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Outcomes of acute appendicitis in patients younger than age 4: a descriptive study

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Abstract

Background: Acute appendicitis is an infrequent pathology in children under 4 years of age, and its diagnosis is a clinical challenge that can lead to late detection. The intention of this study is to describe the clinical and surgical findings and to explore factors and outcomes associated with appendiceal perforation in patients under 4 years of age with histologically confirmed acute appendicitis. Cross-sectional study of historical data is on patients with a pathologic diagnosis of appendicitis. Clinical, surgical, and pathological variables were described. The relationship between the presence of perforation and associated factors and outcomes was explored using odds ratios (OR) and 95% confidence intervals.

Results: Seventy-five patients were found between 2013 and 2019. Seventy-four cases presented with pain on palpation, 56 (75%) with signs of peritoneal irritation, and 70 (93%) with sepsis on admission to the emergency room. An ultrasound was done on 57 patients (76%), and only 26 (45%) were suggestive of appendicitis. Forty-one (55%) cases were operated on by open surgery and 34 (45%) by laparoscopy. In 61 (81%), they were perforated, and 48 (64%) presented peritonitis. Perforation was associated with increased hospital days ($OR = 2.54 [1.60-4.03]$), days of antibiotics ($OR = 4.40 [2.09-9.25]$), and admission to intensive care ($OR = 9.65 [1.18-78.57]$).

Conclusions: Abdominal pain reported by parents, pain on abdominal palpation, and clinical criteria of sepsis on admission to the emergency room are common features. Acute appendicitis complicated by perforation leads to high morbidity due to longer antibiotic treatment, hospitalization days, admission to PICU, and postoperative ileus.

Keywords: Appendicitis, Perforated appendicitis, Children, Diagnostic study, Ultrasound, Pathology, Sepsis, Peritonitis

Background

Acute appendicitis is the most common cause of surgical abdomen in childhood [1]. In children under 5 years of age, the incidence is estimated to be approximately 1.1 per 10,000 cases [2]. In young children, the clinical presentation is challenging and makes early diagnosis difficult because the clinical manifestations are nonspecific or atypical [3]. The most frequent symptoms in this age group are vomiting, pain, fever, and diarrhea. This

suggests gastroenteritis, urinary tract infection, and intussusception [2] and thus delays diagnosis and contributes to a high rate of perforation [4]. Diagnosis in infants and preschoolers has become a challenge since it depends on a high index of suspicion that relies on a careful clinical history and complete physical examination. Perforation frequency is estimated to be 100% in children under 1 year of age and up to 69% in children under 5 years of age with an inverse relationship between age and perforation frequency [3, 5]. Regarding diagnostic studies, there is still no biomarker that differentiates appendicitis from other causes of abdominal pain [6]. Clinical scales such as the pediatric appendicitis score (PAS), leukocyte count, neutrophilia, and C-reactive protein have been devised for diagnosis, but sensitivity and

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specificity are highly variable and include patients up to 18 years of age [7–9]. Procalcitonin has shown a better performance in mainly complicated appendicitis. However, it is not available in all hospitals [10]. Regarding diagnostic studies, an ultrasound should be used in cases of moderate risk of appendicitis according to the PAS. It is a noninvasive test with no risk of ionizing irradiation, although it is operator dependent [11]. Finally, computed tomography (CT) is the diagnostic image with the best sensitivity and specificity, but its use is declining due to the risk of radiation-induced malignancy [12]. There are few studies that describe acute appendicitis in a population of children under the age of 4, so this study was designed to describe the clinical, laboratory, and imaging characteristics, and the surgical procedure, as well as explore the relationship between factors and outcomes associated with perforation.

Methods

Study design and patient selection

A descriptive study that includes an exploratory analytical component was carried out using historical records. Patients under 4 years of age with a histological diagnosis of appendicitis, who were treated at the Sociedad de Cirugía de Bogota-Hospital de San Jose and at the Hospital Infantil Universitario de San Jose in the city of Bogota and who were not referred to other healthcare centers after medical or surgical treatment between 2013 and 2019, were included. The pathology service databases were searched for conclusive data on the diagnosis of acute appendicitis. A sequential and suitable collection of data was carried out based on the selection criteria. The following variables of interest were taken into account: sociodemographic conditions, medical history, preoperative clinical profile (signs and symptoms), systemic inflammatory response syndrome on admission based on the international consensus on sepsis [13], diagnosis tests report on admission, clinical and surgical treatment, histopathological study, postoperative conditions, and mortality. With these variables as a basis, a collection instrument was put together and applied by the researchers who had been trained on it, and the information was input into a database for subsequent statistical analysis using STATA 13.1. To evaluate the consistency of the data collected, 10% of the records were selected randomly and compared with the physical records.

Statistical analysis

A descriptive analysis of the population was done, qualitative variables were expressed in absolute and relative frequencies, and the quantitative variables with central tendency and dispersion measurements were based on the distribution of the data. In addition, an analytical

exploration of cases with perforated appendicitis was done that included associated factors and outcomes such as duration of surgery, hospital stay, days of antibiotic treatment, postoperative ileus, and admission to the pediatric intensive care unit (PICU). A bivariate analysis of perforated and non-perforated appendicitis was done using simple logistic regression and calculating the odds ratios (OR) and their respective 95% confidence intervals.

Ethical aspects

This work took international and national regulations for research involving human subjects into account. It was also presented to and approved by the Human Research Ethics Committee of the FUCS-HSJ and is identified with approval number: 0154-2019.

Results

A total of 2850 confirmed pathology specimens with acute appendicitis were examined, of which 75 (2.6%) corresponded to patients under 4 years of age.

Clinical findings

No preference by gender was found (female: 38 (51%)), and only 8 (10%) patients had a history of prematurity. The median age was 36 months (IQR: 28–43), the minimum was 5 months, and the maximum was 47 months (Table 1). Thirty-one patients (41%) received analgesics prior to admission (acetaminophen or ibuprofen). The most frequent findings after physical examination were pain on abdominal palpation — 74 (99%), abdominal pain was a recurrent symptom reported by the parents — 67 (89%), dehydration — 47 (63%), and peritoneal irritation — 56 (75%). A relevant finding was the presence of sepsis in 70 patients (93%) on admission to the emergency room. The diagnoses on admission to the emergency room were acute appendicitis — 30 (40%), abdominal pain under study — 22 (29%), gastroenteritis — 12 (16.2%), intestinal obstruction — 5 (6.3%), febrile syndrome — 2 (3.8%), urinary tract infection — 2 (2.5%), rhinopharyngitis — 1 (1.3%), and oral intolerance — 1 (1.3%). It was established that 25 (33%) of the patients received an intravenous fluid bolus on admission to the emergency room. The antibiotics used are shown in Table 1. At the end of hospitalization, an increase in the use of piperacillin-tazobactam was noted in 25 patients (33%), mainly in cases in which the intraoperative finding was generalized peritonitis. Other antibiotics used until the end of hospitalization were as follows: ampicillin sulbactam — 27 (36%), metronidazole plus amikacin — 13 (17%), and clindamycin plus amikacin — 8 (11%). No carbapenems were used. The clinical diagnosis of appendicitis on admission was 30 patients (40%).

Table 1 Clinical and laboratory characteristics

	n (%)
Age in months, p50 (p25–p75)	36 (28–43)
Time to consultation (days), p50 (p25–p75)	2 (1–3)
Symptoms	
Parent referred abdominal pain	67 (89)
Fever	59 (79)
Emesis	59 (79)
Hyporexia	42 (56)
Diarrhea	27 (36)
Irritability	24 (32)
Respiratory symptoms	5 (7)
Dysuria	5 (7)
Physical examination	
Pain on abdominal palpation (location)	74 (99)
Right iliac fossa	49 (66)
Lower hemiabdomen	13 (18)
General	11 (15)
Left iliac fossa	1 (1)
Peritoneal irritation ^a	56 (75)
General	14 (19)
Local	42 (56)
Dehydration (DHT) ^a	47 (63)
DHT grade I	16 (34) ^a
DHT grade II	30 (64) ^a
DHT grade III	1 (2) ^a
Respiratory distress	2 (3)
Sepsis on admission to emergency	70 (93)
Laboratories	
Blood count, (%)	
Leukocytes (cells/mm ³) (average ± SD)	69 (92)
Neutrophils (cell/mm ³)	16.685 ± 6.201
Lymphocytes (cell/mm ³)	12.975 ± 5.433
Monocyte (cell/mm ³)	2.706 ± 1.855
Hemoglobin (g/dL)	1.127 ± 809
Hematocrit (%)	12.5 g/dL ± 1.5
Platelets	36.0 ± 8.1
C-reactive protein (CRP)	345.574 ± 104.854
CRP values (mg/dL), p50 (p25; p75)	31 (38.8)
	1.2 (0.25; 3)
Urinalysis and urine gram	
Contaminated	52 (69)
No suggestion of UTI ^b	8 (15)
	44 (84)
Treatment	
Intravenous fluid resuscitation	25 (33)
Blood transfusion	3 (4)
Antibiotic therapy	
Initiation of antibiotics at first evaluation	75 (100.0)
Delayed antibiotic starting time (hours), p50 (p25; p75)	19 (23.7)
	11 (8; 18)
Type of antibiotic	
Ampicillin-sulbactam	32 (43)
Metronidazole + amikacin	28 (37)

Table 1 (continued)

	n (%)
Clindamycin + amikacin	11 (15)
Piperacillin tazobactam	4 (5)
Days of antibiotics, x (± SD)	6 (± 3)
Outcomes	
Days of hospitalization, x (± SD)	27 (33.7)
Admission to ICU	7 (± 4)
Death	27 (36)
Returning to the hospital	0 (0, 0)
	10 (13)

^a Percentage of total dehydration^b UTI: urinary tract infection

Laboratories

A complete blood count was done on 56 (75%) of the patients on admission and on 13 (17%) during hospital follow-up; the results showed a high frequency of leukocytosis and neutrophilia. C-reactive protein (CRP) was not a routine test for 29 patients (39%), and its results indicated wide variability (Table 1). In some cases, a urinalysis was done on 52 patients (69%), and the results for urinary tract infection were negative.

Images

A total abdominal ultrasound (TAU) was done on 57 patients (76%) of which 26 (45%) were reported to have an apparent acute appendicitis. In patients measured by TAU, the mean transverse diameter of the appendix was 8.8 mm (SD 2.63). The most relevant findings are shown in Table 2. Although plain abdominal radiography and contrasted abdominal axial tomography were not routine examinations, 14 patients (19%) underwent radiography with ileus findings (most frequent finding) which were present in 9 patients (64%) or reported as normal in 5 cases (36%). Only 4 patients (5%) that underwent tomography had findings that indicated apparent acute appendicitis in all cases (see Table 2).

Surgery

The surgical findings are shown in Table 3. Thirty-four patients (45%) were operated on using laparoscopy with an average operating time of 88 min (SD 31.43). Open surgery was used to operate on 41 patients (55%) with an average operating time of 78 min (SD 31 min). Sixty-one patients (81%) had perforated appendices. Postoperative complications occurred in 12 patients (16%). The most frequent ones were surgical site infection (SSI), organ-space infection — 5 patients (42%),

Table 2 Findings on diagnostic imaging

	n (%)
Abdominal ultrasound scan	57 (76)
Suggestive of appendicitis	
Appendiceal peristalsis	24 (42)
Alteration of mesenteric fat	1 (1.7)
Suggestive of appendicitis	1 (1.7)
Not suggestive of appendicitis	
Ileus	11 (19.2)
Normal	10 (17.5)
Free fluid in abdominal cavity	5 (8.7)
Free liquid in FID	3 (5.2)
Cecal colitis	1 (1.7)
Intussusception	1 (1.7)
Abdominal X-ray	14 (19)
Ileus	9 (64)
Normal	5 (36)
Abdominal CT scan	4 (5)
Suggestive of appendicitis	4 (5)
Alteration of peri-appendicular fat	1 (25)
Generalized peritonitis	1 (25)
Fecalith	1 (25)
Right-to-left flank collection	1 (25)

intestinal obstruction — 4 (33%), superficial SSI — 1 (8%), and deep SSI — 2 patients (17%). Ten patients (13%) required reoperation due to the following: peritonitis — 2 (2.6%), intraperitoneal abscesses — 7 (9.3%), and adhesive small bowel obstruction — 1 (1.3%). Of these patients, peritoneal fluid cultures were taken from only 9 (12%) with 5 (56%) of the cases showing polymicrobial growth and the remaining 44% showing isolation of multisensitive *E. coli*.

Pathology

Macroscopic findings established that, on average, the transverse diameter of the appendix was 7.9 mm (SD 2.78), with findings of whitish membranes in 55 patients (73%) and the presence of intra-appendiceal fecalith in 25 (33%). Regarding microscopic findings, 70 (93%) had acute appendicitis with periappendicitis, 5 (7%) had focal acute appendicitis, and none had diffuse acute appendicitis.

An exploratory analysis was done which showed that an age of less than 2 years as well as development time in days at the time of the doctor visit was associated with a higher risk of perforated appendicitis. Moreover, perforation is associated with outcomes such as

Table 3 Surgical findings

Surgical findings	n = 75 (%)
Hours of assessment time for pediatric surgery	13.05 (± 25.3)
Duration of surgery in minutes	63.5 (± 21.2)
Surgical description	
Not perforated	14 (19%)
Perforated	61 (81%)
Not complicated	5 (7%)
Complicated by	56 (75%)
Generalized peritonitis	27 (36%)
Local peritonitis	21 (28%)
Plastron	5 (7%)
Abscess	3 (4%)
Collections	10 (16%)
Location of collection	
Peri-appendicular	4 (40%)
Retrovesical	1 (10%)
Pericecal	1 (10%)
No description	5 (50%)
Fecalith in the cavity	5 (7%)
Open surgery	38 (51%)
Laparoscopic surgery	34 (45%)
Surgery converted to open surgery	3 (4%)
Laparostomy bags	2 (3%)
Postoperative NGT	32 (43%)
Days p50 (p25, p75)	3.8 (2.5)
Postoperative ileus	31 (41%)
Days p50 (p25, p75)	3.9 (3.5)
Postoperative fever	11 (15%)
Days p50 (p25, p75)	1.9 (1.2)
Complications	12 (16%)
Surface SSI	1 (8%)
Deep SSI	2 (18%)
Intestinal obstruction	4 (33%)
SSI organ space	5 (43%)
Reoperation	10 (13%)
Abscesses and/or intra-abdominal collections	7 (70%)
Adhesive small bowel obstruction	1 (10%)
Peritonitis	2 (20%)
Managing repeat surgery	
Open surgery	4 (40%)
Percutaneous drainage	4 (40%)
Laparoscopic drainage	1 (10%)
Others	1 (10%)

SSI Surgical site infection

the following: patients are hospitalized longer, on antibiotics longer, and have higher frequency of ileus and admission to the PICU (Table 4).

Table 4 Outcomes associated with perforation in acute appendicitis

Variable	Perforated appendicitis		OR	CI 95%
	No = 14 (18.7%)	Yes = 61 (81.3%)		
Outcomes				
Hospital stay (days), p50 (p25, p75)	2 (1, 3)	7 (6, 10)	2.54	1.60–4.03
Days of antibiotics, p50 (p25, p75)	2 (1.2)	7 (5, 7)	4.40	2.09–9.25
Postoperative ileo, <i>n</i> (%)	1 (7%)	30 (50%)	13	1.59–105.73
Admittance to PICU, <i>n</i> (%)	1 (7%)	26 (43%)	9.65	1.18–78.57

Discussion

This study shows the great variety of symptoms in this age group. The most frequent symptoms were abdominal pain reported by the parents, pain on abdominal palpation, and clinical criteria of sepsis on admission to the emergency room. In addition, perforated appendices were associated with a longer period since onset at the time the patient was seen, hospital stay, days on antibiotics, ileus, and admission to PICU.

Acute appendicitis is a major cause of morbidity in infants and children under 4 years of age because it is an infrequent condition with nonspecific symptoms, which is why its timely diagnosis is sometimes compromised [14]. Early clinical suspicion by the medical team (pediatrics and pediatric surgery) represents the mainstay for priority management and thus prevents unnecessary requests for ultrasound and CT scans [15–17]. Regarding symptoms, abdominal pain continues to be the main symptom in these patients and is associated with other symptoms such as vomiting and fever [17]. At preschool age, the symptoms of acute appendicitis are nonspecific, so the information provided by parents becomes one of the keys to a timely diagnosis [18]. Among the symptoms noted by parents, in order of frequency, were diffuse abdominal pain in 94% of the cases, followed by symptoms such as vomiting, anorexia, diarrhea, fever, and irritability [19]. Signs of peritoneal irritation in infants are difficult to determine. In this series, peritoneal irritation was present in 72% of uncomplicated appendicitis and in 90% of complicated appendicitis. Serial evaluations with abdominal palpation and percussion in the right lower quadrant are sufficient to determine peritoneal irritation [19–22]. The systemic inflammatory response syndrome (SIRS), associated with an infectious focal point, is suggestive of sepsis [13]. Raines et al. established the presence of SIRS in patients with appendicitis and found it had a prevalence of 30% in children under 17 years of age, and that the presence of SIRS was associated with complicated appendicitis [22]. Other studies have demonstrated the presence of SIRS in patients with higher rates

of appendectomy [23]. In our population, the presence of SIRS comes to more than 90% upon admission to the emergency room with high rates of perforation. Therefore, the clinician should look for the presence of SIRS and abdominal pain in young children in order to call in the pediatric surgeon at an early stage.

Diagnosing acute appendicitis is not easy in young pediatric patients. The use of laboratory studies and diagnostic images for these patients is intended to provide a more accurate diagnosis. The recommendation for applying them should be in accordance with the diagnostic impression, the patient's physical examination, the PAS, and the physician's judgment [18, 24]. The use of ultrasound for this condition worldwide has revealed that it has a relatively high sensitivity and specificity (90% and 95%, respectively) [25]. However, even though it represents a reproducible and nonionizing diagnostic aid, especially for the age group in question, it is limited by the fact that it is an operator-dependent test, and its sensitivity and specificity are linked to the radiologist's experience. The study by Mangona et al. [26] shows how ultrasound scans done in training centers and those done at night alter sensitivity and specificity. Without clinical suspicion, the request for an ultrasound scan could delay the diagnosis. For example, in this series, only 45% of the ultrasound scans were conclusive. In spite of the fact that CTs have demonstrated greater sensitivity and specificity than ultrasound [12], their use represents exposure to radiation that is sometimes unnecessary for pediatric patients. In addition to delaying timely management of this condition, it is noteworthy how limited the requests for CTs are in our population.

The performance of the hemogram in the present study was similar to that of other case series [24]. This laboratory test is frequently requested for these patients. However, the increase in leukocytes is nonspecific and has little sensitivity since they may have increased in other infectious diseases and do not differentiate between complicated and uncomplicated appendicitis [18, 19]. Neutrophils together with the total leukocyte count improve

the sensitivity (60–87%) and specificity (53–100%) for acute appendicitis. However, a low count cannot limit the diagnosis to appendicitis [19, 27]. C-reactive protein (CRP) is still a nonspecific laboratory test for this type of pathology with sensitivity (43 to 92%) and specificity (33–95%). Studies show that an elevated CRP together with the sensitivity of leukocytosis and neutrophilia could approach 98% for the diagnosis of appendicitis [9, 27].

Acute perforated appendicitis is directly related to the onset of symptoms, progression time, delay in diagnosis, and time to surgical management with the risk of complicated appendicitis [28]. This reinforces the concept that poor clinical suspicion, the delay in having inconclusive laboratory tests done, and, therefore, a late diagnosis increase the incidence of complicated appendicitis and complications related to surgical findings [29, 30]. A delay of more than 24 h for patients with symptoms has shown a higher rate of complicated appendicitis not only in children but also in adults [31]. This is relevant when a patient with abdominal pain is admitted to the emergency room because of its direct repercussion on the surgical and postoperative outcome. Perforations are very frequent in younger children and account for up to 80% of children under 3 years of age [5, 32]. There are several theories about this including aspects such as anatomical immaturity, lack of an adequate omental barrier to contain peritonitis, a mobile appendix, the presence of a thin appendiceal wall, and the difficulty of infants to express their symptoms [2, 5].

Regarding the surgical management of these patients, in spite of the large number of complicated appendicitis cases, a significant group of patients underwent laparoscopic surgery. This approach has been gaining ground over open surgery in this population group with a surgical complication rate similar to recent world literature [33–38]. It is noteworthy that in spite of being complicated acute appendicitis in 76% of the cases, the need for reoperation was not high, and the most frequent postoperative complication was organ-space type surgical site infection. The vast majority of these were managed with only broad-spectrum antibiotic therapy, mainly upgraded to piperacillin tazobactam [39–41]. No carbapenems were used since they do not fit within the rational use of antibiotics on this population group. These complications continue to represent the greatest risk during the postoperative period due to the high intraperitoneal contamination, especially in complicated appendicitis [42]. The use of minimally invasive methods such as percutaneous drainage could be reevaluated in these cases in subsequent studies.

Recently, the exclusive use of antibiotic therapy for the management of uncomplicated appendicitis has also

been studied. This involves the routine use of specialized imaging such as CT for a proper intra-abdominal assessment of appendicitis that has a success rate of 58 to 100% of cases [43, 44]. In spite of these findings and considering the previously mentioned unusual behavior of appendicitis in infants, it is not possible to determine the applicability of this strategy in this population group. More studies and faster diagnosis are required to define the possibility of exclusive use of antibiotic therapy in patients under 5 years of age with uncomplicated appendicitis. Of the appendices evaluated in this study, 81% were perforated. This percentage is comparable to other published series [2, 5] and correlates with the microscopic findings in the present population. In 93% of the microscopic studies, there was acute appendicitis with peri-appendicitis since, in the majority of cases (advanced stages), there would be some degree of ulceration of the mucosa and acute inflammation and, in the most severe cases, transmural compromise with neutrophilic infiltration of the muscularis propria [45].

Limitations

The retrospective data collection with respect to the exploration of associations is limited by the fact that no sample size calculation was done, so the measurements of association may be overestimated or underestimated.

Conclusion

This study found that abdominal pain reported by the parents, pain on abdominal palpation, and sepsis on admission to the emergency room are common. Acute appendicitis complicated by perforation leads to high morbidity in these patients by triggering longer antibiotic time, admission to PICU, and postoperative ileus. The diagnosis of acute appendicitis begins with clinical suspicion and good teamwork between the pediatrician and pediatric surgeon. Delayed diagnosis and low specificity of symptoms lead to appendiceal perforation. The use of diagnostic imaging should be individualized or based on the PAS. The most commonly used study for this population was abdominal ultrasound, and few patients underwent the risks of CT scanning.

Abbreviations

OR: Odds ratios; PAS: Pediatric appendicitis score; CT: Computed tomography; PICU: Pediatric intensive care unit; CRP: C-reactive protein; TAU: Total abdominal ultrasound; SIRS: Systemic inflammatory response syndrome; DHT: Dehydration; SSI: Surgical site infection.

Authors' contributions

All authors conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. The article has been

approved by all authors and has not been previously submitted in any journal for publication.

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Availability of data and materials

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Declarations

Ethics approval and consent to participate

This work took international and national regulations for research involving human subjects into account. It was also presented to and approved by the Human Research Ethics Committee of the FUCS-HSJ and is identified with approval number: 0154-2019. It does not require consent to participate.

Consent for publication

Yes, approved by the Human Research Ethics Committee of the FUCS-HSJ.

Competing interests

The authors declare that they have no competing interests.

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