Original article:

Prospective evaluation of clinical, biochemical and sonographic findings in the diagnosis of acute appendicitis in children

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Abstract

Background: The appendix was erroneously viewed as a vestigial organ with no known function, though it is one of the most important surgically. It is now well recognized that the appendix is an immunologic organ that actively participates in the secretion of immunoglobulins, particularly immunoglobulin A (IgA).

Materials and method: The study comprised of 100 patients admitted in the emergency department of Surgery, Government Medical College, Srinagar with a provisional diagnosis of acute appendicitis. All patients selected were under 15 years of age and either sex were evaluated on the basis of predetermined proforma, which included, a detailed history from patients or parents, clinical examination, laboratory investigations and high resolution sonography.

Results: Majority of the patients in the study cohort fell in the age range of 11-14 years; the youngest being a 2.4 year old kid and the oldest being children of 14 years. In our study there were more males than females (ratio M: F 58:42). 74 patients out of 79 histological positive appendicitis, had clinical assessment suggestive of appendicitis (sensitivity= 93.7%). Out of 79 patients with histologically positive appendices, 64 patients had leucocytosis. Among 21 negative appendectomies only 5 had leucocytosis. 59 patients of 79 histologically positive appendicitis had raised CRP levels and 10 patients out of 21 negative appendectomies had raised CRP levels. 70 patients out of 79 who had histological positive appendicitis had USG suggestive of appendicitis and 1 patient out of 21 negative appendectomies has ultrasound positive for appendicitis. Out of 100 patients 79 patients had positive histopathology and 21 patients had negative histopathology.

Key words: Leucocyte count, CRP, Ultrasonography

Introduction

The appendix first becomes visible in the eighth week of embryologic development as protuberance of the terminal portion of the cecum. The appendix can vary in length from less than 1 cm to greater than 30 cm; most appendices are 6 to 9 cm in length. Appendiceal absence, duplication, and diverticula have all been described [1,2,3] . The first published account of appendectomy for appendicitis was by Krönlein in 1886. However, this patient died 2 days postoperatively. Fergus, in Canada, performed the first elective appendectomy in 1883[4]. Semm is credited with performing the first successful laparoscopic appendectomy in 1982 [5]. Despite an increased use of ultrasonography, computed tomography (CT) scanning, and laparoscopy between 1987 and 1997, the rate of misdiagnosis of appendicitis has remained constant (15.3%), as has

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the rate of appendiceal rupture. The percentage of misdiagnosis of appendicitis is significantly higher among women than men (22.2 vs. 9.3%) [10,11]. Faecoliths are found in 40% of cases of simple acute appendicitis, 65% of cases of gangrenous appendicitis without rupture, and nearly 90% of cases of gangrenous appendicitis with rupture [6,7,8]. Mild leukocytosis, ranging from 10,000 to 18,000/mm^3, is usually present, White blood cell counts above this level raise the possibility of a perforated appendix with or without an abscess [9].

Material and Methods

The study "prospective evaluation of the clinical, biochemical and sonographic findings in the diagnosis of acute appendicitis in children" comprised of 100 patients admitted in the emergency department of Surgery, Government Medical College, Srinagar with a provisional diagnosis of acute appendicitis. All patients selected were under 15 years of age and either sex were evaluated on the basis of predetermined proforma, which included, a detailed history from patients or parents, clinical examination, laboratory investigations and high resolution sonography. The detailed history and clinical examination was done to rule out any associated co-morbid condition. For the diagnosis of acute appendicitis complete blood count, C reactive protein and high resolution ultrasonography were done pre-operatively. Complete blood count and high resolution ultrasonographic reports were available pre-operatively while C-reactive protein report was available post-operatively. Urine analysis was done routinely to rule out urinary tract infection.

Results

The study was conducted in the department of surgery, Government Medical College Srinagar, Kashmir on 100 patients with clinical diagnosis of acute appendicitis from October 2007 to September 2009. Patients of either sex under 15 years of age were included in the study. Majority of the patients in the study cohort fell in the age range of 11-14 years; the youngest being a 2.4 year old kid and the oldest being children of 14 years. The age distribution is shown in table 1 and depicted by a bar diagram below. In our study there were more males than females (ratio M: F 58:42) [Table1]

Clinical Assessment: 74 patients out of 79 histologically positive appendicitis, had clinical assessment suggestive of appendicitis (sensitivity= 93.7%). This was based on shifting pain, anorexia, nausea, elevated temperature, increased pulse rate, tender RIF, Rebound tenderness and guarding. This gives highest sensitivity for the diagnosis of acute appendicitis by clinical means. The results are shown in [Table 2]

Total Leucocyte Count: Out of 79 patients with histologically positive appendices, 64 patients had leucocytosis. Among 21 negative appendectomies only 5 had leucocytosis, giving a sensitivity of 81%, specificity of 76.2% and accuracy 80% [Table 3]

Neutrophil Percentage: 71 patients had neutrophilia (> 75%), but only 63 had histologically positive appendicitis. Out of 29 patients who had normal neutrophil percentage, 18 had appendicitis [Table 4].

C – Reactive protein: 59 patients of 79 histologically positive appendicitis had raised CRP levels and 10 patients out of 21 negative appendectomies had raised CRP levels [Table 5]. For high resolution Ultrasound abdomen 70 patients out of 79 who had histologically positive appendicitis had USG suggestive of appendicitis and 1 patient out of 21 negative appendectomies has ultrasound positive for appendicitis. This gives the highest specificity (90.47%) and accuracy (90%) of High

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resolution ultrasound in the diagnosis of acute appendicitis. Diagnosis was based on following major criteria: visualization of non-compressible, aperistaltic, painful appendix with an outer diameter of more than 6mm, presenting with a " target-like" cross-sectional view and a tubular appearance with a blind-ending tip on the longitudinal scan, surrounded by echogenic inflamed fat. Additional criteria were appendicolith, and the absence of gas in the lumen. If the appendix was not visualized in addition to having no other findings, the ultrasonographic examination was considered to be negative [Table 6].

Based on operative findings patients were divided into three groups;

a. Simple Appendicitis (n=49) included only those patients who had signs of inflammation- thickened edematous, grossly inflamed appendix with or without faecolith, periappendicular fluid or inflamed omentum.

b. Complicated Appendicitis (n= 30):- patients with perforated/gangrenous appendix, appendicular abscess or lump.

c. Other diagnosis (n = 21)

Combined sensitivity, Specificity, and Accuracy of clinical signs, TLC, NP, CRP and USG:-The table 10 shows the sensitivity, specificity and accuracy of Clinical features, TLC, NP, CRP and USG in the diagnosis of acute appendicitis. It shows highest sensitivity (93.7%) for clinical assessment but specificity and accuracy is highest for USG (94.47%, 90%).

Clinical	Positive Histopathology	Negative Histopathology	Total
Positive	74	14	88
Negative	05	07	12
Total	79	21	100

Table 1: showed correlation between clinical assessment and histopathology

TLC	Positive Histopathology	Negative Histopathology	Total
Elevated	64	05	69
Normal	15	16	31
Total	79	21	100

Sensitivity: 81%

Specificity: 76.2%

Positive Predictive Value: 92.76%

Negative Predictive Value: 51.62%

Accuracy: 80%

Table 2: showed correlation between elevated total leukocyte count and histopathology

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Neutrophil Percentage	Positive Histopathology	Negative Histopathology	Total
Significant	63	08	71
Normal	16	13	29
Total	79	21	100

Sensitivity: 79.75%

Specificity: 61.9%

Positive Predictive Value: 88.73%

Negative Predictive Value: 44.82%

Accuracy: 76%

Table 3: showed correlation between raised neutrophil count and histopathology

C Reactive protein	Positive Histopathology	Negative Histopathology	Total
Elevated	59	10	69
Normal	20	11	31
Total	79	21	100

Table 4: showed correlation between C reactive protein and histopathology

Ultrasound Abdomen	Positive Histopathology	Negative Histopathology	Total
Positive	70	01	71
Negative	09	20	29
Total	79	21	100
Histopathology	79	21	100

Sensitivity : 88.6%

Specificity: 90.47%

Positive Predictive Value: 98.6%

Negative Predictive Value: 68.96%

Accuracy: 90%

Table 5: showed correlation between ultrasound abdomen and histopathology

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	Clinical Assessment	TLC	% Neutrophils	CRP	USG
Sensitivity	93.7	81	77.2	74.68	88.6
Specificity	33.4	76.2	61.9	52.38	90.47
Accuracy	81	80	74	70	90

Table 6: shows the sensitivity, specificity and accuracy of Clinical features

Discussion

The establishment of a diagnosis of acute appendicitis in young children is more difficult than in the adult. The inability of young children to give an accurate history, diagnostic delays by both parents and physicians, and the frequency of gastrointestinal upset in children is all contributing factors. The more rapid progression to rupture and the inability of the underdeveloped greater omentum to contain a rupture lead to significant morbidity rates in children. Children younger than 5 years of age have a negative appendectomy rate of 25% and an appendiceal perforation rate of 45%. This is compared to a negative appendectomy rate of less than 10% and a perforated appendix rate of 20% for children 5 to 12 years of age [10].

Clinical examination and laboratory parameters, such as white blood cell, differential counts (percentage of neutrophil granulocytes and band neutrophil granulocytes), and C-reactive protein were the only diagnostic tools for many years. Perforation rate was high, as well as the number of negative appendectomies. Following the introduction of ultrasonography in the last two decades and computed tomography (CT) in the last decade, the rate of negative appendectomies in children has decreased, but the perforation rate has remained high (22%-62%) [4,5]. Not single test is definitive. A white blood cell count (WBC) is perhaps the most useful laboratory test. Typically, the WBC is slightly elevated in nonperforated appendicitis, but may be quite elevated in the presence of perforation. Abdominal ultrasonography is a popular imaging modality for acute appendicitis. Ultrasound is highly operator-dependent, however, and it is frequently unable to visualize the normal appendix. A recent meta-analysis of 14 prospective studies showed

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ultrasound to have a sensitivity of 0.86 and a specificity of 0.81 [11].

The incidence of major complications after appendectomy in children is correlated with appendiceal rupture. The wound infection rate after the treatment of nonperforated appendicitis in children is 2.8% as compared to a rate of 11% after the treatment of perforated appendicitis. The incidence of intra-abdominal abscess is also higher after the treatment of perforated appendicitis as compared to nonperforated cases (6% vs. 3%) [6]. The total of 100 patients, who were operated upon for suspected acute appendicitis on the basis of clinical parameters, formed the study sample. The age range of patients in our study was between 2.4-14 years with a mean age of 10.1 years. In a study conducted by Mojca Groselj-Grenc et al (2007) the mean age was 10.8 years and there age range was 2.8-14 years [12]. Meier DE et al (2003) retrospectively studied perforated appendicitis in 1196 consecutive children with appendicitis over a period of 5 years. Children between 1-18 years were included and the median age was 9 years [13]. The numbers of male patients were 58 and female patients were 42. Males were more affected as compared to females. Similar results were found in the retrospective study of NANCE M. L (2000) et al [14].

In our study, all patients with diagnosis of acute appendicitis were operated. On the basis of operative findings, patients were divided into three groups:-

Group A - Inflammed but uncomplicated appendix

Group B - complicated appendicitis

Group C - normal appendix/ other diagnosis

In our study, Group A included 49 patients, Group B included 30 patients and Group C included 21 patients. Similar type of grouping was done by Chung JL et al in their study [15].

On the basis of clinical parameters like shifting pain, anorexia, nausea, elevated temperature, increased pulse rate, tender RIF, Rebound tenderness, guarding; 88 patients were suspected to have acute appendicitis. But only 74 patients had operative and histopathological findings suggestive of acute appendicitis. Out of 12 patients whose clinical signs were equivocal, 5 patients had laboratory parameters and ultrasound abdomen suggestive of acute appendicitis and were confirmed by operative and histopathological findings. This gives sensitivity and specificity of clinical parameters of 93.7% and 33.4% respectively. This shows the highest sensitivity of clinical assessment for the diagnosis of acute appendicitis. The sensitivity and specificity of clinical assessment in our study was similar to the study conducted by Mojca Groselj-Grenc et al (2007) that is 93.9% and 33.3% respectively [12]. Our results are comparable with the study conducted by Pruekprasert P et al(2004), they found surgeon's clinical diagnosis had a highest sensitivity of 96% [16]. Clinically, a history of pain migration proved to be reliable as a diagnostic indicator. In Our study, Out of 79 patients with histopathologically positive appendicitis, 66 patients had history of migratory pain. All those patients having history of migration of pain had operative and histopathological findings suggestive of acute appendicitis. Similar finding was observed in a study conducted by John H, Neff U, Kelemen M (1993) [17].

The majority of patients with acute appendicitis had an elevated total leucocyte count that is more than 10,500/cmm. In our study leucocyte count was raised in 64 patients out of 79 who had histologically proven appendicitis and 5 patients among 21 negative

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appendectomies had raised leucocyte count. Total leucocyte count was much more raised in complicated appendicitis than in simple appendicitis. Thus the sensitivity and specificity of total leucocyte count in our study was 81% and 76.2% respectively. This is consistent with the study conducted by Lau W Y (1989) which gives sensitivity and specificity of total leucocyte count of 81.4% and 77.3% respectively. The study concluded that raised total leucocyte count preferably combined with raised neutrophil percentage is useful in the diagnosis of acute appendicitis but should be interpreted in the light of clinical findings [18]. This was comparable with the prospective study by Norback I and Harju E, which gives sensitivity of 78.5% [19]. In a study conducted by Harland RNL (1991), sensitivity and specificity of total leucocyte count in the diagnosis of acute appendicitis was 92% and 70% respectively which is comparable with our study [20].

Neutrophil is body"s first line defence and is the only type of cell involved in acute inflammation. Robert B Sasso et al (1970) reviewed the records of 525 patients with clinical and histological evidence of acute appendicitis between 1966 and 1968; they observed that 78% of the patients had a neutrophil count above 75% [21]. In our study, 63 patients out of 79 histologically proven appendicitis had neutrophil count above 75% and 8 patients out of 21 histologically negative appendectomy had neutrophil count above 75%.This gives sensitivity ,specificity and accuracy of 79.75%, 61.9% and 76% respectively. This is comparable with the study conducted by Robert B Sasso et al.

The preoperative serum C-reactive protein levels were correlated with the histopathology. Out of 79 patients with histopathology positive, 59 patients had raised C-reactive protein level and 20 patients had normal C-reactive protein levels. Out of 21 patients with negative appendix, 10 had raised C-reactive protein level. In our study, sensitivity and specificity of C-reactive protein in the diagnosis of acute appendicitis was 74.68% and 52.38% respectively. In a study conducted by Mojca Groselj-Grenc et al, sensitivity and specificity of C-reactive protein in the diagnosis of appendicitis was 73.9% and 54.5% respectively [12]. All most similar results were found in our study. In a study conducted by Dueholm et al, sensitivity and specificity of C-reactive protein was 75% and 56% respectively [22] which is comparable to our study.

Pruekprasert P (2004) et al studied the accuracy in diagnosis of acute appendicitis by comparing serum C-reactive protein measurements, Alvarado score and clinical impression of surgeons. 231 patients admitted to the hospital with suspected appendicitis were studied prospectively. CRP of > 10 mg/l had a much lower sensitivity (62%) and lower specificity (56%) [16]. The sensitivity of C- reactive protein in our study was higher (74.68%) this is because lower limit of C- reactive protein for positive cases was 6mg/l. In our study specificity of the C-reactive protein was 52.38% which is comparable with above study (56%).

Ultrasonography is a non-invasive investigation in the diagnosis of acute appendicitis and other associated pathologies. The probe used in the present study was 7.5 MHZ. Besides being highly specific in the diagnosis of appendicitis, it accurately excludes diseases that do not require surgery like mesenteric adenitis, terminal ileitis, ureteric stone and gynaecological disorders. Diagnosis was based on following major criteria: visualization of non-compressible, aperistaltic, painful appendix with an outer diameter of more than 6mm, presenting with a

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"target-like" cross-sectional view and a tubular appearance with a blind-ending tip on the longitudinal scan, surrounded by echogenic inflamed fat. Additional criteria were appendicolith, and the absence of gas in the lumen, free fluid in peritoneal cavity.In the present study, ultrasonographic examination was positive in 70 patients out of 79 patients having operative and histopathological findings suggestive of appendicitis and 1 patient had false positive ultrasound, out of 21 patients who had histopathology negative. The sensitivity, specificity and accuracy of ultrasonography in present study are 88.6%, 90.47% and 90% respectively. Thus the specificity of ultrasonography is more than clinical assessment (33.4%), total leucocyte count (76.2%), neutrophil percentage (61.9%) and C-reactive protein(52.38%). Our results are consistent with those observed by Puylaert JB, in 1986 who reported 89% sensitivity of ultrasonography. In 25 (89%) of 28 patients with confirmed appendicitis, the inflamed appendix was visualized by ultrasonography. Perforation was predictable in six of seven patients [23].

Our results were comparable with the study conducted by Jeffery R B, Laing FC, Lewis FR (1987) who used High-resolution, real-time ultrasonography with graded compression to evaluate 90 patients with clinically suspected acute appendicitis. The overall sensitivity was 89%, the specificity was 95%, and the accuracy was 93% [24]. In our study the sensitivity, specificity and accuracy of High-resolution ultrasonography was 88.6%, 90.47% and 90% respectively. Schwerk Wolf B. et al (1990) prospectively evaluated the clinical value of high-resolution real-time sonography for the diagnosis of acute and complicated appendicitis in 857 patients admitted with suspected appendicitis. The ultrasound findings were correlated with history and physical examination on admission. Sonography was able to make the diagnosis of appendicitis with a sensitivity of 89.7%, a specificity of 98.2%, and overall accuracy of 96.3%, respectively [25]. Hahn HB et al (1998) in there prospectively study observed sensitivity, specificity and overall accuracy of sonography in the diagnosis of acute appendicitis of 90%, 97% and 96 %, respectively [26]. Mojca Groselj-Grenc et al (2007) in their study reported a sensitivity of 91.4% and specificity of 95.2% of sonography for the diagnosis of acute appendicitis in children [12]. These results are higher than our study, reason may be that ultrasonography is operator dependent and many of the ultrasound in our study were done by junior sonologist. Francois V et al (1990) in their study reported a sensitivity of 94%, specificity of 89% and a predictive accuracy of 91% of high-resolution sonography for the diagnosis of acute appendicitis which comparable with our study [27]. Charles D Douglas et al (2000) reported a Sensitivity and specificity of ultrasonography for the diagnosis of acute appendicitis in children of 94.7% and 88.9%, respectively [28]. Meier D.E. et al (2003) retrospectively studied perforated appendicitis in 1196 consecutive children with appendicitis over a period of 5 years. They observed perforation rate of 38.9% [13].

In our study there were 30 patients with complicated appendicitis that is perforated/gangrenous appendicitis and appendicular abscess, 0ut of 79 patients whose operative and histopathological findings were suggestive of appendicitis. The perforation rate in our study was 37.9%, consistent with the above study. This high rate of perforation in children may be due to underdeveloped greater omentum, inability of young children to give an

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accurate history, diagnostic delays by both parents and physicians, and the frequency of gastrointestinal upset in children are all contributing factors.

Conclusion

The study prospective evaluation of the clinical, biochemical and sonographic findings in the diagnosis of acute appendicitis in children. The diagnosis of acute appendicitis is primarily a clinical one that is based on proper history and repeated clinical examinations. Raised Total leucocyte count preferably combined with raised neutrophil percentage and raised C-reactive protein is useful in the diagnosis of acute appendicitis but should be interpreted in the light of clinical findings. Sonography is particularly useful in the evaluation of children with suspected appendicitis in whom the clinical findings are equivocal, and in the evaluation of female children with suspected pelvic pathology. Findings at sonography should not supersede clinical judgement in patients who are believed to be at high risk of having appendicitis on the basis of clinical signs and symptoms.

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