Title Page

Original Article

Impact of the COVID-19 Pandemic and the Restrictions on Pediatric Appendicitis in Turkey: A Single Center Experience

Short Title: Pediatric Surgery and Pandemic

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Abstract

Background

In this study, we investigated how the incidence and course of acute appendicitis (AA) changed in children, during the pandemic.

Methods

Children diagnosed with AA during the one-year pandemic period after the first COVID-19 case in Turkey and the previous one year were included in the study. Children were divided into two groups: those hospitalised during the pandemic (group A) and hospitalized in the previous year of the pandemic (group B). Furthermore, we compared the findings obtained for COVID-19-positive and COVID-19-negative children in the whole study group and within group A.

Results

In our study, a significant difference was found between the two groups in terms of gender, the rate of vomiting and number of days of vomiting. Complicated AA findings were found more frequently from the results of patients in group B than in group A. In addition, the hospital stay was longer, and the mean number of days with fever, and mean body temperature were higher in COVID-19 positive patients in the whole study group and within group A.

Conclusions

Contrary to most studies in the literature, in our study patients were admitted to hospital later in the pre-pandemic period, and therefore the frequency of complicated AA might have been more common in these patients. In conclusion, the arrangements and warnings of health authorities during the pandemic, might have reduced the anxiety and the hesitancy of the families to go to the hospital and relatively the rate of complicated acute appendicitis.

Keywords: Acute appendicitis, abdominal pain, children, COVID-19, pediatric surgery

Introduction

Acute appendicitis (AA) is inflammation of the appendix vermiformis. Appendicitis is the most common cause of surgical abdominal pain in children and requires urgent abdominal surgery. The lifetime risk of having appendicitis is between 7-10%. The incidence of appendicitis is 1-2/10000 in children under the age of 4 years, and 9- 28/10000 in children under the age of 14 years. It is most common in the second decade, between the ages of 10-12 years and is more common in boys (1-3). Complications may develop in 25-70% of children diagnosed with AA (4,5). When diagnosed late, its mortality and morbidity rates are high (2-5). AA diagnosis is achieved using clinical, laboratory and imaging findings.

Gastrointestinal symptoms of patients in the pediatric age group with COVID-19 may be confused with appendicitis (6-9). Multisystem inflammatory syndrome in children (MIS-C) should also be considered in children with prominent gastrointestinal symptoms and a history of recent COVID-19 exposure or infection. Radiological examination and laboratory findings are necessary for differential diagnosis (6-9).

In addition, it was reported that there may be a relationship between AA and COVID-19 (6-9). Some studies report that COVID-19 can induce lymphoid follicular hyperplasia in the colonic epithelium lining the appendix leading to luminal obstruction, inflammation, and ischemia (6-10). Case series studies reported that AA cases with COVID-19 have a more complicated disease course (6).

The COVID-19 pandemic has had a significant impact on healthcare systems. Fear of families coming into contact with infected people, warnings of authorities not to leave the house unless necessary, and the effort of emergency services to cope with abnormal patient load has resulted in late diagnosis and complication of diseases other than COVID-19. Some studies have reported an increased rate of complicated and/or perforated appendicitis in children during the pandemic period (1, 2, 5, 7, 11-29).

In this study, we investigated how the incidence and course of AA changed in children, during a one-year period of the pandemic, especially when the restrictions were more intense.

Materials and Methods

A retrospective study was conducted at the State Hospital of Denizli, Department of Pediatric Surgery. Children diagnosed with AA by a pediatric surgeon with clinical, laboratory, and radiological findings, during the one-year pandemic period after the first COVID-19 case in

Turkey (March 18, 2020 and March 18, 2021) and the previous one year (March 18, 2019 and March 18, 2020) were included in the study. Polymerase chain reaction (PCR) tests to detect COVID-19 were performed for all patients who were hospitalized and included in the study during the pandemic. Patient information was obtained from their epicrisis and patient hospital files. Children were divided into two groups: those hospitalised during the pandemic (group A) and hospitalized in the previous year of the pandemic (group B). The demographic information of the two groups, duration of symptoms before admission to the hospital, clinical and laboratory findings, radiological features, treatments, surgical and pathological findings, length of stay in hospital, and prognoses were compared. In addition, we compared the findings obtained for COVID-19-positive and COVID-19-negative children in the whole study group. Furthermore, the clinical and laboratory findings of patients in group A analysed according to their COVID-19 status

Consent from the patient and from their parents to participate in the study was obtained at the time of their hospitalization. Before starting the study, approval of the health ethics committee (Ethical Committee of Pamukkale University Faculty of Medicine, date of approval 16/03/2021 and 06 approval number), the permission of the Ministry of Health, and the chief physician of the hospital were obtained.

Statistical Analysis

For statistical analysis, SPSS (Statistical Package for the Social Sciences) 23.0 software (IBM SPSS Statistics, IBM Corporation) was used. For statistical analyses, the Chi-square test, Student's t-test, and Mann–Whitney U-test were used; $p < .05$ was considered statistically significant.

Results

A total of 285 children diagnosed with AA were included in our study. When all children included in the study were examined, 61.4% (n:175) were boys and the majority were between the ages of 9-15 years (n:150, 52.6%). The most common complaint was abdominal pain and it was present in all cases. Overall, 272 (95.4%) children reported vomiting and 99 (34.7%) fever. On physical examination, abdominal pain was localized to the right lower quadrant in 202 (70.9%) children, diffuse in 83 (29.1%) children, and rebound was detected in 95 (33.3%). About 22% of the patients (n:64) were overweight. Children with atypical findings and children who could not be evaluated with physical examination due to their young age underwent US to rule out conditions that could be confused with AA, especially, MIS-C. CT was performed if

the appendix could not be visualised on ultrasound and if a diagnosis could not be made using ultrasound despite clinical suspicion. Abdominal ultrasound was performed in 218 children and was normal in 49 (22.5%), compatible with simple AA in 160 (73.4%), and compatible with complicated AA in 9 (4.1%). Abdominal CT was performed in 49 patients and was normal in 8 (16.3%), compatible with simple AA in 38 (77.5%), and compatible with complicated AA in 3 (6.2%). Two children diagnosed during the pandemic were treated without surgery. When the operative results were analysed, simple AA was found in 216 (75.8%) patients, and complicated and/or perforated AA was found in 53 (18.6%) patients. By pathological examination, simple AA was found in 221 (77.5%) patients, and complicated and/or perforated AA was found in 49 (17.2%) patients. The negative appendectomy rates in groups A and B were 3.9% and 4.6%, respectively.

Demographic Features of Groups A and B

When the children were divided into two groups, the pre-pandemic period (Group B) and the pandemic period (Group A), their numbers (142 vs 143) (49.8% vs 50.2%) were similar. When the demographic characteristics were examined, a significant difference was found between the two groups in terms of gender. Although the ratio of boys (69.7%, n:99) was higher than that of girls in group B, this difference almost disappeared in group A (53.1%. n:76) (p=0.01). (Table 1)

Clinical Findings in Groups A and B

When the symptoms were questioned, only the rate of vomiting and number of days of vomiting were statistically different between the two groups. Vomiting was more frequent (141 vs 131, 99.3% vs 91.6%) (p=0.01) and the vomiting duration was longer (1.93 days vs 1.90 days) (p=0.04) in Group B. There were no statistically significant differences in physical examination findings between the two groups (Table 2)

Laboratory and Radiological Findings of Groups A and B

There were no statistically significant differences between the two groups in terms of laboratory results other than alanine aminotransferase (ALT). Although within the normal range, the mean ALT was higher in group A (15.95 vs 13.62 U/L) (p=0.01). Abdominal CT was performed more frequently during the pandemic period (32 vs 17, 22.4% vs 12%), however CT findings were not statistically significantly different between the two groups (p=0.12). (Table 3). The findings obtained as a result of the pathological examination of the surgical material also showed a

statistically significant difference between the two groups. Complicated AA findings were found more frequently from the pathological results of patients in group B (34 vs 15, 23.9% vs 10.5%) (p=0.01).

COVID-19 Status

COVID-19 was detected in 10 patients included in our study. All positive patients had fever and underwent surgery. There were no post-operation complications in any patients. However, the hospital stay was longer (6,40 vs 3,81 days, p<0.001), and the mean number of days with fever (2 vs 0,50 days, p<0.001), mean weight (58.4 vs 43.11, p=0.01), and mean body temperature (38.6 vs 37.1, p<0.001) were higher in COVID-19 positive patients. In the COVID-19 negative group, blood leukocyte (11.520 vs 14.871, p=0.45) and thrombocyte (236.200 vs 296.363, p=0.02) numbers were higher than in the COVID-19 positive group. No complicated AA findings were found in any pathological examinations of these patients' surgical material.

We also analysed the clinical and laboratory findings of patients in group A according to their COVID-19 status. Similar to the results obtained when all groups of children were analysed, the hospital stay was longer (7.14 vs 3.83 days, p<0.001) and the mean number of days with fever (1.86 vs 0.53 days, p<0.001), mean weight (61.6 vs 43.4 days, p=0.01), and mean body temperature (38.5 vs 37.1, p<0.001) were higher in COVID-19-positive subjects within group A. In COVID-19-negative subjects within group A, blood leucocyte (10185.71 vs 14619.5, p=0.04) and thrombocyte (224571.4 vs 292128.5, p=0.04) counts were higher than those in the COVID-19-positive subjects within group A

Discussion

When the data of all children included in our study were analysed, the demographic characteristics and clinical findings were similar to those previously reported. As in other studies, AA was more common in boys and the incidence of AA increased above the age of 5 years, especially in the second decade of life (1-3, 30). When the symptoms of the patients were evaluated, abdominal pain was the most common symptom, followed by vomiting and fever similar to that previously reported. In addition, right lower quadrant tenderness was present in most patients. (1-3, 30).

In our study, we noticed that the rate of overweight children was 22.5% (n:64). Although we could not find any data on the frequency of overweight in AA cases, studies have reported a

direct correlation between body mass index (BMI) or age and the rate of complicated appendicitis. Based on these data, there is a need for data on obesity in pediatric AA cases.

For children with AA, radiological examination is performed when necessary and it starts with ultrasound. CT may be preferred if the appendix cannot be visualized on ultrasound and if a diagnosis cannot be made with ultrasound despite clinical findings (31). In our study, the frequency of CT examination was much lower than ultrasound.

When we analysed the operative and pathological results obtained from our study, the rate of complicated AA in Groups A and B was 18.6% and 17.2%, respectively. In the literature, the rate of complicated appendicitis varies between 25-70%, and this rate increases as the time between the onset of symptoms and treatment increases (4). The rate of complicated AA was lower in our hospital compared to the literature. The fact that cases with high clinical suspicion are operated on without delay may explain this. However, our negative appendectomy rates were 4.9% and 4.6%, which were not higher than those previously reported in the literature. Although negative appendectomy was more common, especially in young children and postmenarchial girls, it varied between 1-25% in children (32-34).

Similar to that reported previously, gender changed and male dominance disappeared during the pandemic period (5, 19, 21, 35, 36). However, some studies reported male dominance in AA continued during the pandemic and that only perforated AA was increased in men (13, 14, 34, 37-39).

In our study, we observed that complaints of vomiting were more frequent and longer in patients who were admitted before the pandemic. In addition, complicated AA was more common in these patients. All these findings show that, contrary to most studies in the literature, patients were admitted to hospital later in the pre-pandemic period, when vomiting occurs, and therefore the frequency of complicated AA might have been more common in these patients (1, 2, 5, 15, 17-25). In our hospital, pediatric services are located in a separate building, and our pediatric emergency department is separate from the adult emergency department. Our hospital has served patients in our city and in the surrounding cities for a long time, and this has promoted confidence among patients, especially with regard to pediatric surgeries. This confidence among patients and the complete isolation of pediatric patients from adult patients may have prevented a decrease in patient admissions during the pandemic. In fact, before the pandemic, while patients were waiting for abdominal pain to accompany vomiting, they visited the hospital more frequently, fearing that abdominal pain might be a symptom of COVID-19 during the

pandemic period. In our opinion, the most important reasons associated with the decrease in the number of complicated AAs and prevalence of vomiting in children grup A are as follows: (i) during the pandemic period, patients visited the hospital more frequently, fearing that abdominal pain might be a symptom of COVID-19 and (ii) the decrease in the anxiety of families of the children to be exposed to COVID-19 after the first period of the pandemic, as observed in case of the whole society. However, the arrangement of emergency departments for pediatric patients may have contributed to the outcome indirectly by at least reducing the anxiety of the families and may have prevented the feared decrease in the number of admissions of those with serious illness predicted in the pandemic. In the pre-pandemic period, such arrangements may not have been effective because there was no concern of exposure to COVID-19. In addition, considering that most studies in the literature examined the first 3- 6 months of the pandemic, and we examined the one-year period, a decrease in the anxious approach of families in the latter stages of the pandemic may be an important explanation for these findings (5, 7, 13, 16, 18, 40-42).

When we examined the radiological results, CT was used more diagnostically during the pandemic. This situation supports the idea that in the pandemic, surgeons tend to get quick results for cases where they are not completely sure of the diagnosis, instead of hospitalizing the patients and examining them intermittently for a long time. This may partly be the result of practices aimed at reducing the patient load in the hospital and allocating more areas for excessive numbers of COVID-19 patients.

In our study, the rate of COVID-19 positivity was 3.5% (10 of 285) among all cases and 6.9% (10 of 143) among cases during the pandemic period, which was higher than that reported in the literature where the prevalence of COVID-19 in the AA population varies between 5.1% and 5.8%, and between 2% and 5% in children (35, 43, 44). Similar to some studies, but different from most studies, there was no increase in the frequency of complications among positive cases (6, 10, 27, 30, 45-47). Although there was no increase in the complication prevalence, the frequency and level of fever and the mean length of hospital stay of patients in the pandemic period were higher than in the other group. Fever-related findings may be related to COVID-19 independent of AA. We were able to find only one study that reported that the length of hospital stay was increased in COVID-19 patients who were operated on for AA (12). These results need to be clarified in future studies. The higher blood leukocyte and blood platelet counts of patients in the pre-pandemic period may be due to the late and complicated admission of these patients, as stated above.

The first limitation of our study was its retrospective design. Another limitation was the inclusivity of the study, because it was performed at one centre.

Conclusions

AA is an important surgical problem in childhood and maintained its importance during the pandemic. Disruptions in the health system and problems in accessing health services during pandemic periods further complicated the situation. In our study, although there was no increase in the frequency of complications in pediatric AA cases during the pandemic period, increases were experienced in many centres. It was revealed in our study that the separation of the pediatric department from adult departments, warnings of health authorities to visit hospital when necessary, facilitated patient management during the pandemic. However, more studies are needed to evaluate these findings.

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Disclosure

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Author contributions:

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48. Table 1. Demographic Features of Groups

49.

		Group A		Group B		p
		n	%	n	%	
Gender	male	76	53.1	99	69.7	0.01
	female	67	46.9	43	30.3	
Age distribution	≤5 years	4	2.8	6	4.2	0.84
	5- ≤15 years	106	74.1	107	75.4	
	≥15 years	33	23.1	29	20.4	
		mean±SD	Median (min - max)	mean±SD	Median (min – max)	
Age (months)		139.1±43.5	145,5 (25-213)	143.8±41.3	146 (35-213)	0.35

50.

51.

52. Table 2. Clinical Findings in Groups A and B

53.

		Group A		Group B		p
		n	%	n	%	
Fever	Yes	51	35.7	48	33.8	0.74
	No	92	64.3	94	66.2	
Abdominal pain	Yes	142	99.3	142	100	1.00
	No	1	0.7	0	0	
Vomiting	Yes	131	91.6	141	99.3	**0.02**
	No	12	8.4	1	0.7	
Duration of fever (day)	mean±SD	0.59±0.92		0.51±0.78		0.39
Duration of abdominal pain (day)	mean±SD	1.90±0.96		1.93±0.81		0.79
Duration of vomiting (day)	mean±SD	1.14±0.54		1.26±0.46		**0.04**
		n	%	n	%	
Abdominal tenderness	Right lower quadrant	102	71.3	100	70.4	0.87
	Diffuse	41	28.7	42	29.6	
Rebound	Yes	49	34.3	46	32.4	0.74
	No	94	65.7	96	67.6	

54.

55. Table 3. Radiographic features

		Abdomen US*				p
		No US	Normal	Simple AA	Complicated AA	0.42
Grup A	n	36	27	74	6	
	%	25.2%	18.9%	51.7%	4.2%	
Grup B	n	31	22	86	3	
	%	21.8%	15.5%	60.6%	2.1%	
		Abdomen CT**				

		No CT	Normal	Simple AA	Complicated AA	0.12
Grup A	n	111	6	24	2	
	%	77.6%	4.2%	16.8%	1.4%	
Grup B	n	125	2	14	1	
	%	88.0%	1.4%	9.9%	0.7%	

56. *US:ultrasonography, **CT:computed tomography

57.