

Management of appendicitis in coronavirus disease 2019, severe acute respiratory syndrome coronavirus 2, pandemic era: decreasing incidence with increasing complicated cases?

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SUMMARY

OBJECTIVE: This study aimed to examine the impact of the coronavirus disease 2019 (COVID-19) pandemic on appendicitis and the relevant outcomes in a tertiary hospital, designated as a "pandemic institution" by the Ministry of Health, between pre-COVID-19 and post-COVID-19, i.e., between 2019 and 2020, of the identical period in terms of the annual schedule.

METHODS: The data of cases with acute appendicitis, who were followed up at the Department of General Surgery, a 400-bed, tertiary care, a university-affiliated education and research hospital, providing health care to a population of approximately 450,000 people, during the novel coronavirus SARS-CoV-2, during the identical time intervals of pre-COVID-19 (March 12, 2020 to November 12, 2020) and post-COVID-19 (March 12, 2019 to November 12, 2019), were retrospectively analyzed in a detail.

RESULTS: Of the 212 appendectomy operations in total, 99 (46.7%) were performed in the pre-COVID-19 and 113 (53.3%) were performed in post-COVID-19. Compared to the pre-pandemic period, patients who had undergone appendectomies in post-COVID-19 revealed significantly lower neutrophil counts and significantly greater appendix diameters ($p < 0.001$ for both). A significantly lower ($p = 0.041$) acute appendicitis with abundant gangrenous appendicitis and phlegmonous appendicitis ($p = 0.043$ and $p = 0.032$, respectively) was recognized in post-COVID-19 compared with pre-COVID-19 interval.

CONCLUSION: The number of appendectomy operations decreased in the COVID-19 pandemic. Patients operated during the pandemic period had wider appendix diameter and lower neutrophil levels. The pathological diagnosis was less frequent acute appendicitis, more frequent gangrenous appendicitis, and phlegmonous appendicitis in the pandemic period.

KEYWORDS: Pandemic. COVID-19. SARS-CoV-2. Appendectomy. Appendix. Appendicitis.

INTRODUCTION

Acute appendicitis, defined as inflammation of the vermiform appendix, remains the most frequent emergency face of abdominal pain, accounting for 4.5% of all relevant cases¹. Common factors that complicate definitive diagnoses, such as gynecological disorders in young women, difficulty in patient-physician relationship, delayed administration to health care institutions, and impediments in the referral chain may contribute to delayed or late diagnosis, progression of inflammation, and even perforation. In addition, the effects of extraordinary national or global events, e.g., the novel coronavirus disease 2019 (COVID-19) strain, that burden the local and global health care system on a massive scale can be disastrous for the human being, due to the augmentation in the relevant morbidity and mortality rates²⁻⁴. Crucial alterations have occurred in

the health policies of countries worldwide due to the outbreak of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which has been declared a global pandemic by the World Health Organization (WHO)⁵. Many countries have planned to attenuate the spread of the disease through measures of quarantining at-risk individuals and travel restrictions after the onset of the pandemic. However, some concerns about the patients that may be reluctant to seek essential health care due to these restrictions and also personal preferences have appeared⁶. Attenuation in admissions to emergency service^{6,7}, delayed or late admission of acute appendicitis cases⁸⁻¹⁰, and an augmented frequency of complicated appendicitis cases^{6,11} all these led to worsening appendicitis-related outcomes and post-operative consequences of appendectomy^{6,11}. This study aimed to evaluate the appendectomies that had been performed in a tertiary hospital, designated as a pandemic institution by the

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Ministry of Health, during the COVID-19 pandemic period, i.e., 2020, in comparison to the same period in the previous year, i.e., 2019. Our objective was to compare the effect of SARS-CoV-2 on appendicitis and its outcomes between pre-COVID-19 and post-COVID-19 of the identical period in terms of the annual schedule.

METHODS

This study was a retrospective, backward-looking, cohort investigation of acute appendicitis at a 400-bed, tertiary care, a university-affiliated education and research hospital, providing health care to a population of approximately 450,000 people, during the novel coronavirus SARS-CoV-2. Variables collected included patient age, gender, imagings, labs, histopathology, and length of stay. We identified all adult and pediatric admissions to our pandemic hospital by enrolling the documents, which were identified via searching each through electronic databases of the hospital that are kept in real time, of the consecutive cases with uncomplicated and complicated acute appendicitis during the COVID-19 pandemic (March 12, 2020 to November 12, 2020), in comparison to those for the same period before the pandemic in Turkey (March 12, 2019 to November 12, 2019). *Ab initio*,

March 11 was accepted as the threshold/initiation, since the first confirmed COVID-19 case in Turkey was reported on March 10, 2020. The primary outcome of this study was to identify the numerical value presenting with acute appendicitis pre-COVID-19 and post-COVID-19 associated restrictions and the proportion of cases with complicated acute appendicitis disease. All the statistical analysis was performed using SPSS, version 22 (IBM SPSS Statistics for Windows, version 21.0; Chicago, IL, USA). The descriptive statistics were displayed as mean±standard deviation or median (first quartile to third quartile) percentage unless stated otherwise for categorical variables. Univariable statistics were generated using the Shapiro-Wilk test, Student's t-test, and Mann-Whitney U test. A two-tailed $p < 0.05$ was considered statistically significant.

RESULTS

We identified that a total of 212 patients who had been admitted with acute appendicitis to our institution during the study period. Of these, 113 (53.3%) patients were performed in the post-COVID-19 and 99 (46.7%) were performed in pre-COVID-19, in comparison with the same period of the previous year. Demographic and clinical characteristics for the study population are depicted in Table 1. The mean neutrophil count was 10.83 (7.9–13.01)

Table 1. Demographic and clinical characteristics during the period of admission.

	Period		P
	Pre-COVID-19 (n=113)	Post-COVID-19 (n=99)	
Sex, n (%)			
Female	35 (30.97)	37 (37.37)	0.326
Male	78 (69.03)	62 (62.62)	
Age (years)	36.0 (27.0–52.0)	35.0 (25.0–51.0)	0.269
White blood cell count (×10 ³ /μl)	13.72±4.33	12.87±55.54	0.222
Neutrophil count (×10 ³ /μl)	10.83 (7.91–13.01)	8.33 (5.78–10.20)	<0.001
Diameter of the appendix (mm)	9.10 (8.00–10.00)	11.00 (10.00–12.20)	<0.001
Perforation, n (%)	8 (7.08)	11 (11.11)	0.305
Extraluminal air, n (%)	7 (12.28)	9 (16.07)	0.563
Pathological diagnosis, n (%)			
Acute appendicitis	97 (85.84)	74 (74.75)	0.041
Gangrenous appendicitis	4 (3.54)	11 (11.11)	0.043
Phlegmonous appendicitis	3 (2.65)	9 (9.09)	0.032
Suppurative appendicitis	1 (0.88)	3 (3.03)	0.252
Lymphoid hyperplasia	4 (3.54)	2 (2.02)	0.506
Length of stay (days)	2.0 (2.0–2.0)	2.0 (1.0–3.0)	0.335

Data were given as mean±standard deviation or median (first quartile to third quartile) for the continuous variables according to the normality of distribution and as frequency (percentage) for the categorical variables.

$\times 10^3/\mu\text{l}$ in the pre-COVID-19 and $8.33 (5.78-10.20) \times 10^3/\mu\text{l}$ in the post-COVID-19 period, with the latter being less significant ($p < 0.001$) (Figure 1). The median appendix diameter (first quartile to third quartile) was 11 (10.0–12.2) mm in the post-COVID-19 and 9.1 (8.0–10.0) mm in pre-COVID-19, with the former being significantly higher ($p < 0.001$). Histopathologically, pre-COVID-19 and post-COVID-19 have been recognized to

comprise acute appendicitis (85.8/74.8%), gangrenous appendicitis (3.5/11.1%), and phlegmonous appendicitis (2.7/9.1%) (Figure 2). Last but not least, a comparison of histopathological outcomes of performed appendectomies in 2020 vs. 2019 revealed significantly lower ($p = 0.041$) acute appendicitis with abundant gangrenous appendicitis and phlegmonous appendicitis ($p = 0.043$ and $p = 0.032$, respectively) in the post-COVID-19 period.

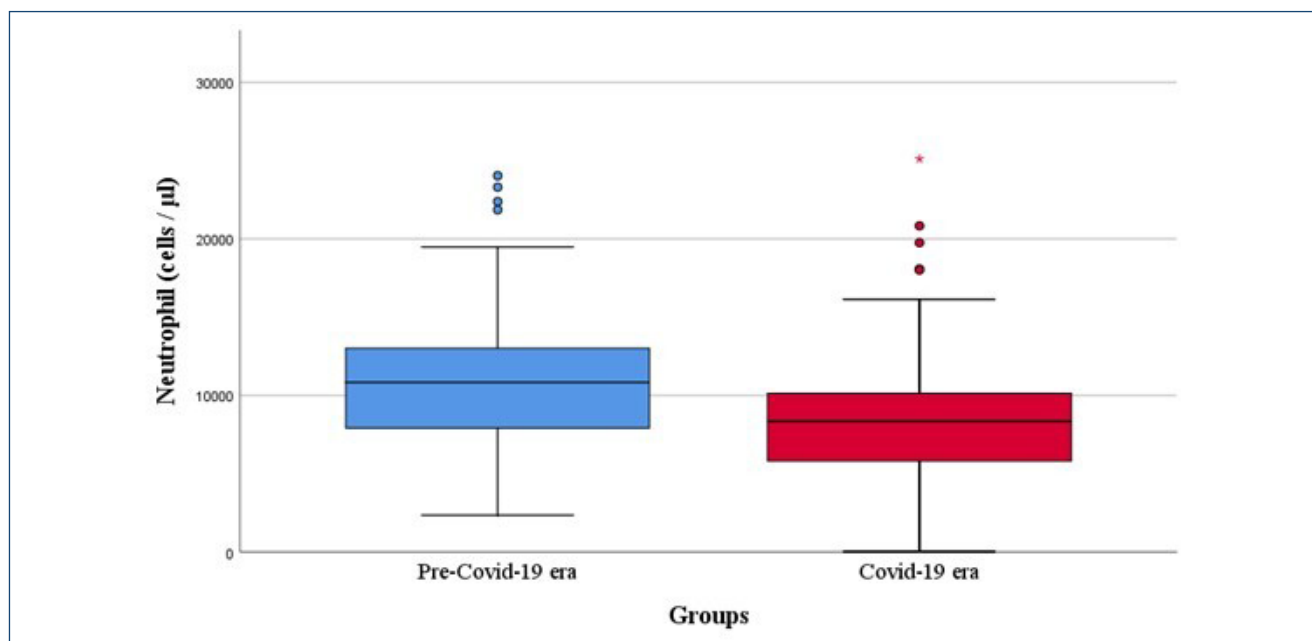


Figure 1. The box-plot of the neutrophil counts for pre-COVID-19 era and post-COVID-19 era.

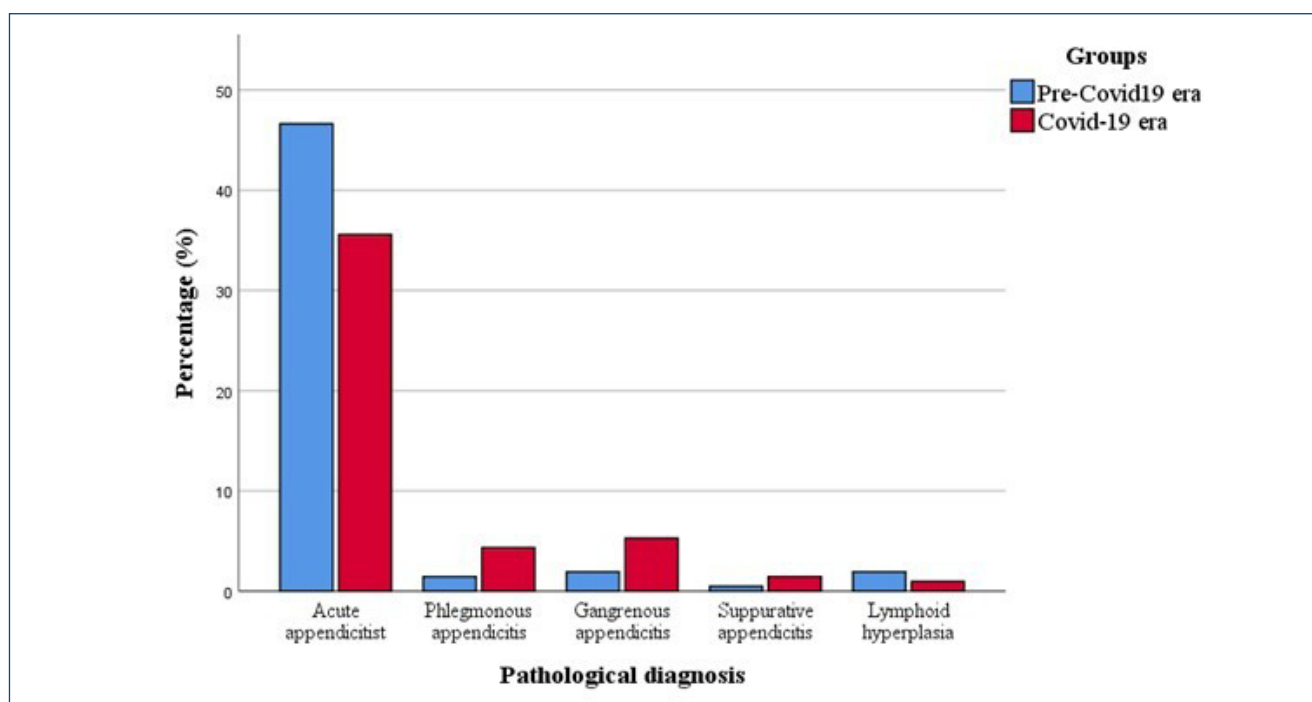


Figure 2. The box-plot of the appendix diameters for pre-COVID-19 era and post-COVID-19 era.

DISCUSSION

Since WHO declared SARS-CoV-2 as a global public health emergency in January 2020, the pandemic has profoundly affected the health care systems and the economies worldwide⁵. Acute surgical emergencies are inevitable, and these cases should be dealt with in a timely and logical manner. The COVID-19 pandemic has had many implications in the management of emergency cases. In this context, postponing all elective surgical and endoscopic cases has been recommended in current guidelines^{12,13}. *Hic et ubique terrarum*, many security measures have been implemented to refrain from the spread of the virus. On the other side of the coin, since most individuals were concerned about contracting COVID-19 and some groups were restricted to staying in their homes, they may have been reluctant to seek medical care until their health status would reach a serious level, necessitating hospital admission.

In the present study, the relevant surgical procedures had been performed by using the same operating room that had been sanitized concerning the COVID-19 protocol. *A posteriori*, the lower neutrophil levels with the greater vermiform appendix diameters were revealed for the cases in the post-COVID-19 compared with pre-COVID-19 period. Moreover, less acute appendicitis with more gangrenous and phlegmonous appendicitis was recognized as another outcome in post-COVID-19, in terms of histopathology. An Italian study reported that pediatric emergency admissions being decreased by 88% during the pandemic period⁷. Another study conducted in Colombia asserted a 57% decrease in the frequency of computed tomography (CT) scans that were ordered to confirm acute appendicitis during the SARS-CoV-2 infection. In contrast, the authors reported acute appendicitis was being diagnosed more frequently in CT scans and the mentioned cases had possessed more severe disease⁶.

Due to the limitations of this study, the possible cases treated conservatively had not been analyzed. Various studies have reported that surgeons may be more inclined to apply conservative treatment under pandemic conditions and concluded that utilizing nonsurgical therapeutic options in non-essential situations may be beneficial^{14,15}. In other words, the main impact of the pandemic may be ascertained as an increase in conservative treatment and a decrease in surgical treatment, which is much more likely than an overall decline in the number of acute appendicitis cases during this period.

Many factors that emerged in the pandemic era have contributed to some delays in hospital admission, directly or indirectly contributing to the development of more severe clinical conditions among the cases. A study conducted in New York City reported that the patients with suspected acute

appendicitis had a considerable delay in hospital admissions; therefore, the duration of symptoms before admission was longer and the patients who were admitted for appendectomy procedure had more severe clinical pictures¹⁵. A study conducted in Israel exhibited that the frequency of complications doubled in acute appendicitis cases that had undergone surgery during the COVID-19 pandemic¹⁰. In addition, different studies conducted in Spain¹⁶, Australia¹⁷, Brazil¹⁸, and Nepal¹⁹ observed that the hospital admissions of patients with symptoms of acute appendicitis were delayed, the number of complicated appendicitis cases had increased, the severity of appendicitis cases had increased, and length of hospital stay was prolonged during the pandemic period compared to the previous year. Consistent with previous studies, compared to the pre-pandemic period, we recognized the frequency of complicated cases and the diameters of the appendixes had significantly increased in the post-COVID-19. Previous studies have shown that the relevant admission delay is a multifactorial problem, even under normal conditions, that may be associated with many variables, involving health perception, socioeconomic status, and educational status¹⁵. Of note, the clinical presentation of patients may have also changed according to the characteristics of the region, preventive measures in practice, and the approach of the local population, for each study, to the relevant health care services.

Appendicitis is an inflammatory condition, and an augmentation in the inflammation markers is expected in cases, regardless of the presence or absence of complications¹. It is well-established that white blood cell count, neutrophil levels, fever, even C-reactive protein (CRP) levels are higher in complicated appendicitis cases than the uncomplicated ones. Considering that complicated cases increased during the pandemic period, we would have expected to observe relatively elevated neutrophil levels in the pandemic period. Nevertheless, contrary to expectations, the mentioned neutrophil levels were expressed to be significantly lower in the relevant literature findings²⁰⁻²².

The most important limitation of the present study was possessing retrospective pattern and single-centered design. The cases who would have normally applied to our pandemic hospital may have preferred not to, and some may not have been able to access our facilities during the SARS-CoV-2 pandemic due to various restrictions (e.g., prohibition of going out and traveling). To this end, the cases were examined in two different time intervals, which might have regional differences that could have altered characteristics. We also did not questionnaire the previous COVID-19 infection status directly and the cases were not analyzed according to these characteristics. Since our hospital was designated as a pandemic hospital,

any individuals with a COVID-19 diagnosis would have been referred to us for surgical treatment. Herein, it is unlikely that screening for COVID-19 would have altered the results considerably. Of note, the early pandemic period and later pandemic period may have had significant differences in terms of patient characteristics, since the restrictions were much greater in the early period of disease spread. We could not examine whether the infection imitated appendicitis clinic or led to it. Last but not least, we did not evaluate acute appendicitis cases treated conservatively, without surgery, which may have had marginal effects on the distribution of patient characteristics. Notwithstanding, emergency surgery remains its significance in the era of emergency cases, prevalently²³⁻²⁵.

CONCLUSIONS

Compared to the previous year, the numerical value of appendectomy attenuated in the COVID-19 era. Patients who had undergone surgery in the post-COVID-19 had greater appendix diameters and lower neutrophil levels. The distribution of histopathological diagnoses had changed in favor of complicated cases, with a lesser frequency of acute appendicitis and a higher frequency of gangrenous and phlegmonous ones, in

the post-COVID-19 era. Hereinbefore, in any SARS-CoV-2 pandemic era, early detection of life-threatening situations with maximum adherence to protective precautions may be critical and vital to reducing complicated cases of both frequent and substantial causes of acute abdomen appendicitis.

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AUTHORS' CONTRIBUTIONS

TK: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft. **IS:** Conceptualization, Investigation, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **IA:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Validation, Visualization. **SV:** Data curation, Project administration, Resources, Validation, Visualization. **DS:** Investigation, Methodology, Project administration, Software, Supervision, Writing – review & editing.

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