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Appendicitis in paediatric age group: Correlation between preoperative inflammatory markers and postoperative histological diagnosis

Peter Mekhail, Nader Naguib[1], Fady Yanni[2], Asal Izzidien[3]

ABSTRACT

Introduction: Clinical diagnosis of appendicitis can be challenging, particularly in the paediatric age group. There is an increased risk of perforation in paediatrics; therefore, a need for sensitive and specific diagnostic tool is mandatory. **Aim:** The aim of this study is to evaluate the role of preoperative inflammatory markers in supporting the clinical diagnosis of appendicitis in the paediatric age group. **Materials and Methods:** Retrospective study of 268 emergency paediatric appendicectomies performed in a District General Hospital in Wales, over a period of seven years (2002–2009). The data collected from hospital database include preoperative inflammatory markers, C-reactive protein (CRP) and white blood cells count (WBCC) and post-operative histology. Statistical analysis was performed using Fisher's exact test. **Results:** The median age group in the study was 12 (2–16). 141 (53%) patients were <12 years, while 127 (47%) patients were 12–16 years old. Male : female ratio = 1 : 1 (134 each). Inflammatory markers were not done for 94 patients (35%). CRP was done for 149 cases (55.6%), while WBCC was done for 172 cases (64%). Both markers were done together for 147 cases (54.8%). Histology was positive (inflamed / gangrenous appendix) in 202 cases (75.4%). Eight cases were associated with *Enterobious vermicularis* infestation and one patient had carcinoid tumour. The sensitivity and specificity of CRP were 82% and 60%, respectively, with positive predictive value (PPV) of 87% (P<0.0001), while those of WBCC were 80% and 59%, respectively, with PPV of 88% (P<0.0001). The sensitivity and specificity of both markers together were 80% and 70%, respectively, with PPV= 81% (P=3.11E-8). 94 patients (35%) had an appendicectomy operation based on clinical diagnosis alone without preoperative inflammatory markers having been tested. In 28 cases (30%) out of these, postoperative histology revealed normal appendix (P = 0.18). **Conclusion:** CRP and WBCC are simple tests that can provide a significant role supporting the clinical diagnosis of acute appendicitis in the paediatric age group.

Key words: Appendicitis, C-reactive protein, inflammatory markers, paediatrics, white blood cell count

Department of Surgery, Specialist Registrar in General Surgery, Aintree University Hospital, Liverpool, UK, [1]Department of Surgery, Associate Specialist in General Surgery, [3]Department of Surgery, Consultant General Surgeon and Lead Paediatric Surgeon, Prince Charles Hospital, Merthyr Tydfil, UK, [2]Department of Surgery, CT2 doctor in General Surgery, Pilgrim Hospital, Boston, Lincolnshire, UK

Address for correspondence:
Mr. Peter Mekhail,
Specialist Registrar in General Surgery,
2 Maes Yr Efail, Llangennech, Llanelli, SA14 8WD, UK.
E-mail: petertadros@hotmail.com

INTRODUCTION

Diagnosis of acute appendicitis is challenging – particularly in the paediatric age group- even in the hands of experienced surgeons.[1] In 1990, Addiss *et al.* mentioned that acute appendicitis represents the most common abdominal emergency in the USA.[2] Acute appendicitis can be atypically presented in children with non-specific abdominal symptoms. In addition, there is increased incidence of perforation within the paediatric age group "20–50%".,[3-5] Hence, finding cheap, quick and reliable investigatory tool is mandatory. The role of CT scan in diagnosing acute appendicitis is controversial, particularly in paediatrics. Some studies showed minimal improvement in the accuracy of the diagnosis of appendicitis using the CT scan.[6] Different studies showed sensitivity of 87% (higher diagnostic accuracy), and decreased negative laparotomy from 14.7 to 4.1 using the CT scan.[7,8] However, CT in this age group carries significant increase in lifetime radiation risk.[9]

White blood cells count (WBCC) and C-reactive protein (CRP) are two inflammatory markers that usually rise with variable inflammatory conditions including

appendicitis; therefore, they can be used to support the clinical diagnosis of acute appendicitis but with low specificity and positive predictive value (PPV).[10,11] Many studies performed on adults showed higher rates of normal appendices in the presence of positive signs and symptoms if WBCC and CRP are within normal limits.[12-15] Therefore, Gronroos *et al.* suggested that we can potentially avoid 25% of negative appendicectomies by measuring WBCC and CRP levels in patients with clinically suspected appendicitis.[12]

The aim of this study is to evaluate the role of preoperative inflammatory markers in supporting the clinical diagnosis of appendicitis in paediatrics.

MATERIALS AND METHODS

A retrospective study of all emergency appendicectomies was performed in paediatric age group in a District General Hospital in Wales over a period of seven years (2002–2009). All elective or interval appendicectomies were excluded from the study. Data was retrieved from theatre system database, operative notes and patient data enquiry computer system "AVALON" The data collected included preoperative inflammatory markers: CRP and (WBCC), intra-operative findings and post-operative histology. Histological results were categorically divided into two groups:

1. Positive appendicitis group including inflamed, gangrenous and perforated appendix.
2. Negative appendicitis group including normal appendix, follicular hyperplasia and non-inflamed appendix with *Enterobious vermicularis* infestation.

Results of the inflammatory markers were interpreted qualitatively as either normal or elevated.

The study population were divided into two age groups: children younger than 12 years old and teenagers between 12 and 16 years.

Table 1: Breakdown of cases

Histology	Normal	Inflamed	Perforated	Gangrenous	Carcinoid
Number	65 EV = 5	170 EV = 3	8	24	1

Table 2: Statistical significance of CRP+WBCC combined, according to gender

	Sensitivity	Specificity	PPV	*P* value
Male	95	63	95	0.0004
Female	87	75	90	0.0002

Statistical analysis was performed using Fisher's exact test.

RESULTS

Two hundred and sixty eight paediatric patients had emergency appendicectomy performed between 2002 and 2009. The median age was 12 (2–16), 53% (141 patients) were children <12 years and 47% (127 patients) were teenagers between 12 and 16 years of age. Male : female ratio was 1 : 1 (134 patients each). Thirty five percent (94 patients) had their operation based on the clinical diagnosis without preoperative inflammatory markers. Approximately 55.6% (149 patients) had preoperative CRP. Sixty four percent (172 patients) had preoperative WBCC done while in 54.8% (147 patients) both markers were performed together.

With regard to histology, 202 patients (75.4%) had positive appendicitis (inflamed, gangrenous or perforated appendix). Sixty five patients (24.3%) had normal appendix and one patient had carcinoid tumour [Table 1].

3% patients had *E. vermicularis* (EV) infestation (three associated with inflamed appendix).

The sensitivity and specificity of CRP alone were 82% and 60%, respectively, with a PPV of 87% ($P<0.0001$). The sensitivity and specificity of WBCC alone were 80% and 59%, respectively, with a PPV of 88% ($P<0.0001$). Assessing both inflammatory markers together was statistically significant with a sensitivity and specificity of 80% and 70%, respectively, PPV = 81% ($P= 3.11E-8$).

Statistical significance of WBCC and CRP analysis according to gender and according to age group is demonstrated in Tables 2 and 3.

Combined CRP and WBCC analysis is statistically more significant among the teenage group (>12 years old) – with sensitivity and specificity of 92% and 100%, respectively, PPV of 100% – compared to the younger children (<12 years old).

There was no significant statistical difference within both genders.

Table 3: Statistical significance of CRP and WBCC combined, according to age group

	Sensitivity	Specificity	PPV	*P* value
Children <12	91	50	88	0.00313
Teenagers	92	100	100	5.25E-7

Among the group of patients who had appendicectomy based on the clinical diagnosis without analysis of inflammatory markers (94 patients), 28 patients (30%) had normal appendix (negative histology), $P = 0.18$. This ratio was smaller in the groups who had preoperative WBCC, CRP or both being 11.6% ($P = 0.0004$), 12.8% ($P = 0.0014$) and 10.9% ($P = 0.0003$), respectively. Table 4 shows Breakdown of data according to age, gender and inflammatory markers.

Although the incidence of perforation was higher in children <12 years than in teens (14.9% vs. 8.7%), it was not statistically significant ($P = 0.13$).

DISCUSSION

Acute appendicitis by definition is characterized by a local inflammatory reaction that will in turn progress to a systemic inflammatory response. Detecting this inflammatory response through an easy, minimally invasive, widely available and cost-effective method is always desirable.[1] Several inflammatory markers have been anticipated to increase diagnostic accuracy in acute appendicitis including serum amyloid A,[16] interleukins and cytokines,[11] phospholipase A[17] and leucocyte elastase.[18]

The clinical diagnosis will remain the corner stone in acute appendicitis; nevertheless, laboratory investigations provide significant complimentary aid in diagnosis. The literature suggests that sensitivity of clinical examination alone in paediatric age group ranges between 54% and 70% compared to 70% and 87% in adults.[19-23] In our cohort, 30% (28/940) of patients who underwent appendicectomy based solely on clinical diagnosis had histologically normal appendices. WBCC and CRP are the most commonly used inflammatory markers that can represent a selective rise according to the stage of the disease i.e. WBCC increases more at the early process of appendicitis while CRP increases more dramatically in advanced appendicitis.[24]

Leucocytosis is a non-specific reaction induced by many conditions. This is reflected in numerous reports by an acceptable sensitivity (79–93%) but a rather low specificity for appendicitis. This is similar to our finding of lower specificity and higher sensitivity for WBCC.[25]

Despite the decreased specificity of WBCC and CRP in confirming acute appendicitis in children and adults,[7,9,10] the combined presence of normal WBCC and CRP in a patient makes the diagnosis of acute appendicitis highly unlikely particularly in adults.[9-12,15] In a study conducted by Stefanutti *et al.* on 100 children, they concluded that WBCC or CRP value alone does not appear to provide any additional information in the diagnosis of acute appendicitis. However, the sensitivity of the combined two tests is extremely high. Normal values of both WBCC and CRP are very unlikely in a pathologically confirmed appendicitis.[1] Our study showed that the increased sensitivity of each inflammatory marker solitarily is comparable to their sensitivity when combined together, while the specificity was significantly higher when both tests were performed together compared to their individual analysis in confirming the diagnosis of acute appendicitis in the paediatric age.

As the leucocyte response is reduced in children below five years of age, it was shown that the WBC count is better than CRP in the correct diagnosis of appendicitis in every age group of children except infants.[26] The number of patients <5 years old in our study was too small (8) to conduct statistical analysis.

Moreover, in a study involving 189 laparotomy for appendicitis, the results showed that measurement of IL-6 or CRP but not WBC had additional diagnostic value on the diagnosis of advanced or perforated appendicitis.[27] Our study, although, did not show significant statistical difference between CRP and WBCC in advanced or perforated appendicitis ($P = 0.12$).

Table 4: Breakdown of data according to age, gender and inflammatory markers

	Histology	Inflamed	Perforated	Gangrenous	Normal
Age	<	47	21	15	25
	12–16 years	96	11	13	40
Gender	Male	76	20	16	22
	Female	67	12	12	43
WBCC	Increased	71	16	20	16
	Normal	23	4	2	20
CRP	Increased	58	17	17	15
	Normal	22	0	1	19
WBCC+CRP	Increased	41	14	15	4
	Normal	10	0	0	16

CONCLUSION

CRP and WBCC levels can support the clinical diagnosis of acute appendicitis in the paediatric age. We recommend those tests in all paediatric patients with suspected acute appendicitis as this may decrease the incidence of negative appendicectomies.

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