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How Did The Covid-19 Pandemic Affected Children Acute Appendicitis?

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ABSTRACT

Aim: This study aimed to reveal the changes in the clinical status and results of pediatric cases with acute appendicitis during the COVID-19 pandemic.

Materials and Methods: The data of pediatric patients who underwent appendectomy for acute appendicitis between March 1 and May 31, 2019 (group B) and March 1 and May 31, 2020 (group A) in our city were reviewed retrospectively. All data were evaluated and the groups were statistically compared.

Results: The mean age of group A (n=29, 9 female, 20 male) was 12.69 years, and the mean age of group B (n=65, 21 female, 44 male) was 11.12 years. It was found that the number of patients undergoing appendectomy decreased significantly during the COVID-19 pandemic compared to the same period of the previous year. The mean duration of symptoms was significantly longer in group A compared to group B (p<0.001). The late admission rate was higher in Group A compared to Group B (p=0.012). While the mean white blood cell (WBC) count did not differ between the two groups, mean C-Reactive Protein (CRP) levels were significantly higher in group A compared to group B (p<0.001). Complicated appendicitis was observed in 7 patients in group A and 10 patients in group B (p=0.532). Duration of surgery was significantly higher in group A (49.82±19.09 min and 40.15±11.61 min). The rate of patients who underwent postoperative drainage was significantly higher In group A (4 patients) compared to group B (1 patient).

Conclusion: The results of this study showed that the number of patients with acute appendicitis who applied to our hospital decreased significantly during the COVID-19 pandemic, and the incidence of complicated appendicitis and more severe clinical symptoms increased due to late admission to healthcare institutions.

Keywords: Acute Appendicitis, Appendectomy, Covid-19, Pandemic, Child

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Introduction

In December 2019, an outbreak of respiratorytransmitted pneumonia of unknown origin occurred in Wuhan, China ^{(1).} On March 1, 2020, the World Health Organization (WHO) declared this as a new type of coronavirus (SARS-CoV-2) pandemic and named the disease "Coronavirus Disease 2019 (COVID-19)". Since then, the disease has spread rapidly throughout the world, affecting billions of people. COVID-19 can lead to a broad spectrum of clinical manifestations, from asymptomatic cases with mild or moderate clinical course to severe pneumonia with a high morbidity or mortality rate ⁽²⁾. COVID-19 has become a serious health problem all over the world, however, it is milder in children compared to adults ⁽³⁾. Countries around the world have adjusted their economic resources and healthcare systems according to this pandemic. They have reserved most of their resources, such as personnel and materials, for the management of COVID-19. In order to reduce the spread, a series of restrictions were introduced to slow down social life, elective health services in hospitals were reduced as much as possible, and the necessary equipment for healthcare workers and healthcare services were allocated to fight the pandemic. Within the scope of these measures, in order to use hospital resources more efficiently, surgeries were re-scheduled, and elective surgical interventions were postponed.

Acute appendicitis (AA) is one of the most common emergency surgical pathologies encountered by adult and pediatric surgeons ⁽⁴⁻⁶⁾. AA is the first consideration in the differential diagnosis of abdominal pain in children, and overlooking AA may lead to medicolegal consequences as well as morbidity and mortality. Rapid diagnosis is critical for AA because of the high morbidity and mortality risk from the perforation of the appendix. Perforation occurs due to delayed diagnosis, and complications such as ileus, intra-abdominal abscess and infertility may occur ⁽⁷⁾.

COVID-19 has been heavily covered in the media since it was announced as a pandemic and has become the most talked about topic worldwide, creating severe fear and panic among people ⁽⁸⁾. During the pandemic, people have tried to avoid hospitals as much as possible, where most COVID-19 cases were gathered. In Turkey, we also observed that admissions to emergency services for emergencies other than COVID-19 have decreased significantly during the pandemic. Although these were not directly related to the occurrence of AA, we observed a significant decrease in AA cases in Siirt during the pandemic, admissions to hospitals were delayed, and the number of complicated cases was higher than normal.

Therefore, this study aimed to compare the data of patients who underwent appendectomy within the first 3 months of the COVID-19 pandemic in Turkey with the same period one year before.

Materials and Methods

This study was conducted in our state hospital, the only hospital in the city with a Pediatric Surgery Specialist. The Pediatric Surgery staff in the hospital was the same during the pre-pandemic and pandemic periods. In both study periods, pediatric appendicitis treatment in our city was only performed in our hospital. Again, during the pandemic, emergency services in our hospital continued without interruption, and appendicitis or other emergency surgical interventions continued to be performed. Data of pediatric patients who underwent appendectomy with the diagnosis of AA in the first 3 months (01 March 2020 - 31 May 2020) after the first COVID-19 case was seen in Turkey and COVID-19 restrictions began to be implemented, and the data of pediatric patients operated in the same time period of 2019 (01 March 2019 - 31 May 2019) were reviewed retrospectively. Age, gender, te from the onset of symptoms to hospital admission, laboratory data, radiology reports, appendix diameters measured by preoperative radiological imaging, operation reports, condition of the appendix and the abdomen in the perioperative examination, duration of operation, need for postoperative drainage, time to transition to oral feeding, length of hospitalization, histopathological examination reports, and postoperative complications were recorded for all patients.

The time from the onset of symptoms to the time patients applied to the hospital was termed symptom duration, and patients with a symptom duration of more than 48 hours were considered 'late admission'. Perforated appendix observed in the perioperative examination, plastron formation, conditions requiring peritoneal debridement, diffuse peritonitis, and conditions requiring postoperative drainage were categorized as complicated appendicitis. The remaining cases were considered non-complicated appendicitis. The transition time to oral feeding was determined as the time elapsed until the patients started adequate oral feeding after the operation. Histopathological diagnosis of gangrenous appendicitis, phlegmonous appendicitis, and suppurative appendicitis were classified as severe inflammation. Patients diagnosed with normal, acute appendicitis, or lymphoid hyperplasia were classified as mild inflammation.

Two groups were created as patients in the pandemic period (March 01, 2020 - May 31, 2020) Group-A, and patients in the pre-pandemic period (March 01, 2019 -May 31, 2019) Group-B. The number of patients, mean age, male/female ratio, mean symptom duration, late admission rates, mean White Blood Cell (WBC) count, mean C-Reactive Protein (CRP) value (reference range 0-10 g/dl), mean appendix diameter measured by computed tomography (CT) and ultrasonography (US), rates of complicated and uncomplicated appendicitis, mean duration of operation, rates of patients requiring peritoneal debridement, rates of patients who underwent postoperative drainage, mean hospital stay, mean time to start oral feeding, severe inflammation and mild inflammation rates in pathology reports, and postoperative complication rates were calculated for both groups. The results were subjected to statistical analysis and the two groups were compared.

Statistical analysis: The conformity of the data to normal distribution was examined with the Shapiro wilk test. Student's t-test was used to compare normally distributed variables between the groups, and the Mann Whitney u test was used to compare non-normally distributed variables between the groups. Relationships between categorical variables were examined with Pearson and Exact chi-square tests. Descriptive statistics were presented as mean±standard deviation for numerical variables. SPSS Windows version 23.0 package program was used for statistical analysis and P<0.05 was considered statistically significant.

Results

A total of 94 patients were included in the study (29 patients in Group A and 65 patients in Group B). It was determined that the number of patients decreased significantly during the pandemic period (Group-A) compared to the pre-pandemic period (Group-B). The mean age was 12.69 ± 3.54 in Group A and 11.12 ± 3.29 in Group B. There was no significant difference between the two groups in terms of mean age (p=0.051). Group A consisted of 9 (31%) girls and 20 (69%) boys, Group B consisted of 21 (32.3%) girls and 44 (67.7%) boys, and

the gender distribution of the two groups was similar (p=0.869).

The mean symptom duration was significantly higher in group A (43.17 ± 36.39 hours) compared to group B (24.73 ± 11.75 hours) (p<0.001). The number of late admissions was 12 (41.3%) in Group A and 8 (12.3%) in Group B. There was a significant difference between the groups (p=0.012).

The mean WBC count was 14.68 × 10 9/L (±3.82) in Group A and 13.54 × 10 9/L (±3.83) in Group B. No difference was found in WBC between the groups. The mean CRP level was 60.44 g/dl (±56.24) in Group A, compared to 20.14 g/dl (±14.55) in Group B. CRP level was significantly higher in Group A (p<0.001). CT and US were performed in 16 (55.2%) patients each in Group A, compared to 36 (55.4%) and 31 (47%) patients in Group B. There was no significant difference between the two groups in terms of radiological imaging. Appendix diameter could be measured in 22 (75%) patients in Group A and 52 (80%) patients in Group B, and the mean appendix diameter was larger in Group A (10.06 ±2.17) compared to Group B (8.21±1.93) (p<0.001).

Although there was an increase in the percentage of complicated appendicitis cases in Group A (n:7, 36.8%) compared to Group B (n:10, 28.6%), this increase was not statistically significant (p=0.532). The number of patients who underwent peritoneal debridement-toilet was 5 (17.2%) in Group A and 4 (6.2%) in Group B (p=0.092). The mean duration of operation was longer in Group A (49.82 ±19.09 min vs. 40.15 ±11.61 min) (p=0.016). Postoperative drainage was applied to 4 (13.8%) patients in Group A and 1 (1.5%) patient in Group B (p=0.030). Although the transition time to oral feeding was longer in favor of Group A (1.51 ±0.83 days vs. 1.28 ± 0.60 days), the difference was not statistically (p=0.160). The mean significant duration of hospitalization was also similar (3.58 ±2.91 days for Group A and 3.0 ±1.63 days for Group B) (p=0.876).

Open appendectomy was performed on all patients included in the study. During postoperative follow-up, wound site infection requiring wound debridement and re-suturation was observed in one patient in Group A, and one patient in Group B developed a brid ileus requiring surgery. The results of the patients are shown in Table 1 together with the statistical analysis results Table 1.

According to the histopathological examination reports, the rate of appendicitis with severe inflammation findings (gangrenous, phlegmonous and suppurative

Variable	GRUP A On the Pandemic (n=29)	GRUP B Off The Pandemic (n=65)	Total (n=94)	p
Age (year) (mean±sd)	12.69±3.54	11.12±3.29	11.6±3.42	0,051
Sex - n(%) -Male	20 (69.0)	44 (67.7)	64	
Sex - n(%) -Female	9 (31.0)	21 (32.3)	30	0,869
Symptom Duration (hour) (mean±sd)	43.17±36.39	24.73±11.75	30.41±23.90	<0.001
Late Applicants n(%)(>48 hours)	12 (41.3)	8 (12.3)	20 (21.3) 0.0	012 0,012
White Blood Cell (× 109/L) (mean±sd)	14.68±3.82	13.54±3.83	13.89±3.84	0,186
C-Reaktif Protein (mean±sd) (Ref. Ran.: 0-10 g/dl)	60.44±56.24	20.14±14.55	32.57±25.83	<0.001
Radiological İmaging - n(%) -Computed Tomography	16 (55.2)	36 (55.4)	52 (55.3)	0,99
Radiological İmaging - n(%) -Ultrasonography	16 (55.2)	31 (47.0)	47 (49.5)	0,461
Appendix Diameter (mm)(mean±sd)	10.06±2.17 (n:22)	8.21±1.93 (n:52)	8.76±2.17 (n:74)	<0.001
Grade of Appendicitis - n(%) -Noncomplicated	12 (63.2)	25 (71.4)	65 (68.5)	
Grade of Appendicitis - n(%) -Complicated	7 (36.8)	10 (28.6)	17 (31.5)	0,532
Length of Surgery (min.)(mean±sd)	49.82±19.09	40.15±11.61	40.35±14.98	0,016
Peritoneal Debridement-Toilet - n(%)	5 (17.2)	4 (6.2)	9 (9.6)	0,092
Postoperative Complication	1 (Surgical Field infection)	1 (lleus)	2	

 Table 1. Descriptive analysis of the sample. quantitative and qualitative variables.

Table 2. Descriptive analysis of the histopathological examination reports

Histopathological result	GRUP A GRUP B On the Pandemic (n=29) Off The Pandemic (n=65)		TOTAL (n=94)	р
Lymphoid hyperplasia	2 (6.9)	10 (15.4)	12 (12.8)	
Acute App.*	15 (51.7)	38 (58.5)	53 (56.4)	
Gangranus App.	4 (13.8)	7 (10.8)	11 (11.7)	
Phlegmatous App.	3 (10.3)	1 (1.5)	4 (4.3)	
Suppurative App.	4 (13.8)	7 (10.8)	11 (11.7)	
* Severe Inflammation n(%)	11 (37.9)	15 (23.1)	26 (27.7)	137
* Mild İnflammation n(%)	18 (62.1)	50 (76.9)	68 (72.3)	216

*Appendicitis

appendicitis) was higher in Group A (n:11, 37.9%) compared to Group B (n:15, 23.1%), but this difference was not statistically significant. Histopathological examination results are shown in Table 2.

Discussion

After being first identified in Wuhan, China in December 2019, COVID-19 continued to spread rapidly and soon turned into a global pandemic (1). This new member of the coronavirus family can easily be transmitted from person to person through respiratory routes and contact, leading to a disease with high morbidity and mortality ⁽⁹⁾. From the moment it was first described, COVID-19 has been and continues to be covered daily by the media around the world. News about COVID-19 related deaths in the media and the global struggle in health sectors to fight against this disease, even in developed countries, has led to tremendous anxiety and panic in people. Furthermore, a series of bans restricting social life, declared by governments in order to prevent the spread of the disease, further increased this fear. This has led to significant hesitations to apply to healthcare facilities, even for urgent health problems, because of the large number of COVID-19 cases in hospitals. Hospitals are high-risk environments for the transmission of respiratory diseases during epidemics, which induces severe anxiety about patient-to-patient transmission in the emergency department ^(10,11). During this period, non-COVID-19 applications to healthcare facilities decreased significantly in almost every center.

Similarly, during previous outbreaks (Influenza and Middle East Respiratory Syndrome (MERS) outbreaks), emergency applications to hospitals for non-respiratory causes decreased significantly as outbreaks progressed ^(12,13). We also observed that admissions to the emergency services of our hospital decreased significantly. In the present study, we demonstrate this decrease in patients who underwent appendectomy and were diagnosed with of acute appendicitis during the COVID-19 pandemic. Our hospital is the only center with a pediatric surgery department in our city, and pediatric surgeons in our center consult every case with suspected acute appendicitis Furthermore, the pediatric surgeons in both periods selected for the study were the same people and the only treatment performed for AA was an appendectomy. These conditions being the same before and during the pandemic period makes the data showing the decrease in AA cases during the pandemic more reliable. Other studies in the literature show a similar decrease in AA cases during the COVID-19 pandemic $^{(14,15)}$.

Since COVID-19 or any other epidemic cannot directly affect AA development, there must be another underlying reason. One of the hypotheses that may explain this decrease may be that AA can regress spontaneously or the symptoms can disappear with symptomatic treatment. In the literature, some studies describe spontaneous recovery from AA ^(16,17). In other words, some AA cases can recover without appendectomy. Probably, during the pandemic, some patients with AA did not apply to hospitals because of fear and anxiety and tolerated their symptoms as long as possible, and they were able to recover spontaneously or with symptomatic treatment during this time at home. On the other hand, patients who do not recover present with a delayed and more complicated clinical picture (18,19).

The present study showed that the duration of symptoms and late admission rates of pediatric patients diagnosed with AA in the first 3 months of the COVID-19 pandemic in Turkey were significantly higher. Other studies show that this period is more extended than usual during pandemics ⁽²⁰⁾. It has also been reported that the incidence of acute appendicitis may vary seasonally ⁽²¹⁾. Therefore, the periods selected for the study covered the same months in 2019 and 2020.

Acute appendicitis is also the most common cause of abdominal surgery in children, and appendectomy remains the most common emergency surgical procedure pediatric surgeons perform (4-6). 1%-8% of cases presenting to the emergency department with abdominal pain are diagnosed with AA ⁽²²⁾. It has been reported that appendicitis is seen 1.1 to 2.9 times more frequently in males during childhood ⁽²³⁾. In the present study, the female/male ratio was similar in the prepandemic and pandemic periods, and, consistent with the literature, AA was more common in male patients.

Even though the mortality and morbidity of AA are decreasing thanks to the widespread use of continuously developing health services, mortality, morbidity and medicolegal incidents can still be seen due to the late diagnosis of AA ⁽²⁴⁾. Furthermore, the diagnosis of AA can be more difficult in children than it is in adults. Factors such as communication difficulties with children, difficulties in physical examination, obesity and gynecological diseases in young girls can further reduce the rate of correct diagnosis ^(25,26). Perforated appendicitis is more common in children

than adults, most likely because of these diagnostic difficulties (27). Patients who fail to present to the hospital within 24 hours of the onset of symptoms have a higher risk of suffering from perforated appendicitis ^(28,29). AA cases presenting late have a higher risk for these complications during pandemics. In the present study, although the rate of complicated appendicitis was higher during the COVID-19 pandemic, the increase was not statistically significant. This may be due to the small number of patients in our series. Similar studies have also shown that the rate of complicated appendicitis is significantly higher during the pandemic ⁽¹⁵⁾. A similar study was conducted in Spain with 66 pediatric patients (41 patients before and 25 patients during the pandemic). It was shown that CRP elevation, length of hospital stay and the rate of complicated appendicitis were higher during the pandemic period ⁽¹⁶⁾. In another study on pediatric appendicitis conducted in Italy, the pandemic period was compared with the previous 3 years and no statistically significant difference was found in terms of the number of patients, duration of symptoms, and complicated appendicitis rate (30).

In recent years, publications have supported that the first-line treatment of uncomplicated AA may be antibiotics instead of appendectomy ^(31,32). Studies also show no superiority between antibiotic treatment and only symptomatic treatment without antibiotics (33). On the other hand, studies argue that appendectomy remains the most effective treatment, even for patients with uncomplicated AA, with higher efficacy and lower complication rates ⁽³⁴⁾. During the COVID-19 pandemic, due to the risk of healthcare workers being infected and a possible COVID-19 case leading to a more severe clinical picture after surgery, it has become important to carry out interventional treatments in accordance with the procedures and measures determined by medical authorities. Accordingly, it is recommended that elective surgeries be postponed and emergency surgical cases should be carried out by taking a series of precautions ⁽³⁵⁾. During the pandemic, several sources also suggested that antibiotic therapy could be the first treatment choice in uncomplicated AA cases ⁽³⁶⁾. A study by The Association of Italian Surgeons in Europe showed that surgeons more commonly preferred nonsurgical antibiotic treatment for AA during the pandemic. One-third of the surgeons participating in the same study reported that patients had more severe appendicitis during the COVID-19 pandemic (37). In our hospital, we did not change pediatric AA's diagnosis and treatment management during the COVID-19 pandemic. We performed an appendectomy on every patient diagnosed with AA before and during the pandemic.

The appendix diameter measured by CT or US was larger during the COVID-19 pandemic (Group A). Another study comparing the anterior-posterior diameter of the appendix between appendicitis cases diagnosed with abdominal CT reported that the mean diameter was larger during the pandemic (20). More complicated appendicitis cases naturally prolong the surgery ⁽¹⁹⁾. Another study reported that blood loss in patients who underwent open appendectomy was higher during the COVID-19 pandemic compared to the pre-pandemic period ⁽²¹⁾. In the present study, the duration of surgery was significantly longer during the pandemic. Although the duration of hospitalization and transition to oral feeding were also longer in this group, the difference was not statistically significant.

According to the histopathology reports, it was found that the rate of patients with severe inflammation findings was higher during the COVID-19 pandemic, but the difference was not statistically significant. Unlike other publications (19), no difference was found in the present study between the two groups in terms of complications. This may be due to the small number of cases, which is also one of the limitations of our study.

Based on the results of the present study and similar studies in the literature, it can be concluded that people refrain from applying to hospitals even for emergency health problems or delay their application during the COVID-19 pandemic. It should not be forgotten that this may lead to more serious health problems, morbidity, and mortality. The media organs constantly sharing warnings or information about COVID-19 should also inform the public about other emergencies and related processes. It should be announced to the public that they should not hesitate to apply to health institutions for oncological, cardiac, or emergency surgical diseases that can cause serious health problems if delayed. Health organizers must assure the public that they can safely benefit from emergency health services. During such extraordinary periods, it is essential to strengthening home health and transport services (ambulance, etc.) to better deal with emergencies.

The management of acute appendicitis may be modified in light of studies providing evidence that acute appendicitis can regress spontaneously or be cured with How Did The Covid-19 Pandemic Affected Children Acute Appendicitis?

symptomatic treatment at home. We think that further, more comprehensive studies are needed on this subject.

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Conflict of interest

All authors declare that they have no conflict of interest.

Ethical standards

This study was approved by the local ethics committee.

References

- 1. He F, Deng Y, Li W. Coronavirus disease 2019: What we know? J Med Virol 2020;92:719–25.
- Dae-Gyun A, Hye-Jin S, Mi-Hwa K, Sunhee L, Hae-Soo K, Jinjong M, et al. Current Status of Epidemiology, Diagnosis, Therapeutics, and Vaccines for Novel Coronavirus Disease 2019 (COVID-19). J Microbiol Biotechnol. 2020 Mar 28;30(3):313-324.
- 3. Yuanyuan D, Xi M, Yabin H, Xin Q, Fan J, Zhongyi Ji, et al. Epidemiology of COVID-19 Among Children in China. Pediatrics 2020 Jun;145(6):e20200702.
- Karabulut R, Sonmez K, Turkyilmaz Z, Demirogullari B, Ozen IO, Demirtola A, et al. Negative appendectomy experience in children. Ir J Med Sci 2011;180:55-8.
- Deng Y, Chang DC, Zhang Y, Webb J, Gabre-Kidan A, Abdullah F. Seasonal and day of the week variations of perforated appendicitis in US children. Pediatr Surg Int 2010;26:691-6.
- Pearl RH, Hale DA, Molloy M, Schutt DC, Jaques DP. Pediatric appendectomy. J Pediatr Surg 1995;30:173-81.
- Mueller BA, Daling JR, Moore DE, Weiss NS, Spadoni LR, Stadel BV, et al. Appendectomy and the risk of tubal infertility. N Engl J Med 1986;315:1506-8.
- Anneliese D, Sam M, Emilie K, Raman P, Annelies WS, Heidi L. The pandemic of social media panic travels faster than the COVID-19 outbreak. J Travel Med. 2020 May 18;27(3):taaa031.
- Yung-Fang T, Chian-Shiu C, Aliaksandr AY, Yi-Ying L, Yung-Hung L, Yi-Tsung L, et. al. A Review of SARS-CoV-2 and the Ongoing Clinical Trials. Int J Mol Sci. 2020 Apr 10;21(7):2657.
- Alenazi TH, Al Arbash H, El-Saed A, Alshamrani MM, Baffoe-Bonnie H, Arabi YM, et al. Identified transmission dynamics of middle east respiratory syndrome coronavirus infection during an outbreak: implications of an overcrowded emergency department. Clin Infect Dis. 2017;65(4):675–679.

- Assiri A, McGeer A, Perl TM, Price CS, Al Rabeeah AA, Cummings DAT, et al. Hospital outbreak of middle east respiratory syndrome coronavirus. N Engl J Med. 2013;369:407–416.
- Schanzer DL, Schwartz B. Impact of seasonal and pandemic influenza on emergency department visits, 2003–2010, Ontario. Canada Acad Emerg Med. 2013;20(4):388–397.
- Paek SH, Kim DK, Lee JH, Kwak YH. The impact of middle east respiratory syndrome outbreak on trends in emergency department utilization patterns. J Korean Med Sci. 2017;32(10):1576–1580.
- James T, Aner K, Ori B, Michael K, Brigitte H, Shahaf S, et al. The Decreasing Incidence of Acute Appendicitis During COVID-19: A Retrospective Multi-centre Study. World J Surg. 2020 May 26:1–6.
- Velayos M, Munoz-Serrano AJ, Estefanía-Fernández K, Sarmiento Caldas MC, Moratilla Lapena L, López-Santamarí M, et. al. Influence of the coronavirus 2 (SARS-Cov-2) pandemic on acute appendicitis. Anales de Pediatría (English Edition). Volume 93, Issue 2, August 2020, Pages 118-122.
- Kirshenbaum M, Mishra V, Kuo D, Kaplan G. Resolving appendicitis: role of CT. Abdom Imaging. 2003;28(2):276–279.
- 17. Andersson RE. The natural history and traditional management of appendicitis revisited: spontaneous resolution and predominance of prehospital perforations imply that a correct diagnosis is more important than an early diagnosis. World J Surg. 2007;31(1):86–92.
- Paige F, Omar P, Kiranmayi M, Henry W, Thomas M, Stephen U, et al. A Retrospective Analysis of the Trends in Acute Appendicitis During the COVID-19 Pandemic. J Laparoendosc Adv Surg Tech A. 2020 Nov 11. doi: 10.1089/lap.2020.0749.
- Javier R, Sergio V, Andres G. Acute Appendicitis During Coronavirus Disease 2019 (COVID-19): Changes in Clinical Presentation and CT Findings. J Am Coll Radiol. 2020 Aug;17(8):1011-1013.
- 20. Yuan Z, Lu-Sha C. Managing acute appendicitis during the COVID-19 pandemic in Jiaxing, China. World J Clin Cases. 2020 Oct 6;8(19):4349-4359.
- 21. Stein GY, Rath-Wolfson L, Zeidman A, Atar E, Marcus O, Joubran S, et al. Sex differences in the epidemiology, seasonal variation, and trends in the management of patients with acute appendicitis. Langenbeck's Arch Surg. 2012;397(7):1087–1092.
- 22. Sivit CJ, Siegel MJ, Applegate KE, Newman KD. Special focus session: When appendicitis is suspected in children. Radiographics. 2001;21:247-62.

- 23. Shrestha R, Ranabhat SR, Tiwari M. Histopathologic analysis of appendectomy specimens. Journal of Pathology of Nepal 2012;2:215-9.
- 24. Callie B, Anupam K. Acute appendicitis in pediatric patients: an evidence-based review. Pediatr Emerg Med Pract. 2019 Sep;16(9):1-20.
- 25. Rothrock SG, Skeoch G, Rush JJ, Johnson NE. Clinical features of misdiagnosed appendicitis in children. Ann Emerg Med 1991;20:45-50.
- 26. Horwitz JR, Gursoy M, Jaksic T, Lally KP. Importance of diarrhea as a presenting symptom of appendicitis in very young children. Am J Surg 1997;173:80-2.
- 27. Bonadio W, Peloquin P, Brazg J, Scheinbach I, Saunders J, Okpalaji C, et al. Appendicitis in preschool aged children: regression analysis of factors associated with perforation outcome. J Pediatr Surg 2015;50:1569-73.
- Williams N, Bello M. Perforation rate relates to delayed presentation in childhood acute appendicitis. J R Coll Surg Edinb. 1998;43(2):101–102.
- 29. Kearney D, Cahill RA, O'Brien E, Kirwan WO, Redmond HP. Influence of delays on perforation risk in adults with acute appendicitis. Dis Colon Rectum. 2008;51(12):1823–1827.
- Enrico LP, Alberto S, Federico R, Daniele V, Giorgio F, Daniela C, et. al. Appendicitis in Children in a Large Italian COVID-19 Pandemic Area. Front Pediatr. 2020 Dec 9;8:600320.
- Hansson J, Körner U, Khorram-Manesh A, Solberg A, Lundholm K. Randomized clinical trial of antibiotic therapy versus appendicectomy as primary treatment of acute appendicitis in unselected patients. Br J Surg 2009; 96: 473–81.
- Corinne V, Caroline B, Sophie M, Karine P, Mahaut L, Bruno C, *et al.* Amoxicillin plus clavulanic acid versus appendectomy for treatment of acute uncomplicated appendicitis: an open-label, non-inferiority, randomized controlled trial. Lancet 2011; 377: 1573– 9.
- Park HC, Kim MJ, Lee BH. Randomized clinical trial of antibiotic therapy for uncomplicated appendicitis. Br J Surg. 2017;104(13):1785–1790.
- 34. Mauro P, Nicola C, Salomone DS, Antonio L, Francesco F, Gianluigi L, et al. Antibiotics-first strategy for uncomplicated acute appendicitis in adults is associated with increased rates of peritonitis at surgery. A systematic review with metaanalysis of randomized controlled trials comparing appendectomy and non-operative management with antibiotics. Volume 15, Issue 5, October 2017, Pages 303-314.
- 35. Ti LK, Ang LS, Foong TW, Ng BSW. What we do when a COVID-19 patient needs an operation: operating

room preparation and guidance. Can J Anaesth 2020;67:756–8.

- Collard M, Lakkis Z, Loriau J, Mege D, Sabbagh C, Lefevre JH, et al. Antibiotics alone as an alternative to appendectomy for uncomplicated acute appendicitis in adults: Changes in treatment modalities related to the COVID-19 health crisis. J Visc Surg. 2020 Jun; 157(3S1):S33-S42.
- Lelpo B, Podda M, Pellino G, Pata F, Caruso R, Gravante G, et al. Global attitudes in the management of acute appendicitis during COVID-19 pandemic: ACIE Appy Study. Br J Surg. 2020 Oct 8: 10.1002/bjs.11999.