ORIGINAL ARTICLE

Diagnostic Utility of Ultrasound in Acute Appendicitis in Correlation with Total Leukocyte Count

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ABSTRACT:
Objective: To evaluate the diagnostic utility of ultrasound (US) in the diagnosis of acute appendicitis in correlation with total leukocyte count (TLC).
Materials and Methods: This cross sectional comparative study was conducted at the Radiology and Pathology Departments of CMH Lahore from 1st February 2007 to 31st January 2008. A total of 125 suspectedpatientsof appendicitis were included in the study through non-probability purposive sampling. They all underwent US evaluation and laboratory assessment (TLC). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of US findings and TLC were calculated keeping surgical findings and histopathology of the removed appendix as gold standard whenever appendecectomy was carried out.
Results: Among 62 patients finally proven to be suffering from acute appendicitis US correctly diagnosed the same in 55 (89%), whereas a normal appendix was visualized in 30 (48%) out of the remaining 63 non – appendicitis patients. The most accurate appendiceal finding for appendicitis was adiameter of 6 mm or larger, with a sensitivity of 96%, specificity of 97%,NPV of 98%, and PPV of 98%.The lack of visualization of the appendixwith US had a NPV of 82%. An increase in TLC had a PPV of 66%, whereas normal TLC had a NPV of 73% whereas those of US were 96% and 90% respectively. By utilizing US as an adjunct to clinical evaluation, negative appendectomy rate was lessened to 3.2%.
Conclusion: US have better diagnostic utility than TLC in the diagnosis of acute appendicitis.
Keywords: Ultrasonography, Appendix. Appendicitis, Appendicectomy.

INTRODUCTION:

Acute appendicitis is a common clinical problem, which needs early surgical decision[1,2]. More than 250,000 appendicectomies are being carried out in the UnitedStates each year [3]. Possibility of suffering from appendicitis in the lifetime is approximately 12 percent in men and 25 percent in women [4]. The diagnosis of acute appendicitis traditionally has been based on clinical features found primarily in the patient's history and physical examination. However, this diagnosis not infrequently becomes difficult and results in unnecessary appendicectomies[5],delays in treatment or needless hospital admissions for observation. Removal rate of a normal appendix (negative appendectomy) up to 20% has been widely reported [6,7,8,9]. To improve the diagnostic accuracy and to curb down negative appendicectomies, the importance oflaboratory findings(both white blood cell counts and C-reactive protein values)[10] and the use of US have been widely evaluated.

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The purpose of this study was to evaluate the sensitivity, specificity, PPV, and NPV of the US (in general and its different acute appendicitis – specific findings) and that of TLC in the final diagnosis of appendicitis.

MATERIALS AND METHODS:

This cross sectional comparative study was carried out in the Radiology and Pathology Departments of CMH Lahore from 1st February 2007 to 31st January 2008.125 cases of clinically suspected acute appendicitis were included in the study through Non-probability purposive sampling**.** Inclusion criteria was:
(1)Patient`s referred by surgeons, with strong clinical suspicion of acute appendicitis (2)any gender (3)any age.Exclusion criteria was(1) patients in whom ultrasound could not be performed (e.g., very obese patients, tense ascites, severe pain)(2)patients with clinical signs of appendicular lump / abscess requiring conservative management or drainage(3)patients with already known abdominal disease(4)history of appendectomy(5)history of any leukocyte disorder.
DATA COLLECTION PROCEDURE: After initial clinical evaluation by the surgeons, patients fulfilling inclusion and exclusion criteria were referred to the radiology department for US. In each patient, the abdomen was initially examined by using a 3.5 / 5.0 MHzconvex-array transducer. Sonographic evaluation of appendix was done by a 7.5 MHz linear-array transducer with graded-compression technique in transverse as well as longitudinal planes. Using psoas major muscle, iliac vessels and cecum as landmarks, visualized appendix was identified as a blind-ended, a-peristaltic tubular structure. Color Doppler US to detect blood flow in appendiceal wall was performed at the end of the grey-scaleultrasound by using a low-velocity scale (pulse repetitionfrequency, 1,500 Hz) and a low wall filter (100 Hz) to detect slow blood flow.US criteria for diagnosing acute appendicitis were grouped into two categories.

(a)Appendiceal findings: These findings were noted for their presence or absence in both normal as well as inflamed appendices.

i. Outer diameter: Appendix was considered inflamed when its outer antero-posterior diameter under compression, measured in transverse plane, was 6 mm or greater.
ii. Lack of compressibility
iii. Fluid in the appendix
iv. Appendicolith
v. Blood flow in appendiceal wall on colour Doppler

(b)Peri-appendiceal findings: These were noted in all patients irrespective of visualization of appendix.

i. Hyperechoic peri-enteric fat in RLQ
ii. Lymph node in RLQ measuring at least 5 mm
iii. Cecal wall thickness of 5 mm or more
iv. Peritoneal fluid

In general, US was considered positive when at least two or more criteria for acute appendicitis were met and negative if a normal looking appendix was visualized or if it was not visualized and / or a definite non-appendicular pathology was noted. The laboratory investigation included total leukocyte count, which was given importance for appendicitis when greater than 10 x 10^9/L. The final decision to operate upon was made by the attending surgeon who was in picture of laboratory as well as US findings. Removed appendices were sent to Pathology Department of CMH Lahore for histopathology. US and TLC findings were compared with those of preoperative surgical findings and histopathology of the removed appendix, the later being the gold standards of diagnosis of acute appendicitis in this study.Patients with negative US findings and those who did not undergo surgery at first place were followed up in respect of clinical and surgical outcomes.Sensitivity, specificity, PPV, NPV and diagnostic accuracy of TLC, US and individual US findings were calculated keeping surgical findings and histopathology of the removed appendices as gold standard.

STATISTICAL ANALYSIS: The McNemar's chi-square test for paired data was applied to analyze the differences between the diagnostic values of US and TLC in the diagnosis of acute appendicitis. Differences were considered statically significant if P values were < 0.05.

RESULTS:

Out of 125patients 73 (58%) were males and 52 (42%) females. Gender wise distribution in 10-year age brackets(Figure1).

US diagnosis of acute appendicitis was made in 57 patients who underwent surgery. Histopathology of the resected appendices showed signs of acute appendicitis in 55, whereas 2 appendices turned out normal, thus making 2 FP US results.

In 68 US negative patients a normal appendix was observed in 30 patients (44% of US negative patients) and in the remaining 38 (56%); it was not seen sonographically. Seven patients, among these 38 US negative patients, persisted to have clinical signs and symptoms of acute appendicitis. Surgical intervention was carried out within 24 h of US examination. These patients had inflamed appendices on surgery and histopathology (thus giving the non-visualizationof the appendix at US a NPV of 82%).These were the FN results of US. Two out of these seven patients had perfoated appendicitis and the other five had Pretrocecal appendices.

In the 63 patients without acute appendicitis, diagnosis was confirmed on US in 30 patients, on surgery in 6 patients (including 2 US false positive cases), at endoscopy in one patient and at clinical follow up in 26 patients. Table1 lists the final diagnoses in these 63 patients.

The number of positive or negative US examinations in respect of acute appendicitis, its TP, TN, FPand FN results and diagnostic accuracy are shown in Table 2.Appendiceal US findings were evaluated in 87 patients. Table3a shows (a) the frequency with which each appendiceal finding was interpreted as positive or negative, (b) the number of TP, TN, FP, and FN results, and (c) the sensitivity, specificity, accuracy, PPV, NPV and diagnostic accuracy of each appendiceal finding. The two most consistentappendiceal findings for appendicitis were a diameter of at least 6 mm or larger and incompressibility. In the non-appendicitis group, the appendiceal diameter was 6 mm or larger in one patient only who had a final diagnosis of pyelonephritis. The periappendiceal US findings were looked for in the entire study group(Table3b). Combining the non-appendiceal findingswith appendiceal findings did not increase the NPV or PPV ofindividualappendiceal findings, such as an appendix 6 mm orlarger in diameter or non-compressibility of the appendix.

The number of TP, TN, FP and FN results and the sensitivity, specificity,accuracy, PPV, NPV and diagnostic accuracy of TLC are shown in Table4. A TLC level above 10 x 10^9/L had a sensitivity of 77% and a specificity of 60% for acute appendicitis in appropriate clinical settings.

US showed more diagnostic utility in comparison to TLC in the diagnosis of acute appendicitis. There was a significant difference between the specificity (97% vs 60%; p value: 0.000), PPV (96% vs 66%; p value: 0.016), NPV (90% vs 73%; p value: 0.016) and diagnostic accuracy (93% vs 69%; p value: 0.009) of US and TLC respectively. However, difference between the sensitivity of both was not much significant (89% vs 77%; p value: 0.189).

Figure: 1
Age and gender distribution of patients with suspected acute appendicitis

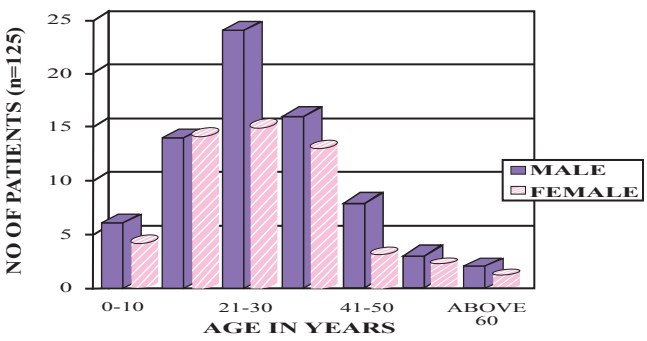

Table:1
Final diagnosis in patients without acute appendicitis

Diagnosis	No of Patients (N= 63)
Non specific abdominal pain	24
Mesenteric adenitis	13
Gynecologic disease	10
Renal and ureteral calculi	8
Ileocolic TB	2
Gastroenteritis	2
Cystitis / UTI	2
Pyelonephritis	1
Duodenal ulcer	1

Table: 2
US results for acute appendicitis

Findings and values	US
Finding at US (n)	
Positive	57
negative	68
Final diagnosis finding (n)	
TP	55
TN	61
FP	2
FN	7
Value (%)	
Sensitivity	89
Specificity	97
PPV	96
NPV	90
Accuracy	93

n = number of patients. Total n = 125
Positive finding mean identification of an inflamed appendix on US. Negative finding means visualization of a normal appendix ornon-visualization of appendix on US

Table: 3a
Appendiceal US signs of acute appendicitis

Finding and value	Diameter > 6 mm	Lack of compress-ibility	Intra-luminal fluid	Appendi-colith	Flow in wall
Finding at US (n)					
Positive	55	55	20	25	28
Negative	32	32	67	62	59
Final diagnosis finding (n)					
TP	54	53	16	15	25
TN	30	29	37	33	30
FP	1	2	4	10	3
FN	2	3	30	29	29
Value(%)					
Sensitivity	96	95	35	34	46
Specificity	97	94	90	77	91
PPV	98	96	80	60	89
NPV	94	90	55	53	51
Accuracy	97	94	61	55	63

n = number of patients. Total n = 87 (in whom appendix was visualized irrespective of its disease status)

Table:3b
Periappendiceal US signs of acute appendicitis

Finding and value	Inflamm-atory fat changes	Cecal wall thickening	Periileal lymph node	Peritoneal fluid
Finding at US (n)				
Positive	65	26	48	55
negative	60	99	77	70
Final diagnosis finding (n)				
TP	50	11	19	31
TN	54	56	40	45
FP	15	15	29	24
FN	6	43	37	25
Value (%)				
Sensitivity	89	20	34	55
Specificity	78	79	52	65
PPV	77	42	40	56
NPV	90	56	52	64
Accuracy	83	54	47	61

n = number of patients. Total n = 125 patients

Table:4
TLC in acute appendicitis

Findings and values	TLC
Finding (n)	
Positive	73
Negative	52
Final diagnosis finding (n)	
TP	48
TN	38
FP	25
FN	14
Value(%)	
Sensitivity	77
Specificity	60
PPV	66
NPV	73
Accuracy	69

n = number of patients. Total n = 125

DISCUSSION:

In our study of 125 patients, US diagnosis of acute appendicitis was made in 57 patients based upon at least 2 of the US criteria of acute appendicitis. Out of these 57 patients, two patients turned out to be having normal appendices on surgery and histopathology. One of these patients was a female in whom a hydrosalpinx was mistaken as a non-compressible pelvic appendix. The other patient had the final diagnosis of non-specific

abdominal pain. Thus the negative appendectomy rate was 3.2%, which is much less as compared to that when diagnosis was made solely on clinical evaluation (10-30% and as high as 47% in women of childbearing age)[6,7,8,9,11,12]. False negative cases were seven. Two out of these seven patients had perforated appendicitis. Perforation of the appendix leads to luminal decompression and reduction in its diameter so that appendix is no longer seen on US.[13,14,15] A non-compressible appendix may be identified in only 38%–55% of patients with perforation.[16] Majority of patients with false negative US results in our study were due to the retrocecal position of the appendix, making it invisible due to overlying cecal gas shadows. False negative US diagnosis of appendicitis owing to its retrocecal position is a commonly reported pitfall in literature [14, 17].

According to our study, identification of an appendix with less than 6 mm diameter was an accurate indication to exclude appendicitis, with a NPV of 94%. Similarly Rettenbacher et al [18]mentioned a NPV of 100%, whereas Rioux[19]reported a NPV of 98%. The appendicular diameter of 6 mm or above for diagnosis of acute appendicitis had high PPV (98%) in our study. The high PPV is out of line with the data obtained by Rettenbacher et al [18], who reported an appendiceal diameter of 6 mm or larger in 32% of symptomatic patients without appendicitis in whom the appendix was identified. Yabunaka[20] had reported the same in 3.6%. We assume that this discrepancy is due to differences in measurement of appendiceal diameter. We thus performed measurements under maximal compression to standardize the measurement because the relevant anteroposterior diameter of a compressible appendix may vary according to the graded compression applied to the abdominal wall, and we hypothesize that we may have compressed some loose feces or air out of the normal patent lumen. However, as mentioned we do have a false positive result based on this criterion. It necessitates the need for addition of at least another US criterion for diagnosing acute appendicitis. In this context, lack of compressibility of appendix was another finding with high PPV (96%) and NPV (90%).

Another finding in our study was Doppler detectable hyperemia in the appendiceal wall was a specific finding for appendicitis that was observed in only three of the patients not having acute appendicitis. Similar high specificity has been reported in already published studies that seldom identified flow in the normal appendiceal wall[21].

Among right lower abdominal quadrant changes, echogenic fat has been observed to be 100% sensitive but not specific to appendicitis at CT[22]. Echogenic fat depicting inflammation in the right lower quadrant may be present in number of differential diagnoses other than appendicitis [23], and we found inflamed fat in 24% of the patients without appendicitis. We did not observe inflamed echogenic periappendicealfat in every patient with appendicitis, which is contrary to known data from CT studies. Right iliac fossa lymphadenopathywas present in 31% of appendicitis positive patients of our study. It is a common finding related to ileal, cecal, or appendiceal inflammatory diseases which may be seen in patients with appendicitis or and also otherwise. We concur with published studies [22, 24]that the much helpful method to differentiate an appendicitis adenopathy from mesenteric adenitis is to identifysonographically either an enlarged inflamed appendix or a normal looking appendix. Cecal wall changes seen on CT include focal cecal apical thickening, arrowhead and cecal bar signs which are suggestive of appendicitis;however, circumferential diffuse wall thickening may also be seen in colitis[22]. However, these observations require adequate cecal distention using the CT technique described by Rao et al [22]. Therefore, we limited our evaluation with US to the identification of cecal wall thickening but did not obtain sufficient predictive values to differentiate appendicitis from non-appendicitis.

Earlier in Pakistan Khan [25]have conducted a prospective study to determine the value of various investigations in the same patient of acute appendicitis including TLC (sensitivity 73%, specificity 80%) and US (sensitivity 86.2%, specificity 91.8%). In our study, TLC and US demonstrated a similar sensitivity of 77% and 89% but specificity of 60% vs 97% respectively for the diagnosis of acute appendicitis. Our study also established that US examinations were superior to TLC for affirming appendicitis (PPV 96% vs 66%; and diagnostic accuracy 93% vs 69%). In addition, more strikingly, US examinations were superior to TLC for excluding appendicitis (NPV 90% vs 73%). Therefore, we do not recommend using TLC as part of an algorithm to restrict imaging indications for patients with increased TLC only. On the other hand, in patients whose appendix is not visualized at US, laboratory tests could be performed to strengthen the NPV of non-visualization of the appendix. However, further studies that include more patients in whom the appendix is not identified at US are necessary to confirm the importance of TLC. Our study faced a number of limitations. First, there was no reliable way to confirm that all patients without appendicitis would have had a normal appendix at histopathologic analysis if surgery had been performed. Second, our study design was based on a prospective evaluation of several US and biologic criteria. We are aware that some additional criteria not included in our protocol may have been interesting to evaluate, especially the thickness of the appendiceal wall, the presence of air in the appendiceal lumen, and the non-compressibility of the periappendiceal fat.

CONCLUSION:

US has better diagnostic utility than TLC in the diagnosis of acute appendicitis. A threshold 6-mm diameter of the appendix under compression is the most accurate US finding with high PPV and NPV for the diagnosis of acute appendicitis. Keeping in view the increasingly high diagnostic accuracy of US for acute appendicitis and its advantages we recommend that US should be carried out more frequently in suspicious patients of acute appendicitis to avoid unnecessary surgical procedures. An US negative patient can be closely

monitored in the hospital instead of being taken straight on to the operation table.

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