UMJ Surgery **2022; 3: e10012201**

Review DOI: 10.5281/zenodo.10100894

Advancing appendicitis care: A comprehensive review of epidemiology, pathogenesis, and evolving treatment strategies

Carlo Firetto

Department of General Surgery of Hospital Santa Julia, Brazil

Correspondence
Carlo Firetto, Department of General Surgery of Hospital Santa Julia, Brazil. E-mail: carlofirettomd@gmail.com

Received: 30 October 2021
Revised: 30 October 2021
Accepted: 5 January 2022
Published: 7 January 2022

Keywords
⇒ Appendicitis
⇒ Diagnosis
⇒ Epidemiology
⇒ Non-surgical management
⇒ Pathophysiology
⇒ Treatment

ORCID ID of the author(s):
CF: 0009-0000-1872-4216

ABSTRACT

Appendicitis is the inflammation of the vermiform appendix and constitutes a significant global health challenge. Traditionally addressed through surgical intervention, the disease's complexity is now better understood, involving a wider array of both surgical and non-surgical management strategies. This review provides a detailed examination of appendicitis from its epidemiological distribution to its pathophysiological underpinnings, clinical presentation, diagnostic modalities, and treatment approaches. The global incidence of appendicitis suggests demographic and geographic disparities, with the highest prevalence among the younger population. Developed countries are witnessing a decline in incidence, attributed to dietary and hygienic improvements, whereas the trend is static or rising in developing regions, compounded by healthcare accessibility issues. Seasonal patterns and gender predilections are noted, with lifestyle factors like diet playing a possible role in prevention. Appendicitis generally begins with an obstruction of the appendiceal lumen, leading to bacterial proliferation, increased pressure, venous outflow impairment, ischemia, and potential perforation. This progression from a simple inflammation to a complex infection underscores the importance of early diagnosis and management. Immunological and genetic Appendicitis is the inflammation of the vermiform appendix and constitutes a significant global health challenge. factors appear to modulate individual susceptibility and disease course, marking an area of active research. The symptomatology of appendicitis is varied, often characterized by a shift of pain from the umbilical region to the lower right abdomen. Diagnostic strategies encompass clinical scoring systems like the Alvarado score, supplemented by laboratory and imaging investigations, with CT scans being particularly diagnostic. While appendectomy remains the definitive treatment, the emergence of non-operative management (NOM) with antibiotics represents a paradigm shift for uncomplicated cases. Complex cases may necessitate an interval appendectomy or percutaneous drainage, with treatment individualized to patient response and health status. Appendicitis, once considered a straightforward surgical condition, is now recognized as a complex interplay of epidemiological, pathophysiological, and clinical factors. This review encapsulates the evolving understanding and approaches, emphasizing the necessity of tailored management strategies to enhance patient outcomes.

Cite as: Firetto C. Advancing appendicitis care: A comprehensive review of epidemiology, pathogenesis, and evolving treatment strategies. UMJ Surg. 2022; 3: e10012201.

INTRODUCTION

Appendicitis, characterized by the inflammation of the appendix—a small, tube-shaped pouch attached to the large intestine—remains one of the most acute surgical emergencies around the globe. Its prevalence and the urgency it demands in medical intervention make it a topic of substantial importance within the realms of healthcare and medical research. This review aims to dissect the multifaceted nature of appendicitis, from its epidemiological reach to the complexities of its management and treatment (1-3). Traditionally, appendicitis has been viewed primarily as a surgical concern, with a standard treatment protocol of an appendectomy—the surgical removal of the appendix. However, recent advancements and debates have brought forth a nuanced perspective that encompasses a broader spectrum of clinical considerations, including non-surgical management options, variations in disease presentation, and a closer examination of the pathophysiology and etiological factors. The incidence of appendicitis fluctuates worldwide, influenced by factors such as age, sex, diet, and perhaps, genetic predispositions. While it can affect individuals at any age, it predominantly strikes the younger population, with a peak incidence in the second decade of life. This review will explore the epidemiological patterns of appendicitis, delving into how these patterns have informed our understanding of the disease and how they continue to guide public health policies and preventative strategies. Appendicitis is a medical enigma in the sense that the appendix, once considered a vestigial organ, now has attributed roles in the body's immune system. This recognition prompts a reevaluation of the implications of its removal and calls for a deeper investigation into the pathophysiological mechanisms that result in its inflammation. Our review will outline the current knowledge on the function of the appendix, the cascade of events leading to appendicitis, and the intrinsic and extrinsic factors contributing to this potentially life-threatening condition (4-7).

The clinical presentation of appendicitis is notoriously variable, often mimicking other intra-abdominal processes, thus complicating the diagnostic pathway. This review will discuss the classic and atypical presentations of appendicitis, the diagnostic challenges they pose, and the role of clinical acumen and investigative modalities in achieving a timely and accurate diagnosis. We will examine the traditional and emerging diagnostic tools, including the various imaging technologies and laboratory tests, highlighting their sensitivities, specificities, and practical applications in different clinical scenarios (8).

With respect to treatment, the landscape is shifting. While appendectomy, whether open or laparoscopic, remains the cornerstone of appendicitis management, there is growing evidence supporting the selective use of antibiotics as a first-line treatment in specific cases. This controversial pivot in management paradigms underscores a critical area of debate and research that our review will address. We will scrutinize the indications, efficacy, and outcomes of both surgical and non-surgical treatments, paying special attention to the evolution of management protocols and their implications for patient care. Lastly, as the adage goes, 'prevention is better than cure', and so we will explore the current understanding of risk factors that may allow for preventive measures against appendicitis, as well as the potential role of dietary and lifestyle modifications. The comprehensive analysis will also include a discussion on the importance of public and professional education in recognizing the early signs of appendicitis to prevent the severe complications that can ensue from delayed treatment (9).

Through this review, we intend to offer an extensive and critical overview of appendicitis, presenting it not just as an anatomical affliction of a seemingly insignificant organ, but as a complex disease process that continues to challenge our medical knowledge and surgical

skills. By examining the latest evidence and exploring the current debates, we hope to contribute to a better understanding and management of this common yet perplexing condition.

Epidemiology

The epidemiology of appendicitis presents a unique pattern, reflecting various demographic and geographical variations. It is predominantly a disease of the young, with the highest incidence reported in individuals aged between 10 and 19 years. Despite its widespread occurrence, there are intriguing disparities in the rates of appendicitis and its outcomes across different regions and populations. These variations offer a window into the complex interplay of environmental, genetic, and lifestyle factors that influence the risk and severity of the disease (10).

Globally, appendicitis has a reported annual incidence of approximately 100 cases per 100,000 people, making it a significant contributor to urgent surgical care. In developed countries, the incidence appears to be declining, a trend that some attribute to changes in dietary habits, improved hygiene, and perhaps more conservative diagnostic criteria. Conversely, in developing nations, the incidence remains stable or is increasing, where it also poses a greater risk of complications due to delayed presentation and limited access to healthcare facilities (1,2,6,11).

Seasonal variations have also been observed, with a higher occurrence noted during the summer months. While the exact reason for this seasonal variation remains unclear, it may be related to changes in dietary habits, physical activity, or even infectious disease patterns that influence the incidence of appendicitis. The male-to-female ratio of appendicitis cases is roughly 1.4:1, indicating a slightly higher prevalence among males. This difference may be due to physiological variations or perhaps differences in health-seeking behavior between genders. Moreover, certain lifestyle factors, such as a high-fiber diet, have been inversely associated with the risk of developing appendicitis, suggesting that dietary choices may play a preventive role. However, the evidence is not entirely consistent, and the potential mechanisms behind such an association warrant further investigation (12-14).

Pathophysiology

The pathophysiology of appendicitis is a complex process, typically initiated by an obstruction of the appendiceal lumen. This obstruction can be due to various factors, including fecaliths (hardened and calcified pieces of stool), lymphoid hyperplasia, foreign bodies, or even neoplasia. Once the lumen is obstructed, bacteria that normally reside within the appendix begin to multiply, leading to the accumulation of mucus and increased intraluminal pressure. The increased pressure impairs venous outflow, which can result in localized ischemia and bacterial invasion of the appendiceal wall. Furthermore, this pressure may compromise the arterial blood supply, exacerbating the ischemia and promoting necrosis (15,16).

The initial phase of appendicitis, often termed the ‘simple’ or ‘catarrhal’ phase, may manifest as an inflammation confined to the mucosa. If the condition is not treated promptly, it can progress to the ‘suppurative’ phase, where inflammation involves the entire wall of the appendix. Bacterial proliferation within the appendix further stimulates the body’s immune response, leading to the accumulation of pus and an increase in intraluminal pressure, which can exacerbate the obstruction. If the pressure continues to rise unchecked, the walls of the appendix become increasingly ischemic and may eventually perforate. Perforation releases bacteria and inflammatory mediators into the peritoneal cavity, which can result in peritonitis—a severe and generalized inflammation of the abdominal cavity lining. In

children and the elderly, the response to inflammation can be less localized, thus increasing the risk of diffuse peritonitis. In an attempt to contain the infection and prevent the spread of inflammation, the body often forms an ‘appendiceal phlegmon’ or mass, which includes the inflamed appendix, surrounding intestine, and omentum (17-21). When the inflammation is walled off by the omentum and adjacent structures, an abscess can form. An abscess, if not properly treated, can lead to further complications, including sepsis. Interestingly, there's an immunological dimension to the pathophysiology of appendicitis. The appendix contains lymphoid tissue that plays a role in the immune system. During periods of high immune activity, such as in response to infection, this lymphoid tissue can swell. This immune response can contribute to the obstruction of the appendix. Recent research suggests that not all appendicitis progresses in a linear fashion from simple to complicated disease. There appears to be a subset of patients in whom appendicitis can resolve spontaneously or with antibiotic treatment, suggesting that there may be different pathophysiological pathways. This revelation is leading to a reevaluation of traditional approaches to appendicitis treatment and has spurred interest in understanding the immunological and microbiological factors at play. Moreover, the variability in clinical presentations and disease progression suggests that genetic factors may influence an individual's susceptibility to appendicitis and their ability to contain the infection and inflammation. Studies are ongoing to identify specific genetic markers that might predict the severity of appendicitis or the likelihood of complications (18,22,23).

Clinical symptoms and diagnosis

Appendicitis is an acute medical condition characterized by the inflammation of the appendix, a small, tube-like structure attached to the large intestine. The clinical presentation of appendicitis can be variable, but it commonly starts with a dull pain near the navel or the upper abdomen that becomes sharp as it moves to the lower right abdomen. This hallmark symptom is often accompanied by additional manifestations such as loss of appetite, nausea, vomiting, and a low-grade fever. As the condition progresses, the intensity of abdominal pain increases and becomes more localized. It is crucial to note that atypical presentations are not uncommon, especially in children, women, and the elderly, where the pain may be diffuse or located in different areas of the abdomen (24).

The pathophysiology behind the pain begins with the obstruction of the appendiceal lumen, typically by fecaliths, lymphoid hyperplasia, or, less commonly, by foreign bodies, tumors, or worms. The obstruction leads to increased intraluminal pressure, compromised blood flow, and eventual bacterial overgrowth. As a result, the appendix becomes inflamed and edematous, which is perceived as the initial, centrally-located abdominal pain. As the inflammation progresses to involve the parietal peritoneum, the pain shifts to the right lower quadrant at McBurney's point (1,7).

The diagnostic approach to appendicitis ideally combines clinical judgment with supportive imaging and laboratory tests. Clinicians often use the Alvarado score, which is a clinical scoring system based on symptoms, signs, and laboratory findings. This score helps to stratify patients according to the likelihood of appendicitis and decide on further investigative steps or surgical intervention (8).

Laboratory tests typically reveal leukocytosis with a left shift, though this finding is not specific to appendicitis. Inflammatory markers such as C-reactive protein (CRP) may also be elevated. However, these laboratory findings must be interpreted within the clinical context, as they can also be elevated in other conditions such as gastroenteritis or ectopic pregnancy (9).

Imaging studies play a pivotal role in the diagnosis of appendicitis. Ultrasonography (US) is often the first-line imaging modality, especially in children and pregnant women, due to its safety profile, cost-effectiveness, and reasonable sensitivity (10). A graded-compression technique is utilized to visualize an inflamed, non-compressible appendix, with the presence of an appendicolith, or fecalith, serving as a strong indicator of appendicitis. However, ultrasound has limitations, particularly in obese patients or those with extensive intestinal gas, which can obscure the view of the appendix. Computed tomography (CT) of the abdomen and pelvis with or without contrast is considered the gold standard for adults with suspected appendicitis, offering higher sensitivity and specificity. CT findings consistent with appendicitis include an enlarged appendix, periappendiceal fat stranding, appendiceal wall thickening, and the presence of an appendicolith. Magnetic resonance imaging (MRI) is an alternative when radiation exposure is a concern, such as in pregnant Women (25).

Management and treatment

The management and treatment of appendicitis are predominantly surgical, with appendectomy being the standard care. However, the approach to treatment can be stratified based on the stage of the disease at presentation and the patient's overall health status. Surgical intervention to remove the inflamed appendix, known as an appendectomy, can be performed using two main techniques: open appendectomy (OA) and laparoscopic appendectomy (LA). The choice of technique generally depends on the surgeon's expertise, the patient's clinical status, and the facility's resources. LA is preferred for its advantages in terms of less postoperative pain, shorter hospital stay, and better cosmetic outcomes, though OA may be chosen in cases where laparoscopic equipment or expertise is not available or when there is a contraindication to pneumoperitoneum or laparoscopy (**Figure 1**) (26-29).

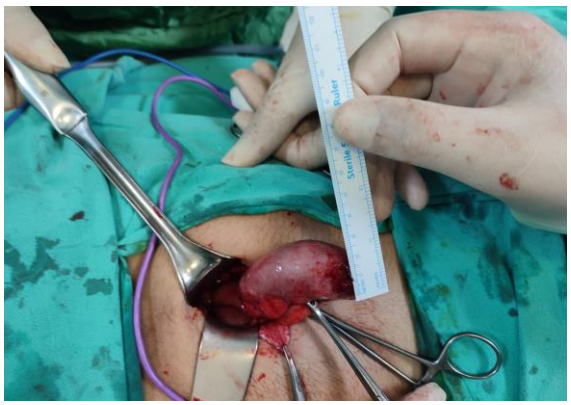

Figure 1: Intraoperative surgical treatment of the appendicitis

In uncomplicated appendicitis, where there is no perforation or abscess, prompt surgical intervention minimizes the risk of perforation and subsequent peritonitis. Preoperative antibiotics are administered to reduce the risk of postoperative infectious complications, with a regimen typically covering gram-negative and anaerobic bacteria. Complex cases, such as those presenting with a phlegmon or abscess, may require a different approach. An initial nonoperative management (NOM) with intravenous antibiotics can be considered, particularly in patients where surgery poses high risk or when inflammation has walled off. In these situations, an interval appendectomy, which is an appendectomy performed weeks to months after the resolution of acute inflammation, may be planned (30). However, recent studies have suggested that interval appendectomy may not always be necessary following successful NOM, and the decision is often individualized based on patient factors and response to treatment. For those who respond well to NOM with antibiotics, some may opt

for conservative management without surgery. This conservative approach has emerged as a potential treatment for selected patients with uncomplicated acute appendicitis. The use of imaging-guided percutaneous drainage has become a valuable adjunct in the management of appendiceal abscesses or localized peritonitis. This less invasive procedure can be employed to drain the abscess, thus potentially avoiding or delaying surgery until the patient is in a more stable condition or inflammation has decreased (31).

The postoperative management of patients includes pain control, early mobilization, and resumption of oral intake as tolerated. The postoperative complications, such as wound infection, intra-abdominal abscess, or ileus, must be promptly recognized and managed (32-35).

CONCLUSIONS

The multifaceted nature of appendicitis calls for personalized treatment, balancing surgical and non-surgical methods, to optimize outcomes in the face of evolving demographic and clinical insights.

Conflict of interest: The authors report no conflict of interest.
Funding source: No funding was required.
Ethical approval: No need for reviews.
Informed consent: No need for reviews.
Acknowledgments: No.
Peer-review: Externally. Evaluated by independent reviewers working in at least two different institutions appointed by the field editor.
Data availability: The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.
Contributions:
Research concept and design: CF
Data analysis and interpretation: CF
Collection and/or assembly of data: CF
Writing the article: CF
Critical revision of the article: CF
Final approval of the article: CF
All authors read and approved the final version of the manuscript.

REFERENCES

1. Schneuer FJ, Adams SE, Bentley JP, et al. A population-based comparison of the post-operative outcomes of open and laparoscopic appendicectomy in children. Med J Aust. 2018;209:80-85.
2. Smith MP, Katz DS, Lalani T, et al. ACR Appropriateness Criteria® Right Lower Quadrant Pain--Suspected Appendicitis. Ultrasound Q. 2015;31:85-91.
3. Schoel L, Maizlin II, Koppelmann T, et al. Improving imaging strategies in pediatric appendicitis: a quality improvement initiative. J Surg Res. 2018;230:131-136.
4. Zosimas D, Lykoudis PM, Pilavas A, et al. Open versus laparoscopic appendicectomy in acute appendicitis: results of a district general hospital. S Afr J Surg. 2018;56:59-62.
5. Gorter RR, Eker HH, Gorter-Stam MA, et al. Diagnosis and management of acute appendicitis. EAES consensus development conference 2015. Surg Endosc. 2016;30:4668-4690.

6. Xie X, Zhou Z, Song Y,et al. The Management and Prognostic Prediction of Adenocarcinoma of Appendix. Sci Rep. 2016;6:39027.
7. Morano WF, Gleeson EM, Sullivan SH, et al. Clinicopathological Features and Management of Appendiceal Mucoceles: A Systematic Review. Am Surg. 2018;84:273-281.
8. Marte A, Sabatino MD, Cautiero P, et al. Unexpected finding of laparoscopic appendectomy: appendix MALT lymphoma in children. Pediatr Surg Int. 2008;24:471-473.
9. Zhang K, Meyerson C, Kassardjian A, et al. Goblet Cell Carcinoid/Carcinoma: An Update. Adv Anat Pathol. 2019;26:75-83.
10. Jiang J, Wu Y, Tang Y, et al. A novel nomogram for the differential diagnosis between advanced and early appendicitis in pediatric patients. Biomark Med. 2019;13:1157-1173.
11. Van de Moortele M, De Hertogh G, Sagaert X, et al. Appendiceal cancer : a review of the literature. Acta Gastroenterol Belg. 2020;83:441-448.
12. Ahmed K, Wang TT, Patel VM, et al. The role of single-incision laparoscopic surgery in abdominal and pelvic surgery: a systematic review. Surg Endosc. 2011;25:378-96.
13. Khashab MA, Kalloo AN. NOTES: current status and new horizons. Gastroenterology. 2012;142:704-710.
14. Hucl T, Benes M, Kocik M, et al. Comparison of Inflammatory Response to Transgastric and Transcolonic NOTES. Gastroenterol Res Pract. 2016;2016:7320275.
15. Turk E, Acimis NM, Karaca F, et al. The effect on postoperative pain of pulling the rectus muscle medially during open appendectomy surgery. Minerva Chir. 2014;69:141-146.
16. Siribumrungwong B, Chantip A, Noorit P, et al. Comparison of Superficial Surgical Site Infection Between Delayed Primary Versus Primary Wound Closure in Complicated Appendicitis: A Randomized Controlled Trial. Ann Surg. 2018;267:631-637.
17. Antonacci N, Ricci C, Taffurelli G, et al. Laparoscopic appendectomy: Which factors are predictors of conversion? A high-volume prospective cohort study. Int J Surg. 2015;21:103-107.
18. Zani A, Hall NJ, Rahman A, et al. European Paediatric Surgeons' Association Survey on the Management of Pediatric Appendicitis. Eur J Pediatr Surg. 2019;29:53-61.
19. Kumar S, Jalan A, Patowary BN, et al. Laparoscopic Appendectomy Versus Open Appendectomy for Acute Appendicitis: A Prospective Comparative Study. Kathmandu Univ Med J (KUMJ). 2016;14:244-248.
20. Kave M, Parooie F, Salarzaei M. Pregnancy and appendicitis: a systematic review and meta-analysis on the clinical use of MRI in diagnosis of appendicitis in pregnant women. World J Emerg Surg. 2019;14:37.
21. Hwang ME. Sonography and Computed Tomography in Diagnosing Acute Appendicitis. Radiol Technol. 2018;89:224-237.
22. Kim DW, Suh CH, Yoon HM, et al. Visibility of Normal Appendix on CT, MRI, and Sonography: A Systematic Review and Meta-Analysis. AJR Am J Roentgenol. 2018;211:W140-W150.
23. Swenson DW, Ayyala RS, Sams C, et al. Practical Imaging Strategies for Acute Appendicitis in Children. AJR Am J Roentgenol. 2018;211:901-909.
24. Pooler BD, Repplinger MD, Reeder SB, et al. MRI of the Nontraumatic Acute Abdomen: Description of Findings and Multimodality Correlation. Gastroenterol Clin North Am. 2018;47:667-690.
25. Withers AS, Grieve A, Loveland JA. Correlation of white cell count and CRP in acute appendicitis in paediatric patients. S Afr J Surg. 2019;57:40.
26. Awayshih MMA, Nofal MN, Yousef AJ. Evaluation of Alvarado score in diagnosing acute appendicitis. Pan Afr Med J. 2019;34:15.

27. Vaos G, Dimopoulou A, Gkioka E, et al. Immediate surgery or conservative treatment for complicated acute appendicitis in children? A meta-analysis. J Pediatr Surg. 2019;54:1365-1371.
28. Gignoux B, Blanchet MC, Lanz T, et al. Should ambulatory appendectomy become the standard treatment for acute appendicitis? World J Emerg Surg. 2018;13:28.
29. Eng KA, Abadeh A, Ligocki C, et al. Acute Appendicitis: A Meta-Analysis of the Diagnostic Accuracy of US, CT, and MRI as Second-Line Imaging Tests after an Initial US. Radiology. 2018;288:717-727.
30. Khan MS, Chaudhry MBH, Shahzad N, et al. Risk of appendicitis in patients with incidentally discovered appendicoliths. J Surg Res. 2018;221:84-87.
31. Stringer MD. Acute appendicitis. J Paediatr Child Health. 2017;53:1071-1076.
32. Bhangu A, Søreide K, Di Saverio S, et al. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet. 2015;386:1278-1287.
33. Addiss DG, Shaffer N, Fowler BS, et al. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol. 1990;132:910-925.
34. van Aerts RMM, van de Laarschot LFM, Banales JM, et al. Clinical management of polycystic liver disease. J Hepatol. 2018;68:827-837.
35. Snyder MJ, Guthrie M, Cagle S. Acute Appendicitis: Efficient Diagnosis and Management. Am Fam Physician. 2018;98:25-33.