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Research Article

Sensitivity and Specificity of Procalcitonin in Pediatric Patients with Complicated Acute Appendicitis

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Abstract

Introduction: Acute appendicitis is the most frequent cause of surgical abdominal pain in pediatric patients.

Objective: This study aimed to determine the sensitivity and specificity of procalcitonin in pediatric patients with complicated acute appendicitis.

Method: Retrospective, analytic, observational, homodemic, and transversal studies. The present study included patients aged 1–15 years with a diagnosis of acute appendicitis, who underwent an appendectomy between January 2018 and February 2022, and whose procalcitonin level was measured at the time of admission. We used the Mann-Whitney U test and Fisher's exact test for statistical analysis, and the ROC to determine the sensitivity and specificity of procalcitonin.

Results: The study included 70 patients, 47 of whom presented with simple appendicitis and 23 with complicated appendicitis. The mean value of procalcitonin for complicated appendicitis was 1.5 ng/ml (p = 0), and 0.3 ng/ml for simple appendicitis. The area under the curve was 0.952, with a cutoff point of 0.74 for complicated acute appendicitis.

Conclusion: Procalcitonin has a sensitivity of 87% and a specificity of 10%.

Keywords: Procalcitonin; Sensitivity; Specificity; Complicated Appendicitis; Children

Introduction

Acute appendicitis is widely recognized as the most common surgical emergency [1]. In most cases, the diagnosis depends on the clinic attended by the patient; however, in pediatric patients, it is difficult to distinguish appendicitis from other diseases. Only 10 to 36% of pediatric patients present the classic symptomatology of an appendicular picture, in contrast to adults, who present with symptoms in 60-70% of the cases [2,3]. Hence, the use of diagnostic auxiliaries is important for timely and appropriate diagnosis.

Procalcitonin is a precursor of calcitonin; it is a peptide of 116 amino acids produced by the C cells of the thyroid gland. In normal conditions, procalcitonin is not released into the circulation, and its normal concentration is lower than 0.5 ng/ml [4].

During inflammation, the production of procalcitonin is caused by endotoxins, exotoxins, and interleukins (FNT, IL 1, 2, and 6). After this stimulus, it appears in the blood three–six hours later, with a maximum of eight hours and a plateau at 24–30 h, with a mean life of 20–24 h [5]. Different studies have shown the relationship between procalcitonin levels and the severity of infectious processes, resulting in the patient's prognosis since it is related to both the severity of the process and the need for urgent surgical intervention [6]. This study aimed to determine the sensitivity and specificity of procalcitonin in pediatric patients with complicated acute appendicitis.

Method

A retrospective, analytic, observational, homodemic, and transversal study was conducted at the General Hospital de la Zona Norte, "Bicentenario de la Independencia" of the state of Puebla from January 2018 to February 2022. We included the clinical files of patients aged 1–15 years with a diagnosis of acute appendicitis who underwent surgery in that unit. We excluded postoperative patients with acute appendicitis without a complete record, pediatric patients with a diagnosis of acute appendicitis who underwent surgery in another unit, and patients with prophylactic appendectomy. Pediatric patients with a diagnosis of acute appendicitis who underwent appendectomy and were transferred to another unit were excluded.

For statistical analysis, continuous variables were expressed in terms of mean and standard deviation. For continuous random variables, we used the Student's t-test of independent samples, and to analyze continuous data with non-normal distribution, we used the Mann-Whitney U test. Statistical significance was established using a two-tailed p-value <0.05.

Using the ROC curves, we determined the sensitivity and specificity for the diagnosis of simple or complicated appendicitis. Subsequently, we calculated the cutoff point of maximal diagnostic precision for each analytic parameter using Youden's index.

The collection was made with a data collection instrument to enter the information into Microsoft Excel version 2013, and they were analyzed with IBM SPSS Statistic, version 25.

Results

From January 1, 2018, to February 28, 2022, we analyzed 107 patients diagnosed with acute appendicitis in the pediatric population. Of these, 37 were excluded because of incomplete files, and none were eliminated. Therefore, we obtained a sample of 70 patients classified as uncomplicated (n = 23) or complicated (n = 47) (Figure 1).

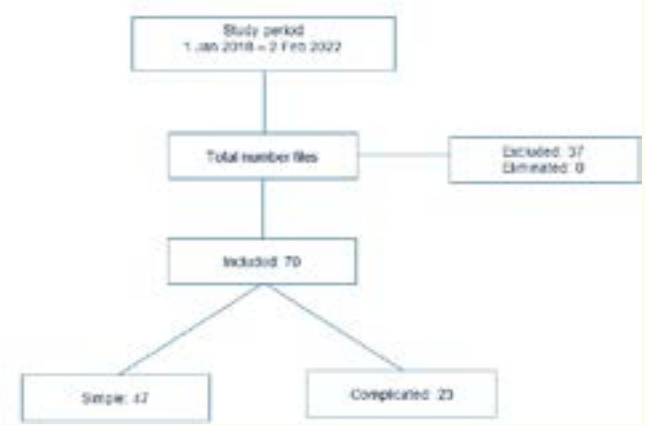

Figure 1: Flow chart of the study.

Regarding the sex of the patients, we found that 44.3% (31) corresponded to the female sex, and the rest (55.7%) (39) were male. The mean age of the group corresponded to 8.4 years, SD = 3.7 with a minimum of 2 years and maximum of 15 years.

Of the studied patients with acute appendicitis, we observed in the perioperative period that 47 corresponded to simple acute appendicitis and 23 to complicated acute appendicitis. In patients with simple appendicitis, we identified a mean leukocyte count of 13.5, SD = +- 4.3, and a rank from 4.7-31.2; for those with complicated acute appendicitis, we observed a mean of 19.5, SD = 2.8, and a rank from 15.3 to 26.1 ($p \leq 0.005$).

Procalcitonin in simple appendicitis was identified with a mean of 0.3, SD = 0.3, and a rank from 0.1 2. However, for complicated appendicitis, the mean was 1.5 with an SD of 0.7 and a rank from 0.3-2.6. Table 1 shows the remaining biochemical parameters and in-hospital stay data.

	Complicated appendicitis				Simple appendicitis				
Variable	**Mean**	**SD**	**Min**	**Max**	**Mean**	**SD**	**Min**	**Max**	**p**
Leukocytes	19.5	2.8	15.3	26.1	13.5	4.3	4.7	31.2	.000*
Lymphocytes	8.4	4.9	2.8	23.6	22.2	10.1	7.9	43.6	
Neutrophils	86.5	3.8	78.1	92.3	74.3	7.7	46	92.1	.000*
Procalcitonin	1.5	0.7	0.3	2.6	0.3	0.3	0.1	2	.000*
Hospital stay	5.13	1.517	3	9	2.57	0.82	1	4	<0.005*

Table 1: Differences between the biochemical markers and in-hospital stay of complicated and simple appendicitis.

SD: Standard deviation; Min: Minimum; Max: Maximum. *U de Mann Whitney.

The mean number of in-hospital days showed a mean of 5.1 days, SD was 1.5, the minimum stay was 3 days, and the maximum was 9 days. In patients with simple acute appendicitis, the mean was 2.5 days, SD = 0.82), and the rank ranged from 1 to 4 days.

On the other hand, procalcitonin in patients with complicated acute appendicitis had an AUC of 0.952, IC 95% (0.906-0.998) with $p < 0.005$, and a cut-off point of 0.74, which corresponds to a sensitivity of 87% and a specificity of 10% for complicated appendicitis (Table 2 and Figure 2).

Complicated appendicitis	AUC	IC95% Li; Ls	p-value
Procalcitonin	0.952	0.906;0.998	<0.005
Leukocytes	0.907	0.837;0.977	<0.005
Neutrophils	0.951	0.901-1.000	<0.005

Table 2: Area Under the Curve for procalcitonin.

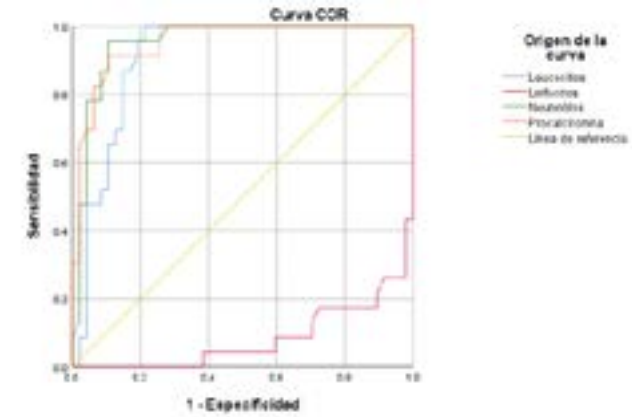

Figure 2: ROC curve.

Regarding the trans-surgical findings and postoperative complications, Table 3 shows that in patients with complicated appendicitis, the highest number corresponded to ileus (6) and seroma (6), followed by 2 patients with wound infection and a patient with a residual abscess and wall abscess, respectively. In the uncomplicated appendicitis, two patients presented with ileus, and two presented with seroma. When associating the complications with the trans-surgical findings, we identified a p-value less than 0.05 (Table 3).

Discussion

Procalcitonin (PCT) is a calcitonin prohormone. PCT levels increase rapidly after systemic bacterial infection but are still low in viral infections and inflammatory diseases. The role of PCT in the diagnosis of pediatric AA remains unclear [7].

	Ileus	Wound infection	Seroma	Residual abscess	Wall abscess	Total	p-value
Complicated	6	2	6	1	1	23	
Simple	2	0	2	0	0	47	
Total	8	2	8	1	1	70	* $p < 0.05$

Table 3: Postoperative complications.

*U de Mann Whitney.

A study conducted by Pian., *et al*. [8] showed that procalcitonin increased significantly in complicated acute appendicitis, with a significance similar to that found in our study ($p < 0.005$).

Khan., *et al*. [9] conducted a prospective cohort study in children aged 5 to 17 years with acute abdominal pain where 48% resulted in acute appendicitis. They found that the medium level of procalcitonin was higher among children with appendicitis ($p = 0.3$) with a cut-off level of 0.39, which is lower than our cut-off value (0.74); nevertheless, this study did not analyze the association with complicated acute appendicitis.

A meta-analysis made by Wei Cui., *et al*. [7] identified seven studies for acute appendicitis and four studies for complicated appendicitis. They found that procalcitonin was more precise in the diagnosis of complicated appendicitis, with a sensitivity of 89%, which is very similar to what we found (87%). On the other hand, they found a specificity of 90%, which was significantly different from the 10% detected in our study.

A prospective study carried out by Gavela., *et al*. [10] for a diagnosis of complicated appendicitis with peritonitis obtained a cut level for procalcitonin of 0.18 ng/ml, which suggested an early surgery and closer monitoring of these patients. In contrast to our study, the cutoff level for the data of complications was found to be too low.

In 103 patients with a clinical diagnosis of appendicitis who underwent an appendectomy, the procalcitonin level was observed to rise considerably in cases of severe inflammation, especially after appendicular perforation or gangrenous appendicitis, which is similar to our study, where the mean procalcitonin level in cases of complicated acute appendicitis (1.5 ng/ml) was higher than that in cases of uncomplicated acute appendicitis (0.3 ng/ml) [11].

Kafetzis., *et al*. [12] found that a PCT level >0.5 ng/ml (which is lower than our cut level) is indicative of perforation or gangrene with a sensitivity of 73.4% (similar to ours, 87%).

A study made by Haghi., *et al*. [13] determined that the sensitivity of procalcitonin for the diagnosis of acute appendicitis was 65% and 80% for simple and complicated, respectively. Nevertheless, this study was conducted in adults, and the values in cases of complicated acute appendicitis were not compared.

Yang., *et al*. [14] conducted a retrospective study of 1895 children with confirmed acute appendicitis. They compared cases of perforation with those without perforation and found no significant differences in procalcitonin levels between the two groups.

In a prospective observational study, Chandel., *et al*. [15] found higher sensitivity (95.65%) compared to ours, with procalcitonin values over 0.5ng/ml in most cases. Nevertheless, in their study, the diagnosis was made based on the histopathological report of the extirpated sample.

None of the above-mentioned studies showed an association between complicated acute appendicitis and postsurgical complications. In our study, these complications were seroma and ileus, with six cases each in the complicated acute appendicitis group ($p < 0.05$).

The results of previous studies are similar to those of our study. However, in the state of Puebla, there are no studies related to procalcitonin in complicated appendicitis in the pediatric population; therefore, there is scope for future studies. A limitation of this study was that during the SARS-CoV-2 pandemic, there were no cases of admission of pediatric patients with a diagnosis of acute appendicitis in our hospital, so the sample may have been affected.

Conclusion

Despite the biochemical and imaging auxiliary studies for the diagnosis of acute appendicitis, there are still many challenges in this matter for the opportune diagnosis. Clinical practice in children, in contrast to that in adults, is variable and atypical in some cases. Therefore, it is of utmost importance to draw on other diagnostic tests that may help clinicians and surgeons in making decisions.

In our study, the value of procalcitonin was significant in cases of complicated acute appendicitis in the pediatric population, with high sensitivity and low specificity.

In clinical practice, the use of this biomarker may help determine which pediatric patients are going through a complicated acute appendicitis picture, offering surgeons and pediatricians a tool to make the right decisions. All the above aims to improve the prognosis of patients, diminish morbidity and mortality, and bring beneficial effects to the health system.

Declarations

This study was approved by the Research Ethics Committee of the General Hospital de la Zona Norte "Bicentenario de la Independencia" of Puebla State. Clinical Trial Number: CI/R18/2021.

This investigation was performed in line with the principles of the Declaration of Helsinki.

Informed consent was obtained from all participants.

Conflict of Interest

The authors declare that they have NO affiliations with or involvement in any organization or entity with any financial interest in the subject matter or materials discussed in this manuscript.

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