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Delaying laparoscopic surgery in pregnant patients with an equivocal acute appendicitis: a step-wise approach does not affect maternal or fetal safety

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Abstract

Background Accurate and timely diagnoses of acute appendicitis (AA) during pregnancy avoids maternal and fetal morbidity and mortality. We present our experience of using an initial transabdominal ultrasound (US) performed at presentation to diagnose AA in pregnant patients as well as the value of a delayed repeat study in those who remain equivocal. We explore the sensitivity and specificity of this algorithm as well as the maternal and fetal safety of this approach.

Methods Of the 225 patients identified within the study period who underwent laparoscopic appendectomy, 216 met the inclusion criteria and were retrospectively analyzed. If the US performed on presentation revealed AA, surgery was performed. Patients with a non-diagnostic US were admitted with surgery performed if there was clinical and/or biochemical deterioration. Patients who remained equivocal underwent a repeat delayed study. The results of the initial versus delayed studies were compared. Maternal and fetal complications were recorded and contrasted.

Results Of the 216 patients included, 164 (75.9%) had AA, 14 (6.5%) had complicated AA and 38 (17.6%) had a normal appendix. Initial US was diagnostic for 125/216 (57.9%) of patients and 19/34 (55.8%) of patients who underwent a delayed repeat study. The remaining patients underwent empirical surgery. The pooled sensitivity and specificity of US for the cohort was 79.2% and 92.1%, respectively. There was no difference in proxies of maternal or fetal safety between the groups.

Conclusion US is a useful tool for diagnosing AA in pregnancy. In this cohort, performing a delayed repeat US during a period of observation in those patients who remained otherwise equivocal increased the diagnostic yield of the US. Delaying surgery in this specific group of patients does not affect maternal or fetal safety.

Keywords Appendicitis · Pregnancy · Laparoscopy

Affecting between 1/500–850 pregnant women [1] acute appendicitis (AA) is the most common surgical emergency faced by women during pregnancy. However, in this group of patients, a particular diagnostic challenge exists as the classical symptoms of gastrointestinal complaints, abdominal pain and malaise are all common in normal pregnancy [2]. Anatomical changes in pregnancy can also result in a misleading clinical examination [3]. Finally with raised inflammatory markers during pregnancy, routine laboratory examinations may also be of limited value [4].

Despite these difficulties, early diagnosis of AA is essential as a higher level of perforated appendicitis is noted in pregnant versus non-pregnant patients [5]. Moreover, a delay in diagnosis may be associated with an increased rate of maternal and fetal morbidity [6]. Yet at any stage of pregnancy, maternal and fetal morbidity and mortality are also associated with unnecessary surgery [7].

In order to reduce the risks to both mother and fetus, early and accurate diagnosis is vital. Due to concern regarding the radiation of computed tomography (CT) during pregnancy [8], abdominal ultrasonography (US) is often utilized as it is cheap, safe and non-invasive. However, the reported value

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of abdominal US in diagnosing AA in pregnancy is variable with some authors reporting relative success with the modality [9], whilst others have found rates of indeterminate studies ranging between 88 and 96% [3, 10, 11].

Although the use of magnetic resonance imaging (MRI) has also been described in the academic literature with promising sensitivity alongside an acceptable safety profile [12], urgent MRI is not available in many hospitals, especially out-of-hours [13].

It has been shown in pediatric patients that in the setting of AA, if the initial US performed on presentation to hospital was non-diagnostic, then in clinically equivocal patients the sensitivity of US can be significantly increased by performing a repeat delayed study without increasing morbidity [14, 15]. Although the process of observing pregnant patients with a suspected AA has been shown to be safe in terms of maternal and fetal outcomes [16], the stepwise approach of performing a delayed repeat US for pregnant patients has not been previously documented in academic literature.

In order to fill this void, we present a retrospective analysis of 216 pregnant patients who underwent laparoscopic appendectomy for a presumed AA. The aim of this study was not only to document our experience with abdominal US in diagnosing AA in pregnant patients but also to assess the safety in terms of maternal and fetal outcomes for those patients for whom a delayed repeat US was performed after a period of observation.

Methods

Approval was attained from the institutional Helsinki ethics committee who waived the requirement for informed consent due to the retrospective nature of this study. The study was performed at the Shaare Tzedek Medical Center, a university affiliated tertiary center for general surgery and obstetrics at which there are almost 25,000 births per annum.

All women of child bearing age who between January 2000 and December 2015 underwent emergency surgery for a presumed AA at the hospital were identified. This was achieved by firstly performing an electronic search of hospital records using Israeli Ministry of Health diagnostic codes 47–47.19 based on the ICD-9 codes for appendicitis or appendectomy. A secondary search was then performed using the diagnostic code v.22 which is based on the ICD 9 code for pregnancy. This gave a cohort of 225 patients.

These patients' electronic and paper notes were retrospectively reviewed. Demographic, clinical and pathological data were extracted including age, gestation at time of surgery, basic observations and white cell count at presentation to the Emergency Department (ED), duration of symptoms, pre-operative imaging results, final pathological diagnosis, duration of surgery and length of hospital stay, APGAR score and incidence of post-operative complications. For the purpose of this study, patients were excluded if an US was not performed on arrival at the Emergency Department (ED) or the files were not available for review. Similarly, women who gave birth at another hospital were also excluded as were those who did not undergo a laparoscopic procedure. This left 216 patients included in the final analysis.

There were two endpoints for this study. Firstly, we wanted to assess the sensitivity and specificity of US in this cohort of patients and whether the diagnostic yield of the study could be increased by performing a delayed repeat study in patients who remained equivocal during a period of observation. Secondly, we wanted to understand whether those patients for whom a repeat US was performed had a higher incidence of either maternal or fetal complications in comparison to those patients who underwent immediate surgery.

In order to assess the former outcome, the pre-operative imaging was reviewed. Abdominal US was performed either by a senior radiology resident or consultant. A standardized protocol using graded compression of the right lower quadrant to acquire longitudinal and transverse images was applied. Sonographic findings such as dilatation of the appendix above 7 mm, non-compressibility, edema of the appendiceal wall and local fat stranding were considered as radiologically confirming the diagnosis of AA. If the appendix was not visualized, the study was considered to be non-diagnostic.

If this first line of pre-operative imaging was diagnostic, laparoscopic appendectomy was performed. Surgery was performed either by a senior general surgery resident or consultant. Post-surgical care was provided in a multidisciplinary approach on the general surgery ward with in-reach assistance by the obstetric team. Fetal US was performed on the day after surgery to assess fetal health.

If the first line imaging study was inconclusive, the practice in our center was to admit the patient for observation with repeat blood tests and serial physical examinations. Patients who clinically and/or biochemically deteriorated underwent surgery without a repeat US being performed. Patients who remained equivocal underwent a delayed repeat US which was typically performed between 12 and 24 hours after the initial study.

In order to assess whether AA was actually present, a comparison of the US findings and the final pathological diagnosis was made. These pathological results were summated into three groups: A normal appendix was confirmed when no inflammatory reaction was noted; AA was defined as the presence of acute inflammation; and complicated AA referred to those specimens in which perforation or gangrene was present.

In order to assess the second endpoint, proxies of maternal and fetal safety such as the incidence of complicated

AA, operative time, length of stay and the incidence of post-operative complications occurring within 4 weeks of surgery were extracted. The fetal APGAR score at delivery was also recorded. This score is a measure of the physical condition of the infant at birth encompassing heart rate, respiratory effort, muscle tone, response to stimulation and skin coloration. This is graded from 0 to 10 with the mean scores presented below. A comparison of these variables was made between two groups of patients. One group consisted of those who underwent 'early' surgery and other of those patients for whom a delayed for a repeat US was be performed.

Statistical analysis was performed using SPSS version 21 (IBM SPSS Statistics for Windows, Version 21.0. Released 2012. Armonk, NY: IBM Corp). Descriptive statistics are displayed as mean or N with standard deviation or percentage in parenthesis unless stated otherwise. Univariate analysis was performed using either Mann Whitney, Chi squared or Fisher's exact test as appropriate. A p value of <0.05 was considered significant. The sensitivity and specificity was also calculated with the 95% confidence internal (CI) stated in parentheses.

Results

Of the 1620 women aged between 18 and 45 years old, who between January 2000 and December 2015 underwent appendectomy for a presumed AA, 225 pregnant patients were identified. After applying the exclusion criteria described above, the final cohort consisted of 216 pregnant patients. The basic demographic and clinical data of these patients was extracted and is displayed in Table 1.

With a mean age of 25.8 (5.3) years old, most patients were in the second trimester of pregnancy (59.3%) at the time of surgery and suffered symptomology for an average of 1.9 days (0.9) before presenting the ED. Although 145/216 (67.1%) of patients presented with an absolute neutrophilia ($>11\times10^{9/L}$), only 20/215 (9.3%) patients presented with a fever of greater than 38 degrees Celsius. When considering the final pathology, 164 patients (75.9%) had AA, 14 (6.5%) had a complicated AA whilst the remaining 38 (17.6%) had a normal appendix.

The flow of patients through the diagnostic pathway is shown in Fig. 1.

In total, 125/216 (57.9%) patients underwent immediate surgery after AA was confirmed on the initial US. Of the 91 patients with a non-diagnostic initial US, 56 (61.5%) deteriorated either biochemically and/or clinically and underwent empirical surgery. The remaining 35 (38.5%) underwent a repeat delayed US followed by surgery. The results of both the initial and delayed US stratified by trimester are presented in Table 2.

Table 1 Basic demographic and clinical data of the 216 patients included in the study

Variable	Mean/N (SD/%)
Age (years)	25.8 (5.3)
Trimester	
1st	69 (31.9)
2nd	128 (59.3)
3rd	19 (8.8)
No previous abdominal surgery	195 (90.3)
Duration of symptoms (days)	1.9 (0.9)
Heart rate (beats per minute)	90.6 (14.6)
Systolic blood pressure (mmHg)	113.2 (23.6)
Temperature > 38 °C	20 (9.3)
Total white cell count > 11 ($\times10^{9/L}$)	145 (67.1)
Pathological diagnosis	
Acute appendicitis	164 (75.9)
Complicated appendicitis	14 (6.5)
Normal pathology	38 (17.6)

The initial US performed at presentation was found to be diagnostic in 125/216 (57.9%) of patients. When stratifying the results by trimester, a significant difference was noted in the distribution of diagnostic studies with US performed in the 1st trimester being more likely to be diagnostic than those preformed in later trimesters ($p=0.004$).

As noted above, of the 91 patients with a non-diagnostic initial US, 56/91 (61.5%) underwent empirical surgery because of clinical or biochemical deterioration. In the 35 patients who remained equivocal and underwent delayed repeat US, the study was diagnostic in 19 (54.3%). However, in this cohort of patients, there was no difference in the distribution of diagnostic versus non-diagnostic studies when comparing between the different trimesters ($p=0.532$). From this group, the remaining 16/35 (45.7%) patients underwent surgery without a radiological diagnosis because of either clinical or biochemical deterioration after the repeat delayed scan was performed.

A comparison of the US findings and final pathology is presented in Table 3. This shows that in the first and second trimesters, patients were significantly more likely to have an US suggestive of AA with subsequent pathological confirmation than they were to have either a non-diagnostic study or a study that was radiologically diagnositic with a pathologically normal appendix. A similar relationship was noted in the third trimester; however, this failed to reach statistical significance ($p=0.088$). Nevertheless, in this group, no patients with an US suggestive of AA who underwent surgery had a pathologically normal appendix.

The overall sensitivity and specificity of US was 79.2% and 92.1%, respectively. Although the sensitivity was higher in the first trimester compared with the second

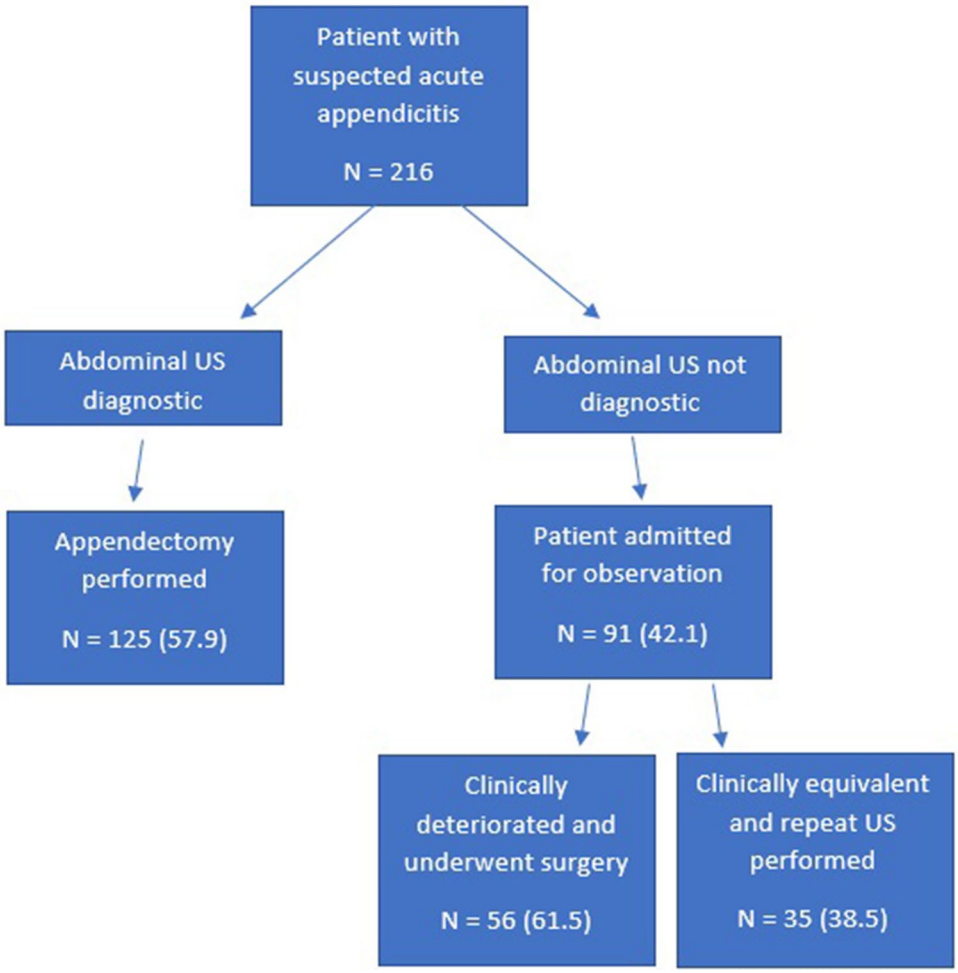

Fig. 1 A diagram showing the flow of 216 pregnant patients with a presumed acute appendicitis through our diagnostic algorithm

Table 2 Results of abdominal US stratified by trimester of pregnancy

Trimester	Initial US		Repeat delayed US	
	Acute appendicitis N (%)	Non-diagnostic N (%)	Acute appendicitis N (%)	Non-diagnostic N (%)
1st	51 (73.9)	18 (26.1)	5 (62.5)	3 (37.5)
2nd	64 (50.0)	64 (50.0)	11 (47.8)	12 (52.2)
3rd	10 (52.6)	9 (47.4)	3 (75.0)	1 (25.0)
Total	125 (57.9)	91 (42.1)	19 (54.3)	16 (45.7)
p value	0.004*		0.523*	

*Chi squared

and third, the sensitivity of studies increased later in pregnancy.

In order to assess the safety of delaying surgery in order to perform a repeat US, several proxies of maternal and fetal safety were extrapolated. These proxies were compared between those who underwent a repeat delayed US and those who did not. This information is presented in Table 4. It was found that there was no statistically significant difference in the length of surgery, length of stay or incidence of complicated AA between the two groups. The mean APGAR score following delivery was also the same.

Discussion

The diagnosis of AA in pregnant women presents a considerable diagnostic challenge. Not only are many of the common symptoms of AA present during pregnancy, but

Table 3 A comparison of US and pathological findings stratified by trimester

Trimester	US result	Pathologically AA[§]	Pathologically normal	*p* value	Sensitivity % (95% CI)	Specificity (95% CI)
1	Diagnostic	55 (79.7)	1 (1.5)	0.000*	91.7 (81.6–97.2)	89.9 (51.8–99.7)
	Non-diagnostic	5 (7.2)	8 (11.6)			
2	Diagnostic	73 (57.0)	2 (1.6)	0.000*	72.3 (62.5–80.7)	92.6 (75.7–99.1)
	Non-diagnostic	28 (21.9)	25 (19.5)			
3	Diagnostic	13 (68.4)	0 (0.0)	0.088**	76.5 (50.1–93.2)	100.0 (15.8–100.0)
	Non-diagnostic	4 (21.1)	2 (10.5)			
Total	Diagnostic	141 (65.3)	3 (1.4)	0.000	79.2 (72.5–84.9)	92.1 (78.6–98.3)
	Non-diagnostic	37 (17.1)	35 (16.2)			

*Chi squared

**Fisher's exact test

[§]Where AA includes acute, perforated and gangrenous appendicitis

Table 4 Comparison of proxies of patient and fetal safety in those who underwent an initial US only and those who underwent a delayed repeat US

Variable	Cohort total median/N (SD/%) N = 216	Single study mean/N (SD/%) N = 181	Delayed repeat study mean/N (SD/%) N = 35	*p* value
Length of surgery (minutes)	38.4 (15.9)	37.9 (97.0)	40.5 (87.0)	0.271
Length of stay (days)	2.3 (1.3)	2.3 (7.0)	2.4 (6.0)	0.308
Post-operative complications	4 (1.9)	3 (1.7)	1 (2.8)	0.542*
Pathology				
Acute appendicitis	164 (75.9)	141 (77.9)	23 (65.7)	0.298**
Complicated appendicitis	14 (6.5)	11 (6.1)	3 (8.6)	
Normal appendix	38 (17.6)	29 (16.0)	9 (25.7)	
APGAR score (0–10)	8.9 (0.8)	9 (4.3)	9 (4.2)	0.625*

*Fisher's exact test

**Chi squared

also routine blood tests and clinical examination can be misleading [6]. However, with pregnant patients tending to suffer a greater incidence of perforated appendicitis than non-pregnant patients [5], and perforation being associated with increased fetal and maternal morbidity and mortality [16], timely surgical intervention is required. This requirement to operate early is balanced by a need to avoid unnecessary surgery with rates of fetal mortality and premature labour of 4% and 10% respectively being described in the literature [7, 17].

To aid decision making in this complex group of patients, attention has historically focused on the role of US to aid in the diagnosis of AA. The availability and non-invasive non-radiating nature of the modality has made it particularly attractive in pregnant patients who present to hospital with abdominal pain [18]. Many studies have examined the role of US in this setting with some heterogenicity in the results. For instance, in a study by Barloon and colleagues of 22 patients, US was found to be diagnostic 3/22 patients [10]. In one study focusing on only second and third trimester pregnancies, 96/99 studies failed to visualize the appendix [11]. Similar low rates of visualization were also found by Drake [3]. Conversely, Lim and colleagues found 42/45 studies to be diagnostic [19].

We found that US was correctly diagnostic in 141/216 (65.3%) of patients with a low rate of false positives leading to an overall sensitivity of 79.2% and specificity of 92.1%. Moreover, repeat delayed US was diagnostic in 19/35 (54.3%) of patients. Hence, performing such a study increased the diagnostic yield without increasing the proxies of maternal or fetal morbidity described above. There were some patients for whom the US was diagnostic of AA; however, pathology ultimately revealed a normal appendix. This is most likely a reflection of the operator dependency of US.

Although our cohort was considerably larger than the others previously published on the topic, our results were in keeping with other smaller studies [9]. Furthermore, we found that 38/216 (17.7%) of our patients had a normal appendix despite using the algorithm described above. This is similar to the rate of negative appendectomies found in a large national

observational study focusing on pregnant women [20]. A study by Wallace et al. found that the use of preoperative US reduced the negative laparotomy rate in pregnant patients with a presumed AA from 54 to 36% [21]. In our experience, an even lower rate of negative appendectomy can be achieved. This implies that the role of US in reducing unnecessary surgery may be greater than previously reported moreover because this study only included those who ultimately underwent surgery.

In terms of patient safety, we postulated that if pregnant patients were observed with serial clinical examinations and repeat blood tests with the option of a repeat US if they remained equivocal there would be no impact on maternal or fetal safety. This stepwise approach is based on literature from pediatric patients in which a similar algorithm significantly increased the rate of pre-operatively diagnosed AA in children [14]. Our approach is based on the observation that only perforation rather than a delay in surgery is associated with maternal and fetal complications [16]. However, despite US being performed in every patient in that cohort, no surgeries were performed laparoscopically. Therefore, the impact of the operative burden and period of observation may have on mother and fetus may be difficult to extrapolate considering modern surgical techniques. We found no greater rate of perforated appendixes in those patients for whom surgery was delayed and a repeat US was performed as long as surgery was not delayed if deterioration occurred.

The value of this study, therefore, lies not only in the size of the cohort but also in the identification and validity of a stepwise approach to managing these patients. Delaying surgery, pending patients were admitted for clinical observation, did not increase maternal nor fetal morbidity. This challenges the dogma that pregnant patients with presumed but unconfirmed AA need to undergo surgery as soon as possible.

This study is not without its limitations. Retrospective in nature a selection bias is present as only those who ultimately underwent appendectomy were included. This will overvalue the role of US as those patients who did not undergo surgery were not included. Also, as some patients were lost to follow-up data regarding late post-operative complications may be lacking especially if they happened outside of our hospital system. Importantly, this includes the rate of miscarriage hence why it was not included here. Furthermore, the proxies of patient safety does not include other important measures such as unplanned readmissions which may again have happened outside of our hospital system.

Conclusions

We present the largest cohort to date examining a stepwise approach to manging pregnant patients with AA utilizing laparoscopic appendectomy. We suggest that if US is available that it is a good first step. Observation with serial clinical examinations and blood tests can be used to identify those patients who require prompt empirical intervention. In those who remain equivocal, a delayed repeat US may be useful. We believe it is a safe approach for both mother and fetus.

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Compliance with ethical standards

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