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Impact of appendicitis during pregnancy: No delay in accurate diagnosis and treatment

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HIGHLIGHTS

- Ultrasonography has a high rate of non-visualization of the appendix.
- (Perforated) appendicitis is known to be associated with a high rate of maternal and fetal morbidity and mortality.
- Prematurity was seen following a negative appendectomy (33%) and perforated appendicitis (33%).
- A rapid and accurate diagnosis of appendicitis is particularly critical in pregnant patients.
- We recommend clinicians to consider an MRI to improve diagnostic accuracy to reduce the rate of negative appendectomies.

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ABSTRACT

Background: Acute appendicitis during pregnancy may be associated with serious maternal and/or fetal complications. To date, the optimal clinical approach to the management of pregnant women suspected of having acute appendicitis is subject to debate. The purpose of this retrospective study was to provide recommendations for prospective clinical management of pregnant patients with suspected appendicitis.
Method: Case records of all pregnant patients suspected of having appendicitis whom underwent appendectomy at our hospital between 1990 and 2010 were reviewed.
Results: Appendicitis was histologically verified in fifteen of twenty-one pregnant women, of whom six were diagnosed with perforated appendicitis. Maternal morbidity was seen in two cases. Premature delivery occurred in two out of six cases with perforated appendicitis cases and two out of six cases following a negative appendectomy. Perinatal mortality did not occur.
Conclusion: Both (perforated) appendicitis and negative appendectomy during pregnancy are associated with a high risk of premature delivery. Clinical presentation and imaging remains vital in deciding whether surgical intervention is indicated. We recommend to cautiously weigh the risks of delay until correct diagnosis with associated increased risk of appendiceal perforation and the risk of unnecessary surgical intervention. Based upon current literature, we recommend clinicians to consider an MRI following an inconclusive or negative abdominal ultrasound aiming to improve diagnostic accuracy to reduce the rate of negative appendectomies. Accurate and prompt diagnosis of acute appendicitis should be strived for to avoid unnecessary exploration and to aim for timely surgical intervention in pregnant women suspected of having appendicitis.

1. Introduction

Acute appendicitis is the most common non-obstetric surgical emergency during pregnancy. A rapid and accurate diagnosis of appendicitis is particularly critical in pregnant patients because non-perforated appendicitis can quickly progress to appendiceal rupture, which is associated with high rates of early delivery, miscarriage, and fetal loss [1–4]. During pregnancy, perforated appendicitis is reported to occur in 14.9%–43% [1–5]. Traditionally, an aggressive surgical approach has been advocated, because the clinical diagnosis of appendicitis is often unreliable and a delay in the correct diagnosis of appendicitis was thought to be associated

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with a higher risk of appendiceal perforation. Until recently, a high negative appendectomy rate of 23–37% [1–8] during pregnancy versus 14%–18% [1,6] in the non-pregnant population was generally accepted and justified in an attempt to avoid possible serious complications associated with perforation. However, a negative appendectomy during pregnancy appears more harmful to mother and child than previously assumed [1,3,6]. Following negative appendectomy, premature delivery and fetal loss are seen in 10%–26% [1,6] and 3.0%–7.3% [1,3,6], respectively.

Currently, the optimal approach of a pregnant patient suspected of having appendicitis is not evident. The need for appropriate and prompt surgical treatment to avoid appendiceal perforation with associated adverse outcome has to be well balanced with the need for additional imaging to enhance preoperative diagnostic accuracy to avoid mortality and morbidity associated with a negative appendectomy. The objective of this retrospective study was to evaluate clinical presentation, imaging, management, and outcome of pregnant patients whom underwent an appendectomy at our hospital. The overall aim of this study was to provide recommendations for the prospective clinical management of pregnant women suspected of having appendicitis.

2. Methods

Case records of all pregnant women whom underwent an appendectomy for suspected appendicitis at the University Medical Center in Groningen (a tertiary care hospital) between 1990 and 2010 were reviewed. Firstly, hospital procedure codes were used to identify all female patients whom underwent an appendectomy during the study period. Secondly, patient identification numbers were matched to those available in the electronic delivery database of the department of obstetrics, which provided us with the hospital numbers of all women, who had a contemporaneous pregnancy. Patient demographics, presenting signs and symptoms, laboratory values, imaging results, details of the surgical intervention, histological results, total length of hospital stay, and maternal and fetal outcome were documented. The Institutional Review Board of the University Medical Center in Groningen approved this study, as part of a large retrospective study concerning various aspects of appendicitis.

Abdominal ultrasonography with graded compression was generally performed as the initial imaging test. When a CT scan was performed as a secondary imaging modality, both intravenous and oral contrast was used. Ultrasonography (US) and computed tomography (CT) scans were recorded as true positive, false positive, true negative, false negative, or equivocal regarding the diagnosis of appendicitis. Consultants or senior registrars in the field of general surgery performed the appendectomies. Pre- and post-operative patient care was provided upon an interdisciplinary basis by the departments of general surgery and obstetrics. Final diagnosis was based upon macroscopic findings during surgery verified by histological examination of the resected specimen. A negative appendectomy was defined as surgical resection of an appendix without histological confirmation of appendiceal inflammation. Non-perforated appendicitis was defined as an inflamed appendix without signs of perforation. Complicated appendicitis was defined as appendicitis with evidence of perforation, appendiceal abscess, and/or (generalized) peritonitis.

The main outcome variables were maternal and fetal morbidity and mortality. Postoperative complications were graded using the Clavien–Dindo classification [9] for surgical complications. Spontaneous abortion was defined as the spontaneous, premature expulsion of a non-viable embryo or fetus from the uterus before 20 weeks of gestation. Fetal loss was defined as the spontaneous loss of pregnancy after 20 weeks of gestation. Preterm delivery was defined as delivery before the gestational age of 37 weeks. Perinatal mortality was defined as fetal loss and early neonatal mortality, which is defined as death of a live-born baby within the first seven days of life.

Relevant variables were analysed using descriptive statistics. Fetal and maternal outcomes were stratified by surgical approach (open versus laparoscopic appendectomy) and final diagnosis (non-inflamed appendix, non-perforated appendicitis, and perforated appendicitis). Moreover, our patients were classified according to gestational age, namely first (0–12 weeks), second (13–27 weeks), and third trimester (28–42 weeks). Statistical analyses were performed using SPSS for Windows, version 19.0 (SPSS inc, Chicago, IL, USA).

3. Results

During the 20-year period under review, a total of 21 pregnant women underwent an appendectomy for suspected appendicitis. Overall, 15 women (71%) had histologically proven appendicitis, of whom nine women (43%) had non-perforated appendicitis and six women (29%) had perforated appendicitis. The negative appendectomy rate was 29% (N = 6). A total of 25.443 deliveries were conducted at the obstetrical department during the same period, corresponding to an incidence of one case of acute appendicitis in 1777 births. Demographic characteristics of the study population are shown in Table 1.

As shown in Table 2, the most frequent presenting symptom was pain located in the right lower abdominal quadrant (95%). Other common presenting symptoms were nausea (90%), vomiting (48%), and loss of appetite (48%). A classical history of periumbilical pain migrating to the right lower abdominal quadrant occurred in ten out of twenty-one women (48%), of whom two turned out to have a normal appendix.

Upon physical examination right lower quadrant abdominal pain or diffuse abdominal tenderness was seen in the majority of our study population (Table 3). Fourteen women showed signs of rebound tenderness (67%) of whom four did not have appendicitis. None of the women showed signs of involuntary guarding. Three of fifteen women with histologically confirmed appendicitis developed fever (20%).

Infection markers such as leucocyte count and c-reactive protein (Table 4) were not significantly raised in pregnant women with appendicitis compared to pregnant women with a normal appendix. Of note is that a normal c-reactive protein value (≤10 mg/L) was seen in five out of nine pregnant women with non-perforated appendicitis.

Abdominal US was performed in eight women (38%). In six cases (75%) the appendix could not be visualized during US, of whom two women were diagnosed with non-perforated appendicitis and one

Table 1
Demographic characteristics of the entire study population (N = 21).

Patient characteristics	Median (range)
Patient age (years)	30.8 (23.6–39.6)
Time interval between onset of symptoms and appendectomy (hours)	48 (11–240)
Surgical details	**Median (range)**
Gestational age at the time of surgery (weeks)	25 (5–39)
Duration of operation (minutes)	60 (25–184)
Length of hospital stay (days)	6.5 (1–73)
Obstetrical details	**Median (range)**
Gestational age at delivery (weeks)	39^{+5} (26^{+2}–42^{+2})
Birth weight (grams)	3670 (1020–5090)
Parity	**No. of women (%)**
Primiparous	18 (85.8)
Multiparous	3 (14.3)

Table 2
Presenting symptoms of the entire study population related to final diagnosis (N = 21).

Symptoms	Final diagnosis (number of cases)		
	Normal appendix (N = 6)	Non-perforated appendicitis (N = 9)	Perforated appendicitis (N = 6)
Abdominal pain			
RLQ[1]	5	9	6
RUQ[2]	1	1	3
Diffuse	3	6	4
Migration of pain	2	4	4
Nausea	3	4	2
Nausea and vomiting	1	5	4
Appetite			
Loss of appetite	3	3	4
Normal appetite	0	2	1
Defecation abnormality	2	3	2

Abbreviations: [1]RLQ = Right Lower Quadrant, [2]RUQ = Right Upper Quadrant.

with perforated appendicitis. Following non-visualization of the appendix during US, CT was used as a secondary diagnostic imaging modality in two patients (10%; both in third trimester of pregnancy). Radiology reports of the CT scans mentioned that both appendices showed signs of inflammation. However, appendicitis was confirmed in only one of the abovementioned cases. Magnetic resonance imaging (MRI) was not used as a diagnostic modality in this population.

The appendix was adequately visualized during US in two cases (25%). The sonographer reported obvious signs of inflammation in one of the two cases, which histologically was verified as a perforated appendix. The other US report mentioned the possibility of an inflamed appendix, which turned out to be a non-perforated appendicitis. Of the thirteen women, whom did not undergo abdominal US, ten turned out to have appendicitis (77%).

Seven women (33%) underwent a laparoscopic appendectomy, of whom two women required peroperative conversion to an open appendectomy. Fourteen women (67%) underwent an open appendectomy. Three women (14%) underwent surgical intervention during the first trimester, ten women (48%) during the second trimester, and eight women (38%) during the third trimester. Peroperatively, a perforated and/or gangrenous appendix was macroscopically seen in eight patients (38.1%) and a peri-appendiceal or pelvic abscess was seen in two patients (10%). Table 5 shows maternal and fetal outcome related to type of surgical intervention, final diagnosis, gestational age, patient delay until presentation, and hospital delay until appendectomy. The median length of delay was 30 h (range 11–50 h) and 88 h (range 24–240 h) in case of non-perforated appendicitis and perforated appendicitis, respectively. Delay in treatment seems to be associated with a higher rate of maternal and fetal complications (Table 5).

Table 5 shows that two women whom underwent an open appendectomy for a perforated appendicitis experienced a postoperative complication. Illustrative, one patient developed intra-abdominal abscesses requiring a relaparotomy and she simultaneously underwent a caesarean section (Clavien–Dindo surgical complication Grade IIIB). Another patient was conservatively treated for a postoperative ileus (Clavien–Dindo surgical complication Grade I). No postoperative maternal complications were seen in patients whom underwent a negative appendectomy. Maternal mortality did not occur.

The majority of women carried their pregnancy to term and all delivered viable infants. Four women (14.3%) underwent a caesarean section. Four women delivered prematurely, of whom two following a negative appendectomy (33% of negative appendectomy cases) and two following an open appendectomy of a perforated appendicitis (33% of perforated appendicitis cases). Fetal loss did not occur.

4. Discussion

To date, the optimal clinical approach to the management of pregnant women suspected of having acute appendicitis is subject to debate. In this retrospective study, we evaluated all pregnant patients whom underwent appendectomy for suspected appendicitis at our tertiary care hospital aiming to be able to provide recommendations for prospective clinical management.

A considerable number of studies on appendicitis during pregnancy have been reported, but are often fairly limited based upon the generally low prevalence of appendicitis during pregnancy. At our tertiary care hospital, the incidence of appendicitis during pregnancy was 1 in 1777 births during the period between 1990 and 2010. The diagnostic accuracy of 71% is comparable to rates reported by other authors (64%–77% [1–4,6–8]).

As reported in other series, the preoperative diagnosis of acute appendicitis is often inaccurate during pregnancy. Clinically establishing the diagnosis of appendicitis remains challenging for the treating physician, as physiological and anatomical changes associated with pregnancy may obscure the diagnosis of appendicitis [1,2,7,10–12]. Symptoms, such as nausea and vomiting, can obscure or even delay correct diagnosis as these symptoms occur frequently during pregnancy [2,7,10–12]. Signs, such as rebound tenderness and muscle guarding, are valuable in non-pregnant patients, but these signs are not often seen in pregnant patients due to alteration of the location of nearby organs owing to augmentation of the gravid uterus and the increased laxity of the abdominal wall [10,12]. These physical alterations result in a diminished response to peritoneal irritation and reference of pain perception. Physiological leucocytosis associated with pregnancy can obscure an increased leukocyte count related to disease [2,7]. Consistent with previous literature, there were no significant differences between patients with and without appendicitis regarding frequency of presenting symptoms or laboratory results [2]. Noticeable, in our study pain in the right lower quadrant of the abdomen was present in all cases with pathologically proven appendicitis, which is mentioned in 76%–82.4% of cases in previous literature [2,7]. Only 53% of our patients with pathologically proven appendicitis reported a classic history of diffuse or periumbilical pain migrating to the right lower abdominal quadrant (versus 29%–48% reported in literature [2,5]). Furthermore, numerous pregnancy-related, gynaecological and other abdominal differential diagnoses must be taking into account when trying to establish the correct diagnosis during pregnancy [4].

The need for prompt surgical intervention in case of suspected appendicitis to avoid adverse outcome related to appendiceal perforation has to be balanced with the need for additional imaging to enhance preoperative diagnostic accuracy to avoid mortality and morbidity associated with unnecessary surgical intervention. In accordance with McGory et al. [1], we found that negative appendectomies are associated with a high rate of fetal morbidity. McGory et al. [1] concluded that it appears that the greatest opportunity to improve fetal outcomes is by improving diagnostic accuracy and reducing the rate of negative appendectomy in pregnant women. Ito et al. [6] recommend careful preoperative assessment and imaging to avoid unnecessary exploration during pregnancy. Perhaps it might be an option to leave a macroscopically non-inflamed appendix in situ during laparoscopy, but further studies are needed in the future in order to establish if this might be a safe option.

Table 3
Signs during physical examination of women suspected of having appendicitis related to final diagnosis (N = 21).

Signs[a]	Final diagnosis (number of cases)		
	Normal appendix (N = 6)	Non-perforated appendicitis (N = 9)	Perforated appendicitis (N = 6)
Generally looks unwell	1	2	3
Auscultation of bowel sounds: normal/increased/decreased	1/0/2	3/0/0	1/1/2
Abdominal tympany: normal/increased	1/0	0/0	1/2
Tender upon palpitation	5	7	5
Rebound tenderness	5	12	8
Flank tenderness	2	0	1
Rovsing's sign positive	2	0	1
Psoas sign positive	0	1	0
Painful digital rectal/vaginal examination	0/1	1/1	1/0
Temperature (°C)			
Fever (≥38 °C)	2	1	2
Afebrile (<38 °C)	2	7	3

[a] Regarding the abovementioned variables, some data may be lacking due to the possibility of incomplete documentation in medical files/partial physical examination of treating physician.

US, MRI and CT are the main imaging techniques used to increase diagnostic accuracy in pregnant patients suspected of having appendicitis [1,10,11]. In the current study, US was performed in only a minority of cases (38%) and thus a number of cases in this study did not undergo primary imaging before surgical intervention. Apparently, rapid surgical intervention seemed indicated and validated by the treating physician based upon clinical suspicion of appendicitis based upon clinical presentation alone or the treating physician might have expected non-visualization of the appendix during ultrasonography. In our study, the diagnosis of appendicitis was confirmed in 77% (10/13) of the women whom did not undergo ultrasonography.

Worldwide, US is widely used as initial imaging technique for evaluation of a pregnant patient suspected of having appendicitis due to near-universal availability, non-invasive character, safety, lower cost compared to cross-sectional modalities, and lack of ionizing radiation/contrast medium [8,10–14]. The reported diagnostic performance of US for detecting appendicitis in pregnancy varies widely in the literature [13]. Sensitivity of 20%–46.1% [5,13,15,16] and specificity of 95.4%–100% [5,15,16] is reported. However, US seems to be of limited utility during pregnancy due to the high rate of non-visualization of the appendix (88%–97%) [13,15]. This is possibly related to altered anatomic location of the appendix, enlarged uterus with viable fetus, obesity, overlying bowel gas, and experience of the operator [7,8,10–12,14–16]. Thus, the advantage of lower cost, availability, and lack of ionizing radiation must be weighed against the time required to perform an US as primary imaging modality despite the high likelihood of non-diagnostic outcome, necessitating further workup and ultimately delaying diagnosis and definitive treatment [13]. US as first-line imaging may result in unnecessary cost and delay in diagnosis in during pregnancy [13].

Wallace et al. [11] compared negative appendectomy rates in pregnant patients suspected of having appendicitis, who were clinically evaluated (54%), who underwent ultrasonographic evaluation (36%), and who underwent ultrasound/CT evaluation (8%). They reported a significant reduction in the negative appendectomy rate in the ultrasound/CT group compared to clinical evaluation group (8% versus 54%, $p < 0.05$) [11]. In the current study, CT was cautiously used as a secondary diagnostic modality in only two patients following an inconclusive ultrasound (during third trimester of pregnancy). Previous literature states that additional CT imaging can reduce the negative appendectomy rate during pregnancy [11,16]. However, ionizing radiation is a significant disadvantage of CT because it is a potential hazard to the developing fetus [11,17]. When the exposure to radiation during a CT scan is less than 500 mGy, no increase in adverse pregnancy outcomes is seen, but the risk for childhood cancer is estimated to increase by 0.1% following a fetal radiation dose of 100 mGy [17]. Therefore, given the potential teratogenic and carcinogenic effects of ionizing radiation on the developing fetus, diagnostic medical imaging should be avoided where possible in a pregnant patient and used only when absolutely necessary [10,11].

Table 4
Laboratory findings in women suspected of having appendicitis related to final diagnosis (N = 21).

Laboratory values	Final diagnosis (number of cases)		
	Normal appendix (N = 6)	Non-perforated appendicitis (N = 9)	Perforated appendicitis (N = 6)
Leucocyte count (cells/mm^3)			
Within normal limits (<10.000 cells/mm^3)	0	0	0
Elevated (≥10.000 and <16.000 cells/mm^3)	4	6	2
Elevated (≥16.000 cells/mm^3)	2	3	4
C-reactive protein (mg/L)			
Missing data	1		1
Within normal limits (≤10 mg/L)		5	
Elevated (>10 mg/L)	5	4	5

Table 5
Maternal and fetal outcome related to type of surgical intervention, final diagnosis, gestational age, patient delay until presentation and hospital delay until appendectomy.

	Maternal and fetal outcome		
	Uncomplicated	Maternal complication	Fetal complication
Type of surgical intervention			
Laparoscopic appendectomy	4	Nil	FII[4]
Open appendectomy	1	Nil	Nil
McBurney's incision	7	Nil	FI[3]
Median laparotomy	3	M2[2]	FIII[5] + FIV[6]
Conversion	1	M1[1]	Nil
Delay			
Unknown delay	2	Nil	Nil
<24 h	1	Nil	Nil
24–47 h	7	M2[2]	FIV[6]
48–71 h	3	Nil	FI[3] + FII[4]
≥72 h	3	M1[1]	FIII[5]
Final diagnosis			
Normal appendix	4	Nil	FI[3] + FII[4]
Non-perforated appendicitis	9	Nil	Nil
Perforated appendicitis	3	M1[1] + M2[2]	FIII[5] + FIV[6]
Trimester of pregnancy			
First	3	Nil	Nil
Second	7	M1[1]	FII[4] + FIII[5]
Third	6	M2[2]	FI[3] + FIV[6]

Abbreviations: [1]M1 = Mother 1, [2]M2 = Mother 2, [3]FI = Fetus I, [4]FII = Fetus II, [5]FIII = Fetus III, [6]FIV = Fetus IV.

However, MRI provides a valuable tool for evaluation of pregnant patients with right lower abdominal quadrant pain due to features such as lack of ionizing radiation, the excellent safety profile, the exceptional characterization of pathologic tissue, and the capability of direct multiplanar cross-sectional imaging [10,12,14]. Moreover, MRI provides a systemic evaluation of the abdomen and/or pelvis, which enables identifying appendicitis as well as numerous other diagnoses [18]. MRI has a reported sensitivity of 80%–100% [5,15,18] and has the major diagnostic strength of being highly specific (93%–100% [5,15,18]). In comparison to ultrasonography, MRI visualizes a higher percentage of appendices (52%–66.7% [13,15] versus 3%–12% [13,15]) Rapp et al. [18] concluded that the routine incorporation of MRI into the clinical workup for suspicion of appendicitis in pregnant patients was associated with a decrease in the negative appendectomy rate of 47% without a significant change in perforation rate. At our institution, MRI was not employed in the diagnostic workup, possibly due to the limited availability and experience.

When initial ultrasound findings are indeterminate, MRI seems the preferred additional imaging modality [5,8,10,15]. However, when MRI is not readily available and the potential risks of radiation to the fetus are outweighed by serious, immediate complications that could result from a missed diagnosis, a CT scan should be considered to increase pre-operative accuracy of the diagnosis [10,12,14,16]. Imaging protocols should be modified to reduce fetal radiation exposure especially during the first trimester and radiation dose according to the ALARA-principle (as low as reasonably achievable) [10]. Another consideration is that improved preoperative diagnostic accuracy may lead to a reduced number of negative appendectomies. A reduction in unnecessary surgical intervention leads to prevention of exposure of pregnant patients to the possible risks associated with surgical intervention and anesthetic agents. These can cause changes in uteroplacental perfusion due to hypotension or aortocaval compression and potential teratogenic effects of anesthetic drugs [19].

Currently, the optimal surgical technique to be used to treat acute appendicitis during pregnancy is yet to be established. Presently, the choice of surgical approach is possibly based upon trimester of pregnancy and surgeon's preference. [3,12] In this study both laparoscopic and open procedures were performed in the first and second trimester, whereas in the third trimester only open appendectomies were performed. Representative results regarding safety issues and outcome of surgical technique cannot be reported based upon our limited sample size.

In this study, a relatively high rate two out of six women with perforated appendicitis (33%) delivered prematurely compared to rates varying between 11% and 28% reported in current literature [1,4,6]. All cases of non-perforated appendicitis delivered at term, whereas in previous literature premature delivery rates varying between 4% and 20% are reported [1,6]. Equally important, one third of our women delivered prematurely following a negative appendectomy, which is also relatively high compared to 10%–26% reported in literature [1,6].

There was no case of fetal demise in this series of 21 patients. Fetal loss rates of 6%–21.4% [1,3,4,6] and 2%–10% [1,3,4,6] are reported in other series for cases with perforated appendicitis and non-perforated appendicitis, respectively. In our series, delay in treatment seems to be associated with a higher rate of maternal and fetal complications. Tamir et al. [2] found that perforated appendicitis (43%) occurred in cases, whom had symptoms exceeding 24 h ($p < 0.0005$). Establishing the diagnosis of appendicitis accurately and promptly is of the utmost importance, as delay in establishing appendicitis during pregnancy and delay until surgical intervention may lead to fetal and/or maternal morbidity or mortality.

This study has several limitations. First and foremost are the limitations inherent to retrospective analysis. Also, the sample size may limit interpretation of some of the outcomes. Another limitation is heterogeneity in diagnostic workup, surgical intervention, and pathological evaluation. Multiple surgeons performed the appendectomies and multiple pathologists evaluated the obtained specimens. However, this set up does reflect real-world practice and the protocol for pathologic evaluation, the indication for appendectomy, and the definitions used remained constant over the study period.

5. Conclusion

This study shows that delay in surgical treatment of appendicitis during pregnancy seems to be associated with a higher rate of maternal and fetal complications. Furthermore, this study confirms that both a negative appendectomy and perforated appendicitis during pregnancy result in increased rates of prematurity. These results indicate that prompt and accurate diagnosis is extremely important. In accordance with other studies, the diagnosis of appendicitis during pregnancy remains inaccurate based upon the combination of history of presenting complaint, physical examination, laboratory results, and ultrasonography. Based upon current clinical literature, we recommend that clinicians should consider performing an MRI as first choice additional investigation when appendicitis is suspected during pregnancy. Appendectomy should be performed as soon as possible when MRI is suggestive of appendicitis.

Ethical approval

The Institutional Review Board of the University Medical Center in Groningen approved this study, as part of a large retrospective study concerning various aspects of appendicitis.

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Author contribution

L. Aggenbach and H.S. Hofker carry joint responsibility for the conception and design of the study; L. Aggenbach was responsible for the acquisition of data, (statistical) analysis, interpretation of data, and drafting of the article; G.G. Zeeman, A.E.P. Cantineau, S.J. Gordijn, and H.S. Hofker also carried equal responsibility for interpretation of the data and were responsible for critically revising the article for important intellectual content; and H.S. Hofker was responsible for supervision of the study. All authors listed have reviewed, approved, and provided written consent for submission of the manuscript for publication.

Conflicts of interest

Nil conflicts of interest.

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