Non-operative Management of Acute Appendicitis in Pediatric Population, A Narrative Review

Taqvai Nakhjiri M. MD[1], Ghavami Adel M. MD[2*]

Abstract:

Background and Objective: Acute appendicitis has traditionally been treated with operative approaches. Recent advances in diagnostic techniques have coincided with the introduction of novel non-invasive treatment options. Original studies on this topic indicate that non-operative management of acute appendicitis in the pediatric population is feasible. This review examines the current literature on the efficacy, safety, and long-term outcomes of non-operative treatments and provides an overview of this management strategy.

Materials & Methods: In the pursuit of conducting this narrative review, a systematic search was performed using the Scopus, Embase, ISI, and Google Scholar databases. The inclusion criteria encompassed original articles, review papers, and meta-analyses focusing on the non-surgical treatment of acute appendicitis in the pediatric population. This study employed a descriptive-analytical approach. All relevant literature was thoroughly evaluated, and data were carefully extracted; the findings and insights obtained from these sources were subsequently integrated into various sections of this review.

Results: Non-operative management has been reported to result in a shorter hospital stay and higher patient satisfaction compared to operative management. Key factors in selecting the appropriate candidates for non-operative treatment include younger age, shorter duration of symptoms and fever, mild clinical presentations, lower white blood cell and C-reactive protein (CRP) levels on laboratory tests, and smaller appendix diameter on imaging. Further Randomized Controlled Trials (RCT) with longer follow-up periods and similar antibiotic regimens are needed to address the heterogeneity of previous studies.

Conclusion: Existing evidence from previous studies supports the non-surgical management of uncomplicated acute appendicitis in children. However, it is crucial to develop comprehensive guidelines for patient selection. These guidelines are necessary to reduce the risk of misdiagnosis and to prevent the occurrence of serious complications resulting from inadequate treatment.

Keywords: Pediatrics, Appendicitis, Antibiotics, non-operative management, appendectomy

[1]General Physician, Research Assistant, Breastfeeding Research Center, Family Health Research Institute, Faculty of Medicine, Tehran University of Medical Sciences, Vali Asr Hospital

[2]Associate Professor, Department of Pediatric Surgery, Faculty of Medicine, Tehran University of Medical Sciences, Imam Khomeini Hospital

Received: 20/02/2025
Accepted: 08/07/2025

Corresponding Author: Dr. Maryam Ghavami Adel
Tel: 61192358

E-mail: maryamghavami5@gmail.com

Background and Objective

Acute appendicitis is the most common condition in children requiring urgent evaluation.[1] Although recent studies have reported a decline in its overall incidence, it remains most frequently diagnosed in children aged 10 to 19 years.[2,3] Diagnosing appendicitis in this age group is particularly challenging due to factors such as ineffective communication, symptom overlap with other medical conditions, and the limitations of physical examinations, all of which can lead to both misdiagnosis and delays in appropriate treatment.[4]

The standard treatment option for acute appendicitis is appendectomy.[5] However, surgical intervention can be discouraging for pediatric patients and their families, particularly considering the associated costs and potential complications.[6,7] Recent advancements in diagnostic techniques and a better understanding of the disease's natural progression have increased interest in Non-Operative Management (NOM) strategies. Consequently, the management of acute appendicitis has evolved significantly, reflecting a shift toward exploring alternative therapeutic options.[8]

This narrative review aims to synthesize the current literature on the NOM of acute appendicitis in children, evaluating its efficacy, safety, and long-term outcomes. The article provides a comprehensive overview of the non-operative approach to managing acute appendicitis.

1. Pathophysiology

Acute appendicitis, the most common surgical emergency in children, is characterized by the inflammation of the vermiform appendix.[3] The onset of appendicitis is often attributed to the obstruction of the appendiceal lumen, which can result from various factors such as fecaliths, lymphoid hyperplasia, foreign bodies, or neoplasms.[9,10] This obstruction leads to increased intraluminal pressure, thereby impairing blood flow and causing ischemic changes in the appendiceal wall.[11,12] Historical research has consistently demonstrated a significant correlation between the presence of fecaliths and the occurrence of appendicitis, supporting the obstruction theory.[13] Additionally, findings from the study by Rogers et al. suggest that the appendiceal environment contains unique microbial communities, such as the species of Fusobacterium, which may play a significant role in the development of appendicitis.[14]

The inflammatory process can progress through several stages. Initially, patients often report pain localized around the peri-umbilical region, which arises from the stimulation of visceral nerves.[12] This early discomfort serves as an indicator of the underlying pathological changes within the abdominal cavity. As the condition advances, the inflammatory response may escalate, potentially involving structures beyond the appendix. This extension of inflammation can affect the parietal peritoneum, resulting in a more pronounced clinical presentation characterized by symptoms such as fever, nausea, and vomiting.[10,11] If the inflammatory process remains untreated, it can lead to perforation of the appendix, a complication that significantly increases the risk of morbidity and mortality.[12]

2. Evolution of treatment options

The management of acute appendicitis has undergone significant transformation over time, evolving from conventional surgical techniques to more advanced approaches. Surgical intervention for appendicitis dates back to the 18th century, beginning with the resection of the cecal appendix trapped in an inguinal hernia, performed by Claudius Amyand in 1735.[15]

The late 19th century marked a pivotal moment in the standardization of surgical procedures. In 1894, Charles McBurney introduced the open appendectomy (OA) technique, characterized by a substantial incision in the right lower quadrant of the abdomen.[16] This method became the gold standard for an extended period, providing direct access to the inflamed appendix. The development of laparoscopic surgery in the

1980s led to the widespread adoption of laparoscopic appendectomy (LA) as the preferred surgical method, primarily due to its minimally invasive nature. This approach is associated with reduced postoperative pain, shorter hospital stays, and faster recovery times. LP involves smaller incisions and the use of a camera, which enhances visualization during the procedure.[17] In recent years, the single-incision laparoscopic appendectomy (SILA) technique has gained prominence. This method uses a single incision, usually located at the umbilicus, to achieve superior cosmetic results and minimize complications. Although SILA is still being refined, it represents a notable progression in surgical techniques.[18]

Alongside surgical interventions, there is an increasing focus on NOM for uncomplicated appendicitis, primarily using antibiotics. Research indicates that this approach can be effective, reducing the need for surgical procedures in many cases.[19] Current management strategies for acute appendicitis are now more personalized, considering factors such as the patient's overall health, the severity of the appendicitis, and any existing complications.[20]

3. Non-Operative Management approaches

Non-surgical management of acute appendicitis primarily involves the administration of antibiotics combined with supportive care measures. Numerous studies have highlighted several key strategies that enhance the effectiveness of this treatment approach.

Individuals should be hospitalized for observation and be provided with supportive treatments such as intravenous fluids, pain relief medications, and antibiotics. This approach may lead to the natural resolution of less severe cases of appendicitis.[21]

Research findings demonstrate that antibiotics, when used as an initial and standalone treatment, can effectively manage acute uncomplicated appendicitis.[22] Commonly recommended treatment protocols typically involve broad-spectrum antibiotics such as amoxicillin-clavulanic acid, piperacillin-tazobactam, or ceftriaxone combined with metronidazole.[23] For example, Perveen et al. prescribed Cefotaxime 100 mg/kg/24h along with Metronidazole 30 mg/kg divided into three doses per day in their study, while Abbo et al. treated patients with intravenous Amoxicillin and Clavulanic acid (100 mg/kg/day) for two days (six doses).[24,25]

NOM may also include oral antibiotics after initial improvement. The regimen might involve administering intravenous antibiotics for 48-72 hours, followed by a course of oral antibiotics to complete a total of 7 days.[23]

Patients undergoing non-operative treatment are closely monitored for any signs of deterioration.[22,24] If symptoms worsen or fail to improve, an appendectomy may be performed.[26]

4. Efficacy and safety of non-operative Treatments

The administration of NOM through antibiotic therapy has demonstrated a success rate ranging from 63% to 80% over one year, depending on the specific study and the demographic characteristics of the patient population involved.[27,28] For example, findings from the NOTA study revealed a recurrence rate of less than 14% after a two-year follow-up period.[28] Tan et al. reported a recurrence rate of approximately 24% at 16 months.[29] A comprehensive meta-analysis has shown that initial antibiotics treatment effectively resolves 97% of pediatric cases with uncomplicated appendicitis, with a recurrence rate of approximately 14%.[30]

Short-term outcomes: most clinical symptoms improve rapidly, often within a single day after initiating non-operative treatment. Research indicates a significant reduction in pain levels after just one day of therapy, with the majority of pediatric patients experiencing relief from nausea and vomiting.[31] The Appendicitis Acuta (APPAC) trial further supports the efficacy of NOM by revealing that it is associated with fewer days lost to disability compared to surgical options.[32,33]

Long-term outcomes: Long-term observational studies have demonstrated that a considerable number of children initially treated non-operatively for appendicitis may later experience a recurrence of the condition. However, it is important to emphasize that many of these cases can be successfully managed with conservative treatment, thereby avoiding the necessity for surgical intervention. For example, research has shown that approximately 14% of pediatric patients who underwent NOM ultimately required an appendectomy due to recurrent appendicitis.[30] Additionaly, a systematic review by Decker et al. reported a failure rate of 32% after one year or more, suggesting that a considerable number of children may eventually require surgical intervention.[32]

Complications and safety: Evidence indicates that NOM is a safe approach, as studies report no fatalities associated with this treatment method.[27] The incidence of complications related to NOM is generally low; however, the potential for severe complications arising from appendicitis itself remains a significant concern.[26,32] The presence of an appendicolith has been identified as a risk factor for treatment failure, underscoring the importance of careful patient selection the success of NOM.[21,34,35]

5. Comparison of non-operative and operative treatments

ü Efficacy:

Appendectomy remains the gold standard for treating appendicitis, with a success rate approaching 100%. In the APPAC trial, 99.6% of patients who underwent appendectomy experienced successful outcomes.[33] NOM with antibiotics has shown variable success rates. For example, in the APPAC trial, 72.7% of patients treated with antibiotics avoided surgery within one year.[33] However, other studies report NOM success rates ranging from 67% to 88%.[36,37] A meta-analysis of 16 studies found that non-operative treatments achieved an overall efficacy rate of 92%.[38]

ü Complication Rates:

The complication rate for appendectomy can be significant, with studies reporting rates of 20.5% for minor complications, 2.8% for major complications, and an overall complication rate of 24.4% at five years.[39] NOM does not involve surgically related complications.[34] The APPAC trial reported a complication rate of only 2.8% in the antibiotic group.[33] In a study focusing on NOM, complications were observed in 20.8% of patients, although most were not severe.[26] However, a meta-analysis demonstrated that antibiotic treatment was associated with a considerably lower rate of uncomplicated recovery compared to surgical procedures.[40] Another meta-analysis by Maita et al. found no significant difference in complication rates between nonoperative treatment and surgical intervention. Nevertheless, they suggested that NOM is a safe and effective approach for nonperforated acute appendicitis in selected pediatric patients.[38]

ü Length of Hospital Stay:

Patients undergoing appendectomy typically experience longer hospital stays. In Svensson's study, the median length of stay for surgical patients was reported as 34.5 hours, whereas in Wolferstetter's study, it was 4.5 days.[21,41] Patients treated non-operatively often have shorter hospital stays. In the APPAC trial, the median length of stay for the antibiotic group was longer due to monitoring protocols; however, it is generally shorter in routine practice.[33] Nevertheless, a meta-analysis demonstrated no significant difference in the length of hospital stay between patients treated non-operatively and those who underwent surgical procedures.[38]

ü Recovery Time and Disability Days:

Patients who undergo surgery may experience longer recovery times, with an average of 10.9 days of disability reported. NOM is associated with fewer disability days, averaging approximately 6.6 days. Patients often return to normal activities more quickly with NOM.[36]

ü Patient Satisfaction and Quality of Life:

While surgery is effective, some patients may experience dissatisfaction due to complications or prolonged recovery periods. Many patients and their families prefer NOM because it avoids surgery and its associated risks. Studies indicate that patient satisfaction is generally high with NOM, especially when the treatment is successful.[37,42]

ü Recurrence Rates:

Recurrence is not a concern after an appendectomy, as the appendix is removed. However, recurrence rates following NOM can be significant, with studies reporting rates between 27% and 39% within one year.[21,39] In situations where recurrence occurs, the preferred initial intervention would be an appendectomy.[27]

6. Patient Selection Criteria

To identify the most suitable candidates for non-operative intervention in cases of uncomplicated appendicitis in children, it is essential to analyze a range of clinical, demographic, and laboratory factors. Evaluating these elements can help in selecting appropriate candidates:

1. Age: Candidates should generally be older than 7 years. Younger children may present more severe symptoms and complications, making them less suitable for NOM.[43]

2. Duration of Symptoms: A shorter duration of symptoms (ideally less than 48 hours) is favorable. Studies indicate that children with symptoms lasting less than 24 hours have better outcomes with NOM.[43-45]

3. Fever Duration: Candidates should ideally have a shorter duration of fever prior to admission. A fever lasting less than one day is associated with a higher likelihood of successful NOM.[43,45]

4. Clinical Presentation: Patients typically present with mild symptoms, such as localized abdominal pain without significant rebound tenderness or signs of systemic infection. The absence of severe abdominal pain or peritonitis is crucial.[46]

5. Laboratory Findings:

- White Blood Cell Count (WBC): A lower WBC count (ideally less than 10,000/μL) is preferable, as higher counts may indicate a more severe inflammatory process.[36,44-46]
- C-Reactive Protein (CRP): Lower CRP levels are also associated with better outcomes in NOM.A CRP level of approximately 15 mg/l or less has been linked to successful NOM.[45,46]

6. Imaging Findings: The absence of an appendicolith and a smaller appendiceal diameter are important factors. Larger diameters (generally greater than 10.5 mm) and the presence of an appendicolith are associated with higher failure rates of NOM.[35,45,46]

7. Parental Consent and Preference: Involving parents in the decision-making process is essential. Parents should be informed about the risks and benefits of NOM, and their consent is necessary to proceed with this treatment approach. In addition, it is important to emphasize the need for access to the hospital for ongoing monitoring and subsequent follow-up care.[43,44]

8. Structured Protocols: Implementing a structured management protocol with clearly defined cut-off criteria for monitoring patient progress can enhance the success of NOM. This approach includes regular assessments of pain, fever, and laboratory results.[43]

7. Future studies

The implementation of NOM for acute appendicitis is both safe and feasible in the pediatric population. However, there is a lack of evidence regarding aspects of this treatment approach, highlighting the need for further studies.

A meta-analysis of original studies revealed heterogeneity in the results.[32] To determine the effects of age, laboratory findings, and imaging results on the success of NOM, more RCTs with similar antibiotic regimens, consistent patient inclusion criteria, and follow-up durations are necessary to minimize the heterogeneity.[32,47] Although parental involvement in the

decision-making process is essential, it is important to remain aware of the potential selection bias their participation may introduce. Hence, minimizing this bias is crucial in future studies.[47] There is a need for further prospective randomized controlled trials that specifically evaluate the long-term clinical outcomes and cost-effectiveness of this approach.[21,30,38]

Research indicates that patients with uncomplicated acute appendicitis may benefit from NOM. Identifying a positive response to nonoperative treatment during the initial evaluation is crucial. Therefore, future studies should focus on the early differentiation of various forms of appendicitis in children -such as simple versus complicated, and progressive versus self-limiting- - to establish gold standard criteria for diagnosis and management.

Conclusion

NOM of acute appendicitis in children has emerged as a considerable alternative to traditional appendectomy, demonstrating a high initial success rate and comparable complication rates between the two treatments approaches. Studies indicate that NOM can avoid surgery in a significant proportion of cases, particularly in patients without appendicoliths or complicated acute appendicitis. Hence, careful patient selection is crucial. While the current evidence supports the safety and efficacy of NOM, further large-scale randomized controlled trials are needed to solidify its role in clinical practice and to establish clear guidelines for its implementation in pediatric patients with uncomplicated appendicitis.

References:

1. Malia L, Sturm JJ, Smith SR, Brown RT, Campbell B, Chicaiza H. Predictors for Acute Appendicitis in Children. Pediatric Emergency Care. 2021; 37(12).
2. Hansen GL, Kleif J, Jakobsen C, Paerregaard A. Changes in Incidence and Management of Acute Appendicitis in Children-A Population-Based Study in the Period 2000-2015. Eur J Pediatr Surg. 2021; 31(4): 347-52.
3. Yadav AK, Resident J, Pawar S. Ultrasonography Technique and Its Role in Diagnosis of Acute Appendicitis. 2021.
4. Almaramhy HH. Acute appendicitis in young children less than 5 years: review article. Ital J Pediatr. 2017; 43(1): 15.
5. Jaschinski T, Mosch C, Eikermann M, Neugebauer EAM. Laparoscopic versus open appendectomy in patients with suspected appendicitis: a systematic review of meta-analyses of randomised controlled trials. BMC Gastroenterology. 2015; 15(1): 48.
6. Bodnar C, Buss R, Somers K, Mokdad A, Van Arendonk KJ. Association of Neighborhood Socioeconomic Disadvantage with Complicated Appendicitis in Children. J Surg Res. 2021; 265: 245-51.
7. Gonzalez KW, Adibe OO, Dalton BG, Desai AA, Sharp SW, St Peter SD. Understanding parental refusal of permission for child participation in surgical prospective trials. Pediatr Surg Int. 2016; 32(5): 505-8.
8. Switzer NJ, Gill RS, Karmali S. The evolution of the appendectomy: from open to laparoscopic to single incision. Scientifica (Cairo).2012;2012: 895469.
9. Levin MD. The pathogenesis of acute appendicitis. The non-specific response of the digestive tract in acute inflammation in the abdomen. Eksp Klin Gastroenterol. 2016(8):67-74.
10. Bhangu A, Søreide K, Di Saverio S, Assarsson JH, Drake FT. Acute appendicitis: modern understanding of pathogenesis, diagnosis, and management. Lancet. 2015; 386(10000):1278-87.
11. Echevarria S, Rauf F, Hussain N, Zaka H, Farwa UE, Ahsan N, et al. Typical and Atypical Presentations of Appendicitis and Their Implications for Diagnosis and Treatment: A Literature Review. Cureus. 2023; 15(4): e37024.
12. Brennan GD. Pediatric appendicitis: pathophysiology and appropriate use of diagnostic imaging. Cjem. 2006; 8(6): 425-32.
13. Singh JP, Mariadason JG. Role of the faecolith in modern-day appendicitis. Ann R Coll Surg Engl. 2013; 95(1): 48-51.
14. Rogers MB, Brower-Sinning R, Firek B, Zhong D, Morowitz MJ. Acute Appendicitis in Children Is Associated With a Local Expansion of Fusobacteria. Clin Infect Dis. 2016; 63(1): 71-8.
15. Amyand C. VIII. Of an inguinal rupture, with a pin in the appendix coeci, incrusted with stone; and some observations on wounds in the guts. Philosophical Transactions of the Royal Society of London. 1997; 39(443): 329-42.
16. McBurney C. IV. The Incision Made in the Abdominal Wall in Cases of Appendicitis, with a Description of a New Method of Operating. Ann Surg. 1894; 20(1): 38-43.
17. Bennett J, Boddy A, Rhodes M. Choice of approach for appendicectomy: a meta-analysis of open versus laparoscopic appendicectomy. Surg Laparosc Endosc Percutan Tech.2007;17(4):245-55.
18. Bhatia P, Sabharwal V, Kalhan S, John S, Deed JS, Khetan M. Single-incision multi-port laparoscopic appendectomy: How I do it. J Minim Access Surg. 2011; 7(1): 28-32.
19. Firetto C. Advancing appendicitis care: A comprehensive review of epidemiology, pathogenesis, and evolving treatment strategies. UMJ Surgery. 2022/01/07; 3.
20. Wagner M, Tubre DJ, Asensio JA. Evolution and Current Trends in the Management of Acute Appendicitis. Surg Clin North Am.2018;98(5):1005-23.
21. Reis Wolfertstetter P, Ebert JB, Barop J, Denzinger M, Kertai M, Schlitt HJ, et al. Suspected Simple Appendicitis in Children: Should We Use a Nonoperative, Antibiotic-Free Approach? An Observational Study. Children (Basel). 2024; 11(3).
22. Clémence P, Olivier A, Caroline M, Lucas R, Damien D, Cécile L, et al. Non-operative treatment of acute appendicitis in children: clinical efficacy of amoxicillin-clavulanic acid in a retrospective single-centre study. BMJ Paediatrics Open. 2023; 7(1): e001855.
23. Lee SL, Islam S, Cassidy LD, Abdullah F, Arca MJ. Antibiotics and appendicitis in the pediatric population: an American Pediatric Surgical Association Outcomes and Clinical Trials Committee systematic review. J Pediatr Surg. 2010; 45(11):2181-5.
24. Abbo O, Trabanino C, Pinnagoda K, Ait Kaci A, Carfagna L, Mouttalib S, et al. Non-operative Management for Uncomplicated Appendicitis: An Option to Consider. Eur J Pediatr Surg. 2018; 28(1): 18-21.
25. Perveen S, Akhtar J, Ali S, Jabbar A. Feasibility of nonoperative treatment of acute appendicitis in children: a prospective cohort study. Singapore Med J. 2023.
26. Gorter RR, van der Lee JH, Cense HA, Kneepkens CM, Wijnen MH, In 't Hof KH, et al. Initial antibiotic treatment for acute simple appendicitis in children is safe: Short-term results from a multicenter, prospective cohort study. Surgery. 2015; 157(5):916-23.

27. Bethell GS, Rees CM, Sutcliffe J, Hall NJ. Outcomes 1 year after non-operative management of uncomplicated appendicitis in children: Children with AppendicitiS during the CoronAvirus panDEmic (CASCADE) study. BJS Open. 2023; 7(3).
28. Di Saverio S, Sibilio A, Giorgini E, Biscardi A, Villani S, Coccolini F, et al. The NOTA Study (Non Operative Treatment for Acute Appendicitis): prospective study on the efficacy and safety of antibiotics (amoxicillin and clavulanic acid) for treating patients with right lower quadrant abdominal pain and long-term follow-up of conservatively treated suspected appendicitis. Ann Surg. 2014; 260(1): 109-17.
29. Tan APP, Yap TL, Cheong YL, Rai R, Choo C, Ong C, et al. Conservative antibiotic treatment of pediatric acute uncomplicated appendicitis during the COVID-19 pandemic: a prospective comparative cohort study. Pediatr Surg Int. 2022; 39(1): 60.
30. Georgiou R, Eaton S, Stanton MP, Pierro A, Hall NJ. Efficacy and Safety of Nonoperative Treatment for Acute Appendicitis: A Meta-analysis. Pediatrics. 2017; 139(3).
31. Knaapen M, van der Lee JH, Heij HA, van Heurn ELW, Bakx R, Gorter RR. Clinical recovery in children with uncomplicated appendicitis undergoing non-operative treatment: secondary analysis of a prospective cohort study. Eur J Pediatr. 2019; 178(2): 235-42.
32. Decker E, Ndzi A, Kenny S, Harwood R. Systematic Review and Meta-analysis to Compare the Short- and Long-term Outcomes of Non-operative Management With Early Operative Management of Simple Appendicitis in Children After the COVID-19 Pandemic. J Pediatr Surg. 2024; 59(6): 1050-7.
33. Salminen P, Paajanen H, Rautio T, Nordström P, Aarnio M, Rantanen T, et al. Antibiotic Therapy vs Appendectomy for Treatment of Uncomplicated Acute Appendicitis: The APPAC Randomized Clinical Trial. Jama.2015;313(23):2340-8.
34. Armstrong J, Merritt N, Jones S, Scott L, Bütter A. Non-operative management of early, acute appendicitis in children: is it safe and effective? J Pediatr Surg. 2014; 49(5): 782-5.
35. Castelló González M, Bueno Rodríguez JC, Hernández Moore E, Aguilar Atanay D. Predictors of recurrent appendicitis after non-operative management of children with perforated appendicitis presenting with an appendicular inflammatory mass. Arch Dis Child. 2014; 99(2): 154-7.
36. Minneci PC, Hade EM, Lawrence AE, Sebastião YV, Saito JM, Mak GZ, et al. Association of Nonoperative Management Using Antibiotic Therapy vs Laparoscopic Appendectomy With Treatment Success and Disability Days in Children with Uncomplicated Appendicitis. Jama. 2020; 324(6): 581-93.
37. Hartwich J, Luks FI, Watson-Smith D, Kurkchubasche AG, Muratore CS, Wills HE, et al. Nonoperative treatment of acute appendicitis in children: A feasibility study. J Pediatr Surg. 2016; 51(1): 111-6.
38. Maita S, Andersson B, Svensson JF, Wester T. Nonoperative treatment for nonperforated appendicitis in children: a systematic review and meta-analysis. Pediatr Surg Int.2020;36(3):261-9.
39. Salminen P, Tuominen R, Paajanen H, Rautio T, Nordström P, Aarnio M, et al. Five-Year Follow-up of Antibiotic Therapy for Uncomplicated Acute Appendicitis in the APPAC Randomized Clinical Trial. Jama. 2018; 320(12): 1259-65.
40. Xu H, Yang S, Xing J, Wang Y, Sun W, Rong L, et al. Comparison of the efficacy and safety of antibiotic treatment and appendectomy for acute uncomplicated appendicitis: a systematic review and meta-analysis. BMC Surg. 2023; 23(1):208.
41. Svensson JF, Patkova B, Almström M, Naji H, Hall NJ, Eaton S, et al. Nonoperative treatment with antibiotics versus surgery for acute nonperforated appendicitis in children: a pilot randomized controlled trial. Ann Surg. 2015; 261(1): 67-71.
42. Prechal D, Post S, Pechlivanidou I, Ronellenfitsch U. Feasibility, acceptance, safety, and effectiveness of antibiotic therapy as alternative treatment approach to appendectomy in uncomplicated acute appendicitis. Int J Colorectal Dis. 2019; 34(11): 1839-47.
43. Ikegami M, Miyano G, Nojiri S, Ochi T, Shibuya S, Yazaki Y, et al. Indications for Nonoperative Management of Uncomplicated Appendicitis in Children: A Prospective Analysis at a Single Institution. J Laparoendosc Adv Surg Tech A. 2020; 30(1): 70-5.
44. Steiner Z, Gilad Y, Gutermacher M, Stackievicz R, Bauer-Rusek S, Arnon S. Acute appendicitis in children: Reexamining indications for conservative treatment - A large prospective analysis. J Pediatr Surg. 2022; 57(10): 373-9.
45. Van den Bogaard VA, Euser SM, van der Ploeg T, de Korte N, Sanders DG, de Winter D, et al. Diagnosing perforated appendicitis in pediatric patients: a new model. J Pediatr Surg. 2016; 51(3): 444-8.
46. Loftus TJ, Brakenridge SC, Croft CA, Stephen Smith R, Efron PA, Moore FA, et al. Successful nonoperative management of uncomplicated appendicitis: predictors and outcomes. J Surg Res. 2018; 222: 212-8.e2.
47. Mosuka EM, Thilakarathne KN, Mansuri NM, Mann NK, Rizwan S, Mohamed AE, et al. A Systematic Review Comparing Nonoperative Management to Appendectomy for Uncomplicated Appendicitis in Children. Cureus. 2021; 13(10): e18901.