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Appendicitis: A medical serious condition - An updated review

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***Abstract*---Background**: Appendicitis, an inflammation of the appendix, is a prevalent medical condition with varied clinical presentations. It primarily affects individuals between 5 and 45 years of age, with a higher incidence in males. Although appendicitis is common in Western countries, its rates are increasing in developing regions. **Aim**: This updated review aims to explore the clinical presentations, diagnostic approaches, and risk factors of appendicitis, with a focus on typical and atypical signs, as well as the role of imaging in diagnosis. **Methods**: A comprehensive literature review was conducted, incorporating studies on appendicitis risk factors, diagnostic challenges, and therapeutic strategies. Data on clinical presentations, anatomical variations, and the effectiveness of imaging modalities were examined. **Results**: The review highlights that typical symptoms of appendicitis include migratory pain, anorexia, nausea, and fever, but atypical presentations are common in children, the elderly, and pregnant women. Delayed diagnosis in these groups can lead to complications such as perforation and peritonitis. Diagnostic imaging, including ultrasonography, CT scans, and MRI, plays a crucial role in identifying appendicitis, with CT scans being the gold

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standard. **Conclusion**: Appendicitis remains a diagnostic challenge in specific populations due to atypical presentations. Early imaging and prompt intervention are key to preventing complications. Advances in imaging and laparoscopic techniques offer improved outcomes, but further research is required to optimize diagnosis and treatment strategies.

Keywords---appendicitis, diagnosis, imaging, atypical symptoms, perforation, appendectomy.

Introduction

The appendix has undergone significant evolutionary variation, and its function has been a topic of discussion and investigation for many years [1]. Recent studies suggest that the appendix plays a role in the body's immune defense by supporting mucosal immunity and regulating the balance of intestinal microbiota [1]. Inflammation of the appendix, termed appendicitis, is a common condition [2]. The prevalence of appendicitis is approximately 100 cases per 100,000 individuals annually, with stable rates in Western countries and increasing incidence in developing regions. It primarily affects individuals between the ages of 5 and 45 years [3]. The rates of morbidity and mortality related to appendicitis differ based on age, with higher prevalence in children and adolescents, while mortality rates are elevated among the elderly [4]. Moreover, research indicates a slight male predominance across all age groups, with a lifetime incidence of 8.6% for men and 6.7% for women [2]. However, females have higher rates of appendectomies due to gynecological conditions that mimic appendicitis [5,6]. Population-based data also show that appendicitis is more prevalent among non-Hispanic whites and Hispanics, while less frequent in Black and other racial-ethnic groups [7,8]. Nevertheless, minority populations face a greater risk of perforation and complications [9,10], likely due to factors such as socioeconomic status, inadequate access to healthcare, and under-resourced medical facilities leading to delays in treatment [11]. Although appendicitis is generally easy to diagnose, it can be more challenging in pediatric, elderly, and pregnant populations, leading to delayed detection and more severe outcomes. While the exact cause of appendicitis remains unclear, it is considered multifactorial, influenced by both environmental and genetic factors [7]. The condition typically begins with luminal obstruction in the appendix, most often due to a fecalith. In children, lymphoid hyperplasia is another significant cause, driven by genetic predispositions or viral infections that stimulate excessive lymphoid tissue growth, blocking the lumen [7,12]. Other causes include foreign bodies, parasites such as Enterobius vermicularis (pinworm), and rare tumors, whether benign (mucinous) or malignant (adenocarcinoma, neuroendocrine) [13,14]. When mucus secretion in the appendix is obstructed, it leads to increased pressure, causing pain and distension due to the activation of visceral nerve fibers. This process results in the accumulation of mucus and bacteria, prompting an immune response as white blood cells infiltrate the lumen.

The severity of appendicitis inflammation plays a crucial role in determining the manifestation of signs, symptoms, and associated complications. As inflammation

progresses, edema and ischemia can result in thrombosis of nearby blood vessels, weakening the epithelial wall, and leading to necrosis, which may culminate in perforation and potentially life-threatening peritonitis. In some cases, the omentum may isolate the infection by forming a peri-appendiceal abscess or phlegmon. Alternatively, appendicitis can resolve on its own or with antibiotic treatment, potentially resulting in recurrent episodes or spontaneous recovery [7,13,15]. Research on risk factors for acute appendicitis remains limited. However, several factors may influence its occurrence, including demographic characteristics such as age, gender, family history, and environmental and dietary factors [6]. Studies indicate that although appendicitis can affect individuals across all age groups, it is more commonly observed among adolescents and young adults, with a higher incidence in males [16,17]. Similar to other conditions, a family history of appendicitis significantly increases the risk, with individuals who have a positive familial history being more susceptible to the disease [18]. Additionally, dietary factors such as a low-fiber diet, increased sugar intake, and inadequate hydration have been associated with a heightened risk of appendicitis [19-22]. Environmental factors, including exposure to polluted air, allergens, cigarette smoke, and gastrointestinal infections, have also been linked to the development of the condition [21,23-25]. Emerging evidence suggests a possible link between high temperatures and acute appendicitis, with dehydration potentially increasing susceptibility to the condition [21]. Moreover, there is an association between appendicitis and SARS-CoV-2, as studies indicate that patients presenting with acute appendicitis may have unrecognized COVID-19, prompting recommendations for testing such patients for the virus [26]. Research has also shown that individuals with psychiatric disorders who are prescribed high doses of antipsychotic medications face an increased risk of developing complicated appendicitis [27]. The classic presentation of appendicitis typically involves epigastric pain that originates near the umbilicus and migrates to the right lower quadrant of the abdomen, often accompanied by nausea, vomiting, anorexia, and a low-grade fever. However, atypical presentations can occur, which may delay diagnosis and treatment. Therefore, this review of the literature aims to consolidate data on both typical and atypical clinical presentations of appendicitis and assess their implications for diagnostic and therapeutic strategies. The **clinical presentation** of acute appendicitis varies depending on factors such as the patient's age, duration of symptoms, and anatomical variations in the appendiceal position [28]. These symptoms are typically classified into **typical** and **atypical** categories.

Typical Signs and Symptoms of Appendicitis

In children, the presentation of appendicitis varies across age groups [29]. It is rare and difficult to diagnose neonates and infants [30], who typically present with abdominal distension, vomiting, diarrhea, a palpable abdominal mass, and irritability [31]. On physical examination, they may appear dehydrated, hypothermic, and in respiratory distress, making the diagnosis of appendicitis challenging. Pre-school children up to the age of 3 often present with vomiting, abdominal pain, diffuse fever, diarrhea, difficulty walking, and stiffness in the right groin [32]. They may also show signs of abdominal distension, rigidity, or a palpable mass on rectal examination [12]. In children aged 5 years and above, classic symptoms such as migratory abdominal pain, anorexia, nausea, and

vomiting are more common, along with physical findings like pyrexia, tachycardia, decreased bowel sounds, and tenderness in the right lower quadrant [33]. Younger children often present with atypical symptoms that can mimic other disorders, leading to delayed diagnosis and increased risk of complications [12,34]. In adults, typical appendicitis symptoms include migratory pain in the right iliac fossa, anorexia, nausea, with or without vomiting, fever, and localized muscle rigidity or generalized guarding [35-39]. The classic symptom progression starts with vague periumbilical pain, followed by anorexia, nausea, and vomiting, before the pain migrates to the right lower quadrant and low-grade fever sets in [36,40]. Approximately 50-60% of patients experience peri-umbilical pain that localizes to the right lower quadrant within 24 hours, with 80-85% reporting anorexia, nausea, and fever [40]. Common diagnostic signs include McBurney's sign (tenderness in the right lower quadrant), Rovsing's sign (pain in the right lower quadrant upon palpation of the left lower quadrant), Psoas sign (pain on passive right hip extension), and Obturator sign (pain on passive right hip flexion with internal rotation) [28,36,40,41]. The sensitivity and specificity of these signs vary, ranging from 39-74% and 57-84%, respectively [40].

Atypical Presentations

The clinical presentation can differ based on the anatomical location of the inflamed appendix. Anatomical variations such as rectocecal/retrocolic (75%), sub-caecal pelvic (10%), and pre-ileal/post-ileal (5%) appendicitis can influence symptoms. Diarrhea and rectal or vaginal irritation may occur in some cases [1,40]. For example, a positive Psoas sign is often seen in patients with retrocecal appendicitis. In sub-caecal pelvic appendicitis, symptoms such as suprapubic pain, urinary frequency, and positive Obturator signs or rectal and vaginal tenderness may dominate the clinical picture. Patients with pre- and post-ileal appendicitis may experience vomiting and diarrhea due to irritation of the distal ileum. In elderly patients, the presentation may be atypical, with fewer classic signs like right lower quadrant pain, fever, anorexia, and vomiting [42]. Abdominal pain remains the most common symptom, with 75% experiencing lower quadrant pain, but other signs such as vomiting (27%), Rovsing's sign (10%), and McBurney's tenderness (9%) may be less frequently observed [41]. Elderly patients are more likely to present with rebound pain, guarding, or a palpable mass, which can complicate diagnosis. In addition, up to 54% of elderly patients may exhibit both rebound pain and tenderness [41]. Appendicitis is also the most common non-obstetric cause of emergency surgery during pregnancy. Pregnant patients typically experience periumbilical pain that shifts to the right lower quadrant, along with symptoms of anorexia, nausea, vomiting, and fever [43].

Severity and Diagnostic Indicators

The severity of acute appendicitis can be gauged through clinical findings such as rebound tenderness and rigidity in the right lower quadrant, which correlate with the degree of histopathological inflammation of the appendix [35]. Migration of pain to the right lower quadrant, anorexia, fever, and elevated white blood cell counts with increased polymorphonuclear leukocytes are all clinical indicators of severe appendicitis [35,44]. Sudden relief or a decrease in pain intensity may

signal appendiceal rupture, as pressure within the appendix decreases. A rigid abdomen on physical examination is a sign of perforation and should prompt immediate intervention to avoid complications [26,33]. In summary, appendicitis can present with a wide range of signs and symptoms depending on factors such as age, anatomical variation, and severity of inflammation. Typical symptoms are more likely in older children and adults, while younger children, elderly individuals, and pregnant women may show atypical features, which can complicate diagnosis and management.

Atypical Signs and Symptoms of Appendicitis

In some cases, appendicitis presents atypical signs and symptoms, such as left-sided abdominal pain, which may localize to the left upper quadrant. Although rare, this occurs in about 0.02% of the adult population, typically in individuals with conditions like gut malrotation or situs inversus [45]. Diarrhea is another atypical symptom of advanced appendicitis, particularly in patients with intra-abdominal abscesses [46]. In children, appendicitis can be challenging to diagnose due to vague symptoms, including pain and tenderness extending from the right upper quadrant to the right iliac fossa, often associated with arrested caecal descent of the appendix into a subhepatic position [47]. Adult males may show atypical symptoms such as severe right hemiscrotal pain that later becomes mild abdominal pain. Meanwhile, females might present with genitourinary complaints, including femoral region tenderness or a mass, accompanied by diarrhea [48,49]. In elderly patients, appendicitis can mimic a strangulated inguinal hernia and present with non-specific symptoms [50]. Pregnancy further complicates the clinical presentation. Pregnant patients may present with symptoms like gastroesophageal reflux, pelvic pain, indigestion, flatulence, dysuria, and altered bowel habits [43]. As pregnancy progresses, the appendix is displaced cranially, causing pain to manifest in the right upper quadrant (RUQ) [51], though right lower quadrant (RLQ) pain remains the most frequent presentation [52]. Diagnosing appendicitis in pregnancy is complicated by physiological leukocytosis and the masking of common signs like tenderness and guarding due to the distended abdomen [43].

Role of Imaging in the Diagnosis of Acute Appendicitis

Imaging modalities such as ultrasonography (USG), contrast-enhanced CT scan (CECT), and magnetic resonance imaging (MRI) are widely used in diagnosing acute appendicitis (AA). CECT is considered the gold standard for diagnosing AA, but USG is recommended as the first-line imaging technique, especially for children and adults. When USG findings are equivocal, a low-dose CECT scan is recommended to confirm appendicitis [67]. In high-risk cases, surgery may be advised without cross-sectional imaging in patients under 40, a recommendation that has sparked debate, as some clinicians advocate for routine CT scans before surgery due to their association with a reduced rate of negative appendectomies [68]. CT and MRI both demonstrate higher sensitivity and specificity than USG in diagnosing AA, although they are not recommended as first-line due to higher radiation exposure and costs. MRI is particularly useful for pregnant women, but USG remains the preferred initial modality. If MRI results are negative but clinical suspicion remains high, surgery is still recommended [55,71].

Role of Diagnostic Laparoscopy in the Diagnosis of Acute Appendicitis

Diagnostic laparoscopy is used in cases with atypical presentations, unclear imaging results, or persistent or worsening symptoms. It serves both diagnostic and therapeutic purposes, allowing for the accurate diagnosis and treatment of AA, reducing the risk of complications [55,72].

Differentiation Between Uncomplicated and Complicated Acute Appendicitis

Distinguishing between uncomplicated and complicated appendicitis is essential, as the treatment approach differs. However, no single diagnostic method reliably differentiates between the two. Clinical scoring systems and biochemical markers can help predict complicated appendicitis to some extent [63,73,74]. A CT scan can reveal findings associated with complicated appendicitis, such as extraluminal appendicolith, abscesses, or appendiceal wall enhancement defects. The presence of appendicolith is a notable predictor of the failure of non-operative management [75]. Additionally, a triad of CRP >60 g/L, WCC >12 × 10^9/L, and age >60 years has been associated with complicated appendicitis [76].

Management of Appendicitis
Non-Operative Management of Appendicitis

Non-operative management (NOM) aims to treat appendicitis with antibiotics, avoiding surgery. Early studies from the 1950s indicated successful treatment of appendicitis with antibiotics, particularly in cases where symptoms had been present for less than 24 hours [77-79]. More recently, NOM for uncomplicated appendicitis has seen renewed interest, with approximately 65% of cases treated successfully with antibiotics alone. However, studies such as APPAC and ACTUAA have reported varying success rates, with failure rates ranging from 11.9% to 39.1% [80-84]. While limited data exist on NOM for complicated appendicitis, it has shown success but is associated with increased readmission rates and prolonged hospital stays [85,86]. The 2016 Jerusalem Guidelines and EAES guidelines recommend appendectomy as the preferred treatment for acute appendicitis and caution against the routine use of NOM [87,88]. However, the 2020 Jerusalem Guidelines endorse NOM as a first-line treatment for uncomplicated appendicitis in both adults and children, albeit with careful counseling on the risk of failure [55]. Studies have shown higher rates of readmission and treatment failure with NOM, but the CODA trial found no significant difference in quality of life (QOL) between NOM and appendectomy [89-91]. Despite these findings, appendectomy remains the standard recommendation. There is no standardized antibiotic regimen for NOM. A recent meta-analysis suggests carbapenems as the optimal antibiotic choice for non-operative management [92]. In cases of complicated appendicitis with abscess or phlegmon, antibiotics and/or percutaneous drainage are recommended as the first-line treatment, with early laparoscopic appendectomy advised to reduce the risk of further interventions and readmissions [93-97]. Interval appendectomy is not recommended unless recurrent symptoms occur, especially in patients under 40. NOM is generally not recommended for elderly patients, obese individuals, or pregnant women due to increased risks [55].

Operative Management of Appendicitis

Surgical intervention remains the primary treatment for appendicitis, a practice first introduced by Reginald Heber Fitz in 1886 and refined by Mc Burney in 1889 with his muscle-splitting incision, now known as Mc Burney's incision [98-100]. Surgical techniques have since evolved from open appendectomy to laparoscopic approaches and, more recently, to single-incision surgery, endoscopic retrograde appendicitis therapy, and natural orifice transluminal endoscopic surgery.

Laparoscopic vs. Open Appendectomy

Open appendectomy was the standard surgical approach for acute appendicitis until laparoscopic appendectomy emerged in 1981, laparoscopic surgery was reserved for uncomplicated appendicitis due to concerns over potential intra-abdominal abscess formation in complicated cases. However, recent studies reveal no significant difference in abscess rates between laparoscopic and open procedures . Laparosince gained preference, offering benefits such as shorter hospital stays, fewer complications, lower rates of surgical site infections, and reduced readmissions . As a result, guidelines now adaparoscopic appendectomy in all patients, including those with complicated appendicitis . Laparoscopic Single-Incision Surgery sion laparoscopic surgery (SILA) was developed to improve the cosmetic outcomes of laparoscopic appendectomy. Studies comparing SILA to conventional multi-incision laparoscopic appendectomy (CLA) found no significant difference in complication rates, hospital stay, or post-operative pain . However, CLA demonstrated shorter operative times and reduce SILA was associated with better cosmetic results. Despite the cosmetic advantage of SILA, recent evidence recommends CLA over SILA as the standard approach .

Endoscopic Retrograde Appendicitis Therapy (ERAT)

Endoscopic retrograde appeerapy (ERAT) is a minimally invasive treatment for appendicitis that has shown success rates between 92.1% and 99.36%, with minimal complications . ERAT offers improved pain outcomes and shorter hospitalization compared to laparoscopic apffective in pediatric patients, with higher success rates than antibiotics alone . However, there is no consensus on the standard use of ERAT, and more research is needed to establish its role in treating apther methods.

Natural Orifice Transluminal Endoscopic Surgery (NOTES)

In 2008, the first successful appendectomy via the natural orifice transluminal endoscopic surgery (NOTES) technique was performed using a transvaginal approach . Various routes such as transgastric, transvesical, transcolonic, and transvaginal have been employed since then . While NOTES appendectomy can bas a standalone procedure or in combination with laparoscopic visualization (hybrid-NOTES), its routine use remaiprovide recommendations for its widespread adoption.

Management of Appendicitis with Atypical Presentation

Managing appendicitis with atypical presentations, such as in children, pregnant females, or elderly patients, can be particularly challenging . Diagnostic laparoscopy has proven effective in diagnosing and treating appendicitis, identifying alternative diagnoses, and preventing unnecessary surgeries . In children, it helps avoid unnecessary aing alternative conditions . For elderly patients, laparoscopic appendectomy is the preferred treatment due to the higher likelihood of complicated appendicit management is generally discouraged. Pregnant females can safely undergo laparoscopic appendut significantly increasing risks of fetal loss or preterm delivery . In cases with persistent symptoms despite normal imaging, diagnscopy is recommended .

Conclusion

Appendicitis continues to be a critical medical condition, with both typical and atypical clinical presentations posing challenges to timely diagnosis and treatment. While the classic symptoms—migratory abdominal pain, anorexia, nausea, and fever—are well recognized, atypical cases are common in vulnerable populations, including children, the elderly, and pregnant women. The diagnostic complexity in these groups often leads to delayed treatment, increasing the risk of complications such as perforation and peritonitis. Furthermore, variations in appendiceal anatomy, such as retrocecal and pelvic appendices, can obscure the clinical presentation and lead to misdiagnosis or unnecessary surgical interventions. The role of diagnostic imaging, particularly ultrasonography, CT scans, and MRI, has been pivotal in improving the accuracy of appendicitis diagnosis. Among these, CT scans are considered the gold standard due to their high sensitivity and specificity. However, concerns about radiation exposure, especially in children and pregnant women, make ultrasonography the preferred initial diagnostic tool, with MRI as an alternative in complex cases. Laparoscopy has also gained prominence as both a diagnostic and therapeutic tool, offering minimally invasive solutions with lower complication rates. In addition to diagnostic advancements, this review underscores the importance of understanding the multifactorial nature of appendicitis. Risk factors such as low-fiber diets, genetic predispositions, and environmental influences play significant roles in their development. Notably, recent studies suggest an association between appendicitis and COVID-19, highlighting the need for further research into the effects of viral infections on appendiceal inflammation. In conclusion, while appendicitis is generally manageable with early diagnosis and intervention, ongoing research into its atypical presentations, risk factors, and advanced diagnostic techniques is essential to enhance patient outcomes, especially in high-risk populations.

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التهاب الزائدة الدودية: حالة طبية خطيرة - مراجعة محدثة

الملخص:
الخلفية: التهاب الزائدة الدودية هو التهاب في الزائدة الدودية، ويُعد حالة طبية شائعة تختلف في مظاهرها السريرية. يؤثر بشكل أساسي على الأفراد الذين تتراوح أعمارهم بين 5 و45 عامًا، مع ارتفاع معدل الإصابة بين الذكور. ورغم أن التهاب الزائدة الدودية شائع في الدول الغربية، إلا أن معدلاته في تزايد في المناطق النامية.
الهدف: تهدف هذه المراجعة المحدثة إلى استكشاف المظاهر السريرية وطرق التشخيص وعوامل الخطر المرتبطة بالتهاب الزائدة الدودية، مع التركيز على العلامات النموذجية وغير النموذجية، ودور التصوير الطبي في التشخيص.
الطرق: تم إجراء مراجعة شاملة للأدبيات شملت دراسات حول عوامل خطر التهاب الزائدة الدودية، وتحديات التشخيص، واستراتيجيات العلاج. تم تحليل البيانات المتعلقة بالمظاهر السريرية، والاختلافات التشريحية، وفعالية وسائل التصوير .
النتائج: تُبرز المراجعة أن الأعراض النموذجية لالتهاب الزائدة الدودية تشمل ألمًا متنقلًا، فقدان الشهية، الغثيان، والحمى، ولكن الأعراض غير النموذجية شائعة بين الأطفال وكبار السن والنساء الحوامل. قد يؤدي التأخر في التشخيص لدى هذه الفئات إلى مضاعفات مثل الانثقاب والتهاب الصفاق. يلعب التصوير التشخيصي، بما في ذلك التصوير بالموجات فوق الصوتية، والأشعة المقطعية، والرنين المغناطيسي، دورًا حاسمًا في تشخيص التهاب الزائدة الدودية، مع اعتبار الأشعة المقطعية المعيار الذهبي.
الاستنتاج: لا يزال التهاب الزائدة الدودية يمثل تحديًا تشخيصيًا في بعض الفئات بسبب الأعراض غير النموذجية. يعد التصوير المبكر والتدخل السريع أمرًا أساسيًا لمنع المضاعفات. تقدم التطورات في تقنيات التصوير والجراحة بالمنظار نتائج محسنة، ولكن هناك حاجة لمزيد من البحث لتحسين استراتيجيات التشخيص والعلاج.
الكلمات المفتاحية: التهاب الزائدة الدودية، التشخيص، التصوير، الأعراض غير النموذجية، الانثقاب، استئصال الزائدة