

Changes in the frequency, presentation and surgical outcomes of complicated appendicitis during the pandemic

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ABSTRACT

OBJECTIVE: Coronavirus Disease 2019 (COVID-19) has affected every aspect of human life and all health care systems globally. The aim of this study was to investigate the effect of COVID-19 pandemic on the frequency, presentation and surgical outcomes of complicated appendicitis.

METHODS: Patients who underwent appendectomy for acute appendicitis one year before and one year after the declaration of the pandemic were investigated. Demographics and diagnostic findings as well as surgical and histopathological outcomes were recorded and statistically analyzed.

RESULTS: The study group of 409 patients was composed of 241 cases in the pre-pandemic group and 168 cases in the pandemic group revealing that the weekly total number of appendectomies decreased during the pandemic [pre-pandemic, median (IQR): 5 (3–6); pandemic, median (IQR): 3 (2–5); $p=0.005$]. The pandemic group was significantly associated with a longer time from emergency department admission to hospitalization, increased mean blood C-reactive protein levels and increased rate of postoperative complications ($p=0.024$, $p=0.038$ and $p=0.004$, respectively). Most importantly, pathological examinations revealed a higher number of complicated appendicitis cases in the pandemic group when compared to the pre-pandemic group [26 (15.5%) vs. 19 (7.9%), respectively] which corresponded to a 2.1-fold higher risk of being diagnosed with complicated appendicitis during the pandemic [OR: 2.1 (95% CI: 1.1–4.1), $p=0.024$].

CONCLUSION: While fewer appendectomies were performed during the pandemic, the incidence of complicated appendicitis and postoperative complications increased considerably.

Keywords: Appendicitis; COVID-19; general surgery; pandemics.

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Coronavirus Disease 2019 (COVID-19) is an infectious disease mostly in the form of mild to moderate and in some cases, severe respiratory illness caused by the SARS-CoV-2 virus. First identified in December 2019 in China, the disease was declared a pandemic by the World Health Organization (WHO) on March 11th, 2020 which initiated a series of control measures including quarantine orders throughout the world to prevent its transmission [1]. By the end of April 2020, most of the countries as well as Turkey were under lockdowns. Even after the lockdowns, people were mandated to stay at home which led to a fear of public areas, especially hospitals. Studies investigating the effects of the pandemic on emergency departments (EDs) in Istanbul reveal approximately a 50% reduction in emergency admissions, a 30% reduction in emergency consultations and a 25% reduction in surgical patient admissions in the city [2, 3].

Acute appendicitis (AA) is one of the most common surgical emergencies worldwide. As a global disease with a stable incidence over the past years, appendicitis can be useful to determine the impact of the pandemic on emergency surgery [4]. Studies focusing on the relation between the duration of symptoms in AA and the severity of the disease show that delayed presentation for medical care is a risk factor for complicated appendicitis [5, 6]. The aim of this study was to investigate the effect of the pandemic on the frequency, diagnostic features and surgical outcomes of complicated appendicitis.

MATERIALS AND METHODS

The Turkish Ministry of Health reported the first case of COVID-19 on March 11th, 2020, which was the same date that the disease was declared a pandemic by the WHO. This date was acknowledged as the beginning of the pandemic for the present study. With the intention of comparing AA patients before and during the pandemic, patients who underwent an emergency appendectomy at the Department of General Surgery during one year period of the pre-pandemic era (from March 11th, 2019 to March 10th, 2020) and one year period of the pandemic era (from March 11th, 2020 to March 11th, 2021) were investigated retrospectively. This study was conducted in accordance with the Declaration of Helsinki, the ethics committee approval was obtained from the Istanbul Medeniyet University Goztepe Training and Research Hospital Clinical Research Ethics Committee (date: 26.05.2021, number: 2021/0272) and signed informed consent forms were obtained from all patients.

Highlight key points

- A decrease in the number of appendectomies, a longer time from emergency to admission for appendicitis patients, and higher pre-operative C-reactive protein levels were recorded during the pandemic.
- Postoperative findings of patients who underwent appendectomy during the pandemic revealed an increased rate of 'complicated' appendicitis and postoperative complications.
- Patients with appendicitis during the pandemic had a 2.1-fold higher risk of being diagnosed with complicated appendicitis.

All patients who underwent appendectomy due to a suspicion of AA were included in the study. Patients who were below 18 and above 90 years of age, who had a chronic inflammatory or malignant disease (Familial Mediterranean Fever, inflammatory bowel disease, cancer, etc.), patients whose histopathological examination of the appendectomy specimen revealed a result other than acute appendicitis (i.e., adenocarcinoma, carcinoid tumor, mucocele, etc.) were excluded.

Patient data including age, sex, time from ED admission to surgery, preoperative laboratory findings such as; complete blood count (CBC) values, C-reactive protein (CRP) and bilirubin levels as well as preoperative abdominal ultrasonography and abdominal computerized tomography scan (CT) findings were recorded. Postoperative histopathological examination results of the appendectomy specimens, length of hospital stay, presence of postoperative complications, a need for postoperative percutaneous drainage and readmission rates were investigated.

All appendectomy specimens were evaluated by the same pathologist, and complicated appendicitis was defined as the presence of gangrenous or perforated appendicitis, as determined by postoperative histopathological examinations. The patients received follow-up at approximately 10 days post-discharge at the General Surgery outpatient clinic. Complications were defined as any deviation from the stable postoperative course during hospitalization and during the first month after surgery.

Two patient groups were created where the first group was comprised of AA cases during the pre-pandemic period (pre-pandemic group), while the AA cases during the pandemic were included in the second group (pandemic group).

Statistical Analysis

Descriptive data were presented as numbers (n), percentages (%), mean \pm standard deviation (Mean \pm SD) and median with interquartile range (IQR). Normality was assessed with the Shapiro-Wilk test. Non-normally distributed continuous variables were compared using the Mann-Whitney U test. The chi-squared and Fisher's exact tests were used to compare categorical variables. Measure of risk was presented as odds ratio (OR) with 95% confidence interval (CI). Double-sided p-values of less than 0.05 were considered statistically significant. The R Project for Statistical Computing version 4.0.0 (Vienna, Austria: R Core Team) was used for statistical analysis.

RESULTS

Between March 11th, 2019 and March 11th, 2021, a total of 409 patients consisting of 250 (61.1%) men and 159 women (38.9%) with a mean age of 34.5 ± 13.7 (median: 31, range: 18–90) years underwent surgery for acute appendicitis. All appendectomies were carried out laparoscopically, and conversion to open surgery was not necessary in any of the patients. The number of surgeries performed in the pre-pandemic and the pandemic periods were 241 (58.9%), and 168 (41.1%), respectively (Table 1). The median weekly total number of operations was significantly lower in the pandemic period (median, IQR: 3, 2–5) when compared to the pre-pandemic period (median, IQR: 5, 3–6) ($p=0.005$) (Fig. 1). The mean duration between the patients' ED admission to hospitalization was calculated as 1.5 ± 1.3 (median: 1.0, range: 1.0–15.0) hours. The preoperative laboratory test results of the patients are listed in Table 1.

The mean length of hospital stay of the patients was 1.6 ± 1.1 (median: 1.0, range: 1.0–10.0) days. Out of 409 patients, 201 (49.1%) underwent abdominal ultrasonography while an abdominal CT scan was performed on 273 (66.8%) patients for diagnostic purposes preoperatively. According to ultrasound reports, 23 (11.4%) patients had a normal appendix and 178 (88.6%) had AA. On the other hand, according to the CT scan results, 26 (9.5%) patients were reported to have a normal appendix, while 247 patients (90.5%) were found to have AA (Table 1).

Histopathological examinations of the appendectomy specimens revealed that 20 (4.9%) patients had a normal appendix while 334 (84.1%) were diagnosed with uncomplicated AA, and 45 (11.0%) cases were diagnosed with complicated appendicitis.

Postoperative complications were encountered in 15 (3.7%) patients. Intraabdominal fluid collection detected by postoperative imaging took place in 8 (3.7%) cases and 3 (0.7%) of these cases underwent percutaneous drainage. Additionally, postoperative fever was detected in 4 (1.0%) and surgical site infection in 3 (0.7%) cases. Readmission was necessary for 4 (1.0%) patients (Table 1). None of the patients tested positive for COVID-19 postoperatively, and all complications were successfully managed nonoperatively.

When the pre-pandemic and pandemic patient groups were compared regarding demographics, CBC values, neutrophil / lymphocyte ratio, total bilirubin levels, length of hospital stay and imaging results, no significant differences were determined (Table 2).

In terms of the time period between ED admission and hospitalization, the pre-pandemic group had a mean duration of 1.5 ± 1.4 (range: 1.0–15.0) hours while the pandemic group had a mean duration of 1.6 ± 1.2 (range: 1.0–7.0) hours showing a significant delay in the pandemic group ($p=0.024$) (Table 2). Another comparison between the groups revealed an escalation in the CRP levels during the pandemic period as the mean CRP levels for the pre-pandemic and pandemic groups were 3.4 ± 4.8 (range: 0.3–4.6) mg/dL and 4.4 ± 5.5 (range: 0.5–6.5) mg/dL, respectively ($p=0.038$) (Table 2). Moreover, fewer CT scans were performed during the pandemic period compared to the pre-pandemic period. In the pre-pandemic group CT scans were performed in 171 patients (60.7%) whereas 102 patients (71.0%) had CT scans in the pandemic group ($p=0.04$) (Table 2).

Detailed comparisons of the pathology results in both groups showed no significant difference in uncomplicated appendicitis frequencies. Nevertheless, the numbers of complicated appendicitis cases, which were 19 (7.9%) for the pre-pandemic and 26 (5.5%) for the pandemic groups, were significantly different as it was determined that the cases in the pandemic period had 2.1 times higher risk of being diagnosed with complicated appendicitis [OR: 2.1 (95% CI: 1.1–4.1), $p=0.024$] (Table 2).

In terms of postoperative complication rates, the two groups also revealed significant difference. In the pre-pandemic group 3 patients (1.2%), and in the pandemic group 12 (7.1%) patients were diagnosed with postoperative complications ($p=0.004$). Further examinations of complication types showed higher rates of intraabdominal fluid collections, postopera-

TABLE 1. Demographics, diagnostic findings and surgical outcomes of the appendectomy patients (n=409)

	Min–Max	Median	Mean±SD
Age (years)	18.0–90.0	31.0	34.5±13.7
Time from ED admission to hospitalization (hours)	1.0–15.0	1.0	1.5±1.3
Hematocrit (%)	30.0–63.0	42.0	41.8±4.7
Hemoglobin (g/dL)	9.1–19.6	14.4	14.1±1.7
White blood cell count (10 ³ /μL)	2.6–31.0	14.4	14.7±4.5
Platelet count (10 ³ /μL)	72.0–476.0	244.0	247.0±63.2
Neutrophil count (10 ³ /μL)	0.6–81.1	11.5	11.9±5.5
Lymphocyte count (10 ³ /μL)	0.2–14.5	2.0	2.1±1.2
Neutrophil / lymphocyte ratio	0.4–71.0	5.7	7.7±6.9
CRP (mg/dL)	0.1–31.8	1.7	3.8±5.1
Total bilirubin (mg/dL)	0.1–3.3	0.7	0.9±0.6
Length of hospital stay (days)	1.0–10.0	1.0	1.6±1.1
		%	
Gender			
Male		61.1	
Female		38.9	
Group			
Pre-pandemic		58.9	
Pandemic		41.1	
Imaging			
Ultrasonography		49.1	
Normal appendix		11.4	
Acute appendicitis		88.6	
Computerized tomography scan		66.8	
Normal appendix		9.5	
Acute appendicitis		90.5	
Pathology			
Normal appendix		4.9	
Acute appendicitis		95.1	
Uncomplicated appendicitis		84.1	
Complicated appendicitis		11.0	
Postoperative complications		3.7	
Intraabdominal fluid collection		3.7	
Postoperative fever		1.0	
Surgical site infection		0.7	
Percutaneous drainage		0.7	
Readmission		1.0	

Min: Minimum; Max: Maximum; SD: Standard deviation; n: Number of patients; ED: Emergency department; CRP: C-reactive protein.

tive fever and surgical site infections during the pandemic. Among these complications, only postoperative fever, which was recorded in 2 (2.4%) patients of the pandemic group, reached statistical significance ($p=0.028$) (Table 2).

DISCUSSION

In the early stages of the COVID-19 pandemic, the measures and restrictions taken around the world affected every aspect of human life. To control the person-to-person

TABLE 2. Comparison of the pre-pandemic and the pandemic periods regarding patient characteristic and surgical outcomes (n=409)

	Pre-pandemic (n=241) Mean±SD	Pandemic (n=168) Mean±SD	p
Age (years)	34.3±13.6	34.8±13.9	0.743
Time from ED admission to hospitalization (hours)	1.5±1.4	1.6±1.2	0.024*
Hematocrit (%)	41.8±4.7	41.8±4.6	0.837
Hemoglobin (g/dL)	14.1±1.8	14.1±1.7	0.888
White blood cell count (10 ³ /μL)	14.5±4.5	14.9±4.4	0.284
Platelet count (10 ³ /μL)	249.0±64.5	243.0±61.4	0.494
Neutrophil count (10 ³ /μL)	11.8±6.3	12.0±4.2	0.150
Lymphocyte count (10 ³ /μL)	2.2±1.3	2.0±0.9	0.136
Neutrophil/lymphocyte ratio	7.3±6.2	8.2±7.7	0.123
CRP (mg/dL)	3.4±4.8	4.4±5.5	0.038*
Total bilirubin (mg/dL)	0.9±0.6	0.8±0.5	0.091
Length of hospital stay (days)	1.5±0.9	1.7±1.4	0.282
	n=241 (%)	n=168 (%)	p
Gender			0.388
Male	63.1	58.3	
Female	36.9	41.7	
Imaging	95.0	92.9	0.483
Ultrasonography	45.6	54.2	0.130
Computerized tomography scan	71.0	60.7	0.040*
Pathology			
Acute appendicitis	93.8	97.0	0.206
Uncomplicated appendicitis	85.9	81.5	0.296
Complicated appendicitis	7.9	15.5	0.024*
Postoperative complications			
Intraabdominal fluid collection	0.8	3.6	0.069
Postoperative fever	0.0	2.4	0.028*
Surgical site infection	0.4	1.2	0.571
Overall	1.2	7.1	0.004**

SD: Standard deviation; ED: Emergency department; CRP: C-reactive protein; n: Number of patients; *: P<0.05; **: P<0.01.

transmission of the virus, people were advised by the WHO and the Ministry of Health departments to “stay (at) home”. With the beginning of the pandemic, due to understaffing, elective procedures were canceled in our department as only emergency and oncological surgeries were performed.

According to the comparison of our study groups, it is noteworthy that the number of appendectomies decreased during the pandemic. Studies comparing the number of appendectomy procedures during and before the COVID-19 pandemic mostly reported similar findings [7, 8]. In their study with a total of 163 AA patients, Gao et al. [9] suggested that the decrease in appendecto-

my cases during the pandemic was due to more patients asking for non-surgical treatment options after the outbreak. As a result, the prevalence of complicated appendicitis was significantly higher in the epidemic group than in the pre-epidemic group ($p<0.001$) [9]. Other studies suggested a possibility of an association between the widely known seasonal variations in AA cases and the pandemic period [10, 11]. Before the pandemic, Fares [12] defined some of the factors causing an increase in AA cases during summer as air pollution and a rise in the incidence of gastrointestinal infections, both of which could be decreased due to COVID-related lockdowns.

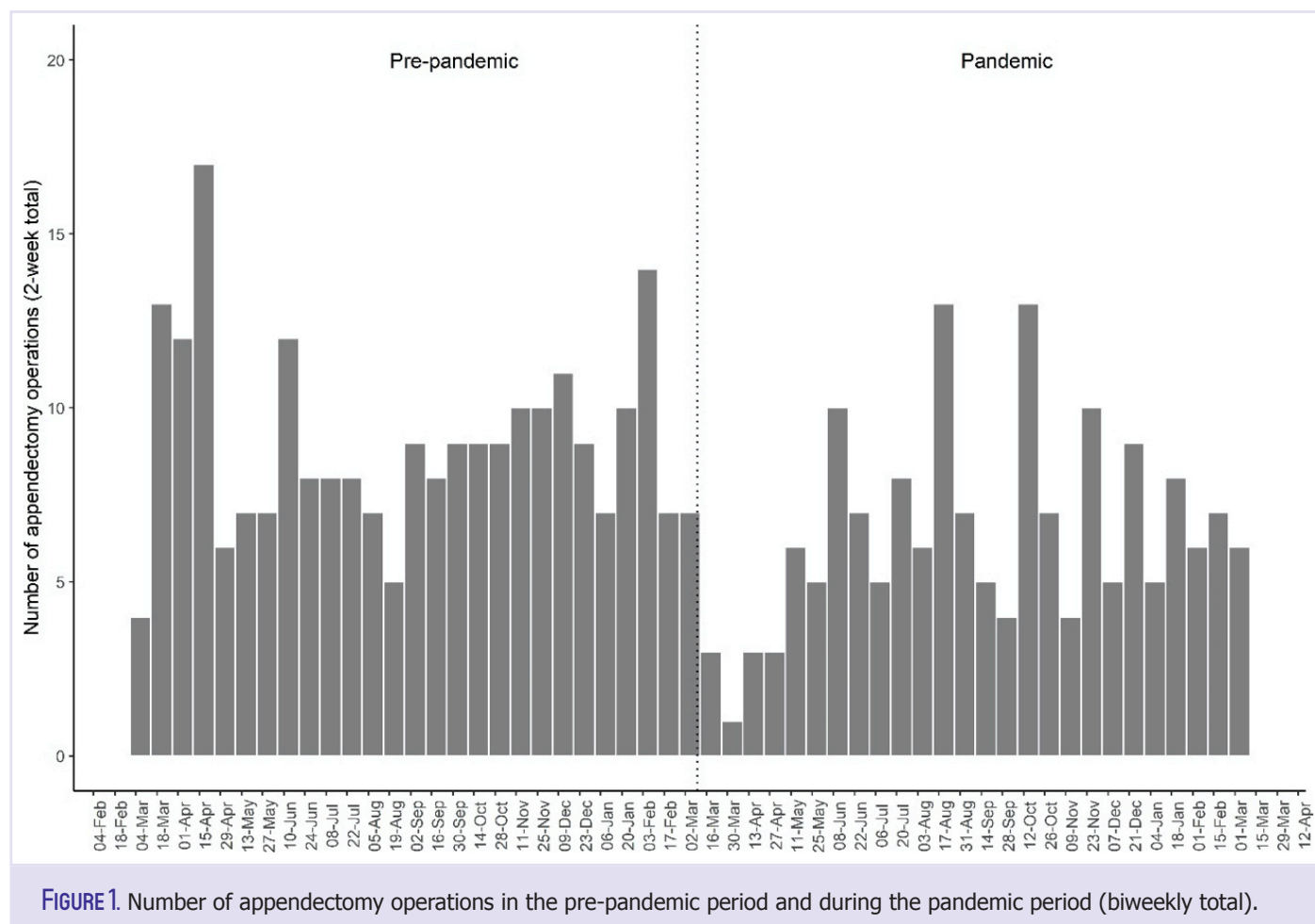


FIGURE 1. Number of appendectomy operations in the pre-pandemic period and during the pandemic period (biweekly total).

The majority of research, that looked into how the COVID-19 outbreak affected EDs, mostly shared the same results. Throughout the world during the pandemic, patients had to spend longer time waiting at their emergency department visits. Alarthi et al. [13] reported longer waiting times for 83% of the patients presenting to the ED during the pandemic in non-COVID hospitals. A similar study by Guo et al. [14] comparing ED length of stay for pre-pandemic and pandemic periods also revealed a significant increase in the length of stay during the pandemic. The time from the onset of symptoms to admission was 17.3 hours for the pre-pandemic group and 65.0 hours for the pandemic group ($p < 0.001$). In our study, the time period from the ED admission to hospitalization to the Department of General Surgery with the diagnosis of AA was prolonged in the pandemic group ($p < 0.05$). This could be a reflection of the decline in emergency medical professionals' ability to diagnose AA due to the understaffing and the overcrowding of the ED during the pandemic.

Studies questioning the diagnostic value of serum inflammatory markers in AA share the conclusion that increased CRP levels correlate with the increased incidence of complicated appendicitis [15, 16]. In a study examining the diagnostic markers of inflammation in AA, it was reported that when WBC, bilirubin and CRP were compared, CRP had the highest specificity (80%) for complicated appendicitis [17]. Another important aspect of CRP levels in AA patients, as advocated by Blok et al. [18], is that CRP's sensitivity in AA diagnosis increases when symptoms last longer than 48 hours. Our pandemic group of patients presented with statistically higher CRP levels ($p < 0.05$). The elevation of CRP levels may have occurred due to the delayed admissions of the patients to the ED.

An additional difference in AA diagnosis during the pandemic period, in contrast to the pre-pandemic period, was the decrease in the use of abdominal CT imaging after the outbreak. Although a small number of studies comparing cases before and after the outbreak of the pandemic showed an increase in CT scans

during the pandemic, our study had the opposite outcome [19]. This drop in the percentage of CT imaging could be a result specific to our hospital's pandemic conditions. The real-time polymerase chain reaction (RT-PCR) test was the most important diagnostic tool for COVID-19 throughout the pandemic. Additionally, with a high sensitivity of 67–100%, chest CT scans were also used routinely for diagnosis and follow-up [20]. The increased necessity of the CT devices for COVID-19 diagnosis may have led to their decreased availability for the diagnosis of non-COVID diseases like AA during the pandemic.

Undoubtedly, the most important result of our study is the 2.1-fold increased rate of complicated appendicitis cases during the pandemic. Similar outcomes are reached when studies comparing appendectomies performed for AA before and after the outbreak are examined. Gao et al. [9] compared 105 pre-pandemic and 58 pandemic group of patients and found a statistically significant increase in the proportion of complicated appendicitis in the pandemic group (pandemic: 51.7% vs. pre-pandemic: 12.4%, $p < 0.001$). Nevertheless, in this study, complicated appendicitis was defined as the presence of gangrenous appendicitis on pathological examination together with perforation as a surgical finding and periappendiceal abscess based on CT scans. On the other hand, in our study, complicated appendicitis was defined only by the postoperative histopathological examinations of the specimens. Another similar study by Angeramo et al. [21] also concluded that there was an increase in the complicated appendicitis rate during the pandemic by examining the intraoperative findings (pre-pandemic: 15% vs. pandemic: 42%, $p < 0.0001$). Having compared 55 pandemic and 141 non-pandemic cases, Romero et al. [22] demonstrated increased complicated appendicitis rates during the pandemic according to CT findings (pre-pandemic: 57.1% vs. pandemic: 97%, $p = 0.003$). A study by Orthopoulos et al. [10], with the results of a 21% increase in perforated appendicitis and a 29% increase in gangrenous appendicitis after the outbreak, also defined complicated appendicitis based on intraoperative findings. The multicenter cohort study by Huijgen et al. [19], with a total of 4401 cases, advocated that no differences were observed in the number of appendectomies and the proportion of complicated appendicitis before and during the COVID-19 pandemic. In this study, complicated appendicitis was also defined by operative findings of necrosis, perforation,

abscess or peritonitis by different surgeons from nine different hospitals.

Furthermore, the results of our research showed an increased rate of overall postoperative complications and an increased rate of postoperative fever in the patients of the pandemic group ($p = 0.004$ and $p = 0.028$, respectively). Most of the studies comparing rates of complicated appendicitis in both eras did not include postoperative complications in their data. Orthopoulos et al. [10] had stable complication rates for all of their patient groups. A study on pediatric AA cases by Snapiri et al. [23] concluded that delays in the diagnosis of AA resulted in increased complications although this conclusion could not be supported by statistical results. Huigen et al.'s [19] cohort did not find differences between the two patient groups in terms of postoperative complications, but the same study also found no difference in the incidence of complex appendicitis for pandemic and pre-pandemic groups, either. Since most of the studies reported increased rates of complicated appendicitis during the pandemic, it would be sensible to expect an escalation in postoperative complications. In the case of severe disease, the rise in postoperative complications is a logical consequence.

Study Limitations

The limitations of the present study are its retrospective nature and, although relatively larger than most of the studies on this subject, its limited number of patients. Due to its being a single-center study, it may not be possible to make generalizations about the pandemic conditions and effects in other hospitals. Since the study only focuses on AA patients who underwent appendectomies, those who underwent medical treatment were not included, which may have increased during the pandemic period.

Conclusion

In conclusion, during the pandemic while the total number of appendectomies decreased, the rate of complicated appendicitis significantly increased. Although it is difficult to pinpoint the exact reason for the increased severe presentations, delayed admission to the hospital seems to be the most logical explanation. We consider that, despite a global pandemic, patients should be warned and encouraged to have the sense and ability to continue seeking prompt treatment for urgent diseases.

Ethics Committee Approval: The Istanbul Medeniyet University Goztepe Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 26.05.2021, number: 2021/0272).

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