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Histopathological examination of acute appendicitis tissue in children during the COVID-19 pandemic

Semra Gurunluoglu[1], Mehmet Gul[2], Sami Akbulut[3], Hasan Ates[4], Necmettin Akpinar[4], Ecem Serbest Cin[4], Elif Kayhan Kustepe[2], Serpil Kaplan[5], Mehmet Aslan[6], Ahmet Selim Ozkan[7], Mehmet Demircan[4], Kubilay Gurunluoglu[4]

[1]*Inonu University, Faculty of Medicine Department of Pathology, Malatya, Türkiye*
[2]*Inonu University, Faculty of Medicine Department of Histology and Embryology, Malatya, Türkiye*
[3]*Inonu University, Faculty of Medicine Department of General Surgery, Malatya, Türkiye*
[4]*Inonu University, Faculty of Medicine Department of Pediatric Surgery, Malatya, Türkiye*
[5]*Malatya, Education and Research Hospital, Pathology Laboratory, Malatya, Türkiye*
[6]*Inonu University, Faculty of Medicine Department of Pediatrics, Malatya, Türkiye*
[7]*Inonu University, Faculty of Medicine Department of Anesthesiology, Malatya, Türkiye*

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Abstract

In this study, we prospectively investigated the histopathological features of the removed appendix tissue in pediatric patients who were operated on with the preliminary diagnosis of appendicitis. A catarrhal appendicitis group (n=43), a phlegmonous appendicitis group (n=28), a gangrenous appendicitis group (n=19), a perforated appendicitis group (n=35), and an appendicitis +COVID-19 group (n=7) were formed. The control group consisted of 21 children. A section of each patient's appendix tissue from the part with the highest diameter was taken for histopathological examination. The sections were routinely stained with hematoxylin and eosin (H&E). The two pathologists evaluated all H&E sections in a light microscope. The evaluation results were analyzed statistically. No significant differences in age and gender were found between all groups. The results of neutrophil and lymphocyte counts in all tissue layers of all groups were significantly different. Neutrophil count in the mucosa and muscularis propria in the appendix tissues of the control group were found to be zero. Among all groups, the highest number of neutrophil counts in the mucosa and muscularis propria were found in the perforated group. Among all groups, the highest number of lymphocyte counts in mucosa and muscularis propria were found in the Covid-19 group. The mucosal erosion, intraluminal neutrophils, and reactive lymphoid hyperplasia were negative in all samples in the control group. Neutrophil accumulation in the mucosa and muscularis propria layers in appendix tissue together with other inflammation findings are important in the histopathological diagnosis of appendicitis. In patients with Covid-19 infection, appendicitis may occur, in which case, severe accumulation of lymphocytes appears in the mucosal layer in addition.

Keywords: Pediatric appendicitis, histopathological features, COVID-19 pandemic

Introduction

Acute appendicitis is the most common intra-abdominal pathology requiring emergency surgical intervention in children all over the world [1]. Although the diagnosis of acute appendicitis is made by radiology findings together with scoring systems consisting of anamnesis-clinical-laboratory findings, the definitive diagnosis is made by histopathological examination of the appendix tissue removed in operation [1-3]. Despite all advanced diagnostic methods, histological examination revealed that 8.9% of the pediatric patients who were operated on with the presumptive diagnosis of appendicitis did not have appendicitis [4]. This rate varies between 1% and 40% in different studies [4]. Therefore, it is important to know the histological features of appendix tissue in normal children and appendicitis patients.

Coronavirus disease 2019 (COVID-19), which first appeared at the end of 2019, rapidly developed into a pandemic in 2020. The pandemic has placed extraordinary burdens on health systems globally and has affected the treatment process of many diseases

*Corresponding Author: Kubilay Gurunluoglu, Inonu University, Faculty of Medicine, Department of Pediatric Surgery, Malatya, Türkiye
E-mail: kgurunluoglu@hotmail.com

and patients of different ages [5].

This study aims to investigate the histopathological features of the removed appendix tissue in pediatric patients who were operated on with the preliminary diagnosis of appendicitis during the Covid-19 pandemic.

Material and Methods

Our study was conducted in a single center Turgut Ozal Medical Centre, Malatya, Türkiye Pediatric Surgery Clinic between June 2020 and May 2022.

Ethical approval was obtained from Inonu University Faculty of Medicine Clinical Research Ethics Committee in Malatya, Turkey (Decision number: 2020/84). This study was carried out following the Helsinki Declaration. The informed consent forms signed by the legal guardians of all patients included in the study were obtained and these documents are available in the archives of our clinic.

Study Groups

In our study, all appendix tissues removed during surgery in patients who were operated on with the preliminary diagnosis of appendicitis were divided into groups according to intra-operative macroscopic evaluation. Within these groups, a separate group of Covid-19 positive patients was formed.

Histopathological examinations of all appendix tissues were routinely performed and two cases that were diagnosed as negative appendicitis in the intraoperative macroscopic evaluation were diagnosed as catarrhal appendicitis on histopathological evaluation.

Accordingly, a total of 6 groups were formed control, catarrhal, phlegmonous, gangrenous, perforated, and Covid-19 positive appendicitis. Patients who were operated on with preoperative diagnosis of appendicitis but intra-operatively were not considered as appendicitis constituted the control group, besides two cases that were diagnosed as catarrhal appendicitis in histopathological examination and added to the catarrhal appendicitis group.

The criteria for inclusion in the study were: i) clinical diagnosis of appendicitis, ii) patient aged between 4-17 years, iii) patient with appendix tissue removed in one piece during surgery, iv) the patient does not have a chronic disease such as diabetes or epilepsy, v) presence of parental informed consent and vi) performed operation was open surgical appendectomy. According to these criteria, 153 patients were included in the study, and groups were formed as 43 catarrhal, 28 phlegmonous, 19 gangrenous, 35 perforated, and 7 Covid-19 appendicitis patients. The control group consisted of 21 children.

Our evaluation protocol for the basic diagnosis consisted of abdominal and lung radiographs, laboratory parameters, and the Alvarado score system for pediatric patients with abdominal pain. All patients underwent routine laboratory tests, and the same physical and radiological examinations. The abdominal and chest X-ray images were performed for all patients. We performed the X-ray images of the abdomen to find free air and the chest X-rays to assess right lower lobe pneumonia. Radiographic examinations of all patients in this study revealed no free air and no right lower lobe pneumonia. Abdominal ultrasound was performed only in female patients over 10 years of age to rule out tubal, ovarian, and uterine pathologies.

All patients were given Alvarado scores at the time of diagnosis. We have been using the Alvarado scoring system (ASS) in our clinic for a long time and we were more experienced in using this scoring system than the others. Therefore, in our study, we used ASS for the diagnosis in the emergency department. Only patients with a score of 7 or higher were considered as having acute abdomen and underwent surgery. In the preoperative period, all patients were given sulbactam-ampicillin IV (Ampicillin 50mg/kg single dose) as a prophylactic antibiotic.

General Anesthesia Protocol

The preoperative fasting periods for all appendicitis patients were six hours for solid foods and two hours for clear fluids [6]. Covid-19-positive patients underwent anesthesia with additional precautions. High-level personal protective equipment consisting of N95 masks, impermeable body suits, glasses, face visors, shoe covers, and double-layered medical gloves was used by the entire team, including the pediatric surgeon, anesthesiologist, nursing staff, and assistants [6]. The patients wearing N95 masks were then transferred to the operation room through a corridor in which all other patient and hospital staff movement was stopped to minimize the risk of contamination.

General anesthesia with rapid-sequence induction and intubation was administered according to a standardized protocol by an experienced anesthesiologist after low-flow preoxygenation. Propofol (2–3mg/kg), rocuronium (0.6–1,1mg/kg), and fentanyl (1µg/kg) were administered intravenously in amounts calculated according to the actual body weight [6]. We used double gloves during intubation and changed the outer gloves immediately after the laryngoscopy procedure. All the staff wore appropriate personal protective equipment during the operation. The patients were then extubated, and a surgical mask was placed over their airways. Analgesia was administered to all patients by using appropriate doses of fentanyl and paracetamol (10mg/kg, IV) at the time of skin suturing.

Surgical Procedures

All surgeries were performed by the same surgical and anesthesiology teams. All appendicitis patients received standard appendicitis surgical (open appendectomy) and medical treatment proposed by Dunn [1].

Preparation of histopathological sections

A section of each patient's appendix tissue from the part with the highest diameter was taken for histopathological examination. If there was no diameter difference throughout the entire appendix tissue, a section was taken 2cm proximal to the appendicular tip. The sections were 1cm in length and the full appendicular wall thickness was included. The sections were first washed with saline and then placed in a container containing 10% formalin and left for 24 hours. After this process appendix tissue samples were further divided into 0.3cm long pieces passed through a routine tissue processing procedure and embedded in paraffin blocks [7]. Then, sections of 3-5µm thickness were taken by a microtome from each paraffin block. The sections were stained by routine hematoxylin

and eosin (H&E) procedures.

Histopathological evaluation of tissue sections

The two pathologists evaluated all H&E sections by a light microscope (Eclipse E 200 MU Ri Nikon Corporation, Tokyo, Japan) at 40-400 magnifications. In each tissue section, the mucosa, submucosa, muscularis propria, and subserosa layers were identified first [7,8]. Then the mucosa was further divided into superficial, middle, and deep layers. In each layer from superficial mucosa to sub-serosa, 5 random areas were evaluated at X400 magnification by counting, neutrophils, and lymphocytes separately; and an average was calculated for every layer of every sample. Lymphocyte count was performed by excluding lymphoid follicle areas [7,8]. In addition, the presence of mucosal erosion, intraluminal neutrophils, and reactive lymphoid hyperplasia in each tissue section was investigated [7,8]. The results obtained were analyzed statistically.

Biostatistical analysis

Shapiro Wilk test of normality was used to determine whether the variables had a normal distribution. Data were given as median (minimum-maximum) and number (percent). Pearson chi-square test and Kruskal Wallis test were used where appropriate in statistical analysis. Conover test was used for pairwise comparison of the groups. A value of $p<0.05$ was considered statistically significant. IBM SPSS Statistics 26.0 program was used in the analysis.

Results

The results of the statistical analysis of the characteristic parameters of the patients in the study are shown in table 1. In our study, negative appendectomy patients were 21 patients in total. We found the negative appendectomy rate in our study to be 13.7%. No significant differences in age and gender were found between all groups. The groups with the highest Alvarado scores were gangrenous, perforated, and Covid-19 appendicitis (Table 1). The group with the highest operative time was found to be the perforated group (Table 1). The groups with the highest mean hospitalization time were gangrenous and perforated. ICU stay was found to be the highest in the gangrenous group (Table 1).

Statistical analysis of neutrophil and lymphocyte counts in all layers of the appendix tissues of the groups is shown in table 2. The results of neutrophil and lymphocyte counts in all layers of all groups were significantly different (Table 2). Neutrophil count in the mucosa and muscularis propria of the control group was found to be zero (Table 2 Figure 1-4). Among all groups, the highest number of neutrophil counts in the mucosa and muscularis propria were found in the perforated group (Table 2 Figure 1,2, 5-6). Among all groups, the highest number of lymphocyte counts in mucosa and muscularis propria were found in the Covid-19 group (Table 2, Figure 7,8).

Statistical analysis of the parameters of mucosal erosion, intraluminal neutrophils, and reactive lymphoid hyperplasia in the appendix tissue of all groups is shown in table 3. Each of these three parameters was found to be significantly different among all groups (Table 3). In the control group mucosal erosion, intraluminal neutrophils, and reactive lymphoid hyperplasia were negative in all samples (Table 3). Mucosal erosion was positive in all samples in the catarrhal, perforated and gangrenous groups. Intraluminal neutrophils were found to be positive in all samples of the catarrhal, perforated, gangrenous, and Covid-19 groups (Table 3). Reactive lymphoid hyperplasia was found to be negative in all samples of the control and perforated groups, but positive in all samples of the Covid-19 group (Table 3).

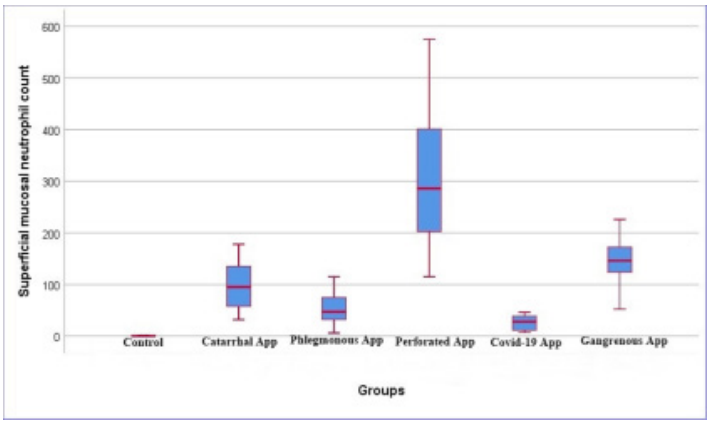

Figure 1. The superficial mucosa neutrophil count of all groups is shown in the graphic

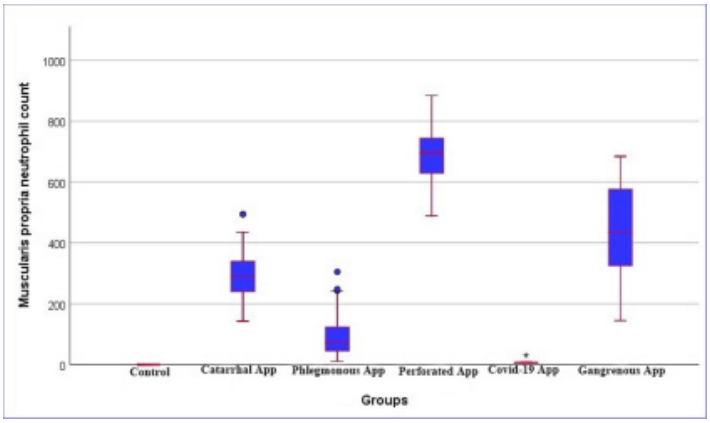

Figure 2. The muscularis propria neutrophil count of all groups is shown in the graphic

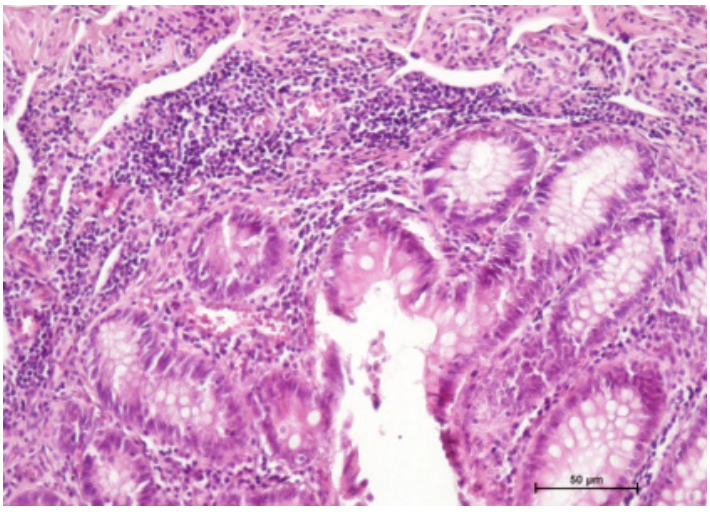

Figure 3. Normal appendix mucosa of the control group is shown in the picture at X 200 magnification (H&E)

Table 1. Patient characteristics

Variables**		Groups*						p
		Control (n=21 13.7%)	Catarrhal App (n=43 28.2%)	Phlegmonous App (n=28 18.3%)	Perforated App (n=35 22.8%)	COVID-19 App (n=7 4.5%)	Gangrenous App (n=19 12.5%)	
Gender (%)	Male	11 (52.4)	23 (53.5)	15 (53.6)	27 (77.1)	2 (28.6)	12 (63.2)	0.116***
	Female	10 (47.6)	20 (46.5)	13 (46.4)	8 (22.9)	5 (71.4)	7 (36.8)	
Age		12 (5-17)	9.2 (5-16.8)	11.5 (5-17)	12 (4-17)	14.5 (9-16)	12 (4.5-17)	0.2329****
Alvarado Score		8^{ce} (5-9)	8^{ce} (5-9)	7.5^{ce} (5-9)	9 (8-10)	8 (8-9)	9 (8-10)	<0.001****
Operation time (min)		65^{ce} (35-120)	60^{ce} (30-120)	64^{ce} (30-120)	95^{d} (55-120)	65 (30-120)	95 (55-120)	<0.001****
Hospital stay (days)		3^{acde} (2-5)	2^{bcde} (1-3)	2.5^{cde} (2-5)	6 (5-12)	5^{e} (5-7)	7 (5-12)	<0.001****
ICU stay (days)		0^{ae} (0-2)	0^{bce} (0-2)	0^{ce} (0-3)	0^{e} (0-2)	0^{e} (0-5)	2 (1-4)	<0.001****

*: a: Catarrhal App is different by group, b: Phlegmonous App is different by group, c: Perforated App is different by group, d: Covid_19 App is different by group, e: Gangrenous App is different by group. **: The variables are summarized as 'median (min.-max.)', ***:Pearson chi-square test. ****:Kruskal Wallis Test

Table 2. Neutrophil and lymphocyte count in the appendix tissue of the all groups histopathological examination results

Variables**	Groups*						p***
	Control	Catarrhal App	Phlegmonous App	Perforated App	COVID-19 App	Gangrenous App	
SMNC	$0^{a,b,c,d,e}$ (0-2)	$95^{b,c,d,e}$ (32-178)	$47^{c,d,e}$ (6-115)	$286^{d,e}$ (115-575)	28^{e} (7-46)	146 (52-226)	<0.001
SMLC	$148^{a,b,d}$ (63-256)	$608^{b,c,e}$ (358-896)	$423^{c,d,e}$ (115-734)	$156^{d,e}$ (82-442)	885^{e} (249-1354)	108 (58-245)	<0.001
MMNC	$0^{a,b,c,e}$ (0-3)	$445^{b,d,e}$ (285-758)	$43^{c,e}$ (3-185)	$455^{d,e}$ (342-758)	3^{e} (2-15)	405 (265-615)	<0.001
MMLC	$178^{a,b,d,e}$ (68-238)	$612^{c,d,e}$ (385-896)	$569^{c,d,e}$ (295-845)	110^{d} (45-285)	985^{e} (480-1168)	128 (45-228)	<0.001
DMNC	$0^{a,b,c,e}$ (0-1)	$459^{b,d,e}$ (350-785)	$32^{c,d,e}$ (2-146)	$456^{d,e}$ (223-752)	5^{e} (3-8)	186 (42-452)	<0.001
DMLC	$268^{a,b,c,d,e}$ (90-343)	$369^{b,c,d,e}$ (254-586)	$333.5^{c,d,e}$ (64-482)	154^{d} (78-289)	1122^{e} (443-1363)	145 (59-228)	<0.001
SNC	$1^{a,b,c,e}$ (0-1)	$498^{b,c,d,e}$ (254-725)	$138^{c,d,e}$ (3-255)	$302^{d,e}$ (121-616)	5^{e} (4-24)	223 (111-396)	<0.001
SLC	$148^{a,c,d}$ (68-255)	$125^{b,d,e}$ (56-178)	$142^{c,d}$ (47-523)	$101^{d,e}$ (56-155)	596 (43-887)	155 (17-222)	<0.001
MPNC	$0^{a,b,c,d,e}$ (0-0)	$291^{b,c,d,e}$ (143-495)	$74^{c,d,e}$ (11-305)	$695^{d,e}$ (489-884)	7^{e} (5-31)	435 (145-684)	<0.001
MPLC	$11^{a,b,c,d,e}$ (5-17)	$156^{b,c,d,e}$ (56-282)	$41.5^{c,d,e}$ (12-82)	$144^{d,e}$ (63-282)	289^{e} (58-584)	66 (28-146)	<0.001
SSNC	$2^{a,b,c,e}$ (1-3)	$458^{b,c,d,e}$ (243-690)	$67^{c,d,e}$ (16-192)	$342^{d,e}$ (106-556)	5^{e} (2-27)	157 (105-448)	<0.001
SSLC	$28^{a,b,c,d,e}$ (12-47)	$142^{c,d,e}$ (56-215)	$12^{0c,d,e}$ (42-228)	$105^{d,e}$ (54-164)	189 (106-436)	242 (31-289)	<0.001

SMNC=Superficial mucosa neutrophil count, SMLC= Superficial mucosa lymphocyte count, MMNC= Middle mucosa neutrophil counti, MMLC= Middle mucosa lymphocyte count, DMNC= Deep mucosa neutrophil count, DMLC= Deep mucosa lymphocyte count, SNC= Submucosa neutrophil count, SLC= Submucosa lymphocyte count, MPNC= Muscularis propria neutrophil count, MPLC= Muscularis propria Lymphocyte count, SSNC= Subserosa neutrophil count, SSLC= Subserosa Lymphocyte count. *: a: Catarrhal App is different by group, b: Phlegmonous App is different by group, c: Perforated App is different by group, d: Covid_19 App is different by group, e: Gangrenous App is different by group. **:**: The variables are summarized as 'median (min.-max.)', ***:Kruskal Wallis test

Table 3. In the all groups, Mucosal Erosion (ME), Intraluminal Neutrophil (ILN), Statistical analysis result of reactive lymphoid hyperplasia (RLH) variables

Variables**	Categories	Groups (n;%)						p
		Control	Catarrhal App	Phlegmonous App	Perforated App	Covid-19 App	Gangrenous App	
Mucosal Erosion (ME)	**Negative**	21 (100)	0 (0)	12 (42.9)	0 (0)	2 (28.6)	0 (0)	<0.001
	Positive	0 (0)	43 (100)	16 (57.1)	35 (100)	5 (71.4)	19 (100)	
Intraluminal Neutrophil (ILN)	**Negative**	21 (100)	0 (0)	12 (42.9)	0 (0)	0 (0)	0 (0)	<0.001
	Positive	0 (0)	43 (100)	16 (57.1)	35 (100)	7 (100)	19 (100)	
Reactive lymphoid hyperplasia (RLH)	**Negative**	21 (100)	21 (48.8)	10 (35.7)	35 (100)	0 (0)	10 (52.6)	<0.001
	Positive	0 (0)	22 (51.2)	18 (64.3)	0 (0)	7 (100)	9 (47.4)	

*:Pearson chi square test

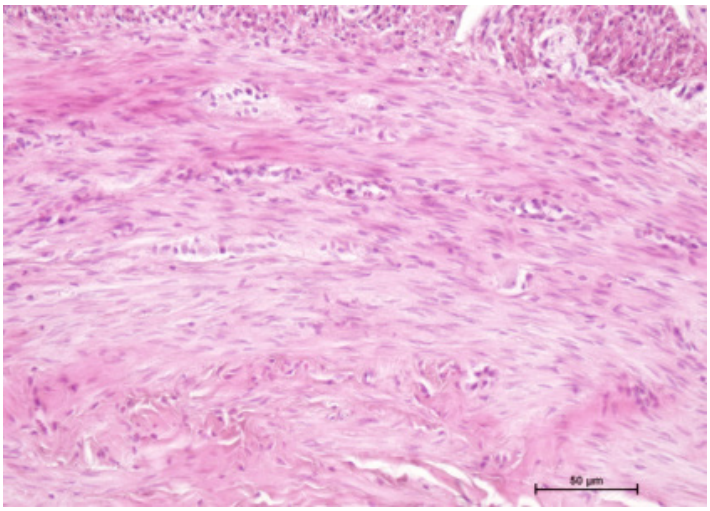

Figure 4. Normal appendix muscularis propria of the control group is shown in the picture at X 200 magnification (H&E)

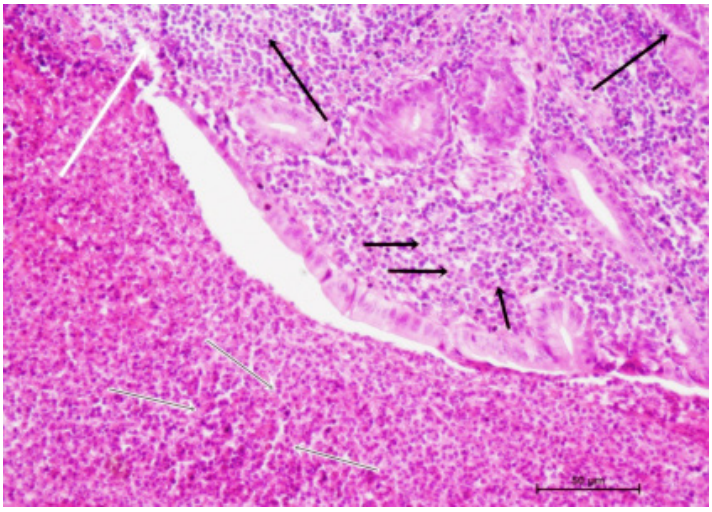

Figure 5. The mucosal erosion (white arrow), neutrophils (black arrows), and intraluminal neutrophils (white-sheathed black arrows) in the appendix mucosa of the perforated group are shown in the picture at X 200 magnification (H&E)

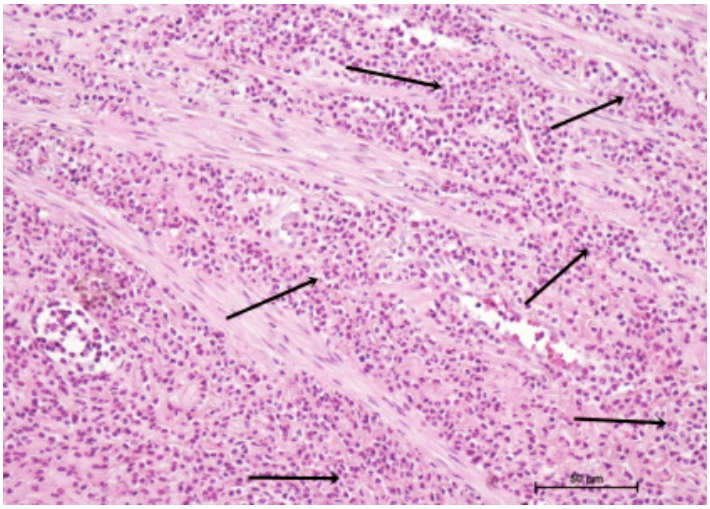

Figure 6. Neutrophil accumulation (black arrows) in the muscularis propria layer of the perforated group is shown in the picture at X 200 magnification (H&E)

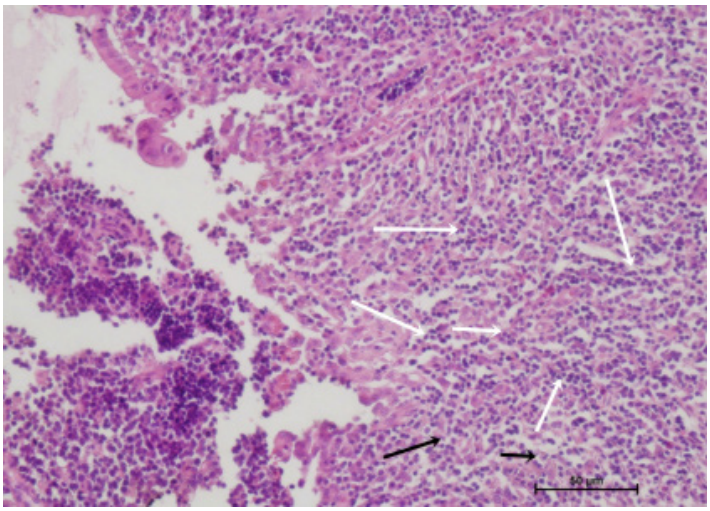

Figure 7. Neutrophil (black arrows) and lymphocyte accumulation (white arrows) in the mucosal layer of the Covid-19 group is shown in the picture at X 200 magnification (H&E)

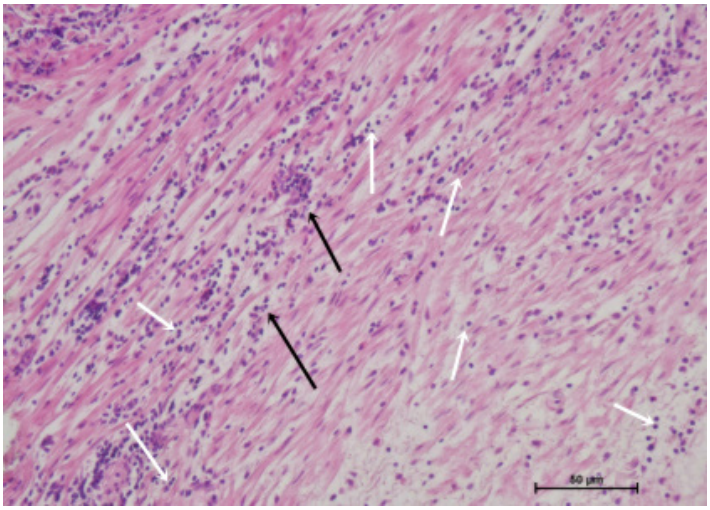

Figure 8. Neutrophil (black arrows) and lymphocyte accumulation (white arrows) in the muscularis propria layer of the Covid-19 group is shown in the picture at X 200 magnification (H&E)

Discussion

We found striking results in our study in which we examined the histological features of the appendix tissue in pediatric patients who were operated on with the preliminary diagnosis of appendicitis. We found that there were different amounts of neutrophil and lymphocyte accumulation in catarrhal, phlegmonous, perforated, and covid-19 appendicitis patients in all layers of appendix tissue. In the control group, there were no neutrophils in the layers of mucosa and muscularis propria. We found that the greatest accumulation of neutrophils in the layers of mucosa and muscularis propria was in patients with perforated appendicitis. With these results, we think that it is important to examine the mucosa and muscularis propria layers to diagnose appendicitis histologically. We claim that if no neutrophils were detected as a result of the examination of the mucosa and muscularis propria layers, the diagnosis of appendicitis can be excluded.

In a study by Barcia et al, they accepted the presence of more than 10 neutrophils in the mucosa layer and the presence of neutrophils in the muscularis propria layer as findings in favor of appendicitis

[7]. Rodriguez et al. considered the presence of neutrophil infiltration in the lamina propria on histological examination of the appendix tissue as appendicitis in their study [9]. They considered perforation as the presence of ulcers on the mucosa, submucosa, and muscular layer. They found that there was a moderate agreement between the surgeon and the pathologist in terms of diagnosis [9]. They found that this concordance did not depend on the surgeon's experience or the surgical method. They found that 70 patients were accepted to be non-perforated by the surgeon even though the pathologist accepted them to be perforated [9]. In our study, there was a diversity in terms of negative appendicitis. Since two intraoperatively negative appendicitis cases were diagnosed as catarrhal appendicitis on histopathologic examination.

Bolmers et al. examined 1850 appendicitis patients, as a result of their study, they claimed that histological examination was unnecessary to confirm the diagnosis of appendicitis and that intraoperative evaluation would be sufficient for diagnostic accuracy [10]. They claimed that histopathological examination would be valuable in terms of tumor or malignancy [10]. As a result of our study, we can say that histological evaluation is especially important for differentiating catarrhal stage appendicitis from negative appendicitis. In our study, we did not find tumors or malignancies in the appendix tissue.

Maloney et al. conducted a study to determine negative appendectomies in 1435 pediatric appendicitis patients [4]. In their study, they compared histopathological examination with clinical diagnosis [4]. Histopathologically, they accepted the presence of transmural inflammation in the appendix tissue as appendicitis [4]. As a result of their study, they found that the negative appendectomy rate was 4.5%. They argued that it was important to complete clinical diagnosis with histopathological examination because in this way, the detection of tumors, malignancies, and parasite infections could be performed and this was important in postoperative treatment; furthermore the number of negative appendectomies could be determined also [4]. In their study, they claimed that the negative appendectomy rate was a valuable parameter in determining the quality of a clinic [4]. Ma et al. evaluated the appendix tissue of 1492 adult patients and found 18.2% negative appendectomy and claimed that histopathological examination was very important in determining the negative appendectomy rate [11]. As a result of our study, we think that histopathological examination of the appendectomy material is especially important in determining negative appendectomy. We found our negative appendectomy rate to be 13.7%.

Butler et al. argued in their study that not only neutrophil accumulation in mucosa would be sufficient for the diagnosis of appendicitis, but also mucosal ulceration should be present [12]. Carr et al. argued that some intraluminal neutrophil deposits can be seen in very early-stage appendicitis, but if no transmural neutrophil residue is detected, then inflammation may be in a reversible period [13]. They even recommended that if such a patient had severe abdominal pain, then another cause of abdominal pain should be investigated clinically [13]. Akbulut et al. performed an appendectomy on donors of liver transplantation and found that 6.9% of the tissue samples they received contained transmural inflammation [14]. These patients are those who did not have abdominal pain and had no clinical signs of appendicitis. In our opinion, histopathological examination alone may not be sufficient for the diagnosis of appendicitis. Rabah et al. evaluated 324 pediatric patients who were clinically thought to have appendicitis in their study [15]. Although negative appendectomy was considered in 60 of these patients, they found serosal neutrophil accumulation in 29 of the negative appendectomies. However, there was no mucosal neutrophil accumulation [15].

In a study by Herd et al. 3 different pathologists evaluated 100 appendectomy specimens and found that the results were discrepant in 27 cases [16]. However, 3 pathologists expressed a consistent opinion that mucosal neutrophil accumulation necessarily develops in all cases of appendicitis [16].

Otake et al. examined appendiceal tissue samples of pediatric patients who were operated on for appendicitis and claimed that the presence of inflammatory infiltration and/or fibrosis was a sufficient criterion for appendicitis [17]. We did not detect fibrosis in the tissue samples of the patients in our study.

Tayfur et al. drew attention to the detection of parasites on histopathological examination of the tissue specimens of patients operated on for clinical appendicitis [18]. In their study, they detected parasites in 1.3% of specimens. We did not detect parasites in the appendix tissues in our study.

Yılmaz et al. found in their study, consisting of 1621 adult patients, that inflammation in 8.3% of the appendix tissues was accompanied by some other pathologic findings such as parasite infection, fibrosis, tumors, and mucocele [19].

Akbulut et al. examined the appendectomy material of 5262 adult patients, in their study they found unusual appendicitis in only 52 (1%) patients [20]. We did not detect any unusual appendicitis cases in our study in pediatric patients.

Dasso et al. examined the histological structure of human and rabbit normal appendix tissue in their study, and they claimed that the presence of T lymphocytes in this tissue was natural, especially since this tissue is a primary lymphoid organ [21].

Sucic et al examined the appendix tissue of pediatric patients immunohistochemically and found that regulatory T lymphocytes were increased in the dome part [22]. Cianni et al. examined the histological characteristics of the appendix tissue in 200 cases in their study and found that there was predominantly lymphocyte infiltration in the subserosa and muscularis propria layers in 80 cases [8]. They thought these findings were due to the late admission of cases [8]. In our study, we took the tissue sample from the most dilated part (if dilation was not present from the part close to the dome) and the density of lymphocytes was especially evident in the mucosal layer of the Covid-19 group.

Limitations

This study has certain limitations. First, the numbers of patients in the groups were not equal, although there were no statistically significant differences in terms of age and gender. Second, not every region of the appendix tissue was included in the study; only a section of the largest diameter area was included.

Conclusion

Histopathological examination of appendix tissue in pediatric

patients operated on for appendicitis is important in determining the negative appendectomy rate. Neutrophil accumulation in the mucosal layer and muscularis propria layer in appendix tissue together with other inflammation findings are important in the diagnosis of appendicitis. In patients with Covid-19 infection, appendicitis may occur, in which case, severe accumulation of lymphocytes appears in the mucosa layer in addition.

Conflict of interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
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Ethical approval
Ethical approval was obtained from Inonu University Faculty of Medicine Clinical Research Ethics Committee in Malatya, Turkey (2020/84).

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