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#### **Original Contribution**

# Predictive value of C-reactive protein, ultrasound and Alvarado score in acute appendicitis: a prospective pediatric cohort ♣,♣♠,★



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#### ABSTRACT

*Purpose:* To evaluate whether C-reactive protein (CRP) level and ultrasound (US) results on admission could aid the diagnostic accuracy of Alvarado score.

*Methods*: A prospective study was performed on children < 14 years admitted for suspected acute appendicitis. Patients were categorized into three groups based on the Alvarado score: group II: score 7-10, group III: score 5-6, group III: score 0-4.

Results: The difference between predictive values of Alvarado score alone and Alvarado score with CRP was not statically significant. The PPV increased from 74.29% (Alvarado score and CRP) to 93.75% (Alvarado score and US) in group 1 (P = .001) and the NPV increased from 64.86 and 79.69% (Alvarado score and CRP) to 82.6 and 88.2% (Alvarado score and US) in group 2 (P = .01) and group 3 (P = .001), respectively.

*Conclusions*: Alvarado score and ultrasound taken together improve the predictive value of diagnosing acute appendicitis in children.

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#### 1. Introduction

Acute pain represents one of the most common cause for children consultation in the emergency department [1]. Clinical diagnosis of appendicitis in children is often challenging even for experienced surgeons. Different disease processes mimic the diagnosis of acute appendicitis as there are a number of causes leading to pain in the right iliac fossa particularly in female patients [2,3]. These difficulties likely contribute to the 28% to 57% rates of initially misdiagnosed appendicitis in children younger than 12 years [4–6]. Recently, different clinical scoring systems aiding in the diagnosis of appendicitis have been developed. Alvarado score is one of the most used scores in children (Table 1) [7]. It provides measurably useful diagnostic information in evaluating children with suspected appendicitis. However, Alvarado score doesn't provide adequate predictive values to be used in clinical practice as the gold method for determination of the need for surgery [8,9].

The aim of the study was to evaluate whether C-reactive protein (CRP) level and ultrasound (US) results on admission could aid the diagnostic accuracy of Alvarado score in a prospectively identified cohort of pediatric patients with suspected appendicitis.

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#### 2. Materials and methods

A prospective study was performed on children admitted for suspected acute appendicitis at the Paediatric Surgery Unit, Hedi Chaker Hospital, Sfax, Tunisia, between January 2013 and December 2014. The diagnosis of suspected appendicitis was established preoperatively by one of the consultant pediatric surgeons on the basis of clinical history and physical examination. Laboratory tests including white blood cell count and CRP were ordered on admission. C-reactive protein levels were measured by a highly sensitive immunonephelometric method; the upper reference limit for CRP was 6.0 mg/L. Decision for US evaluation was left to the discretion of the pediatric surgeon during the initial assessment. Ultrasound was performed by experienced pediatric radiologists during weekdays with all exams interpreted by a radiology resident and attending radiologist. Senior radiology residents performed and interpreted US during night-time hours (7 PM to 8 AM) and weekends. Ultrasound radiology reports were classified as positive or negative. A positive report was considered to be a maximum outer diameter of the appendix greater than 6 mm. Negative reports included those in which the appendix measured less than 6 mm and those in which there was no appendix seen on ultrasound with no indirect signs of appendicitis (large amounts of free fluid, phlegmon, or pericecal inflammatory fat changes). The Alvarado score, CRP value, and US result were correlated with the histopathological findings of the removed appendix. Patients were categorized into three groups based on the Alvarado score (Fig. 1). A score of  $\geq 7$  was indicating acute appendicitis, a score of 5 to 6 suggested the need for serial examination and follow-up

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**Table 1**The Alvarado scoring system

Mnemonic (MANTRELS)		Value
Symptoms	Migration	1
	Anorexia-acetone	1
	Nausea-vomiting	1
Signs	Right iliac fossa tenderness	2
	Rebound pain	1
	Elevation of temperature > 37.3°C	1
Laboratory	Leukocytosis	2
	Shift to the left	1
Total score		10

and a score below this level meant normal appendix, but the decision to undergo surgery was purely clinical. Patients were operated by conventional method of appendectomy in 122 cases and by laparoscopy in 26 cases. Appendicitis was considered present when patients who had undergone surgery had a final histology showing acute appendicitis. Patients who did not undergo surgery were considered not to have appendicitis if they did not re-present within 2 weeks from initial discharge with acute appendicitis. Negative (NPV) and positive predictive values (PPV) of Alvarado score, CRP and ultrasound were calculated. The differences between groups are presented as 95% confidence intervals. P < .05 was considered to indicate statistical significance. All data was analyzed by SPSS version 13.

#### 3. Results

There were 402 patients admitted for suspected appendicitis from January 2013 to December 2014. One hundred and ten patients were not evaluated with US scans and were excluded from the study. Two hundred ninety-two patients were included in the study after taking informed consent. There were 170 (58.2%) males and 122 (41.8%) females. The mean age was 8.54  $\pm$  3 years, ranging from 3 to 13.8 years. At the time of consultation, the mean duration of pain was 46.8 hours (4–168 hours). Pain was associated with nausea and vomiting in 86 patients. Right iliac fossa tenderness was found in 68 patients.

Among the 292 patients, 144 were treated without surgical approaches and were then discharged from our hospital. None of these

patients has re-presented within 2 weeks from initial discharge with acute appendicitis. The rates of normal appendix, non-perforated appendicitis, and perforated appendicitis were 6.1%, 73%, and 20.9%. The final diagnoses of patients with normal appendices included colitis, functional gastrointestinal disorders, and mesenteric lymphadenopathy.

The sensitivity, specificity, positive and negative predictive values of Alvarado score, CRP, and US are illustrated in Table 2. The PPV of Alvarado score  $\geq 7$  was 71.1% in group I, the NPV of Alvarado score  $\leq 7$  were 50.78% in group II and 68.9% in group III. The PPV of high CRP, the NPV of normal CRP, the PPV of positive ultrasound scan and the NPV of negative ultrasound result are presented in Table 3. The difference between predictive values of Alvarado score alone and Alvarado score with CRP was not statically significant (P=.453 in group 1, P=.43 in group 2, P=.08 in group 3). On the contrary, ultrasound was very helpful to diagnose acute appendicitis: The PPV increased from 74.29% (Alvarado score and CRP) to 93.8% (Alvarado score and ultrasound) in group 1 (P=.001) and the NPV increased from 64.86 and 79.69% (Alvarado score and CRP) to 82.6 and 88.2% (Alvarado score and ultrasound) in group 2 (P=.01) and group 3 (P=.001), respectively (Fig. 2).

#### 4. Discussion

Our study showed that CRP level on admission could not aid the diagnostic accuracy of Alvarado score in acute appendicitis. Despite substantial research, the diagnosis of pediatric appendicitis remains challenging. Recent studies have proposed different clinical scoring systems aiding in the diagnosis of appendicitis [8]. Ideally, a clinical score could accurately distinguish those patients that need immediate operative care from those that may benefit from further investigation or observation. Two well-studied appendicitis scores were developed by Alfredo Alvarado and Madan Samuel, with the explicit purpose of diagnosing appendicitis [10]. Several studies validated the Alvarado score as simple, practical and reproducible diagnostic tool for assessing an acute abdomen [11–15]. It has been useful both to reduce the incidence of negative appendectomy and to avoid delay in therapy [14,16,17]. However, other studies suggest that Alvarado score doesn't provide adequate predictive values to be used in clinical practice as the sole method for determination of the need

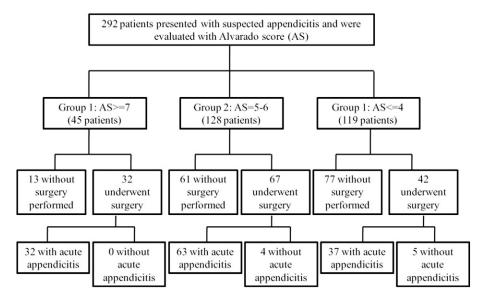


Fig. 1. Management course and outcomes of study cohort.

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