Prognostication of Pediatric Appendicitis with Three Scoring Systems

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Abstract: Background: Appendicitis represents one of the most prevalent abdominal emergencies in the pediatric group of population. In spite of being a comparatively common disease, appendicitis diagnosis in children may be challenging in some cases. Scoring systems of appendicitis have been proposed as a diagnostic aid to increase accuracy of decision-making in children with doubtful cases of acute appendicitis. The present prospective study evaluates three scoring systems in children suspected to have acute appendicitis (Appendicitis Inflammatory Response score, Alvarado score, and Pediatric Appendicitis Score). **Patients and Methods:** 278 child (less than 18 years old) suspicious to have acute appendicitis were involved in the study from January 2013 to December 2016. Variables were recorded for subsequent evaluation of 3 different scoring systems concerning appendicitis diagnosis (Appendicitis Inflammatory Response score, Alvarado score, and Pediatric Appendicitis Score). The diagnostic accuracy of each of the three scoring systems were construed by calculating the diagnostic performances at different cut-off points. **Results:** 78 child (28%) had non-appendicitis causes of abdominal complaint and eliminated from the study. Two hundred patients underwent appendectomy. There were 116 boys (58%) and 84 girls (42%) with a mean age of 8.6 years (range, 2.6–16.2 years). The sensitivity, specificity, accuracy and positive predictive value of the Appendicitis Inflammatory Response score were superior to Alvarado and Pediatric Appendicitis Scores in prognostication of acute appendicitis. In children with low-risk acute appendicitis, false negative rates of 2.2% for the Appendicitis Inflammatory Response, 4% for the Alvarado, and 9.7% for the Pediatric Appendicitis Score were measured. Appendicitis Inflammatory Response score correctly classified 95.6% of all patients confirmed with histological acute appendicitis to the high probability group (at optimal cutoff threshold of ≥ 9), compared with 85.9% with Alvarado score (at optimal cutoff threshold of ≥ 7.5), and with 83.4% with Pediatric Appendicitis Score (at optimal cutoff threshold of ≥ 6; p-value is 0.001). **Conclusion:** Appendicitis Inflammatory Response scoring system is the most convenient, accurate and specific scoring system for the pediatric Egyptian population suffering from acute appendicitis followed by Alvarado scoring system and lastly Pediatric Appendicitis scoring system. Elimination of acute appendicitis safely in pediatric population with scoring systems still remains unreliable especially in female population.

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1. Introduction

Abdominal pain considered to be one of the commonest presentations of children seen in the casualty department. Appendicitis considered to be one of the commonest surgical emergency in the pediatric group of population. Proper diagnosis of appendicitis especially in children is challenging despite being a very common clinical condition. The ability of the clinician to diagnose acute appendicitis is variable especially when he depends on history and physical examination alone (with a sensitivity of 75% and specificity of 78%).[1]

This diagnostic uncertainty, beside the attention to reduce negative appendectomy, has led to heavy dependence on diagnostic imaging studies as ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI). In a retrospective cohort study of 13,328 patients, Rice-Townsend et al.[2] stated that there is wide variation in the diagnostic tools of suspected acute appendicitis among children′s clinicians, in preoperative imaging there is 3.5-fold variation and in laboratory utilization there is 5-fold variation. The American College of Surgeon′s Pediatric National Quality Improvement Program (ACS NSQIP) stated that 65% of pediatric group of population with suspected appendicitis received preoperative ultrasound before appendectomy and 42% received preoperative computed tomography (CT) scan.[3] Several factors may clarify this practice variation, including differences of available resources among hospitals and in the perceived value of different diagnostic adjuncts used individually and in combination.

Although appendicitis is less common in young children, diagnosis is confusing and offer special difficulties. It may be hard to get medical history from a child and clinical signs can be misleading. Non-specific abdominal pain and mesenteric lymphadenitis are common alternate diagnoses, and sometimes these are impossible to differentiate from acute appendicitis on clinical grounds. This results in wrong or delayed diagnosis in 19–57% of children with a suspected appendicitis. This will result in prolonged observation time with an increase in complications, including perforated appendicitis (23–73%), pelvic abscesses, and bowel obstructions.[4]

The standard protocol for children suspected to have appendicitis is proper history taking, general and local examination, and laboratory tests. Routine imaging examination of children at the casualty department consume time, and there is no confidence that acute appendicitis will be diagnosed or ruled out. Visualization of the appendix with ultrasound may be difficult and also operator dependent. Computed tomography is not suitable for use in children due to radiation exposure and the associated long-term risks of cancer.[5]

Clinically based scoring systems may help in identification of patients at high or low hazard for acute appendicitis. Unluckily, prospective effectiveness of these scores has shown mixed test performance, thus limited their approval as alternatives to diagnostic imaging.[4] The heterogeneous presentation of children with query appendicitis, particularly in females and young children, is an important reason for the lack of success of these rules.[6] In comparison, male patients are known to present with more typical findings for appendicitis and have fewer alternative etiologies for right lower abdominal pain, and might serve as better sector of populations for appendicitis clinical scoring systems.[7]

The most frequently used scoring systems are Alvarado score and the Pediatric Appendicitis Score (PAS). The score of Alvarado is constructed and advocated to predict appendicitis for patients irrespective of ages, and the PAS is constructed for children and adolescents. Both scoring systems produce widespread diagnostic results in validation studies and vary in usability.[8]

Appendicitis Inflammatory Response (AIR) scoreis a relatively novel scoring system. AIR score is constructed and advocated to predict suspected appendicitis in adults. AIR score is different from Alvarado and PAS systems because it include C-reactive protein (CRP) as an important value. Two studies have shown that AIR score significantly more accurate than Alvarado score for diagnosing acute appendicitis.[9, 10] The aim of this study is to evaluate and compare the accuracy of AIR, Alvarado, and PAS in the diagnosis of children suspected to have appendicitis.

2. Patients and Methods

Two hundred child were evaluated in this study between January 2013 and December 2016. They were below 18 years. They presented with non-traumatic abdominal pain (i.e., diffuse, epigastric regions, periumbilical, or right lower quadrant). Patient records were initialized immediately at presentation. In all patients, multiple variables were scored (anorexia, nausea, vomiting, and RLQ pain either primary or migrating). Physical examination involved fever assessment, rebound tenderness, rigidity and cough tenderness in the RLQ. Blood tests included leucocytic count (total and differential), and serum CRP.

Each variable assigned points according to the original scoring systems (AIR score[9], Alvarado score[11], and PAS characteristics[12]). If a variable was not mentioned, no point was assigned to the child. The total points of each system indicates the likelihood of acute appendicitis. Higher scores conforming to a greater probability. However, each system has its cut-off value for the probability of acute appendicitis and its total number of points. The original cut-off points of each scoring system as described by their authors were used. The AIR has a score of (0–4) low, (5–8) intermediate, and (9–12) high. The Alvarado has a score of (0–4) low, (5–6) intermediate, (7–8) high probably acute appendicitis and (9–10) highly likely acute appendicitis. The latter 2 groups considered as high probability acute appendicitis. The PAS score only separates into a low (≤5) and high (≥6) probability of acute appendicitis. Details of the 3 scoring systems points were provided in Table I.

The primary assessment of each child who presented with manifestations of appendicitis was made by a single surgeon. The judgment to perform imaging was the preference of the surgeon. Children with presumed low risk of acute appendicitis, depending on history, physical examination, and laboratory findings, were candidates for re-evaluation at the clinic after 24 hours. These children included in the present study. They were followed up until a correct diagnosis was made or symptoms resolved.

If additional diagnostic ultrasound imaging was positive for acute appendicitis, the decision of operation was taken. An open appendectomy was performed. The diagnosis of acute appendicitis in the present study was based on histopathologicl examination of the appendix (neutrophil granulocyte infiltrate muscularis propria).[13] Patients with acute appendicitis were classified into 2 subgroups: (1) the suppurative appendicitis group and (2) the advanced appendicitis group. The latter group included any form of gangrene of the appendix (including that with perforation).

Measurement of leucocytic count (total and differential) was performed routinely in the standard laboratory request. It was found that polymorphonuclear leukocytes shift only occurred when a WBC ≥12 × 10^9/L was measured. In the AIR score, a 2-point score can be given if the PLS is ≥85%. Data analysis was processed by IBM SPSS statistics (version 21.0). Fisher exact test was used for binominal variables with a frequency of <5 and Student *t* test for continuous variables.

3. Results

Table 1. Points of the three scoring systems and its significance.*

	AIR score[9]	Alvarado score[11]	PAS[12]
Vomiting	1	—	—
Nausea or vomiting	—	1	1
Anorexia	—	1	1
RLQ tenderness	1	2	2
Migration of pain to the RLQ	—	1	1
Rebound tenderness or muscle rigidity	—	1	—
Light	1	—	—
Medium	2	—	—
Strong	3	—	—
Cough/percussion/hopping tenderness in RLQ	—	—	2
Body temperature			
≥37.3°C	—	1	—
≥38.0°C	—	—	1
≥38.5°C	1	—	—
Leukocytosis			
>10.0 × 10^9/L	—	2	1
10.0–14.9 × 10^9/L	1	—	—
≥15.0 × 10^9/L	2	—	—
Polymorphonuclear leukocytes shift			
70–84%	1	—	—
>75%	—	1	1
≥85%	2	—	—
CRP concentration			
10–49 mg/L	1	—	—
≥50 mg/L	2	—	—
Total score	12	10	10

*AIR score: 0–4 = low probability of AA, 5–8 = indeterminate group, in-hospital observation with additional imaging or diagnostic laparoscopy, 9–12 = high probability of AA, operation recommended. Alvarado score: 0–4 = not likely AA, 5–6 = compatible of AA and observation is recommended, 7–8 = probability of AA and operation is recommended, 9–10 = high probability of AA and operation is recommended. PAS: ≥ 5 = no AA and observation is recommended, ≥ 6 = AA and operation is recommended.

Table 2. The distribution of patients with individual scoring systems AIR, ALVARADO, and PAS.

AIR		**Alvarado**		**PAS**	
Score	**No. (%)**	**Score**	**No. (%)**	**Score**	**No. (%)**
0–4	4 (2%)	0–4	6 (3%)	≤5	32 (16%)
5–8	28 (14%)	5–6	14 (7%)	-	-
9–12	168 (84%)	7-10	180 (90%)	≥6	168 (84%)
Total	200 (100%)	**Total**	200 (100%)	**Total**	200 (100%)

From the 278 patients included in the study 78 child (28%) had non-appendicitis causes of abdominal pain and excluded from the study. Two hundred cases (72%) underwent surgery for the diagnosis of acute appendicitis. The most frequent alternate diagnosis was nonspecific abdominal pain 22(28.2%) that resolved spontaneously during follow-up, followed by gastroenteritis 16(20.5%), mesenteric lymphadenitis 15(19.3%), constipation 12(15.4%), urinary tract infection 8(10.3%), pelvic inflammatory disease 2(2.5%), colitis 2(2.5%), and intussusception 1(1.3%).

Of the total of 200 patients, there were 116 boys (58%) and 84 girls (42%) with a mean age of 8.6 years (range, 4.6–16.2 years). Right iliac fossa pain was present in 200 (100%) patients in the study group. Pain migration was present in 150 (75%). Anorexia was present in 180 patients (90%). Nausea and vomiting was present in 160 patients (80%). Fever was present in 121 patients (60.5%) and patients presenting with duration of symptoms <48 h were 140 (70%).

Tenderness was present in 184 patients (92%) of the study group. Rebound tenderness was present in 112 patients (56%). Guarding was present 84 patients (42%) and Rovsing's sign was present in 64 patients (32%). Total leucocytic count was raised in 107 patients (53.5%) with shift to the left in 83 patients (41.5%). Urine analysis was normal in 186 patients (93%). Of all the symptoms right iliac fossa pain, anorexia, nausea and vomiting and duration of symptoms came out to be statistically significant with p value 0,001, 0.03, 0.01 and 0.03, respectively. Of all the signs only right iliac fossa tenderness came out to be highly statistically significant with p value 0.001.

The distribution of patients with individual scoring systems ALVARADO, PAS, and AIR were shown in Table 2. Of the total 200 patients, 169 (84.5%) were histopathologically positive and 31 (15.5%) were negative for appendicitis. The suppurative appendicitis group were 142 (84%) and the advanced appendicitis group were 27 (16%).

Chi-square analysis of gender distribution between the groups was significant (p=0.01) with more male patients 14 (12%) in negative appendectomy group compared to 102 (88%) in the positive group in contrast to female patients 20 (23.8%) in negative appendectomy group compared to 64 (76.2%) in the positive group. Other statistically significant findings between the groups using t-test were higher values for the true appendectomy group regarding pre-operative symptom duration (hours) 26.2 ± 4.6 ($p < 0.01$), admission body temperature 37.8^{o} C (p=0.01) and AIR score 9.2 ± 1.5 ($p < 0.01$).

All scoring systems were compared and an area under the curve (AUC) of the receiver operating characteristic (ROC) was calculated. Table 3 shows the ROC analysis for the three scoring systems. The best scoring system in the current study was the AIR score with an AUC of 0.92 (95% confidence interval [CI], 0.88–0.96). A comparison of the AIR score with the AUC of Alvarado 0.86 (95% CI, 0.83–0.89) or PAS 0.80 (95% CI, 0.75–0.85) showed a statistical significant difference with a *P* value of 0.008 and 0.003, respectively. The AIR score gave statistically better results than the Alvarado and PAS in the sub-analysis of acute appendicitis in boys especially in the group aged 7 to 12 years (Table 3).

At optimal cutoff threshold of ≥ 9 the sensitivity and specificity of the AIR scoring system were 97.8% and 84.3% respectively. At optimal cutoff threshold of ≥ 7.5, the sensitivity and specificity of the ALVARADO scoring system were 95.9% and 33.3% respectively. Similarly, at optimal cutoff threshold of ≥ 6 the sensitivity and specificity of the PAS scoring system were 90.3% and 47% respectively. The overall accuracy of AIR, ALVARADO, and PAS scoring systems was 95.6%, 85.9%, and 83.4% respectively. Positive predictive and negative predictive values of AIR score were 97% and 87.8% respectively. Positive predictive and negative predictive values of ALVARADO score were 88.4% and 39.3% respectively. Positive predictive and negative predictive values of PAS score were 90% and 48% respectively. The detailed statistical values of the three scoring systems is outlined in Table 4.

Table 3. ROC curve analysis.

	No. (%)	**AIR score**	**Alvarado score**	**PAS**
All AA	169 (89.5%)	0.92	0.86□	0.80□
Suppurative	142 (84%)	0.82	0.79	0.70□
Advanced	27 (16%)	0.90	0.82□	0.80□
Sex				
Boys	116 (58%)	0.90	0.86□	0.79□
Girls	84 (42%)	0.91	0.90	0.80□
Age				
Group 1 (1–<7 y)	26 (13%)	0.88	0.85	0.84
Group 2 (≥7–<13 y)	96 (48%)	0.92	0.86□	0.81□
Group 3 (≥13–18 y)	78 (39%)	0.88	0.86	0.81□

*Denotes P < 0.05 when compared with AIR score.

Table 4. Statistical values of AIR, ALVARADO, and PAS.

	AIR	Alvarado	PAS
Sensitivity	97.8%	95.9%	90.3%
Specificity	84.3%	33.3%	47%
Accuracy	95.6%	85.9%	83.4%
Positive predictive value	97%	88.4%	90%
Negative predictive value	87.8%	39.3%	48%
False positive rate	18.7%	52.9%	66.7%
False negative rate	2.2%	4%	9.7%

4. Discussion

The goals of evaluating a pediatric patient with suspected appendicitis should include a timely diagnosis with minimal radiation exposure and risk of negative appendectomy. Appendicitis risk scores can be used as a useful screening aid to detect moderate to high risk patients where additional imaging or observation may be warranted, although their value as a single diagnostic tool may be limited. When imaging is being indicated, ultrasonography should be the initial modality (when available), and use of standardized sonographic technique, reporting methods and dedicated pediatric sonographers have been shown to improve accurate diagnosis. When CT is considered, dose reduction protocols should be implemented to limit radiation exposure. The preliminary data of MRI for detecting appendicitis is promising, but more data is needed to confirm ideal imaging protocols and the role MRI should play in the context of other diagnostic adjuncts.[14]

The diagnosis of acute appendicitis is predominantly depends on clinical grounds.[15] Few cases can be managed conservatively but most of them have to be operated upon. The risk of appendectomy in emergency is 12% and 23% in men and women, respectively.[16] Modern medical practice and surgical techniques reduced the overall risk but complications still high for certain subgroups e.g. extremes of age, diabetics, and immuno-compromised patients.[17] Unnecessary appendectomies are associated with increased morbidity and cost ineffective. Mortality complicating acute appendicitis has been brought down to <1% with modern surgical practice.[18]

Removal of normal appendix has been associated with increased risk of abdominal adhesions, as compared to acute appendicitis, and puts a healthy patient at risk for operative morbidity. A delay in performing appendectomy to improve its diagnostic accuracy increases the rate of appendicitis complications (perforation and peritonitis), which in turn increases morbidity and mortality.

The opposite is also true with decreased diagnostic accuracy, the negative appendectomy rate is increased, and this is generally reported to be approximately 20-40%.[19] Several authors considered higher negative appendectomy rates acceptable in order to minimize the incidence of perforation.[20, 21] Diagnostic accuracy can be improved through the use of abdominal ultrasonography, magnetic resonance imaging, or computed tomography. However, such routine practice increase the cost of health care substantially. A recent study has suggested that such indistinctive use of CT may lead to diagnosis of early low-grade appendicitis with subsequent unnecessary appendectomies which would simply resolved spontaneously by antibiotics therapy.[22] Hence, scoring system were derived in order to increase accuracy of acute appendicitis diagnosis.

Although hematological parameters such as leucocytic count and serum C-reactive protein can assist in more confident diagnosis, both are non-specific and may be raised in a many inflammatory and infective conditions. Radiological tools utilized to aid in acute appendicitis diagnosis including abdominal ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) have cost issues, require experienced personnel and are not available 24 hours a day in the majority of hospitals. Additionally, none of them is confirmatory.[20]

Appendicitis scoring systems were proposed as a predictive tool to ameliorate decision-making in patients with a preliminary suspicious of acute appendicitis. These clinically applied scoring systems rate the probability of acute appendicitis and could participate in the decision-making because of their simple layout and application.

There are many reasons to use scoring systems in the management of patients with appendicitis. A clinical scoring system may be appropriate as an agent for selecting patients for further imaging techniques examination or next-day re-examination. Scoring system can be repeated and impact the decision to perform imaging. It must be confirmed that scoring system is not intended to establish a primary diagnosis of acute appendicitis, but simply to distinguish objectively when there is uncertainty. Better description of the patients who are included in clinical studies is another reason to use such a scoring system in order to facilitate comparison of the results. Objective validated scoring system could legally augment decisions made in the emergency room and lessen malpractice liability.

Many scoring systems have been developed to boost the accuracy of diagnosis of acute appendicitis and reduce negative appendectomy rates. The Alvarado, RIPASA, and Lintula are the three most common used scoring systems in the Western populations.[23] The 2 most studied scoring approaches in pediatrics are those reported by Alvarado (Alvarado score), and Samuel (Pediatric Appendicitis Score, PAS).[11, 12]

The present work compared sensitivity and specificity between AIR, Alvarado, and PAS systems. Sensitivity (true positive rate) is the proportion of actual positives which is correctly identified that is the percentage of sick people who are correctly detected as having the condition. Specificity (true negative rate) is the proportion of negatives which are correctly identified that is the percentage of healthy people who are correctly detected as not having the condition.[24]In the present study the AIR score statistically outperformed the Alvarado score and PAS as a diagnostic tool in the prediction of acute appendicitis in pediatric population. The AIR score revealed the best diagnostic accuracy with a low percentage of negative appendectomies.

Many studies in the literature have evaluated appendicitis scoring systems in adult patients. The first prediction tool for patients with suspected acute appendicitis was Alvarado score. The sensitivity ranges between 70–98%, specificity between 39–100%, PPV between 74–100%, and NPV between 41–98% in the literature.[5, 25-27] Alvarado score developed in a population that already had undergone operation. This has a major effect on the pretest prospect of the score and may explains the variations of the outcome in the literature. PAS has been introduced specifically for use in children, but it also displayed varying diagnostic values, with sensitivities between 82–100%, specificities between 50–98, PPVs of 54–97%, and NPVs of 79–99%.[4,26, 28, 29] A recent article that prospectively compared Alvarado score with PAS for predicting acute appendicitis in children concluded that neither scoring systems has sufficient predictive value to diagnose acute appendicitis safely. No significant differences were detected between Alvarado score and PAS. The authors complemented that the scores are not applicable as an exclusive standard in diagnosing acute appendicitis in children.[30]

The AIR score has unparalleled advantage in the pediatric population as all variables can be applied in children very easily. The Alvarado score and PAS needs subjective signs as nausea, anorexia, and migration of pain while the AIR score only has objective variables. The original Alvarado score did not comprise many children and subsequently probably compares better with the AIR score in the juvenile age. The original AIR score was constructed to suspect acute appendicitis in patients of all ages. Andersson et al[18] demonstrated that the AIR score statistically was superior to Alvarado score in predicting acute appendicitis in the general population.[9, 10]

The finding of relatively low specificity found in many studies for both the PAS and Alvarado score is particularly noteworthy as many children without appendicitis will meet the scoring threshold and potentially be at risk for a negative appendectomy. With this consideration, many have proposed the use of risk scores as a screening tool to identify patients who might benefit from further imaging or serial abdominal examinations prior to appendectomy. [4, 26, 29, 31, 32] The classical Alvarado score includes left shift of neutrophil maturation, which is not routinely done in many laboratories. The modified Alvarado score which includes extra-sign (e.g. cough test, Rovsing sign and rectal tenderness) is helpful in minimizing unnecessary appendectomy and is practical, reliable and easily done.

Kanumba et al. study demonstrated that modified Alvarado score provides high degree of sensitivity, specificity, PPV, NPV and accuracy in the diagnosis of suspected acute appendicitis and has found to be better in male patients with lower negative appendicectomies and high positive predictive value for male patients as compared to females.[33] On the contrary, PEYVASTEH and his colleagues stated that modified Alvarado score has high sensitivity but low specificity for diagnosis of acute appendicitis in children.[34]

The question arises as to whether PLS have any clinical relevance in the prediction of acute appendicitis in the studied scoring systems. In 2004, Andersson et al[35] examined in a meta-analysis the discriminatory power of clinical signs and laboratory variables in patients with appendicitis. The laboratory data expressed as AUC were 0.75 for CRP, 0.77 for WBC, and 0.77 for PLS. The summation of CRP and WBC levels showed an increase of the AUC to 0.96.[35] Van Dieijen-Visser et al[36] found an AUC of 0.85 for the combination of CRP and WBC levels. Unfortunately, the AUC decreased to 0.79 when PLS was incorporated with both inflammatory variables. Similar results were encountered in the present study. Addition of PLS to each element of the scoring system did not elevate the statistical recognition of acute appendicitis in children. Therefore, deleting PLS may make the scoring system easier without loss of its predictive power.

In daily practice, such a system could reduce unnecessary hospitalization and diagnostic procedures. A perfect scoring system may be used as anagent for selecting pediatric patients for immediate diagnostic imaging to assert the diagnosis, observation with or without additional diagnostic imaging (repeated ultrasonography or magnetic resonance imaging/computed tomography) or discharge and re-examination the next day.

The present study showed that the AIR score is statistically more beneficial than Alvarado and PAS for this purpose in children population. The clinical relevance of such a scoring system has yet to be confirmed. High AIR score had the best distinguishable power in predicting acute appendicitis in children. With a low AIR score, one cannot simply rule-out appendicitis and discharge patients, as this would result in an unacceptable 12.2% rate of missed appendicitis.

Conclusion

The AIR score had the best distinguishable power and statistically is superior to Alvarado score and PAS in prognostication of acute appendicitis in children population. Usage of AIR score in the diagnosis of suspected acute appendicitis in pediatrics increases clinical accuracy and reduces the negative appendicectomy rate. This results in a decrease in unnecessary admissions, the healthcare burden and cost and increases the overall efficiency of emergency surgical services.

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