

Research Article

Comparison of Clinical, Pathological, and Procedural Characteristics of Adult and Pediatric Acute Appendicitis before and during the COVID-19 PandemicGoran Augustin^{1,2*}, Jurica Žedelj, Nora Knez and Karmen Jeričević¹University Hospital Centre Zagreb, Zagreb, Croatia²School of Medicine, University of Zagreb, Croatia

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ABSTRACT

Aims: This study aims to examine the impact of the COVID-19 pandemic on the clinical, pathological, and surgical features of acute appendicitis (AA) in a tertiary referral center - Clinical Hospital Centre Zagreb, through a patient data comparison before and during the pandemic. **Methods:** Demographic (age, gender), clinical (duration of hospitalization), pathological (gangrenous AA, perforated AA, complications), and surgical data (type of appendectomy, negative appendectomy, conversion, revision) were retrospectively collected from an electronic database for all consecutive patients admitted for AA before and during the COVID-19 pandemic. **Results:** Demographic data were comparable between groups. There was statistically no significant difference in the type of appendectomy ($p=0.331$). The median hospital length of stay was 3 (2-5) days ($p=0.078$). There was an increase in the conversion rate (4.2% to 7.7%, $p=0.031$). The negative appendectomy rate did not differ significantly (5.6% vs. 4.2%, $p=0.338$). There was no significant difference in the incidence of perforated AA (13.3% vs. 15.7%, $p=0.339$). **Conclusion:** We did not observe a significant increase in the rate of AA complications during the COVID-19 pandemic at the Clinical Hospital Centre Zagreb. This could be because AA is typically diagnosed and treated in emergency care, which remained available during the pandemic. Additionally, diagnostic and therapeutic protocols remained unchanged despite the pandemic.

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1. Introduction

Acute appendicitis (AA) is one of the most common emergencies in abdominal surgery, with an estimated lifetime risk of 7% [1]. Subsequently, appendectomy is one of the most common surgical procedures, which represents a significant burden for healthcare systems [2]. COVID-19 (Corona Virus Disease-19) is an infectious disease caused by the novel coronavirus SARS-CoV-2, first identified in December 2019 in Wuhan, Hubei province, China [3]. The virus quickly spread worldwide, leading the World Health Organization to declare a pandemic on March 11, 2020 [4]. The first case in Croatia was confirmed on February 25, 2020.

During the COVID-19 pandemic, studies have been published linking SARS-CoV-2 infection and AA. One of the presumed mechanisms is the infection of intestinal cells by SARS-CoV-2 due to the high expression of the viral receptor, angiotensin-converting enzyme 2 (ACE2), which compromises barrier function and facilitates the translocation of microorganisms [5]. The atypical histopathological appearance of appendiceal issue, including microthrombi, fibrinoid necrosis of blood

vessels, and perivascular lymphocytic inflammatory infiltrate, supports the association between SARS-CoV-2 infection and AA, given that such findings are indicative of SARS-CoV-2 infection based on lung tissue sample findings [6, 7]. Furthermore, it is known that viral infections uncommonly can cause AA through several mechanisms, including lymphoid hyperplasia, which obstructs the appendix, and mucosal ulcerations, which lead to bacterial superinfection [8].

According to the guidelines of the World Society of Emergency Surgery (WSES), the Society of Gastrointestinal and Endoscopic Surgeons (SAGES), and The European Association for Endoscopic Surgery (EAES), appendectomy is the gold standard for AA treatment instead of non-operative management (NOM) with antibiotics [9-11]. The COVID-19 pandemic has significantly impacted healthcare systems worldwide, and its effects on various areas of medicine, including general surgery, are still undetermined [12]. Restrictions and fear of infection have led patients to postpone seeking medical help and using healthcare services, which could have contributed to delayed recognition, accurate diagnosis, and treatment [13, 14].

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During the pandemic, there was a significant decrease in patients seeking medical attention for non-COVID-19-related emergency conditions such as acute coronary syndrome, stroke, and acute abdomen [15]. From March to April 2020, hospitals worldwide experienced a 42% drop in emergency department visits, with a significant decrease seen in visits for abdominal pain [16]. Delayed or canceled appointments and treatments for other diseases could lead to serious health complications, potentially worse than the infection with the virus itself [17]. The pandemic necessitated prolonged surgical delays and waiting for COVID-19 PCR results, except for urgent cases like trauma or severe peritonitis with unstable vital signs. This inevitably impacted the management of AA [18].

The study aimed to evaluate the impact of the COVID-19 pandemic on the clinical, pathological, and surgical characteristics of patients with AA in the University Hospital Center Zagreb.

2. Patients, Materials, and Methods

2.1. Study Design

The data were retrospectively collected from the electronic database for all consecutive patients admitted for appendectomy at the Department of Surgery at University Hospital Centre (UHC) Zagreb between January 1 and December 31, 2019, and between March 11, 2020, and March 11, 2021. March 11, 2020, marked the beginning of the pandemic period.

Patients were divided into two comparable groups, the pre-COVID-19 group, defined as patients treated before the COVID-19 pandemic (January 1, 2019, until December 31, 2019), and the COVID-19 group, defined as patients treated during the pandemic (March 11, 2020, until March 11, 2021). The patients were then stratified and compared according to age groups. Pediatric patients are defined as those younger than 16. At our center, adult AA is managed by abdominal surgeons, and pediatric AA is managed by pediatric surgeons. Individual medical records were reviewed for demographic (age, gender), clinical (duration of hospitalization), pathological (gangrenous AA, perforated AA, complications), and surgical data (type of appendectomy, negative appendectomy, conversion, revision).

The primary objective was to compare clinical, pathological, and procedural characteristics of AA before and during the COVID-19 pandemic to evaluate the impact of the pandemic on AA complications incidence. The secondary objective was to compare those characteristics separately for the pediatric and adult populations. The study was approved by the Institutional Review Board of the University Hospital Centre Zagreb, and due to the study's retrospective nature, written informed consent was not required.

2.2. Statistical Analysis

All data were collected into the EXCEL database (Microsoft, Washington, DC, USA). The statistical analysis was performed using SPSS version 29.0.0.0 (SPSS, Inc, Chicago, Ill). The normality of distribution for quantitative variables was tested using the Kolmogorov-Smirnov test. Continuous data are presented as median with interquartile range (IQR) and compared between groups using the Mann-Whitney U

test. Categorical data are presented as absolute numbers with percentages and compared between groups using the χ^2 (chi-square) test or Fisher's exact test when the number of events was <5 . A p-value of <0.05 was considered statistically significant.

3. Results

During the two study periods, 855 appendectomies (open and laparoscopic) were performed, with 427 in the pre-pandemic period and 428 during the pandemic. The median age of the entire cohort was 27 (16-42) years, and 450 (52.6%) patients were male. Demographic characteristics did not significantly differ between the groups (age: 26 (16-41) vs. 29 (16-44), $p=0.181$; male gender: 49.4% vs. 55.8%, $p=0.06$). Of the total cohort, 225 patients (26.3%) were younger than 16 years, 57 (13.3%) and 67 (15.7%) in the pre-pandemic and pandemic periods, respectively ($p=0.339$).

The groups did not differ according to the surgical approach type (open or laparoscopic) ($p=0.331$). The median duration of hospitalization was 3 (2-5) in both groups ($p=0.078$). During the pandemic, a significantly higher conversion rate was observed (4.2% vs. 7.7%, $p=0.031$). The difference in revision rates was not statistically significant (0.5% vs. 1.2%, $p=0.451$). The overall negative appendectomy rate was 4.9%, with no observed difference between the periods (5.6% vs. 4.2%, $p=0.338$). There was no statistically significant difference in the incidence of perforated AA between the periods (13.3% vs. 15.7%, $p=0.339$). There were no differences in the frequency of other complications between the two periods (7.7% vs. 7%, $p=0.687$). The rates of perforated AA with other complications also did not differ between the periods (3.7% vs. 3.5%, $p=0.85$).

3.1. Adult Patients

The study included 630 adult patients who underwent open or laparoscopic appendectomy, with 313 patients in the pre-pandemic group and 317 in the pandemic group. Demographic data were comparable between the groups (age; 33 (29-49) vs. 36 (26-51), $p=0.08$, male gender; 46.3% vs. 52.4%, $p=0.129$). There was no statistically significant difference in the appendectomy modality (open or laparoscopic) between the two groups ($p=0.652$). The median length of hospitalization was 3 (2-5) days in both groups ($p=0.3$). A significant increase in the conversion rate in the pandemic group was observed (4.8% vs. 8.8%, $p=0.044$). The negative appendectomy rate was similar before and during the pandemic (5.8% vs. 5%, $p=0.696$). There was no significant difference in the frequency of perforated appendicitis (14.7% vs. 16.7%, $p=0.485$). There were no significant differences in the rates of other complications (8.6% vs. 6.9%, $p=0.429$).

3.2. Pediatric Patients

The study included 225 pediatric patients with AA, 114 of whom were treated before and 111 during the pandemic. The median age in the entire group was 11 (9-14) years ($p=0.778$). Demographic characteristics did not differ significantly between the groups (age: 11 (8-14) vs. 11 (9-14), $p=0.778$; male sex: 57.9% vs. 65.8%, $p=0.224$). There was no significant difference in the choice of surgical treatment between the groups ($p=0.328$). The median length of hospital stay was 4 (3-5) days in both

groups (p=0.047). The negative appendectomy rate did not differ significantly before and during the COVID-19 pandemic (5.3% vs. 1.8%, p=0.281). There was no difference in the rate of perforated AA

between the two periods (9.6% vs. 12.6%, p=0.479). No significant differences in the rate of other complications were found between the groups (5.3% vs. 7.2%, p=0.546).

TABLE 1: Comparison between acute appendicitis factors before and during the COVID-19 pandemic.

Adult patients:				
Variable	All (n=630)	Pre-COVID-19 (n=313)	During COVID-19 (n=317)	p-value
Age, median (IQR)	34 (24-51)	33 (23-49)	36 (26-51)	0,08
Female, n (%)	319 (50,6)	168 (53,7)	151 (47,6)	0,129
Male, n (%)	317 (50,3)	145 (46,3)	166 (52,4)	0,129
Laparoscopic approach, n (%)	612 (97,1)	305 (97,4)	307 (96,8)	0,652
Hospitalization (days), median (IQR)	3±3	3±3	3±3	0,3
Conversion, n (%)	43 (6,8)	15 (4,8)	28 (8,8)	0,044
Revision, n (%)	7 (1,1)	2 (0,6)	5 (1,6)	0,451
Gangrenous appendicitis, n (%)	231 (36,7)	115 (36,7)	116 (36,6)	0,969
Negative appendectomy, n (%)	34 (5,4)	18 (5,8)	16 (5)	0,696
Perforated appendicitis, n (%)	99 (15,7)	46 (14,7)	53 (16,7)	0,485
Complications, n (%)	49 (7,8)	27 (8,6)	22 (6,9)	0,429
Complications + perforated appendicitis, n (%)	25 (4)	14 (4,5)	11 (3,5)	0,519
Pediatric patients:				
Variable	All (n=225)	Pre-COVID-19 (n=114)	During COVID-19 (n=111)	p-value
Age, median (IQR)	11 (9-14)	11 (8-14)	11 (9-14)	0.778
Female, n (%)	86 (38,2)	48 (42,1)	38 (34,2)	0.224
Male, n (%)	139 (61,8)	66 (57,9)	73 (65,8)	0.224
Laparoscopic approach, n (%)	612 (97,1)	305 (97,4)	307 (96,8)	0.652
Hospitalization (days), median (IQR)	4 (3-5)	4 (3-5)	4 (3-5)	0.047
Conversion, n (%)	8 (3,6)	3 (2,6)	5 (4,5)	0.495
Revision, n (%)	0	0	0	/
Gangrenous appendicitis, n (%)	55 (24,4)	30 (26,3)	25 (22,5)	0.508
Negative appendectomy, n (%)	8 (3,6)	6 (5,3)	2 (1,8)	0.281
Perforated appendicitis, n (%)	25 (11,1)	11 (9,6)	24 (12,6)	0.479
Complications, n (%)	14(6,2)	6 (5,3)	8 (7,2)	0.546
Complications + perforated appendicitis, n (%)	6 (2,7)	2 (1,8)	4 (3,6)	0.442
All:				
Variable	All (n=855)	Pre-COVID-19 (n=427)	During COVID-19 (n=428)	p-value
Age, median (IQR)	27 (16-42)	26 (16-41)	29 (16-44)	0.181
Pediatric patients, n (%)	225 (26,3)	114 (26,7)	111 (25,9)	0.8
Female, n (%)	405 (47,4)	216 (50,6)	189 (44,2)	0.06
Male, n (%)	450 (52,6)	211 (49,4)	239 (55,8)	0.06
Laparoscopic approach, n (%)	828 (96,8)	416 (97,4)	412 (96,3)	0.331
Hospitalization (days), median (IQR)	3 (2-5)	3 (2-5)	3 (2-5)	0.078
Conversion, n (%)	51 (6)	18 (4,2)	33 (7,7)	0.031
Revision, n (%)	7 (0,8)	2 (0,5)	5 (1,2)	0.451
Gangrenous appendicitis, n (%)	286 (33,5)	145 (34)	141 (32,9)	0.753
Negative appendectomy, n (%)	42 (4,9)	24 (5,6)	18 (4,2)	0.338
Perforated appendicitis, n (%)	124 (14,5)	57 (13,3)	67 (15,7)	0.339
Complications, n (%)	63 (7,4)	33 (7,7)	39 (7)	0.687
Complications + perforated appendicitis, n (%)	31 (3,6)	16 (3,7)	15 (3,5)	0.85

4. Discussion

The onset of the SARS-CoV-2 pandemic has led to substantial global changes in routine healthcare and daily life [14]. This study is the most comprehensive analysis of AA outcomes during the COVID-19 pandemic in Croatia. While several studies have reported a higher

incidence of complicated AA and an increased complication rate during the COVID-19 outbreak [19-22], the present study at UHC Zagreb did not identify significant differences in the clinical, pathological, and surgical characteristics of patients diagnosed with AA.

Delayed presentation of AA leads to a more complicated AA, which is one of the risk factors for conversion from a laparoscopic to an open approach [9]. Although we did not observe a significant increase in the rates of complicated AA, there was a notable increase in conversion rates during the pandemic (4.2% vs. 7.7%, $p=0.031$). After stratifying patients into pediatric and adult populations, a statistically significant difference in conversion rates was also observed for adult patients (4.8% to 8.8%, $p=0.044$). Potentially, the increased conversion rates during the pandemic were due to factors unrelated to the severity of AA, such as the surgical team performing the procedure.

The meta-analysis and systematic literature review conducted by Kariya *et al.* reported a significant increase in the rate of complicated acute appendicitis during the COVID-19 pandemic. One possible explanation for the higher complication rates observed during the COVID-19 pandemic is that patients may have been reluctant to seek medical attention due to fear of infection or recommendations to reduce visits to emergency services [23].

According to the systematic literature review and meta-analysis by Pogorelič *et al.*, there was a significant increase in the rate of complicated pediatric AA during the COVID-19 pandemic compared to the pre-pandemic period. Furthermore, there was an increase in the proportion of children who received NOM during the pandemic [24].

Regarding uncomplicated AA, a systematic review and meta-analysis by Xu *et al.* indicates that the 1-year success rate of NOM is lower compared to surgical treatment. However, delayed appendectomy due to the failure of NOM did not increase complication rates compared to the classical approach [25]. In the context of the COVID pandemic, low complication rates and the possibility of repeating the treatment make NOM a possible treatment strategy for delaying or avoiding surgery for AA altogether.

In UHC Zagreb, surgical management was the exclusive treatment approach for all patients diagnosed with AA during the pandemic. Our results align with the findings of a similar study conducted at UHC Rijeka, which showed no difference in the complications of AA before and during the pandemic [26]. Since Zagreb and Rijeka are both major urban centers, possibly the findings may not be generalizable to other Croatian regions. Further studies, encompassing other centers where appendectomy is performed, are needed to determine whether the impact of the COVID-19 pandemic on AA is consistent across the country.

The results of this study can be argued in several ways. The healthcare system in Croatia was not as burdened by the COVID-19 pandemic as in some other countries, which may have affected the continuity of healthcare for patients with AA. The results indicate that AA was still recognized as an emergency requiring prompt medical intervention, and emergency medical care and surgical protocols remained unchanged during the COVID-19 pandemic. During the COVID-19 pandemic, most medical centers worldwide postponed or canceled regular elective procedures, and the same trend was applied in Croatia. Surgical procedures were limited to emergency cases to reduce unnecessary burdens on the healthcare system and the number of hospitalized patients.

At the UHC Zagreb, a separate operating room was set up in the premises of the unified emergency hospital admission department for COVID-19-positive patients due to the risk of virus transmission through the medical gas pipeline system and contamination of the operating room.

During the pandemic, we did not observe a decrease in patients treated for AA. This could be attributed to the fact that UHC Zagreb treated a larger volume of patients from Clinical Hospital Dubrava, designated as one of Croatia's primary COVID-19 treatment centers. On the other hand, COVID-19-positive patients were operated on at the Clinical Hospital Dubrava during the pandemic.

5. Conclusion

This study did not observe a significant increase in the rate of complicated AA during the COVID-19 pandemic in UHC Zagreb, despite the imposed restrictions. The study suggests that the absence of changes in clinical, pathological, and surgical characteristics can be attributed to the fact that AA is typically diagnosed and treated in emergency settings, which remained available before the COVID-19 pandemic. Diagnostic and therapeutic protocols for emergency conditions remained unchanged despite the pandemic. Additionally, it can be noted that the pandemic did not strongly affect our region as it did in some other countries.

Limitations of the Study

The main limitations of this study are the retrospective design and the fact that it is based on an experience of a single university hospital that may not be generalizable to other hospitals.

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