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Validation of the Appendicitis Inflammatory Response (AIR) score during pregnancy: A nested case–control study

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Abstract

Objectives: Appendicitis poses diagnostic challenges. A correct diagnosis is important during pregnancy to avoid unnecessary surgery on the one hand and delayed surgery on the other hand, as both may negatively affect pregnancy outcomes. Clinical scores for risk-stratified management of suspected appendicitis are well established in adults but have not been validated during pregnancy. This nested case–control study evaluated the diagnostic accuracy of the Appendicitis Inflammatory Response (AIR) score and imaging during pregnancy.

Methods: By cross-linking national Swedish health registries from a defined geographical area, we identified a cohort of 154 women who underwent appendectomy for suspected appendicitis during pregnancy and a matched cohort of 232 pregnant women admitted for acute abdominal pain and suspected appendicitis but with a discharge diagnosis of nonspecific abdominal pain (NSAP). All variables were extracted from medical records. The diagnostic value of AIR score and imaging was estimated for patients with a final diagnosis of appendicitis compared with patients with negative appendectomy and NSAP patients.

Results: The final diagnoses for the operated patients were uncomplicated and complicated appendicitis in 49.4% and 26.6%, respectively, and negative appendectomy in 24.0%. Nearly half of all the patients underwent diagnostic imaging (41%), mainly by ultrasonography. The sensitivity and specificity of diagnostic imaging were 44.9% (95% CI 32.9%–57.4%) and 42.2% (95% CI 31.9%–53.1%), respectively. The area under the receiver operating characteristic curve of AIR score was 0.88 (95% CI 0.84–0.92) for all appendicitis and 0.90 (95% CI 0.84–0.95) for complicated appendicitis. The sensitivity for complicated appendicitis was 100% at a score of ≥4. The specificity for all appendicitis was 97% at a score of ≥9.

Conclusions: The results of this study suggest that the AIR score may be a suitable diagnostic tool for risk stratification of pregnant women with abdominal pain and suspected appendicitis but further validation among pregnant women is needed.

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INTRODUCTION

Acute abdominal pain is common during pregnancy. Although appendicitis is rare in pregnant women, with an incidence of approximately one per thousand births,[1,2] it is still an important differential diagnosis and the most frequent cause of nonobstetric surgery during pregnancy.[3] The proportion of patients with negative appendectomy is high during pregnancy.[2,4] This may reflect diagnostic difficulties and the need to treat patients without delay to avoid progression of the disease and minimize the risk of adverse pregnancy outcomes, such as miscarriage, intrauterine fetal death (IUFD), and premature birth.[5,6] Other studies suggest that appendectomy itself is a risk factor for adverse pregnancy outcomes, and making an accurate diagnosis is equally important for avoiding unnecessary surgery.[4,7]

The clinical presentation of acute appendicitis may be obscured by the pregnancy itself. The growing uterus may render evaluation of peritonitis more difficult, and the relevance of leukocytes and C-reactive protein (CRP) has been questioned due to the physiologically increased inflammation during pregnancy.[8,9] Furthermore, imaging may be less helpful during pregnancy because abdominal ultrasonography (US) has reduced specificity and sensitivity for identifying appendicitis during pregnancy, and computed tomography (CT) is generally avoided due to ionizing radiation.[10–12]

The diagnostic value of clinical signs and inflammatory parameters during pregnancy has not been well studied. Most of the previous studies of the diagnostic process were retrospective, based only on pregnant women operated on for suspected appendicitis and not including patients with suspected appendicitis who were deemed not to have appendicitis after diagnostic assessment. As a consequence, the diagnostic value of clinical parameters during pregnancy is commonly estimated from women with either appendicitis or negative appendectomy, which induces selection bias.[13–15] This tendency precludes conclusions about the utility of clinical and laboratory parameters in the management of pregnant women with abdominal pain and possible appendicitis since the most common differential diagnosis in patients with abdominal pain and suspected appendicitis is nonspecific abdominal pain (NSAP). We found two previous studies that included nonoperated pregnant women with a differential diagnosis of NSAP; the results indicated that inflammatory parameters, including the white blood cell (WBC) count and neutrophil-to-lymphocyte ratio (NLR), are elevated in pregnant women with appendicitis compared to women with NSAP.[16,17]

Clinical scoring systems for appendicitis are used to obtain a more objective assessment by combining symptoms, clinical signs, and laboratory test results. These clinical scores provide a basis for risk stratification that can guide decision making for patients with suspected appendicitis. Among the several clinical scoring systems for appendicitis, few have been validated for pregnant women.[14,18,19] The Appendicitis Inflammatory Response (AIR) score has shown the highest discriminating and predicting ability in many reviews but has not been validated for pregnant women[20–23] (Table 1).

TABLE 1 AIR score.

Symptoms/findings	Points
Right inferior fossa pain	1
Vomiting	1
Rebound tenderness or muscular defense	
Light	1
Medium	2
Strong	3
WBC count ($\times 10^9$/L)	
10.0–14.9	1
≥15.0	2
Proportion of neutrophil granulocytes	
70%–84%	1
≥85%	2
CRP concentration (g/L)	
10–49	1
≥50	2
Body temperature (°C)	
≥38.5	1

Note: 0–3 points = low probability, outpatient follow-up recommended; 4–8 points = intermediate group, in-hospital active observation with rescoring or diagnostic imaging recommended; 9–12 points = high probability, surgical exploration recommended.

Abbreviations: AIR, Appendicitis Inflammatory Response; CRP, C-reactive protein; WBC, white blood cell.

The aim of this nested case–control study was to assess the diagnostic value of the clinical findings and inflammatory parameters included in the AIR score as well as imaging for suspected appendicitis during pregnancy. The study included pregnant women who were diagnosed with appendicitis at operation (appendicitis patients) compared to patients who had negative appendectomy at operation or who were diagnosed with NSAP after assessment for abdominal pain and suspected appendicitis (nonappendicitis patients).

METHODS

Study population

This study is based on two extracts obtained from registers held by the Swedish National Board of Health and Welfare. One extract included all women in the Swedish National Patient Register with a discharge diagnosis of appendicitis (ICD8, 54000–54208; ICD9, 540A–542; ICD10, K350–K370) or NSAP (ICD7, 785.50–785.99; ICD8, 785.51–785.59; ICD9, 789A; ICD10, R10*) or a code indicating appendectomy (procedural codes 4500–4511, 4517 [1964–1996], JEA00–JEA10) from 2010 to 2013. The second extract included all women who gave birth between 2010 and 2013 and was obtained from the Swedish Medical Birth Register (MBR). All pregnancies resulting in stillbirth after 22 weeks of gestation were also included in the MBR.

These two extracts were cross-linked using the unique personal identity number assigned to all Swedish residents. From this merged database, two cohorts of women were identified and included in a nested case–control study design: all women who had an appendectomy during pregnancy and all women discharged for NSAP while pregnant. For practical reasons, we limited the inclusion of women from these two national cohorts to women from the 21 hospitals with a surgical emergency department (ED) and a maternity ward in the southern, southeastern, and western health care regions (representing a population of 4.9 million) of Sweden during 2010–2013. For each pregnant woman who underwent appendectomy, we selected two patients from the NSAP cohort who were matched for age in years and admitted to the same hospital within one calendar month.

Copies of the medical and maternity care records were obtained and completely reviewed three times for all included women to ensure the accuracy of the extracted data. Information about gestation week at admission, date of birth, mode of delivery, and clinical information, including the parameters of the AIR score (localization of pain, vomiting, presence of muscular defense or rebound tenderness, body temperature, concentration of CRP and leukocytes, and the proportion of neutrophils) was extracted. Any indication of muscular defense or rebound tenderness was noted as medium, yielding 2 points in the AIR score. We noted information on management, including duration from onset of symptoms to arrival at the hospital, length of stay, readmission within 30 days after the index admission, and results of diagnostic imaging when performed.

The results of diagnostic imaging were interpreted according to the intention to diagnose the patient. In accordance with the recommendations of the literature,[24] we counted patients with a nonvisualized appendix as false negatives if the final diagnosis was appendicitis and as false positives if the final diagnosis was not appendicitis. For the operated patients, the duration from arrival at the hospital until the start of surgery, surgical method, postoperative complications, and macroscopic and microscopic diagnoses of the appendix were registered. Transmural invasion of inflammatory cells was the histopathological criterion for uncomplicated appendicitis, transmural tissue necrosis was the criterion for gangrenous appendicitis, and intraoperative perforation was the criterion for perforated appendicitis. Gangrenous and/or perforated appendicitis or abscess was defined as complicated appendicitis. If no microscopic diagnosis of the appendix was available, we used the intraoperative macroscopic diagnosis.

Statistical analysis

Differences were analyzed using the chi-square test, Fisher's exact test, *t*-test, Kruskal–Wallis ANOVA, and Mann–Whitney *U*-test where appropriate. The Bonferroni test was used for the post hoc paired analyses. The diagnostic value of the clinical parameters for identifying appendicitis during pregnancy was estimated from the patients with a final diagnosis of appendicitis (appendicitis cases) compared to the combined group of patients with negative appendectomy and the nonoperated patients with a discharge diagnosis of NSAP (nonappendicitis controls), expressed as the sensitivity and specificity and the area under the receiver operating characteristic curve (ROC area). Multiple imputation with chained equations was used to compensate for missing values.[25] A p-value of <0.05 was regarded as statistically significant. Stata statistical software, Release 15, was used for all calculations. The Regional Ethical Review Board in Linköping, Sweden, approved this study on September 17, 2014 (dnr 2014/338-31), and on November 18, 2015 (dnr 2015/364-32).

RESULTS

In total, we identified 178 patients treated with appendectomy for suspected appendicitis during pregnancy and selected 302 matched pregnant NSAP patients examined for acute abdominal pain and suspected appendicitis (Figure 1). Medical records could not be retrieved for 71 patients even after the hospital's archives were reviewed. An additional 23 women were excluded because the reason for appendectomy or admission for abdominal pain was due to another cause than suspected appendicitis (malignancy, trauma, etc.). As a result, 24 operated patients and 70 NSAP patients were excluded. The final study population consisted of 386 women, of whom 154 patients underwent appendectomy; 117 had a final diagnosis of appendicitis (appendicitis cases), 37 had a negative appendectomy, and 232 had NSAP, for a total of 269 nonappendicitis controls (Figure 1).

Characteristics of operated patients and NSAP patients

The characteristics of the patients with appendicitis or negative appendectomy and a NSAP diagnosis are presented in Table 2. The duration of symptoms on arrival at the hospital was similar for all groups. The patients with negative appendectomy had longer length of stay than did the patients with appendicitis (median 3 days compared with 2 days; $p<0.001$). The length of stay was 1 day for the patients with an NSAP diagnosis. Most of the patients were admitted during the first or second trimester, at an earlier stage of pregnancy, for patients with appendicitis than for patients with negative appendectomy or NSAP diagnosis (median 17 weeks vs. 22 and 21 weeks, respectively; $p=0.012$). Among the operated patients, 49.4% (76/154) had uncomplicated appendicitis, 26.6% (41/154) had complicated appendicitis, and 24.0% (37/154) had negative appendectomy (Table 2).

Diagnostic accuracy of diagnostic imaging in pregnant patients

Diagnostic imaging was used more frequently in 59.8% (70/117) of the operated patients with appendicitis than in 48.6% (18/37) of the operated patients with negative appendectomy and 37.1% (86/232) of the NSAP patients ($p<0.001$; Table 2). Abdominal US was by far

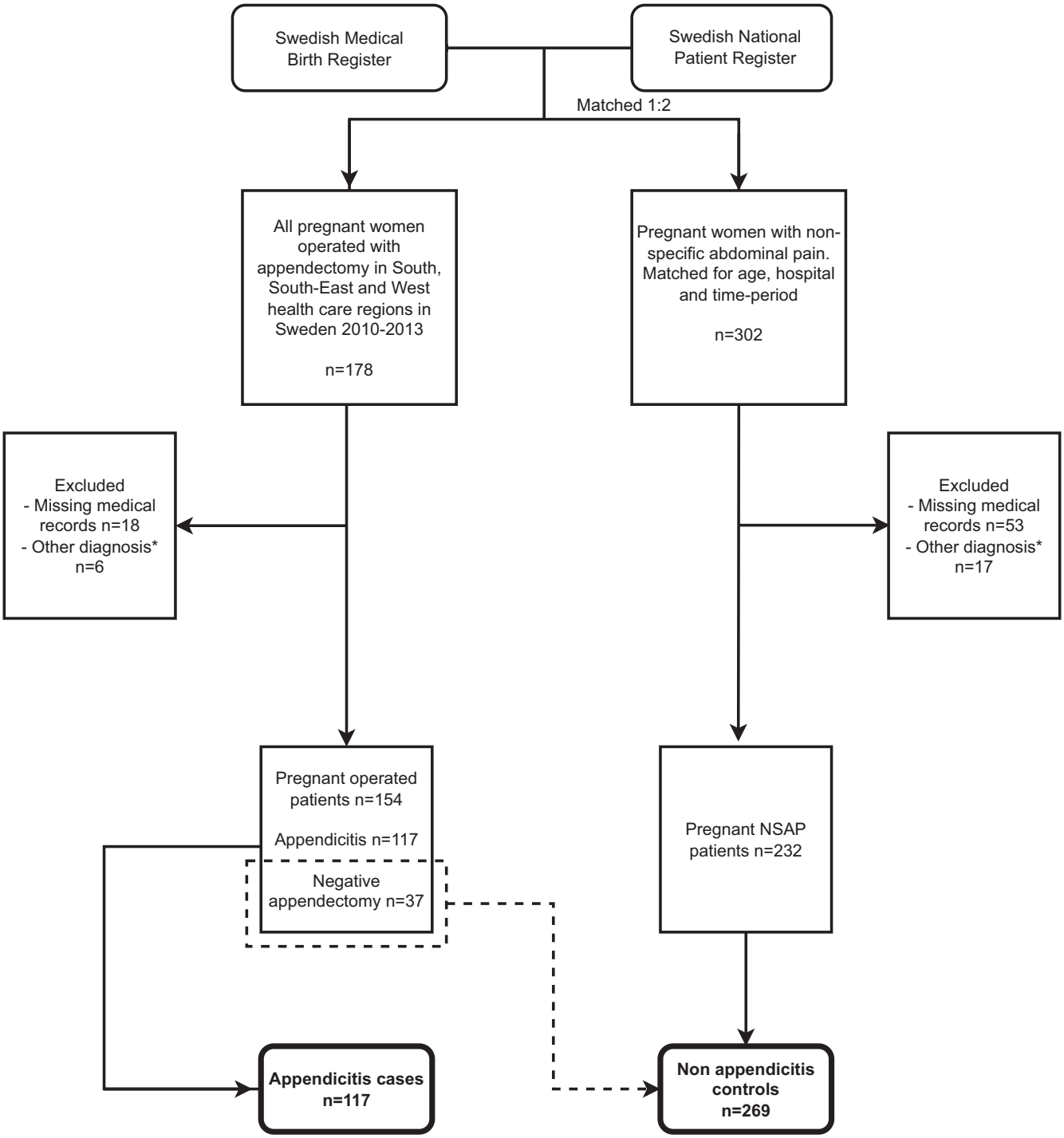

FIGURE 1 Flowchart of the study population. *Other diagnoses consisted of other indications for appendectomy/admission for abdominal pain known in advance other than appendicitis, including trauma, malignancy, cholecystitis, or urolithiasis. NSAP, nonspecific abdominal pain.

the most common modality, with a greater proportion of patients with appendicitis (54.7%, 64/117) than of patients with negative appendectomies (45.9%, 17/37) and NSAP patients (20.7%, 48/232; $p < 0.001$). Among the 154 operated patients, six women (3.9%) were examined by CT, none by magnetic resonance imaging (MRI) compared to nine women (3.9%) by CT, and one woman (0.4%) by MRI of the NSAP patients.

The proportion of patients in whom visualization of the appendix was not possible via abdominal US was 65.1% (84/129), with both false-positive and false-negative results when the imaging results were compared with the final diagnosis, as shown in Table 3. The sensitivity and specificity for diagnostic imaging were 44.9% (95% confidence interval [CI] 32.9–57.4) and 42.2% (95% CI 31.9–53.1), respectively.

TABLE 2 Demographic and study characteristics of operated patients with appendicitis or negative appendectomy and NSAP.

	Operated patients (n = 154)			
	Appendicitis (*n* = 117)	Negative appendectomy (*n* = 37)	Patients with NSAP (*n* = 232)	*p*-value
Age (years)	29.69 (±4.84)	28.49 (±5.96)	28.98 (±5.78)	0.40
Parity				
0	53 (45.3)	24 (64.9)	110 (47.4)	0.063
1	44 (37.6)	8 (21.6)	65 (28.0)	
2+	20 (17.1)	5 (13.5)	57 (24.6)	
Gestation week at admission				0.011
0–21	82 (70.1)	17 (45.9)	118 (50.9)	
22–27	12 (10.3)	4 (10.8)	38 (16.4)	
28–31	5 (4.3)	8 (21.6)	29 (12.5)	
32–36	11 (9.4)	2 (5.4)	27 (11.6)	
37–42	7 (6.0)	6 (16.2)	20 (8.6)	
Median (IQR)	17 (10–25)	22 (15–31)	21 (12–29)	0.012
Duration of symptoms on arrival (h)	21.5 (19.5–29.2)	24.1 (21.1–51.8)	21.5 (16.5–38.6)	0.32
Diagnostic imaging				<0.001
No imaging	47 (40.2)	19 (51.4)	146 (62.9)	
Abdominal US	64 (54.7)	17 (45.9)	48 (20.7)	
CT	5 (4.3)	1 (2.7)	9 (3.9)	
MRI	0 (0.0)	0 (0.0)	1 (0.4)	
US and CT	1 (0.9)	0 (0.0)	0 (0.0)	
Imaging with other question	0 (0.0)	0 (0.0)	28 (12.1)	
Diagnosis at appendectomy				<0.001
Not appendicitis	0 (0.0)	37 (100.0)	232 (100.0)	
Uncomplicated	76 (65.0)	0 (0.0)	0 (0.0)	
Complicated	41 (35.0)	0 (0.0)	0 (0.0)	
Gestation week at partus				0.38
22–27	1 (0.9)	0 (0.0)	1 (0.4)	
28–31	3 (2.6)	1 (2.7)	1 (0.4)	
32–36	8 (6.8)	4 (10.8)	11 (4.7)	
37–41	105 (89.7)	32 (86.5)	219 (94.4)	
Days to delivery from first admission/operation				0.001
0	13 (11.1)	6 (16.2)	1 (0.4)	
1–7	0 (0.0)	1 (2.7)	11 (4.7)	
8+	104 (88.9)	30 (81.1)	220 (94.8)	
Mode of delivery				0.010
Vaginal delivery	84 (71.8)	26 (70.3)	187 (80.6)	
Cesarean section	33 (28.2)	11 (29.7)	45 (19.4)	
IUFD	1 (0.9)	1 (2.7)	1 (0.4)	0.62
Length of stay (days), median (IQR)	2 (1–4)	3 (2–5)	1 (1–2)	<0.001
Readmission within 30 days	3 (2.6)	1 (2.9)	14 (7.3)	0.17

Note: Data are reported as mean (±SD), *n* (%), or median (IQR).

Abbreviations: IQR, interquartile range; IUFD, intrauterine fetal death; MRI, magnetic resonance imaging; NSAP, nonspecific abdominal pain.

Diagnostic properties of AIR score parameters for identifying appendicitis in pregnant patients

The diagnostic properties of the AIR score parameters during pregnancy were estimated for the 117 pregnant cases with appendicitis compared with the 269 nonappendicitis pregnant controls admitted for suspected appendicitis, i.e., the 37 patients with a negative appendectomy combined with the 232 matched NSAP patients (Table 3). The AIR score was elevated in the cases with appendicitis compared with the pregnant nonappendicitis controls, except for

TABLE 3 AIR score variables and results of diagnostic imaging according to final diagnosis.

	Appendicitis		NSAP/negative appendectomy	*p*-value
	Complicated	Uncomplicated		
	41 (10.6)	76 (19.7)	269 (69.7)	
Inflammatory parameters (%)				
Body temperature (°C)	37.4 (±0.6)	37.2 (±0.6)	37.1 (±0.6)	0.007
WBC count ($\times 10^9$/L)	15.5 (±4.3)	14.9 (±4.6)	11.2 (±3.4)	<0.001
Neutrophil granulocytes ($\times 10^9$/L)	12.2 (9.0–15.6)	11.9 (9.1–15.3)	6.5 (5.5–8.6)	<0.001
Proportion neutrophil granulocytes	0.87 (0.80–0.91)	0.86 (0.80–0.89)	0.68 (0.52–0.80)	<0.001
CRP (g/L)	66.0 (37.0–119.0)	38.5 (20.5–65.5)	11.0 (5.0–41.0)	<0.001
Clinical signs				
Vomiting	23 (56.1)	35 (46.1)	82 (30.5)	<0.001
Right iliac fossa pain	35 (85.4)	69 (90.8)	129 (48.0)	<0.001
Defense or rebound tenderness	20 (48.8)	38 (50.0)	27 (10.0)	<0.001
AIR score				<0.001
0–3	0 (0.0)	1 (1.3)	114 (42.4)	
4–8	22 (53.7)	51 (67.1)	147 (54.6)	
9–12	19 (46.3)	24 (31.6)	8 (3.0)	
Result imaging				<0.001
Appendicitis	14 (34.1)	16 (21.1)	4 (1.5)	
Not appendicitis	0 (0.0)	2 (2.6)	13 (4.8)	
Appendix not visible or unclear diagnosis	16 (39.0)	22 (28.9)	46 (17.1)	
Other diagnosis	0 (0.0)	0 (0.0)	19 (7.1)	
Imaging not done or other indication than appendicitis	11 (26.8)	36 (47.4)	187 (69.5)	

Note: Data are reported as n (%), mean (±SD), or median (IQR).

Abbreviations: AIR, Appendicitis Inflammatory Response; CRP, C-reactive protein; NSAP, nonspecific abdominal pain.

one patient. Among the 115 patients with AIR score ranging from 0–3, one had uncomplicated appendicitis. None of the women admitted for acute abdominal pain and possible appendicitis with a discharge diagnosis of NSAP at the index admission were readmitted for appendicitis during their pregnancy.

The area under the ROC curve for the estimated AIR score was 0.88 (95% CI 0.84–0.92) for all patients with appendicitis and 0.90 (95% CI 0.84–0.95) for those with complicated appendicitis (Figure 2). An AIR score of ≥4 had a sensitivity for complicated appendicitis of 100% (95% CI 91%–100%). An AIR score of ≥9 had a specificity of 97% for all cases of appendicitis (95% CI 94%–99%; Table 4).

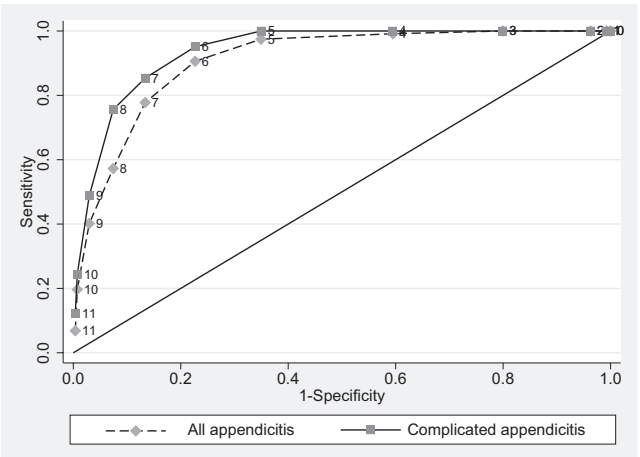

FIGURE 2 ROC curve for all appendicitis and complicated appendicitis at different cutoff levels for the AIR score. AIR, Appendicitis Inflammatory Response; ROC, receiver operating characteristic.

Perioperative management and surgical treatment of pregnant patients

The most common surgical approach was open appendectomy through a gridiron incision above McBurney's point, but 18.2% (28/154) of the patients underwent nonstandard placement of the gridiron incision. The alternative placement was motivated either by the punctum maximum pain or by the location of the appendix on imaging. Some 19 women (12.3%) underwent synchronous appendectomy and cesarean section. Seven procedures were performed before 37 weeks of gestation. An obstetric indication for a cesarean

TABLE 4 Sensitivity and specificity for all appendicitis and complicated appendicitis at different cutoff levels for the AIR score.

AIR score cutoff	Sensitivity (%)	95% CI	Specificity (%)	95% CI
All appendicitis				
≥4	99	95–100	42	36–49
≥9	37	28–46	97	94–99
Complicated appendicitis				
≥4	100	91–100	42	36–49
≥9	46	31–63	97	94–99

Abbreviation: AIR, Appendicitis Inflammatory Response.

section was present for five women; one woman had suspected appendicitis and no progress after labor induction, one woman had a combination of suspected appendicitis and breech position, and in three cases, a cesarean section was performed due to worsening of the patient's abdominal pain. For most of the remaining 14 women, synchronous cesarean section was justified by better access to the appendix. Among the 19 women who underwent synchronous appendectomy and cesarean section, six (31.6%) had uncomplicated appendicitis, six (31.6%) had complicated appendicitis, and seven (36.8%) had negative appendectomy.

Postoperative complications Grade 3a or 3b according to the Clavien–Dindo grade occurred in 3.2% (5/154) of the operated patients. One woman had signs of postoperative bowel obstruction and underwent diagnostic laparoscopy, one woman had a postoperative abscess, and one woman had a miscarriage in the first trimester in close relation to the appendectomy. Among the women who underwent appendectomy and synchronous cesarean section, one patient had multiple complications and required intensive care, and one woman had wound dehiscence requiring reoperation.

Pregnancy outcome in the operated patients and NSAP patients

No delivery started spontaneously during the first week after appendectomy (Table 2). In addition to the 19 women (12.3%) who underwent synchronous appendectomy and cesarean section described above, one woman gave birth by cesarean section the day after appendectomy because of persistent abdominal pain and fever. The proportion of premature deliveries (<37 weeks of gestation) did not differ between the groups: 12/117 (10.3%) among the operated patients with appendicitis, 5/37 (13.5%) of the negative appendectomies versus 13 of 232 (5.6%) of the NSAP patients ($p=0.38$). A greater proportion of the patients operated on for suspected appendicitis were delivered by cesarean section (44 of 154, 28.6%) than were the NSAP patients (45 of 232, 19.4%; $p=0.010$). IUFD occurred in two of the operated patients. Both were diagnosed with IUFD 21 weeks after appendectomy performed in Gestation Weeks 6 and 9, respectively. Among the patients with NSAP, one patient was diagnosed with IUFD the day after admission for NSAP in Gestation Week 29 (Table 2).

DISCUSSION

To the best of our knowledge, this is the largest study on the clinical diagnosis of appendicitis in pregnant women. Since prospective studies of appendicitis in pregnant women are difficult to conduct owing to its rarity, most of those previous reports are retrospective and compare the diagnostic properties between patients who underwent surgery for appendicitis and patients operated with negative appendectomy, resulting in severe selection bias. In this study, we overcame this problem by using a nested case–control study design. By including nonoperated patients, assessed for suspected appendicitis, our results should be more representative of the real-life setting where clinicians need to manage unselected pregnant women with acute abdominal pain and suspected appendicitis. The multicenter design included 21 hospitals of varying sizes, and the geographically defined catchment area covering approximately half the Swedish population increased the generalizability of the study. Like most retrospective studies, ours had some missing values. Multiple imputation of random missing data is now accepted to increase the validity of the results.[25,26] As the intensity of peritoneal irritation was seldom graded in the medical records, we assigned any indication of muscular defense or rebound tenderness as medium, yielding 2 points in AIR score. As a consequence, some of the patients´ AIR scores were at risk of a minor under- or overestimation. Another limitation of the study was that a majority of the included patients were ethnic Swedes (Caucasian) and so the results may be less applicable to other ethnicities.

In addition to common perceptions, inflammatory parameters and clinical signs also have diagnostic value for pregnant women. Like outside of pregnancy, this is particularly true when combining various inflammatory parameters and clinical signs since none of them used alone has the discriminating power to rule in or rule out appendicitis.[27,28] The utility of a combination of clinical parameters for determining the AIR score was demonstrated by the ROC area of 0.88 for all appendicitis cases and 0.90 for complicated appendicitis in pregnant women. Our results indicate that outpatient follow-up is safe for pregnant women with AIR score ranging from 0 to 3 (a low probability of having appendicitis) and that diagnostic imaging via abdominal US for this group has no further value. These results are in keeping with previous studies of AIR scores in nonpregnant populations.[20–23,29]

The high proportion of negative appendectomy during pregnancy (24.0%) is in line with the findings of previous population-based studies and underlines the need for improved diagnostics in pregnant women with suspected appendicitis.[2,4] Nevertheless, our results indicate that the AIR score can correctly classify most women with suspected appendicitis during pregnancy, whereas diagnostic imaging can be saved for women with an intermediate AIR score of 4–8 points or for differential diagnosis in patients when other diagnoses are suspected or need to be ruled out.

This study is based on data from 2010–2013, and the management of pregnant women with abdominal pain and suspected appendicitis may have changed since then. One reason may be that uncomplicated and complicated appendicitis are currently considered two different entities, the focus of which has shifted toward identifying patients with complicated appendicitis requiring prompt surgery.[30]

Clinical signs and inflammatory parameters, sometimes combined in clinical scores, constitute the basis for the diagnosis and management of patients with suspected appendicitis. The World Society of Emergency Surgery (WSES) guidelines for the diagnosis and treatment of acute appendicitis recommend the use of clinical signs and inflammatory parameters in combination when examining pregnant patients with abdominal pain.[30] Neutrophil granulocytes are now routinely analyzed in most EDs for patients seeking care for abdominal pain, and the NLR improves the accuracy of acute appendicitis diagnosis in nonpregnant and pregnant women.[16,17]

The use of diagnostic imaging during pregnancy has undergone some changes since the studied period.[11] Nevertheless, abdominal US has a low specificity and sensitivity for identifying appendicitis during pregnancy, as our and other's results indicate.[10,12,31] A consequence of the high proportion of indeterminate US findings is the difficulty in ruling out appendicitis. This seems to be the case even outside pregnancy. Poortman et al.[32] conducted a prospective cohort study of nonpregnant women with suspected appendicitis and evaluated US and clinical observation. The authors concluded that the high false-negative rate with US limits its value and that observation is safe in women with equivocal signs of appendicitis. CT has high sensitivity and specificity for identifying appendicitis but is often avoided during pregnancy due to ionizing radiation.[12,33] Abdominal MRI has the advantages of being a radiation-free modality with both high sensitivity and high specificity for identifying appendicitis during pregnancy but is expensive and time-consuming. It might be needed when the diagnosis is uncertain, but necessary surgery should not be delayed.[34,35]

Laparoscopic appendectomy has gradually become more common in recent years in pregnant women, mainly in the first and second trimesters, whereas open surgery predominates in the third trimester.[36] Surprisingly, almost one-fifth of the operated patients in our study had an alternative placement of the gridiron incision. This might reflect the widespread view among surgeons that the appendix is displaced cranially by the growing uterus during pregnancy. A Japanese study reported that 16 of 33 (48.5%) pregnant women who underwent appendectomy had an alternative incision in the form of a pararectal incision, motivated by the fact that less manipulation of the uterus was possible with that incision.[15] However, clinical and radiological evaluation of the location of the appendix during pregnancy concluded that the appendiceal location is only marginally changed during pregnancy and can be reached through a conventional grid iron incision over McBurney's point in most cases even during term pregnancy.[37,38]

In our study, the risk of premature delivery (<37 weeks) was 10.3% among pregnant patients with appendicitis who underwent surgery and did not differ from the risk among pregnant NSAP patients. According to the Swedish Medical Birth Register, which includes virtually all births in Sweden, the percentage of premature births (<37 weeks) was 5.9%–6.1% for the years 2010–2013.[39] For most of the pregnant operated patients, admission for appendectomy and date of birth were not closely related. Obviously, women who underwent synchronous appendectomy and cesarean section were an exception to this and constituted seven of 12 (58%) of all premature deliveries. The 19 women who underwent synchronous appendectomy and cesarean section represented nearly half of the cesarean sections in total and contributed to the high proportion of deliveries via surgical intervention. Interestingly, no delivery started spontaneously during the first week after appendectomy, indicating that the risk for surgery-induced labor is low regardless of disease severity.

CONCLUSIONS

Contrary to current views, symptoms, clinical signs, and inflammatory parameters appear to have diagnostic value in identifying appendicitis during pregnancy. The findings of this study suggested that the Appendicitis Inflammatory Response score is an appropriate diagnostic tool for risk stratification of pregnant women with abdominal pain and suspected appendicitis. The accuracy of Appendicitis Inflammatory Response score in pregnant women is similar to that in nonpregnant patients, but further validation among pregnant women is needed.

AUTHOR CONTRIBUTIONS

Roland E. Andersson, Marie Blomberg, and Elin Moltubak planned the study. Roland E Andersson, Elin Moltubak, and Kalle Landerholm analyzed the data, and all authors interpreted the results. Roland E. Andersson prepared the tables and Elin Moltubak prepared the figures. All the authors contributed to the writing and review of the manuscript. All the authors have read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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