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Appendicitis on Pediatric Patients: Current Evidence in Diagnosis and Treatment

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ABSTRACT

Appendicitis is a common surgical condition in pediatric patients, with a higher prevalence among males by 55 – 60%. The etiology is not definitively established, but luminal obstruction caused by stool, lymphoid hyperplasia, or parasites is a commonly cited cause. The classic presentation includes the gradual onset of periumbilical abdominal pain with migration to the right lower quadrant within 24 hours, fever, anorexia, nausea, and vomiting. However, infants and young children may present differently. Risk scores have been developed to improve the accuracy of diagnosis by using clinical symptoms, physical examination, and laboratory results. Ultrasound is the recommended imaging modality due to its low cost and avoidance of radiation, with reported sensitivity ranging from 72.5% to 94.8% and specificity of 95% to 99%, depending on the operator's experience. In young preschool-age children, acute appendicitis carries a higher risk of complications, including surgical site infections and abscesses. The risk of appendix perforation increases with delayed diagnosis. Treatment involves fluid resuscitation, pain control, antibiotics, and appendectomy. In cases of perforation, percutaneous drainage may be necessary. Hospital readmissions are often due to infection, bowel obstruction, or abdominal pain.

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INTRODUCTION

Appendicitis is a common surgical condition diagnosed in 1-8% of children evaluated in the emergency room. [(1)] The risk of developing this condition is up to 7 - 8%, with a higher incidence during adolescence. [(2)]

The appendix, ileum, and colon originate from the midgut and first appear at 8 weeks of gestation. Afterward, the cecum becomes fixed in the right lower quadrant as the gut rotates medially, determining the final position of the appendix. [(3)] It is considered a true diverticulum of the cecum and measures 6 to 9 cm. Its blood supply comes from the appendicular branch of the ileocolic artery, while its visceral innervation is from the superior mesenteric plexus and vagus nerve. [(3,4)] The appendix is located intraperitoneally and retrocecal, but it may be pelvic in about 30% of patients and retroperitoneally in 7%. [(3)]

Uncomplicated appendicitis is defined as an inflamed appendix with an intact wall. On the contrary, complicated appendicitis includes a hole in the appendix, a fecalith, formation of pus or abscess, accounting for around 30% of hospital admissions for pediatric patients. [(1)] This review aims to summarize current evidence on diagnosing and managing acute appendicitis in pediatric patients.

EPIDEMIOLOGY

The annual incidence of appendicitis among pediatric patients is estimated to be 83 per 100,000. [1] It's considered the fifth most common reason for hospitalization, with an incidence rate that has increased over the years, with the number of affected children ranging from 1 – 6 per 10,000 for those younger than 4 years, and 19 – 28 per 10,000 for those between 4 to 14 years. [1,5]

Appendicitis is more prevalent among males than females by 55 - 60%, with a lifetime risk of 9% and 7% each. [6] The general risk of developing this condition is up to 7 - 8%, with a higher incidence during adolescence. [2] On the other hand, pediatric patients under six often have advanced disease due to nonspecific symptoms, causing delayed diagnosis in up to 57% of the cases. [7]

PATHOGENESIS

The appendix is frequently situated in the right lower quadrant of the abdomen, coming from the posteromedial aspect of the cecum, below the ileocecal junction, and with a retrocecal location in 60% of the cases. [4]

The etiology of acute appendicitis has been studied over time; however, no definitive explanation has been established. [1,6] The most cited cause of this condition describes a luminal obstruction caused by stool, lymphoid hyperplasia, or parasites that increase intraluminal pressure, causing a vascular compromise with mucosal ischemia and bacterial invasion leading to a possible perforation commonly after 72 hours. [1,8] This bacterial overgrowth includes *Escherichia coli*, *Bacteroides fragilis*, *Peptostreptococcus* species, and *Pseudomonas* species. [8] However, *Enterobius vermicularis* and *Ascaris lumbricoides* may also cause direct obstruction of the appendix. [9]

On the other hand, recent theories include genetic factors and environmental influences that should explain the risk of having appendicitis being three times higher in patients with a positive family history. [6,8]

CLINICAL PRESENTATION AND DIAGNOSIS.

The classic presentation includes the gradual onset of periumbilical abdominal pain with migration to the right lower quadrant, usually within 24 hours. Pediatric patients may also present with fever, anorexia, nausea, vomiting, and diarrhea. [1, 2] However, infants and young children may not present this pattern at all. Therefore, a physical examination is important to establish a diagnosis. [1] An experienced physician can diagnose acute appendicitis with over 90% accuracy. [6] Local tenderness at McBurney's point, situated approximately one-third of the distance along a line from the anterior superior iliac spine to the umbilicus, is the most reliable clinical sign of appendicitis. However, it could be less evident in patients with a retrocecal, retroileal, or pelvic appendix position. [10]

On the other hand, signs of peritonitis include involuntary muscle guarding, rebound tenderness, rovsing sign (palpation of the left lower quadrant causes right lower quadrant pain), obturator sign (pain caused by the flexion and internal rotation of the right hip), and iliopsoas sign (pain elicited by the right hip extension). [1] These last three have an estimated sensitivity of 16-44% and 86-98% specificity in diagnosis. [1]

The physical examination may be challenging for some pediatric patients due to the amount of pain. For this reason, The American Academy of Pediatrics recommends using early analgesia to make the examination and imaging more comfortable for patients. [11,12] Previously, analgesia was discouraged due to the mistaken belief that it would mask symptoms and cause surgeons to overlook signs of acute appendicitis. Nowadays, the evidence indicates that diagnosis is not significantly impacted in patients who receive pain control. [12]

Laboratory findings.

Although there's no known biomarker specific to appendicitis, the white blood cell count (WBC), absolute neutrophil count (ANC), and the c-reactive protein (CRP) are used to differentiate appendicitis from other inflammatory conditions. [1,2,6] These values can be more helpful to the diagnosis in combination with imaging and clinical presentation. It is crucial to note that laboratory exams should not be used solely to exclude or diagnose appendicitis. [2]

Risk scores.

Over time, risk scores have been developed to enhance the diagnostic accuracy of acute appendicitis by using clinical symptoms, physical examination, and laboratory results. The most used scores include The Alvarado score, Pediatric Appendicitis Score (PAS), and Pediatric Appendicitis Risk Calculator (pARC). [1,6]

The Alvarado Score is a 10-point scoring system based on clinical signs and symptoms such as migration of pain, anorexia, nausea, and vomiting. [Table 1] This system recommends discharging patients with a score of 1-4, monitoring those with a score of 5-6, and considering surgical intervention for those with a score of 7 or higher. [1]

ALVARADO SCORE

Parameter	Score
Signs	
Right lower quadrant tenderness	2
Increase in temperature (> 37.5 °C)	1
Rebound tenderness	1
Signs	
Migration of pain	1
Anorexia	1
Nausea	1
Signs	
Leukocytosis (>10,000/uL)	2
Left shift in WBC count (>75% neutrophils)	1

Table 1. Alvarado Score. Information retrieved from Alvarado A (1986) A practical score for the early diagnosis of acute appendicitis

On the other hand, the PAS is a tool that uses history, physical examination, and laboratory findings to categorize the risk of appendicitis on a 10-point scale. [1,13] [Table 2] The frequency of appendicitis in pediatric patients with PAS <2 to 3 points is about 2%, PAS 3 to 6 points up to 48%, and PAS >7 points with 96%. [13]

The Pediatric Appendicitis Risk Calculator (pARC) has been recently developed, and it includes age, sex, temperature, nausea/vomiting, pain, duration, location, pain with walking, migration of pain, guarding, WBC, and ANC. [1,14] This score system ranges from 0% to 100% probability of acute appendicitis. However, to use the pARC, sophisticated calculations must be programmed and integrated into an electronic health record. [1,14]

Although using these scores alone does not appear to be sufficient to determine the diagnosis of appendicitis, they are essential tools to identify children who may benefit from diagnostic imaging and surgical consultation. [1]

PEDIATRIC APPENDICITIS SCORE

Parameter	Score
Migration of pain	2
Anorexia	1
Nausea / Vomiting	1
Right lower quadrant tenderness	2
Pain with cough, percussion or hopping	1
Fever >38°C	1
Leukocytosis (>10,000/uL)	1
Polymorphonuclear neutrophilia (75 %)	1

Table 2. Pediatric Appendicitis Score (PAS). Information retrieved from: Samuel, M. Pediatric appendicitis score.

Imaging.

Ultrasound is the study the American College of Radiology recommended to diagnose acute appendicitis in pediatric patients. [15,16] It is the imaging modality of choice due to its low cost and avoidance of radiation. [1,2,6] Reported sensitivity ranges from 72.5% to 94.8%, with a specificity of 95% to 99%, depending on the operator experience and sonographer. [1,3] Ultrasound findings that support the diagnosis of appendicitis include noncompressible tubular structure in the right lower quadrant, wall thickness of the appendix >2 mm, overall diameter > 6 mm, free fluid in the right lower quadrant, localized tenderness with graded compression, and the presence of a calcified appendicolith. [3]

Although ultrasound is the first-line imaging study, computed tomography is still performed in over 50% of pediatric patients, most at non-pediatric hospitals. [1] The CT scan has a sensitivity of 97% and a specificity of 99% with a positive predictive value of 98%. [2] However, one CT scan in a five-year-old increases the lifetime risk of radiation-induced cancer to 26.1 per 100,000 in women and 20.1 per 100,000 in men. [1] Therefore, its unjustified use cannot be ignored and should be avoided.

On the contrary, magnetic resonance can be helpful in cases of a non-visualized appendix on ultrasound with an overall sensitivity of 96.8% and specificity of 97.4%, with a negative appendectomy rate of 3.1%. [1,2] However, it is utilized less frequently due to its higher costs, potential need for sedation, and limited availability. [1,3]

DIFFERENTIAL DIAGNOSIS

Acute appendicitis may present with the classic clinical features. However, certain conditions have similar symptoms. Mesenteric adenitis is the most common differential diagnosis in pediatric patients. [17] This condition's etiology includes viral and bacterial gastroenteritis, inflammatory bowel disease, and lymphoma. [2] It is characterized by multiple enlarged lymph nodes in the right lower quadrant and mesentery. [15] Compared with acute appendicitis, mesenteric adenitis causes more prolonged symptoms with average WBC counts and C-reactive protein levels. [17]

Other conditions that can mimic acute appendicitis in pediatric patients include inflammatory bowel disease, constipation, intussusception, and omental infarction. [17] Henoch-Schonlein purpura, can also cause severe abdominal pain. [17,2] Additionally, genitourinary causes include pyelonephritis, nephrolithiasis, and ovarian torsion. [2] The presentation of genitourinary symptoms can mimic appendicitis, while appendicitis can also be accompanied by urological symptoms due to the topographic variations of the appendix and urogenital organs, causing in some cases bacteriuria, leukocyturia, proteinuria, and hematuria. [18] The presence of bacteriuria caused by appendicitis is more evident when the appendix is in a posterior position and after 48 hours when the degree of inflammation is severe. [19]

Therefore, it´s important to evaluate these urological symptoms correctly to avoid delaying the diagnosis of appendicitis.

TREATMENT

Management for uncomplicated appendicitis.

Uncomplicated appendicitis can be treated with antibiotics alone or with surgery. Over time, non-operative management has been studied, and results have shown that it is safe and effective for selected uncomplicated cases. [1] A common antibiotic regimen includes a combination of cephalosporin and nitroimidazole, such as metronidazole. Subsequently, penicillin with a beta-lactamase inhibitor or quinolones is recommended. [20] However, if the patient has abdominal pain for more than 48 hours, WBC over 18 000 uL, elevated C-reactive protein, appendicolith in an imaging study, or preoperative concern based upon clinical findings, it is recommended to perform an appendectomy. [17]

Preoperative and medical management.

After confirming the diagnosis, the initial steps involve fluid resuscitation and intravenous antibiotics. [2] For patients with mild pain, acetaminophen or ketorolac can provide good analgesia; patients with moderate to severe pain may require preoperative administration of intravenous opioids. [6]

The preferred treatment for appendicitis is an appendectomy, which should be done within 24 hours of diagnosis, either through laparoscopy or open surgery, to minimize the risk of perforation. [1, 20] In cases where perforation is identified before surgery, treatment options include surgical intervention or percutaneous drainage, followed by a delayed interval appendectomy. [21]

Antibiotic treatment is administered intravenously for one to three days, then transitioned to oral administration for five up to seven days. [20] It is important to note that the optimal duration of this antibiotic therapy remains uncertain and is typically determined based on the patient's clinical progress and the normalization of inflammatory markers. [20] Additionally, antibiotics are recommended to be administered perioperatively as a part of the treatment protocol for all forms of appendicitis. [20, 21] Using cefuroxime combined with metronidazole was associated with a significantly lower incidence of surgical site infections compared to amoxicillin/clavulanic acid, with a rate of 1.1% for those treated with cefuroxime plus metronidazole, in contrast to 2.8% for those receiving amoxicillin/clavulanic acid. [22]

Surgical management.

In 1894, McBurney described the traditional method for performing an appendectomy, involving an incision in the lower right quadrant of the abdomen that required splitting the muscle. [2] Nowadays, laparoscopic appendectomies have predominantly taken over the conventional open surgical approach. [2, 22] More than 91% of appendectomies are conducted laparoscopically, a substantial increase from the 22% rate in the late 1990s. [2,6]

Laparoscopic appendectomy is performed by inserting a camera through the umbilical area via a five or 10-mm port [6, 22], along with two lower abdominal ports or small incisions. The recommended technique includes ligating the base of the appendix close to the cecum and aspirating all purulent fluid. [1,2] In patients with complicated appendicitis, it is important to consider a search for an appendicolith in the pelvis or peri-appendiceal area when the appendix is perforated, and inserting a drain is recommended if there is an abscess. [1] Another option is single-incision laparoscopy, where instruments are introduced through the same umbilical port, and the appendix can be removed inside or outside the body. [22] It's important to emphasize that the overall outcomes are similar, and any lasting differences in appearance are typically minimal. [6]

In the past, appendicitis was considered a surgical emergency that required immediate intervention to prevent complications. However, evidence has shown that patients with uncomplicated appendicitis who receive antibiotics and undergo surgery within 24 hours of diagnosis do not face an increased risk of complications. In contrast, those with complicated appendicitis should be done earlier. [1,2]

Postoperative management.

Nowadays, treating uncomplicated acute appendicitis has evolved into an outpatient procedure at numerous children's hospitals, and the typical hospital stay for these patients typically ranges from 4 to 5 days. [2,6] Upon awakening, most patients can start with liquids and advance to solid food as tolerated. [22]

In cases of perforated appendicitis, the administration of antibiotics continues until patients are free of fever and can resume their regular diet. [22] Patients with perforated or gangrenous appendicitis require intravenous antibiotic therapy postoperatively. Most of these cases can be benefited by piperacillin/tazobactam or ceftriaxone and metronidazole. [2] It's important to acknowledge that returning white blood cell (WBC) counts to normal is not an absolute criterion for discharge. [2] Instead, if WBC remains elevated, additional oral antibiotics are recommended. [6]

Evidence suggests pediatric patients with uncomplicated appendicitis may be discharged within 24 hours post-surgery. However, the discharge timing should be based on the patient's clinical condition. [1,2]

OUTCOMES

In young preschool-age children, acute appendicitis is associated with a higher risk of complications, with an overall rate of 10% to 15%. [6, 21, 22] Postoperative complications may include surgical site infections, such as wound infections and intra-abdominal abscesses. [22] The frequency of these complications varies between open appendectomy, with an overall complication rate of 11.1%, and laparoscopic appendectomy, 8.7%. [21] Patients with uncomplicated appendicitis have a risk of surgical site infection or abscess of 1 to 5%; on the contrary, cases with complicated appendicitis may experience surgical site infection, bowel obstruction, or unplanned hospital re-admission in up to 55% of the cases. [23]

The risk of appendix perforation within 36 hours ranges from 16% to 36%, and perforation increases by 5% for every 12-hour delay. [22] This emphasizes the critical importance of a timely diagnosis and adequate treatment. Additionally, it's noteworthy that <1% of patients require a second surgical operation, except those undergoing interventional radiology drainage for managing abscesses. Postoperative intra-abdominal abscesses develop in 15-20% of children with perforated appendicitis and 1% of cases involving non-perforated appendicitis. [6]

Regarding hospital readmissions, 5-10% are due to infection, bowel obstruction or ileus, and pain. [6] However, when appendicitis progresses to perforation, it is associated with higher morbidity and mortality rates than non-perforated cases. [6,21] The risk of mortality in cases of acute non-

gangrenous appendicitis is less than 0.1%, but in gangrenous cases, the risk increases up to 0.6%. [21]

CONCLUSION

Acute appendicitis is presented commonly among pediatric patients and is diagnosed through clinical presentation, physical examination, and imaging studies. Evidence has shown us the importance of a prompt diagnosis for reducing life-threatening complications. The physical exam plays an important role in diagnosis, changing the paradigm about using analgesia for patients difficult to examine. Nowadays, experts have developed several risk scores, such as the Alvarado score, Pediatric Appendicitis Score (PAS), and Pediatric Appendicitis Risk Calculator (pARC), that can improve the accuracy of diagnosis and save time.

The recommended treatment for appendicitis involves administering fluids, pain relief, antibiotic therapy, and early surgery. There is evidence about using conservative management in selected cases of uncomplicated appendicitis; however, it depends on the evolution of the patient, and it requires close monitoring. On the contrary, an appendectomy can be performed by open surgery or laparoscopically with faster recovery time and fewer complications. After surgery, it is recommended to complete antibiotic therapy for up to seven days, depending on the clinical progress. The prognosis for pediatric patients with uncomplicated acute appendicitis is excellent, with low rates of morbidity and mortality.

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