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Complicated Acute Appendicitis during COVID-19 Pandemic: The Hidden Epidemic in Children

Carlos Delgado-Miguel[1] Antonio J. Muñoz-Serrano[1] Miriam Miguel-Ferrero[1]
María De Ceano-Vivas[2] Cristina Calvo[3] Leopoldo Martínez[1,4]

[1] Department of Pediatric Surgery, La Paz Children's Hospital, Madrid, Spain
[2] Pediatric Emergency Department, La Paz Children's Hospital, Madrid, Spain
[3] Pediatric Infectious Diseases Department, Fundación IdiPaz. Traslational Research Network in Pediatric Infectious Diseases, Madrid. Spain
[4] Institute for Biomedical Resarch La Paz (IdiPaz), Network for Maternal and Children Health (SAMID), La Paz Children's Hospital, Madrid, Spain

Address for correspondence Carlos Delgado-Miguel, MD, Department of Pediatric Surgery. La Paz Children's Hospital., Paseo de la Castellana 261, Madrid 28041, Spain (e-mail: carlosdelgado84@hotmail.com).

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Abstract

Introduction Since home confinement for novel coronavirus disease 2019 (COVID-19) pandemic began, pediatric visits to the emergency department (ED) have decreased, including consultation for abdominal pain. Our aim is to investigate the incidence of complicated acute appendicitis (AA; peritonitis or appendicular mass) during confinement for COVID-19 pandemic and to compare it with the previous 5 years.

Materials and Methods A retrospective study was performed in children with AA who underwent surgery between March 9 and April 13 from 2015 to 2020; patients were divided into six groups according to the year of surgery. We analyzed demographic variables, time from onset of symptoms, mean hospital stay, cumulative incidence, and incidence rate of complicated appendicitis.

Results A total of 168 patients were included with no differences in the number of patients, gender, and age between groups. Patients in 2020 (COVID-19 group) presented longer symptom progression time (46.8 hours; $p = 0.046$), higher rate of complicated appendicitis (48.4%; $p = 0.004$), longer mean hospital stay (4.9 days; $p < 0.001$), increased cumulative incidence (8.27 cases per 100,000 children per 0.1 years; $p < 0.001$), and increased incidence rate of complicated appendicitis (83 cases per 100,000 children; $p < 0.001$) when compared with other groups.

Conclusion Delayed ED visit of children with AA during home confinement lead to an increased rate of complicated appendicitis. It is crucial to make parents aware of the importance of early diagnosis and treatment of abdominal pain.

Keywords
- SARS-CoV-2
- COVID-19
- perforated appendicitis
- peritonitis
- children

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Introduction

In March 2020, the World Health Organization announced that novel coronavirus disease 2019 (COVID-19) had reached pandemic status.[1] Accumulated evidence suggests that the virus plagues people ubiquitously, although pediatric patients seem to present with distinct characteristics from infected adults.[2,3] The number of confirmed pediatric cases is very low compared with adults, and the severity and mortality rates are even lower.[4,5] During the current outbreak of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), the number of confirmed cases in children under 19 years of age represents approximately 2% of the total number of cases worldwide, only 7.9% of them present with severe disease and the overall mortality rate is 2 to 3% compared with 8 to 10% in adults.[6] Symptoms in children include fluctuating fever, upper respiratory signs (cough, sore throat, nasal congestion, sneezing, and rhinorrhea), flu-like syndrome and pneumonia, being fever, and cough the most common clinical manifestations.[7,8] A few children do not exhibit fever but only manifest cough or diarrhea, and even fewer can be asymptomatic carriers. Vomiting and abdominal pain can also occur in SARS-CoV-2 infection but are not common symptoms.[3,9]

Modeling studies predict that transmission chains can be interrupted by sustained social interventions, mainly through health education such as handwashing, masking, and home confinement.[10] In China, where the SARS-CoV-2 outbreak began in December 2019, strong mandatory quarantines and infection control efforts were initiated in January 2020, and by March 2020, they proved to be effective in stopping the increase in COVID-19 new cases.[11] For this reason, during the month of March, these measures have been implemented in the United States and in most European countries. Since confinement in our country began, the number of visits to the pediatric emergency department (ED) has decreased dramatically. Fever or cough has become the main reason for consultation in this population, probably due to the social alarm that makes parents pay more attention to this type of symptoms. Other common reasons for consultation, such as abdominal pain, vomiting, or diarrhea have decreased notably, as children are only brought to the ED when symptoms persist after symptomatic treatment at home. Subsequently, there has been a decrease in the number of nonspecific abdominal pain, gastroenteritis, or uncomplicated diarrhea diagnosed in the ED during the time of enforced home confinement. On the other hand, when compared with the months prior to the onset of quarantine, we have observed a significant increase in the number of children who waited for several days before consulting for abdominal pain complaint, and were finally diagnosed with complicated acute appendicitis (AA; with peritonitis or appendicular mass).

The aim of this paper is to investigate the incidence of complicated AA (peritonitis or appendicular mass) during the time of enforced confinement in the outbreak of COVID-19, and to analyze it when compared with the same period of time of the previous 5 years.

Materials and Methods

A retrospective observational study was performed in patients diagnosed with AA who underwent surgery at our institution between March 9 and April 13 of the past 6 years (2015–2020). Patients were divided into six groups according to the year in which they were operated on for AA. We analyzed demographic variables (age and sex), time from onset of symptoms (hours), presence of fever or vomiting, intraoperative diagnosis (phlegmonous AA, gangrenous AA, peritonitis, and appendicular mass), mean hospital stay (days), and early postsurgical complications, such as surgical wound infection, intra-abdominal abscess, and bowel obstruction, which were defined according to the U.S. Centers for Disease Control and Prevention's criteria.[12] We identified as phlegmonous appendicitis those with mild inflammation of the wall without perforation, as gangrenous those with moderate inflammation without perforation, as peritonitis those AA perforated, and as appendicular mass those perforated with localized abscess formation. All data were collected from each patient's medical history. Exclusion criteria were age over 18 years, absence of some of the data of the variables analyzed, and absence of intraoperative diagnosis of AA.

All patients who had been diagnosed of AA by ultrasound, received a preoperative dose of antibiotics with amoxicillin–clavulanic acid (40 mg/kg, maximum dose, 2 g). After surgery, the postoperative antibiotic was only continued in gangrenous appendicitis (amoxicillin–clavulanic acid for 5 days), and in appendicitis complicated by peritonitis or appendicular mass (gentamicin, metronidazole, and amoxicillin–clavulanic acid for 7 days). A screening for SARS-CoV-2 infection was performed on all patients with AA diagnosed in the year 2020 prior to the intervention. A nasopharyngeal mucosal swab was obtained on which the virus genome was identified using real-time polymerase chain reaction (PCR) test.[13] The study protocol was conformed to the guidelines of the 1975 Declaration of Helsinki and was approved by our institutional review board. Because of the nature of aggregated data, the retrospective design of this study, absence of human or animal samples, as well as importance of sharing the research findings, and bridging the knowledge gaps, an ethical approval was waived by institutional review board.

For the statistical analysis, data were collected in Microsoft Excel software version 2010 (Redmond, Washington, United States, EE.UU.), and analyzed with SPSS Statistic version 22 (Chicago, Illinois, United States). Continuous variables were expressed as mean and standard deviation. To check whether the variables were normally distributed, the Kolmogorov–Smirnoff and Shapiro–Wilk tests were used. For the continuous variables normally distributed, the analysis of variance (ANOVA) of independent samples was used, and to analyze the continuous variables not normally distributed data, the Kruskal–Wallis test was used. Discrete variables were expressed as frequency and percentage, and were analyzed by the Chi-square test or Fisher's test when the first one could not be applied. Statistical significance was established with a value of $p < 0.05$.

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Cumulative incidence rate of complicated AA was calculated by dividing the number of patients operated on for AA during the same period of time each year (from March 9 to April 13), among the pediatric population served by our institution, expressed per-100,000 inhabitants. Incidence density rate was calculated by the cumulative incidence rate of AA divided by the duration of the follow-up time, which in our study was 36 days (0.1 years). Cumulative incidence and incidence density rate of complicated appendicitis (appendicular peritonitis or mass) were performed in the same way. The pediatric population served by our institution in our health area was obtained from the annual register of the Statistical Institute of the Community of Madrid.[14]

Results

A total of 168 patients (99 males and 69 females), with a mean age of 9.9 ± 3.5 years, who were operated on for AA between March 9 and April 13 from 2015 to 2020 were included: 31 patients in 2020 (COVID-19 group), 26 in 2019, 31 in 2018, 24 in 2017, 28 in 2016, and 28 in 2015. No patient was excluded. There was no statistically significant difference in the number of patients between these groups. PCR test for SARS-CoV-2 was positive in one patient from COVID-19 group who was taken to the ED for abdominal pain and vomiting, without associated fever, cough, or other associated respiratory symptoms. Respiratory isolation protection measures were used during surgery and subsequent hospital admission, and he was discharged after 24 hours with adequate oral intake. No significant differences were observed when comparing the distribution by sex and age between the six groups. However, COVID-19 group patients attended the ED with a longer time of evolution from the onset of symptoms, with a mean of 46.8 ± 13.5 hours, being this difference statistically significant when comparing to patients in the previous 5 years ($p = 0.046$). In addition, COVID-19 group presented a higher frequency of associated fever and vomiting (61.3 and 64.5%, respectively) compared with patients in other groups, with no statistical significance. ►Table 1 shows demographic and clinical features of patients distributed by groups according to the year in which they were diagnosed with AA.

When analyzing the intraoperative diagnosis of AA, patients in COVID-19 group presented a higher proportion of peritonitis (25.8%) and appendicular mass (22.6%), this difference being statistically significant when compared with the rest of the groups, in which a higher proportion of phlegmonous and gangrenous appendicitis was observed. The rate of complicated AA was 48.4% in COVID-19 group, which was significantly higher than in other groups, where percentages ranging from 15 to 21% ($p = 0.004$) were observed. The mean hospital stay was also increased in COVID-19 group, with a mean of 4.9 ± 2.2 days, significantly higher when compared with the rest of the groups ($p < 0.001$). Early postoperative complications occurred in 7 to 15% of patients, with no significant differences between groups. Intraoperative findings, average hospital stay, and postoperative complications in each group of patients are described in ►Table 2.

No significant differences have been found in the cumulative incidence or incidence density rate of AA in the past 6 years. However, patients in COVID-19 group had a cumulative incidence of complicated AA of 8.27 cases per-100,000 children per 0.1 year and an incidence density rate of 83 cases per 100,000 children-year. Both data were significantly higher than those observed in the other groups, being these differences statistically significant ($p < 0.001$). Data related to cumulative incidence and incidence density rate are shown in ►Table 3.

Discussion

This paper describes the clinical features, intraoperative findings, and early postoperative complications of children diagnosed with AA during home confinement due to COVID-19 infection, and compares them with those of patients who underwent surgery in the same period of time

Table 1 Demographic and clinical features distributed by groups (2015–2020)

	2020	2019	2018	2017	2016	2015	*p*-Value
Patients (*n*)	31	26	31	24	28	28	0.57
Age (y) Mean (SD)	10.4 (3.3)	11.2 (3.8)	9.5 (4.1)	10.6 (3.8)	9.4 (2.4)	9.1 (3.3)	0.073
Gender *n* (%)							0.692
• Male	21 (67.7)	16 (61.5)	18 (58.1)	15 (62.5)	16 (57.1)	15 (53.6)	
• Female	10 (32.3)	10 (38.5)	13 (41.9)	9 (37.5)	12 (42.9)	13 (46.4)	
Time from onset of symptoms (h) Mean (SD)	46.8 (13.5)	22.9 (11.5)	32.8 (21.7)	25.4 (12.7)	25.9 (14.9)	24.1 (12.2)	0.046
Fever *n* (%)	19 (61.3)	6 (23.1)	12 (38.7)	10 (41.7)	9 (32.1)	10 (35.7)	0.076
Vomiting *n* (%)	20 (64.5)	15 (57.7)	16 (51.6)	15 (50)	12 (42.9)	14 (50)	0.66

Abbreviation: SD, standard deviation.

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Table 2 Intraoperative findings, average hospital stay and postoperative complications distributed by groups (2015–2020)

	2020	2019	2018	2017	2016	2015	*p*-Value
Total acute appendicitis (*n*)	31	26	31	24	28	28	0.47
Type acute appendicitis *n* (%)							0.004
• Phlegmonous	13 (41.9)	18 (69.2)	17 (54.8)	18 (75)	20 (71.4)	16 (57.1)	
• Gangrenous	3 (9.7)	4 (15.4)	9 (29)	3 (12.5)	5 (12.5)	6 (21.4)	
• Peritonitis	8 (25.8)	4 (15.4)	5 (16.1)	1 (4.2)	2 (7.1)	6 (21.4)	
• Appendicular mass	7 (22.6)	0	0	2 (8.3)	1 (3.6)	0	
Complicated appendicitis (peritonitis or appendicular mass) *n*	15	4	5	3	3	6	0.004
Complicated appendicitis rate (complicated appendicitis ×100/total acute appendicitis)	48.4%	15.4%	16.1%	12.5%	10.7%	21.4%	0.004
Mean hospital stay (d) Mean (SD)	4.9 (3.2)	2.5 (1.4)	3.6 (2.8)	2.5 (1.4)	3.6 (2.0)	3.3 (3.3)	<0.001
Postoperative complications *n* (%)	4 (12.9)	4 (15.4)	5 (16.1)	2 (8.3)	2 (7.2)	3 (10.7)	0.68
• Intra-abdominal abscess	3	4	1	0	1	1	
• Surgical site infection	1	0	3	2	1	0	
• Bowel obstruction	0	0	1	0	0	2	

Abbreviation: SD, standard deviation.

Table 3 Cumulative incidence and incidence density rate distributed by groups (2015–2020)

	2020	2019	2018	2017	2016	2015	*p*-Value
Pediatric population (0–16 years) served by our institution	181,368	181,159	180,582	182,135	179,345	177,478	0.57
Acute appendicitis (*n*)	31	26	31	24	28	28	0.47
• Cumulative incidence (cases per 100,000 children per 0.1 years)	17.1	14.4	17.2	13.2	15.6	15.8	0.45
• Incidence density rate (cases per 100,000 children-years)	171	144	172	132	156	158	0.45
Complicated appendicitis (*n*)	15	4	5	3	3	6	0.004
• Cumulative incidence (cases per 100,000 children per 0.1 years)	8.27	2.21	2.77	1.65	1.67	3.44	<0.001
• Incidence density rate (cases per 100,000 children-years)	83	22	28	17	17	34	<0.001

during the previous 5 years. Since home confinement began, the number of children diagnosed with AA has been similar to that of the past 5 years; however, during the same period of time this year, children have been brought to the ED with a higher number of hours of evolution since the onset of symptoms, and consequently, we have observed a significant increase in the rate of complicated AA.

The first confirmed case of COVID-19 infection in the Madrid region was declared on February 27, 2020, and since then, Madrid has become the hot spot of infection in Spain, with more than 60,000 people infected, which is approximately one-third of the people infected in our country. Recently published data on infection in children agree with those previously published, suggesting that only 2% of affected individuals are younger than 19 years.[15] In Madrid, 60% of confirmed infections in children required admission, the main criteria for admission being respiratory problems.[16] In the largest study of severity of COVID-19 in 2,143 identified cases among children, Dong et al reported an inverse relationship between age and proportion of severe and critical cases, which was 10.6, 7.3, 4.2, 4.1, and 3.0% for the age groups of <1, 1 to 5, 6 to 10, 11 to 15 and >15 years, respectively.[17] This suggested that young children were more likely to progress to severe disease than older ones. All this, added to the appearance of the first deaths in children due to COVID-19 infection, has caused a significant social alarm in parents with a high fear of the infection spreading to their children.[18]

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Consequently, there has been a notable decrease in the number of pediatric visits to ED since home confinement began compared with previous years, which has also been reported in other countries that have suffered a high number of COVID-19 cases such as in Italy.[19] This can be partly explained by the fact that since March 9, the Regional Government decreed the closure of schools and sports activities in Madrid, so it is understandable that accidental injuries and trauma in children have decreased as a result of this measure.[20] However, children continue getting sick with occasional infections and complications or acute onset of chronic conditions. This substantial decrease in pediatric care access during home confinement might reflect the reticence on the part of parents and caregivers to risk exposure to SARS-CoV-2 in a health care setting, in addition to lower rates of accidental injuries and trauma. However, this decrease in pediatric visits to the ED has been associated with a delay in the diagnosis and treatment of severe acute diseases, with children attending ED after several days of evolution from the onset of symptoms, as we have observed in our study, leading to negative consequences for children's health. This may explain the increased cumulative incidence and incidence density rate of complicated appendicitis with peritonitis or appendicular mass that we have observed during home confinement. Consequently, while the incidence of AA has not varied significantly from the previous 5 years, the incidence of complicated appendicitis has four-fold increased during the same time period in 2020. Furthermore, the rate of complicated appendicitis has tripled when compared with previous years in this same period of time, reaching 48.4% since home confinement had begun, while this rate is usually around 10 to 15% of all patients diagnosed with AA in our area.[21] As a result, the average hospital stay of these patients has increased significantly, with an increase in direct and indirect costs, arising from the need for care by parents throughout the period of hospitalization.

In our hospital, PCR test in COVID-19 group of patients was performed at the arrival to the emergency department, at the same time as laboratory studies, and the result of both is obtained in approximately 1 hour, so there was no delay in the surgical treatment for that reason in these patients. Only one of the 31 patients operated on COVID-19 group presented a positive PCR test for SARS-CoV-2, although this did not cause a delay in surgical treatment either because the emergency operating room was full equipped and prepared to perform surgery on patients with COVID-19. During the pandemic, the hospital staff in the operating room was the same as in previous months, so there was no difference in this regard either.

This is one of the first studies to analyze the negative consequences of the COVID-19 pandemic on children. Several studies have been published on the epidemiology, clinical management, and treatment of COVID-19 infection in children, but to date, there are few studies that reflect the negative side effects on children during the pandemic. In Italy, 12 cases of delayed access to hospital care have been recently reported.[19] These include two children who were brought to the ED with acute onset of type-1 diabetes and severe ketoacidosis, a 3-year-old girl who arrived at the ED after 6 days at home with very high fever (>39°C), with sepsis secondary to pyelonephritis, or a newborn who was brought to the hospital after vomiting for several days due to hypertrophic pyloric stenosis and reached the ED in hypovolemic shock. Half of the children of this series were admitted to an intensive care unit, and four of them finally died. In all cases, parents reported avoiding access to hospital because of fear of infection with SARS-CoV-2.

There is a need to prevent delays in accessing hospital care and to increase provision of high-quality coordinated care by health care providers. Parents should be made fully aware that the risks of delayed access to hospital care for emergency conditions can be much higher than those posed by COVID-19. To this end, the Spanish Society of Pediatric Emergencies has developed a guide for parents where it establishes the situations in which parents should take their children to the ED, using a series of signs and symptoms easily recognized by parents.[22] The delay in medical care in children with urgent diseases, such as AA, leads to an increase in negative consequences, with more advanced diseases and a longer mean hospitalization time. It is essential to make parents aware that children can suffer from the same diseases as before the COVID-19 pandemic, and their early diagnosis is really important to avoid complications derived from this.

Limitations

This study has several limitations, mainly those derived from being a unicentric study, as well as those of its retrospective design features. Multicenter studies with a greater number of patients are needed to evaluate the negative side effects of COVID-19 pandemic in children.

Conclusion

To sum up, children diagnosed with AA during home confinement in COVID-19 infection presented an increased rate of complicated appendicitis, with a significantly higher cumulative incidence and incidence density when compared with the previous 5 years. They presented a longer time from onset of symptoms at the time of ED visit and an increased average hospital stay, with no difference in early postoperative complications.

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Conflict of Interest

None declared.

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