Original Article

Acute Appendicitis in Children in the Era of Covid-19

Muhamed Jassim Fadhle, Ali Farooq Al-Mayoof

Department of Surgery, Division of Pediatric Surgery, Mustansiriyah University, College of Medicine, Baghdad, Iraq

Abstract

Background: Abdominal pain is a common complaint encountered by paediatric surgeons. This complaint could be related to surgical or non-surgical causes. With coronavirus disease 2019 (COVID-19), the incidence of abdominal pain has increased and mimicked acute appendicitis in paediatric patients. **Objective:** The objective of this study was to assess the impact of the COVID-19 pandemic on paediatric acute appendicitis in terms of demographic data (age and sex), and operative findings, specifically, the complicated appendicitis and negative appendectomy rates. **Materials and Methods:** This retrospective cohort study reviewed the records of children aged 5–15 years, who were diagnosed with acute appendicitis and underwent surgery between January 2018 and December 2021. The patients were divided into pre-pandemic and pandemic groups. Demographic, operative and histopathological findings were compared between the two groups. **Results:** A significant increase in the incidence of acute abdominal pain amongst the admitted children (39.8% vs. 32.7%, $P < 0.0001$) and a significant decrease in the incidence of acute appendicitis (27% vs. 33%, $P < 0.013$) were observed in the pandemic group. An associated non-significant increase in the rates of complicated appendicitis (30% vs. 26%, $P = 0.299$) and negative appendectomy (5.8% vs. 3.8%, $P = 0.359$) was noted. During the pandemic period, no statistically significant differences were found between polymerase chain reaction (PCR)-positive and PCR-negative patients in complicated appendicitis or negative appendectomy rates (30% vs. 29.7%, $P = 0.841$, and 6.7% vs. 4.2%, $P = 0.424$, respectively). **Conclusion:** COVID-19 is associated with an increased incidence of acute abdominal pain in children but a decreased rate of acute appendicitis. The latter tends to present at a younger age than usual. The rates of complicated appendicitis and negative appendectomy increased but were not significantly affected by the pandemic or severe acute respiratory syndrome coronavirus 2 infection status.

Keywords: Abdominal pain in children, acute appendicitis in children, complicated acute appendicitis, coronavirus disease 2019, negative appendectomy

Introduction

At the end of 2019, an outbreak of unexplained pneumonia manifested as dry cough, fever and fatigue in Wuhan, Hubei Province, China.[1] The causative agent was identified as a new variant of the coronavirus, which was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the infection as coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO). The viral epidemic spread rapidly worldwide which made the WHO declare a pandemic status in March 2020 as the disease reached an alarmingly dangerous level.[2]

The clinical presentation of COVID-19 is highly variable, ranging from completely asymptomatic to severe respiratory failure.[3] The major challenges faced by healthcare professionals in the early stages of the pandemic included the infection risk in children which were related to various factors, such as poor compliance of the children to follow preventive and control measures, including mask wearing and social distancing, and immature immune systems.[4] However, most reports have stated that the paediatric age group (up to 18 years) tends to have mild illness and short hospitalisation compared to the adult population, and only 2.4% of the total cases occurred in children.[1]

In May 2020, many reports from the United States, United Kingdom and Europe described an increasing number of children with exaggerated inflammatory reactions and manifestations of multiorgan failure in the setting of previous or concurrent SARS-CoV-2 infection.[5] This condition

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Address for correspondence: Prof. Ali Farooq Al-Mayoof, Zayouna Sect 718, St.,18, Baghdad, Iraq.
E-mail: alialmayoof@uomustansiriyah.edu.iq

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is termed the multisystem inflammatory syndrome in children (MIS-C) by the WHO and the Centers for Disease Control and Prevention.[6] The diagnostic criteria for the MIS-C are age <21 years, fever (38°C or more) for more than 24 h, two or more organ involvement, increased inflammatory markers, COVID-19 positivity or exposure within 4 weeks before the development of symptoms, lack of other alternate possible diagnoses and disease severity that necessitate hospital admission.[5,6] Gastrointestinal manifestations of MIS-C, such as nausea, vomiting, abdominal pain and/or diarrhoea, are reported in >70% of patients. Abdominal pain can be severe enough to mimic acute appendicitis or peritonitis. Thus, MIS-C must be considered in the differential diagnosis of acute abdomen in children after an outbreak of SARS-CoV-2 infection.[7,8]

The COVID-19 pandemic has caused significant changes to the presentation, diagnosis and management of various medical conditions, including acute appendicitis. Increasing evidence suggests a potential link between COVID-19 and acute appendicitis in children. The association between both conditions is an area of abundant interest, as one condition may be misdiagnosed as another, or both conditions may present simultaneously.[9] Some hypotheses have suggested that COVID-19 predisposes patients to acute appendicitis. This is based on the three factors related to SARS-CoV-2 infection. First, there are abundant angiotensin-converting enzyme 2 (ACE-2) receptors in the intestine and colon, which are receptors for SARS-CoV-2. Second, COVID-19 is commonly associated with mesenteric adenopathy, which may obstruct the lumen of the appendix and subsequent appendicitis. Third, appendicitis may occur because of the hyper-inflammatory state in MIS-C.[7,8]

This study aimed to assess the impact of COVID-19 pandemic on paediatric population with acute appendicitis in terms of demographic data (age and sex) and operative findings, specifically complicated appendicitis and negative appendectomy rates.

Materials and Methods

This retrospective cohort study reviewed the records of children diagnosed with acute appendicitis and operated at a paediatric surgery centre in Baghdad, Iraq, over 4 years. Patients were divided into two groups. The pre-pandemic group included children who underwent appendectomy before the COVID-19 pandemic between January 2018 and December 2019. The pandemic group included children who underwent appendectomies between January 2020 and December 2021. Demographic data and operative and histopathological findings were compared between the two groups. The status of the appendix was classified according to operative findings, with or without histopathology, into normal and inflamed. The inflamed appendix involves both non-complicated acute appendicitis and complicated acute appendicitis (perforation, peritonitis and abscess). During the pandemic period and according to the Ministry of Health regulations, it was mandatory for all admitted patients to undergo a polymerase chain reaction (PCR) test for COVID-19. Informed consent was not obtained due to the retrospective nature of the study. The Institutional Ethics and Scientific Committee approved this study (No. 366–2022). The inclusion criteria were children who were diagnosed with acute appendicitis and underwent appendectomy, aged 5–15 years, with complete medical records. Patients diagnosed with acute appendicitis or its complications who were treated conservatively were excluded. In addition, any child diagnosed and operated on beyond the age limit of the study or those who had incomplete records were excluded.

Statistical analysis

Data analysis was performed using the statistical package SPSS-28 (Statistical Package for the Social Sciences, version 28 by IBM (International Business Machines Corporation), Armonk, New York, USA. Released on 2021). Data were presented as simple measures of frequency, percentage, mean, standard deviation and range (minimum–maximum values).

The significance of differences in different means (quantitative data) was tested using the Student's *t*-test for differences between two independent means. The significance of differences in different percentages (qualitative data) was tested using the Pearson Chi-square test with the application of Yates' correction or Fisher's exact test, whenever applicable. Statistical significance was set at $P \leq 0.05$.

Results

During the study period, 4129 children with an age range of 5–15 years were admitted to the paediatric surgery emergency department due to different complaints, of which 1893 children were admitted during the pre-pandemic period and 2236 during the COVID-19 pandemic period. Amongst these patients, acute abdominal pain was reported in 620 (32.7% [620/1893]) patients during the pre-pandemic period and in 891 (39.8% [891/2236]) patients in the pandemic period, reflecting a significant increase in the incidence of acute abdominal pain during the COVID-19 period ($P < 0.0001$) [Table 1].

Acute appendicitis was reported during the pre-pandemic period in 206 patients, which comprised one-third (33% [206/620]) of the patients with acute abdominal pain, while in COVID-19 era, acute appendicitis was reported in 243 (27% [243/891]) patients. The difference in the acute appendicitis rates between the two periods was significant, $P < 0.013$. In addition, there was a significant difference in the mean age of the children ($P < 0.0001$), while there was no significant difference in the male-to-female ratio between the two groups ($P = 0.793$) [Table 1].

After performing appendectomy in patients in the two groups, an innocent appendix was found in 8 (3.8%) patients in the pre-pandemic period and 14 (5.8%) patients during the pandemic period, which was not significant ($P = 0.359$). Of the total patients with acute appendicitis, the rates of complicated appendicitis were 26% (54/206) and 30% (73/243) in the

pre-pandemic and pandemic periods, respectively, which were also insignificant ($P = 0.299$) [Table 2].

During the COVID-19 era, 149 (61.3% [149/243]) patients were PCR positive, and 94 (38.7% [94/243]) patients were PCR negative. In the PCR-positive group, a normal appendix was found in 10 (6.7%) patients, whereas in the PCR-negative group, only 4 (4.2%) patients had a normal appendix. No significant differences were found between the PCR-positive and PCR-negative groups in terms of operative and histopathological findings ($P = 0.424$). Of the total cases of acute appendicitis, the rate of complicated appendicitis was 30% (45/149) and 29.7% (28/94) in PCR-positive and PCR-negative patients, respectively, which was not significant ($P = 0.841$) [Table 3].

Discussion

Abdominal pain is a common complaint during childhood and may have both surgical and non-surgical causes.[8] Acute appendicitis is the most common surgical condition in paediatric patients worldwide, with an overall incidence of approximately 7%–8%.[8] Although antibiotics alone have been described as a treatment modality for uncomplicated appendicitis, appendicectomy remains the treatment of choice for acute appendicitis.[10] Many case reports in children and adults described patients with a clinical picture of acute appendicitis but were diagnosed with COVID-19, as there is an overlap between the clinical presentations of acute appendicitis and COVID-19 with predominant gastrointestinal manifestations.[11,12]

In Iraq, COVID-19 has affected 2,465,545 patients and resulted in 25,375 deaths, placing it in the 15th position amongst 50 Asian countries and 44th amongst 231 countries worldwide. The first confirmed case of COVID-19 in our country was on 23 February 2020, and the total number of cases reached 596,193 by the year-end. On 31 December 2021, the reported cases were 2,093,740 and the highest number of new daily cases was 13,515 on 28 July 2021.[13]

Acute abdominal pain was reported in 620 (32.7%) out of 1893 patients aged between 5 and 15 years who were admitted to the paediatric surgery emergency department during the pre-pandemic period. During the pandemic, 891 (39.8%) of the total 2236 patients were admitted for acute abdominal

Table 1: Demographic data of patients in pre-pandemic and pandemic periods

Variables	Pre-pandemic period	Pandemic period	*P*
Total number of visits	1893	2236	-
Children with abdominal pain, *n* (%)	620 (32.7)	891 (39.8)	0.0001*
Children with acute appendicitis, *n* (%)	206 (33)	243 (27)	0.013*
Mean age±SD (range) of patients with acute appendicitis	10.5±3.8 (7–15)	8.1±2.7 (5–14)	0.0001#
Male, *n* (%)	117 (56.8)	141 (58)	0.793
Female, *n* (%)	89 (43.2)	102 (42)	

*Significant difference between percentages using Pearson Chi-square test at 0.05 level, #Significant difference between two independent means using Student's *t*-test at 0.05 level. SD: Standard deviation

Table 2: Operative and histopathological findings of patients with acute appendicitis during pre-pandemic and pandemic eras

Operative and histopathological report	Pre-pandemic period, *n* (%)	Pandemic period, *n* (%)	*P*
Normal appendix	8 (3.8)	14 (5.8)	0.359
Inflamed appendix	198 (96.2)	229 (94.2)	
Non-complicated acute appendicitis	144 (70.2)	156 (64.2)	0.229
Complicated acute appendicitis	54 (26)	73 (30)	
Total	206 (100)	243 (100)	

*Significant difference between percentages using Pearson Chi-square test at 0.05 level

Table 3: Operative and histopathological findings of patients with acute appendicitis during pandemic period according to polymerase chain reaction test

Operative and histopathological report	Results of PCR test for COVID-19 virus		*P*
	Positive, *n* (%)	Negative, *n* (%)	
Normal appendix	10 (6.7)	4 (4.2)	0.424
Inflamed appendix	139 (93.3)	90 (95.8)	
Non-complicated acute appendicitis	94 (63.3)	62 (66.1)	0.841
Complicated acute appendicitis	45 (30)	28 (29.7)	
Total	149 (100)	94 (100)	

*Significant difference between percentages using Pearson Chi-square test at 0.05 level. PCR: Polymerase chain reaction, COVID-19: Coronavirus disease 2019

pain. The increase in the incidence of acute abdominal pain during the pandemic was significant. However, this was expected, as paediatric cases of COVID-19 predominantly present with gastrointestinal symptoms such as abdominal pain, nausea, vomiting and diarrhoea with mild respiratory manifestations.[8,9]

On the other hand, there was a significant decrease in the percentage of acute appendicitis cases in the pandemic period compared to the pre-pandemic period in our study (243 [27%] vs. 206 [33%] patients, respectively). Many studies conducted in different countries have reported similar findings. In Italy, La Pergola *et al*. conducted a study in a large pandemic area and found that the incidence of acute appendicitis cases at the pandemic peak in 2020 was less than the incidence at the same period in the previous three consecutive years (86 in 2020 and 121, 96 and 92 in 2017, 2018 and 2019, respectively).[14] Similarly, a wide multicentre study of 146 various United States hospitals observed a significant reduction in the overall incidence of acute appendicitis during the pandemic period (approximately 25.4%), with a greater reduction in paediatric acute appendicitis by approximately 33.8%.[15] Similarly, a Croatian study reported a decrease in the number of acute appendicitis cases in paediatric and adult patients during the pandemic period by approximately 22% compared with the pre-pandemic period.[16] This finding can be attributed to two factors. First, most people were afraid of acquiring an infection from the crowded environment of hospitals. Second, accessing healthcare centres and specialised hospitals was challenging due to the stay-at-home policy and the lockdown rules enforced by health authorities worldwide. This made most parents treat their children with mild abdominal pain and low suspicion of acute appendicitis symptomatically at home and sought medical help and treatment if needed from nearby private clinics and general hospitals.

The demographic data analysis revealed a significant difference in patient age between the pandemic and pre-pandemic periods. The mean age of patients during the pandemic period was less than that during the pre-pandemic period by approximately 2 years, while other studies did not find a significant difference in patient age between the two periods.[17,18] This significant difference may be related to the abundant presence of lymphoid tissues in young children, as SARS-CoV-2 infection may cause mesenteric lymphadenitis or gut associated lymphoid hyperplasia, which may predispose patients to, or misdiagnosed as acute appendicitis.[7,19]

There was a 4% increase in the complicated appendicitis rate in the pandemic period compared to the pre-pandemic period in our study (73 [30%] vs. 54 [26%] patients, respectively); however, the difference was not significant. This was comparable to other studies that found the rate of complicated appendicitis was not affected significantly by COVID-19.[17,18,20] In a multicentre study of 19 United States paediatric hospitals, there was an insignificant difference in complicated appendicitis cases between the pre-pandemic and pandemic periods. This was explained by the increased rate of non-operative treatment of acute appendicitis during the pandemic and low treatment failure rate in patients with complicated appendicitis who were treated non-operatively.[20] In other studies, the unchanged rate of complicated appendicitis during the pandemic was partially attributed to the increased use of abdominal computed tomography (CT) scans for the evaluation and diagnosis of acute abdominal pain during the pandemic period, especially where frequent and serial assessment was required. This decreased the rate of misdiagnoses or incorrect diagnoses, and only confirmed cases of appendicitis were admitted to the hospital.[17,18] In our study, the long duration of the pandemic period, which extended over 2 years and involved both total and partial lockdown periods, may be the underlying reason why the increased complicated appendicitis rate did not reach a statistically significant level. The total lockdown was applied for only 6 months (from March to September 2020), and the rest of the pandemic period was a partial lockdown. Although most patients were afraid of contracting SARS-CoV-2 infection in hospitals, they did not hesitate to seek medical help and advice for their persistent symptoms that did not respond to symptomatic treatment at home, as transportation became easier and stay-at-home instructions became less intense during the partial lockdown period. Interestingly, within the pandemic era, the complicated appendicitis rates in PCR-positive and PCR-negative patients were comparable, with no statistical significance. This reflects the opinion that SARS-CoV-2 infection did not increase the severity of acute appendicitis by itself but caused a delayed presentation as patients feared the outdoor environment.[21]

In contrast, many studies from different parts of the world have reported a significant increase in the complicated appendicitis rate during the pandemic. In New York City, for example, the rate of perforated appendicitis increased by approximately 18% during the pandemic in comparison to the usual rate from the preceding 5 years (45% vs. 27%, respectively).[21] In addition, Lee-Archer *et al*. found that the rate of complicated appendicitis doubled during the pandemic period compared to the previous year (60.5% vs. 30.4%).[22] This finding was explained mainly as a delayed presentation of acute appendicitis cases due to public fears and wariness of contracting SARS-CoV-2 infection from the hospitals, fear of social crowding and external restrictions for transport from quarantine rules. All these factors made families reluctant to seek medical help and acted as barriers that prevented patients from receiving timely and early assessment during the course of acute appendicitis. In other words, there was an increased time period from the onset of symptoms to the start of treatment, which negatively impacted the outcome of acute appendicitis, as the latter is a known time-dependent condition.[23] An additional source of the increased complicated appendicitis rate during the pandemic may be the increased dependency on outpatient clinics as all hospital wards were converted to isolation units for COVID-19 patients. A study in The Netherlands revealed that the increased complicated appendicitis rate in adults during the pandemic was partly due to decreased admitted cases of mild appendicitis that could

be resolved spontaneously or treated as outpatients or even at home.[24]

The negative appendectomy rate increased by approximately 2% during the pandemic period compared to the pre-pandemic period in our study (14 [5.8%] vs. 8 [3.8%] patients, respectively). This slight increase in the negative appendectomy rate was insignificant but could be attributed to the extreme similarity in the presentations between COVID-19 and acute appendicitis in some cases. This explanation is supported by similar findings between PCR-positive and PCR-negative patients during the pandemic. PCR-positive patients had a 2.5% higher risk of undergoing a negative appendectomy than PCR-negative patients (10 [6.7%] vs. 4 [4.2%] patients, respectively); however, the result was also insignificant. In our study, during the pandemic, 10 patients were PCR positive and presented with features suggestive of acute appendicitis, such as abdominal pain, vomiting and fever accompanied by tenderness, and guarding in the right lower abdomen; however, surgical exploration revealed a normal-looking appendix, which was confirmed later by histopathological examination. Six patients had mesenteric adenitis, two had terminal ileitis and two had small ascites. In contrast to our study, many studies reported a reverse finding, as the negative appendectomy rate decreased significantly during the pandemic. In the United Kingdom, Salgaonkar *et al*. found a significant decrease in the negative appendectomy rate from 17.1% in the pre-pandemic period to 6.8% in the pandemic period, which was related to strict recommendations for antibiotic use in the early stages of appendicitis and reservation of surgical interventions only in cases with persistent symptoms or complications.[25] Another study in Turkey reported a significant reduction in the negative appendectomy rate from the pre-pandemic to pandemic period (16.9%–7.2%). This was attributed to patients' fear of contracting SARS-CoV-2 infection; hence, they presented in advanced stages of the disease and to precise and meticulous assessment and evaluation to establish the diagnosis before taking patients to operative theatres.[26] Thus, COVID-19 has both direct and indirect effects on paediatric patients with acute appendicitis. The direct effect related to inflammation of the appendix from viral invasion of the gastrointestinal tract through ACE-2 receptors, appendiceal obstruction from mesenteric lymphadenopathy or appendicitis may develop as part of the exaggerated inflammatory reaction in MIS-C. The indirect effect is related to the increased complication rate of acute appendicitis due to delayed initiation of appropriate treatment. Given these findings, it is crucial that healthcare providers remain vigilant in managing children who present with acute abdominal pain during the COVID-19 pandemic, through a thorough assessment of potential COVID-19 symptoms and prompt referral to imaging or surgical specialists. It is also essential to educate parents and caregivers about the signs and symptoms of acute appendicitis and encourage timely access to healthcare services.

Our study had some limitations. First, the retrospective nature of the study may have resulted in a selection bias during data collection. Second, this was a single-institution study, which may not reflect the actual situation of acute appendicitis during the pandemic in our community because the severity of the COVID-19 pandemic varied amongst different locations.

Conclusion

COVID-19 is associated with an increased incidence of acute abdominal pain in children but a decreased rate of acute appendicitis. The latter tends to present at a younger age than usual. Complicated appendicitis and negative appendectomy rates increased but were not significantly affected by the pandemic or SARS-CoV-2 infection status.

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Conflicts of interest

There are no conflicts of interest.

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