



## APPENDICITIS IN PREGNANCY

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### ABSTRACT

Appendicitis is the commonest non-obstetric emergency in pregnancy. The management is challenging in pregnancy due to the physiological and anatomical changes occurring in pregnancy that lead to delays in diagnosis and intervention. Delayed intervention adversely affects the maternal and fetal well-being. This article reviews the various aspects related to appendicitis in pregnancy in the light of recent literature.

**Keywords:** Appendicitis, Pregnant, Perforation, Imaging, labour, Complications.

### INTRODUCTION

Appendicitis is an infrequent but the commonest non-obstetric surgical emergency in pregnancy, occurring in approximately 1/800 to 1 in 1500 pregnancies. [1, 2]. Multiple theories have been proposed to explain the etiopathogenesis and some studies in recent literature even suggest a protective effect of pregnancy [3].

The clinical presentation and course of appendicitis is similar in the pregnant and non-pregnant states but the management is particularly challenging in pregnancy due to the physiological and anatomical changes occurring in pregnancy that lead to difficulty and/or delays in diagnosis [4].

Perforation of inflamed appendix occurs more frequently in pregnancy, due to delayed diagnosis and reluctance to operate on pregnant women, thereby adversely affecting the maternal and fetal state of health. Hence, achieving an accurate diagnosis and institution of early treatment are crucial to prevent complications [5-6]. This article presents the summarized review of the etiopathogenesis, epidemiology clinical presentation, investigations, complications and treatment of acute appendicitis in pregnancy with emphasis on the recent advances.

### METHODS AND MATERIALS

A systematic review of English-language articles related to appendicitis in pregnancy was performed after

deriving references from sources including Pubmed Central, Medline, Cochrane Database, HINARI, Bioline International, AJOL, CINAHL, Scopus, Cogprints, Openmed, MD Links, and IndMed. The search items /MeSH terms included appendicitis in pregnancy, acute abdomen in pregnancy, surgical emergencies in pregnancy, non-obstetric acute abdomen in pregnancy, and recent trend of acute appendicitis in pregnancy. References published in last decade were preferred and a total of 49 references were used. Older references were cited only when no appropriate reference was available from the recent literature.

### Etiopathogenesis

The etiopathogenesis remains uncertain but it is postulated that the initiating event in appendicitis is the obstruction of its lumen most commonly by a calcified "stone" made of faeces called faecolith and uncommonly by inflamed lymphoid tissue, parasites, gallstones, foreign bodies or tumours. Irrespective of the source of obstruction, intraluminal pressure increases with continued mucosal secretion causing lymphatic and venous obstruction culminating in oedema, congestion of the inflamed appendix, breakdown of mucosal barrier and bacterial proliferation [1]. If left untreated treated at this stage, further increases in intraluminal pressure would compromise arterial blood flow culminating in necrosis of the appendicular wall and perforation of the appendix. In

non-pregnant state, omentum tends to wall off the inflamed appendix but in later stages of pregnancy, there may be an upward and lateral displacement of the appendix that may adversely affect the omentum from effectively walling off and containing the inflamed appendix and thereby may contribute to a higher risk of inflammatory spread and generalised peritonitis [7].

### Epidemiology

Acute appendicitis can occur at any time during pregnancy, although it has been reported most often during the second trimester. Borst AR [8] found 45% of cases in second trimester, 30% during the first trimester and the remaining 25% in the third trimester. In the series of Ghazanfar et al.[6], 52% of these patients were in their second trimester, followed by first trimester (38%) and third trimester (10%). Kazim et al [4] however found equal proportion of cases in all the three trimesters (30% in the 1st trimester, 37% in 2nd trimester, and 34% in the 3rd trimester). The overall incidence of appendicitis has been reported to be about 0.15 to 2.10 per 1000 pregnancies [9]. A study done in Sweden by Andersson and Lambe [3] showed an inverse relation between pregnancy and appendicitis, suggesting thereby that pregnancy affords protection against appendicitis, especially in the last trimester [3]. They also noted that perforation in pregnancy varied with gestational age approximating 6% in the first trimester, 10% in second and 13 % in the third trimester [3]. Yilmaz et al. [10] found a significant difference in the rate of complications (52% vs. 17%) between perforated and non-perforated patients. In the presence of perforation, perinatal mortality and fetal mortality can reach up to around 35% and 8 - 14% [9-10] respectively though maternal deaths are rare and fetal mortality ranges from 0-1.5% in cases of simple appendicitis [9]. The histopathological diagnosis of appendicitis is confirmed in only 30% to 50% of cases due to the lack of specificity of the preoperative evaluation [2]. Greater accuracy is yielded in the first trimester, but more than 40% of cases in the second and third trimester will have a normal appendix on evaluation of specimen.

### Clinical Features

#### Patient Presentation

The clinical course of appendicitis in pregnant patients is similar to the non-pregnant patients; it is the physiological and anatomical changes occurring in pregnancy that lead to difficulty and/or delays in diagnosis. Abdominal pain, predominantly in right lower quadrant (RLQ) is the most common presenting symptom, regardless of the stage of pregnancy [4-6, 8, 11]. In a significant number of patients, the pain starts as diffuse or peri-umbilical colics which migrates to the RLQ and attains constant character. Kazim et al. [4] has found pain in RLQ in 74% of cases and Ghazanfar et al. [6] reported

this symptom in 72% of cases, whereas 18% had a vague generalized abdominal pain and 10% had backache. Patients may present with pain over right upper quadrant which is attributed partly to an upward displacement of appendix toward the costal margin in the later stages of pregnancy [7]. Other common presenting symptoms include anorexia, nausea, vomiting, uterine contractions, dysuria, and diarrhoea [7]. Fever, hypotension and tachycardia may not be present and are not considered reliable in pregnancy [7-8]. On physical examination, tenderness is present over right lower quadrant in most of the cases. This sign was elicited in 87% of cases in the series of Kazim et al.[4] irrespective of the trimester of pregnancy. However, rebound tenderness and guarding of the abdominal wall, which are important signs of appendicitis in non-pregnant state, are less commonly elicited in pregnancy due to the stretching of the abdominal wall muscles away from the inflamed appendix, thereby impeding the direct contact between the area of inflammation and the parietal peritoneum. For similar reasons, the classical signs like Rovsing's, Obturator and Psoas signs are encountered in 30-55% of patients [4, 12-13]. A patient of acute appendicitis in a labour is especially difficult to diagnose and requires a high index of suspicion. Labour may be associated with pain that lateralizes, fever if some degree of chorioamnionitis is present and vomiting. Persistence or progression of the symptoms after delivery should prompt re-evaluation to confirm or rule out appendicitis.

### Laboratory

Blood tests, particularly the white blood cell count (WBC) and differential (DLC) is usually done in patients with RLQ pain to confirm or exclude the suspected appendicitis and approximately 80 % of non-pregnant patients with documented appendicitis have a preoperative leucocytosis (white blood cell count >10,000 cells/  $\mu$ L) and shift to the left in the differential [14]. However, Lurie et al [15] states that it may not be helpful and reliable in pregnant women as the WBC and neutrophil counts gradually and significantly increase from the first to the third trimester (WBC count as high as 17000/ $\mu$ L). In a retrospective review of 66,993 consecutive deliveries by Mourad J et al.[16], including 67 (0.1%) women with a probable diagnosis of acute appendicitis, the WBC count in women with histologically proven appendicitis and in those with histologically normal appendices were 16,400 cells/  $\mu$ L and 14,000 cells/  $\mu$ L, respectively.

Urine analysis is not a specific aid in ruling out appendicitis. Pyuria and microscopic hematuria is reported in about 20 % of cases of appendicitis patients but urinary tract symptoms are frequent in acute appendicitis and hence their presence should not exclude the diagnosis of this disease [17].

Similarly elevated levels of C-reactive protein (CRP) are detectable in appendicitis, but this is a nonspecific sign of inflammation and hence unreliable [11,13]. Sand M et al.[18] have postulated that mild elevations in serum bilirubin (total bilirubin >1.0 mg/dL) may be considered as a marker for appendiceal perforation (sensitivity 70 %; specificity 86 %).

### Imaging

Due to non-classical presentation and non-specific laboratory investigations, diagnosis gets delayed. Hence imaging plays an important role in management of appendicitis in pregnancy in reducing delays in surgical intervention due to diagnostic uncertainty [13, 19-23]. Furthermore, imaging can aid in reducing negative appendectomies by revealing other probable causes of the patient's symptoms and signs. The imaging modalities include:

#### Ultrasonography (US)

Graded compression Ultrasonography (US) is the initial modality of choice for accurate diagnostic imaging of the appendix in pregnancy, especially in early gestation [19-21]. The sonographic features supporting the diagnosis of appendicitis include identification of a non-compressible, blind-ended, tubular multi-layered structure in the right lower quadrant with a maximal diameter greater than 6mm [19-20]. Other findings include periappendiceal fluid and thickening of the caecum. However, the normal appearing appendix does not exclude appendicitis unless sonographic findings suggest a likely alternative diagnosis (e.g., ovarian torsion, rupture corpus luteum, ectopic pregnancy etc).

In later gestation, the gravid uterus can interfere with visualization of the appendix and performing graded compression, leading to inconclusive ultrasound findings. In multivariate analysis, Hirsch et al. [20] found early gestational age to be independently associated with higher rate of accurate US results (OR = 0.92, 95% CI 0.85-0.99,  $p=0.39$ ). For diagnosing appendicitis in pregnancy, Williams and Shaw [22] found the sensitivity to range between 67 to 100 % and specificity ranged from 83 to 96 %, compared to general population where sensitivity and specificity were 86 and 96 %, respectively.

#### Magnetic Resonance Imaging (MRI)

Where readily available, MRI is an imaging modality of choice for pregnant patients for excluding acute appendicitis in pregnant women when clinical examination is inconclusive [23].

Long *et al.* [24] conducted a meta-analysis for evaluation of MRI in pregnant women with suspected appendicitis and included 6 studies of 12 to 148 patients of whom 2 to 14 patients subsequently had confirmed acute appendicitis. The results showed the pooled sensitivity and pooled specificity to be 91 percent (95%

CI 54-99) and 98 percent (95% CI 87-99), with positive predictive and negative predictive values of 86 and 99 percent, respectively. Pedrosa et al. [25] found the sensitivity, specificity, positive and negative predictive values of MRI for diagnosis of acute appendicitis in pregnancy to be 100, 93, 61, and 100 percent, respectively. Fonseca et al. [26] in his series found that magnetic resonance imaging in pregnant patients with suspected appendicitis does increase hospital charges but allows safe discharge from the emergency department and improves resource use.

MRI offers a feasible alternative to computed tomography (CT) because it avoids exposure to ionizing radiation. Gadolinium is not routinely administered due of theoretical fetal safety concerns, but may be used if essential [27]. However, if prolonged wait before MRI is anticipated, the increasing risk of perforation over time should be considered and undue delays for imaging studies should be avoided.

#### (Computed Tomography) CT-Scan

MRI and CT performs equally well in the confirming or ruling out appendicitis in pregnancy but due to the ionizing radiation, CT is less preferred modality in settings where MRI is available[28]. However, if MRI is not available and physical examination/ US is inconclusive, CT plays an important role [29]. Typical CT findings include the swollen appendix with a thickened wall and periappendiceal fat stranding. Peri-appendiceal fluid, faecolith and worms can also be detected. The CT may also detect other surgical and gynaecologic pathologies, which are included in the differential diagnosis. Shetty et al. [30] after analysis of CT scans during pregnancy for suspected appendicitis over 5 years found CT to provide an accurate diagnosis and be of value in avoiding false negative exploratory laparotomy with its consequent risk of maternal and fetal mortality and morbidity and hence justifies its use to reduce maternal mortality and mortality in patients with appendicitis.

#### Differential diagnosis

There is a wide range of diseases that may mimic appendicitis [3, 9, 31-32] and hence make it challenging to arrive at the diagnosis, without any significant delay [Table1]. The list includes disorders typically considered in non-pregnant individuals as well as pregnancy-related causes of lower abdominal pain, fever, leucocytosis, nausea/vomiting, and changes in bowel function[2, 31]. Only a thorough history and meticulous physical examination can lead the evaluating clinician to formulate a differential diagnosis that is appropriate for a particular patient. Hee and Viktrup [2] demonstrated that appendicitis occurred in approximately half of their cases and the other half suffered from pathologies including ovarian cysts, mesenteric adenitis, fibromyoma uteri, varicose veins in the parametria, ileus, salpingitis, and torsion.

There have also been reported cases in literature where appendicitis concurrently with conditions that form the differential diagnosis making the situations even more difficult and hazardous. Ankouze *et al.* [33], Hazebroek EJ *et al.* [34], and Riggs JC *et al.* [35] reported cases of simultaneous appendicitis and ectopic pregnancy.

### Complications

The most severe complication of appendicitis is perforation and in pregnancy, the percentage of perforated appendix can be as high as 43%, compared to 19% in the general population [36]. The risk of perforation also increases with the gestational age [37]. Anderson *et al.* [1] reported that perforation varied with gestational age approximating 6% in the first trimester, 10% in second and 13% in the third trimester. The consequences of perforation include localised or generalized peritonitis, sepsis, miscarriage, preterm labour and fetal or maternal death. In the series of Mourad *et al.* [16], of 23 patients of appendicitis at or greater than 24 weeks' gestational age, 19 (83%) had preterm contractions and an additional 3 patients (13%) had preterm labour with documented cervical change. In the series by Lemieux *et al.* [38], 8.1% patients delivered prior to 35 weeks' gestation and 18.1% delivered before term (<37 weeks) but there was no significant differences in the rates of preterm delivery, adverse outcome or operative time between trimesters of pregnancy. Butte *et al.* [39] had 15% premature delivery rate in their series. Tracey *et al.* [36] had premature deliveries in about 45% cases but all of the cases were late gestational with perforated appendix.

For the fetus, appendicitis is associated with a fetal loss risk of 1.5% to 14%, however the risk increases up to 35% after perforation [16, 40]. Lemieux *et al.* [38] did not observe any fetal loss. Ghazanfar *et al.* [6] had 14% fetal mortality rate in their series. Maternal mortality ranging from 0-2% has been reported in literature. Kazim *et al.* [4], Tracey *et al.* [36], Ghazanfar *et al.* [6] and Lemieux *et al.* [38] had no maternal mortality in their series of 38 patients.

### Treatment

#### Appendicitis

Urgent surgical intervention in the form of appendectomy is recommended, once the diagnosis of appendicitis is established. Intervention within 24 hours has a relatively lower rate of perforation of appendix and subsequent complications. Yilmaz *et al.* [10] recommends that the interval between the symptom onset and operation should never exceed 20 hours. The aim of the surgeon should be to operate upon the patient before perforation as studies have shown that after 36 hours of onset of symptoms the rate of perforation is between 16% and 36% and the risk of perforation increases 5% for every subsequent 12-hour period [41]. Perioperative antibiotic treatment should provide coverage for Gram-negative,

Gram-positive and anaerobes. The choice and dosage of a particular antibiotic should take into consideration the following factors [42]:

1. Teratogenic potential of the drug
2. Pregnancy related pharmacodynamic changes that result in reduced maternal plasma levels of antibiotics.

In a series by Hale *et al.* [43], perioperative antibiotics were administered to 94% of the patients undergoing appendectomies and second-generation cephalosporins were preferred in 60% of cases due to safer profile. There are reports of prophylactic usage of various colytic agents for uterine irritability; however their efficacy is debatable [4, 40].

### Perforation

The management of perforated appendix depends on whether the perforation is free or walled-off.

#### Free perforation

A free perforation causes intraperitoneal dissemination of pus and faecal material and increases the chances of preterm labour and delivery and fetal loss. These patients are typically quite ill and may be septic. The management includes urgent laparotomy with appendectomy and irrigation / drainage of the peritoneal cavity followed by intensive care.

#### Walled – off perforation

There is sparse literature on management of pregnant patients who present with long duration of symptoms and clinical/radiological findings of contained perforation though non-operative medical management is a reasonable option if the patient is not ill appearing as in non-pregnant states, immediate surgery is associated with increased morbidity due to dense adhesions and inflammation [44].

### Surgical approach (Open Vs Laparoscopic)

Open appendectomy and laparoscopic appendectomy are the two surgical techniques used in treating appendicitis. In recent years, laparoscopic surgery has been in vogue and has been propagated because of early ambulation, less wound infection, less postoperative pain, less narcotic use, lower risk of ileus and short postoperative recovery period but this approach still remains debated, especially in cases of suspected appendicitis in later gestation. Lemieux *et al.* [38], Sadot *et al.* [45] and Walsh *et al.* [46] consider laparoscopic approach to be a valuable option for pregnant, regardless of trimester due to the low rate of complication in their series. Walsh *et al.* [46] found significantly lower overall interruption of pregnancy rate of 11.3% by laparoscopic approach compared to the open method (11.3% vs. 7.7%  $p < 0.0068$ ).

However, Wilasrusmee *et al.* [47], on the basis of results of a systematic review and meta-analysis of studies

comparing laparoscopic and open appendectomy in pregnancy identified using Pub Med and Scopus search engines from January 1990 to July 2011, suggested that laparoscopic appendectomy in pregnant women might be associated with a greater risk of fetal loss.

The main concern of the laparoscopic method is the use of carbon dioxide (CO<sub>2</sub>) to create a pneumoperitoneum which exposes the fetus to CO<sub>2</sub>, increases intra abdominal pressure, which can potentially lead to preterm labour, decrease uterine blood flow and cause fetal acidosis [48]. Furthermore, the placement of a primary port or Veress needle can also potentially injure the fetus and cause a pneumoamnion [8]. To overcome the potential adverse effects of, it has been suggested to keep pneumoperitoneum pressures up to 12 mm Hg only and put the first trocar by an open entry/directly visualized optical trocar insertion technique.

If open surgical approach is adopted, then such an incision should be made that appendectomy is facilitated together with ability to perform peritoneal toilet in indicated cases with minimal manipulation of the pregnant uterus. Popkin *et al* [49] postulated that the incision for the removal of the appendix in pregnant patients in all trimesters can be successfully made over McBurney's point. Hodjati *et al*. [50] also did not notice any significant shift in the position of appendix that would mandate change in location of incision.

Due to concerns for maternal and fetal outcomes, a higher rate (23-40 %) of negative appendectomies is reported in literature, irrespective of the surgical approach efforts have to be made towards new diagnostic modalities to lower the negative appendectomy rate in this specific population [38].

### Fetal Monitoring

In view of the risks of preterm labour and fetal loss, fetal monitoring before and after surgery especially in later gestational age, is important. Dedicated fetal surveillance for the few days after surgery is expected to decrease the incidence of fetal loss. If there are no complications post-operatively and pregnancy progresses

without adverse event, the patient is recommended to resume the routines of effective pregnancy care [32].

### Post operative complications and long term outcome

Pregnant females can potentially suffer from all the complications that non-pregnant females have due to surgical intervention under general anaesthesia. However, infection, premature labour and deep vein thrombosis are the areas of concern. Butte *et al* [39] reported superficial wound infection in 15% and Kazim *et al* [4] reported superficial wound infection in 8% and organ space infection in 3% patients

Risk of premature onset of labour due to is generally quoted as 8 – 15% in the literature.(4, 38-39). The use of tocolytics in this situation is not well defined in literature (4, 40). Deep vein thrombosis (DVT) / pulmonary embolism (PE) is significant cause of morbidity and mortality during pregnancy and an area of concern that continues to be neglected (4). In the series by Kazim *et al* [4], only 8 (21%) of patients had been started on preoperative heparin prophylaxis and 2 patients had developed clinically significant PE.

The long-term prognosis for patients who undergo appendectomy during pregnancy seems to be good, but the data on the subject are limited to small observational series. Such women do not appear to be at increased risk of infertility or other complications. Viktrup and Lee [51], after studying 101 patients who underwent appendectomy during pregnancy postulated that appendectomy during pregnancy of a normal, inflamed or perforated appendix does not lead to clinically significant intraperitoneal adhesions or infertility .

Choi *et al* [52] followed up the progeny of 29 patients who underwent appendectomy during pregnancy and found that appendectomy during pregnancy is not associated with developmental delays in children, irrespective of the trimester in which the procedure was performed. All children in their study had normal motor, sensory, and social development by 3 years of age.

**Table1. Differential diagnosis of appendicitis in pregnancy**

Obstetric/Gynaecological	
Ectopic pregnancy	Miscarriage (early gestation) <i>Complete/Incomplete/Septic</i>
Twisted or ruptured ovarian/Corpus luteum cyst	Pelvic inflammatory disease
Preterm labor (advanced gestation)	Abruptio placentae
Red degeneration of uterine leiomyoma	Rupture of endometrioma
Non obstetric/non-gynaecological	
Urinary tract infection	Acute cholecystitis
Acute gastroenteritis	Right ureteric colic
Acute pyelonephritis	Perforated peptic ulcer
Mesenteric adenitis	Intestinal obstruction
Abdominal tuberculosis	Typhlitis

Meckel's diverticulitis	Terminal ileitis
Pneumonia	Diabetic ketoacidosis
Porphyria	Preherpetic pain on right tenth and eleventh dorsal nerves
Colonic/appendicular diverticulitis	Rectus sheath hematoma
Acute pancreatitis	Caecal tumour

## CONCLUSION

Appendicitis is the commonest non-obstetric emergency seen in pregnancy. The accurate diagnosis of appendicitis during pregnancy requires a high level of suspicion, clinical skills and appropriate utilization of imaging modalities. Delay in surgical intervention leads

to higher maternal and fetal complication rates and hence early surgical intervention is essential. The surgical approach can be open or laparoscopic. There are no long-term adverse effects on patients who undergo appendectomy in pregnancy or in their progeny.

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