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FACTORS ASSOCIATED WITH COMPLICATED ACUTE APPENDICITIS IN A PERUVIAN PEDIATRIC EMERGENCY HOSPITAL

FACTORES ASOCIADOS A APENDICITIS AGUDA COMPLICADA EN UN HOSPITAL PERUANO DE EMERGENCIAS PEDIÁTRICAS

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ABSTRACT

Introduction: Acute appendicitis is more frequent in males and affects pediatric and adolescent patients aged 10 to 20 years. It is caused by obstruction of the appendiceal lumen due to fecaliths, lymphoid follicle hyperplasia, parasites, or primary carcinomas. In children, there is a higher risk of complications, because the symptoms are very nonspecific. **Objectives:** To determine the risk factors associated with complicated acute appendicitis in pediatric patients at the Pediatric Emergency Hospital for the period 2019-2021. **Methods:** Analytical, observational, retrospective case-control study through data collection from medical records and operative reports. **Results:** An association was found between leukocytosis (ORa=2.79, 95% CI: 1.30-6.01, p=0.008), delay in presenting to emergency greater than 24 hours (ORa=1.72, 95% CI: 1.21-2.45, p=0.003), and the time from the appearance of the first symptom to the surgical act greater than 49 hours (ORa=3.01, 95 % CI: 1.54-5.93, p=0.001) with the possibility of developing complicated acute appendicitis (CAA).een 24 to 48 hours or greater than 49 hours .**Conclusions:** Factors related to developing CAA include a high white blood cell count, a delay in emergency presentation greater than 24 hours, and the time from the appearance of the first symptom to the surgical act between 24 to 48 hours or greater than 49 hours.

Keywords: Risk factors; Pediatrics; Pediatric surgery; Complicated acute appendicitis (CAA). (Source: MESH-NLM)

RESUMEN

Introducción: La apendicitis aguda es más frecuente en varones y afecta a pacientes pediátricos y adolescentes de 10 a 20 años. La causa es por obstrucción de la luz apendicular, debido a fecalitos, hiperplasia del folículo linfoide, parásitos o carcinomas de tipo primario. En los niños, se observa mayor riesgo de complicaciones, porque la sintomatología es muy inespecífica. **Objetivos:** Determinar los factores de riesgo asociados a apendicitis aguda complicada en pacientes pediátricos del Hospital de Emergencias Pediátricas del periodo 2019-2021. **Métodos:** Estudio de tipo analítico, observacional, retrospectivo de casos y controles a través de recolección de datos de historias clínicas y reportes operatorios. **Resultados:** Se encontró asociación entre la leucocitosis (ORa=2,79 IC=0,95; 1,30 – 6,01 p=0,008), tiempo que demora en acudir a emergencia mayor a 24h (ORa=1,72; IC=0,95 1,21-2,45 ; p=0,003), tiempo en aparición del primer síntoma hasta el acto quirúrgico mayor a 49 horas (ORa =3,01; IC:0,95 1,54-5,93 ; p=0,001) con la posibilidad de desarrollar apendicitis aguda complicada (AAC). **Conclusiones:** Los factores relacionados a desarrollar AAC son recuento alto de leucocitos, demora en emergencia mayor a 24 horas, aparición del primer síntoma hasta el acto quirúrgico entre 24 a 48 horas o mayor a 49 horas.

Palabras clave: Factores de riesgo; Pediatría; Cirugía pediátrica; Apendicitis aguda complicada (AAC). (Fuente: DeCS- BIREME)

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INTRODUCTION

Acute appendicitis (AA) is the most common surgical pathology in cases of acute abdomen across different age groups; 1-2% of hospitalized pediatric patients are admitted for surgical reasons. In general, pediatric patients with abdominal pain represent 1-8% of the population with acute appendicitis. However, acute appendicitis is rare among preschool students. Despite the availability of imaging techniques such as ultrasound and tomography, diagnosing AA in pediatric patients remains challenging, leading to a high proportion of children experiencing late complications such as perforation, which in turn causes obstructions, or the presence of sepsis and peritonitis that prolong hospital stays and are associated with a higher frequency of death[1].

The incidence of AA is heterogeneous; for example, in children aged 0-4 years, it is observed in two out of every 10,000. In low- or middle-income countries, the higher frequency of complications is due to limited access to healthcare services, the distance between homes and specialized care centers, or delayed diagnoses caused by poor or absent symptom expression in children, making diagnosis more challenging in younger ages[2]. In pediatric patients, the high cost generated by complications is evident; however, in recent years, there has been significant progress in perioperative care [3]. In a previous study conducted in Peru, it was observed that appendectomy is performed through emergency rooms, with open and laparoscopic surgeries accounting for 51.6% and 48.4%, respectively, in patients aged 2 to 14 years [4].

This research is crucial due to the high incidence and severity of complications associated with acute appendicitis, particularly in the pediatric population. In contexts like Peru, where access to healthcare services can be limited and diagnoses are often delayed, identifying these risk factors is essential to improve early intervention strategies and reduce morbidity and mortality rates. Understanding the specific factors contributing to the progression of complicated appendicitis can guide healthcare professionals in implementing more effective protocols and optimizing available resources for the adequate management of these cases.

The objective of the present study was to determine the risk factors associated with appendectomy in patients at a pediatric emergency hospital in Peru.

METHODS

Study design

This is an analytical, observational, retrospective case-control study, as the design allows for the discovery of causal agents related to complicated acute appendicitis.

Study population

People admitted with complicated acute appendicitis, under 18 years of age, post operated, and treated at the General Surgery Department of the Hospital de Emergencias Pediátricas during the period 2019-2021 (n=300).

Eligibility criteria

Cases were defined as male or female patients, under 18 years of age, with an operative report, whose diagnosis was of complicated acute appendicitis in the necrotic and perforated stages (n=67). Meanwhile, controls included patients with the same characteristics described as cases, except for the absence of complicated acute appendicitis (n=67). The power found for the leukocytosis variable was 94.6%.

Definition of variables

The dependent variable was complicated acute appendicitis, and the independent variables were: age, sex, prior medication, leukocytes (more than 11,000), time taken to seek emergency care, and the time from the onset of symptoms to the surgical procedure. Covariates included clinical characteristics such as abdominal pain, fever, vomiting, nausea, diarrhea, McBurney's sign, and Blumberg's sign.

Procedures

The researchers collected information from medical records, with prior authorization from the Universidad Ricardo Palma and the hospital, and the variables of interest were transferred to a spreadsheet.

Statistical analysis

Data were collected from the review of medical records and surgical reports from the Surgery Department of the Hospital de Emergencias Pediátricas for the period 2019-2021. Subsequently, the obtained data were processed using Microsoft Excel and STATA software. For the univariate analysis of qualitative variables, absolute and relative frequencies were calculated; for quantitative variables, the mean and standard deviation were estimated, previously determined according to their normal distribution. For the bivariate analysis, contingency tables were used: chi-square or Fisher's exact test, and for multivariate analysis, logistic regression was performed to determine the crude and adjusted odds ratio (OR), as well as 95% confidence intervals.

Ethical considerations

This research study was approved by the Ethics Committee of the Faculty of Human Medicine of the Universidad Ricardo Palma (PG-78-021) and the Hospital de Emergencias Pediátricas (official letter No. 162-DG-094-2021-OADI-HEP/MINSA). Confidentiality of the information was maintained according to the Peruvian General Health Law, which stipulates that the information obtained should only be used for research purposes.

RESULTS

A total of 134 pediatric patients were analyzed, of which 67 had complicated acute appendicitis (cases). Regarding age, the mean age of the controls was 10.7 years, while that of the cases was 13.1 years. The predominant sex in both cases and controls was male. Among the controls, 62.7% received prior non-analgesic medication, while among the controls, analgesic use was observed in 50.7%. With respect to those presenting with leukocytosis, the number of patients with complicated AA was higher compared to the control group (92.5% vs. 68.7%, p=0.001). The time to seek emergency care longer than 24 hours was more frequent in the cases (59.7% vs. 34.3%, p=0.001), as was the time from the onset of symptoms to the surgical procedure longer than 49 hours, observed in patients with complicated AA (38.8% vs. 17.9%, p=0.002).

The predominant symptoms in both groups were vomiting, fever, diarrhea, and Blumberg's sign. The incidence of vomiting in patients with complicated acute appendicitis was higher than in the control group (85.1% vs. 65.7%, p=0.009). The diagnosis of necrotized and perforated appendicitis was 70.1% and 29.9%, respectively (Table 1).

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Table 1. General characteristics of patients with acute appendicitis at a Peruvian pediatric emergency hospital.

Variables	Cases (n=67)	Controls (n=67)	p-value
Categorized age			
Infancy (0-5 years)	8 (11.9)	7 (10.4)	
Childhood (6-11 years)	41 (61.2)	38 (56.7)	0.748*
Adolescence (12-18 years)	18 (26.9)	22 (32.8)	
Sex			
Male	45 (67.2)	43 (64.2)	
Female	22 (32.9)	24 (35.8)	0.716*
Prior medication			
No analgesia	33 (49.2)	42 (62.7)	
Analgesia	34 (50.7)	25 (37.3)	0.117*

Leukocytes			
Normal	5 (7.5)	21 (31.3)	
Leukocytosis	62 (92.5)	46 (68.7)	0.001**
Delay in emergency care (categorized)			
Less than 24 hours	27 (40.3)	46 (68.7)	
24 hours or more	40 (59.7)	21 (34.3)	0.001*
Time from the onset of symptoms to surgery (categorized)			
Less than or equal to 24 hours	7 (10.4)	21 (31.3)	
24-48h	34 (50.7)	34 (50.7)	0.002*
49 hours or more	26 (38.8)	12 (17.9)	
Symptoms			
Nausea			
No	57 (85.1)	51 (76.1)	
Yes	10 (14.9)	16 (23.9)	0.190 *
Vomiting			
No	10 (14.9)	23 (34.3)	
Yes	57 (85.1)	44 (65.7)	0.009*
Fever			
No	31 (46.3)	39 (58.2)	
Yes	36 (53.7)	28 (41.8)	0.166*
Diarrhea			
No	49 (73.1)	55 (82.1)	
Yes	18 (26.9)	12 (17.9)	0.214*
McBurney's sign			
No	4 (6.0)	1 (1.5)	
Yes	63 (94.0)	66(98.5)	0.183**
Blumberg's sign			
No	41 (61.2)	45 (67.2)	
Yes	26 (38.8)	22 (32.8)	0.471*
Diagnosis			
Congestive	0 (0.00)	17 (25.4)	
Suppurative	0 (0.00)	50 (74.6)	<0.001**
Necrotic	47 (70.1)	0 (0.00)	
Perforated	20 (29.9)	(0.00)	

* Chi-square ** Fisher's exact test

For the analysis using simple regression, it was found that patients with leukocytosis were 2.9 times more likely to present with complicated acute appendicitis compared to those with normal leukocyte counts (OR=2.87; 95% CI: 1.285 – 6.411). Those with a delay of more than 24 hours in emergency care were 1.8 times more likely to present with complicated acute appendicitis compared to those with a delay of less than 24 hours (OR=1.77; 95% CI: 1.25 – 2.52); patients with a time from the onset of the first symptom to surgery exceeding 49 hours were 2.7 times more likely (OR=2.74; 95% CI: 1.39 – 5.39), and those with a time from the onset of the first symptom to surgery of 24-48 hours were 2.00 times more likely (OR=2.00; 95% CI: 1.01 – 3.97) to present with complicated acute appendicitis compared to those with a time from symptom onset to surgery of less than 24 hours. Then, in the multiple regression analysis, the observed association in terms of direction and magnitude was maintained. It was observed that pediatric patients with leukocytosis were 2.8 times more likely to present with complicated acute appendicitis compared to those with normal leukocytes (OR=2.79; 95% CI: 1.30 – 6.01). Those with a delay in emergency care exceeding 24 hours were 1.7 times more likely to present with complicated acute appendicitis compared to those with a delay of less than 24 hours (OR=1.72; 95% CI: 1.21 – 2.45); those with a time from the onset of the first symptom to surgery exceeding 49 hours were three times more likely (OR=3.01; 95% CI: 1.54 – 5.93), and those with a time from the onset of the first symptom to surgery between 24-48 hours were 2.3 times more likely (OR=2.25; 95% CI: 1.14 – 4.44) to present with complicated acute appendicitis compared to those with a time from symptom onset to surgery of less than 24 hours. Variables such as age, sex, medication use, diagnosis of necrotizing or perforated appendicitis, and symptoms like nausea, fever, diarrhea, McBurney's and Blumberg's signs were not risk factors for complicated acute appendicitis in our study (Table 2).

Table 2. Risk factors for complicated acute appendicitis in a Peruvian pediatric emergency hospital.

Characteristics	Crude analysis			Adjusted analysis*		
	OR	95% CI	p	OR	95% CI	p
Categorized Age						
Infancy (0-5 years)	Ref			Ref		
Childhood (6-11 years)	0.973	0.58-1.64	0.918	0.96	0.58-1.63	0.900
Adolescence (12-18 years)	0.844	0.47-1.52	0.570	0.89	0.49-1.61	0.711
Sex						
Male						
Female	0.935	0.649 – 1.348	0.72	1.05	0.76 – 1.441	0.771
Prior Medication						
No analgesia	Ref			Ref		
Analgesia	1.31	0.935 – 1.835	0.117	1.10	0.79 – 1.53	0.551
Leukocytes						
Normal	Ref			Ref		
Leukocytosis	2.87	1.285 – 6.411	0.01	2.79	1.30 – 6.01	0.008
Symptoms						
Nausea						
No	Ref			Ref		
Yes	0.729	0.433 – 1.225	0.233	0.92	0.577 – 1.477	0.740

Vomiting						
No	Ref			Ref		
Yes	1.86	1.078- 3.218	0.026	1.583	0.91 – 2.76	0.105
Fever						
No	Ref			Ref		
Yes	1.27	0.903- 1.787	0.17	1.06	0.760 – 1.475	0.734
Diarrhea						
No	Ref			Ref		
Yes	1.273	0.891 – 1.821	0.185	1.269	0.901- 1.788	0.171
McBurney's Sign						
No	Ref			Ref		
Yes	0.611	0.379 – 0.981	0.041	0.719	0.389- 1.328	0.293
Blumberg's Sign						
No	Ref			Ref		
Yes	1.14	0.806 – 1.601	0.466	1.05	0.76 – 1.446	0.747
Others						
No	Ref			Ref		
Yes	0.99	0.641 – 1.557	1.000	1.069	0.668-1.71	0.781
Delay in emergency care (categorized)						
Less than 24 hours	Ref			Ref		
24 hours or more	1.77	1.25-2.52	0.001	1.72	1.21-2.45	0.003
Time from onset of symptoms to surgery (categorized)						
Less than or equal to 24 hours	Ref			Ref		
24-48 h	2	1.01-3.97	0.048	2.25	1.14-4.44	0.018
49 hours or more	2.74	1.39-5.39	0.004	3.01	1.54-5.93	0.001
Diagnosis						
Congestive	Ref			Ref		
Suppurative	1	0.575 – 1.737	1.000	1	0.568 – 1.759	1.00
Necrotic	1.091	0.6791 – 1.761	<0.001	1.09	0.664 – 1.78	<0.001
Perforated	1.091	0.6791 – 1.761	<0.001	1.9	0.664 - 1.78	<0.001

*Adjusted for all variables: age, sex, leukocytes, prior medication, clinical characteristics, time to seek emergency care, and time between the first symptom and the surgical procedure.

**Significant p-value <0.05

OR: Odds ratio, 95% CI = 95% Confidence Interval

DISCUSSION

In the present study, the results show an association between the presence of complicated acute appendicitis (CAA) and leukocytosis, a delay of more than 24 hours in seeking emergency care, and the time from the onset of symptoms to the surgical procedure, which ranged between 24-48 hours and exceeded 49 hours.

In our research, pediatric patients with leukocytosis had an OR of 2.79 for developing complicated acute appendicitis (CAA). This is similar to another study conducted on a pediatric population in Trujillo, where an OR of 2.39 (95% CI: 1.04-5.51; p=0.0038) was found for the development of CAA [5]. In another study on pediatric patients from northern Peru, an OR of 7.36 (95% CI: 1.66-32.76; p=0.003) was reported for presenting with CAA[6]. In a study conducted on pediatric patients in India, it was found that leukocyte counts above 15,000/ml were associated with a higher likelihood of CAA. In our study, the cutoff point for determining leukocytosis was above 11,000/ml. Another investigation, with a similar cutoff point, observed that leukocytosis was associated with an increased likelihood of developing CAA (OR=16.38; 95% CI: 1.836-146; p=0.012) [7]. In another study, a leukocyte count equal to or greater than 14,000/ml was found to be a predictive factor for CAA in children, with an OR of 2.07 (p<0.001) [5]. One possible explanation, from a healthcare perspective, could be that the failure to diagnose and treat patients promptly at referral centers might prolong the inflammatory response. Another possible explanation may involve weaknesses in care provided by primary care centers and first-level management[8].

Leukocytes play an important role in protecting against harmful agents, including bacteria; various organisms present in the appendix lumen can cause acute appendicitis, infectious complications, and sepsis. A study found that the incidence of infectious complications increased in proportion to leukocyte count, with all children developing abdominal infections when leukocytes exceeded 7,000 cells/dl of the upper normal limit [9]. Additionally, it has been shown that, although infection may be present, the total leukocyte count can be normal, suggesting that elevated counts could be an indicator of prognosis when they are elevated. However, it has been observed that leukocyte counts vary depending on the duration of the illness; elevated total leukocyte counts may be found in a later phase of the disease [10]. In our study, 92.5% of children with leukocytosis had complicated acute appendicitis, while 68.7% of children with leukocytosis had uncomplicated acute appendicitis.

In our research, patients whose symptoms lasted between 24-48 hours before surgery had an OR of 2.25, and those with symptoms lasting more than 49 hours had an OR of 3.01 for developing CAA. Additionally, children with a delay in emergency care exceeding 24 hours had an OR of 1.72 for developing it. In a study conducted on children in India, it was found that those with pain lasting more than 72 hours had a higher likelihood of complicated appendicitis, with an OR of 14.6 (95% CI: 2.40-89.77; p=0.004)[11]. In a previous publication, multivariable analysis confirmed that the duration of symptoms exceeding 24 hours (OR=5.5, 95% CI: 3.5-8.9, p<0.01) was an independent predictor of complications[12].

A duration of illness greater than 72 hours is a factor associated with CAA (OR=5.118; 95% CI: 1.702-15.389; p=0.003)[13]. Another prior publication showed that the time between symptom onset and hospital admission was predominantly associated with 59% of patients with complicated acute appendicitis, with a delay between 12-24 hours, and the time between hospital admission and surgery was associated with 48% of patients with complicated acute appendicitis, with a time span between 7-12 hours; the longer the delay, the higher the complication rate [14,15]. Another study found that the duration of appendicitis symptoms did not directly correlate with the stages of disease presentation [10]. A prior report observed that 60% of children with complicated appendicitis had abdominal pain lasting more than 48 hours. In a study conducted in India (n=102), it was observed that symptoms lasting more than 72 hours were more likely to result in complications[16]. A systematic review determined that a delay of 24 to 48 hours in symptom presentation or hospital wait times increased the likelihood of developing complicated appendicitis by 1.99 to 1.84 times [17].

In a study conducted in the United States, it was observed that if the presentation occurred within 36 hours, the risk of perforation was less than 2%, but if the presentation was longer than 36 hours, the risk of perforation increased by 5% every 12 hours [17]. Another study found that there is an early risk of perforation and necrosis within the first 36 hours[18]. In our work, 70.1% of pediatric patients with CAA presented with necrotic appendicitis, and 20.9% with perforated appendicitis. In another study conducted in the United States, it was found that the perforation rate increased linearly from 10% at 18 hours to 44% at 36 hours [19]. Another study observed that if symptoms persisted for more than two days, the risk of perforation and necrosis exceeded 40% [20]. A possible explanation, according to the literature, is that the longer the duration of symptoms, the greater the possibility of developing perforated appendicitis[21]; this can range from symptoms present for 24 hours[12], 36 hours, or more than 48 hours[22]. However, there is still no consensus among studies on the precise time limit for having a significant risk of necrosis or perforation [22].

A limitation of the study is that it does not establish the temporal relationship between the dependent variable and the covariates, nor can causality or directionality be determined. That is, participants may have presented the risk factors first and then developed complicated acute appendicitis or vice versa. Additionally, variables such as C-reactive protein (CRP) and neutrophils, which may influence complicated acute appendicitis, were not considered. However, we believe that the study's findings are useful in providing an overview of complicated acute appendicitis in pediatric patients at a hospital in Lima.

CONCLUSIONS

The research reveals a significant association between leukocytosis and an increased risk of developing complicated acute appendicitis in children. Additionally, the results indicate that delays of more than 24 hours, both in surgical emergency care and the interval from the onset of symptoms to surgery, significantly increase the likelihood of developing complicated acute appendicitis. These findings highlight the importance of a prompt and efficient medical response to minimize complications in pediatric patients with acute appendicitis, emphasizing leukocytosis as a key predictor and the need to optimize diagnostic and treatment times to improve clinical outcomes.

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