

Rare Parasitic Causes of Acute Appendicitis: Enterobius Vermicularis in Focus

Akut Apandisitinin Nadir Paraziter Nedenleri: Enterobius Vermicularis Üzerine Bir İnceleme

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ABSTRACT

Background: Acute appendicitis is one of the most common causes of emergency surgery. Usually, it occurs due to luminal obstruction. However, enterobius vermicularis (EV) infections can also contribute to appendiceal pathology. EV may mimic symptoms of appendicitis, complicating diagnosis. Anthelmintic therapy emerges as a potential alternative to surgery in cases without inflammation.

Materials and Methods: Appendectomy cases from May 2020 to April 2024 were retrospectively analyzed. EV-positive patients were compared with age- and gender-matched controls. Parameters such as white blood cell count (WBC), appendix diameter, and imaging findings were examined using blood tests and computed tomography (CT) imaging.

Results: Among 2,599 cases, 13 were EV-positive (0.5%). WBC levels ($10.6 \pm 1.8 \times 10^3/\text{mm}^3$) and appendix diameter (10.1 ± 1.0 mm) were significantly lower in the EV group compared to controls. No significant differences were observed in neutrophil count, C-reactive protein levels, or signs of inflammation. The appendix diameter on CT has shown high sensitivity in excluding EV cases, but its specificity is low.

Conclusion: EV infestation often presents symptoms like appendicitis without causing histological inflammation, potentially leading to unnecessary surgeries. Anthelmintic therapy is a promising alternative. Retrospective analysis limits this study and underlines the need for prospective research, which should include symptoms like pruritus ani, to enhance diagnostic accuracy. Differentiating EV-related appendiceal symptoms from acute appendicitis is crucial to avoid unnecessary surgeries. Developing diagnostic tools and clinical algorithms could allow for non-operative management with targeted anthelmintic therapy, providing a promising alternative for EV-positive cases.

Keywords: Acute appendicitis, enterobius vermicularis, appendectomy

ÖZ

Amaç: Akut apandisit, cerrahi müdahale gerektiren yaygın bir acil durumdur ve genellikle lümen obstrüksiyonu ile ilişkilendirilir. Ancak enterobius vermicularis (EV) enfeksiyonları, daha az rastlanan bir neden olarak apendiks patolojilerinde önemli bir rol oynayabilir. EV, apandisit belirtilerini taklit edebilir ve tanıda zorluklara yol açabilir. Parazitin tedavi edilmesi, enflamasyon olmadığında cerrahiye alternatif bir yaklaşım sunabilir.

Gereç ve Yöntemler: Mayıs 2020-Nisan 2024 arasında yapılan apendektomi olguları retrospektif olarak incelenmiştir. EV pozitif hastalar ve benzer yaş-cinsiyet özelliklerine sahip kontrol grubu karşılaştırılmıştır. Kan testleri ve bilgisayarlı tomografi görüntüleme ile beyaz kan hücresi (WBC), apendiks çapı gibi parametreler analiz edilmiştir.



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Bulgular: Toplam 2.599 olgudan 13'ü EV pozitif bulunmuştur (%0,5). EV grubunda WBC düzeyi ($10,6 \pm 1,8 \times 10^3/\text{mm}^3$) ve apandiks çapı ($10,1 \pm 1,0$ mm), kontrol grubuna göre anlamlı derecede düşüktür. Ancak, nötrofil, C-reaktif protein ve enflamasyon gibi diğer parametrelerde fark saptanmamıştır. BT'deki apandiks çapı, EV olgularını dışlamakta yüksek hassasiyet göstermiştir ancak özgüllüğü düşüktür.

Sonuç: EV enfestasyonları, apandisit belirtilerini taklit eder ve sıklıkla enflamasyon görülmez. Bu durum, gereksiz cerrahi müdahalelere yol açabilir. Antelmintik tedavi, cerrahiye alternatif bir yaklaşım olarak değerlendirilebilir. Ancak, mevcut çalışma retrospektif olduğundan, ileriye yönelik çalışmalarda pruritus ani gibi semptomların dahil edilmesi önerilmektedir. EV ile ilişkili apandiks belirtilerini akut apandisitten ayırmak, gereksiz cerrahiden kaçınmak için önemlidir. Uygun tanısal araçlar ve klinik algoritmalar geliştirildiğinde, birçok hasta cerrahiden kurtarılabilir. Non-operatif izlem ve hedefe yönelik antelmintik tedavi, umut vadeden bir alternatif olarak dikkat çekmektedir.

Anahtar Kelimeler: Akut apandisit, enterobius vermicularis, appendektomi

Introduction

Acute appendicitis remains a predominant cause of surgical emergencies globally, with individuals facing a 7% to 8% lifetime risk (1). Traditionally, the etiology has been attributed to luminal obstruction resulting from fecalith, lymphoid hyperplasia, or neoplasms, which leads to increased intraluminal pressure, bacterial proliferation, and subsequent inflammation (2). However, parasitic infections, particularly those caused by enterobius vermicularis (EV), represent a less frequent but clinically significant contributor to appendiceal pathology.

EV, commonly referred to as pinworm, is the most widespread human helminth infection worldwide, predominantly affecting children and populations of lower socioeconomic status (3,4). Although typically inhabiting the cecum and proximal colon, EV can migrate to the appendix, potentially inducing appendiceal colic or mimicking symptoms of acute appendicitis (5,6). It is noteworthy that multiple studies have indicated a correlation between EV infestation and negative appendectomies, as histological evidence of acute inflammation may be lacking in these instances (7-9).

Cases associated with EV may exhibit clinical presentations indistinguishable from acute appendicitis. This similarity in symptomatology presents diagnostic challenges and may result in unnecessary surgical procedures. Elevated eosinophil levels have been observed in patients undergoing appendectomy due to EV-related complications (10). While preoperative imaging techniques such as ultrasound or computed tomography may provide valuable insights in certain cases, the definitive diagnosis is typically established through pathological examination (11).

As conservative management of uncomplicated appendicitis gains traction, EV-related appendiceal inflammation may similarly benefit from anti-helminthic

therapy (12). Consequently, the ability to establish a preoperative diagnosis of EV-related acute appendicitis-like presentation is of paramount importance.

Our retrospective investigation sought to enhance preoperative diagnostic accuracy by analyzing imaging and laboratory findings in cases of EV-related appendicitis. The Neutrophil to lymphocyte ratio (NLR) and systemic immune-inflammatory (SII) Index were employed to assess the inflammatory response in EV-related appendicitis compared to conventional acute appendicitis. We propose that EV-associated appendicitis may be amenable to medical management, contingent upon accurate preoperative evaluation that considers EV as a potential etiological factor.

Materials and Methods

Patients who had undergone appendectomy in our clinic between May 2020 and April 2024 were retrospectively reviewed. Patients older than 18 years of age and those who had undergone appendectomy for acute abdomen or had a prediagnosis of acute appendicitis were included in the study. Patients under 18 years of age and those who underwent appendectomy for unrelated conditions were excluded.

Demographic data and pathology results of the patients were analyzed. For each patient whose pathology slides indicated EV, four control group patients were selected who met similar age and gender criteria. The matching was conducted using the propensity score matching method. Neutrophil (Neu), lymphocyte (Lym), NLR, platelet (Plt), platelet-to-lymphocyte ratio (PLR), C-reactive protein (CRP), and white blood cell (WBC) levels, as well as appendix diameter and periappendicular inflammation, were examined in preoperative blood tests and computed tomography images of the EV positive and control groups. The widest diameter of the appendix was measured on computed tomography scans. Periappendicular inflammation was recorded categorically.

Approval for this study was obtained from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Local Ethics Committee (approval number: 28, date: 06.11.2024).

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics (version 24) and R software (version 4.3.2). The Shapiro-Wilk test was applied to assess the normality of continuous variables. For non-normally distributed data, the Mann-Whitney U test was employed, while the Pearson chi-square test was used to analyze categorical variables. Matched logistic regression analysis was applied to determine the factors predicting the EV positive group. In this analysis, the effect of each parameter on the EV positive group was reported using odds ratios (ORs) and 95% confidence intervals (CIs). The accuracy of the model was measured by concordance. The predictive power of the model was evaluated by receiver operating characteristic (ROC) analysis. Cut-off points for appendix diameter and WBC were determined, and sensitivity and specificity of both variables were calculated. Parameters with an area under the curve (AUC) value greater than 0.600 were considered significant in terms of diagnostic accuracy. The results of the analyses were presented as mean and standard deviation for quantitative data and as frequency (n) and percentage for categorical data. The statistical analyses were conducted with a significance level set at $p < 0.05$.

Results

A total of 2,599 appendectomy cases were retrospectively analyzed, and 13 EV-positive cases were identified according to pathology reports. The EV rate in our case series was determined to be 0.5%. One patient was excluded from the EV group due to missing data. For each patient with EV, four age- and sex-matched patients were selected as the control group. Sixty cases were included in the analyses in total.

WBC levels were significantly elevated in the control group compared to the EV-positive group (13.2 ± 2.1 vs. 10.6 ± 1.8 , $p = 0.039$). The control group exhibited a significantly larger appendix diameter (12.5 ± 1.3 mm) compared to the study group (10.1 ± 1.0 mm, $p = 0.009$). Whereas no significant difference was detected between the groups in terms of Neu, Lym, eosinophils, CRP, Plt, NLR, PLR, and SII. There was no statistically significant variation in eosinophil percentage between the two groups ($p = 0.853$, Table 1).

There was no significant difference between the EV-positive and EV-negative groups in the presence of periappendiceal inflammation as assessed by computed tomography (CT) imaging ($p = 0.764$).

Analysis with conditional logistic regression was conducted to evaluate the predictive power of WBC and appendix diameter for EV-positive cases. The OR for WBC was 0.930 (95% CI: 0.740-1.168) and was not statistically significant ($p = 0.531$). Similarly, the OR for appendix diameter was 0.803 (95% CI: 0.592-1.090), and this association was also not statistically significant ($p = 0.160$). The overall predictive accuracy of the model was assessed using the Concordance Index, and was calculated as 0.604 (standard error: 0.111), indicating limited predictive power (Table 2).

ROC analysis was performed to evaluate the diagnostic accuracy of WBC count and appendix diameter. The AUC value for WBC was calculated as 0.568 (95% CI: 0.357-0.779), with an optimal cut-off value determined to be 12,785, providing 58.3% sensitivity and 64.6% specificity. The AUC for appendix diameter on CT imaging was 0.632 (95% CI: 0.469-0.795), with an optimal cut-off value of 12.15 mm, which provided 100% sensitivity and 29.2% specificity. Although appendix diameter demonstrated high sensitivity in detecting positive conditions, its low specificity suggests a potential for high false-positive rates (Table 3, Figures 1, 2).

Table 1. Comparison of laboratory and clinical data between study and control groups

Parameter	EV + group (mean ± SD)	Control group (mean ± SD)	p-value
WBC ($\times 10^3/\text{mm}^3$)	11.25±3,306	13.83±3.88	0.039*
Neutrophil ($\times 10^3/\text{mm}^3$)	6.60±4.79	7.35±4.89	0.605**
Lymphocyte ($\times 10^3/\text{mm}^3$)	1.75±0.866	1.94±0.81	0.622**
CRP (mg/dL)	46.50±51,856	28,71±49,279	0.168**
Appendix diameter (mm)	8.08±1,730	10.10±2,425	0.009*
Platelet ($\times 10^3/\text{mm}^3$)	259.58±74,650	258.08±51,820	0.935*
PLR	193.85±149.99	163.20±78.92	0.712**
SII	1577.17±930.08	1868.08±1352.65	0.606**

*: Pearson chi-square test was used for categorical variables, **: Mann-Whitney U test or t-test was used for continuous variables. EV: Enterobius vermicularis, SD: Standard deviation, WBC: White blood cell count, CRP: C-reactive protein, PLR: Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammatory

Table 2. Conditional logistic regression analysis of WBC and appendix diameter

Parameter	Coefficient (β)	OR (95% CI)	z-value	p-value
WBC ($\times 10^3/\mu\text{L}$)	-0.073	0.930 (0.740-1.168)	-6.26	0.531
Appendix diameter (mm)	-0.219	0.803 (0.592-1.090)	-1.405	0.160

Model statistics
 Concordance Index (C-index): 0.604 (S.E.: 0.111)
 Likelihood ratio test: $\chi^2=2.79$, $p=0.2$
 Wald test: $\chi^2=2.29$, $p=0.3$
 Score (log-rank) test: $\chi^2=2.5$, $p=0.3$

WBC: White blood cell count, OR: Odds ratio, CI: Confidence interval, S.E.: Standard error

Table 3. Receiver operating characteristic analysis of WBC and appendix diameter for diagnostic accuracy

Parameter	Optimal cut-off	Sensitivity, (%)	Specificity, (%)	AUC	95% CI for AUC	Youden index
WBC ($\times 10^3/\mu\text{L}$)	12,785	58.3	64.6	0.568	0.357-0.779	0.229
Appendix diameter (mm)	12.15	100	29.2	0.632	0.469-0.795	1.292

Sensitivity: True positive rate (%), Specificity: True negative rate (%), AUC: Area under the curve, CI: Confidence interval

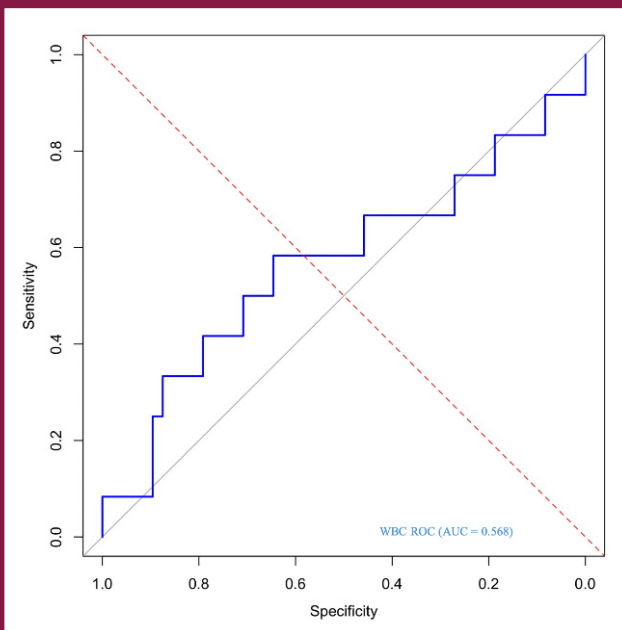


Figure 1. ROC curve for WBC
 ROC: Receiver operating characteristic, WBC: White blood cell count

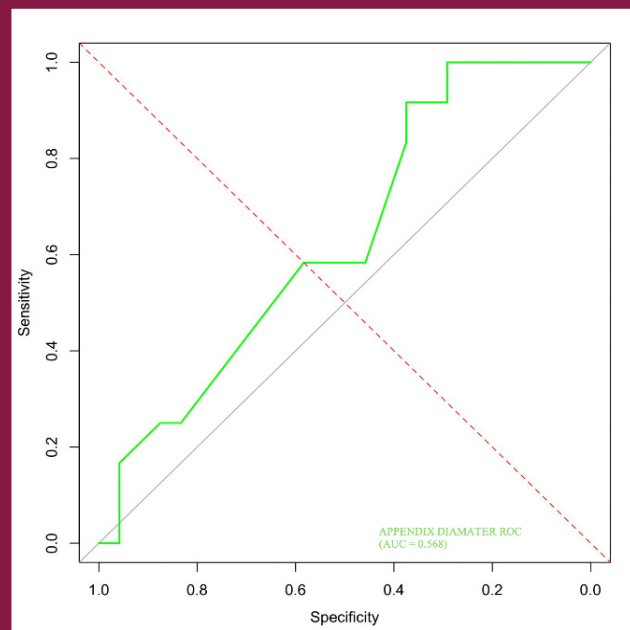


Figure 2. ROC curve for appendix diameter
 ROC: Receiver operating characteristic

Discussion

This study elucidates the clinical and diagnostic challenges associated with EV-related appendiceal symptoms, particularly in differentiating them from acute appendicitis requiring surgical intervention (13,14). Among the 2,599 appendectomy cases reviewed, EV infestation was identified in 13 patients, constituting a small but clinically significant subset. These findings raise important

considerations regarding the necessity of surgery in these cases and the potential for targeted non-operative management.

In the literature, EV was found in appendectomy specimens with a rate ranging between 2 to 9% (3). Its frequency increases in young patients and low socioeconomic regions. In our study, the rate of patients found to be EV positive was 0.5%. These rates also suggest which patients, targeted for our study, might benefit from potential medical treatments.

There are reports in the literature that eosinophil values may be higher in patients who underwent EV-related appendectomy (5). Nevertheless, no significant difference was found between the groups in terms of eosinophil values in our study.

In accordance with the literature, we found that WBC values were higher in the acute appendicitis control group (15,16). Although the mean CRP values were lower in EV cases mimicking acute appendicitis compared to other cases, no significant difference was found. Moreover, no difference significantly was observed in NLR and SII between the groups.

There are reports that preoperative imaging of patients who underwent EV-related appendectomy showed no or fewer signs of classical acute appendicitis inflammation (11,15). In the CT images analyzed, the appendix diameter in the EV group was significantly smaller than that in the control group. This finding supports the literature and suggests that inflammation is less severe in comparison to previous reports. However, while we hypothesized that the findings of periappendicular inflammation on CT images would be less pronounced in the EV group, we could not significantly detect a difference between the two groups.

The potential for non-operative management in EV-related cases is an emerging area of interest. The use of anthelmintic therapy (e.g., albendazole or mebendazole) has been shown to resolve symptoms effectively in similar cases, suggesting that surgery may not be necessary for all patients with EV infestation (7). In our cohort, the absence of gangrenous or perforated appendices in EV-positive patients further supports the feasibility of a conservative approach.

By incorporating clinical indicators such as pruritus ani, eosinophilia, and imaging findings, a diagnostic algorithm could be developed to identify patients who may benefit from medical therapy. Such a framework could reduce unnecessary surgeries, particularly in pediatric populations where EV prevalence is higher (10). As our study was retrospective, complaints such as pruritus ani were not recorded. It should be analyzed as an additional symptom in prospective studies.

Our findings are consistent with Budd and Armstrong (2), who observed that EV is rarely associated with histological acute appendicitis and is more frequently found in appendices removed for non-specific abdominal pain. Similarly, Dahlstrom and Macarthur (1) reported that most EV-related cases present with clinical features of appendicitis but lack histological inflammation, supporting the role of EV in mimicking appendicitis rather than causing it.

Study Limitations

This study has a few limitations. The retrospective nature of the investigation imposed certain constraints. Furthermore, the detection of fewer EV-related appendicitis cases than anticipated could be considered a limitation of the study. Considering our results, such as low WBC and smaller appendix diameter, in patients with an appendicitis-like clinical presentation, the possibility of EV should be considered. Prospective studies incorporating different biomarkers or findings in addition to our research are necessary. If new diagnostic methods are developed and diagnosis is facilitated, non-operative follow-up and medical treatment, particularly anti-helminthic therapy, may be recommended for this patient group. Consequently, the risk associated with surgery could be potentially mitigated, and the burden on the healthcare system potentially reduced.

Conclusion

The objective of our study was to develop parameters to aid in the diagnosis of patients with EV-associated appendicitis, who present with clinical features similar to acute appendicitis, and to provide these patients with an opportunity for medical treatment. EV-associated appendicitis should be considered in patients with low WBC values on preoperative evaluation and small appendix diameter on imaging.

Ethics

Ethics Committee Approval: This study was ethically approved by the Local Ethics Committee of the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital (approval number: 28, date: 06.11.2024).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Y.Y.K., Concept: Y.Y.K., Design: Y.Y.K., M.Ş.K., Data Collection or Processing: Y.Y.K., M.Ş.K., Analysis or Interpretation: F.T.K., Literature Search: Y.Y.K., F.B.S.K., Writing: Y.Y.K., F.T.K., F.B.S.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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