

***Review Article***

**ACUTE APPENDICITIS IN PREGNANCY-CURRENT MANAGEMENT-REVIEW ARTICLE**

**Abstract**

The management of acute appendicitis in pregnancy is considered controversial, as there is no consensus in terms of the diagnosis, investigation, and treatment. Blood investigations like full blood count are of limited value due to the physiological changes that occur in pregnancy. The use of ultrasound abdomen has always been mandatory but magnetic resonance imaging (MRI) is slowly becoming an alternative in the investigation of this condition. Open appendectomy has always been the treatment of choice, but laparoscopic appendectomy is becoming an emerging trend in the management of acute appendicitis in pregnancy. We conducted this narrative review article to evaluate the diagnosis and management of acute appendicitis in pregnancy.

Keywords- Appendicitis in pregnancy, Laparoscopic appendectomy, Open appendectomy, Diagnosis of appendicitis in pregnancy.

**Introduction**

Acute appendicitis is one of the most common non- obstetric emergencies that occur in pregnant patients. It is seen in approximately one in 500 pregnancies per year, and mostly seen in the second trimester of pregnancy. The diagnosis is difficult due to the anatomical and physiological changes that occur during pregnancy.(1)

There is a difficulty in performing blood investigations like full blood count due to the physiological changes that occur during pregnancy and imaging is limited due to the risk of exposure of ionizing radiation to the fetus. (2)

The three management options for acute appendicitis in pregnancy are 1) open appendectomy,2) laparoscopic appendectomy and 3) non-operative management. The world society of laparoscopic surgeons (WSES) have suggested laparoscopic appendectomy as the preferred treatment of choice as it is associated with less pain, earlier recovery, and better wound infection rates.(3,4)

As there is no consensus on the diagnosis and management of acute appendicitis in pregnancy, we have conducted this review article to evaluate the clinical presentation, diagnosis, and treatment of this condition. We conducted a literature review using PUBMED, the Cochrane database of clinical reviews and Google scholar looking for clinical trials, observational studies, systemic reviews, review articles and meta-analysis from 1990 to 2022. The following keywords were used, “acute appendicitis in pregnancy”, “laparoscopic appendectomy in pregnancy”, “open appendectomy in Pregnancy” and “diagnosis of appendicitis in pregnancy”. All articles were in English language only and case reports and editorials were excluded.

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**Comment [Ma1]:** May be the spaces between hyphenations could be more spacious

**Comment [Ma2]:** Abdominal ultrasound?

**Comment [Ma3]:** A narrative review does not have the power to evaluate the diagnosis/management. For this it is better to do a retrospective or prospective series. A narrative review is a tool to find useful and good quality information about a topic, as in this case, so the authors can learn about it and spread the knowledge

**Comment [Ma4]:** There are no difficulties to perform the blood tests. The difficulty is about the result's interpretations

**Comment [Ma5]:** May be this is the main purpose of this paper. Should be stated and declared as it

**Comment [Ma6]:** The introduction should be written in present tense.

**Comment [Ma7]:** This part is how the authors do it, so should be placed in “Methods”

**Comment [Ma8]:** The key-words are only a few, and the authors comment about the clinical presentation, lab tests, imaging, treatment. Every item should have their own group of keywords. And this part should be posted in **Materials and methods**

**Comment [Ma9]:** At the end of the introduction the “main purpose” or “aim” of the work or “Objective” should be stated.

**Comment [Ma10]:** After the introduction the “Materials and methods” or just “Methods” should be placed. This section should be written in past tense and how the authors did it should be described. Please detail how many papers you chosen, how many rejects (and why), and specify how many papers were used for every discussed item. This is a narrative review, not a systematic one, so the authors could choose one publication and reject others, but is fully important to declare how the election was done. This could inform to the reader of a selection bias. If the authors have some bias before (that it is fine...), also should be stated. For example, if the authors are surgeons, may have a bias against the abx treatment.

Moreover, the authors may/ should comment this bias in the "discussion". This is very honest and transparent

**Comment [Ma11]:** After the methods, the results should be placed. In this case, the author should divide the results sections in 4 subsections

### Clinical presentation of acute appendicitis in pregnancy

The classical clinical presentation is abdominal pain in the periumbilical region that migrates to the right iliac fossa. Symptoms of anorexia, nausea and vomiting may also be present. But in the pregnant patient they are less likely to present with the classical symptoms, as the pregnancy progresses to the third trimester, the pain may migrate to the right flank or hypochondrium. Tenderness at McBurney's point is also less sensitive in pregnant patients as the pregnant uterus lifts and stretches the anterior abdominal wall and increases the distance from the inflamed appendix.(5)

Only one third of pregnant patients with acute appendicitis present with symptoms of rebound tenderness at McBurney's point and guarding over the right iliac fossa and one third have very minimal symptoms like pain in the right iliac fossa.(6)

Due to the alteration of the adjacent organs due to the augmentation of the gravid uterus and increased laxity of the anterior abdominal wall leads to diminished response to peritoneal irritation and reference of pain like tenderness over the right iliac fossa.(7)

It is important to note that none of the common clinical signs and symptoms are of help in the diagnosis of acute appendicitis in pregnancy. The specific signs like Rovsing's sign and the psoas sign have not been of any use in the diagnosis of acute appendicitis in pregnancy. General symptoms of fever and tachycardia may also not be present.(8)

The conclusion from these studies is that clinical examination is not specific in the diagnosis of acute appendicitis in pregnancy.

### Investigations in acute appendicitis in pregnancy

The most common laboratory test that is performed is the full blood count that can reveal leukocytosis, but this is seen in almost all pregnant patients, and has limited value in the diagnosis of acute appendicitis in pregnancy. Up to 80% of pregnant patients will have mild leukocytosis with the number increasing to 16,000 during the third trimester of pregnancy. Other parameters like urine Feme examination and C-reactive protein are non-specific markers of inflammation and are not sensitive in the diagnosis of acute appendicitis in pregnancy. The increase in the leukocyte count may increase the accuracy of diagnosis of acute appendicitis but its sensitivity is low in pregnant patients. (9)

Hence laboratory investigations have limited use in the diagnosis of acute appendicitis in pregnancy as physiological leukocytosis makes interpretation of the results difficult for the diagnosis. CRP is a phase reactant that increases in acute inflammation, but the increase is slower than with the white cell count and it reaches a maximum value in 24 to 48 hours. Blood investigations should be used as support parameters with other investigations like ultrasound to aid in the diagnosis of acute appendicitis in pregnancy.(10)

The use of the total white cell count-reactive protein, Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) when used with clinical examination and imaging are useful to aid in the diagnosis of acute appendicitis in pregnancy and to reduce negative appendectomy rates.(11,12)

Clinical scoring systems that include variables like history of abdominal pain and clinical signs, like tenderness at McBurney's point and blood investigations like leukocytosis perform better in pregnant patients. The RIPASA system was found to be the most suitable for guiding pregnant

**Comment [Ma12]:** In the narrative reviews, the authors will comment or present to the readers not their own knowledge about clinical presentation of acute appendicitis but the chosen paper's findings. So they have to cite their findings in every item or subsections.

Otherwise this article should be only a review's theme, like a chapter of a book, usually done by someone who knows a lot of the topic

**Comment [Ma13]:** This statement is one of the results or findings of the author's review and the source deserves to be cited

**Comment [Ma14]:** Please cite all the reviewed studies for this ( and every one) item

**Comment [Ma15]:** Laboratory tests could be more clear for the readers ?

**Comment [Ma16]:** Please cite

**Comment [Ma17]:** The acronyms should be explained at the first time, then could be used freely

**Comment [Ma18]:** Same as above for acronyms. Please cite the ref were RIPASA was described first

patients with suspected acute appendicitis for imaging and this can improve the outcome. Clinical scoring systems can be used as a guide for admitting patients with suspected acute appendicitis and performing imaging modalities like ultrasound and for monitoring patients, but their use is still limited in clinical practice. Although pain over the right iliac fossa is the most consistent sign on examination of a pregnant patient presenting with acute appendicitis, there is no single symptom or investigation that is diagnostic for this condition. A combination of clinical symptoms, blood investigations and imaging are required to diagnose patients that may require appendectomy.(13–15)

**Comment [Ma19]:** Please cite in which ref this is mentioned

**Comment [Ma20]:** Others well-known scoring systems like the Alvarado's score and AIRS its is also fine to mention it, because they are widespread. (Kollar D, McCartan DP, Bourke M, Cross KS, Dowdall J. Predicting acute appendicitis? A comparison of the Alvarado score, the appendicitis inflammatory response score and clinical assessment. World J Surg 2015; 39: 104–09)

### Imaging in acute appendicitis in pregnancy

The imaging of choice for acute appendicitis in pregnancy is ultrasound abdomen due to its easy assessable and does not involve any radiation exposure. It has the advantage of excluding other pathologies like twisted ovarian cyst and its sensitivity ranges from 67% to 100% and specificity of 83% to 96%. The following factors affect the performance of the ultrasound include the gestational age of the pregnancy, the body mass index (BMI) and the experience of the examiner. The study by Segev et al on the diagnostic performance of ultrasound in the diagnosis of acute appendicitis in pregnant and non-pregnant women. The cohort included 586 patients of which 494 patients were not pregnant and 92 were pregnant. The positive predictive value of ultrasound was 0.94 and 0.91 in the pregnant and non-pregnant group and the negative predictive value was 0.40 and 0.43 respectively. This study concluded that the diagnostic performance of ultrasound was the same for both pregnant and non-pregnant patients. The limitations of this study were that it was retrospective in nature.(1,16)

Kezamini et al conducted a prospective analytical study on accuracy of ultrasound in diagnosing acute appendicitis in pregnancy. A total of 58 patients were included in the study and they had undergone ultrasonography. The positive predictive value and negative predictive value were 80% and 52.9% respectively. This study concluded that ultrasonography is a helpful nonionizing imaging modality but due to its sensitivity and specificity further imaging modalities may be required for suspected cases of acute appendicitis in pregnancy. (17)

Magnetic resonance imaging (MRI) is useful to acute appendicitis in a pregnant woman when the clinical examination and ultrasound are inconclusive, and it avoids radiation exposure.

Cho et al conducted a systemic review to look at the diagnostic accuracy of magnetic resonance imaging (MRI) for acute appendicitis in pregnancy. A total of 22 studies were included, 2392 patients were included in the study. The diagnostic sensitivity and specificity were 91-98% and 90-98% and the conclusion from this systemic review was that magnetic resonance imaging (MRI) has a high accuracy for diagnosis of acute appendicitis in pregnancy and should be used in cases where ultrasound results are inconclusive.(18)

**Comment [Ma21]:** Systematic?

Motavaselian et al performed a systemic review and meta-analysis on the diagnostic performance of magnetic resonance imaging (MRI) in the detection of acute appendicitis in pregnancy. 26 studies were included and the sensitivity and specificity were 92% and 98% respectively, the positive likelihood ratio and negative likelihood ratio were 29.52 and 0.10. The conclusion of this study was that magnetic resonance imaging was highly sensitive, specific and accurate in the diagnosis of acute appendicitis in pregnancy and hence reduce unnecessary appendectomies.(19)

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Burns et al conducted a retrospective review on the performance of magnetic resonance imaging (MRI) for the diagnosis of acute appendicitis in pregnancy. A total of 63 patients were included

**Comment [Ma24]:** Here is an interesting topic that should be mentioned also: negative appendectomies rate: Which is the rate in non-pregnant population and in pregnancy trough the trimesters ?, as as it is a marker of good diagnosis, and the surgeons should compare their numbers.

and the results showed that the sensitivity and specificity were 75% and 100% respectively. This study concluded that magnetic resonance imaging (MRI) is useful as a first line investigation in the diagnosis of acute appendicitis in pregnancy. (20)

Magnetic resonance imaging (MRI) is useful to acute appendicitis in a pregnant woman when the clinical examination and ultrasound are inconclusive, and it avoids radiation exposure. Kave et al conducted a systemic review and meta-analysis on the clinical use of MRI in the diagnosis of acute appendicitis in pregnant women. 19 studies were included; 17 was retrospective and two were prospective and it involved 2400 patients. The sensitivity of Magnetic resonance imaging (MRI) in the diagnosis of acute appendicitis in pregnancy was 91.8% and the specificity was 97.9%. Hence the conclusion from this study was that Magnetic resonance imaging (MRI) is an excellent investigation for pregnant patients with suspected acute appendicitis as there is no radiation exposure and can be performed in any stage of pregnancy with no evidence of side effects to the fetus. The drawback of this study was that it was predominantly retrospective in nature. (21)

The World Society of Emergency Surgeons (WSES) recommended that graded compression trans abdominal ultrasound is the preferred initial imaging for suspected pregnant patients with acute appendicitis and magnetic resonance imaging (MRI) being reserved for pregnant patients with inconclusive ultrasound. (4)

Computed tomography (CT) is readily available, but it is generally not indicated due to the exposure of ionizing radiation and the use of oral and intravenous contrast that exposes the fetus to these risks. (22)

The summary of all these studies were that ultrasound should be the initial imaging of choice and if the findings were inconclusive, then magnetic resonance imaging (MRI) should be done for patients who are suspected of having acute appendicitis in pregnancy.

### **Treatment of acute appendicitis in pregnancy**

The treatment of acute appendicitis in pregnancy is appendectomy and it should not be delayed as the risk of perforation of the appendix is increased. The traditional treatment option has always been open appendectomy. The maternal mortality is comparable to non-pregnant patients with acute appendicitis. The risk of fetal loss increases with delay in the diagnosis and the presence of complications like abscess formation or generalized peritonitis. Laparoscopic appendectomy is emerging as a procedure that can be performed successfully in pregnant patients with acute appendicitis but the long-term data on its safety and efficacy are still limited. (23,24)

Several systemic reviews looked at the safety and efficacy of laparoscopic appendectomy versus open appendectomy in the management of acute appendicitis in pregnancy. Most of the cases were performed on patients with a gestational age of 24 and there were higher fetal losses in the laparoscopic appendectomy group, but the incidence of preterm labor was lower. The conclusion of these systemic review was that the complication rates of laparoscopic appendectomy was low but due to the higher rate of fetal loss when compared to open appendectomy, and in the interest of fetal wellbeing the open procedure should be offered to the patient. The limitations of the systemic review were that the cases were from retrospective studies. (25–27)

A few meta-analyses were done on the safety and perioperative mortality on laparoscopic appendectomy in the management of acute appendicitis in pregnancy. There was no significant difference in the wound infection rate, duration of operation and hospital stay. The conclusion of

Comment [Ma25]: systematic

Comment [Ma26]: systematic

the systemic review and meta-analysis was that laparoscopic appendectomy was associated with a higher risk of fetal loss when compared to open appendectomy.(28–30)

The World Society of Emergency Surgeons suggested that laparoscopic appendectomy should be the preferred to open appendectomy in the treatment of acute appendicitis in pregnancy as it is safe and feasible when the expertise is available. The European Association of Emergency Surgeons (EAES) concluded that no recommendations can be made in the management of acute appendicitis in pregnancy with regards to the surgical approach and until more evidence becomes available, the surgical approach should be at the discretion of the operating surgeon.(4,31) Based on the reviewed studies, it can be concluded that laparoscopic appendectomy is associated with a slight increase in fetal loss when compared with open appendectomy, but it is still recommended in the management of acute appendicitis in pregnancy. Further large prospective studies are needed to evaluate the efficacy of laparoscopic appendectomy in pregnancy.

Primary conservative treatment in the management of acute appendicitis in pregnancy is not indicated as it is associated with a higher risk of maternal morbidity and fetal loss and several retrospective studies concluded that it should not be recommended for treatment of acute appendicitis in pregnancy.(32–34)

Based on these studies, the conclusion was that laparoscopic appendectomy is associated with a slight increase in fetal loss when compared with open appendectomy, but it is still recommended in the management of acute appendicitis in pregnancy. Further large prospective studies are needed to evaluate the efficacy of laparoscopic appendectomy in pregnancy.

### Conclusion

Based on the available evidence the diagnosis of acute appendicitis in pregnancy should not be delayed, clinical examination and blood investigations are of limited use. Ultrasound abdomen should be the first line imaging of choice due to its easy availability, but magnetic resonance imaging (MRI) is emerging as an alternative in case where the diagnosis is uncertain. The treatment of acute appendicitis in pregnancy is surgical treatment. Open appendectomy is the treatment of choice, but laparoscopic appendectomy is slowly emerging as a treatment, although it is associated with a slightly increased risk of fetal loss. There is no role for conservative treatment in the management of acute appendicitis in pregnancy. There is no consensus on the management of acute appendicitis in pregnancy and the surgeon managing the patients will decide the treatment option for the patient.

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**Comment [Ma27]:** A systematic review has been appear recently : Candrawinata V, Hanafi R, Baskoro BA *et al*. Antibiotic versus surgery in the treatment of acute appendicitis in the pregnant population: A systematic review and meta-analysis [version 1; peer review: awaiting peer review]. *F1000Research* 2023, 12:188 (<https://doi.org/10.12688/f1000research.129906.1>)

**Comment [Ma28]:** May be it is better to state that “the surgeon in charge of every patient...” and emphasize that the treatment decision is made always in accordance or together with her (informed consent)

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Table 1

Study	N=numbers	Positive predictive value(PPV)	Negative predictive value	Study type
Segev et al	92	0.94	0.40	Case control study
Kezamini et al	58	80%	52.9%	Prospective study

Summary of the studies that involved ultrasound in the diagnosis of acute appendicitis in pregnancy.

Table 2

Study	N=numbers	Sensitivity	Specificity	Study type
Kave et al	2,400	91.8%	97.7%	Meta-analysis
Cho et al	2,392	91-98%	90-98%	Systemic review
Motavaselian et al	709	92%	98%	Systemic review
Burns et al	63	75%	100%	Retrospective study

Summary of the studies that involved magnetic resonance imaging (MRI) in the diagnosis of acute appendicitis.

Table 3

study	N=numbers	Fetal loss	Study type
Wilarusmee et al	599	1.9% relative risk	Meta-analysis
Walsh et al	637	5.6%	Meta-analysis
Zhang et al	2,477	3.8%	Meta-analysis

Summary of the studies that show fetal loss after laparoscopic appendectomy for acute appendicitis in pregnancy.

UNDER PEER REVIEW