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PEDIATRIC APPENDICITIS SCORE / PEDIATRIC APPENDICITIS RISK CALCULATOR / ALVARADO - WHICH IS SUPERIOR IN PREDICTING THE INCIDENCE OF CONFIRMED APPENDICITIS? (DIAGNOSTIC TEST OVERVIEW)

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Abstract

Background: Acute appendicitis is one of the most common causes of acute abdominal pain in children. The most severe complication is perforation of the appendix, which can lead to peritonitis and sepsis. Early diagnosis could prevent deterioration, therefore scoring systems were made to help clinicians to diagnose appendicitis. Aim: This study aims to review the diagnostic test of the Alvarado, Pediatric Appendicitis Score (PAS), and Pediatric Appendicitis Risk Calculator (pARC) scoring systems in predicting the incidence of confirmed acute appendicitis in pediatrics. Material and Methods: This study is an analytical study with a case-control study design and total sampling method. The accessible population is cases of acute appendicitis in children with a limited population in Depati Hamzah Regional Public Hospital from 1st January 2019 to 31st July 2020. Results: PAS has the highest true-positive value (80%), followed by Alvarado score (55%), and pARC (30%). The results of sensitivity, specificity, PPV, and NPV between Alvarado scores and PAS were 68.75%; 100%; 100%; 44.44%. The results of sensitivity, specificity, PPV, and NPV between the pARC against the PAS were 37.5%; 100%; 100%; 71.43%. The results of sensitivity, specificity, PPV, and NPV between the pARC against the Alvarado score were 36.36%; 77.78%; 66.67%; 50%. Conclusion: This study shows that Alvarado score has a better level of sensitivity, specificity, PPV, and NPV in predicting the incidence of acute appendicitis in confirmed children.

Keywords: ***acute appendicitis, PAS, pARC, Alvarado, pediatric***

INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdominal pain in children. Appendicitis is a process of obstruction caused by a fecalith then an infectious process and followed by inflammation of the vermiform appendix.(1–3) Patients need to be educated that appendicitis in this age group has a higher risk of perforation, and duration of the hospital stay may be longer.(4) The most severe complication is perforation of the appendix, which can lead to peritonitis and sepsis. So it is necessary to know as early as possible to prevent deterioration.(5)

As many as 250,000 cases of appendicitis are reported annually. The estimated risk of appendicitis is 12% for male and 25% for female.(4) The incidence of acute appendicitis decreased from 3.6 / 10,000 to 1.1 / 10,000 in preschool children, from 18.6 / 10,000 to 6.8 / 10,000 in children aged 5-9 years, and from 29.2 / 10,000 to 19.3 / 10,000 in children aged 10-14 years. Although appendicitis can occur at any age, the incidence of appendicitis is most common in the age range of 10-19 years.(6,7) The diagnosis of acute appendicitis can be achieved by several clinical, radiological, and laboratory criteria.(8) The diagnosis of appendicitis in pediatric patients may be challenging,

therefore scoring systems were made to help clinicians to diagnose appendicitis.(9)

The most frequently used appendicitis scoring in general population is Alvarado score with total score of 10 that helps clinicians to decide whether to discharge the patient (Alvarado score < 5), stay alert (Alvarado score 5-6), and to operate (Alvarado score > 6). Some authors suggest that this system could facilitate the diagnostic process especially in low-resource countries where imaging modalities are not widely available.(10,11) Samuel (2002) developed the Pediatric Appendicitis Score (PAS) in a prospective cohort study of 1,170 patients aged 4 to 15 years with abdominal pain. Clinical history, physical examination, and laboratory data were analyzed for 8 variables that showed statistical significance for acute appendicitis, and a 10-point estimation system was constructed.(12) Various large-scale research studies have described variability in clinical presentation and have emphasized the importance of group analysis and interactions among covariates. Age, gender, and symptom symptoms may affect laboratory findings and diagnostic imaging accuracy in children with acute abdominal pain. The Pediatric Appendicitis Risk Calculator (pARC) is a new scoring system that assessed variables to estimate the risk of appendicitis in children. The variables consist of age, sex, temperature, nausea/vomiting, duration of pain, location of pain, pain on walking, migratory pain, abdominal guarding, leukocyte count, and absolute neutrophil count.(13)

This study aims to review the diagnostic test of the Alvarado, PAS, and pARC scoring systems in predicting the incidence of confirmed acute appendicitis in pediatrics.

METHODS

This study is an analytical study with a case-control study design with the ultimate goal of comparing which questionnaire is the most superior in predicting the incidence of acute appendicitis in children. This research took place at the Depati Hamzah Regional Public Hospital, Pangkalpinang, Bangka Belitung, from 1st August 2020 to 20th August 2020. This study has an accessible population, which is cases of acute appendicitis in children with a limited population in the Depati Hamzah Regional Public Hospital area, Pangkalpinang in the period of 1st January 2019 to 31st July 2020. The sample in this study was part of the accessible population that met the inclusion criteria. This study's large sample is following the number of incidence of appendicitis in children, namely 1.1 / 10,000 among preschool children, 18.6 / 10,000 in children aged 5-9 years, and 19.3 / 10,000 in children. Age 10–14 years with the mean total incidence rate of 13 / 10,000 events, which makes the minimum sample size in this case 20 respondents (preliminary 1 was 5% and clinical assessment was 0.015).

The sampling method used in this study was total sampling. The inclusion criteria were children with acute appendicitis and aged less than 18 years, while the exclusion criteria in this study were data from respondents who did not have a good record of history, physical examination, and related supporting examinations. The investigation of this procedure starts with a proposal of investigation, asking permission from the hospital regarding proper permits and data collection, coordination with related parties, especially the medical record division, sorting medical records, recording medical records, and processing data for publication and accountability purposes. The variables in

this study are divided into two, namely the independent variable and the dependent variable. The independent variables in this study are the results of the scoring from the Pediatric Appendicitis Score (PAS) questionnaire, the Pediatric Appendicitis Risk Calculator (pARC), and the Alvarado score, which are then converted into an ordinal data scale to nominal according to their interpretation according to applicable regulations. This study's dependent variable was the incidence of acute appendicitis diagnosed with the gold standard, namely through surgery and imaging. The procedure between variables in this study begins with processing descriptive data in examiners (%) for categorical data and centralized distribution data (mean, standard deviation, median, minimum, maximum) and testing with diagnostic examiners. This study's diagnostic test procedure was to compare the true-positive rate between the scoring types in predicting the incidence of acute appendicitis in children. The scoring system with the highest true-positive value is the most superior questionnaire when compared to other questionnaires, which will then be tested for sensitivity, specificity, false-positive values, and false negative values between these questionnaires.

RESULTS

The study included 20 children with acute appendicitis involving 13 (65%) males, mean age 11.7 (3.2) years, 15 (75%) acute appendicitis without peritonitis, and 5 (25%) acute appendicitis with peritonitis. The symptoms that arose from 20 respondents were 6 (30%) experienced migrating of pain, 17 (85%) experienced anorexia, 13 (65%) experienced nausea/vomiting, 19 (95%) experienced right lower quadrant (RLQ) tenderness, 12 (60%) experienced cough/hopping/percussion tenderness in RLQ, 12 (60%) had elevated temperature (> 38°C), 11 (55%) rebound tenderness, 1 (5%) had pain while walking. From a laboratory perspective 11 (55%) had leukocytosis and 16 (80%) had polymorphonuclear (PMN) neutrophilia >75%. All outcome variables are presented in Table 1.

Table 1. Basic terms of respondents with acute appendicitis in children in Depati Hamzah Hospital, 1st August 2020 to 20th August 2020

Parameter	N (%)	Mean (SD)	Median (Min – Max)
Gender			
• Male	13 (65%)		
• Female	7 (35%)		
Age		11,7 (3,2)	11,5 (6 – 18)
Diagnosis			
• Appendicitis	15 (75%)		
• Peritonitis	5 (25%)		
Migrating of pain			
• Yes	6 (30%)		
• No	14 (70%)		
Anorexia			
• Yes	17 (85%)		
• No	3 (15%)		
Nausea/Vomiting			

• Yes	13 (65%)
• No	7 (35%)
RLQ Tenderness	
• Yes	19 (95%)
• No	1 (5%)
Cough/Hopping/Percussion Tenderness in the RLQ	
• Yes	12 (60%)
• No	8 (40%)
Elevated Temperature (>38°C)	
• Yes	12 (60%)
• No	8 (40%)
Leukocytes > 10.000	
• Yes	11 (55%)
• No	9 (45%)
PMN Neutrophilia >75%	
• Yes	16 (80%)
• **No**	4 (20%)
Rebound Tenderness	
• Yes	11 (55%)
• No	9 (45%)
Duration of Pain	
• <24 hours	5 (25%)
• 24 – <48 hours	5 (25%)
• 48 – 96 hours	5 (25%)
• >96 hours	5 (25%)
Pain while Walking	
• Yes	1 (5%)
• No	19 (95%)
Abdominal Guarding	
• Yes	13 (65%)
• No	7 (35%)
Referred Pain to RLQ	
• Yes	8 (40%)
• No	12 (60%)
PAS Interpretation	
• ≥ 5 Appendicitis likely	16 (80%)
• 5 Appendicitis likely	3 (15%)
• < 5 likely	1 (5%)
pARC Interpretation	
• 76 – 90% (Moderate – High)	6 (30%)
• 51 – 75% (Moderate)	8 (40%)
• 26 – 50% (Moderate)	1 (5%)
• 16 – 25% (Moderate)	4 (20%)
• 6 – 15% (Low)	1 (5%)
Alvarado Score Interpretation	11 (55%)

• 7-8 Appendicitis probable	6 (30%)
• 5-6 Appendicitis possible	3 (15%)
• 1-4 Appendicitis unlikely	

The descriptive examiner between the scoring results from the Pediatric Appendicitis Score (PAS) questionnaire, the Pediatric Appendicitis Risk Calculator (pARC), and the Alvarado score used in the acute appendicitis group in children received the Pediatric Appendicitis Score (PAS) questionnaire which has the highest true-positive value (80%), followed by Alvarado score (55%), and the Pediatric Appendicitis Risk Calculator (pARC) (30%). All categorical interactions between systems are presented in table 2.

Table 2. Cross-tabs Interpretation between 3 diagnostic questionnaires for acute appendicitis in children.

Parameter		Scoring 1 Pediatric Appendicitis Score (PAS)		
		≥ 5 Appendicitis likely	**5 Appendicitis likely**	**< 5 Appendicitis likely**
Scoring 2 Alvarado score	7-8 Appendicitis probable	-	11 (55%)	-
	5-6 Appendicitis possible	-	3 (15%)	3 (15%)
	1-4 Appendicitis unlikely	1 (5%)	2 (10%)	-
Scoring 3 Pediatric Appendicitis Risk Calculator (pARC)	76 – 90% (Moderate – High)	-	2 (10%)	2 (10%)
	51 – 75% (Moderate)	1 (5%)	-	-
	26 – 50% (Moderate)	0	8 (40%)	-
	16 – 25% (Moderate)	-	-	1 (5%)
	6 – 15% (Low)	-	6 (30%)	-

Parameter		Scoring 2 Alvarado score		
		7-8 Appendicitis probable	**5-6 Appendicitis possible**	**1-4 Appendicitis unlikely**
Scoring 3 Pediatric Appendicitis Risk Calculator (pARC)	76 – 90% (Moderate – High)	-	2 (10%)	4 (20%)
	51 – 75% (Moderate)	1 (5%)	1 (5%)	6 (30%)
	26 – 50% (Moderate)	1 (5%)	-	-
	16 – 25% (Moderate)	1 (5%)	2 (10%)	1 (5%)
	6 – 15% (Low)	0	1 (5%)	-

The follow-up test converts the ordinal scale to a nominal scale to see anything for sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) between acute appendicitis diagnostic questionnaires. The results of

sensitivity, specificity, PPV, and NPV between Alvarado scores and Pediatric Appendicitis Scores (PAS) were 68.75%; 100%; 100%; 44.44%. The results of sensitivity, specificity, PPV, and NPV between the Pediatric Appendicitis Risk Calculator (pARC) against the Pediatric Appendicitis Score (PAS) were 37.5%; 100%; 100%; 71.43%. The results of sensitivity, specificity, PPV, and NPV between the Pediatric Appendicitis Risk Calculator (pARC) against the Alvarado score were 36.36%; 77.78%; 66.67%; 50%. (Table 3)

Table 3. Comparison of sensitivity, specificity, PPV, and NPV between acute appendicitis diagnosis questionnaires

Parameter		Scoring 1 Pediatric Appendicitis Score (PAS)		Diagnostic Test Overview			
		Positive	Negative	Sensitive	Specific	PPV	NPV
Scoring 2 Alvarado score	Positive	11 (55%)	0	68,75%	100%	100%	44,44%
	Negative	5 (25%)	4 (20%)				
Scoring 3 Pediatric Appendicitis Risk Calculator (pARC)	Positive	6 (30%)	0				
	Negative	10 (50%)	4 (20%)	37,5%	100%	100%	71,43%

Parameter		Scoring 2 Alvarado score		Diagnostic Test Overview			
		Positive	Negative	Sensitive	Specific	PPV	NPV
Scoring 3 Pediatric Appendicitis Risk Calculator (pARC)	Positive	4 (20%)	2 (10%)	36,36%	77,78%	66,67%	50%
	Negative	7 (35%)	7 (35%)				

DISCUSSION

Our study shows that appendicitis incidence in children is more common in boys (65%) than in girls (35%). The results of the study contradict research conducted by Arifuddin et. Al. (2017) who experienced a higher incidence of appendicitis in women (63%) than men (37%), but this study concluded that gender was not a risk for the incidence of appendicitis (OR 0.657; 95% CI; 0.337-1,284).(14) The relationship in the event of an emergency cannot be identified because of the female and female forms' anatomy.(15)

Our study assessed the presenting signs of acute appendicitis based on the contents of Alvarado, PAS, and pARC. Signs found in this study were anorexia in 17 (85%) of respondents, nausea/vomiting in 13 (65%) of respondents, cough/tenderness in 19 (95%), and migratory pain in 6 (30%) of respondents. In a study by Hossain, Sobhan and Talukder (2012) who studied the signs

of acute appendicitis sufferers, 70 (92%) experienced typical pain in the right lower abdomen, 62 (81.6%) respondents experienced anorexia, 68 (89 %) experienced nausea, followed by 65 (85.5%) respondents who experienced vomiting.(16) Nausea appears as a defense, source of organisms to avoid possible ingestion of toxins. Central and peripheral pathways are involved in the pathogenesis of nausea and vomiting. Afferent stimulation of various stimuli is transmitted to the solitary tract's nucleus through four routes, one of which is the gastrointestinal tract via the vagus nerve. The stimulation of the vagus nerves will increase and provide a sensation of nausea with or without vomiting. Information such as the solitary nucleus tract is also responsible for activating the autonomic nerves via the vagal pathway. It is also associated with gastric dysrhythmias and vasopressin release.(17)

Our study found that 11 (55%) people with appendicitis experienced leukocytosis and 16 (80%) increased neutrophil values >10,000 cells/mm^3. This incident is in line with Saiiq (2012) findings, which showed that 67.38% of leukocytes >10,000 cells/mm^3 in acute appendicitis patients.(18) Another study conducted by Baso (2015) obtained an average neutrophil count value of 48.2%. increased neutrophils indicate acute inflammation of lymphatic tissue.(19)

This study is the first to analyze the comparison of sensitivity, specificity, PPV, and NPV for each scoring for all samples, which are patients with acute appendicitis. We did not find any previous studies that carried out similar studies.

Kharbanda et. Al. (2018) conducted a study of predictors of appendicitis using pARC. This study showed that all components in pARC had a significant association with the risk of appendicitis in children with acute abdominal pain (p <0.05). this study found that the area under curve (AUC) for pARC was 0.85 (95% CI: 0.83 - 0.87).(13) another study by Cotton, et. Al. (2018) using pARC successfully diagnosed 353 (16.9%) respondents as appendicitis from 2089 respondents, of which 55 (15.6%) respondents were perforated appendices. 54% of respondents had a predicted risk of being very low (<5%) or low (5% to 14%), 43% having a moderate risk (15% to 84%), and 4% have a high risk (≥85%). In the deficient and low-risk groups, 1.4% and 3.0% of patients had appendicitis. The area under the receiver operating characteristic (ROC) curve for pARC was 0.89 (95% CI 0.87-0.92) compared to 0.80 (95% confidence interval 0.77 to 0.82) for PAS. This study demonstrates that pARC is accurate for diagnosing the risk of appendicitis in children over five years compared to PAS.(20) Gudjonsdottir et. Al. (2020) stated that pARC had a much higher specificity and positive predictive value (PPV), and a lower rate of false positives (2%), than PAS and Alvarado scores (36 and 28%, p <0.001). Among the different genders and age groups, pARC generally received fewer peer-positive PAS and Alvarado scores. There were no significant differences in sensitivity, negative predictive value (NPV), missed appendicitis rates, or ROC curve analysis.(21)

PAS specifically addresses and unique physical marks for children.(12) Parveen et. Al (2017) conducted a validation test on PAS in diagnosing appendicitis in children. The study found as many as 15 (75%) children with PAS ≥7 who underwent surgery and biopsy showed appendicitis results. The PAS score helps the clinician make decisions about outpatient care or the need for an appendectomy in a child with an acute abdomen.(22) Another study by

Khanafer et. Al. (2016) found the sensitivity, NPV, and specificity of PAS scores were 80.0%, 86.4%, 5.0%, respectively. The PAS score can be used to screen for children at low risk who can be closely observed at home without laboratory testing.(23) Shah et. Al (2016) developed a diagnostic algorithm used prospectively in 840 patients, 267 of whom were ultimately diagnosed with appendicitis. The sensitivity algorithm had a 98.6% sensitivity and specificity of 94.4%, with a decrease in CT utilization from 75.4% to 24.2%.(24)

The Alvarado score, also known as MANTRELS, is a 10-point scoring system used to diagnose acute appendicitis symptoms, signs, and diagnostic tests in patients with suspected acute appendicitis. The Alvarado score allows risk stratification in persons presenting with abdominal pain, the probability of appendicitis being linked to recommendations regarding discharge, observation, or surgical intervention.(11) Study by Ramadhanti (2016) at Tangerang found that Alvarado's sensitivity score at the age of 5-14 years of children was 35.3% with a specificity of 66.7% and the 15-24 year age group obtained 33.3%. The Alvarado score can diagnose acute appendicitis from ages 4-80 years, which explains that this scoring system is highly specific across all age groups.(25) Zenon. Et al. (2015) assessed the validity of using the Alvarado score in 265 children with acute appendicitis. This study obtained a sensitivity of 89%, a 59% specificity, and a positive predictive value of 93.1%. There was no significant difference in both sensitivity and specificity between Alvarado and PAS in diagnosing appendicitis in children.(26) Another study by Wu et. Al (2012) concluded that Alvarado's AUC score was higher than that of PAS (day 1: 0.09 vs 0.87; day 2: 0.87 vs 0.84; day 3: 0.88 vs 0.82).(27)

CONCLUSION

The results of sensitivity, specificity, PPV, and NPV between Alvarado score and Pediatric Appendicitis Score (PAS) were 68.75%; 100%; 100%; 44.44%. The results of sensitivity, specificity, PPV, and NPV between the Pediatric Appendicitis Risk Calculator (pARC) against the Pediatric Appendicitis Score (PAS) were 37.5%; 100%; 100%; 71.43%. The results of sensitivity, specificity, PPV, and NPV between the Pediatric Appendicitis Risk Calculator (pARC) against the Alvarado score were 36.36%; 77.78%; 66.67%; 50%. This study shows that Alvarado score has a better level of sensitivity, specificity, PPV, and NPV in predicting the incidence of acute appendicitis in confirmed children.

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