Diagnostic accuracy of white cell count and C-reactive protein for assessing the severity of paediatric appendicitis

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Summary

Objectives Simple investigations like white cell count (WCC) and C-reactive protein (CRP) may help to improve the accuracy of diagnosis in paediatric appendicitis. We evaluated the diagnostic accuracy of WCC and CRP for the severity of acute appendicitis in children.

Design Cross-sectional study.

Setting This study was conducted on all children who underwent open appendectomy from January 2007 to December 2008 at a District General Hospital. Data regarding demographics, WCC, CRP, histology and postoperative complications were analysed.

Participants All children who underwent open appendectomy during the study period.

Main outcome measures Diagnostic accuracy of WCC and CRP for simple acute appendicitis and a perforated appendix.

Results Out of 204 patients, 112 (54.9%) were girls. At surgery, appendix was grossly inflamed in 175 of which 32 had perforation. Histology revealed simple acute appendicitis in 135 (66.2%) and gangrenous appendicitis in 32 (15.7%). The rest were normal. The duration of symptoms, temperature, length of stay, WCC and CRP were significantly worse in the perforated group (P value <0.05). Postoperative complications included wound infection ($n = 18$), pelvic collection ($n = 5$) and intestinal obstruction ($n = 6$); and were more common among patients with a perforated appendix (P value <0.05). WCC had a higher diagnostic accuracy and higher sensitivity than CRP in diagnosing simple acute appendicitis. The combined sensitivity of WCC and CRP increased to 95% and 100% for the diagnosis of simple acute appendicitis and a perforated appendix, respectively.

Conclusion Accuracy of WCC is higher than CRP for diagnosing simple acute appendicitis. The combined sensitivity of WCC and CRP increases for simple acute appendicitis as well as a perforated appendix.

Introduction

The incidence of paediatric appendicitis in the UK has been declining for the last four decades.[1] However, appendicitis still remains the commonest abdominal emergency in the paediatric population[2] and the mainstay of diagnosis is clinical,[3] but the accuracy of diagnosis is variable mainly due to other childhood illnesses[4] and atypical presentation.[5] Therefore, misdiagnosis is still common (28–57%) in children under 12 years of age[6,7] resulting in conflict and litigation.[8]

White cell count (WCC), C-reactive protein (CRP) and imaging modalities are used by clinicians to diagnose appendicitis accurately.[9,10] Blood tests have been shown to have low sensitivity and specificity in differentiating simple acute appendicitis from a perforated appendix in a majority of the studies.[2,11] However, in a few studies the WCC was more sensitive than CRP in diagnosis of simple acute appendicitis[12] and CRP was reported as more sensitive than WCC in cases of a perforated appendix.[12,13]

The aim of our study was to evaluate the accuracy of WCC and CRP in the diagnosis of severity of appendicitis in children.

Patients and methods

Study design and data collection

This cross-sectional study was conducted at our district general hospital (DGH) from January 2007 to December 2008. All children up to 16 years of age who underwent open appendectomy based on clinical diagnosis during this period were included. Data were collected on patient demographics, duration of symptoms, clinical presentation, blood tests results (WCC and CRP), diagnosis at surgery (simple acute appendicitis, a perforated or normal appendix), and investigations including histology of the removed appendix (simple acute appendicitis, gangrenous or normal appendix), postoperative complications and readmission rate. Standardized procedures were carried out for WCC and CRP results uniformly in all the children attending the DGH. Moreover, histology of the appendix was performed by a single pathologist decreasing the chances of information bias.

Statistical analysis

Data were statistically analysed using SPSS version 14.0 (SPSS Inc., Chicago).[14] Proportions were computed for categorical variables. Mean and standard deviations were calculated for continuous variables having normal distribution, median and interquartile range calculated for those having skewed distribution. One way ANOVA and chi-square test were conducted to look for difference in continuous and categorical variables respectively in children with a normal appendix, simple acute appendicitis and those having a perforated appendix. The Kruskal-Wallis test was conducted as a test of significance for continuous variables having skewed distribution among the three groups. The Fisher's exact test was applied for comparison of categorical variables between the three groups when any of the cell count was less than 05. A P value of less than 0.05 was considered significant.

The validity (sensitivity and specificity), yield (positive predictive value [PPV] and negative predictive value [NPV]) and diagnostic accuracy of WCC and CRP for simple acute appendicitis and a perforated appendix were computed with normal appendix as the reference category. Cut-off level for WCC was taken as 11 X 10^9/L and that of CRP as 10 mg/dL. These cut-offs were finalized using receiver-operating characteristic (ROC) curve analysis. Cut-off value is based on optimal level of sensitivity and specificity, which is reflected by the upper left most part of the ROC curve.[15]

We did not stratify the diagnostic accuracy of WCC and CRP with regards to age as our data showed very weak correlation between WCC and age ($r = 0.01$, P value = 0.89) and CRP and age ($r = 0.02$, P value = 0.77). The histology of appendix was taken as the reference standard for simple acute appendicitis and macroscopic perforation at surgery for a perforated appendix.

Results

During the study period, 219 patients had an appendectomy. Data were missing on 15 patients; and therefore excluded from the study. Out of the 204 patients, 112 (54.9%) were girls and 92 (45.1%) were boys. The median age was 13 years (range 3–16) years. Symptoms included localized right iliac fossa pain in 152 (74.5%), migratory abdominal

pain in 40 (19.6%) and lower abdominal pain in 12 (5.9%). Vomiting was present in 84 (41.2%) and diarrhoea in 18 (8.8%). The mean temperature at admission was 37.16 ± 0.68°C.

The operative details showed that a grossly inflammed appendix was reported in 175 (85.7%) cases, out of which 32 (18.3%) had a perforated appendix. Histology showed simple acute appendicitis in 135 (66.2%), gangrenous appendicitis in 32 (15.7%) and a normal appendix in 37 (18.1%) cases.

Patients with a normal appendix were comparable to those having simple acute appendicitis and a perforated appendix with respect to age and gender. The duration of symptoms, temperature on admission, WCC and CRP were significantly worse (*P* value <0.001) in patients having a perforated appendix than those having simple acute appendicitis or a normal appendix (Table 1).

Postoperative complications were seen in 23 (13.4%) patients and were common among patients with a perforated appendix (Table 2). Conservative management was done for 19 patients while exploratory laparotomy was necessary in four cases (two with unresolving intestinal obstruction and two with persistent pelvic sepsis).

Out of the 204 patients, nine (4.4%) were readmitted; five originally had a perforated appendix while the other four had simple acute appendicitis (Table 2). The median postoperative stay was significantly longer in patients with a perforated appendix than those having simple acute appendicitis (5 [3–15] vs. 2 [1–5] days, *P* value= 0.014). There was no reported mortality during the study period.

Validity, yield and diagnostic accuracy of WCC and CRP

Sensitivity of WCC was higher than CRP in the diagnosis of simple acute appendicitis while both the WCC and CRP had similar sensitivity in the diagnosis of a perforated appendix. On the contrary, the specificity of WCC was less than CRP in the diagnosis of simple acute appendicitis. However, the specificity was the same for both, WCC and CRP, in the diagnosis of a perforated appendix. It was noted that both tests had a higher sensitivity but low specificity in diagnosis of simple acute appendicitis and a perforated appendix (Table 3).

Both tests had high positive predictive value for diagnosing acute simple appendicitis and high negative predictive value for a perforated appendix (Table 3).

Table 1
Characteristics of patients with a normal appendix compared with simple acute appendicitis and a perforated appendix

Variable	*Normal appendix (n = 37)*	*Simple acute appendicitis (n = 135)*	*Perforated appendix (n = 32)*	*P value*
Age in years (median, range)	13 (7–16)	13 (3–16)	13 (4–16)	0.46*
Gender (*n*, %)				
Boy	16 (43.2)	61 (45.2)	15 (46.8)	0.43†
Girl	21 (56.8)	74 (54.8)	17 (53.2)	
Duration of symptoms (days) (mean ± SD)	1.7 ± 1.1	2.2 ± 2.6	4.4 ± 7.6	<0.001‡
Temperature at admission (°C)(mean ± SD)	36.1 ± 0.5	36.4 ± 0.6	38.2 ± 1	<0.001‡
WCC ($x10^9$/L)mean ± SD	6.9 ± 1.3	13.8 ± 3.1	15 ± 3.6	<0.001‡
CRP (mg/dL)mean ± SD	18 ± 54	49.4 ± 30	154 ± 86.3	<0.001‡

*Kruskal-Wallis test – conducted as a test of significance for continuous variables having skewed distribution
†Chi-square test – to look for the difference in categorical variables
‡One way ANOVA – to look for the difference in continuous variables

Table 2
Postoperative complications and readmission rate

Postoperative complication	*Normal appendix (n = 37)*	*Simple acute appendicitis (n= 135)*	*Perforated appendix (n = 32)*	*P value*
Wound infection (*n*, %)	0 (0)	5 (3.7)	11 (34.4)	<0.001*
Pelvic collection (*n*, %)	0 (0)	1 (0.7)	3 (9.3)	0.02*
Intestinal obstruction (*n*, %)	0 (0)	0 (0)	3 (9.3)	0.004*
Readmission rate (*n*, %)	0 (0)	4 (3)	5 (15.6)	0.008*

*Fisher's exact test – conducted as a test of significance for categorical variables as the cell counts are ≤5

Discussion

Clinical diagnosis has always been the decisive factor for exploration in patients with suspected appendicitis. Since, the clinical presentation is variable especially among children; the reported diagnostic errors are high.[16] A perforation rate of up to 50% has been reported as a result of delayed diagnosis and treatment.[2] Various new diagnostic techniques like computed tomography, leucocyte scintigraphy, ultrasonography, diagnostic laparoscopy have been utilized to improve the diagnostic accuracy of acute appendicitis.[3,4] However, most of these tests have cost implications, require expertise, and are not available out of hours in the majority of institutions. WCC and CRP are simple laboratory tests which are cheap, readily available and carried out routinely. Various studies have been conducted to evaluate their role in improving the diagnostic accuracy of appendicitis with varying results.[17]

Table 3
Diagnostic accuracy, sensitivity and specificity of WCC and CRP in simple acute appendicitis and a perforated appendix

Diagnostic test	*Simple acute appendicitis*	*Perforated appendix*
WCC (percentage)		
Sensitivity	80.5	93.0
Specificity	68.0	40.0
PPV	89.0	21.0
NPV	50.0	96.0
Diagnostic accuracy	77.0	44.0
CRP (percentage)		
Sensitivity	75.0	93.0
Specificity	72.0	40.0
PPV	90.0	23.0
NPV	46.0	97.0
Diagnostic accuracy	75.5	50.0
Net sensitivity (percentage)	95.0	100
Net specificity (percentage)	50	20

Our study highlights the diagnostic predictability of WCC and CRP for simple acute appendicitis and a perforated appendix. A higher sensitivity of CRP than the WCC in the diagnosis of simple acute appendicitis has been reported in a few studies.[2] However, our results have shown that WCC is more sensitive than CRP in the diagnosis of simple acute appendicitis; a similar finding has been reported by Grönroos *et al.*[12] Another important finding of our study is that both CRP and WCC have high sensitivity in the diagnosis of a perforated appendix (Table 4).

Regarding the cut-off values of WCC and CRP, the review of literature did not show any reliable cut-off values to signify simple acute appendicitis in children. Studies have been carried out to determine the cut-off values from the onset of symptoms to diagnosis; but they all vary in results, moreover most of the studies were conducted among the adult patients.[18] Therefore we used ROC curve analysis, which is one of the best methods to determine cut-off values of the test for a given disease.[15]

In our study, a high WCC was as sensitive as the high CRP; in the diagnosis of simple acute and perforated appendicitis; a finding that has not been observed in the previous studies.[2,12] When the sensitivities of WCC and CRP were combined, the overall sensitivity increased to 95% and 100% for diagnosis of simple acute appendicitis and a perforated appendix, respectively. This reflects superior reliability of clinical diagnosis in combination with both the WCC and the CRP. Therefore, we suggest that both WCC and CRP level could be the decisive factors

Table 4
Comparison of our results with the other studies

Diagnostic test (sensitivity and specificity in percentage)			*Rodríguez-Sanjuán JC* et al.[13]	*Beltran* et al.[21]	*This study*
WCC	Simple acute appendicitis	Sensitivity	–	90	80.5
		Specificity	–	20	68
	Perforated appendix	Sensitivity	–	60	93
		Specificity	–	90	40
CRP	Simple acute appendicitis	Sensitivity	58	100	75
		Specificity	80	20	72
	Perforated appendix	Sensitivity	–	40	93
		Specificity	–	90	40
WCC and CRP combined	Simple acute appendicitis	Net sensitivity	–	90	95
		Net specificity	–	20	50
	Perforated appendix	Net sensitivity	–	50	100
		Net specificity	–	90	20

in cases with equivocal clinical signs. Relying on equivocal signs only, can lead to increased complications and missed diagnosis.[19,20] A similar conclusion has been drawn by a meta-analysis by Anderson, who concluded that the clinical diagnosis of appendicitis is a combination of clinical findings (signs of peritoneal irritation) as well as the other discriminators like simple laboratory tests (WCC and CRP).[11] Contrary to the common opinion, the meta-analysis showed that the values of WCC and CRP were an equally important discriminator; as were the clinical signs. In other words, the higher the values of WCC and CRP, the more likely was appendicitis and vice versa.[11] This is also evident from our study which showed that the mean value of WCC and CRP increased significantly as the severity of appendicitis increased, being the lowest for the patients having a normal appendix.

A high positive predictive value (PPV) of both WCC and CRP in cases of simple acute appendicitis suggests their high yield in the diagnosis of appendicitis. Comparison of our results with the other studies shows that a high sensitivity of both WCC and CRP in case of simple acute and perforated appendicitis,[13] however the study by Beltran *et al.*[21] has showed a high specificity of both in a perforated appendix (Table 4).

The symptoms of acute appendicitis may vary with age.[2] In our study, the commonest symptom was abdominal pain (100%) followed by vomiting (41%), fever (40%) and diarrhoea (9%). Similar findings have been reported in the other studies in which children presented with abdominal pain (89–100%), fever (80–87%) and vomiting (66–100%),[21,22] though our results show that localized abdominal pain was more common compared to migratory pain. A high temperature and a long duration of symptoms were associated with appendicular perforation and this difference was found to be statistically significant (Table 1). Diarrhoea, though less common, may be the presenting symptom of appendicitis[23] especially if accompanied by abdominal pain, as seen in our study.

The postoperative wound infection rate at our institute was comparable to the study by Cappendijk *et al.*[24] The length of postoperative stay in patients with a perforated appendix was longer than those having simple acute appendicitis. This may be attributed not only to the delay in presentation but also due to the slow recovery owing to the severity of appendicitis and more postoperative complications in the former group. Other studies have also reported a prolonged recovery in patients who either had a perforated appendix or other complications.[24]

The strength of this study is that to our knowledge, these are the largest reported data on paediatric appendectomies from a DGH in the UK. WCC and CRP were conducted by standardized procedures for all the children with suspected appendicitis. Moreover, histology of the removed appendix was performed by a single pathologist. This minimized the information bias. Retrospective nature of this study made it less time consuming and minimized the cost.

One of the weaknesses of this study is that WCC and CRP were performed at a single point, i.e. at the time of admission. Repeated sampling may be done at fixed intervals from the symptom onset to study the sequential increase or decrease in diagnostic accuracy of these two tests for the severity of appendicitis. A prospective study may inquire into this dimension further.

Demographic profile of the patients in this study is comparable to the other DGHs.[25] Therefore the results may be generalized to children aged 3–16 years of age who present with suspected appendicitis to DGHs in the UK.

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