Incidence of *Enterobius vermicularis* in acute appendicitis: A systematic review and meta-analysis

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**ABSTRACT**

**Objective:** To evaluate the incidence of *Enterobius vermicularis* (*E. vermicularis*) in appendectomies in Iran from 1993 to 2018.

**Methods:** Data were systematically collected on the electronic databases including PubMed, GoogleScholar, ScienceDirect, Scopus, Web of Science, Magiran, IranDoc (Bareket), IranMedex, and Scientific Information Database in English or Persian. Six articles including 29694 cases of appendicitis with 258 positive cases of infection with *E. vermicularis* were eligible to enter into this systematic review and meta-analysis.

**Results:** The overall prevalence of *E. vermicularis* in appendicitis in Iran was 1% (95% CI: 0.00-0.02) with the highest rate of 3% (95% CI: 0.02-0.03) and lowest rate of 0% (95% CI: 0.00-0.01).

**Conclusions:** Prevalence of *E. vermicularis* infection in appendicitis in Iran is low and has no statistically significant correlation with age and gender.

**KEYWORDS:** *Enterobius vermicularis; Appendicitis; Iran; Systematic review; Meta-analysis*

**1. Introduction**

Acute appendicitis, the most common reason for emergency abdominal surgery, is usually caused by increased pressure within lumen following obstruction. The obstruction occurred by fecaloid matters, and infection consequently takes place. The most common reasons for acute appendicitis are viral infections and fecal matters while parasitic infections, tumors, and inflammatory bowel diseases rarely lead to this condition[1].

Although role of parasites in causing acute appendicitis is not clear enough, it is believed that some of them such as *Enterobius vermicularis* (*E. vermicularis*) and *Ascaris* may cause appendiceal colic due to lumen obstruction characterized as right lower quadrant pain. *E. vermicularis*, also known as *Oxyuris vermicularis* (pinworm) is the most common helminth in the world, which inhabits in cecum. In some cases, the parasite has reported from appendix but the real role of *E. vermicularis* in pathophysiology is still controversial with no histological evidence of acute inflammation[2-5]. The life cycle of *E. vermicularis* is a little different from other mentioned parasites as the worm lives in terminal ileum, caecum, vermiform appendix, and proximal parts of colon. The female worm migrates to the anal and perianal regions to lay eggs. This happens especially at night and the hatching consequently leads to itching, which results in contamination of hands, bed, clothes, and air of the room. Retro infection also occurs as a result of larval migration through anus to intestine[6]. In Iran, the prevalence of appendicitis has evaluated to be 15.3% among 2173 individuals in 2019. In a global survey, the incidence of appendicitis during 3 times estimation was 15/100000 from 1970 to 2014.

There is no exact estimation about the prevalence of *E. vermicularis* in acute appendicitis[7] and the present systematic review and meta-analysis aimed to evaluate this subject.


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2. Materials and methods

2.1. Data collection

A comprehensive bibliographic search was performed according to following topics:
(1) Type of articles, type of studies, epidemiological parameters of interest. Complete articles including descriptive studies (designated as cross-sectional) in appendicitis caused by *E. vermicularis* parasite were concerned. Also, the prevalence of *E. vermicularis* in acute appendicitis and main factors such as age and gender were considered;
(2) Search strategy: This review was conducted according to the preferred reporting items for systematic reviews and meta-analyses guidelines by using terms: “appendicitis”, “acute”, “*Oxyuris vermicularis*”, “*Enterobius*”, “enterobiosis”, “*Enterobius vermicularis*”, “pinworm”, “Iran”, “prevalence” alone or in combination, both in Persian and English;
(3) Databases: We searched both English and Persian databases including PubMed, Google Scholar, ScienceDirect, Scopus, Web of Science, Cochrane Library, Magiran, Irandoc, IranMedex, and Scientific Information Database and chose relevant studies from 1993 to 2018.

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) Retrospective randomized study format; (2) Studies reporting acute appendicitis with pathologic examination revealing *E. vermicularis* as a causative agent.

Exclusion criteria: (1) Non-randomized studies; (2) Studies out of Iran; (3) Meta-analysis studies. The process is shown in Figure 1.

2.3. Data extraction and quality assessment

Two authors independently extracted data from all eligible studies, and data includes first author, country, year of publication, sex, age, the size of appendectomy, and the size of appendectomy due to *E. vermicularis*. The Jadad scale was used to evaluate the overall quality of all included articles[8]. According to the recommendation of Kjaergardet et al., low-quality studies should have a score of <2 and high-quality studies should have a score of ≥3[9].

2.4. Statistical analysis

After extracting sample size (n) and number of positive cases from each included primary study, the proportion of the number of positive cases divided to sample size assigned as the prevalence of *E. vermicularis* in appendicitis, and the standard error (SE) was calculated using the following equation:

$$SE = \sqrt{\frac{p(1-p)}{n}}$$

To evaluate the effect of each study on pooled effect size, a sensitivity analysis was performed. To assess heterogeneity, we used both the Cochran’s Q test (P<0.1 as heterogeneity) and the I² statistic (I²>50% as heterogeneity). In the event of substantial heterogeneity, a random effect model (Der Simonian and Laird

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**Figure 1.** The study flowchart.
method) otherwise a fixed-effect model (Mantel-Haenszel method) was employed to estimate the pooled prevalence. Pooled prevalence and prevalence of each study with 95% CI were estimated and displayed in a forest plot.

To explore the source of heterogeneity, meta-regression was conducted by covariates as gender (male, female), sample size, and the year of publication. Funnel plot and Eager’s test (P<0.1 considered significant) simultaneously were conducted to detect potential publication bias among studies. All statistical analysis was performed by Stata MP version 14.

2.5. Sensitivity analysis

To assess whether each of the primarily included study had a substantial influence on the pooled effect size, each study were excluded from meta-analysis and estimated pooled effect size.

2.6. Heterogeneity

Before estimating the pooled effect prevalence of *E. vermicularis* in appendicitis, we conducted a fixed effect model on all included studies. The result showed that no evidence of heterogeneity among the studies (I\(^2\)=13.8%, P=0.32). So, the results of fixed effect model presented as pooled estimate of prevalence.

3. Results

Among all databases searched from 1993 to 2018, six articles including a total of 29,694 cases of appendicitis with 258 positive cases for infection with *E. vermicularis* were eligible to enter in this systematic review and meta-analysis. The results of sensitivity analysis demonstrated all studies located in 95% CI, which indicated that we can involve all six studies in meta-analysis (Figure 2). The results of the literature searching are shown in Table 1. According to a fixed-effect model, the pooled estimate of prevalence of *E. vermicularis* in appendicitis is 1% (95% CI: 0.4%-2.3%; I\(^2\)=97.89%, P=0.00). Totally, there is no significant difference among prevalence of these six studies (z=1.79; P=0.074) (Figure 3).

Figure 4 shows the funnel plot which indicates evidence of publication bias. Also, the results of Egger’s regression test of the funnel asymmetry confirmed the asymmetric of the funnel plot (z=2.20, P=0.07).

As showed in Table 2, demographic characteristics had no effect on the prevalence of *E. vermicularis* in appendicitis. In other words, these variables were not potential sources of heterogeneity of the included studies (P>0.1). Although only six studies entered in the meta-analysis, the sample size was great enough for statistical analysis.

### Table 1. Baseline information of the included studies.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Province/city</th>
<th>Sample size</th>
<th>Positive cases</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarmast et al.</td>
<td>2005</td>
<td>Khuzestan</td>
<td>5,981</td>
<td>38</td>
<td>[10]</td>
</tr>
<tr>
<td>Ramezani et al.</td>
<td>2007</td>
<td>Kerman</td>
<td>1,253</td>
<td>9</td>
<td>[11]</td>
</tr>
<tr>
<td>Fallah et al.</td>
<td>2008</td>
<td>Tehran</td>
<td>5,981</td>
<td>38</td>
<td>[12]</td>
</tr>
<tr>
<td>Kazemzadeh et al.</td>
<td>2008</td>
<td>Esfahan</td>
<td>1,533</td>
<td>9</td>
<td>[13]</td>
</tr>
<tr>
<td>Ziaei et al.</td>
<td>2013</td>
<td>Mazandaran</td>
<td>5,048</td>
<td>144</td>
<td>[14]</td>
</tr>
<tr>
<td>Mardani et al.</td>
<td>2017</td>
<td>Qom</td>
<td>13,744</td>
<td>31</td>
<td>[15]</td>
</tr>
</tbody>
</table>
Table 2. Correlation between some characteristics and prevalence of Enterobius vermicularis in appendicitis in Iran.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coeff</th>
<th>Std.Err</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>-0.003</td>
<td>0.003</td>
<td>-0.95</td>
<td>0.517</td>
</tr>
<tr>
<td>Sample size</td>
<td>0.0002</td>
<td>0.0003</td>
<td>3.46</td>
<td>0.180</td>
</tr>
<tr>
<td>Sex</td>
<td>0.017</td>
<td>0.014</td>
<td>1.17</td>
<td>0.452</td>
</tr>
<tr>
<td>Age</td>
<td>0.0003</td>
<td>0.0004</td>
<td>0.77</td>
<td>0.884</td>
</tr>
</tbody>
</table>

4. Discussion

Although E. vermicularis has been found in many cases of acute appendicitis, the real role of pinworms in causing acute appendicitis has not been demonstrated[16]. Parasitic infections rarely cause acute appendicitis, but their presence in appendectomy specimens is a considerable point. The prevalence of infection with E. vermicularis in Iranian children has been reported to be 1.6% to 66.14% in different studies[15]. Also, the overall prevalence of appendicitis in Iranian patients with acute abdominal is 15.3% (95% CI: 13.9%-16.8%; F= 98.9%)[17]. This shows the relatively high prevalence of pinworms in the Iranian population. The incidence of appendicitis in men and women is 8.6% and 6.7%, respectively, and it increases in the second and third decades of life[15]. As a most common helminthic infection in the world, the infection can occur in people at all ages and socioeconomic levels and is estimated to affect up to 209 million people all around the world[5]. The direct oral-fecal mod is the most common route of human infection, but parasite eggs may remain alive for two or three weeks on beds and clothes, which is the easy way for spreading among family members and compact populations[18]. Human is the only natural host for E. vermicularis, and embryonated eggs measuring 30-60 μm are found in fingernails, house dust, clothing, and bed sheets. Ingestion of eggs leads to hatching of eggs in the stomach and consequently releasing larvae. These larvae migrate to the cecum and mature as adult worms. Adult gravid female worms can deposit up to 10000 eggs daily that are infective 6 h after deposition[3]. E. vermicularis is reported as the responsible parasite causing 0.2% to 41.8% of appendicitis in the world[19]. The presence of E. vermicularis in the appendix can cause abdominal pain mimicking features of acute appendicitis or appendiceal colic mostly in children with no histological evidence of acute inflammation[20-22]. Symmers was the first one who described the inflammation in ileocolic region caused by pinworm in 1919[22]. In another study during 1980 and 1987, Wiebe histologically examined 2 267 cases of appendicitis and E. vermicularis infection was identified in 4.1%. The presence of E. vermicularis in histological specimens is rare, and in our study among 29694 appendectomies, only 258 (1%) positive cases were identified as E. vermicularis by meta-analysis. In a study, Arca et al. reported that 1.4% of 1 549 appendectomies were associated with E. vermicularis infestation in the USA[3]. Zouari et al. in a study declared that fifty percent of children enrolled in their study with negative appendectomy were positive for infection with E. vermicularis while appendectomy rate was significantly higher in the infected group compared with the non-infected group. They concluded that presenting with right iliac fossa pain could be explained by E. vermicularis infection. Their research made it possible to identify features that could clinically differentiate true appendicitis from appendiceal colic caused by E. vermicularis[23,24]. The main standard diagnosis of appendicitis is physical examination, but it is not specific enough to differentiate parasitic and ordinary appendiceal pain. In some cases, a history of perianal itching should be helpful. Other surveys including cellophane test, which is conducted with pressing a cellophane tape to the perianal skin to detect attached eggs and has a low diagnostic sensitivity. Either the worms or eggs don’t passing with stool, so the stool examination would be unnecessary. Otherwise, other techniques including Alvarado score and acute inflammatory response can be helpful for establishing the diagnose but generally are not acceptable[25]. CT scan and ultrasonography seems to be beneficial for the diagnosis. The worms strongly attach to the mucosa by their head and carefully thermal dissection of the appendix will be useful to inspect the lumen. The endoscopic suction should be performed in cases that the worms are visible in the lumen. This is practical in laparoscopic operations with hazard of peritoneal contamination by worms[25]. It is clear that medication with anti-helminthics such as mebendazole is needed[23].

Infection with E. vermicularis is usually the main cause of appendiceal pain in the absence of histological inflammation. It is important to consider infection with E. vermicularis in children presenting right iliac fossa pain. Careful consideration of laboratory examinations such as eosinophilia or other symptoms like pruritis especially in children would be helpful in the prevention of unnecessary appendectomies. Medication with anti-helminthics even after appendectomy is necessary to eradicate the worms from the whole body. Prevention programs and hand hygiene should be implemented especially in kindergartens and primary schools. Our study had some limitations including publication bias. It is recommended to expand study search and enter unpublished data, data of desertation and conferences for eradicate the publication bias.

Conflict of interest statement

The authors report no conflict of interest.

Authors’ contributions

S.A.H., F.V., A.M. and A.S.H. were responsible for conception and designing the study. A.G. was responsible in data gathering, S.H.T., was responsible for data analysis. All authors participated in interpretation of the data. A.S.H. drafted the manuscript. A.M. responsible for the critical review of the paper.
References


