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Histopathologic Changes of Appendicitis Stage During the COVID-19 Pandemic

Mohsen Khaleghian[1], Adnan Tizmaghz[2]*, Majid Rezaei-Tavirani[2], Mohammad Amin Abbasi[3], Fatemeh Montazer[4], Ghazaal Shabestanipour[5], Emad Alamoutifard[5], Ali Tayebi[2], Faranak Olamaeian[2]

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Abstract

Background: We decided to compare the pathology stage of appendicitis in patients referred to Firoozabadi Medical Center before and after the official announcement of the coronavirus outbreak in Iran because we believe that people's fears of COVID-19 are keeping them away from hospitals and it likely causes them to come in later stages of the disease. Therefore, this study aims at investigating the effect of the COVID-19 pandemic on the stage of appendicitis at presentation.

Methods: In this retrospective study, histopathology records of all acute appendicitis patients who underwent an emergency appendectomy in the surgical unit in our institute between December 2019 and April 2020 were reviewed retrospectively. The study period was designed to include 2 months before and 2 months after the officially announced onset of the COVID-19 outbreak in Iran on February 20, 2020. All cases of complicated appendicitis (perforated appendicitis, phlegmonous appendix, itis or abscess) were excluded. Descriptive statistics were used to describe our study variables. Furthermore, ordinal logistic regression was used to investigate the effect of the COVID-19 pandemic and demographic variables on the stage of appendicitis at presentation. Data were analyzed using SPSS Statistics Version 22.

Results: The study was conducted on 170 clinically diagnosed acute appendicitis patients. The odds ratio for gender was equal to 0.45 (0.23, 0.86), which means that women presented at an earlier pathological stage than men (p = 0.016). Also, patients who had health insurance were 50% less likely to present in later pathological stages than those who did not (p = 0.024). The COVID-19 outback did not have a significant role in the pathological stage at presentation (p = 0.235).

Conclusion: The number of appendicitis patients was down by about 50% following the outbreak announcement in Iran. Surprisingly, we did not find any significant changes in the distribution pattern of appendicitis pathological staging after the outbreak. Being uninsured and male sex were found to have the most significant roles in delayed hospital presentation and higher pathological stages in patients with acute appendicitis.

Keywords: Appendectomy, Histopathological Examination, Coronavirus Outbreak

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Introduction

An ongoing outbreak of novel coronavirus (2019-nCoV) pneumonia was first identified in Wuhan, China, in De-

Corresponding author: Dr Adnan Tizmaghz, *tizmaghz.a@iums.ac.ir*

1. Department of Vascular Surgery, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran
2. Department of General Surgery, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran
3. Firoozabadi Clinical Research Development Unit (FCRDU), Iran University of Medical Sciences, Tehran, Iran
4. Department of Pathology, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran
5. Private Office, Tehran, Iran

↑What is "already known" in this topic:
Previous reports suggested that SARS-CoV-2 can infect the digestive system and presents with gastrointestinal symptoms, occasionally mimicking acute appendicitis. In addition, fears of coronavirus disease 2019 (COVID-19) may also keep people away from hospitals and probably lead to come in later stages of the diseases. An early report (limited evidence) suggested that COVID-19 vaccine may also contribute to acute appendicitis as an adverse event.

→What this article adds:
The severity of appendicitis increased during the COVID-19 pandemic in a uninsured male subgroup due to the most delayed hospital presentation following the outbreak announcement.

cember 2019 (1-3). On February 11, 2020, the World Health Organization announced a name for the novel coronavirus disease: coronavirus disease 2019 (COVID-19). The Iranian Health Ministry announced the first cases of COVID-19 on February 19, 2020, in Qom (4, 5). In response to the COVID-19 epidemic, most hospitals canceled all elective or nonurgent medical procedures and operating theatres were converted into additional intensive care units.

In these circumstances, COVID-19 phobia kept people with serious surgical events requiring urgent management, for instance, appendicitis, et cetera, away from emergency rooms.

In the case of appendicitis, based on the delay rate between symptom onset and hospital presentation, the stages of the disease may be varied from early acute appendicitis to gangrenous and perforated appendicitis. The pathological stages of appendicitis can be divided into early acute, acute, acute suppurative, acute suppurative with periappendicitis, gangrenous, perforated, and chronic (6).

The primary pathogenetic event in most patients with acute appendicitis is luminal obstruction. As intraluminal pressure increases, appendiceal wall perfusion decreases due to arterial insufficiency. This stage results in mucosal ischemia (early appendicitis). The next stage occurs when bacteria are able to enter the luminal wall, causing transmural inflammation (suppurative appendicitis). In this stage, the parietal peritoneum and other structures also experience inflammation (periappendicitis). Finally, intramural venous and arterial thromboses develop at the final stages, leading to gangrenous appendicitis. If a patient with appendicitis does not undergo an operation at this phase, it will result in appendiceal infarction and perforation (complicated appendicitis) (7, 8).

Considering that fears of COVID-19 are keeping people away from hospitals and it probably leads to come in later stages of the disease, we decided to examine the pathology stage of appendicitis in patients referred to Firoozabadi Medical Center before and after the official announcement of the outbreak of the coronavirus in Iran. Therefore, this study aims at investigating the effect of the COVID-19 pandemic on the stage of appendicitis at presentation.

Methods

In this retrospective study, histopathology records of all acute appendicitis patients who underwent an emergency appendectomy in the surgical unit in our institute between December 2019 and April 2020 were reviewed retrospectively. The study period was designed to include 2 months before and 2 months after the officially announced onset of the COVID-19 outbreak in Iran on February 20, 2020. All cases of complicated appendicitis (perforated appendicitis, phlegmonous appendicitis, or abscess) were excluded.

Records of 170 patients were then reviewed in detail to find the effect of outbreak announcement on the histopathological stage when appendicitis patients come to the hospital. Before February 20, 2020, 111 patients had appendicectomies overall, while 59 patients had them after that day.

The parameters including age, gender, health insurance, and histopathology records were evaluated.

The frequency, percentage, mean, and standard deviation of the variables were first described. Then, a logistics regression model was used to examine the effect of independent variables, including gender (female or male), health insurance (whether or not), time (before or after the COVID-19 outbreak) and age on the ordinal scale-dependent variable; the stage of appendicitis at presentation (I, early acute appendicitis; II, acute appendicitis; III, acute appendicitis with periappendicitis + acute suppurative appendicitis; IV, acute suppurative appendicitis with periappendicitis; V- gangrenous appendicitis).

The logistic regression model was processed in 2 steps. First, simple ranked logistic regression was used to evaluate the effect of each independent variable on the stage of appendicitis at presentation, and then multiple ranked logistic regression was used to observe the effect of each of these independent variables by modifying the effect of other variables.

Results

The study was conducted on 170 clinically diagnosed acute appendicitis patients. Of the studied patients, 70.6% (120 cases) were men and 29.4% (50 cases) were women. The mean ± SD age of patients was 66/25 ± 72/11, respectively. Also, 91 (53.5%) of the samples had health insurance, but 79 (46.5%) did not have any insurance coverage. A total of 111 (65.3%) cases were admitted to the hospital for appendectomy surgery before the COVID-19 outbreak and the remaining 59 cases (34.7%) were admitted during the corona outbreak.

Patients were also classified into 5 groups in terms of disease status and severity (Table 1).

In the next step, a simple ordinal logistic regression model was used to evaluate the effect of each variable on the pathological stage of the disease (Table 2). The effect of gender was statistically significant (estimated beta = -0.80, SE = 0.33, p = 0.016) and the odds ratio (95% CI) was equal to 0.45(0.23, 0.86). It can be interpreted that

Table 1. Frequency Distribution and Percentage of Variables

Variable	Class	Frequency	Percentage
Gender	Male	120	70.6
	Female	50	29.4
Health insurance	Yes	91	53.5
	No	79	46.5
Date of Admission	Before the outbreak announcement	111	65.3
	After the outbreak announcement	59	34.7
Pathological Stage of Appendicitis in Microscopic Examination	Early Acute	3	1.8%
	Acute	33	19.4%
	Acute + periappendicitis	96	56.5%
	Acute suppurative + periappendicitis	33	19.4

women are 0.45 times less likely to present with later stages. This means that the severity of the disease is 55% lower in women than in men. The effect of the date of admission was equal to -0.38 (SE = 32) and its odds ratio (95% CI) was estimated to be 0.68 (0.36, 1.28), which was not significant at the level of 0.05 (p = 0.235). Also, having health insurance with a coefficient of -0.69 (SE = 30) and an odds ratio (95%CI) of 0.50 (0.28, 0.90) at the level of 0.05 was significant (p = 0.024). The results showed that those who had health insurance were 50% less likely to present in later pathological stages than those who did not have health insurance. in other words, those who did not have health insurance were twice as likely as those with insurance. The effect of the age was not significant at the level of 0.05 (p = 0.902), with a regression coefficient close to zero and an odds ratio close to 1.

As the results of the multiple ordinal logistic regression model are shown in Table 3, the effect of gender was estimated to be -0.69 (SE = 0.35), with an odds ratio of 0.50 (0.25, 0.99), which was significant at the level of 0.05 (p = 0.049). It means that if the other variables are constant, the severity of the disease for female patients is 50% less than for male patients. However, the odds ratio for the date of admission was lower but still was not significant (p = 0.098). Also, the effect of health insurance was not significant at the level of 0.05 (p = 0.068). Additionally, the effect variable of age was not significant as well (p = 0.796).

The frequency and bar chart of each pathological stage before and after the COVID- outbreak announcement is presented in Table 4 and Figure 1.

Discussion

This study aimed to examine whether there are any changes in the severity of appendicitis pathological staging in patients who presented for urgent surgical care after the pandemic crisis of the coronavirus disease.

Appendicitis pathological staging and severity are associated with the overall elapsed time from symptom onset to admission or operation (9). The risk of perforation increases with delay in a hospital visit, timely recognition, and surgery for acute appendicitis (10). Emergency department visits all over Iran are down as fear of COVID-19 keeps people with milder and tolerable discomforts away from hospitals. As can be seen in this study, the number of patients with a diagnosis of acute appendicitis was down by about 50% after the outbreak announcement in Iran. Surprisingly, we did not find any significant changes in the distribution pattern of appendicitis pathological staging. It was against Chang et al study that reported an increased severity in acute appendicitis presentation during the COVID-19 pandemic. (11) This discrep-

Table 2. Results of simple ordinal logistic regression model

Variable	Class	Regression coefficient	Odds Ratio (Confidence Interval)	*P*-Value
Gender	Female	-0.80 (0.33)	0.45 (0.23, 0.86)	0.016
	Male	Reference	---	---
Date of admission	After the outbreak announcement	-0.38 (0.32)	0.68 (0.36,1.28)	0.235
	Before the outbreak announcement	Reference	---	---
Health insurance	Yes	-0.69 (0.30)	0.50 (0.28, 0.90)	0.024
	No	Reference	---	---
Age	(01)	0.00 (02)	1 (0.96, 1.04)	0.902

Table 3. Multiple ordinal logistic regression

Variable	Class	Regression Coefficient	Odds Ratio	*P*-Value
Gender	Female	-0.69 (0.35)	0.50 (0.25, 0.99)	0.049
	Male	Reference	---	---
Date of admission	After the outbreak announcement	-0.54 (0.33)	0.58 (0.30, 1.11)	0.098
	Before the outbreak announcement	Reference	---	---
Health insurance	Yes	-0.59 (0.32)	0.55 (0.30, 1.04)	0.068
	No	Reference	---	---
Age	(01)	0.00 (0.01)	1 (0.98, 1.02)	0.796

Table 4. Time-pathologic stage of appendicitis cross tabulation

Variable		Pathologic Stage of Appendicitis					Total
		I	II	III	IV	V	
Time	Before the outbreak announcement	1	15	73	19	3	111
	After the outbreak announcement	2	18	23	14	2	59
Total		3	33	96	33	5	170

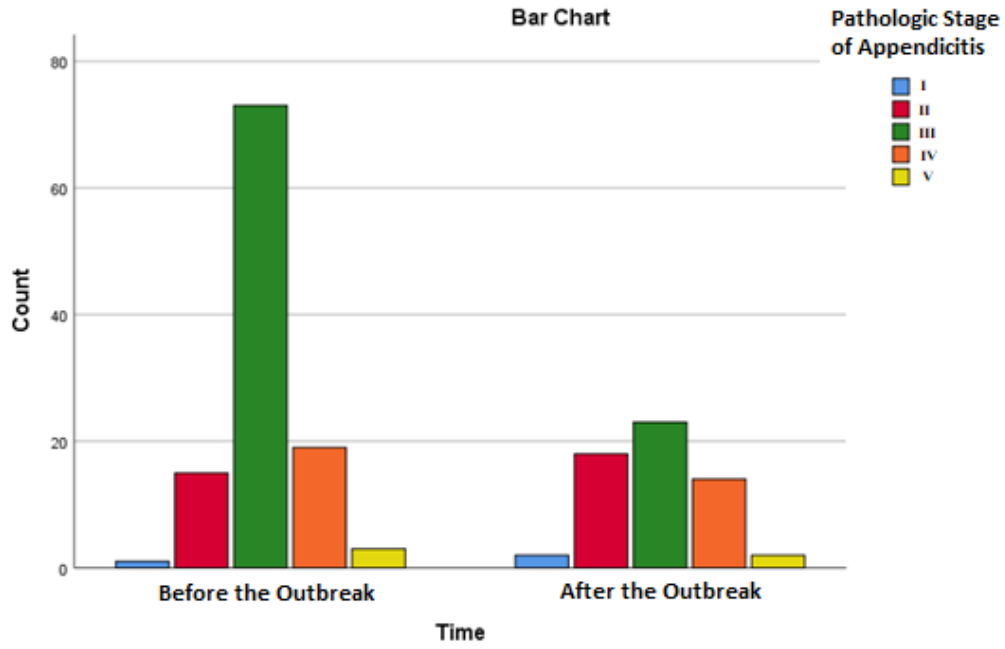

Fig. 1. Time-pathologic stage of appendicitis bar chart

ancy could be attributed to the Iranian population's greater level of fear of the coronavirus than the Chinese population being studied by Chang et al. In the present study, being uninsured and male sex were found to have the most significant roles in delayed hospital presentation and higher pathological stages in patients with acute appendicitis. This result was consistent with Choi et al in 2016, which showed that "patients with no insurance present for care later than patients who have health insurance"(12). Also, Sheu study stated male sex as a risk factor for delayed emergency department presentation (13). An early report (limited evidence) suggested that COVID-19 vaccine may also contribute to acute appendicitis as an adverse event (14). However, the exact nature of the relationship of COVID-19 vaccine with acute appendicitis, if any, requires further longitudinal study to extend this initial explanation, as this case series by Mitchell et al cannot be used to prove or disprove a causal relationship.

However, the rapid decline in emergency department visits could be attributed to closures ordered by governments in an effort to stop the spread of COVID-19 as well as increased travel and people returning to their rural homes.

Conclusion

The number of appendicitis patients was down by about 50% after the outbreak announcement in Iran. However, there was not any significant changes in the distribution pattern of appendicitis pathological staging after the outbreak announcement. Male sex and lack of insurance were revealed to play the biggest roles in patients with acute appendicitis presenting to the hospital later and having higher pathological stages.

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None.

Authors' Contribution

M.K., A.T.M., M.R.T., M.A. and F.M. designed the study. E.A., G.S., A.T.A., and F.O. conducted the statistical analyses and generated the tables and figures. Each author contributed to the interpretation of the results, wrote the manuscript, and gave their final approval to the version that was submitted.

Ethical Considerations

This was a retrospective study and used an already-existing database, and prior to entering the patients' information into the database, informed consent was sought for its use.

Conflict of Interests

The authors declare that they have no competing interests.

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