Section: Surgery

Original Research Article

EVALUATION OF DIAGNOSTIC PERFORMANCE OF PAS IN CHILDREN OPERATED ON FOR SUSPECTED APPENDICITIS COMPARING CHILDREN < 4 YEARS OF AGE WITH CHILDREN > 4 YEARS OF AGE

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Abstract

Background: Appendicitis is the most common disease requiring abdominal surgery in children. However, the diagnosis of pediatric appendicitis is still a challenge, resulting in perforation and negative appendectomies, especially in girls and young children. Further, the pathogenesis of acute appendicitis is not known. The objective is to evaluate the diagnostic performance of PAS in children operated on for suspected appendicitis comparing children < 4 years of age with children > 4 years of age. **Materials and Methods:** A single, institution-based, retrospective study was conducted at a tertiary teaching hospital. All children 15 years of age who underwent appendectomy for suspected appendicitis or who were conservatively treated for an appendiceal abscess, from 2019 to 2022. **Result:** Young children had lower PAS despite more severe appendicitis. Gender differences were found, especially that preoperative imaging, negative appendectomies and operative complications were more common in girls. Two--trocar laparoscopic appendectomy (LA) resulted in shorter surgery time and fewer scars compared to conventional LA, and the rate of wound infection was low. No relation could be seen between different bacteria and the degree of inflammation, and there was a wide variation of abundances at phylum, genus and species level within each specific group of patients. **Conclusion:** PAS should be used with caution in children < 4 years. Diffuse symptoms in younger children lead to delay and to later diagnosis and more complicated appendicitis. Two--trocar LA is a safe and quick technique with a low rate of postoperative wound infections. LRG is a promising novel urinary biomarker for appendicitis in children. In most cases of appendicitis, a specific bacteria does not seem to be the primary event.

INTRODUCTION

There are several findings of drawings of what is thought to be appendix and appendicitis in early history, going back to the ancient Egyptians and further on to Hippocrates.[1,2] The first specific documentation is from 1492 when Leonardo da Vinci sketched the appendix (3) and in 1521 it was described in words by Berengario da Carpi (3). In 1543, Andreas Vesalius, a professor in anatomy, both illustrated and described the appendix, but naming it caecum (blind pouch).[1]

The appendix is involved in the digestion of cellulose in some mammals. Charles Darwin classified the appendix as a rudimentary organ in humans, emphasizing its vestigial nature, although very aware of its potency to cause illness: “not only is it useless, but it is sometimes the cause of death”.[2] However, data suggests that the appendix has been preserved in mammalian evolution for 80 million years or longer (19). Since Darwin, many theories have been put forward of the function of the human appendix, but in conclusion, none has been recognized. Two main theories are the safe house theory and the sampling theory.

Another theory is that the appendix acts as a sentinel sampling organ. This theory is supported by the fact that the appendix is part of gut-associated lymphatic tissue (GALT), the significant increase in lymphatic follicles from birth to a peak in adulthood, and its production of immunoglobulins.[3] This, together with the highly strategic position after small intestines and the ileocecal valve makes it a candidate for being responsible for sampling of antigens.[4] The history of appendicitis is somewhat diffuse, often due to not being specifically separated from other acute diseases in the abdomen and because of the confusion between cecum and appendix.[5] Probably, Jean Fernel, a French physician, mathematician and philosopher, presented the first true description of appendicitis in 1544.[5] But it was not until 1886 that the term appendicitis became commonly recognized when introduced by the Harvard professor, Reginald Fitz, who combined the Latin word, appendere, to hang upon, with the Greek suffix, -itis, relating to.[5] Interestingly, in his article "Perforating inflammation of the vermiform appendix, with special reference to its early diagnosis and treatment", Fitz noted that the disease may spontaneously resolve.[5]

The first appendectomy, that is, removal of the appendix and not just drainage, was performed in 1735 by Claudius Amyand.[6] The patient was an 11-year-old boy with a congenital scrotal hernia in which the appendix had become incarcerated; the incision was made through the hernia.[5] The patient recovered slowly but survived. The first abdominal appendectomy was performed in 1880 by the Scottish surgeon, Robert Lawson Tait.[7] In 1884, the work of Charles McBurney was published regarding the now famous point and incision.[7]

PAS was the first true score for pediatric appendicitis, published in 2002 by Samuel, and based on a prospective study of 1170 patients between 4 – 15 years of age. The study uses eight variables and ranges from 0–10 points. A child with a score > 6 has probable appendicitis. It was in the original study said to have a 100% sensitivity, 92% specificity, 96% PPV,and 99% NPV. PAS has been evaluated in children before, but not specifically in children < 4 years of age which were not an age group included in the original cohort from Samuel.[8]

MATERIALS AND METHODS

The patients were all treated at the tertiary teaching hospital associated with Maharaja Suheldev Autonomous State Medical College, Bahraich, India. The center covers an area of nearby 4 district with 5 million inhabitants with primary surgical care for children. If there is suspicion of appendicitis, the patients are referred for a pediatric surgery consultation.

The referral may be issued by either a pediatrician at the pediatric ER or directly from a general practitioner. The consultation is often carried out by a resident in surgery.

The study included all children who underwent appendectomy, from December 2019 through December 2022. After excluding patients who had undergone an appendectomy during operations for other diseases (N = 32), patients with interval appendectomy (N = 6), and patients lacking data for calculation of PAS (N = 30), a total of 122 patients were included in the study. There were 102 children > 4 years of age with a mean age of 10.5 years (± 2.9) and 62% males, and 20 children < 4 years of age with a mean age of 2.6 (± 0.7) and 55% males.

Statistical Analyses

Comparison of different parameters between two groups was carried out. A power analysis was carried out. Significance was set to a p-value < 0.05 in all Papers. Statistical Package for the Social Sciences (IBM SPSS Statistics), version 22, was used for the statistical calculations.

RESULTS

When comparing younger (< 4 years) with older (> 4 years) children, clear significant differences were seen regarding the presence of parent's and doctor's delay. The younger children were brought later to hospital and were also more often sent home from the ER without a planned reevaluation [Table 1]. Further, 15% of the younger children were not even triaged with abdominal pain. Younger children had a significantly higher rate of complicated appendicitis (75% and 33%, respectively) (p = 0.001).

Table 1: Comparison of parent's and doctor's delay, and severity of appendicitis between younger and older children operated on for suspected appendicitisValues presented as median (range) or as the absolute number and percentage of patients (n (%)).

> 4 years(N = 102)		< 4 years(N = 20)	p--value
Parent's delay(Time from onset of symptoms to seeking care, hours)	24 (2–144)	48 (12–168)	0.005
Triaged as acute abdomen	102 (100)	17 (85)	0.004
Doctor's delay(Sent home from pediatric ER without suspicion of appendicitis and no planned reevaluation)	6 (6)	5 (20)	0.017
Presumed diagnosis in patients with doctor's delay	Unspecified abdominal pain (4),constipation (2)	Gastroenteritis (2), pyelonephritis, constipation, virus infection.	
Complicated appendicitis(gangrenous, perforated, abscess)	34 (33)	15 (75)	0.001
Negative appendectomy	7 (7)	3 (15)	0.211

When comparing symptoms between the two age groups, fever was more common in the younger child (80% and 36%, respectively) ($p < 0.001$). None of the children < 4 years was described to have migration of pain, compared to 48% of the older children ($p < 0.001$). Diarrhea was, after exclusion of patients with appendiceal abscess, still more common in younger children (20% and 5%, respectively) ($p = 0.039$). Despite the higher rate of complicated appendicitis, the children under 4 years were less likely to have tenderness in the RLQ (65% and 88%, respectively) ($p = 0.016$), and did not have a higher rate of peritonitis (50% and 52%, respectively). No differences between the two age groups were seen when comparing the presence of nausea/vomiting, anorexia, leukocytosis, neutrophilia, or symptoms of urinary tract infection.

Girls and boys taken to the operating room due to suspicion of appendicitis were compared regarding symptoms, findings at the abdominal examination, and results from routine blood tests. No significant differences were found except that boys more often had local peritonitis in the RLQ (61% and 51%, respectively) ($p = 0.042$).

Girls were more likely to have preoperative imaging (50% and 38%, respectively) ($p = 0.021$), but had a higher rate of negative appendectomy (Table 2). Despite no difference in time to operation, boys had a significantly higher rate of perforated appendicitis. Boys were also more likely to undergo open appendectomy. There was a trend towards laparoscopic appendectomy taking longer time in girls than in boys.

No difference was found when comparing length of hospital stay between boys and girls. Neither were any differences found when comparing postoperative pain treatment with regard to the number of patients receiving morphine, amount of morphine administered, or the use of NSAIDs or paracetamol. Finally, boys and girls received equally long postoperative treatment with antibiotics in cases of complicated appendicitis.

Girls had a significantly higher frequency of operative complications, and when sub-analyzed with regard to the operative modality, the significance was observed in open but not in laparoscopic appendectomy When comparing postoperative complications, no difference was seen between the genders.

Table 2: Preoperative radiology, severity of appendicitis, method of operation and surgery time in girls and boys operated on for suspected appendicitis Values presented as the absolute number and percentage of patients (n (%)), or as mean + SD (standard deviation).

Girls(N = 174)		**Boys (N = 234)**	**p--value**
Preoperative imaging	87 (50)	90 (38)	0.021
Ultrasound	72 (41)	80 (34)	0.148
Computed tomography	15 (9)	10 (4)	0.094
Grade of inflammation			
Negative appendectomy	33 (18)	17 (7)	0.005
Phlegmonous	82 (45)	137 (56)	0.032
Gangrenous	33 (18)	27 (11)	0.047
Perforated	19 (10)	44 (18)	0.043
Abscess	16 (9)	19 (8)	0.724
Method of operation			
Laparoscopic appendectomy (LA)	116 (67)	145 (62)	0.405
Open appendectomy (OA)	28 (16)	57 (25)	0.048
LA comverted to OA	30 (17)	31 (13)	0.274
Surgery time			
LA	62 + 23	57 + 21	0.056
OA	54 + 27	52 + 22	0.683
LA converted to OA	77 + 31	75 + 23	0.785

Table 3. Diagnoses at negative appendectomy and operative complications in girls and boys operated on for suspected appendicitisValues presented the absolute number of patients (n), or as the absolute number and percentage of patients (n (%)).

<table>
<tr><th colspan="2">Girls</th><th>Boys</th><th>p--value</th></tr>
<tr><td>Diagnoses at negative appendectomy</td><td>Unspecified abdominal pain (15), ovarian cyst rupture (5),
retrograde menstruation (4),
mesenteric lymphadenitis (3), pyelonephritis (2), terminal ileitis (2), pneumonia (1), constipation(1)</td><td>Unspecified abdominal pain (9), mesenteric lymphadenitis (2), omental torsion (2), terminal ileitis (1), infected urachal cyst (1), gastroenteritis (1), parasitic infection with Enterobius vermicularis (1)</td><td></td></tr>
<tr><td>Operative complications</td><td rowspan="4">12 (7)
6 (10)

6 (5)
Iatrogenic perforations (9),
diathermic injury (1), postoperative bleeding event that required reoperation (1),
intestinal injury (1).</td><td>4 (2)</td><td>0.015</td></tr>
<tr><td>Open appendectomy</td><td>1 (1)</td><td>0.016</td></tr>
<tr><td>Laparoscopic appendectomy</td><td>3 (2)</td><td>0.192</td></tr>
<tr><td>Type of complication</td><td>Iatrogenic perforations (3),intestinal injury (1).</td><td></td></tr>
</table>

Pediatric appendicitis score (I, II, IV)

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The pediatric appendicitis score (PAS) was compared between younger (< 4 years) and older children (> 4 years) and this was significantly lower in younger patients. The sensitivity when using a cut-off at > 6 points was low in both groups but significantly lower in the younger children. PAS was of no help for patients with doctor's delay . When comparing the mean PAS between girls and boys no difference was seen. The sensitivity and specificity was low in both groups at a cut-off at > 6 points and < 5 points, respectively, but girls had a significantly higher specificity (Table 3), PAS was prospectively evaluated in the 44 patients (22 with appendicitis, 22 with other causes of the abdominal pain) as a part of the study. PAS had a 90% sensitivity, 86% specificity, 87% PPV, and 90% NPV.

Table 4: Evaluation of the pediatric appendicitis score Values presented as median (range) or mean + SD (standard deviation). PAS: pediatric appendicitis score; PPV: positive predictive value; NPV: negative predictive value; ROC: receiver operating characteristic; AUC: area under the curve

PAPER I	> 4 years(N = 102)	< 4 years(N = 20)	p--value
PAS	7 (2–10)	5 (2–9)	0.005
PAS > 5 (%)	Sensitivity: 87 Specificity: 14 PPV: 93 NPV: 8	Sensitivity: 71 Specificity: 67 PPV: 92 NPV: 29	0.085
PAS > 6 (%)	Sensitivity: 71 Specificity: 14 PPV: 92 NPV: 3	Sensitivity: 41 Specificity: 100 PPV: 100 NPV: 23	0.018
PAS in patients with doctor's delay	5.5 (2–6)	4 (3–5)	0.317

Two-trocar LA had significantly shorter surgery time, even when excluding patients with surgical complications and negative appendectomies. No differences were seen between the two methods in surgical complications, or in the rate of wound infection, which was low in both groups (1%). Postoperative pain treatment did not differ between the two groups with regard to rate and total amount of morphine administered, NSAID administration, or doses of intravenously administered paracetamol.

Table 5: Comparison between two-- and three--trocar LA with regard to severity of inflammation, surgery time and complications values presented as mean + SD (standard deviation), or as the absolute number and percentage of patients (n (%)); LA: laparoscopic appendectomy

Two--trocar LA (N = 91)		Three--trocar LA (N = 168)	p--value
Degree of inflammation Negative appendectomyPhlegmonous GangrenousPerforated	21 (23) 56 (92) 9 (10) 5 (5)	19 (11) 114 (68) 21 (13) 14 (18)	0.023 0.341 0.682 0.462
Surgery time all included(min)	47 + 16	66 + 22	<0.001
Surgery time with negative appendectomies andpatients with surgical complications excluded(min)	46 + 16	65 + 20	<0.001
Excluded patients	23 (25)	26 (15)	
Surgical complications	2 (2)	7 (4)	0.501
Type of complication	Iatrogenic perforation (2)	Iatrogenic perforation (5), postoperative bleeding (1), diathermic injury (1)	
Wound infection	1 (1)	1 (1)	

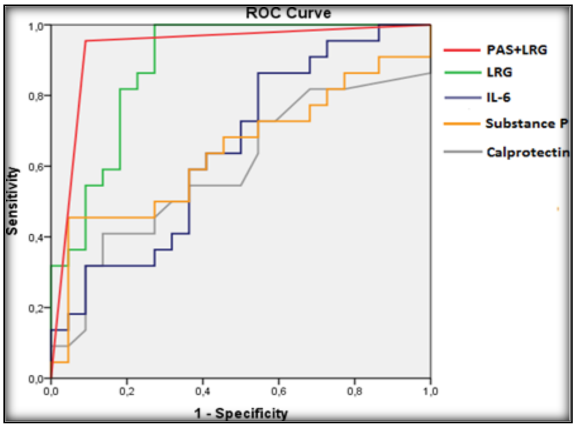

Figure 1: Diagnostic performance of novel urinary biomarkers in 44 children with suspected appendicitis ROC: receiver operating characteristic; PAS: pediatric appendicitis score; LRG: leucine--rich alpha--2--glycoprotein; IL-- 6: interleukin 6.

DISCUSSION

When studying the wide research field of pediatricappendicitis it almost feels as though the diagnosis and treatment of the disease are like a lottery, with pathogenesis, diagnostic methods, and treatment all mixed up in a big tombola. Fortunately, this is most often not the case when managing the child with suspected appendicitis in the clinical setting.

However, not forgotten are all the children who did not present with a typical, straightforward appendicitis, and did not go home the next day after an uneventful appendectomy: The nine-year-old girl with complications to a negative appendectomy, or the four-year-old boy misdiagnosed with pyelonephritis and two days later operated on due to intestinal obstruction and perforated appendicitis. the misdiagnosis and morbidity mentioned above was confirmed. The younger children (< 4 years) had severer appendicitis and longer hospital stay. As seen in other studies, we saw a significant rate of both parent's and doctor's delay in the younger children.[9,10]We also saw that 15% of the young children were not even triaged with "acute abdomen", giving further evidence of the diffuseness of the symptoms. Finally, the rate of diarrhea was significantly higher among the young children, which of course may confuse the clinician.

The main purpose of the study was to evaluate the pediatric appendicitis score (PAS) in younger children to see if this could be an aid for the clinician. The original study describing PAS did not include children < 4 years of age 8, and no study had evaluated the score between younger and older children before. Unfortunately, the results showed that PAS was not helpful; the younger children had a lower mean score, despite the severer appendicitis. The sensitivity of this test was low in both age groups, and this was despite the evaluation of children operated on for suspicion of appendicitis.

The main disadvantages of the study were that it was retrospective, and that the cohort consisted of children who were appendectomized, instead of children with abdominal pain and suspicion of appendicitis. This of course, makes it hard to interpret the predictive values.

One speculation is that no present clinical prediction score really aids the diagnosis of appendicitis in the young children. Looking at the parameters in the different scores,[11,12] one can see the problem: pain migration is of course difficult for the young child to describe, intensity of pain hard to evaluate in the young child, peritonitis less evident in the abdomen with less developed muscles, and nausea/vomiting and anorexia frequently seen in young children with extra abdominal disease. One might conclude that other diagnostic modalities are probably the right way to go when evaluating the young child with abdominal pain. Maybe we should be more liberal with ultrasound? Another possibility is the development of accurate biomarkers.

It is probably hard to lower the perforation rate among young children to levels on a par with that of older children, since most perforations occur prehospitally.[13] Hence, the main part of perforations could be speculated to be due to parent's delay. However, perforated appendicitis is missed in hospital as well, and with improved diagnostics this doctor's delay can be eliminated.

CONCLUSION

PAS seems to be a scoring system for pediatric appendicitis, especially in younger children, and was of no help in the children with parent's delay. Parent's and doctor's delay were contributing factors in the delayed diagnosis of appendicitis in younger children, which may explain the higher rate of complicated appendicitis in this group. Parameters in patient history, symptoms, and abdominal examination are more diffuse in younger children.

REFERENCES

1. Collins D. Historic phases of appendicitis. Ann Surg. 1931;94(179-96).
2. Darwin C. The descent of man and selection in relation to sex, in Charles Darwin, The origin of species and The descent of man (combined volume). J Anat Physiol. 1871;5(Pt 2):363–72.
3. Spencer J, Finn T, Isaacson PG. Gut associated lymphoid tissue: a morphological and immunocytochemical study of the human appendix. Gut. 1985;26(7):672–9.
4. Gebbers JO, Laissue JA. Bacterial translocation in the normal human appendix parallels the development of the local immune system. In: Annals of the New York Academy of Sciences. 2004. p. 337–43.
5. Hamill JK, Liley A, Hill AG. Historical aspects of appendicitis in children. ANZ J Surg. 2014;84(5):307–10.
6. Milanchi S, Allins AD. Amyand's hernia: History, imaging, and management. Hernia. 2008;12(3):321–2.
7. Thorén L. Appendicitenshistoria under 400 år 1521–1921. Nordisk MedicinhistoriskÅrsbok; 1989.
8. Samuel M. Pediatric appendicitis score. J Pediatr Surg. 2002;37(6):877–81.
9. Alloo J, Gerstle T, Shilyansky J, Ein SH. Appendicitis in children less than 3 years of age: A 28-year review. Pediatric Surgery International. 2004. p. 777–9.
10. Addiss DG, Shaffer N, Fowler BS, Tauxe R V. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol. 1990;132(5):910–25.
11. Lintula H, Pesonen E, Kokki H, Vanamo K, Eskelinen M. A diagnostic score for children with suspected appendicitis. Langenbeck's Arch Surg. 2005;390(2):164–70.
12. Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med. 1986;15(5):557–64.
13. Andersson RE. The natural history and traditional management of appendicitis revisited: Spontaneous resolution and predominance of prehospital perforations imply that a correct diagnosis is more important than an early diagnosis. World Journal of Surgery. 2007. p. 86–92.