VALUE OF SECONDARY INFLAMMATORY SIGNS ON ULTRASOUND IN EVALUATION OF ACUTE APPENDICITIS

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ABSTRACT

Objective: To determine the sensitivity, specificity, positive and negative predictive values using secondary Ultrasound features of inflammation, in suspected patients of acute appendicitis

Study Design: Cross sectional validation study.

Place and Duration of Study: Radiology department, Combined Military Hospital Bahawalpur, from Apr 2016 to Mar 2017.

Methodology: A total of 178 suspected patients of acute appendicitis having right lower quadrant pain were referred for ultrasound. Patient's ages ranges from 5-55 years. Primary and secondary signs of inflammation of acute appendicitis were assessed on ultrasound. Patient having positive primary sign alone or at least two or more secondary signs were labeled as acute appendicitis and underwent surgery. Statistical data was analyzed using Medcalc 17.5.5.

Results: When only Secondary sonographic signs of inflammation were considered in suspected cases of acute appendicitis, then Sensitivity was 88.2%, specificity 72.5%, positive predictive value 81.1%, accuracy 81.5% and negative predictive value was 82.2%. Sensitivity and accuracy were increased to 93.7% and 87.6% % respectively, when primary and secondary signs were considered collectively.

Conclusion: Ultrasound examination should be the first imaging modality to be carried out in suspected cases of acute Appendicitis with particular emphasis on secondary ultrasound features, as primary features are not always present. Presence of both these signs confidently diagnose Acute Appendicitis.

Keywords: Appendicitis, Computed tomography, Ultrasound.

INTRODUCTION

Acute appendicitis is a fairly common disease; rapid and accurate diagnosis is mandatory to prevent its complications. It is one of the most common abdominal surgical emergencies and has about 7% lifetime prevalence[1]. The accurate diagnosis of appendicitis relies on a combination of clinical and imaging findings. Imaging is vital to accurate and prompt diagnosis when the clinical presentation is equivocal. Negative appendectomy rate can be markedly reduced with the use of proper imaging modality like ultrasonography in a clinically suspicious patient of acute appendicitis. Negative appendectomy rate has been reported to be as high as 15%[2-5].

Computed tomography (CT) is the most accurate imaging modality for evaluation of suspected acute appendicitis and alternative diseases with lower right quadrant pain according to American College of Radiology[6]. In children, ultrasound is more preferred over CT scan as an initial examination, because it is readily available and nearly as accurate as CT for the diagnosis of acute appendicitis. Moreover, there is no use of ionizing radiations for children. In pregnant women, ultrasound is also preferred initial investigation; while MRI remains a second imaging examination in in conclusive cases[7].

Non-visualization of the appendix is the most common situation in which interpretive uncertainty exists, occurring in approximately half of ultrasound examinations performed to evaluate for appendicitis. Cases in which the appendix is not seen but in which sonographic findings suggest a right lower quadrant inflammatory process constitute a greater diagnostic dilemma[8]. Acute Appendicitis is mostly caused due to obstruction of the lumen of appendix. This leads to buildup of fluid, evolution of secondary infection, venous congestion followed by ischemia and necrosis. The location of the tip of the appendix is verydifficult to demarcate, as the length of the appendix has an extensive range of 2-20cm[9].

When Appendix is not visualized and there are no secondary sonographic features of inflammation, itis considered as negative for acute appendicitis. Moreover, in cases where the appendix is not directly visualized on ultrasound, then presence of secondary features of inflammation are often deemed equivocal[10]. This study is aimed at these equivocal cases in which appendix are not directly visualized. In this study, we assessed the importance of secondary inflammatory

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changes of acute appendicitis, when inflamed appendix is not directly visualized on ultrasonography. Sensitivity, specificity, accuracy, positivepredictive values and negative predictive values were calculated, using secondary ultrasound features alone and in combination with primary features taking operative findings as Gold Standard.

METHODOLOGY

This cross sectional study was carried out in Radiology department of Combined Military Hospital Bahawalpur, from April 2016 to March 2017. A total of 178 suspected patients of acute appendicitis having right lower quadrant pain were referred from surgical department for ultrasound. Patient's ages varied from 5-55 years. Sample was collected by nonprobability purposive sampling and sample size was calculated by CPSP calculator which appeared to be 178. Toshiba color Doppler Ultrasound Machine (NEMIO 17) with 3.5 and 7.5 MHz probes was used to look for primary and secondary signs of inflammation for acute appendicitis.

All of these patients underwent abdominal ultrasound by experienced radiologist for assessment of primary and secondary sonographic signs. Primary signs (direct signs) include direct visualization of thick walled, aperistaltic, blind-ended, reproducible, non-compressible appendix (diameter of >6 mm or single wall thickness of > 3mm) and presence of appendicolith (fig-1). Secondary sonographic signs (indirect signs) include presence of adjacent free fluid (fig-2), phlegmon formation, peri-cecal inflammatory fat changes and mesenteric lymph nodes in right lower quadrant.

Patient having positive primary sign were labeled as having acute appendicitis and after correlation with laboratory investigations, underwent surgery for acute appendicitis. Patients having at least two or more secondary signs were also labeled as acute appendicitis and underwent surgery.Children having age greater than 5 year and pregnant patients are included inthis study. Patients with known history of crohns disease and ileo-cecal Tuberculosis were excluded from this study. Gold standard was per operative assessment of inflamed appendix and histological evaluation of surgically removed appendix.

Data was analyzed using Med-calc 17.5.5. The continuous data such as age was described in terms of mean ± SD (Standard deviation) while frequencies or percentages were calculated for categorical variables like gender, presence or absence of primary and secondary signs on Ultrasound and accuracy is calculated. Outcome was based on the surgical pathologic result for patients who underwent surgery. The negative appendectomy rate was calculated as the number of normal appendixes removed (confirmed at surgical pathologic examination) divided by the total number of operations performed in the sample set.

All results are presented as tables and/or graphs. Sensitivity, specificity, positive predictive values, negative predictive values and accuracy of secondary sonographic signs for acute appendicitis was calculated with help of 2x2 table. Further analysis for specificity and sensitivity of the models and of isolated variables was performed with Microsoft Excel software.

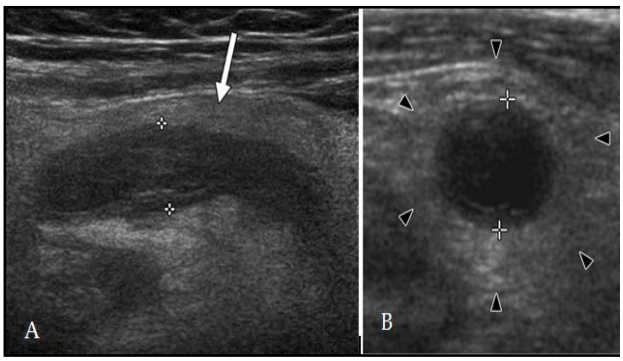

Figure-1: (Primary feature) (A&B) Thick walled inflamed appendix, 6mm thick with surrounding echogenic inflamed mesentery.

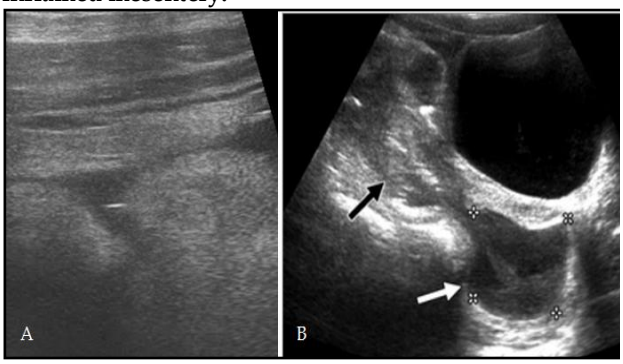

Figure-2: (Secondary features) (A) Free fluid in right iliac fossa. (B) Localized collection of fluid in pelvis with thick walled loop.

RESULTS

Out of 178 patients 63 (35 %) were female and 115 (65 %) were males (table-I). From total of 178 patients 45 (25%) patients were having no primary sign or less than two secondary sonographic signs of acute appendicitis. Other causes of right lower quadrant pain were identified in 24 patientsout of 45. Only 8 out 45 (False Negative) patients were labeled as acute appendicitis, keeping in view the clinical assessment and laboratory parameters of inflammation (increasedwhite blood cell

count and C-reactive protein). They alsounderwent surgery for acute appendicitisthat proved correct.

In remaining 133 (178-45) patients, 74 (42%) were having two or more secondary sonographic signs on ultrasound. Out of these, 60 patients (true positive) were having acute and chronic inflammatory changes of appendicitis in surgically removed appendix. Fourteen cases were reported normal (False positive) out of 74 patients. When only secondary sonographic signs were considered then sensitivity was 88.2%, specificity was 72.5%, positive predictive value was 81.1%, negative predictive value was 82.2% and accuracy was 81.5% (table-II). Primary sonographic signs of inflamed appendix were seen in 59 (33%) patients out of 133 patients, that proved to be correct according to peroperative assessment of inflamed appendix and histological evaluation of surgically removed appendix. When primary and secondary sonographic signs were collectively considered (59 ± 60=119), sensitivity was 93.7%, specificity was 72.5%, positive predictive value was 89.5%, accuracy was 87.6% and negative predictive value was 82.2% (table-II).

Table-I: Primary and secondary signs for diagnosis of acute appendicitis (n=178).

	Secondary Inflammatory Signs	Primary and Secondary Inflammatory Signs	Difference (%)
Sensitivity	88.2%	93.7%	5%
specificity	72.5%,	72.5%	-
PPV	81.1%	89.5%	8%
NPV	82.2%	82.2%	-
Accuracy	81.5 %.	87.6%	6%

Table-II: Frequencies (n=178).

Variables	n (%)
Male	63 (35)
Female	115 (65)
No primary sign or <2 secondary sonographic sign of acute appendicitis	45 (25)
Two or more secondary sonographic signs on ultrasound	74 (95)
Primary sonographic signs of inflamed appendix	59 (75)
Total	178

When only primary sonographic signs were considered sensitivity was 88%, specificity was 72.5%, positive predictive value was 80.8%, negative predictive value was 82.2% and accuracy was 81.3%.

DISCUSSION:

Acute appendicitis is the one of most common emergency presentations requiring surgical intervention in both adults and children. A study carried out by Jin *et al* revealed that in a year almost 29,000 appendicectomies were performed, that is approximately 10% of all surgical emergencies[11]. Despite the availability of ultrasound for more than 25 years, consistent accurate prediction of appendicitis with this modality remains a challenge. Ultrasound and CT are the most commonly used imaging modalities to evaluate patients with symptoms of acute appendicitis, particularly because the findings can lead to a change in the treatment plan in patients with acute appendicitis. Over the past decade, the use of abdominal CT to evaluate suspected cases of appendicitis has been reevaluated because of broadening awareness of the risks of exposing patients to radiation. As a result, there has been increasing support for an "ultrasound-first" paradigm in the imaging evaluation of appendicitis in which ultrasound is used as the initial imaging modality and CT is used if the ultrasound results are equivocal or raise additional questions for diagnosis[12].

Ultrasonography is very reliable imaging modality to identifying abnormal appendix, particularly in lean patients. However, the identification of inflamed appendix is more problematic in obesepatientsand in many instances, appendicitis cannot be ruled out. Imaging modality such as ultrasonography with compression technique has become important tool in diagnosis of acute appendicitis[13]. It is readily available, there is no use of ionizing radiations andis cost effective. In our study we found primary ultrasonographic signs (direct signs) as direct visualization of thick walled, non-compressible appendix diameter of >6 mm or single wall thickness of greater than 3mm and presence of appendicolith. Secondary sonographic signs (indirect signs) in our study include presence of free fluid, phlegmon formation, peri-cecal inflammatory fat changes, and mesenteric lymph nodes in right lower quadrant. These findings are in consistent with other studies by Azhar *et al*[14], and Lin *et al*[15].

Computed tomography provides a more precise diagnosis of appendicitis than ultrasound and has high negative predictive value when compared to ultrasound. However, it is associated with increased radiation risks. Therefore, cautionary use in children is recommended and can be used as complementary second line modality in cases of acute appendicitis[16]. Perforation of appendix occurs with rates ranging between 23% and 73%[17]. With the trend toward conservative management of perforated appendicitis as opposed to immediate appendectomy for non-perforated appen-

dicitis, differentiation between the two conditions has become increasingly important. Because clinical differentiation is not always possible, clinicians often rely on imaging findings[18].

This study particularly focused on using secondary ultrasound features alone and in combination with primary features to diagnose acute appendicitis. It shows that when only secondary sonographic signs were considered then diagnostic sensitivity was 88.2%, specificity 72.5%, positive predictive value 81.1%, accuracy 81.5%, and negative predictive value was 82.2%. When primary and secondary sonographic signs were collectively considered in our study, sensitivity was increased to 93.7% and specificity to 72.5%. These results are similar to study carried out by Al-Khayal *et al*[19], that showed sensitivity of 83.7%, specificity of 95.9%, accuracy of 92.2%, positive predictive value of 89.8% and negativepredictive value of 93.2% using primary and secondary sonographic signs for the diagnosis of acute appendicitis.

In another study carried out by Estey *et al*[20], in the presence of secondary ultrasound features of appendicitis, the specificity of marked free fluid is 98%, specificity of phlegmon is 100%, peri-cecal inflammatory fat changes specificity is 98% and free fluid with prominent lymph nodes is 81%. These results are better than our study having sensitivity of 82.2%. This slight difference when compared to our study is because; aforementioned study was carried out in pediatric population[20].

Although the trend has been to use ultrasound as the initial imaging modality to diagnose appendicitis, the lower sensitivity of ultrasound has led to diverging opinions. Some favor judicious use of CT, citing the risk of perforation and worsening peritonitis versus unnecessary surgery in patients with symptoms[21]. Gorter *et al*[22], suggested the effectiveness of a staged ultrasound and CT protocol in which ultrasound is performed first with suspected acute appendicitis; CT is performed if the ultrasound findings are equivocal. In our study, we expanded this approach, aiming to further reduce the use of CT by stratifying patients with equivocal (inconclusive) ultrasound findings into groups based on primary and secondary signs in appendicitis.

Study by Xu *et al*[23], that when primary and secondary sonographic signs were collectively considered, sensitivity was increased to 93.3% that is near to CT scan sensitivity of 94%. This was in accordance to our study at this setup.CT scan may not be readily available in peripheral medical institutes; therefore, ultrasound examination is very reliable and cost-effective imaging modality in diagnosis of acute Appendicitis. On ultrasound particular emphasis should be on secondary inflammatory signs of acute appendicitis when primary features of inflammation are not present. With the application of an interpretive scheme incorporating equivocal categories and recognizing the high negative predictive value of a non-visualized appendix without secondary findings in the right lower quadrant, we found that the accuracy of sonographic interpretations of positive or negative improved from 94.1-96.8%[24].

This study put emphasis on the diagnostic accuracy of ultrasound in the identification of acute appendicitis, with a particular attention on the utility of secondary sonographic signs as an adjunct to traditionally examined criteria. These secondary signs can be very helpful in cases where the appendix cannot be identified on ultrasound and a more meaningful finding may be made by incorporating the presence or absence of these secondary sonographic signs. According to this study integrating these secondary signs into the final ultrasound diagnosis can improve the diagnostic yield of ultrasound in cases where appendicitis is expected[25].

CONCLUSION

A careful clinical assessment complemented by ultrasound as imaging tool should be used to accurately diagnoseacute appendicitis. Depending on the available local expertise, Ultrasound examination should be the first imaging modality to be carried out in suspected cases of acute Appendicitis with particular emphasis on secondary ultrasound features as primary features are not always present. Moreover, combining these features will yield better diagnostic results.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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