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Review Article

Enterobius vermicularis infection at time of appendicectomy: is it a neglected risk factor?

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ABSTRACT

Obstruction of the appendiceal orifice is well established as a potential cause of appendicitis. However, it remains debated as to if appendiceal orifice obstruction secondary to *Enterobius vermicularis* is considered a risk factor for appendicitis or appendiceal colic. *Enterobius vermicularis* maintains an increased prevalence within lower socioeconomic and human development index regions. Whilst Australia has an overall high human development index it has significant variability in health literacy and socioeconomics. The purpose of this literature review is to evaluate the relationship between *Enterobius vermicularis* and appendicitis, to review the prevalence of *Enterobius vermicularis* appendicectomies in lower human development index and socioeconomic status communities, and to review the Australian based *Enterobius vermicularis* literature available. A comprehensive review of the literature was performed to review the prevalence of *Enterobius vermicularis* at time of appendicectomy. PubMed, Scopus, and Google Scholar databases were investigated for applicable studies published until December 2023. *Enterobius vermicularis* within the appendiceal lumen may cause irritation and lymphoid hyperplasia resulting in appendiceal colic with a similar clinical presentation to that of acute appendicitis. An increased association between *Enterobius vermicularis*, low human development index, and socioeconomic status is suggested. Public health interventions reduce Enterobius prevalence. A single Australian based study from 1994 was identified. *Enterobius vermicularis* infection is a neglected risk factor for appendiceal colic. A high index of suspicion for *Enterobius vermicularis* infection should be taken for clinically stable patients with normal inflammatory biochemistry and low human development index. Further research is required to assess if there is a disparity in *Enterobius vermicularis* in relation to human development index, socioeconomic status, and remoteness within Australian communities.

Keywords: *Enterobius vermicularis*, Enterobius, Appendicectomy, Appendectomy, Appendicitis

INTRODUCTION

Acute appendicitis remains a global healthcare issue and a significant cause for emergency abdominal surgery.[1] An increase of approximately 20% in the prevalence and incidence of acute appendicitis from 1990 to 2019 has been observed.[2,3] Obstruction of the appendiceal orifice is well established as a potential cause of appendicitis. However, it remains debated as to if appendiceal orifice obstruction secondary to *Enterobius vermicularis* infection is considered a risk factor for appendicitis or appendiceal colic. *Enterobius vermicularis*, also known as pinworm or threadworm, is a contagious helminth infection. It is one of the most prevalent helminth infections globally affecting more than 200 million individuals, with a prevalence cited as up to 38% in specific endemic populations.[3-5] *Enterobius vermicularis* retains an increased prevalence within lower socioeconomic and human development index (HDI) regions.[1,4] Whilst Australia has an overall high HDI it has significant variability in health literacy and socioeconimics.[6,7]

Subsequently, a high HDI and socioeconomic status is not necessarily reflected within all Australian communities.[6,7] The purpose of this literature review is to evaluate the relationship between *Enterobius vermicularis* and appendicitis, to review the prevalence of *Enterobius vermicularis* appendicectomies in lower human development index and socioeconomic status communities, and to review the Australian based *Enterobius vermicularis* literature available.

METHODS

An international database search was conducted using PubMed, Google Scholar, and Scopus from the database establishment to 31 December 2023. Relevant literature relating to the following search terms was identified: ("*Enterobius vermicularis*" OR "E vermicularis" OR, "pinworm" OR "threadworm" OR "roundworm" OR "oxyura" OR "oxyuris vermicularis") AND ("appendicectomy" OR "appendectomy" OR "appendicitis" OR "appendix"). To identify literature outside of the databases the reference and bibliography lists were reviewed. A total of three hundred and fifty-six articles were identified. Of the identified literature inclusion criteria specific to retrospective studies, literature review, systematic reviews, and meta-analysis studies published in English were applied yielding twenty-six articles, of which two were systematic meta-analysis articles

DISCUSSION

Appendicitis typically occurs secondary to appendiceal luminal obstruction.[4] Obstruction of the appendiceal lumen results in stasis, bacterial overgrowth, inflammation, and infection.[4] In severe cases of appendicitis the appendix may become ischaemic or perforate as a consequence of luminal obstruction.[4] Laparoscopic appendicectomy remains the mainstay of treatment for acute appendicitis despite emerging data for antibiotic only treatment.[1,4] The literature recognises aetiologies such as tumours and faecoliths as cause for appendicitis.[3,4] However, obstruction causing appendicitis secondary to helminth infections remains controversial.[1,5]

Enterobius vermicularis infection occurs following either inhalation or ingestion of the helminth oocytes.[4] The oocytes enter the intestinal tract taking approximately two to four weeks to mature into adult *Enterobius vermicularis* worms.[1,4,8] This predominately occurs in the terminal ileum, caecum, and appendix.[3] Once matured the adult female worms migrate to the perianal region to undertake oviposition laying and affixing of oocytes to the perianal folds.[4] Oviposition commences between two to six weeks of host oocyte ingestion.[4] Following oviposition an inflammatory reaction between the host and oocytes or adult female worms occurs, resulting in a perianal itch.[4] Oocytes are typically transferred to hosts via clothing, bedding, or fingers secondary to perianal itching.[1,3,4] Additionally, larvae may migrate from the perianal region into the colon resulting in retroinfection.[3] In addition to perianal itch, symptoms such as vomiting, anorexia, and abdominal discomfort can occur in the setting of an significant *Enterobius vermicularis* infection.[1,4]

Diagnosis of *Enterobius vermicularis* can be obtained by either the macroscopic or microscopic presence of adult worms or oocytes at the anal verge or on household items such as clothing or bedding.[4] Microscopically, *Enterobius vermicularis* infection can be confirmed through a cellophane or scotch-tape test.[3] Whereby the cellophane or tape is pressed against the anal verge in the morning prior to passing faeces and examined under a microscope.[3] Although, it is noted that tape tests have a low diagnostic sensitivity, requiring perianal oocytes or worms to be present at time of testing.[3] Once diagnosed the treatment of *Enterobius vermicularis* infection requires anti-helminth medications and maintains a high cure rate.[4] For individuals who undergo an appendicectomy and obtain a diagnosis of *Enterobius vermicularis* either intraoperatively or on appendiceal histological examination helminth treatment is still required regardless of previous appendicectomy.[4]

Enterobius vermicularis and appendicitis

A few theories exist surrounding the pathophysiology of *Enterobius vermicularis* and appendicitis.[5] The first is that either oocytes or adult worms cause a physical obstruction of the appendiceal lumen.[5] The second theory surrounds mucosal invasion of *Enterobius vermicularis*.[5] However, the majority of appendicectomies with *Enterobius vermicularis* infection histologically do not demonstrate acute inflammation and mucosal invasion of *Enterobius vermicularis*.[4,5] The mucosal invasion of *Enterobius vermicularis* is considered to possibly be due to the helminths attempt to evade hypoxia following appendicectomy.[5]

Zouari et al demonstrated *Enterobius vermicularis* helminth infection was present in 50% of the appendicectomies negative for acute appendicitis within their study.[1,3,9] However, histological examination does commonly display lymphoid hyperplasia.[4,12] A literature review completed by Pehlivanoglu et al reviewed 3,222 appendicectomies in which 24 appendixes had *Enterobius vermicularis* infections at the time of appendicectomy.[5] Histological examination of the appendixes with *Enterobius vermicularis* infection demonstrated lymphoid hyperplasia in 100%, congestion in 91.7%, and evidence of acute appendicitis 33.3%.[5] *Enterobius vermicularis* mucosal invasion was present in only one individual.[5] Da Silva et al and Akkapulu et al also established lymphoid hyperplasia as a major finding in *Enterobius vermicularis* at time of appendicectomy.[10,11]

Furthermore, a systematic review and meta-analysis, by Hashemi et al, assessing a total of 29,694 appendicectomies concluded that in the absence of histological appendiceal inflammation *Enterobius*

vermicularis is the leading cause of appendiceal related pain or discomfort.[3] To make diagnosis of *Enterobius vermicularis* more challenging patients who had *Enterobius vermicularis* infection identified on histology at time of appendicectomy had normal inflammatory markers preoperatively.[4] Additionally, it should be noted that lymphoid hyperplasia may not necessarily be distinguishable from acute appendicitis on medical imaging.[5] Following appendicectomy if *Enterobius vermicularis* infection is identified anti-helminth medical treatment is still required.[3,4] Raising the question as to if appendicectomy was required in this cohort of patients.[4] Consideration with a high index of suspicion could be taken into *Enterobius vermicularis* infection as a differential diagnosis for clinically stable patients with normal inflammatory biochemistry.[4] This potentially avoiding the risks associated with appendicectomy.[3] With the hypothesis that *Enterobius vermicularis* worms within the appendiceal lumen may cause irritation and lymphoid hyperplasia resulting in appendiceal colic with a similar clinical presentation to that of acute appendicitis.[3-5,11,13-15]

Prevalence within lower HDI and SES countries

Taghipour et al performed a systematic review and meta-analysis analysing 59 studies with total of 103,195 appendicectomies.[1] The pooled prevalence of *Enterobius vermicularis* infection at time of appendicectomy was 4%.[1] However, it was noted that prevalence varied between 2-8% dependent on geographical location.[1] Additionally, subgroup analysis of human development index (HDI) and income level were performed demonstrating an increased prevalence of *Enterobius vermicularis* infection in low HDI (33%) and lower middle to lower level income (9%) countries.[12] Recognition of *Enterobius vermicularis* infection as a neglected risk factor for appendicitis or appendiceal colic allows for the initiation of public health interventions to reduce disease prevalence within at risk communities.[1] The introduction of *Enterobius vermicularis* screening and public health programs such as handwashing has demonstrated a reduction in *Enterobius vermicularis* prevalence from 22.1% to 5.2% in Greece and 45.9% to 16% in Turkey.[1,16,17]

Australian based literature

A single retrospective study on the prevalence of *Enterobius vermicularis* at time of appendicectomy in Australia was identified.[18] The retrospective study was completed by Dahlstrom et al in 1994.[18] A total of 1967 appendices were reviewed with *Enterobius vermicularis* identified in 63 appendices.[18] Of the infected appendices 63% demonstrated no mucosal invasion or acute appendicitis.[18] However, 98% of the *Enterobius vermicularis* infected appendices presented with symptoms in keeping with appendicitis.[18] It is important to note that this retrospective study is approximately three decades old and may no longer accurately reflect the burden of *Enterobius vermicularis* associated appendicectomies within Australia. In particular, if there is a disparity in *Enterobius vermicularis* infection at time of appendicectomy in relation to HDI, SES, and community remoteness.

CONCLUSION

The literature reveals a hypothesis that *Enterobius vermicularis* worms within the appendiceal lumen may cause irritation and lymphoid hyperplasia resulting in appendiceal colic with a similar clinical presentation to that of acute appendicitis. Additionally, an increased association with low HDI is suggested. Recognition of *Enterobius vermicularis* infection as a neglected risk factor for appendiceal colic could allow for the initiation of public health interventions to reduce disease prevalence within at risk communities. Furthermore, consideration with a high index of suspicion could be taken into *Enterobius vermicularis* infection as a differential diagnosis for clinically stable patients with normal inflammatory biochemistry. Thus potentially avoiding an appendicectomy in individuals with appendiceal colic secondary to *Enterobius vermicularis* infection. Further research is required to assess if there is a disparity in *Enterobius vermicularis* infection at time of appendicectomy in relation to HDI, SES, and remoteness within Australian communities.

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