The Contribution of Alvarado Score and Ultrasonography to the Diagnosis of Childhood Appendicitis during and before COVID-19 Pandemic Period

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ABSTRACT

Introduction: This study aimed to evaluate the changes made by the pandemic in pediatric appendicitis, the Alvarado score and the contribution of ultrasonography to the diagnosis.

Methods: This study was conducted on patients who underwent surgery for appendicitis to compare the COVID-19 pandemic period versus the same period the year before. Data regarding demographics, age, the time between symptom onset and admission to hospital, laboratory, ultrasonography and pathology results and Alvarado score were considered.

Results: A total of 211 patients were operated on for appendicitis, 132 patients in the control group and 79 patients in the COVID-19 group. No significant differences between the groups in terms of age, gender and the distribution of appendicitis severity were found. The median time between the onset of symptoms and admission to the hospital was 2.72 days during the COVID-19 pandemic period and there was a significant difference between the two groups(p=0.043). Alvarado score and ultrasonography were evaluated together, in the control group sensitivity 98.4%, specificity 87.5%, PPV 96.9% and NPV 93.3%; if in the COVID-19 group were 94.5%, 88.8%, 97.2% and 80%, respectively.

Conclusions: This study has shown that the evaluation of the Alvarado score and ultrasonography together, increases both sensitivity and specificity for the diagnosis of childhood appendicitis. That's why the combination of these tests becomes more important in special situations such as the COVID-19 period.

Keywords: Appendicitis; COVID-19 Pandemic; Ultrasonography

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INTRODUCTION
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reason for the Coronavirus disease 2019 (COVID-19) was first reported by China in December 2019 and has spread rapidly around the world. The first case in our country was seen on March 11, 2020, when the World Health Organization declared the COVID-19 outbreak a pandemic.[1] The COVID-19 pandemic has caused changes in health services, as in all areas of our lives. Acute appendicitis, the most common cause of abdominal surgery in children, is thought to develop due to facilities or lymphoid hyperplasia.[2] A definitive diagnosis is made by histopathological examination.[3] In the early stages and especially in young children diagnosis of appendicitis is not always easy. The risk of complications increases when the diagnosis is delayed, and therefore various scoring systems have been developed. Alvarado score (AS) is one of them.[4] In addition, it can be more difficult to diagnose, as can be seen from the publications on patients who applied with the complaint of abdominal pain mimicking acute appendicitis during the COVID-19 pandemic period.[5-8] In this study, we aimed to observe the changes made by the COVID-19 pandemic in the number and qualified of cases by measuring the diagnostic values of AS and ultrasonography (US) according to the histopathological results of the patients we operated on for appendicitis.

METHODS
A retrospective study on patients under the age of 18 by creating two groups was conducted whom we operated with the diagnosis of appendicitis in our clinic from experiencing the COVID-19 pandemic 01.03.2020 to 31.12.2020 and in the same period of 2019 (control group) after ethical approval was taken from both our university clinical research ethics committee(Number:24.03.2021-310) and the Ministry of Health.
Patient demographics, age, the time between symptom onset and admission to hospital, laboratory results, ultrasonography evaluation, pathology results and Alvarado Score (AS) were considered. Appendicitis cases were classified as complicated (peritonitis, abscess, perforation), uncomplicated and normal.
AS was calculated out of 10 points as migration of pain 1 point, anorexia 1 point, nausea/vomiting 1 point, right lower quadrant tenderness 2 points, rebound pain 1 point, the elevation of temperature 1 point, leukocytosis 2 points and neutrophilia 1 point. The AS was done in previous studies, patients with an AS of ≥ 7 were considered to have appendicitis, ie positive, and those with an AS of < 7 were considered negative.[3,7] US findings were divided into two groups positive and negative. According to the histopathology results, the sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) of the AS system, US and both together were calculated. Those with negative or positive AS or US results alone were not included in the evaluation.
Statistical analysis was performed with SPSS Version 22 (IBM Corp, Armonk, NY). Data were analysed using the Chi-Square test or Fisher’s exact test for categorical data and Student t- or Mann-Whitney U tests for continuous data. 132 patients before the COVID-19 period and 79 patients during COVID-19 treated with the diagnosis of appendicitis were included in this retrospective study, no sample calculation was made. p ≤ 0.05 was considered statistically significant.

RESULTS
In our study, a total of 211 patients were operated on, 132 patients in the control group and 79 patients in the COVID-19 group. Basic demographic and outcome details for all patients undergoing appendectomy are summarized in Table 1. Pathology results of the patients were reported as 32 normal
appendix, 93 non-complicated appendicitis and 7 complicated appendicitis in the control group; In the COVID-19 group, 25 normal appendicitis, 46 non-complicated appendicitis, and 8 complicated appendicitis were reported. There were 84 male and 48 female patients in the control group, and 46 male and 33 female patients in the COVID-19 group. The mean age of the patients in the control group, whose ages ranged from 3 to 17 years, was 11.8, the age range of the patients in the COVID-19 group was 4 to 17 and the mean was 11.6. No significant differences between the groups in terms of mean age and gender distribution of patients were found.

In the analysis of the time from the onset of symptoms to the hospital admission of the patients; It was determined that patients applied later (2.72±2.20 days) during the COVID-19 pandemic period and there was a significant difference between the two groups (p=0.04) (Table 1). Although the rate of complicated appendicitis increased from 5.3% to 10.1% compared to the previous year in the COVID-19 period, no statistically significant difference was found in the distribution of appendicitis severity (p=0.154).

In addition, while the number of patients presenting with symptoms for more than 5 days was higher in the period of COVID-19 and statistically significant (p=0.003), no significant difference was found for complicated appendicitis in the same period for each group (p=0.333) (Table 1).

In the control and COVID-19 groups, sensitivity, specificity, PPV and NPV as a result of AS and US evaluation of both together are summarized in Table 2. The sensitivity of the AS was 78% and the NPV was 56.8% in the control group, it increased to 88.8% and 76% in the COVID-19 group, respectively. Specificity of AS decreased from 90.6% and PPV from 96.3% in the control group to 76% and 88.6% in the COVID-19 group, respectively.

While the specificity of US increased in the COVID-19 group compared to the control group, sensitivity, PPV and NPV decreased (Table 2). In the control group, we found 64 true positives and 2 false positives when the AS and US were positive, and 14 true negatives and 1 false negative when both were negative. These patients were operated on because there was no clinical regression or the right lower quadrant pain continued to increase. In the COVID-19 pandemic period, we detected 35 true positives and 1 false positive when AS and US were positive, and 8 true negatives and 2 false negatives when both were negative. When AS and US were evaluated together, in the control group sensitivity 98.4%, specificity 87.5%, PPV 96.9% and NPV 93.3%; whereas in the COVID-19 group were 94.5%, 88.8%, 97.2% and 80%, respectively. No statistically significant difference between the control and COVID-19 groups in the diagnosis of appendicitis by AS and US evaluation was found (p=0.30 for AS, 0.11 for the US).
Table 1: Demographic and Outcome Details of Patients

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>COVID-19</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of case</td>
<td>132</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>84 (63.63%)</td>
<td>46 (58.22)</td>
<td>0.43</td>
</tr>
<tr>
<td>Female</td>
<td>48 (36.37)</td>
<td>33 (41.78)</td>
<td></td>
</tr>
<tr>
<td>Age, years (range)</td>
<td>11.8 (3-17)</td>
<td>11.6 (4-17)</td>
<td>0.712</td>
</tr>
<tr>
<td>Time from symptom onset to presentation, days (range)</td>
<td>2.16(±1.24) (1-7)</td>
<td>2.72(±2.20) (1-14)</td>
<td>0.043</td>
</tr>
<tr>
<td>Presentation ≥ 5 days after the onset of symptom (number)</td>
<td>8</td>
<td>10(12.6%):/</td>
<td>0.154</td>
</tr>
<tr>
<td>Grade of appendicitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal appendix M/F</td>
<td>15(11.4%)/17</td>
<td>15(19%)</td>
<td></td>
</tr>
<tr>
<td>Uncomplicated appendix M/F</td>
<td>(12.8%)</td>
<td>31(39.2%):</td>
<td></td>
</tr>
<tr>
<td>Complicated appendix M/F</td>
<td>67(50.8%)/26</td>
<td>15(19%)</td>
<td>0.333</td>
</tr>
<tr>
<td>Presentation ≥5 days in the complicated appendicitis</td>
<td>2(1.5%):5(3.8%):</td>
<td>(3.8%):2</td>
<td></td>
</tr>
</tbody>
</table>

M= Male, F= Female

Table 2: Comparison of Alvarado Score and Ultrasonography during COVID-19 Period

<table>
<thead>
<tr>
<th></th>
<th>CONTROL</th>
<th>COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alvarado score N=132</td>
<td>Ultrasonography N=132</td>
</tr>
<tr>
<td>True positive, n</td>
<td>78</td>
<td>85</td>
</tr>
<tr>
<td>False positive, n</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>True negative, n</td>
<td>29</td>
<td>15</td>
</tr>
<tr>
<td>False negative, n</td>
<td>22</td>
<td>15</td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>78</td>
<td>85</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>90.6</td>
<td>46.8</td>
</tr>
<tr>
<td>Positive predictive value, %</td>
<td>96.3</td>
<td>83.3</td>
</tr>
<tr>
<td>Negative predictive value, %</td>
<td>56.9</td>
<td>50</td>
</tr>
</tbody>
</table>

DISCUSSION

Acute appendicitis is one of the most common emergencies which requires surgical treatment in children. Signs and symptoms may vary depending on the age of the child. Various scorings have also been developed for appendicitis, which is not always easy to diagnose in childhood.[9]

During the COVID-19 pandemic period, non-emergency cases were postponed in our country as in most countries, but hospitals continued to serve non-COVID emergency patients. During this pandemic period, there has been a decrease and changes in admissions...
Kaya C et al. Diagnosis of childhood appendicitis

to hospitals due to severe restrictions or fear of contamination risk. Snapiri et al. reported a twofold increase in the incidence of complicated appendicitis during the COVID-19 pandemic period, although there was no statistically significant difference.[10] Similarly, in our study, although there was no statistically significant difference, the cases of complicated appendicitis increased from 5.3% in the control group to 10.1% in the COVID-19 group. We think that the increase in these complicated appendicitis cases is due to the delayed admission of the patients to the hospital (2.72±2.20 days).

There are publications in the literature on the nonoperative management of appendicitis with antibiotic therapy.[11,12] No significant difference was found in the study of Park et al. in which they compared those who received antibiotic treatment and those who did not, on adult patients diagnosed with acute appendicitis with a diameter of up to 11 mm without radiological faeces.[13] In our study, according to the histopathology results, while there is no significant difference in the number of the normal appendix and complicated appendicitis during the COVID-19 period and the previous year, there is a 50% decrease in the number of non-complicated appendicitis during COVID-19 period. The decrease in the number of non-complicated appendicitis in our study may be because patients do not come to the hospital due to the risk of COVID-19 infection, and the appendix spontaneously resolves when it is not complicated as Tankel et al. stated. or applied to other centres.[14]

In the literature, SARS-CoV-2 PCR tests both positive and negative Multisystem Inflammatory Syndrome in Children (MIS-C) cases are presented.[5,6,15,16] MIS-C can cause symptoms such as cardiovascular, respiratory and neurological symptoms in addition to causing the most common gastrointestinal symptoms in children that can sometimes be confused with acute abdomen. [5] Although we think that the reason for the increase in the number of patients who were operated on during the COVID-19 pandemic period and whose histopathology results were normal from 24.2% to 31.6%, may be due to this gastrointestinal involvement of the disease mimicking acute abdomen. We did not encounter any SARS-CoV-2 PCR positivity in patients or any complaints or symptoms related to other systems in their follow-up. This could be related to MIS-C without positive SARS-CoV-2 PCR test.

Considering the decrease in uncomplicated appendicitis cases, it cannot be excluded that there may be patients with gastrointestinal symptoms who do not apply to health institutions due to the risk of infection in hospitals. As a result of this, the number of children with SARS-CoV-2 infection, which may be asymptomatic, may be much higher than we thought.

One of the scoring systems developed for the correct diagnosis of acute appendicitis in patients presenting with abdominal pain is the AS. There are many studies published in the literature and their diagnostic values differ. [3,4,7,17] Khanafer et al. reported sensitivity as 68.5%, specificity 74.6%, PPV 54.9%, NPV 85.3% in their study with patients who were considered to have appendicitis when AS was ≥ 7; while Pogorelic et al. reported sensitivity as 89%, specificity 59%, PPV 93.1%, NPV 46%.[7,17] In our study, sensitivity was 78%, specificity was 90.6%, PPV was 96.3%, and NPV was 56.9% in the control group; sensitivity was 78%, specificity was 89.6%, sensitivity was 90.6%, PPV was 96.3%, and NPV was 56.9% in the control group.

Despite the US is dependent on the person performing the procedure, it cannot be ignored in the diagnosis of acute appendicitis. In the study where the AS took the cut-off value of 6, Bappayya et al. reported that PPV increased from 86.3% and NPV from 44.1%, PPV to 94.1% and NPV to 76.2% when evaluated together with the US. [18] Kurane et al. reported sensitivity as 78.2%, specificity as 83.7%, PPV at 75%, and NPV at 86.1% in their study with modified AS. In the same study,
when they evaluated the modified AS and US, they reported that the sensitivity increased to 88.8%, the specificity to 96.5%, PPV to 94.1% and NPV to 93.3%.[19] In our study, sensitivity was 98.4%, specificity 87.5%, PPV 96.9%, and NPV 93.3% in the control group when AS and the US were evaluated together. In addition, we found the sensitivity to 94.5%, specificity at 88.8%, PPV at 97.2% and NPV at 80% during the COVID-19 Pandemic period. Limitations of this study; it was a single-centre and retrospective study and the ultrasonography procedure was performed by different doctors.

CONCLUSION
This study has shown that the evaluation of AS and US together, increases both sensitivity and specificity for the diagnosis of childhood appendicitis. In cases where the diagnosis of childhood appendicitis is difficult, it should be considered that the evaluation of AS and US together can guide surgeons in the decision of operation. That's why the combination of these tests becomes more important in special situations such as the COVID-19 period.

CONFLICT OF INTEREST
None

SOURCE OF FUNDING
None

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