



Acute Appendicitis in Pediatrics: Clinico-Histopathological Perspectives on a Disease with Many Faces

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التهاب الزائدة الدودية الحاد عند الأطفال: منظورات سريرية ونسجية مرضية حول مرض ذي أوجه متعددة

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Abstract:

Background: Appendicitis is a common condition in childhood and adolescence that frequently requires urgent surgical intervention. For almost two centuries appendicitis has been recognized as a medical problem with a surgical solution. Currently the appendix can be removed with a minimally invasive procedure. The present study aimed to study the incidence of various parameters regarding appendicitis in pediatric age group. Objective: To evaluate the incidence and peaks of age, the most common symptoms, the ability to diagnose the disease and the post-surgery outcomes. Methods: This retrospective study was conducted during March and April 2024 It included cases attending Pediatric Hospital, Department of Surgery, Benghazi. Results: The peak of age was (11-15), males outnumber the females, abdominal pain was the most common presentation and blood leukocytosis is not correlated with degree of temperature. Conclusion: Incidence of acute appendicitis is higher in male gender pediatric age group and the diagnostic modality are always accurate for confirming the diagnosis.

Keywords: Appendicitis, Histology, Surgery, Pediatrics.

الملخص:

التهاب الزائدة الدودية هو حالة شائعة في مرحلة الطفولة والمراهقة والتي تتطلب في كثير من الأحيان التدخل الجراحي العاجل. منذ ما يقرب من قرنين من الزمان، تم الاعتراف بالتهاب الزائدة الدودية كمسكلة طبية لها حل في الوقت الحالي، يمكن إزالة الزائدة الدودية بإجراءات جراحية طفيفة. تهدف الدراسة الحالية إلى دراسة مدى حدوث عوامل مختلفة تتعلق بالتهاب الزائدة الدودية في الفئة العمرية للأطفال. الهدف: تقييم نسبة حدوث وذروة العمر والأعراض الأكثر شيوعاً والقدرة على تشخيص المرض ونتائج ما بعد الجراحة. طرق البحث: أجريت هذه الدراسة بأثر رجعي خلال شهري مارس وأبريل 2024م وشملت الحالات المترددة على مستشفى الأطفال، قسم الجراحة، بنغازي. النتائج: ذروة العمر كانت (11-15)، عدد الذكور يفوق عدد الإناث، وكانت آلام البطن هي العرض الأكثر شيوعاً، كما أن زيادة عدد الكريات البيضاء في الدم لا علاقة لها بدرجة الحرارة. الاستنتاج: إن معدل الإصابة بالتهاب الزائدة الدودية الحاد أعلى لدى الذكور من الجنسين في الفئة العمرية للأطفال والتشخيص باستعمال السونوگراف ليس دائماً دقيقاً.

الكلمات المفتاحية: التهاب الزائدة الدودية، أنسجة، جراحة، أطفال.

Introduction:

Appendicitis is among the most prevalent causes for visits to the emergency department in children, with men having a lifetime risk of 8.6% and women 6.7%, typically occurring during the second decade of life. While patients are generally diagnosed based on clinical signs, various scoring systems have been suggested to assist in making the diagnosis. Moreover, laboratory tests such as a complete blood count, absolute neutrophil count, and C-reactive protein (CRP) levels are frequently conducted. Additionally, imaging studies like ultrasound, CT scans, and MRI are performed to validate the diagnosis of appendicitis. (Syed, S., & Naji, H. 2021)

The division of acute appendicitis into two categories, complex appendicitis (also known as necrotizing/perforating) and simple appendicitis (also known as non-perforating/uncomplicated), has become widely accepted in recent years (Knaapen M et al. 2021).

Due to its ambiguous appearance and unusual symptoms, appendicitis is still difficult to diagnose, particularly in younger children. For emergency physicians, prompt and precise diagnosis of appendicitis is crucial due to the increased risks of misdiagnosis, delay, and perforation. (Kharbanda A. & Becker C. 2019)

Urgent appendectomy, a less invasive procedure with limited surgical and anesthetic risk, has historically been used to treat appendicitis (Nepomuceno H., Pearson E G. 2021).

Appendix Embryology:

The vermiform appendix develops alongside the midgut, starting in the fifth week of embryonic life. Initially, in the fourth week, the midgut herniates into the umbilical cord while upper and lower intestinal segments stay fixed by retention bands.

By the fifth week, counterclockwise intestinal rotation brings the midgut back into the abdomen, triggering histological differentiation. The appendix emerges histologically in the cecum around week 8.

At week 12, the cecum ascends by shortening the post-arterial gut and further rotating the intestine 270°, fusing mesentery to fix the ileum, ascending, and descending colon to the posterior wall. This stretches the colon, forming the cecum pouch from which the appendix buds near the ileocecal junction, reaching its final position (Constantin et al., 2023).

Appendix Anatomy:

The vermiform appendix, a tube-like diverticulum of the cecum, is typically 4.5 cm long in newborns and 9.5 cm long in adults. Neonates and babies have a larger, funnel-shaped base and a lower risk of luminal obstruction. At the age of one to two years and at the urogenital system's exterior orifices, it assumes the cylindrical adult shape. The vermiform appendix's tip is very variable in position, while its base, which is located on the posteromedial surface of the cecum near the intersection with its three taenia coli, is less likely to be. The appendicular tip is retrocaecal in 28–68% of cases, pelvic in 27–53%, subcaecal in 2%, anterior or preileal in 1%, inside the hernial sac in 2%, in the right upper quadrant in 4%, and in the left upper and lower quadrants in less than 0.1% of cases (H. H. Almaramhy, 2017).

The Histological Structure:

The appendix is composed of the four layers, characteristic of the gastrointestinal tract, mucosa, sub-mucosa, muscularis externa and serosa. Lymphoid follicles are initially present in the lamina propria of mucus, but they later become large and extend into the sub mucosa. Muscle coat consists of outer longitudinal layer and inner circular layer. Outer most is serous coat. (Bharti JP 2016)

1. Mucosa:

- Simple Columnar Epithelium - neither villi nor plicae circularis are present.
- Few short intestinal crypts.
- Few goblet cells: secrete mucus for lubrication.

- Lamina propria: comprises almost the entire mucosa. Nodules (fill the lamina propria) They are part of gut-associated lymphoid tissue (GALT), which functions in immunologic defense. Germinal centers in these nodules are sites of B-lymphocyte production.
 - Plasma cells, lymphocytes, eosinophils and macrophages are present
 - M (Micro-Fold Cells) - cover nodules and have a lower profile than absorptive cells.
2. **Submucosa:** A layer of loose connective tissue that surrounds the mucosa filled with Lymph follicles, and lymphatic nodules.
 3. **Muscularis Externa:** Two orthogonal layers of smooth muscle (inner circular and outer longitudinal).
 4. **Serosa:** A thin layer of collagenous connective tissue containing fibrocytes and macrophages and a network of elastic fibers covers the outer surface of the appendix (Sorenson, R.L. & Brelje, T.C. 2014) (Figure 2, 3).

Epidemiology:

From birth to age four, the annual rate of acute appendicitis rises from one to six per 10,000 to 19–28 per 10,000 for children under the age of 14. The lifetime risk is nine percent for males and seven percent for females, with a peak incidence occurring between the ages of eleven and twelve. Less than 5% of occurrences of appendicitis occur in children under the age of five. These younger children are more difficult to diagnose due to their relative rarity, as evidenced by a higher incidence of perforated appendicitis. With rates of about 100% at one year of age, 50–69% at five, and more inconsistently reported but often less than 30% in older children, the rate of perforation decreases with age.

African-American and Hispanic children in the US have greater incidence of perforated appendicitis, according to recent studies. While there may be ethnic differences in the way care is delivered, these discrepancies in rates were not solely due to care delays and may indicate that various populations had different paths to perforation (Podany AB and others, 2017). Numerous studies from various geographical places have observed seasonal variation in the prevalence of acute appendicitis. Summertime brings higher temperatures and more humidity, which raises the risk of appendicitis. It is still unknown if the pathophysiology of appendicitis is directly influenced by temperature and humidity, or if the relationship is due to seasonal variations in air pollution or a rise in gastrointestinal illnesses over the summer (A. Fares, 2014).

Etiology and Pathophysiology:

The exact pathogenesis of acute appendicitis is multi factorial, and it is still unclear. But it is irrefutable that obstruction of the lumen is the usually present. In pre-school children this obstruction is usually due to lymphoid hyperplasia and less likely due to fecolith, as the appendix contains an excessive amount of lymphoid tissue in the submucosa which increase in size and number with growing age, reaching maximum in number and size during teenage with a higher possibility of developing acute appendicitis (Almaramhy, H. H. 2017).

Faecoliths are formed by over layering of calcium salts and fecal debris on the inspissated feces within the lumen of the vermiform appendix. Luminal obstruction with continuous secretion and stagnation of fluids and mucus from epithelial cells result in increased intra-luminal pressure and distension of the appendix. Intestinal bacteria within the appendix multiply, and the edematous wall precipitates bacterial invasion. (5) Increased abundance of anaerobic bacteria from the phylum Fusobacteria and a reduced abundance of Bacteroides species was found by 16 s ribosomal RNA sequencing in appendiceal specimens from cases of pediatric appendicitis. Also, the resulting compromise of the blood supply, decreased venous return, and eventually thrombosis of the appendicular artery and vein aggravates the inflammatory process, resulting in ischemia, necrosis, gangrene, and perforation (Podany AB et al. 2017).

Signs and symptoms of the disease:

Although abdominal pain is the most common presenting symptom for children in the emergency department, the diagnosis of appendicitis remains a challenge, especially in younger children, due to a nonspecific presentation and atypical symptoms. Examples of differences in signs and symptoms of acute appendicitis, by age, are reviewed in (Table 1) (Becker C, Kharbanda A. 2019).

Table (1): Signs and Symptoms of appendicitis

Age Group	Historical Features	Examination Findings
Infancy	Vomiting, diarrhea, irritability, fever, unusual use of right hip	Temperature elevation, diffuse abdominal tenderness
Preschool	Abdominal pain, fever, vomiting, "hamburger sign," vomiting followed by pain	Right-lower-quadrant tenderness more often than diffuse tenderness

School age and adolescence	Periumbilical pain that localizes to right lower quadrant, associated with nausea, vomiting, anorexia	Right-lower-quadrant tenderness, +/- diffuse tenderness, guarding, rebound (more likely following perforation)
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The diagnosis of appendicitis is usually made using some combination of clinical examination skills, history-taking, laboratory analysis, and imaging studies. It is important to keep the age of the patient in mind while obtaining history and performing the physical examination. Patients may present with pain to different sites based upon the location of the appendix.

Classic signs of appendicitis on physical examination are:

- Local tenderness with some rigidity of the abdominal wall at or near McBurney point (the point over the right side of the abdomen that is one-third of the distance from the anterior superior iliac spine to the navel. This point roughly corresponds to the most common location of the base of the appendix where it is attached to the cecum.)
- Rovsing sign - pain in the right lower quadrant on palpation of the left side.
- Obturator sign - pain on internal rotation of the right hip.
- Iliopsoas sign - pain on extension of the right hip, which is found in retrocecal appendicitis (Becker C, Kharbanda A. 2019)

The Pediatric Appendicitis Score (PAS) is a tool that utilizes history, physical examination, and laboratory results to categorize the risk of appendicitis in children with abdominal pain as shown in Table 2 (Samuel M. 2002).

Table (2): Pediatric Appendicitis Score

Item	Score
Anorexia	1
Nausea or vomiting	1
Migration of pain	1
Fever > 100.5°F (38°C)	1
Pain with cough, percussion, or hopping	2
Right-lower-quadrant tenderness	2
White blood cell count > 10,000 cells/mcL	1
Neutrophils plus band forms > 7500 cells/mcL	1
Total	10 points

Treatment of acute appendicitis:

A surgical consultation is recommended for a youngster receiving an appendicitis workup. In order to get ready for the operating room, the patient should be maintained NPO. The patient should begin receiving IV fluids if they are found to be dehydrated. Pain should be managed as necessary, and the patient should be regularly reevaluated. For individuals with appendicitis, antibiotic prophylaxis is advised to lower the risk of wound infection and intra-abdominal abscess development (Kharbanda A. & Becker C. 2019).

Aims of the study:

In this study we aim to:

1. Find out the incidence and peak of age of acute appendicitis in pediatric age group.
2. Find out the sex distribution
3. Analyze the incidence of presenting symptoms, fever, abdominal pain and vomiting.
4. Analyze the level of leukocytosis and their correlation with the symptoms.
5. Analyze the ability to diagnose the disease clinically and using imagery.
6. Analyze the outcomes post the surgical treatment.
7. Observe the histomorphology for the available specimens.

Materials and Methods:

The study was conducted in The Pediatric Hospital, department of surgery, City of Benghazi – Libya. It included the admitted cases complaining of acute abdominal pain that most likely diagnosed as (acute appendicitis). The study period was two months, March and April 2024. Information regarding cases were retrospectively gathered from the patents archives with respect to privacy. A total number of 84 cases. The data analyzed with the next consideration: age, sex, symptoms including Fever (Recorded Temperature), abdominal pain, vomiting, and level of blood leukocytosis. Confirming the disease clinically and confirming the disease by imaging, lastly whether the operation faced complications or not.

Statistical analysis: The whole data were evaluated statistically by using SPSS which has also been applied along with Microsoft word to make tables, graphs, pie diagrams, etc. The clinical data so received were evaluated. A comparison with other similar studies was done.

Results:

A total number of 84 cases included in the study, over period of two months. 50% of the cases between (11-15) years old (peak). The mean age was 10 years, with maximum 15 years and minimum 2 years old as presented in Table 3 and 4.

Descriptive Statistics (Age Peaks):

Table (3): Frequency and peak of age

		Frequency	Percent %	Valid Percent	Cumulative Percent
Valid	1-5	5	6.0	6.0	6.0
	6-10	37	44.0	44.0	50.0
	11-15	42	50.0	50.0	100.0
	Total	84	100.0	100.0	

Descriptive Statistics (Age Deviations):

Table (4): Minimum, maximum and mean age

	N	Minimum	Maximum	Mean	Std. Deviation
Age	84	2.0	15.0	10.179	2.5467
Valid N (listwise)	84				

In this current study, there was male predominance, male patients were 63 (75%), while females were 21(25%) as presented in Figure 1.

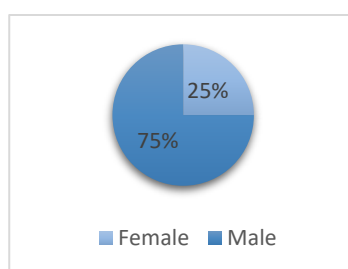


Figure (1): Sex distribution of the cases

In this study the maximum recorded temperature in degree Celsius was 39.5, while the minimum temperature was 35, Mean of temperature 37.08. as presented in Table 5).

Descriptive Statistics (Temperature):

Table (5): Maximum, minimum and Mean of recorded temperature

	N	Minimum	Maximum	Mean	Std. Deviation
fever To	84	35.00	39.50	37.0857	.72430
Valid N (listwise)	84				

Regarding other symptoms, abdominal pain was predominant, 84 cases (98.8%), not present in 1 case (1.2%) as shown in Table 6.

Descriptive Statistics (Abdominal Pain):

Table (6): Incidence of abdominal pain

		Frequency	Percent %	Valid Percent	Cumulative Percent
Valid	False	1	1.2	1.2	1.2
	True	83	98.8	98.8	100.0
	Total	84	100.0	100.0	

In this study the of incidence of vomiting was 69 (82.1%) the rest of the cases presented without vomiting 15 (17.9%) as illustrated in Table 7.

Descriptive Statistics (vomiting):

Table (7): Incidence of vomiting

		Frequency	Percent %	Valid Percent	Cumulative Percent
Valid	False	15	17.9	17.9	17.9
	True	69	82.1	82.1	100.0

	Total	84	100.0	100.0	
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With absolute percentage the diagnosis of appendicitis was confirmed clinically after examination in all of the cases 84 (100%). While confirmed by imaging in 76 (90.5) % of the cases as illustrated in Table 8 and 9.

Descriptive Statistics (Clinical examination):

Table (8): Clinically confirmed diagnosis

		Frequency	Percent %	Valid Percent	Cumulative Percent
Valid	True	84	100.0	100.0	100.0

Descriptive Statistics (Ultrasound Imaging):

Table (9): Diagnosis confirmed by imaging

		Frequency	Percent %	Valid Percent	Cumulative Percent
Valid	False	8	9.5	9.5	9.5
	True	76	90.5	90.5	100.0
	Total	84	100.0	100.0	

The maximum level of blood leukocytes in (MI) was 26.5, the minimum was 4.9, mean level was 14.08 as outlined in Table 10.

Descriptive Statistics (WBC level):

Table (10): Maximum level of blood leukocytes.

	N	Minimum	Maximum	Mean	Std. Deviation
leukocytosis WBC (ml)	84	4.9	26.5	14.089	4.8907
Valid N (listwise)	84				

In this current study no correlation was found between the recorded temperature and leukocytosis level as outlined in Table 11.

Descriptive Statistics (Temperature vs WBC level):

Table (11): Relation between Temperature and WBC level

		fever To	leukocytosis WBC (ml)
fever To	Pearson Correlation	1	-.122-
	Sig. (2-tailed)		.270
	N	84	84
leukocytosis WBC (ml)	Pearson Correlation	-.122-	1
	Sig. (2-tailed)	.270	
	N	84	84

In this study, after confirming the diagnosis, 74 (88.1%) of the cases had surgery without complications, while 10 (11.9%) of the cases faced post-operative complications as shown in Figure 2.

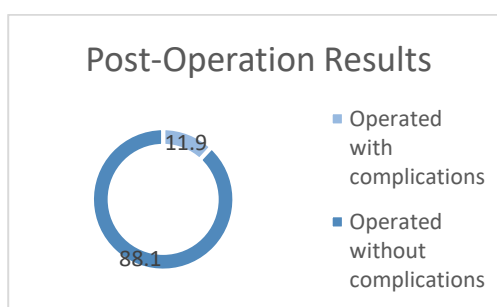


Figure (2): Incidence of operations with and without complications.

The Histopathological evaluation:

Various presentations observed histopathologically regarding the specimens obtained.

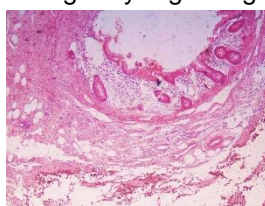


Figure (3): Section of acute appendicitis, showing ulcerated mucosa Edematous submucosa showed inflammatory cells,the serosa was loose and infiltrated by inflammatory cells (H&E X40)

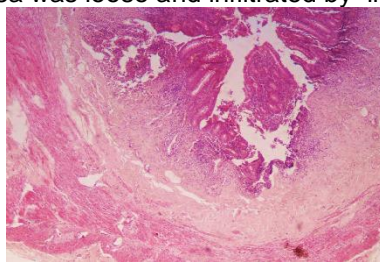


Figure (4): Section of Acute appendicitis ,with lymphoid follicular hyperplasia, Showed inflamed ulcerated mucosa with depleted glands and lymphoid follicles With loose inflamed fibrotic submucosa . (H&E X40)

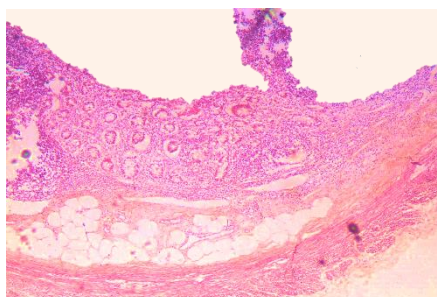


Figure (5): Section of Acute suppurative appendicitis, the lumen showed inflammatory cells. The mucosa is severely atrophic. All layers are infiltrated by neutrophils (H&E, X40).

Discussion:

In this current study regarding incidence of acute appendicitis in the pediatric age group, 84 cases of both genders, different ages below 16 were collected, their data arranged and analyzed.

The peak of age was (11-15) years old, with maximum 15 years and minimum 2 years old. The mean age was 10 years old. Those results strongly agree with a prospective observational study conducted at an academic urban teaching hospital by (Sivitz, et al. 2014), in the latter study, the mean age for children diagnosed with acute appendicitis was 10.8

Also another recent study conducted in Pediatric Surgery, a unit of the Department of General Surgery, Midnapore, West Bengal, India by (Ray et al 2023) reported (11-14) peak of age among children diagnosed by the same disease, which supports our results.

On the other hand, the results in this current study disagree with another study conducted by (Knaapen et al 2019) where the mean age for children diagnosed with acute appendicitis in one pediatric surgical center and two teaching hospitals in the Netherlands was 13 years old with minimum of 7 years.

In This study the male patients were more than the females, a predominance constituting (75%), while females were (25%). This finding is in strong agreement with so many studies, for example one retrospective descriptive cohort study was conducted at Mediclinic Parkview Hospital, Dubai, where the male gender outnumber the female according to Syed, S., & Naji, 2021. Also, Knaapen M. et al 2019 reported a male predominance.

There is variation in the reported incidence of acute appendicitis in male and female paediatric patients. (Alloo et al. 2004) and (Ngim et al.2014) reported a 60:40 male-to-female ratio in their study. It also correlated with results from a South African study which showed a male-to-female ratio of 1.74. (Moore SW, Schneider J.1995)

Regarding signs and symptoms of acute appendicitis, in this current study, most of the patients presented with fever, maximum recorded temperature in degree Celsius was 39.5 C, while in the study conducted by (Ray S. et al 2023) in India, fever as a symptom presented by only (38.9%) of the cases. Incidence of the abdominal pain in this study, mostly starting in the right iliac fossa, was (98.8%) a very high percentage in comparison to (66.7%) which reported also by (Ray et al 2023). In the clinical study conducted by (Knaapen M. et al 2019) the abdominal pain presentation in the emergency was (100%), totally consistent with our results.

The incidence of vomiting (88.1%) in this study, while (Sivitz, 2014) reported a higher presentation of voting (97.3%) and (Ray S. et al 2023) reported less presentation (86%)

Evaluating the cases by the clinical examination and the ultrasound imaging revealed incidence (100%) regarding the clinical signs, (90.5%) percentage of confirming the diagnosis by imaging. So

many studies discussed the reasons behind not visualizing all presented cases of appendicitis by ultrasound. According to (Sivitz, 2014) The appendix may not be visualized after rupture, replaced by extensive inflammation and abscess formation, still ultrasonography remains highly operator dependent, with frequencies of radiologist appendiceal visualization ranging from 22% to 98%. (Jo YH et al. 2010)

Taking in consideration the blood profile, we observed the maximum level of leukocytes in the lab reports was (26.5 x10³/mL) with mean value of (14). While in the study conducted by (Sivitz, 2014) the maximum leukocyte level was (14.9) and the mean was (10.9), values less than our results. We tried statistically to relate the recorded temperature to the level of blood leukocytes, the finding values were not correlated, an interesting finding that must be taken in consideration for further research.

Lastly evaluating the outcome of acute appendicitis after the surgery, (88.1%) of the cases operated without complications, with minimum days of admission, while (11.9%) of the operated cases ended up with complications. This results perfectly in agreement with current literature, the reported overall incidence of post-appendectomy complications in children varies between 5% and 15% according to (Markar et al., 2004) and (Fujishiro et al., 2020). The complications may vary and they include Intra-abdominal abscess, Incisional hernia, ARDS, Wound infection and Urinary tract infection.

Conclusion:

This study included 84 cases of acute appendicitis, all with emergency symptoms. We concluded that the most common age group were (11-15) with mean age of (10) years old. Male gender (75%) much more affected than the female gender (25%) We observed that analyzing the clinical symptoms revealed that the most common symptom is the RIF pain (98.8%) next followed by the fever, with maximum temperature of 39.5 C and lastly the vomiting (82.1%)

Revising signs of the appendicitis to confirm the diagnosis, we concluded that clinically it was confirmed in (100%) of the cases, but using imaging modality the diagnosis confirmed in (90.5%) only. In the blood profile, leukocytosis peaks reached 26.5 and their values were not related to the recorded temperature.

Regarding the surgery itself (88.1%) were smooth operations ended without complications, while (11.9%) of the cases faced post-operative complications.

In summary, the appendicular disease is common in teenage male children. Fever, vomiting, and rebound tenderness at the RIF are clinically significant findings. The imaging modality can sometimes lead to differential diagnosis other than appendicitis and appendectomy complication could always occur.

Recommendation:

In order to prevent pediatric appendicitis from going undiagnosed, it is advised not to undervalue a two-year-old child's persistent vomiting. This diagnosis can still be given to a 2-year-old child. Because rates of perforation are much higher in this age range, especially in a child with persistent symptoms, the danger of appendicitis should always be taken into account.

Additionally, a normal WBC count and negative pictures may not rule out the diagnosis. A normal WBC count may not rule out appendicitis. If the ultrasound is not conclusive and the symptoms persist, the emergency physician should order more imaging.

Data Availability: The corresponding author will provide all data sets collected for this work upon reasonable request.

Ethical Approval: This study was conducted following approval from the Faculty of Biomedical Science, Benghazi University, and the Department of Surgery, Pediatric Hospital, Benghazi. Data collection was performed only after obtaining the necessary institutional permissions.

Limitation of the study:

- This study designed to include 100 cases but due to lack of data and incomplete files, we managed to evaluate retrospectively 84 cases.
- Limitation and shortage in information regarding the specimens and histopathological reports of operated cases, unfortunately made it difficult for us to evaluate all specimens, nonetheless we managed to observe the histomorphology of some of the cases.

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