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Enterobius vermicularis: A cause or an incidental finding in pediatric appendicitis?

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Abstract

Objectives: This study aimed to investigate the incidence of *Enterobius vermicularis (E. vermicularis)* in appendectomy specimens and its contribution to the pathogenesis of appendicitis.

Patients and methods: The files of appendectomy specimens from patients who had *E. vermicularis* between June 2016 and June 2022 were reviewed retrospectively. The samples of patients whose appendectomy specimens showed *E. vermicularis* were analyzed in three groups according to the results of histopathological evaluation: reactive lymphoid hyperplasia, acute appendicitis, and perforated appendicitis.

Results: The files of 1,334 patients were examined, and *E. vermicularis* was found histopathological in 24 (1.8%) patients (15 males, 9 females; mean age: 11.2±2.9 years; range, 7 to 17 years). Histopathological examination of appendectomy specimens revealed reactive lymphoid hyperplasia in 15, acute appendicitis in six, and perforated appendicitis in three. Only neutrophil counts were significantly different in patients with reactive lymphoid hyperplasia and acute appendicitis ($p<0.05$).

Conclusion: The high rate of histopathological reactive lymph nodes in appendectomy specimens with *E. vermicularis* suggests that this parasite is found incidentally in the appendix. Differentiating enterobiasis from true appendicitis may prevent unnecessary appendectomies.

Keywords: Appendicitis, children, enterobiasis, *enterobius vermicularis*, histopathology.

Appendicitis is the most common surgical emergency in children. Appendicitis develops as a result of obstruction of the appendix vermiformis lumen, most commonly due to fecaliths and lymphoid hyperplasia and less frequently owing to intestinal parasite infections and tumors.[1]

The most common parasites encountered in appendectomy specimens are Enterobius, Schistosoma, Taenia, and Ascaris.[2,3] Occlusion of the appendix lumen due to the presence of parasite eggs, cysts, and trophozoites may cause right lower quadrant pain.[4,5]

Enterobius vermicularis (E. vermicularis), also known as pinworm, affects more than 200 million people around the globe and is more common in children than in adults.[6] *Enterobius vermicularis* is transmitted by the fecal-oral route and settles in the gastrointestinal tract of the human host.

The role of *E. vermicularis* in the etiology of acute appendicitis is controversial; some authors advocate that the presence of *E. vermicularis* in the appendix may clinically imitate acute appendicitis, but it is most likely incidental.[7] A careful histopathological examination may reveal helminths and their eggs in appendectomy specimens.[8] In previous systemic reviews and meta-analyses, the prevalence of *E. vermicularis* in acute appendicitis samples was 4% (95% confidence interval 2-6).[9]In this study, we

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aimed to investigate the incidence of *E. vermicularis* in appendectomy specimens and its role in the pathogenesis of appendicitis.

PATIENTS AND METHODS

The files of the patients who underwent appendectomy at the Şanlıurfa Training and Research Hospital and Mehmet Akif İnan Training and Research Hospital, Department of Pediatric Surgery between June 2016 and June 2022 were reviewed retrospectively. Patients whose histopathological evaluation revealed *E. vermicularis* were included in the study. Patients who underwent incidental appendectomy were excluded from the study. The white blood cell (WBC), neutrophil, lymphocyte, and eosinophil counts, C-reactive protein (CRP) values, and histopathological evaluation results of the patients were compared. The samples of patients whose appendectomy specimens showed *E. vermicularis* were analyzed in three groups according to the results of histopathological evaluation: reactive lymphoid hyperplasia, acute appendicitis, and perforated appendicitis (Figure 1). Albendazole treatment was started in patients with *E. vermicularis* according to the outcome of pathology.

Statistical analysis

Statistical analysis was performed using IBM SPSS version 23.0 software (IBM Corp. Armonk, NY, USA). Descriptive analysis was expressed as mean ± standard deviation (SD). Since the sample size was small, the Shapiro-Wilk test was used to evaluate the normal distribution. One-way analysis of variance and Student's t-test were used for comparisons between groups. A p-value <0.05 was considered statistically significant.

RESULTS

This study group examined 1,334 patients who underwent surgery with a clinical diagnosis of acute appendicitis, and *E. vermicularis* was histopathologically detected in the appendectomy specimens in 24 (1.8%) patients (15 males, 9 females; mean age: 11.2±2.9 years; range, 7 to 17 years). There was a significant difference between the ages of the patients and their pathological diagnoses ($p<0.05$).

Histopathological examination of appendectomy specimens revealed reactive lymphoid hyperplasia in 15 (62.5%), acute appendicitis in six (25%), and perforated appendicitis in three (12.5%). The histopathological results and demographic characteristics of the patients are shown in Table 1. However, histopathologic examination of appendectomy specimens of children not infected with *E. vermicularis* revealed reactive lymphoid hyperplasia in 101 (7.7%), acute appendicitis in 976 (74.5%), and perforated appendicitis in 233 (17.8%).

In the complete blood count parameters of the patients, the WBC value was $8.70\pm3.21\times10^3/\mu L$ and within normal limits in patients with reactive lymphoid hyperplasia, $12.74\pm4.8\times10^3/\mu L$ in patients with acute appendicitis, and $24.87\pm0.30\times10^3/\mu L$ in patients with perforated appendicitis. While there was no significant difference between patients with reactive lymphoid hyperplasia and patients with acute appendicitis, WBC was significantly higher in patients with perforated appendicitis ($p<0.05$).

The neutrophil level was $4.70\pm1.40\times10^3/\mu L$ in patients with reactive lymphoid hyperplasia, $9.88\pm1.38\times10^3/\mu L$ in patients with acute appendicitis, and $21.74\pm0.36\times10^3/\mu L$ in patients with perforated appendicitis. Neutrophil values were significantly different between all three groups ($p<0.001$).

When lymphocyte values were compared, they were found to be $3.07\pm0.06\times10^3/\mu L$ in patients with reactive lymphoid hyperplasia, $2.05\pm1.14\times10^3/\mu L$ in patients with acute appendicitis, and $0.54\pm0.01\times10^3/\mu L$ in patients with perforated appendicitis. There was a significant difference between the groups ($p<0.05$).

The eosinophil values of the patients were $0.18\pm0.01\times10^3/\mu L$ in patients with reactive lymphoid hyperplasia, $0.24\pm0.18\times10^3/\mu L$ in patients with acute appendicitis, and $0.01\pm0.0\times10^3/\mu L$ in patients with perforated appendicitis. There was no significant difference between the groups ($p>0.05$), but when we compared the groups among themselves, there was no significant difference between patients with reactive lymphoid hyperplasia and patients with acute appendicitis, while it was found to be significantly lower in patients with perforated appendicitis compared to the previous two groups ($p<0.05$).

When CRP values were compared, they were 0.51±0.42 mg/dL in patients with reactive lymphoid hyperplasia, 1.15±1.22 mg/dL in patients with acute appendicitis, and 6.06±0.06 mg/dL in patients with perforated appendicitis. There was an exceedingly

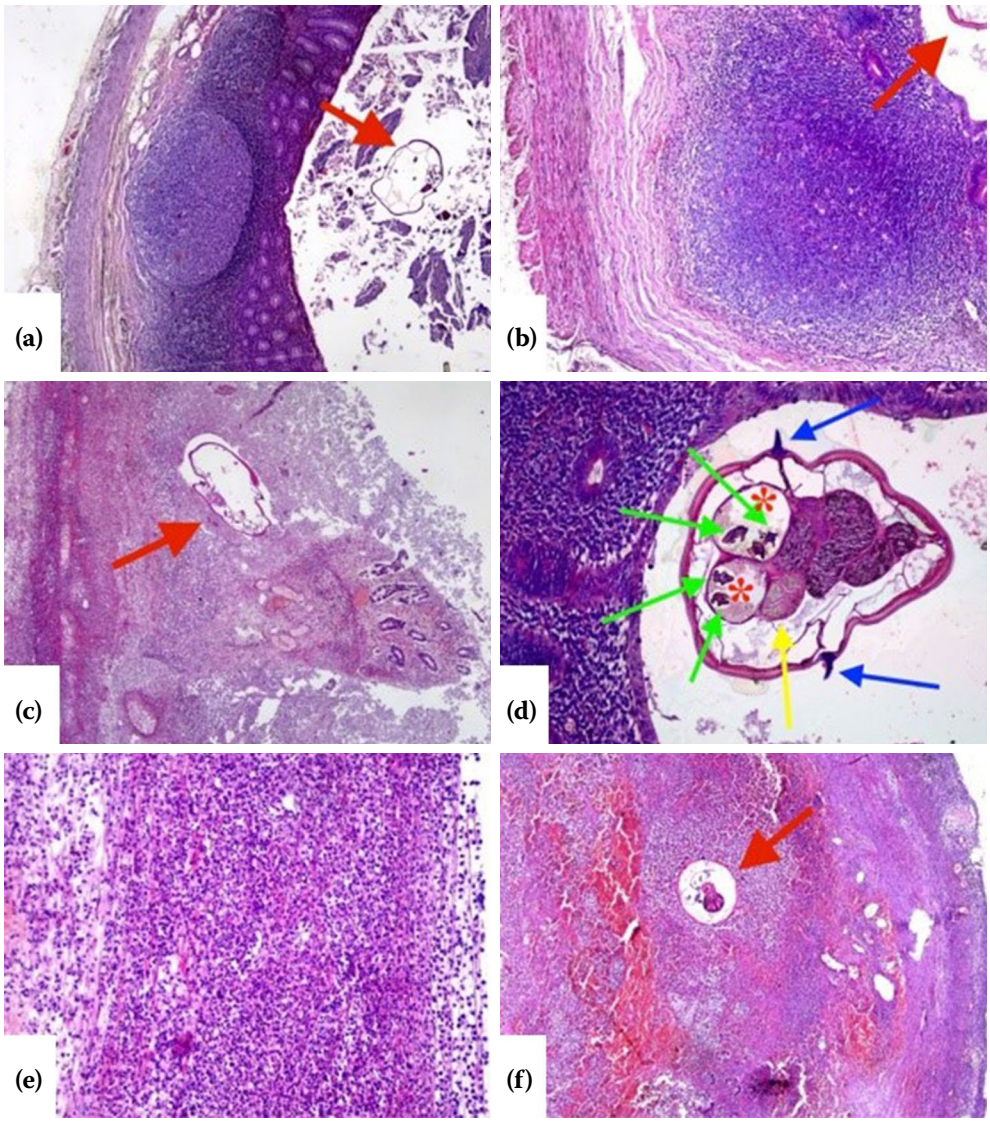

Figure 1. *Enterobius vermicularis* infestation in the appendix. **(a, b)** *Enterobius vermicularis* (red arrow) detected in the lumen of the appendix showing reactive lymphoid hyperplasia (H&E, ×40 and H&E, ×100, respectively). **(c)** In a case of phlegmonous appendicitis characterized by dense neutrophilic infiltration throughout the whole wall, *E. vermicularis* (red arrow) was observed in the submucosa of the appendix (H&E, ×40). **(d)** High-power images of cross sections of *E. vermicularis* in a female adult with the presence of alae (blue arrow), intestine (yellow arrow), and eggs (green arrow) containing ovaries (red star; H&E, ×200). **(e)** Gangrenous appendicitis characterized by intense neutrophilic infiltration and necrotic destruction in all wall layers (H&E, ×200). **(f)** *Enterobius vermicularis* (red arrow) invading the appendix wall in a case of gangrenous appendicitis (H&E, ×40).

significant difference between the groups ($p<0.001$). When we compared the groups themselves, there was no significant difference between patients with reactive lymphoid hyperplasia and patients with acute appendicitis ($p<0.05$), but it was found to be significantly higher in patients with perforated appendicitis than in the previous two groups ($p<0.001$).

All patients with *E. vermicularis* detected in appendectomy specimens were treated with 200 mg albendazole twice daily at one-week intervals.

TABLE 1
Demographic and laboratory characteristics of the patients

	Reactive lymphoid hyperplasia		Acute appendicitis		Perforated appendicitis		
	n	Mean±SD	n	Mean±SD	n	Mean±SD	*p*
Age (year)		12.3±3.1		9±1.4		10±1	0.044
Sex Male Female	 9 6		 3 3		 3 0		0.357
White blood cell (10^3/μL)		8.70±3.21		12.74±4.8		24.87±0.30*	<0.05
Neutrophil (10^3/μL)		4.70±1.40		9.88±1.38		21.74±0.36**	<0.001
Lymphocyte (10^3/μL)		3.07±0.06		2.05±1.14		0.54±0.01*	<0.05
Eosinophil (10^3/μL)		0.18±0.01		0.24±0.18		0.01±0.0*	<0.05
C-reactive protein (mg/dL)		0.51±0.42		1.15±1.22		6.06±0.06†,‡	<0.001

* p<0.05 with respect to reactive lymphoid hyperplasia and acute appendicitis groups; ** p<0.001 with respect to reactive lymphoid hyperplasia and acute appendicitis groups; † p<0.001 with respect to reactive lymphoid hyperplasia group; ‡p<0.05 with respect to acute appendicitis group.

An appointment in the first week was scheduled for all the patients in the pediatric surgery outpatient clinic setting after the appendectomy, and in case of any complaints that would arise afterward, they were recommended to present to the emergency service anytime. Thus far, a late complication was observed in only one patient who was operated on for perforated appendicitis, in which an intra-abdominal abscess was detected in the third week after the operation, and it was treated with percutaneous drainage with appropriate antibiotic therapy. *Escherichia coli* was found in the abscess culture, and no *E. vermicularis* was detected by direct microscopy.

DISCUSSION

Enterobius vermicularis is an endemic disease encountered in developing countries, particularly in rural areas.[10] It is one of the most common helminthic infections in humans; approximately half of the children aged between five and 10 years of age are affected, and 4% of these children have appendix infestation.[11] In this study, 62.5% of the patients were younger than 10 years old.

In a review study by Taghipour et al.,[9] the frequency of *E. vermicularis* in appendectomy specimens was found to be in the range of 2 to 8%. In several studies involving pediatric patient groups, the rate of *E. vermicularis* was reported to be 1.07 to 7%.[12-15] In this study, we found a rate of 1.8%, similar to the literature. In addition to the articles stating that *E. vermicularis* is equally common in both sexes, there are also studies stating that it is more common in females.[16,17] In this study, it was found 1.6 times more frequently in males, akin to the study of Yıldız et al.[14] This is because the city where the study was conducted is in a rural area, and male children are more involved in life.

The presence of parasites in the appendix lumen may cause various pathological conditions, including lymphoid hyperplasia mimicking appendicitis.[17,18] Previous studies have described the phenomenon of "appendix colic," in which physical obstruction of the appendix lumen by *E. vermicularis* causes symptoms and signs similar to those in acute appendicitis.[13]

In recent years, lymphoid follicles have been accepted as a part of functional appendix histology due to their important role in the intestinal immune system.[19] It was assumed that *E. vermicularis* instigated appendicitis by blocking the lumen, although only 23 to 71% of the pathology samples showed inflammation histologically.[11] Sousa et al.[12] concluded that *E. vermicularis* causes neutrophils to accumulate in the submucosa and muscularis mucosa, possibly leading to pain symptoms and clinical suspicion of appendicitis. Additionally, they detected the presence of inflammation in 64.8% of pathology samples; however, in our series, the rate of inflammation (acute and perforated appendicitis) detected in the pathology samples with *E. vermicularis* was only 37.5%. Again, in our study, patients with

reactive lymphoid hyperplasia had normal WBC, neutrophil count, and CRP values, which are common inflammation markers. This suggests that inflammation in appendectomy specimens is due to secondary causes, such as fecalith and bacteria, rather than the presence of *E. vermicularis* invading the appendix lumen. The perforation rate of 12.5% that we found in our patients was similar to that of Alemayehu et al.[20]

If *E. vermicularis* is detected during appendectomy or in the examination of pathology specimens, anthelmintic treatment should promptly be initiated.[7] It is important to diagnose and treat this clinical entity, particularly after perforated appendicitis, as there is an elevated risk of *E. vermicularis* contamination of the abdominal cavity.[12] In this study, *E. vermicularis* was not detected in the direct microscopy of the abscess fluid obtained from the percutaneous drainage fluid of our patient, who developed intra-abdominal abscess three weeks after an appendicitis perforation. This leads us to believe that abscess formation is a bacterial infection secondary to a perforation rather than an *E. vermicularis* infestation.

Common medical treatment modalities for *E. vermicularis* are mebendazole, albendazole (200 mg doses, a single dose one week apart), and pyrantel pamoate (10 mg/kg single doses two weeks apart). These are safe and effective drugs with 90 to 100% cure rates.[21] As suggested in the literature, we followed the same protocol and gave albendazole 200 mg in single doses repeated after one week to our patients and did not see any complications related to *E. vermicularis* in the postoperative period.

The study has a few limitations, such as being retrospective in design, having a small sample size, and having a sample evaluation of pathology specimens by different pathologists. Increasing the number of samples, working with a single pathologist, and performing long-term follow-up of patients may provide us with more detailed information in future studies.

In conclusion, the high rate of reactive lymphoid hyperplasia in appendectomy specimens with *E. vermicularis* makes us assume that this parasite is found in the appendix by chance rather than being a solid factor in the etiology of appendicitis. Since *E. vermicularis* can be treated with oral anthelmintic drugs, distinguishing enterobiasis from true acute appendicitis in patients presenting with right lower quadrant pain may prevent unnecessary appendectomies. Furthermore, nonoperative treatment has recently come to the fore in the treatment of acute appendicitis. With an early diagnosis of *E. vermicularis* in such patients, the addition of anthelmintic drugs to medical treatment may increase the success of management.

Ethics Committee Approval: The study protocol was approved by the Harran University Clinical Research Ethics Committee (date: 03.10.2022, no: HRÜ/22.19.16). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from the parents and/or legal guardians of the patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Study idea/concept: G.G., A.İ.A., O.H.K.; Design and writing the article, references: G.G., O.H.K.; Data collection and/or processing/materials: G.G., A.İ.A., C.Y.; Literature review: G.G.; Critical review: G.G., O.H.K.; Control/ supervision: O.H.K.

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