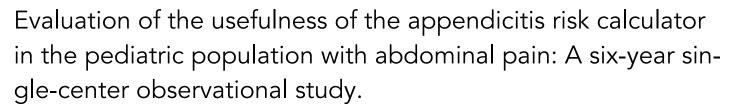
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Abstract

Introduction: Acute appendicitis is a frequent cause of acute abdomen; in pediatrics, the diagnosis is mainly clinical, but it can present in an atypical way. The probability of a diagnosis of appendicitis can be measured with the Pediatric Appendicitis Risk Calculator (pARC) and the Alvarado Index. This study aimed to evaluate the diagnostic capacity of these scales in pediatric patients with abdominal pain assessed at a reference center.

Methods: The present cross-sectional study was carried out with patients from 5 to 19 years of age with acute abdominal pain treated at the Hospital de Los Valles, Quito-Ecuador, between January 2015 and December 2020. pARC and the Alvarado index were applied. A descriptive analysis and diagnostic tests are performed. ROC, PPV, NPV, concordance, correlation between both scales, specificity, and sensitivity were calculated.

Results: There were 284 cases. The prevalence of appendicitis was 8.9% (95% CI 7.27-10.79), and the Alvarado scale and the pARC calculator presented ROC values of 0.919 (95% CI = 0.885-0.953) and 0.926 (95% CI = 0.896-0.955), respectively. The cutoff point for sensitivity and specificity was 4 for the Alvarado Index and 12 for pARC. The Alvarado Index was 82.11 (95% CI 72.9-89.2) and 88.36 (95% CI 82.9-92.6), and for pARC, it was 83.16 (95% CI 74.1-90) and 86.77 (95% CI 81.1- 91.2). The PPV and NPV in the Alvarado Index were 78.00 (95% CI 68.6-85.7) and 90.76 (95% CI 85.6-94.5), pARC 75.96 (95% CI 66.5-83.8) and 91.11 (95% CI 85.9-94.8), respectively.

Conclusions: The ability to predict the diagnosis of acute appendicitis was the same between the pARC calculator and the Alvarado Index; both are valuable and reliable tools.

Keywords: MESH: Appendicitis, pARC Calculator, Alvarado Index.

Introduction

Appendicitis, an inflammatory process of the vermicular appendix, is generally caused by an obstruction in the

lumen of this structure, which, if it persists, allows the invasion of bacterial agents that locate and alter the wall. Subsequently, this infectious process progresses,

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giving rise to the formation of an abscess in the submucosa; the rest consists of necrosis, perforation, and peritonitis [1].

Acute appendicitis has been established worldwide as the most frequent indication in nontraumatic emergency abdominal surgery, with a frequency of 16.33% in men and 16.34% in women. The annual incidence reaches 140 cases per 100,000 inhabitants, and in many cases, it has been associated with overweight in 18.5% and obesity in 81.5% of these patients [2].

In pediatrics, it causes 1 to 8% of pain located in the abdomen, with an incidence that increases in schoolchildren and adolescents, the latter presenting the classic manifestations of central and diffuse abdominal pain, which is located in the right iliac fossa and then continues with vomiting and fever; in preschool-age children, the presentation is often atypical and nonspecific [3].

Appendicitis represents a diagnostic challenge that often must be done without support methods, especially in health institutions that need the technology for imaging studies. Therefore, it is essential to carry out a good anamnesis, active observation, exhaustive physical examination, and critical complementary tests to avoid unnecessary surgical intervention or achieve timely intervention without delaying the correct diagnosis and thereby preventing future complications [3].

The clinic contributes to the diagnosis; however, abdominal pain that migrates to the right iliac fossa does not occur in all patients, and in the population under three years of age, 44% may present more than six atypical signs, especially symptoms such as anorexia, fever, diffuse abdominal pain, and diarrhea, which can confuse the diagnosis with other gastrointestinal pathologies [4]. Other diagnostic support tests are elevated C-reactive protein, computed tomography, and elevated leukocyte count [5].

The Alvarado Scale approximates the diagnosis of appendicitis promptly based on classifying patients based on scores and according to symptoms, signs, and laboratory values [<u>6</u>].

On the other hand, the Pediatric Appendicitis Risk Calculator (pARC) is a validated clinical tool to assess the probability that a child may develop appendicitis with high specificity and sensitivity [Z].

The objective of this research was to evaluate the diagnostic capacity of the appendicitis risk calculator (pARC) in patients between the ages of 5 and 19 with abdominal pain who attended an emergency service of a reference hospital, comparing its predictive capacity with the Index of Appendicitis. Alvarado.

Materials and methods

Type of study

The present observational study is cross-sectional.

Scenery

The study was carried out in the Hospital de los Valles emergency service in Quito, Ecuador. The study period was from January 1, 2015, to December 31, 2020.

Universe and Sample

The population consisted of all patients aged between 5 and 19 years who attended the emergency department with acute abdominal pain. According to the hospital statistics service, the figure reaches 1,065 cases.

Sample

The sampling was carried out by the discard method, taking into account the inclusion and exclusion criteria. The sample was nonprobabilistic, census type, where all cases with an established diagnosis of acute appendicitis were included.

Inclusion and exclusion criteria

Cases of patients aged 5 to 19 years with acute abdominal pain with a definitive diagnosis of acute appendicitis were entered into the study. A second control group was established in whom the diagnosis of abdominal pain was established and with a different diagnosis of acute appendicitis. Appendectomized patients were excluded, and incomplete cases were removed for analysis.

Variables

Age, sex, abdominal pain, presence of migration of pain, location of pain in the right iliac fossa, duration of pain, presence of anorexia, presence of nausea or vomiting, tenderness in the right lower quadrant, presence of abdominal pain rebound, presence of temperature increase, presence of leukocytosis, neutrophilia, histological diagnosis, Alvarado index, and pARC calculator were recorded.

Instrument

The Alvarado test and the pARC calculator.

Statistical analysis

A descriptive analysis of the qualitative variables was performed with absolute and relative frequencies (percentages). The numerical variables were expressed with measures of central tendency and dispersion, stratifying by the group that had appendicitis to compare it with the group that did not.

The validation analysis was carried out by dividing the participants into two groups: (i) children with abdominal pain who were finally diagnosed with acute appendicitis confirmed by histopathology or by the surgeon's report according to the results of the surgical act.

(ii) Those children with abdominal pain who were not finally diagnosed with acute appendicitis or any entity that required surgery and with pain in the abdominal region, which ultimately presented a surgical diagnosis other than acute appendicitis.

To estimate the predictive capacity of the Alvarado scale and that of pARC and to compare this capacity, ROC curves were made for each scale, obtaining the area under the curve (AUC). The sensitivity, specificity, and positive and negative predictive value of each scale were calculated for the cutoff values (obtained by the Youden index) at which the Alvarado scale and pARC revealed the best value of sensitivity and specificity

from the scores obtained with the appendicitis risk calculator (pARC) and the Alvarado index, comparing children with a diagnosis of appendicitis versus those who did not have appendicitis. The diagnostic concordance between the pARC scale and the Alvarado index was calculated, calculating the simple concordance index and the Kappa concordance index. For this, the different categories of the pARC scale were recategorized as follows: ultralow and low, low-moderate and moderate, and moderate-high and high to compare their agreement with the Alvarado scale in its low, intermediate, and high categories. To establish the correlation, the Pearson correlation coefficient was calculated. To carry out the statistical analysis, the Statistical Package for the Social Sciences SPSS 26.0 program (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp) was used.

Procedure to guarantee bioethical aspects

Once the purpose of the research was disclosed and with prior authorization, the information collected was used solely for the analysis and development of the study. The clinical histories were obtained confidentially and were not disclosed to people outside of this project.

Biases

To avoid possible interviewer, information, and memory biases, the principal investigator always kept the data with a guide and records approved in the research protocol. Observation and selection bias was avoided by applying the participant selection criteria. All the clinical and paraclinical variables of the previous period were recorded. Two researchers independently analyzed each record in duplicate, and the variables were recorded in the database once their concordance was verified.

Results

Participants

A total of 1065 cases with abdominal pain were registered, of which 95 presented appendicitis, with a prevalence of 8.9% (95% CI 7.27 to 10.79). The 95 cases in the appendicitis group and 189 cases with abdominal pain in the control group were analyzed.

General characteristics of the population

The general characteristics of the study groups are presented in Table $\underline{1}$.

pARC criteria

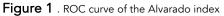
Table <u>1</u> shows that the age of the patients who presented appendicitis analyzed with the criteria of the pARC calculator registered a statistically higher mean than in the patients without appendicitis (*P value* =0.0006). There were no differences in distribution by sex (*P* =0.07). The average duration of pain among those who presented appendicitis was lower, and concerning leukocytes and neutrophils, the results were higher: 73.7% in the group diagnosed with appendicitis. The percentage of patients with pain when walking, tenderness in the DIC, defense in the DIF, and pain migration were significantly higher in patients with appendicitis than those without appendicitis (Table <u>1</u>).

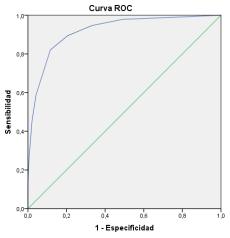
Alvarado criteria

Table <u>1</u> shows the frequency of presentation of the Alvarado scale criteria. Patients with a diagnosis of appendicitis presented a statistically significantly higher frequency of expression in all requirements, that is, migratory pain, anorexia, nausea/vomiting, defense in the right iliac fossa, painful decompression, temperature >38 degrees, leukocytosis count > 10,000 cells/L and neutrophilia > 75%, compared with patients without appendicitis.

Diagnostic tests

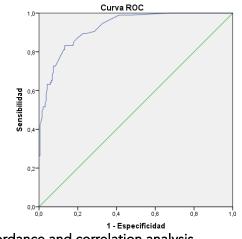
Diagnostic tests are presented in Table 2. The area under the ROC curve of the results obtained by applying the Alvarado Index was 0.919 (95% CI = 0.885 - 0.953) (*P value* <0.0001), so it is established that it has a high discriminative capacity to diagnose patients with appendicitis (Figure 1).

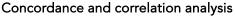




The area under the curve from the pARC calculator P value <0.0001; therefore, it is established that it has a high discriminative capacity to diagnose patients with appendicitis (Figure <u>2</u>).







The expected concordance was 91.76%, the concordance index was 71.06%, and the kappa index showed a statistically significant concordance between

the	two,	0.7153	(P	value	<	0.0	0001).	The	e Pearson	
corr	elatio	n coeffic	cien	t show	/ed	а	positiv	ve d	correlation	

between the Alvarado scores and pARC r 2 = 0.84, *P* value <0.0001 (Figure <u>3</u> and Table <u>3</u>).

Tak	ble	1.	Relationshi	p between	pARC	calculator	criteria	and	appendicitis
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	pARC criteria	
	Group with Appendicitis n=95	Group without appendicitis n=189
Age	(10.9 ± 3.4)	(9.3 ± 3.77)
Gender: Men vs. Women	51 (53.7)	80 (42.3)
	44 (46.3)	109 (57.7)
Duration of pain (hours)	(22.2 ± 21.8)	(31.8 ± 47.3)
Leukocytes (cell/L)	(12.7 ± 4.4)	(7.2 ± 5.5)
Neutrophils (%)	(73.7 ± 12.9)	(45.7 ± 32)
Pain when walking ^a	8 (8.4%)	0 (0)
*RLC sensitivity ^a	83 (87.4%)	13 (6.9)
**Defense in RIF ^a	81 (85.3%)	36 (19)
Migration of pain to RLC ^a	63 (66.3%)	19 (10.1)
	Alvarado Index	
Migratory pain	63 (66.3%)	19 (10.1%)
Anorexy	20 (21.1%)	12 (6.3%)
Nausea/vomiting	52 (54.7%)	83 (43.9%)
Defense in RFI	81 (85.3%)	36 (19.0%)
Painful decompression	55 (57.9%)	14 (7.4%)
Temperature >38 degrees C	37 (38.9%)	36 (19.0%)
Leukocytes >10 thousand u/ul	68 (71.6%)	52 (27.5%)
Neutrophilia >75%	59 (62.1%)	50 (26.5%)

*RLC: Right Lower Quadrant **RIF: Right iliac fossa.

 $^{\rm a}$ All criteria comparisons were statistically significant p value <0.05. FID: Right iliac fossa

Table 2. Diagnostic tests.

	Alvarado Index	pARC calculator
Values	Cut point=4	Cutoff point= 12
Sensitivity	82.11 (95% CI 72.9-89.2)	83.16 (95% CI 74.1-90)
Specificity	88.36 (95% CI 82.9-92.6)	86.77 (95% CI 81.1-91.2)
PPV	78.00 (95% CI 68.6-85.7)	75.96 (95% CI 66.5-83.8)
NPV	90.76 (95% CI 85.6-94.5)	91.11 (95% CI 85.9-94.8)
ROC	0.9193 (95% CI 0.885-0.953)*	0.9256 (95% CI 0.896-0.955)*
*D <0 0001 DD\/	a status a sea alterativa sua luca INIDV/, sea seativa se seativa	

*P<0.0001. PPV: positive predictive value, NPV: negative predictive value, ROC: receiver operator curve.

Tab	le 3.	Concordance	between	Alvarado	Index ar	id pARC	Calculator.
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Study scales		pARC calculator					
Alvarado Index	Ultra low/low No. =185 (%)	Low moderate/moderate No.=85 (%)	Moderate high/High No.=14 (%)				
Low	173 (93.5)	11 (12.9)	0 (0)				
Intermediate	11 (5.9)	41 (48.2)	1 (7.1)				
High	1 (0.5)	33 (38.8)	13 (92.8)				

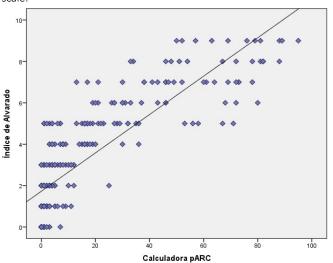


Figure 3. Correlation between the Alvarado scales and the pARC scale.

Discussion

Acute appendicitis has been determined to be the leading cause of surgical urgency worldwide; pediatric patients represent a diagnostic challenge due to its high prevalence and the atypical clinical characteristics that can occur, especially in young children; however, pediatricians have support tools such as validated diagnostic approximation scales that allow evaluating the probability of presenting appendicitis. This observational and cross-sectional study was carried out to compare the diagnostic capacity of the Alvarado Index and the pARC calculator for the diagnosis of appendicitis in children from 5 to 19 years of age with abdominal pain.

This study found that the prevalence of appendicitis in the Hospital de los Valles was 8.9% (95% CI 7.27 to 10.79) from January 2015 to December 2020. It was also found that the Alvarado scale and the pARC calculator are excellent tools with a high discriminative capacity to diagnose patients with appendicitis, with a ROC of 0.919 (95% CI= 0.885 - 0.953) and 0.926 (95% CI= 0.896 - 0.955), respectively. The cutoff point in this group of patients, in this hospital center, maximizes the sensitivity and specificity in the two scales was, in general, a low value. This is for the Alvarado Index, which was estimated at 4, and for the pARC calculator

at 12. Both scales, therefore, at the cutoff above points, presented the highest possible sensitivity and specificity; in the case of the Alvarado Index, it was 82.11%. (95% CI 72.9-89.2) and 88.36% (95% CI 82.9-92.6), and for the pARC calculator, 83.16% (95% CI 74.1-90) and 86.77% (95% CI 81.1-91.2). The PPV and NPV with the two scales were high; these values in the Alvarado Index were 78% (95% CI 68.6-85.7) and 90.76% (95% CI 85.6-94.5), and for the pARC calculator, 75.96% (95% CI 85.6-94.5). 95% 66.5-83.8) and 91.11% (95% CI 85.9-94.8), respectively. The two scales registered concordance and a statistically significant correlation between them.

The prevalence of appendicitis in the present study was 8.9%, taking into account that it is a figure at the hospital level and during a period of 5 years; this, compared to the figure worldwide that is estimated at 7% [2] and 16.9% according to Cotton et al., (2019) [7] whose study was carried out in a total of 11 emergency departments and included a total of 2089 patients of whom 353 presented appendicitis, these two aspects may explain the higher prevalence compared to our study. Although it is not possible to make a comparison with the national estimate since it is calculated at a rate of 22.97 per 10,000 inhabitants, a study in Ecuador [8] indicates that the prevalence of appendicitis was 54.4% among 614 pediatric patients with abdominal acute hospitalized (regionally transferred) to the pediatric surgery service at a regional specialty hospital.

In the Alvarado Index, when calculating the sensitivity and specificity, values were 82.11% and 88.36%, and for the PPV and NPV, these were 78% and 90%, and the ROC area was 0.9193. The findings in the literature present some variations concerning our result, as is the case of the study by Bolívar et al. (2018) [9], where a higher sensitivity and a much lower specificity are evidenced, while the PPV and NPV in the present study were higher. It is essential to highlight that this study does not mention the cutoff point used for such calculations. In contrast, when comparing the results we obtained with other references, such as the

study by Peña & Proaño (2014) [10], these researchers took into account a cutoff point of 7, above the point estimated in this study of 4; these authors describe the sensitivity at 90%, specificity at 72% and PPV 83%, which is slightly closer to what was obtained in this study, corroborating that it is a perfect predictive tool for acute appendicitis. The cutoff point used by these authors was higher than in the present study, so the sensitivity obtained was higher, which may be related to the inclusion of patients between the ages of 5 and 17 who attended the service with acute abdominal pain. Department of the San Francisco de Quito Hospital of the Ecuadorian Institute of Social Security, a second-level teaching center, where according to these authors, the hospital prevalence of appendicitis is 15.37%.

For the pARC calculator, we obtained that the ROC area was 0.926, the sensitivity was 83.16%, the specificity was 86.77%, and the PPV was 75.96%. NPV was 91.11%, except for the ROC area; all the remaining values were higher in other studies, such as the one by Cotton et al. (2019) [7], who included a much larger sample and divided the calculations individually for high and low strata of the calculator.

The pARC calculator is less well known than the Alvarado Index, and they have been studied separately and compared with other scales; however, there are no studies that compare concordance and correlation between these two scales. In our research, the two scales recorded perfect concordance and correlation with each other.

The two scales evaluated are good tools in our environment as a guide in the context of what they claim to measure. The present analysis shows that the Alvarado Index and the pARC calculator are excellent tools with a high discriminative capacity to diagnose patients with appendicitis without significant differences between the two.

A potential limitation of this study was that we could not work with all the patients since eight who presented inconsistency in the diagnostic codes

according to the Department of Statistics concerning the data recorded in the respective clinical histories were excluded; however, given the final size of the included sample, we believe that the lack of inclusion of these patients, in the final analysis, did not substantially affect the results obtained.

Among the strengths of this analysis, it is essential to highlight that the data collection was carried out in a very systematic and complete manner; generally, in the exercise of the pediatric clinic, the medical records do not usually measure the Alvarado or pARC scale or any other evaluation tool so that in this analysis, a systematic collection of all the parameters was carried out for the calculation of both the Alvarado scale and the pARC scale, which was favored by the fact that the clinical histories in the institution where the study was carried out are electronic and digitized, which does not allow mistakes due to the data described or poorly legible. This translates into an accurate estimate of the calculation made for the scales since all the necessary data for each were available.

It is considered essential to point out that the cutoff points used in this study to estimate the best sensitivity and specificity, 4 for the Alvarado Index and 12 for the pARC calculator, were calculated only to perform the sensitivity and specificity calculations in the case of the reference values for this procedure. We do not recommend using these values as a prediction for surgical treatment and maintain the use of these scales as established by their respective authors.

Conclusions

Based on the results obtained in this study and comparison with the theoretical references, we can conclude that both the Alvarado Index and the pARC calculator are beneficial as diagnostic support tools for pediatricians to have a reliable prediction of acute appendicitis. Alvarado and pARC scores as low as 4 and 12 have excellent sensitivity and specificity for the diagnosis of appendicitis. This study showed that the prevalence of acute appendicitis in the child population that attends the Hospital de los Valles is relatively low compared to other hospitals.

The Alvarado Index and the pARC calculator are highly sensitive and specific for diagnosing appendicitis; both have high predictive capacity and are highly concordant and correlated when compared between two. No difference was found in the ability to predict the diagnosis of acute appendicitis between the pARC calculator and the Alvarado Index.

Therefore, with the results of this study, we recommend that it would be potentially helpful to systematically apply either of the two tools in the pediatric service; prior training in the calculation and interpretation of these scales to pediatricians will allow better discrimination between patients presenting with sufficient symptoms to suspect the diagnosis of acute appendicitis.

Abbreviations

LRC: Lower right quadrant. RIF: right iliac fossa. pARC: Pediatric appendicitis risk calculator. ROC: receiver operator curve. NPV: negative predictive value. PPV: positive predictive value.

Supplementary information

No supplementary materials are declared.

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Author contributions

María Fernanda Parra Iñiguez: Conceptualization, data curation, formal analysis, fundraising, research, writing - original draft.

Luis Stalin Donoso León: Methodology, project administration, resources, software, supervision, validation, visualization, writing – review, and editing. Pablo Francisco Endara Dávila: Methodology, project administration, resources, software, supervision.

All authors read and approved the final version of the manuscript.

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Availability of data and materials

Data were collected from medical files and are not publicly available due to patient confidentiality but are available through the corresponding author under clearly justified academic requests.

Statements

Ethics committee approval and consent to participate

The Research Committee and the Ethics Committee of the Faculty of Medicine of the Pontificia Universidad Católica del Ecuador approved this study.

Publication Consent

Not required when patient-specific images, radiographs, and studies are not published.

Conflicts of interest

The authors declare they have no conflicts of interest.

Author Information

Not declared.

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