

EVALUATION OF DIAGNOSTIC ACCURACY OF ALVARADO SCORE, LABORATORY INVESTIGATIONS AND ULTRASOUND FINDINGS IN ACUTE APPENDICITIS AND TO CORRELATE THE RESULTS WITH OPERATIVE AND HISTOPATHOLOGY FINDINGS

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ABSTRACT

BACKGROUND

Acute appendicitis is the most common surgical emergency. So far no single criteria can accurately confirm the preoperative diagnosis of acute appendicitis in the suspected cases. Every effort should be made to establish an exact diagnosis. This has resulted in considerable research to find out the role of various clinical scores, laboratory, radiological parameters and diagnostic laparoscopy in diagnosing appendicitis. However, despite availability of various biochemical and radiological diagnostic investigations like total leucocyte count (TLC), C-reactive protein (CRP), Procalcitonin (PCT), D-dimer and ultrasonography (USG) and computed tomography (CT) scan, a negative appendectomy rate of 5% - 30% has been reported in literature. A wide variation exists in sensitivity, specificity, positive predictive value and negative predictive value of these parameters in various studies conducted earlier.

The present study is aimed to evaluate, correlate and compare the diagnostic efficacy of clinical score, various biochemical investigations and USG in cases operated with pre-operative diagnosis of acute appendicitis with confirmation of final diagnosis by histopathology.

MATERIALS AND METHODS

This study was carried out during a period from February 2014 to July 2015 and included 100 consecutive patients of acute appendicitis. Alvarado score, total leucocyte count, C-reactive protein, Procalcitonin, D-dimer and ultrasonography were performed in all cases preoperatively and histopathological examination done postoperatively.

RESULTS

Age of patients ranged from 10 to 74 years with mean age of 29.24 years; 71 were males and rest were females with the male-to-female ratio being 2.44: 1. Alvarado score was ≥ 7 in 75 cases of proven appendicitis and in 4 cases of normal appendix with sensitivity, specificity, PPV, NPV and diagnostic accuracy of 78.94%, 20.00%, 94.93%, 4.76% and 76%. TLC was $\geq 10,000/\text{mm}^3$ in 55 cases of the patients with acute appendicitis and in 3 cases of normal appendix. The sensitivity, specificity, PPV, NPV and diagnostic values of TLC were 57.89%, 40.00%, 94.83%, 4.76% and 57.00% respectively. CRP was $\geq 5 \text{ mg/dL}$ in 90 cases and 86 cases had acute appendicitis on histopathology. The sensitivity, specificity, PPV and NPV of CRP were 90.53%, 20.00%, 95.56% and 10.00% respectively with a diagnostic value of 87%. D-dimer $\geq 0.5 \mu\text{g/dL}$ was seen in 69 cases and 65 cases were having acute appendicitis on histopathology. The difference was not found to be significant ($p = 1$). Sensitivity, specificity, PPV, NPV and diagnostic accuracy were 68.42%, 80%, 98.48%, 11.76%, 66% respectively. Procalcitonin level in 33 cases was $\geq 1 \text{ ng/dL}$, out of which 32 cases had acute appendicitis on histopathology. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of PCT were 33.68%, 80%, 96.97%, 05.97% and 36% respectively. USG findings suggested acute appendicitis in 90 cases, out of which 86 patients had acute appendicitis. The sensitivity, specificity, PPV, NPV and diagnostic accuracy were 90.53%, 20.00%, 95.55%, 10.00%, 87% respectively. Histopathological findings of acute appendicitis were confirmed in 95 cases, while in five cases appendix was normal on histopathology.

CONCLUSION

Negative appendectomy rate in our study was 5%. Alvarado score, various laboratory investigations or USG are not sufficient on their own for taking the decision for surgery. USG and CRP were the most sensitive investigations with equal diagnostic value. Among the inflammatory markers, the diagnostic value of CRP was higher than PCT and D-dimer. CRP and USG along with Alvarado score can increase the diagnostic accuracy in acute appendicitis.

KEYWORDS

Acute Appendicitis, Alvarado Score, USG, Laboratory and Histopathology.

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BACKGROUND

Acute appendicitis remains most common emergency surgery. The accurate diagnosis of acute appendicitis on clinical examination alone remains a challenge in assessment of women of child bearing age and children. The initial misdiagnosis rate for appendicitis range from 28% - 57% for older children and may reach up to 100% for those 2 years or younger.¹ A delay in diagnosis of acute appendicitis is associated with increased risk of perforation (35%) and further complications.² Surgeons have accepted higher rate of negative appendectomies in order to decrease the incidence of perforation. This approach has been increasingly questioned in today's era of cost effective health care conflicts and litigation.³ The goal of surgical treatment is removal of inflamed appendix before perforation with minimal number of negative appendectomies. Many attempts have been made to determine ways of decreasing the negative laparotomy rate after a clinical suspicion of acute appendicitis. A negative appendectomy rate of 3% - 30% has been reported in literature and many surgeons would accept a rate of up to 20% as inevitable.⁴ Clearly, other aids for diagnosis are required and it would be of interest to know whether the additional use of laboratory, radio-imaging or laparoscopy could reduce the negative appendectomy rate in this group.⁵ This has resulted in considerable research on various clinical scoring system, laboratory and radiological studies to improve the diagnostic accuracy in acute appendicitis.^{6,7,8} Leucocyte count and C-reactive protein (CRP) are the most commonly used laboratory tests. Procalcitonin (PCT) and D-dimer have been studied as novel biomarkers for the diagnosis of acute abdomen in recent years.⁹ Ultrasound (USG) has been increasingly used in the past years for the diagnosis of acute appendicitis with high sensitivity and specificity rates.¹⁰ Plain abdominal films and barium studies are considered of limited value. Computed Tomography (CT) scan is complimentary to ultrasonography, but with disadvantages of greater cost exposure to ionising radiation and contrast agents. However, in doubtful cases it may be helpful to diagnose the condition.¹¹ Tc-labelled WBC (white blood cell) scan has a sensitivity of about 90% and specificity of 80% - 90%.¹² Laparoscopy has advantage in suspected cases of acute appendicitis to visualise and exclude other causes of right iliac fossa pain.¹³ In various studies a wide variation exists in sensitivity, specificity, positive predictive value and negative predictive value of clinical score, laboratory investigations and USG in diagnosing acute appendicitis. Very few studies are there, in which efficiency of different

diagnostic modalities for the diagnosis of acute appendicitis is evaluated and correlated. Thus, we planned to evaluate the role of Alvarado score, total leukocyte count, C-reactive protein, procalcitonin, D-dimer and ultrasound in acute appendicitis and correlate their efficacy with the operative and histopathological findings.

Recognition of acute appendicitis as a clinical entity is attributed to Reginald Aeber Fitz who presented a paper on it in 1886.¹⁴ Charles McBurney is credited with the first attempt to make a diagnostic criterion for acute appendicitis by describing the McBurney's point.¹⁵ While Claudius Amyand F.R.S records the first removal of the human appendix in 1735, during the course of operation for hernia.¹⁶ Mestivier in 1759 was the first to wilfully open an appendiceal abscess.¹⁷ Hancock in 1948 did the laparotomy for peri-appendicular suppuration and proposed such treatment for all such cases with abscess before pointing or fluctuation had occurred, or even before adhesions to the anterior abdominal wall had formed. The procedure looked to be temerarious in the extreme, in spite of excellent recovery made by his patient.¹⁷ In 1886, Hall was the first American surgeon to remove a gangrenous appendix found incidentally in a strangulated inguinal hernia.^{18,19} In the same year, Fitz published the first 100 cases of successful drainage of abscess of the appendix that covered the period from 1848 to 1886 that he was able to find in the literature of his country. The greatest contributor to the advancement in the treatment of appendicitis is of Charles McBurney. In 1889, he published his landmark paper in the New York medical journal describing the indications for early laparotomy for the treatment of appendicitis.^{20,21} Semm is widely credited with performing the first successful laparoscopic appendectomy in 1982.²² Roy G et al (1969) found that out of 451 cases of appendicitis, 408 cases had inflamed appendix, 27 looked normal and 16 had doubtful inflammation and signs of previous inflammation in 51 cases.²³ Samsi et al (1969) in their study of consecutive cases of acute appendicitis with their histological findings that in the series of 100 cases operated for acute appendicitis 71 showed definitive evidence of acute appendicitis, 22 showed no evidence of acute inflammation, while 4 appeared normal.²⁴ Chang FC et al (1977) in their study of rate of the negative appendectomies stated that in 183 patients, 33% of the patients were found to have a disease other than appendicitis.²⁵

Alvarado (1986) conducted a retrospective study of 305 patients hospitalised with abdominal pain suggestive of acute appendicitis. Signs, symptoms and laboratory findings were analysed for specificity, sensitivity, predictive value and joint probability. The total joint probability, the sum of a true positive and a true negative result was chosen as a diagnostic weight indicative of the accuracy of the test. Eight predictive factors were found to be useful in making the diagnosis of acute appendicitis. Their importance according to their diagnostic weight was determined. This score help in interpreting the confusing picture of acute appendicitis.²⁶

Ultrasonography examination using graded compression is the examination of choice if there is doubt whether appendectomy should be performed.⁸ Abu-Yosuf MM et al (1987) showed ultrasonography technique was found to be accurate in the diagnosis of acute appendicitis with a specificity of 85%, a sensitivity of 80% and an accuracy of 90%.²⁷ Stephens PL and Mazzucco JJ (1999) compared ultrasound to the Alvarado score for the diagnosis of acute appendicitis, neither one was found to be absolutely accurate. However, the false positive rate is reduced to zero when both studies are positive and ultrasound improved diagnostic accuracy when the Alvarado score was negative or equivocal. Ultrasound is unnecessary when one's degree of clinical suspicion is high. However, the additional information provided by the ultrasound does improve diagnostic accuracy in case of negative or equivocal score.^{28,29} Johansson et al studied the role of USG, CT scan and laboratory findings in the diagnosis of acute appendicitis. The sensitivities and specificities were 91% and 94% for CT and 83% and 98% for USG respectively. Diagnostic accuracy was high for USG as well as for CT. USG was better for diagnosing positive finds, while CT was better for excluding of appendicitis.³⁰

Though several markers of inflammation have been proposed, TLC is the most common and most studied laboratory investigation for appendicitis.³¹ Leukocytosis increases with the duration of disease process, but on the contrary even in perforated appendix a normal white cell count may be observed.³² Also TLC may be elevated in up to 70% of patients with other causes of right lower quadrant like non-specific mesenteric lymphadenitis, right ureteric colic, etc. An elevated CRP is common in appendicitis, but studies disagree for its sensitivity and specificity. In case of both CRP and TLC, there is increase in sensitivity to 55%, specificity of 100% and an accuracy of 77% in diagnosing acute appendicitis. Increased CRP appears to have better sensitivity and TLC has better specificity.^{33,34} The diagnostic value of leucocyte count and CRP in acute appendicitis was higher than that of the other markers, whereas leucocyte count showed very low specificity. CRP values were higher in perforated appendicitis when compared with the phlegmonous appendicitis. However, PCT and D-dimer showed lower diagnostic values 26% and 31%, respectively. Studies concluded that an increase in CRP levels alone is not sufficient to make the diagnosis of acute appendicitis. However, CRP levels may differentiate between phlegmonous appendicitis and perforated appendicitis. Due to their low sensitivity and diagnostic value, PCT and D-dimer are not better markers than CRP for the diagnosis of acute appendicitis.⁹ Vaziri et al (2014) conducted a study on 100 patients and found sensitivity of 44%, specificity of 100%, PPV of 100% and NPV of 10%.³⁵ Kouame et al (2005) found PCT > 0.5 ng/dL in 12% of their patients with acute appendicitis reflected no role of PCT as a diagnostic marker.³⁶

Aims and Objectives

Evaluation of the diagnostic value of Alvarado score, laboratory investigations and ultrasound in acute appendicitis and to correlate the results with operative and histopathology findings.

MATERIALS AND METHODS

This observational study was carried out in the Department of Surgery in collaboration with Department of Biochemistry, Department of Radiodiagnosis, Department of Pathology at Government Medical College and Hospital, Chandigarh (GMCH) with the ethical clearance taken from Institutional Ethical Committee.

A total of 100 subjects of any age and sex who presented with pain in right iliac fossa and were suspected to have acute appendicitis based on typical history and clinical diagnosis requiring surgery were enrolled for the study.

Exclusion Criteria

1. Patients who had appendicular mass.
2. Patients who did not undergo surgery on clinical suspicion.

Patient's demographic profile, duration of symptoms, Alvarado score were recorded and blood samples were sent for the WBC count and differential leucocyte count and pre-operative C-reactive protein. Blood sample was taken for Procalcitonin and D-dimer and stored at -20°C and results were observed retrospectively. The cut-off value for white cell count was taken as 10,000/mm³. CRP and D-dimer were quantitated by immunoturbidimetric method on autoanalyzer (modular-P 800 automated chemistry analyzer), the value of ≥ 5 mg/dL was taken as positive for CRP and ≥ 0.5 µg/dL for D-dimer. PCT was done by chemiluminescence method on Advia Centaur XP and the value taken into consideration was ≥ 1 ng/dL.

Variables	Clinical Feature	Score
Symptoms	Migratory pain in RIF	1
	Anorexia	1
	Nausea/ vomiting	1
Signs	Tenderness in RIF	2
	Rebound pain	1
	Elevation of temperature	1
Lab	Leukocytosis	2
	Shift to the left	1
Total		10
Table 1. Alvarado Score was Calculated depending upon the Clinical Symptoms, Signs and Laboratory Investigations		

A score of 5 or 6 is compatible with the diagnosis of acute appendicitis. A score 7 or 8 indicates a probable appendicitis, and a score of 9 or 10 indicates a very probable acute appendicitis.²⁸ A score of ≥ 7 was taken into consideration.

Ultrasound was done in all cases. The ultrasonic positive findings suggestive of appendicitis were: identification of a tubular intestinal structure located in the lower right lower quadrant of the abdomen, closed at one end with a

transverse diameter exceeding 6 mm, not compressible and aperistaltic, the appearance of appendicolith and/or the presence of extra-appendicular alterations such as inflamed perienteric fat, periappendicular abscess. After the diagnosis of acute appendicitis was made, all required investigations for the anaesthesia and surgery were done. Appendectomy was done with standard muscle splitting incision. Detailed operative findings were recorded.

Confirmation of acute appendicitis as the final diagnosis was obtained from histological analysis of the appendix in the Department of Pathology. All the observations were recorded in and analysed statistically using appropriate statistical test.

Statistical Analysis

At the end of the study, all the collected data were entered in Microsoft Excel spreadsheet. The overall accuracy of each test was assessed by sensitivity, specificity, positive predictive value, negative predictive value and diagnostic value. Measurement of concordance between diagnostic evaluation and gold standard histopathology was analysed by applying Chi-square test. The level of statistical significance was taken as 'p' value ≤ 0.05 . All the analyses were done in SPSS (statistical package for social sciences).

Observations

The mean age of patients presenting with clinical picture of appendicitis was 29.24 years. The youngest patient was 10 years and oldest was 74 years. Maximum number of cases were in 21 - 30 years' age group (33) followed by 10 - 19 years (25 cases) and only 6 cases were more than 60 years old; 29 cases were females and 71 cases were males.

Histopathological Findings

Histopathology	No. of Patients
Acute Appendicitis with Periappendicitis	25
Acute Diffuse Suppurative Appendicitis with Periappendicitis	31

Follicular Appendicitis	3
Gangrenous Appendicitis with Periappendicitis	12
Healing Appendicitis with Periappendicitis	24
Normal	5
Total	100
Table 2. Distribution of Cases according to Histopathologic Diagnosis	

Maximum cases were of acute diffuse suppurative appendicitis with periappendicitis in 31 cases and normal appendix in 5 cases (Table 2).

The most common symptom was pain in right iliac fossa, which was present in all the patients. Other symptoms were nausea and vomiting, shifting of pain, fever and anorexia.

27 patients presented within 24 hours, 17 patients had acute appendicitis and 1 patient had perforated appendicitis with a significant Alvarado score; 53 patients presented to us in emergency within 48 hours of pain and in 44 (67.7%) cases had appendicitis histopathologically; 47 cases reported after 48 hours of pain and in these 23 (maximum cases) had perforated appendicitis (76.7%). This difference was found to be statistically significant ($p = 0.001$). Alvarado score was significantly raised in 21 patients out of these 23 patients. This difference was not found to be statistically significant.

TLC was raised in 58 patients of clinically suspected acute appendicitis. Out of 95 cases of proven acute appendicitis, only 55 cases were having raised TLC. This difference was found to be not statistically significant ($p = 1$). TLC $\geq 10,000/\text{mm}^3$ had sensitivity, specificity, PPV, NVP and DV of 57.89%, 40.00%, 94.83%, 4.76% and 57% respectively. TLC was raised in 14 (51.85%) cases out of 27 cases those presented early after the onset of pain and 31 (65.95%) cases out of 47 patients those who presented late; 22 cases were of acute appendicitis those presenting late and it was raised in only 10 (45.45%) patients. This difference was found to be statistically significant after 48 hours.

Duration of Onset of Pain	CRP	Appendicitis	Perforated Appendicitis	Normal	Total	P-value
<24 hours	<5 mg/mL	2	0	1	27	0.184
	≥ 5 mg/mL	22	1	1		
24-48 hours	<5 mg/mL	3	0	0	26	0.600
	≥ 5 mg/mL	17	6	0		
>48 hours	<5 mg/mL	4	0	0	47	0.083
	≥ 5 mg/mL	18	23	2		
Total		66	30	4	100	
Table 3. Analysis of CRP with Duration of Time and Operative Findings						

CRP was raised in 24 (88.88%) patients out of 27 cases at 1st day of presentation and in 44 (93.62%) cases those who presented late. It was raised in all 23 (100%) cases of perforated appendicitis and 18 (81.82%) cases of acute appendicitis. This difference was not found to be statistically significant. C-reactive protein was raised in 90 patients out of 100 patients of suspected acute appendicitis. However, 86 patients had acute appendicitis on histology, while it was

also raised in those 4 cases also who were not having acute appendicitis on histology. This difference was found to be not statistically significant ($p = 0.999$). C-reactive protein ≥ 5 mg/dL had sensitivity, specificity, PPV, NVP and DV of 90.53%, 20.00%, 95.56%, 10.00% and 87% respectively (Table 3).

PCT was raised in 8 (29.62%) cases out of 27 cases those who presented early after the onset of pain and 15

(31.91%) cases out of 47 patients those who presented late; 22 cases were of acute appendicitis those who presented late and it was raised in 4 (18.18%) patients and 11 (23.82%) cases of perforated appendicitis. This difference was not found to be statistically significant. PCT was raised in 33 patients out of 100 patients of suspected acute appendicitis. However, 32 patients had appendicitis on histology. PCT was < 1 ng/dL in 63 cases of acute appendicitis and 4 cases with normal appendix. This difference was found to be not statistically significant ($p=0.664$). PCT ≥ 1 ng/dL had sensitivity, specificity, PPV, NPV and DV of 33.68%, 80.00%, 96.97%, 5.97% and 36% respectively.

D-dimer was raised in 69 cases. Acute appendicitis was seen in 65 patients and appendix was normal on histology in 4 cases. D-dimer was not raised in 30 patients. This difference was found to be not statistically significant ($p=1$). D-dimer had sensitivity, specificity, PPV, NPV and DV of 68.42%, 80.00%, 98.48% and 11.76% and 66% respectively. D-dimer was raised in 13 (56.52%) cases out of 27 cases those who presented early after the onset of pain and 37 (78.72%) cases out of 47 patients those who

presented late; 14 (63.64%) cases were of acute appendicitis those who presented late and it was raised in 21 (91.30%) patients of perforated appendicitis. This difference was not found to be statistically significant.

In the present study, 90 patients were having USG findings positive for suspected acute appendicitis; 86 patients were having acute appendicitis on histology, whereas only 4 cases with normal appendix had normal findings on USG. This difference was found to be not statistically significant ($p=0.43$). USG had sensitivity, specificity, PPV, NPV and DV of 90.53%, 20.00%, 95.55%, 10.00% and 87% respectively. USG was positive in 13 (92.59%) cases out of 27 cases those who presented early after the onset of pain and 41 (87.23%) cases out of 47 patients those who presented late. However, it shows perforation of appendix in 3 cases, out of which only 1 (33.33%) had perforated appendicitis within 24 hours of presentation. Out of 23 patients of perforated appendicitis who presented late, it shows appendicitis in 8 cases and perforated appendicitis in 11 cases. This difference was found to be statistically significant after 48 hours.

Investigations	Appendicitis	Perforated Appendicitis	Normal	P value
Alvarado score				
≤ 6	17	3	1	0.209
≥ 7	49	27	3	
TLC*				
$<10,000/\text{mm}^3$	34	6	2	0.014
$\geq 10,000/\text{mm}^3$	32	24	2	
CRP**				
$<5 \text{ mg/mL}$	9	0	1	0.077
$\geq 5 \text{ mg/mL}$	57	30	3	
PCT+				
$<1 \text{ ng/mL}$	50	14	3	0.018
$\geq 1 \text{ ng/mL}$	16	16	1	
D-dimer				
$<0.5 \mu\text{g/mL}$	28	2	1	0.002
$\geq 0.5 \mu\text{g/mL}$	38	28	3	
USG++				
Normal	4	4	0	<0.001
Appendicitis	56	10	4	
Perforated appendicitis	6	16	0	

Table 4. Analysis of Alvarado Score, TLC, CRP, Procalcitonin, D-Dimer and Ultrasound with Operative Findings

*TLC= Total leucocyte count, **CRP= C-Reactive Protein.

+ PCT= Procalcitonin, ++ USG= Ultrasonography.

Alvarado score was ≤ 6 in 21 cases of suspected acute appendicitis. Intraoperative inflamed appendix was found in 20 patients and normal in 1 case. It was > 6 in 79 cases, out of which 76 cases had inflamed appendix. This difference was not statistically significant ($p=0.209$). Total leucocyte count was raised in 58 patients and only 2 cases had normal appendix. TLC was not raised in 42 cases and only 1 case was not having inflamed appendix. This difference was

found to be statistically significant ($p=0.014$). C-reactive protein was raised in 90 patients, out of which 87 patients were having either appendicitis or perforated appendicitis, while it was raised in 3 patients out of 4 patients of normal appendix. This difference was found to be statistically not significant ($p=0.077$). Procalcitonin was raised in 33 patients, out of which only 1 patient had normal appendix; 67 patients had normal value of procalcitonin, while appendicitis was seen in 64 patients. This difference was found to be statistically significant ($p=0.018$). D-dimer was raised in 69 cases and normal in 31 cases, but it was raised in 3 cases of having normal appendix. This difference was

found to be statistically significant ($p= 0.002$). Ultrasound was showing appendicitis in 70 patients and perforated appendicitis in 22 patients. Normal appendix on ultrasound was seen in 6 patients, while all these cases were having intraoperative appendicitis. Negative appendectomy was

done in 4 cases of ultrasound proven appendicitis. This difference was found to be statistically significant ($p=< 0.001$), Table 4.

Parameters	Sensitivity	Specificity	PPV	NPV	DV
Alvarado score	78.95%	20.00%	94.94%	04.76%	76%
TLC	57.89%	40.00%	94.83%	04.76%	57%
CRP	90.53%	20.00%	95.56%	10.00%	87%
PCT	33.68%	80.00%	96.97%	05.97%	36%
D-dimer	68.42%	80.00%	98.48%	11.76%	66%
USG	90.53%	20.00%	95.55%	10.00%	87%

Table 5. Showing Relative Accuracy of Various Diagnostic Tests

In our study, CRP and USG were the most sensitive investigations (90.53%) and both had equal diagnostic value, whereas PCT had least sensitivity (33.68%) and diagnostic value. PCT and D-dimer had maximum specificity (80.00%) and D-dimer also had maximum PPV (98.48%). Least specific were Alvarado score and TLC (20.00%). TLC had least PPV among all parameters (94.83%), Table 5.

Alvarado Score	USG		CRP	
	Positive (86)	Negative (09)	>5 mg/dL (86)	<5 mg/dL (09)
≥7 in 75 (78.94%)	66 (69.47%)	9 (09.47%)	70 (73.68%)	5 (05.26%)
≤6 in 20 (21.05%)	20 (21.05%)	0 (00.00%)	16 (16.84%)	4 (04.21%)

Table 6. Correlation of Alvarado Score with USG and CRP in Histopathological Confirmed 95 Cases of Acute Appendicitis

Out of 75 patients who had ≥ 7 Alvarado score, 66 patients (69.47%) had positive USG findings suggested of acute appendicitis and 70 cases (73.68%) had significant CRP values. Alvarado score was ≤ 6 in 20 cases, while all these cases were having positive USG findings (Table 6).

DISCUSSION

Acute appendicitis is the most common non-traumatic abdominal surgical emergency, but still remains a diagnostic challenge despite availability of various diagnostic modalities. Mean age in the present study was 29.24 years, which is comparable to other similar studies conducted in the past. In studies conducted by Jat et al and Noudet et al in 2007, about 80% of appendicitis occurred below 40 years of age in concordance with our study where 79 out of 100 patients (79%) were under 40 years of age.^{4,37} In the present study, 71 were males and 29 were females.

27 patients reported within 24 hours of onset of pain and only one had perforated appendix in this early group; 53 patients reported within 48 hours of onset of pain and out of these 53 patients 44 patients had acute appendicitis and 7 patients had perforated appendix; 30 cases presented after 48 hours of pain, out of which 23 patients (76.7%) had perforated appendix. This difference was found to be statistically significant ($p= 0.001$). Bickell et al stated that

risk of rupture in ensuing 12-hour periods rises to 5% after 36 hours of untreated symptoms.³⁸

In this study Alvarado score was 78.94% sensitive, 20.00% specific, had PPV of 94.93% and NPV of 4.76%. The diagnostic value was 76%. The sensitivity was in concordance with the studies of Ohle et al and Shogilev et al.^{39,40} Alvarado score was ≤ 6 in 21 cases and out of these 20 cases had TLC $< 10,000/\text{mm}^3$. USG was positive in all these 21 cases. Out of 27 patients who presented within 24 hours, 17 patients of acute appendicitis and 1 patient of perforated appendicitis had significant Alvarado score. Out of 23 patients of perforated appendicitis who presented late, Alvarado score was significantly raised in 21 patients. This difference was not found to be statistically significant. Out of 30 cases of perforated appendicitis, 27 (90.00%) had raised Alvarado score of ≥ 7 and out of 66 cases of acute appendicitis 49 had raised Alvarado score of ≥ 7 . Although, it has low specificity, it has high PPV. It is a non-invasive, simple, fast, reliable and repeatable diagnostic scoring which can be used without expensive and complicated supportive diagnostic methods. Hence, Alvarado score should be calculated preoperatively to improve the diagnosis accuracy of acute appendicitis. NPV was very low and hence Alvarado score ≤ 6 does not rule out acute appendicitis.

There is wide variation in specificity of TLC (32% - 93%) in different studies.⁴¹⁻⁴³ This may be because of different cut-off values of TLC used in different studies. In this study, TLC was raised in 14 (51.85%) cases, out of 27 cases those who presented early after the onset of pain and 31 (65.95%) cases out of 47 patients those who presented late; 22 cases were of acute appendicitis those who presented late and it was raised in only 10 (45.45%) patients. Eriksson et al found that TLC can decrease to normal values during the observation period. This difference was found to be statistically significant after 48 hours.⁴⁴ TLC was raised in 32 cases (48.48%) of acute appendicitis and 24 cases of perforated appendix (80.00%). This difference was found to be statistically significant. Kaya et al also showed raised TLC in 100% cases of perforated appendicitis.¹² Raised TLC level help to differentiate between normal and inflamed appendix and it does not differentiate between inflamed and perforated appendix.⁴⁵ Although, a raised leucocyte count is a useful test for detecting acute appendicitis, it has variable

sensitivities and specificities, and a negative result does not rule out acute appendicitis.

Several studies have addressed the accuracy of CRP in diagnosing appendicitis, and it is agreed that its level increases in appendicitis which is related to the severity of inflammation.^{9,43,45,46} Gross variations have been reported in the sensitivity (65 - 95.6), specificity (68 - 77.77), PPV (34 - 95.6) and NPV (5 - 77.77) by different authors. In a study by Kaya et al, sensitivity, specificity, PPV and NPV of CRP were 72%, 75%, 95% and 5% respectively.⁹ In the present study, C-reactive protein was raised in 90 patients of suspected acute appendicitis. Out of 95 patients of acute appendicitis, 86 patients have raised CRP. Sensitivity, specificity, PPV, NPV and diagnostic values were 90.53%, 40.00%, 95.56%, 10.00% and 87% respectively. The specificity was only 40.00% suggesting that the presence of raised CRP is not a good discriminator for patients with acute appendicitis. CRP was raised in 24 (88.88%) patients out of 27 cases at 1st day of presentation and in 44 (93.62%) cases out of 47 cases who presented after 48 hours. It was raised in all 23 (100%) cases of perforated appendicitis and 18 (81.82%) cases of acute appendicitis. This difference was not found to be statistically significant. CRP was raised in all 30 cases (100%) of perforated appendicitis; 57 patients (86.36%) of acute appendicitis out of 66 patients had significantly increased CRP. This observation was in concordance with Kaya et al study, in which CRP was raised in 100% cases of perforated appendicitis.⁹ In our study also, CRP was raised in all cases of perforated appendicitis.

Diagnostic utility of PCT is not better than CRP in identifying complicated appendicitis and it has little diagnostic value in diagnosing appendicitis. However, it has better diagnostic value in identifying complicated appendicitis.^{9,35,47} In our study of 95 patients of confirmed diagnosis of appendicitis, 32 had PCT \geq 1 ng/dL. The sensitivity, specificity, PPV, NPV and diagnostic values of PCT for the diagnosis of appendicitis were 33.68%, 80%, 96.97%, 05.97% and 36%. This difference was not found to be statistically significant ($p = 0.664$), when comparing with histological findings. PCT was raised in 8 (29.62%) cases out of 27 cases those who presented early after the onset of pain and in 15 (31.91%) cases out of 47 patients those who presented late; 22 cases were of acute appendicitis those who presented late and it was raised in 4 (18.18%) patients and 11 (23.82%) cases of perforated appendicitis. This difference was not found to be statistically significant. Out of 30 cases of perforated appendicitis, PCT was raised in 16 cases (53.33%) and out of 66 cases of acute appendicitis 16 cases (24.24%) have raised acute appendicitis. This difference was found to be statistically significant. Kaya et al showed PCT was raised in 50.00% cases of perforated appendicitis and 12.76% cases of phlegmonous appendicitis.⁹

Sensitivity, specificity and PPV of D-dimer in our study were 68.42%, 80% and 98.48% respectively. Kaya et al (2012) had sensitivity, specificity and PPV of 29%, 75% and 95% respectively.⁹ It was raised in 28 cases (93.33%) out of 30 cases of perforated appendicitis. This difference was

found to be statistically significant ($p = 0.002$). On the basis of histology, 65 patients out of 95 of acute appendicitis confirmed on histology were having raised D-dimer value. Significant D-dimer value was observed in 4 patients, out of 5 normal histopathological findings. This difference was found to be not statistically significant ($p = 1$). Thus, it cannot be used as a diagnostic modality for diagnosing acute appendicitis. D-dimer was raised in 13 (56.52%) cases out of 27 cases those who presented early after the onset of pain, in 37 (78.72%) cases out of 47 patients those who presented late and in 14 patients out of 21 (91.30%) patients of perforated appendicitis. This difference is not found to be statistically significant. D-dimer was raised in 28 cases (93.33%) of perforated appendicitis and 38 cases (57.57%) of acute appendicitis. This difference was found to be statistically significant. Kaya et al studied D-dimer significant in 50.00% of perforated appendicitis and 23.40% in phlegmonous appendicitis.⁹

In the present study, out of 100 patients USG findings were positive in 90 patients of suspected acute appendicitis. Out of 95 patients of acute appendicitis, USG was positive in 86 patients. It had sensitivity of 90.53%, specificity of 20.00% and PPV of 95.55%. The diagnostic value was 87%. USG was positive in 13 (92.59%) cases out of 27 cases those who presented early after the onset of pain and 41 (87.23%) cases out of 47 patients those who presented late. However, it shows perforation of appendix in 3 cases, out of which only 1 (33.33%) had perforated appendicitis within 24 hours of presentation. Out of 23 patients of perforated appendicitis who presented late, it shows appendicitis in 8 cases and perforated appendicitis in 11 cases. This difference is found to be statistically significant after 48 hours.

A wide variation exists in sensitivity, specificity, positive predictive value and negative predictive value of these parameters in various studies conducted earlier.^{41,45,47,48} Leukocytosis count and CRP are the most frequently used tests in acute appendicitis for their easy availability and cost effectiveness, but the sensitivity and specificity are limited. The sensitivity and specificity of TLC in our study were 57.89% and 40%, respectively. In our study, CRP and USG were the most sensitive investigations (90.53%) with equal diagnostic value; 2nd most sensitive tool was Alvarado score (78.95%). Alvarado score was ≤ 6 in 20 biopsy confirmed cases, while all these cases were having positive USG findings. Out of 5 patients of normal appendix on histopathology, 4 had ≥ 7 Alvarado score and significant CRP and 3 had positive findings on USG. However, out of these 4 patients, in 2 patients although there was no appendicitis but these patients had Meckel's diverticulitis and this can be the reason of > 7 clinical score and raised CRP; 1 patient who had ≤ 6 Alvarado score, USG showed positive findings.

SUMMARY

The diagnostic efficiency of clinical examination, Alvarado score, TLC, CRP, D-dimer, PCT and USG in acute appendicitis was evaluated and correlated in our study. Alvarado score of > 7 was observed in 75 histopathologically proven cases of appendicitis and < 6 in 5 cases with no evidence of

appendicitis on histopathological examination. It had a sensitivity of 78.94%, specificity of 20.00%, PPV of 94.93% and NPV of 4.76% and diagnostic accuracy of 76%. Maximum cases of perforated appendicitis, i.e. 23 out of 30 cases presented late, after 48 hours of onset of pain. TLC was $\geq 10,000/\text{mm}^3$ in 55 cases of the patients with acute appendicitis and 3 cases of normal appendix. The values of sensitivity, specificity, PPV, NPV and diagnostic accuracy were 57.89%, 40%, 94.83%, 4.76% and 57% respectively. In this study, CRP was found to have higher sensitivity and diagnostic accuracy (90.53% and 87%) for acute appendicitis when compared to TLC (57.89% and 57%), D-dimer (68.42% and 66%) and PCT (33.68% and 36%). Out of 100 cases, CRP and USG both suggested appendicitis in equal and maximum number of cases (90.00%) followed by Alvarado score (79.00%). D-dimer $\geq 0.5 \mu\text{g/dL}$ was seen in 69 cases and 65 cases were having acute appendicitis on histopathology. The difference was not found to be significant ($p=1$). Sensitivity, specificity, PPV, NPV and diagnostic accuracy of D-dimer were 68.42%, 80%, 98.48%, 11.76% and 66% respectively. Procalcitonin level was $\geq 1 \text{ ng/dL}$ in 33 cases and 32 cases had acute appendicitis on histopathology. PCT is a better marker for bacterial sepsis and is specially increased in perforated and gangrenous appendicitis. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of PCT were 33.68%, 80%, 96.97%, 05.97% and 36% respectively. These results show that PCT is not a useful marker for the diagnosis of acute appendicitis.

CONCLUSION

No single modality at its own has been able to reduce the rate of negative appendectomy to 0%, although by using various diagnostic modalities the incidence of negative appendectomy and risk of perforation can be reduced. Diagnostic accuracy of CRP and USG was equal in our study and diagnostic accuracy of acute appendicitis on clinical examination (Alvarado score) can be increased with the aid of USG and CRP. The incidence of negative appendectomy was 5% in our study. The accurate diagnosis of acute appendicitis still remains an enigmatic challenge despite extraordinary development in modern radiographic imaging and diagnostic laboratory investigations.

REFERENCES

- [1] Rothrock SG, Pagane J. Acute appendicitis in children: emergency department diagnosis and management. *Ann Emerg Med* 2000;36(1):39-51.
- [2] Sack U, Biereder B, Elouahidi T, et al. Diagnostic value of blood inflammatory markers for detection of acute appendicitis in children. *BMC Surg* 2006;6:15-22.
- [3] Rusnak RA, Borer JM, Fastow JS. Misdiagnosis of acute appendicitis: common features discovered in cases after litigation. *Am J Emerg Med* 1994;12(4):397-402.
- [4] Jat MA, Al-Swailmi FK, Mehmood Y, et al. Histopathological examination of appendectomy specimens at a district hospital of Saudi Arabia. *Pak J Med Sci* 2015;31(4):891-894.
- [5] Ooms HWA, Koumans RKJ, Kung PJH. Ultrasonography in the diagnosis of acute appendicitis. *Br J Surg* 1991;78:315-318.
- [6] Kalan M, Rich AJ, Talbot DR, et al. Evaluation of modified Alvarado score in the diagnosis of acute appendicitis: a prospective study. *Ann R Coll Surg Engl* 1994;76(6):418-419.
- [7] Paajanen H, Mansikka A, Laato M, et al. Are serum inflammatory markers age dependent in acute appendicitis? *J Am Coll Surg* 1997;184:303-308.
- [8] Puylaert JBCM. Acute appendicitis: ultrasound sonography evaluation using graded compression. *Radiol* 1986;158(2):35-60.
- [9] Kaya B, Sana B, Eris C, et al. The diagnostic value of D-dimer, Procalcitonin and CRP in acute appendicitis. *Int J Med Sci* 2012;9(10):909-915.
- [10] Jaffrey RB, Laing FC, Lewis FR. Acute appendicitis high resolution real time ultrasound findings. *Radiol* 1987;163(1):11-14.
- [11] Lessin MS, Chan M, Catallozzi M, et al. Selective use of ultrasonography for acute appendicitis in children. *Am J Surg* 1999;177(3):193-196.
- [12] Rypins EB, Evans DG, Hinrichs W, et al. Tc-99m-HMPAO white blood cell scan for diagnosis of acute appendicitis in patients with equivocal clinical presentation. *Ann Surg* 1997;226(1):58-65.
- [13] Smith HF, Fisher RE, Everett ML, et al. Comparative anatomy and phylogenetic distribution of the mammalian cecal appendix. *J Evol Biol* 2009;22(10):1984-1999.
- [14] Collins DC. Historic phases of appendicitis. *Ann Surg* 1931;94(2):179-196.
- [15] McBurney C. The incision made in the abdominal wall in case of appendicitis, with a description of a new method of operating. *Ann Surg* 1894;20(1):38-43.
- [16] Ellis H, Nathanson LK. Appendicitis and appendectomy. In: Ziner MJ, ed. *Maingot's abdominal operations*. 10th edn. McGraw-Hill 1997:1191-1227.
- [17] Mestivier. Observation sur une tumeur situee proche la region ombilicale, du ctedroit, occssionnee par une grosse epingle trouvee dans l'appendice vermiculaire du caecum. *Jour de med, de chir. Et de pharm* 1759:441.
- [18] Hall RJ. Suppurative peritonitis due to ulceration and suppuration of the vermiform appendix; laparotomy; resection of the vermiform appendix; toilet of the peritoneum; drainage; recovery. *New York Med Jour* 1886;13:662-663.
- [19] Hall JN, Dyas FG. Appendicitis at camp logan as a sequel to influenza and pneumonia. *JAMA* 1919;12(10):726-727.
- [20] McBurney C. Experience with the early operative interference in cases of diseases of the vermiform appendix. *NY State Med J* 1889;50:676-684.
- [21] Fitz RH. The relation of the perforating inflammation of the vermiform appendix to perityphilitic abscess. *NY Med J* 1888;67:505-508.

- [22] Li X, Zhang J, Sang L, et al. Laparoscopic versus conventional appendectomy—a meta-analysis of randomized controlled trials. *BMC Gastroenterol* 2010;10:129.
- [23] Roy G, Ray G, Dass G, et al. Acute appendicitis: a clinical appraisal of 500 cases. *J Ind Med Assoc* 1969;52(11):509-513.
- [24] Samsi AB, Adaskar NB, Kamad RS. A study of 100 consecutive cases of acute appendicitis with their histopathological findings. *Ind J Surg* 1969;31:574-579.
- [25] Chang FC, Hogle HH, Welling DR. The fate of the negative appendix. *Am J Surg* 1977;126(6):752-754.
- [26] Evans C, Rashid A. An appraisal of peritoneal lavage in the diagnosis of the acute abdomen. *Br J Surg* 1975;62(2):119-120.
- [27] Abu-Yousef MM, Bleicher JJ, Maher JJ, et al. High resolution sonography of acute appendicitis. *A J R Ann J Roentgenol* 1987;149(1):57-58.
- [28] Stephens PL, Mazzucco JJ. Comparison of ultrasound and the Alvarado score for the diagnosis of acute appendicitis. *Conn Med* 1999;63(3):137-140.
- [29] Kurane SB, Sangoli MS, Gogate AS. A one-year prospective study to compare and evaluate diagnostic accuracy of modified Alvarado score and ultrasonography in acute appendicitis, in adults. *Ind J Surg* 2008;70(3):125-129.
- [30] Johansson EP, Rydh A, Riklund KA. Ultrasound, computed tomography and laboratory findings in the diagnosis of appendicitis. *Acta Radiol* 2007;48(3):267-273.
- [31] Okamoto T, Sano K, Ogasahara K. Receiver-operating characteristic analysis of leukocyte counts and serum C-reactive protein levels in children with advanced appendicitis. *Surg Today* 2006;36(6):515-518.
- [32] Schwarz A, Bolke E, Peiper M, et al. Inflammatory peritoneal reaction after perforated appendicitis: continuous peritoneal lavage versus non-lavage. *Eur J Med Res* 2007;12(5):200-205.
- [33] Ahmad QA, Muneera MJ, Rasool MI. Predictive value of TLC and CRP in the diagnosis of acute appendicitis. *Annals* 2010;16(2):116-119.
- [34] Kessler N, Cyteval C, Gallix B, et al. Appendicitis: evaluation of sensitivity, specificity and predictive values of US, Doppler US and laboratory findings. *Radiol* 2004;230(2):472-478.
- [35] Vaziri M, Ehsanipour F, Pazouki A, et al. Evaluation of procalcitonin as a biomarker of diagnosis, severity and postoperative complications in adult patients with acute appendicitis. *Med J Islam Repub Iran* 2014;28:50.
- [36] Kouame DB, Garrigue MA, Lardy H, et al. Is procalcitonin able to help in pediatric appendicitis diagnosis? *Ann Chir* 2005;130(3):169-174.
- [37] Noudeh YJ, Sadigh N, Ahmadnia AY. Epidemiologic features, seasonal variations and false positive rate of acute appendicitis in Shahr-e-Rey, Tehran. *Int J Surg* 2007;5(2):95-98.
- [38] Bickell NA, Aufses AH, Rojas M, et al. How time affects the risk of rupture in appendicitis? *J Am Coll Surg* 2006;202(3):401-406.
- [39] Ohle R, O'Reilly F, O'Brien KK, et al. The Alvarado score for predicting acute appendicitis: a systematic review. *BMC Med* 2011;9:139.
- [40] Shogilev DJ, Duus N, Odom SR, et al. Diagnosing appendicitis: evidence-based review of the diagnostic approach in 2014. *West J Emerg Med* 2014;15(7):859-871.
- [41] Agrawal CS, Adhikari S, Kumar M. Role of serum C-reactive protein and leukocyte count in the diagnosis of acute appendicitis in Nepalese population. *NMCJ* 2008;10(1):11-15.
- [42] Yang HR, Wang YC, Chung PK, et al. Laboratory tests in patients with acute appendicitis. *ANZ J Surg* 2006;76(1-2):71-74.
- [43] Ortega-Deballon P, Ruiz de Adana-Belbel JC, Hernandez-Matias A, et al. Usefulness of laboratory data in the management of right iliac fossa pain in adults. *Dis Colon Rectum* 2008;51(7):1093-1099.
- [44] Eriksson S, Granstrom L, Carlstrom A. The diagnostic value of repetitive preoperative analyses of C-reactive protein levels and total leucocyte count with suspected acute appendicitis. *Scand J Gastroenterol* 1994;29(12):1145-1149.
- [45] Sengupta A, Bax G, Paterson-Brown S. White cell count and C-reactive protein measurement in patients with possible appendicitis. *Ann R Coll Surg Engl* 2009;91(2):113-115.
- [46] Shafi SM, Afsheen M, Reshi FA. Total leucocyte count, C-reactive protein and neutrophil count: diagnostic aid in acute appendicitis. *Saudi J Gastroenterol* 2009;15(2):117-120.
- [47] Yu CW, Juan LI, Wu MH, et al. Systematic review and meta-analysis of the diagnostic accuracy of procalcitonin, C-reactive protein and white blood cell count for suspected acute appendicitis. *Br J Surg* 2013;100(3):322-329.
- [48] Andersson RE. Meta-analysis of the clinical and laboratory diagnosis of appendicitis. *Br J Surg* 2004;91(1):28-37.