominal pain and mimic appendicitis. Obstruction of the appendicular lumen is implicated through sub mucosal lymphoid follicle hyperplasia following infection. Although parasitic infestation may initiate the process, it is not a common etiology in adults. Faecolith or foreign body is also implicated. Whatever the source of obstruction, intraluminal pressure increases with continued mucosal secretion and bacterial infection causing lymphatic and venous obstruction culminating in oedema and congestion of the inflamed appendix. A thorough history and a careful physical examination should lead the evaluating clinician to formulate a differential diagnosis that is appropriate for the individual. Nonobstetrical/no gynecological conditions. Difficulty in diagnosis is further compounded by abdominal pain in pregnancy being less classical than in the non-pregnant state. Fever, nausea and vomiting, pus cells on urine analysis and leukocytosis all lack sensitivity and specificity. As mentioned above, nausea and vomiting are seen as part of the symptoms of early pregnancy. [35]

Clinical sense and maintaining a high degree of suspicion through close observation and repeated clinical reviews remains the mainstay of establishing the diagnosis. Ancillary imaging tests have not been routinely instituted as positive predictive values depend on state of the pathology and clinical experience. However, they are becoming more relevant in reducing the high percentage of negative appendectomies following clinical diagnosis made in error. Negative appendectomies rates vary from 18% to 27%. [36]. Pregnant women are less likely to have a classic presentation of appendicitis, but the most common symptom of appendicitis, i.e. pain in the lower right quadrant, occurs near Burney's point in most pregnant women, regardless of the stage of pregnancy. [37,38,39]. As the location of the appendix migrates a few centimeters toward the head with the increase in uterine volume, in the third trimester, the pain may be located in the flank or in the right upper quadrant. [40,41] In addition, the causes related to pregnancy leading to abdominal pain, fever, leukocytosis, nausea/vomiting, and changes in bowel function are to be considered. The possibility of ectopic pregnancy should be excluded for any woman with a positive pregnancy test and pain in the right lower quadrant. Round ligament pain is a common cause of light pain in the right lower quadrant in early pregnancy, but is not associated with other symptoms and is not progressive. Pyelonephritis is more common in pregnant women than in non-pregnant women. Pregnant women with pain on the right side, fever, leukocytosis and leukocyturia may be treated for pyelonephritis without investigation, where the effective diagnosis of appendicitis may be delayed. In the second half of pregnancy, pre-eclampsia and HELLP syndrome may be associated with nausea, vomiting and abdominal pain, but in contrast to appendicitis, the pain is usually in the upper right quadrant or epigastric; hypertension is usually present and fever and leukocytosis are atypical. Premature detachment of the placenta and uterine rupture are associated with median or lateral lower abdominal pain. Unlike appendicitis, both diagnoses are often associated with vaginal bleeding, changes in fetal heart rate and significant increase of the uterine tonus (stiffness). [42] Acute appendicitis is a histological diagnosis. Clinical diagnosis should be strongly suspected in pregnant women with classic findings, such as abdominal pain, which migrates to the right lower quadrant, tenderness in the right lower quadrant, nausea and/or vomiting, fever and leukocytosis with a left shift. [43]. With an atypical presentation, which often occurs during pregnancy, imaging studies are recommended.

The main objective of these examinations is to reduce delays in surgical interventions due to diagnostic uncertainty. A secondary objective is to reduce, but not eliminate, the negative appendectomy rate. In such cases, ultrasounds can reveal the possible cause of the patient's symptoms (e.g. ovarian cyst or torsion, degeneration or torsion of myoma, nephrolithiasis, and cholecystitis). [5] Diagnosis of acute appendicitis in a patient during labor requires a high level of suspicion, is especially difficult and may not be possible. Labor may be associated with pain, which may be lateralized, fever and chorioamnionitis, leukocytosis and vomiting. Persistence or progression of these symptoms after delivery should be followed by a detailed physical examination and imaging studies to evaluate appendicitis [43]. The initial method of choice for imaging the appendix in pregnancy is ultrasound. [44]. The main finding is the identification of a non-compressible, blind-ended tubular structure in the lower right quadrant, with a maximum diameter exceeding 6 mm [45]. Several studies have reported non-visualization of the appendix in a large percentage of pregnant women with suspected appendicitis. [46, 47]. However, in a review of studies on the value of ultrasound diagnostics during appendicitis in pregnancy, sensitivity ranged from 67 to 100% and specificity of 83 to 96%, compared with the general population, in which sensitivity and specificity were 86 and 96%, respectively. [48]. Several factors

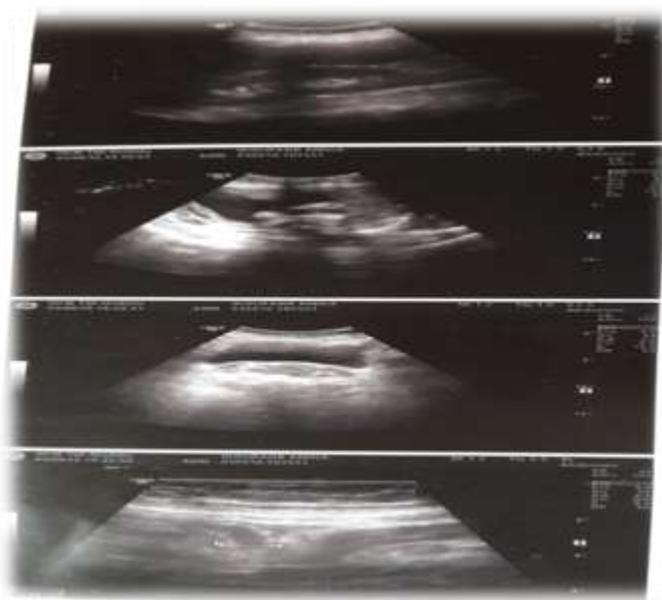
influence the performance of ultrasound diagnosis of appendicitis in pregnancy, including gestational age, body mass index (BMI), and most importantly, the training and experience of the examiner.[49]. Nuclear magnetic resonance imaging (MRI) is an excellent method to exclude acute appendicitis in pregnant women when the clinical examination and ultrasound are inconclusive. MRI is an attractive alternative to computerized tomography (CT), avoiding exposure to ionizing radiation[50]. Gadolinium is not administered routinely because of theoretical concerns about fetal safety, but can be used if essential[51]. According to the American College of Radiology, the preferred test after an inconclusive ultrasound in the evaluation of suspected appendicitis during pregnancy is MRI. However, conduct should not be delayed awaiting magnetic resonance imaging, as the increased risk of rupture over time must be considered.[52]. Computed tomography (CT) is generally more available than MRI, but is still inaccessible in many places in some regions. The main appendicitis findings in CT are inflammation in the lower right quadrant, a hollow elongated tubular structure and/or appendicolith/fecalith.[53]. The initial experience with helical computed tomography for the diagnosis of appendicitis in pregnancy seems promising, but the data are limited to small series of cases. Changes to the CT protocol can limit exposure to fetal radiation estimated at less than 3 mGy, well below the doses related to adverse fetal effects (30 mGy for the risk of carcinogenesis, 50 mGy for deterministic effects), without limiting diagnostic performance[51, 53]. A digital abdominal CT protocol with a preparation of intravenous and oral contrast, especially for the visualization of the appendix, may also be used but is associated with increased fetal exposure to radiation (20 to 40 mGy).[53, 54].

In our study, ultrasound has been a great contribution in confirming the diagnosis of acute appendicitis in the first trimester in all cases. The sensitivity of ultrasound was 100% and specificity of 95%. The second and third trimesters, ultrasound was hampered by uterine volume [55, 56]. CT scan was not performed in our patients because of radiation especially in the first trimester. Selective imaging of the appendix using Helical Computed Tomography has recently shown to be a safe and potentially reliable tool to accurately identify appendiceal changes in appendicitis. Radiation exposure using this test is 300 mrad, which is below an accepted safe level of radiation exposure in pregnancy of 5 rad. Reliance on radiographic studies may not be cost-effective, and may deter from careful and timely serial physical exams.[57]. Finally the Laboratory evaluation may not be helpful and cannot be relied on. [58]. Leukocytosis in pregnancy can be as high as 16,000 cells/mL with bandemia present and still considered a normal variant and not a clear indicator of appendicitis. During labor, it may rise to 30,000 cells/mL, and not all pregnant patients with appendicitis have leukocytosis. It is not a reliable marker, as up to 33% of cases may have a leukocyte count greater than 15,000/mm. [59]. The treatment of acute appendicitis is appendectomy. Perioperative antibiotics should cover Gram-negative and Gram-positive bacteria. Antibiotic therapy alone is not recommended as it is associated with poor outcomes in the short and long term, with minimum data on pregnant patients.[60]. Despite a recent meta-analysis published in the British Medical Journal suggesting that antibiotic therapy may be effective in patients with uncomplicated appendicitis, these data cannot be extrapolated to pregnant women.[61]. Repetitive use of radiologic imaging, magnetic resonance imaging (MRI) and computerized tomography (CT) has the potential to reduce the incidence of negative appendectomy.

There is some evidence suggesting that the higher negative laparotomy rate in pregnant women is associated, at least in part, to a hesitancy to perform the pre-operative CT in such patients.[62, 63]. Cesarean section is rarely indicated at the time of appendectomy. For patients who remain pregnant, the risk of dehiscence of the appendectomy incision during labor and vaginal delivery should not be increased when the aponeurosis is properly approximated.[64]. Assessment for open laparotomy is dependent on gestational age since the appendix progressively relocates. This is typically from McBurney's point, and then rising above the iliac crest. McBurney's point is the point situated about one-third the distance between the right anterior-superior iliac spine and the umbilicus. This area provides effective access for appendectomy throughout pregnancy, even in the third trimester. [65]. Management of a perforated appendix depends on the nature of the perforation: free versus locked. Free perforation may cause intraperitoneal dissemination of purulent and/or fecal material. Such patients are usually very serious cases and may be septic, which exposes them to increased risk of premature birth and fetal loss. Urgently laparotomy is needed for appendectomy with thorough washing and drainage of the peritoneal cavity.[66]. Pregnancy is not considered to be a contraindication for laparoscopic approach to appendectomy.[67]. Fetal health complicates the management of the gravida patient with acute abdominal pain. When appendicitis is suspected, timely obstetric as well as a general surgical consult is necessary. Laparoscopic surgery in the pregnant patient has not been broadly accepted in the latter second and third trimester due to the concern regarding fetal wastage, the effects of carbon dioxide on the developing fetus and the long-term effects of this exposure.[68]. Laparoscopy procedures take approximately 50% longer with conflicting studies showing decreased length of stay and hospitalization.[69]. Questions arise regarding the risk for decreased uterine blood flow due to increased intraabdominal pressures from insufflation and the possibility of fetal carbon dioxide absorption.[70]. Use of nitrous oxide pneumoperitoneum has been advocated[67] although technical difficulties arise with the gravid uterus. Blind placement of the Veress needle,

or primary port, has resulted in puncturing and subsequent pneumoamion. [69, 71]. With improved technique, laparoscopy surgery has been shown to offer some advantages over open laparotomy: decreased postoperative pain, reduced hospital, and wound morbidity. [71]. Postoperatively, early mobilization is advantageous for prevention of thromboembolism as occurrence rates of deep vein thrombosis are higher in pregnancy. Early mobilization also reduces the occurrence of incision scars, hernias, and decreases fetal depression secondary to pain and narcotic use. [72]. The Cochrane Library Systematic Review about laparoscopy in the management of acute abdominal pain in the lower abdomen of women of childbearing age examined eight randomized clinical trials, in which laparoscopy was compared to open appendectomy. Laparoscopy was associated with an increased rate of specific diagnoses, but there was no evidence of a reduction in the rates of adverse events. There was a significant difference favoring laparoscopy in specific diagnostic rates but there was no difference in adverse event rates. Therefore, the authors concluded that the benefits of laparoscopy in women with nonspecific abdominal pain and suspected appendicitis include a high rate of specific diagnoses and low rate of removal of normal appendices, compared with the open technique. There was no evidence of an increase in adverse events with any of the strategies. [73]. In view of the perceived risk of fetal loss and pre-term labor, fetal monitoring before and after surgery especially in later gestational age, can be re-assuring to both the mother and the care-giver. Continued fetal surveillance for the next few days after surgery will direct care givers to the need for receiving a premature fetus or address management of a miscarriage. The routines of effective pregnancy care are recommended if there are no complications post-operatively and pregnancy progresses without event. [35]. In our study, the woman who had aborted was operated after four days of onset of symptoms.

The perforation of the appendix was designated as the most important predictor factor of maternal morbidity [74]. Fetal mortality is over 35% in case of appendiceal peritonitis. It varies between 1 and 8% in women with uncomplicated acute appendicitis. [11] Prematurity and spontaneous delivery are the main risk to the fetus complications. Prematurity rate can reach 20%. We observed one premature birth due to acute appendicitis with peritonitis in the fourth postoperative day.



USE of a 27 year old woman with acute appendicitis and pregnancy of 19 weeks showing:

- Latérocaecal swollen Appendix measuring 10 mm with thick periappendicular fat with no intraperitoneal fluid
- Singleton ongoing pregnancy with positive fetal cardiac activity

VI. Conclusion

Appendicitis is not a common surgical complication and diagnosis can be difficult. Fetal morbidity and mortality are high in the presence of perforation and generalized peritonitis. Diagnostic difficulties arise because of displacement of the vermiform appendix with advancing pregnancy. The accurate diagnosis of appendicitis during pregnancy requires a high level of suspicion and clinical skills, and not merely relying on the classic signs and diagnostic testing. Delay of operation correlates to more inflammatory changes in the appendix and to higher maternal and fetal complication rates. Early surgical intervention is essential. Suspected

cases of this condition require serial physical exams as well as general surgery and obstetric consultation, since they are most qualified to evaluate all aspects of a gravid patient and maternal physiology. It remains to be determined which diagnostic test is best suited to facilitate or determine a diagnosis of acute appendicitis in pregnancy and often the correct diagnosis is determined only at surgical intervention.

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