

Research Article

Validity of Procalcitonin as diagnostic tool among acute appendicitis in pediatric patients

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Abstract: Acute appendicitis is a medical emergency that dictates an urgent operative procedure to prevent complications that are potentially life-threatening. Diagnosis of acute appendicitis presents challenges, more so among children. Ultrasonography and CT have improved the diagnostic accuracy, but these investigations require resources and technical expertise that may not be available in all hospital settings in rural India. Hence, there is a need to explore additional diagnostic tools to augment early and more precise diagnosis of acute appendicitis. This study has been carried out to identify validity of plasma procalcitonin for diagnosis of acute appendicitis among children. The Patients and Methods were in this study was conducted among 30 children diagnosed as acute appendicitis in a tertiary care hospital. WBC count, levels of C-reactive proteins & serum procalcitonin and ultrasonography were carried out in these patients. The excised appendix was subjected to histopathology, and results of histopathological examinations were utilized as gold standard to calculate sensitivity, specificity, positive- and negative-predictive values of four investigations. In results the study revealed high validity of procalcitonin as a tool for diagnosis of acute appendicitis among children. The comparative results of validity of four investigations are reported. In discussion the results of the study with similar studies carried out in India and abroad are discussed. In conclusion the Authors recommend that multi-centric study on validity and cost-effectiveness of plasma procalcitonin as a diagnostic tool for acute appendicitis should be undertaken to include this test in the protocol of management of acute abdomen with high index of suspicion of acute appendicitis.

Keywords: Acute appendicitis, Children, Investigation, Predictive Value, Procalcitonin, Sensitivity, Specificity

INTRODUCTION:

Appendicitis, the most common emergency abdominal surgery is commonly seen in the younger population with a slight male preponderance [1]. Its incidence rises slowly from birth, peaks in the late teen years and gradually declines in the elderly age group [2]. Since uncomplicated appendicitis can progress to perforation, a complication associated with a significantly higher morbidity and mortality, the surgeons often choose to operate when the diagnosis is probable, rather than wait until it is certain [3]. This has resulted in acceptance of 'a surgical security zone' which permits negative laparotomy rate between 15-30% [4]. This rate of negative appendectomy has been considered "acceptable" because the morbidity associated with complicated appendicitis is significantly higher than that of non-therapeutic appendectomy. However, removing normal appendix is an economic burden both on patients and health resources, and

surgical fraternity would like to narrow the safety zone without compromising the health and safety of the patients [5]. These issues get further compounded in children in whom diagnosis of appendicitis in absence of pathognomonic symptoms, variability of clinical picture, frequency of atypical forms, difficulty in detection of local signs, and absence of sensitive and specific haematological indicators make the diagnosis more challenging. Thus, timely and precise diagnosis of acute appendicitis deserves continued research to identify laboratory and radiological tools to prevent morbidity and mortality due to delay in diagnosis as well as over-diagnosis. One such biomarker that has been studied extensively, and even found reliable in bacterial infections and traumas is procalcitonin. Increasing levels of procalcitonin in blood in case of infections and inflammation was first described in 1993 [6]. More recently, it has been shown that concentration of procalcitonin selectively increases in case of bacterial

infections, while in case of other infections (viral, autoimmune) its concentration remains normal [7-9]. In addition, investigations have been carried out demonstrating the role of procalcitonin for diagnoses and prognosis of the post operational complications in case of various surgical pathologies [10, 11]. The significance of procalcitonin level to differentiate infections of bacterial origin from nonbacterial inflammations, predict outcome of disease, and probability of post operational complications has been well established. Thus quantitative estimation of procalcitonin is widely used parameters and is considered as sensitive and specific as fever, leukocyte count, or erythrocytes' sedimentation rate.

However, there is glaring lack of studies on role of procalcitonin, as a biomarker of inflammation in pediatric surgeries. This study aims to study the role of procalcitonin, as an inflammatory biomarker in children with acute appendicitis, and to compare the validity of Procalcitonin (PCT) with C-reactive protein (CRP), White Blood Cell count (WBC) and Ultrasonography (USG) as a diagnostic test among pediatric acute appendicitis cases.

PATIENTS AND METHODS:

The case-series study included thirty patients under the age of 15 years admitted to department of General

Surgery, Kamineni Institute of Medical Sciences, Narketpally, during the period October 2011-September 2013. Written informed consent from the parents of patients, and approval from institutional ethical committee were obtained. Detailed history and findings of clinical examination were recorded in a pretested structured questionnaire. Blood samples were collected from each patient and subjected to WBC count, CRP levels, and serum PCT levels. Ultrasonographies (USG) of abdomen/pelvis were requisitioned in all cases. Surgical findings were recorded and the appendix specimen was sent for histopathological examination. Taking histopathology as gold- standard, the validity parameters of CRP, WBC count, serum PCT and USG were calculated.

RESULTS:

The study included 30 patients up to 15 years of age admitted in the department of General Surgery who underwent surgery for acute appendicitis. Age and sex distribution of the patients is shown in Table 1. Table reveals that two-third of the patients were in age group 11 to 15 years and 14 (73.3%) were males.

Histologically 24 out of 30 patients were confirmed as cases of acute appendicitis. The test positive and negative for each investigation is tabulated in Table 2.

Table 1: Age and Sex distribution of Study Patients (n=30)

Age in years	Number of Boys (%)	Number of Girls (%)	Total (%)
< 5	1	-	1
6-10	7	2	9
11-15	14	6	20
Total	22 (73.3)	8 (26.7)	30 (100.0)

Table 2: Results of various Investigations in Appendicitis among Children

Diagnostic Test	Result of Diagnostic tests	Acute appendicitis Present n=24 (confirmed by histopathological report)	Acute appendicitis Absent n=6 (confirmed by histopathological report)
WBC count (12,000/cmm)	Suggestive of Appendicitis (Test Positive)	16 (True positive)	3 (False positive)
	Non-suggestive of Appendicitis (Test Negative)	8 (False negative)	3 (True negative)
CRP	Suggestive of Appendicitis (Test Positive)	8 (True positive)	4 (False positive)
	Non-suggestive of Appendicitis (Test Negative)	16 (False negative)	2 (True negative)
Procalcitonin	Suggestive of Appendicitis (Test Positive)	22 (True positive)	0 (False positive)
	Non-suggestive of Appendicitis (Test Negative)	2 (False negative)	6 (True negative)
USG	Suggestive of Appendicitis (Test Positive)	20 (True positive)	4 (False positive)
	Non-suggestive of Appendicitis (Test Negative)	4 (False negative)	2 (True negative)

Table 3 and Fig 1 depict the sensitivity, specificity, positive and negative predictive values for each investigation. Table reveals that serum procalcitonin had the highest sensitivity and specificity as well as positive and negative predictive value out of

the four investigations. On the other hand, CRP was detected to have the lowest sensitivity, specificity as well as positive and negative predictive values out of four investigations.

Table 3: Comparison among Validity of Investigations for Acute Appendicitis among Children

Investigation	Sensitivity (Percentage)	Specificity (Percentage)	Positive Predictive Value (Percentage)	Negative Predictive value (percentage)
WBC count	66.67	50.00	84.21	27.27
C-reactive Protein	33.33	33.0	66.67	11.11
Serum Procalcitonin	91.67	100	100	75.00
USG	83.33	33.0	83.33	33.33

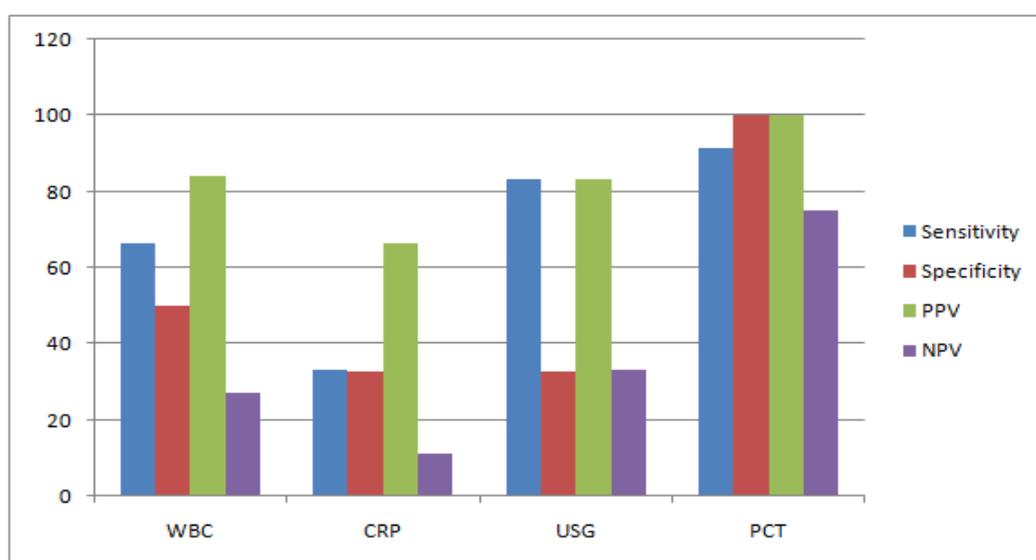


Fig-1: Validity parameters of WBC count, CRP, USG and procalcitonin among study patients

DISCUSSION:

Procalcitonin is a calcitonin precursor and has emerged as one of the useful early laboratory signs for systemic bacterial and fungal infections. In healthy individuals, the normal plasma PCT levels are < 0.5 ng/ml. In recent decades, scientific evidence has gathered in favour of utilizing plasma PCT level as a biomarker for acute appendicitis. This concept is based on the hypothesis that fecaliths that carry a high load of gram-negative bacteria play a predominant role in pathophysiology of acute appendicitis by causing obstruction of appendiceal lumen. Experimental studies have demonstrated that the injection of bacterial endotoxin into healthy subjects cause an increase in PCT after a latency period of 2-3 hours and reaching a plateau after 6-12 hours. This increase is significantly higher (up to 1,000ng/ml) during bacterial invasion while viral infection causes a minimal increase to 1.5ng/ml. However, a biomarker can be clinically useful only if it is Sensitive & Specific, Measurable,

Affordable, Responsive and Reproducible (SMART). The present study attempted to study the validity (specificity, sensitivity, positive & negative predictive Values) of PCT as compared to other commonly used diagnostic tests for acute appendicitis among children using histological evidence as the gold standard. The study revealed the sensitivity, specificity, positive and negative predictive value of PCT in acute appendicitis among children as 91.67%, 100%, 100% and 75%, respectively. These results were higher for other tests including USG. The study results are comparable to study results reported by Chandel *et al.*; [12] (sensitivity 95.65%, specificity 100%) and by Kafetzis *et al.*; [13] (sensitivity 73.4%, specificity 94.6%). However, a study by Bulent *et al.*; [14] reported a significantly lower sensitivity and specificity level of 24% and 50%, respectively.

CONCLUSION:

The study supports that plasma levels of procalcitonin is a sensitive and specific diagnostic test for early and accurate diagnosis of acute appendicitis among children with high positive and negative predictive values. Authors recommend that multi-centric study with large sample should be conducted to define validity parameters and cost-effectiveness of plasma procalcitonin as a diagnostic tool for acute appendicitis so that this test is included in the protocol of management of acute abdomen with high index of suspicion of acute appendicitis.

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