Role and Incidence of Parasitic Infection in Adult Egyptian Patients with Acute Appendicitis

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ABSTRACT
Background: Appendicitis is the most important acute surgical condition of the abdomen, and appendectomy constitutes one of the most common surgical operations worldwide. Many factors can cause appendicitis but the intestinal parasitic infections are one of the most important causes.

Objective: The present study aimed to evaluate and detect the role and incidence of various parasitic infections in appendectomy specimens from Egyptian adult patients with acute appendicitis attending the General Surgery Emergency room at Al-Azhar University Hospitals, Cairo, Egypt (Al-Hussein and Sayed Galal Hospitals).

Patients and methods: The present study was carried out on 200 patients undergoing appendectomy with a provisional diagnosis of acute appendicitis during the period from December 2015 to November 2016. The removed appendices were fixed in 10% buffered formalin, sectioned, stained with H&E and examined for histopathological changes and presence of parasites. Stool examination was also done by direct smear, formol ether concentration techniques as well as CBC examination for all patients.

Results: Stool examination revealed 120 (60%) out of the total 200 appendectomy patients were positive for parasitic infections, while CBC examination revealed leucocytosis among 167 (83.5%), and eosinophilia in 40 (20%) as well as anemia in 43 (21.5%) in all the studied patients. Histopathological examination revealed parasitic infections in 6 (3%) of appendectomy specimens. The presence of E. vermicularis worms and their eggs as well as Schistosoma ova were observed in 4 (2%) and 2 (1%) of cases respectively. Features of acute suppurative appendicitis were observed in 143 (71.5%) of cases, of which, 98 (49%) cases had luminal obstruction by fecalith and 45 (22.5%) showed patent lumen. Non suppurative appendicitis were presented in 57 cases (28.5%) which included lymphoid hyperplasia in 21 cases (10.5%) and neuronal hyperplasia in 6 cases (3%) as well as granulomatous appendicitis with features consistent with appendiceal Crohn’s disease (CD) in 30 cases (15%). Conclusion: The study concluded that parasitic infections constitute 3% of the surgically removed appendixes where Schistosoma eggs and E. vermicularis (adults and eggs) were the parasites recorded. So differential diagnosis of parasitic infections in the etiology of acute appendicitis should be made properly which can save patients from a negative laparotomy, morbidity and even mortality.

Keywords: Appendicitis, Enterobius vermicularis, Schistosoma species, Histopathology, Parasitic infection, Stool and CBC examination.

INTRODUCTION
Appendicitis is the most common cause of acute abdominal pain that requires surgical treatment. The prevalence of appendicitis is reported to be around 7%. It is more common in males than females (1.4:1) and can be seen at any age but it is more commonly seen in older children and in young adults. It is more common in urban, industrialized societies and relatively rare in developing countries where a less-refined, high-fibre diet is typically consumed. Presumably, the diet in industrialized countries leads to hard stool, higher intra colonic pressure and formation of fecaliths that can serve as obstructing agents in the appendiceal lumen 1. The cause of acute appendicitis is unknown but is probably multifactorial; luminal obstruction, dietary and familial factors have all been suggested 2. Faecal stasis, fecaliths, lymphoid hyperplasia and foreign bodies are the most common cause of appendiceal obstruction 1. Another important cause of appendicitis is parasitic infection but the actual role as co-factor in appendicitis is still to debate. There is little evidence regarding the relationship between parasites and acute appendicitis. In even tropical countries, where intestinal parasitic infection is quite common, appendiceal disease is not unusual 3. Obstruction of the appendiceal lumen can occur with parasites and their eggs. If the lumen is obstructed, continued secretion and proliferation of bacteria or the parasites may cause an increase in the intra luminal pressure. Increased pressure impairs the circulation of the wall and mucosal damage may cause bacterial invasion, inflammation, sepsis and finally necrosis and perforation 4. Most prominent parasitic agents
reported to be related with appendicitis are Enterobius vermicularis, Schistosoma spp, Trichuris trichiura, Taenia spp, Ascaris lumbricoides and Entamoeba histolytica. Pinworm is considered the most common helminthic infection postulated with acute appendicitis and varies from 0.2% to 41.8% worldwide.

Eggs of Schistosoma mansoni have been found in the lumen of the appendix leading to transmural inflammation, granulomatous reactions and purulent exudates. Sometimes, the fibrosis that follows the infection causes a luminal obstruction and later secondary bacterial appendicitis.

Trichuris trichiura can be asymptomatic but can be visible in the stool and they can cause rectal prolapse and appendicitis. Appendicitis due to ascariasis can be diagnosed by Ultrasound that shows long filling defects in the right iliac fossa.

Entamoeba histolytica may stay in the appendix as well as protostrongyl and the adult tapeworms, Taenia saginata and Taenia solium which may be found in the lumen of the appendix.

PATIENTS AND METHODS
The present study was carried out during the period from December, 2015 to November, 2016 where a total of two hundred (200) patients with clinical manifestations of appendicitis underwent appendectomy at General Surgery Departments of Al-Hussein and Sayed Galal University Hospitals, Faculty of Medicine, Al-Azhar University, Cairo, Egypt. Right Macberny incision was done, followed by delivery of the caecum, devascularisation of the appendix, base ligation and removal. After appendectomy, each appendix was immediately preserved in 10% formalin in a clean container labelled and transported to the laboratory. The patient's consent was obtained before surgery as per norm. Data for each patient was recorded. All the specimens delivered to the laboratory were examined after obtaining consent from the institutional ethical committee.

Histopathological evaluation
All appendectomy fixed materials were sampled longitudinally in the distal parts and cross-sectionally in the other parts. After overnight tissue processing of specimens, 4 microns (μm) sections were prepared and stained with hematoxylin and eosin (HE) then examined. Stool samples were collected from each patient in a clean container, labelled and examined by direct smear method after staining with iodine and formol ether concentration techniques. Venous blood samples were also collected and analyzed by an automated hematology cell counter analyzer (DIAGON® D-cell 60 hematology analyzer).

RESULTS
Among the two hundred patients suffering from acute appendicitis, 126 (63%) were males and 74 (37%) were females. The age of them was ranging from 18 to 70 years. Stool examination revealed positive parasitic infection among 120 (60%) of them and the distribution of infection was presented in table (1) and figure (1) as E. histolytica 43(21.5%), E. vermicularis 15(7.5%), Fasciola sp.2(1%), G. lamblia 10 (5%), S. mansoni 7(3.5%), T. trichiura 10(5%), A. lumbricoides 19 (9.5%), T. saginata and T. solium which may be found in the lumen of the appendix.

Parasitic infection was detected in 6 specimens (3%) out of the total (200) investigated cases, see figure (3). Four patients of them (2%) were positive for (E. vermicularis and their eggs) and one of these four cases (0.5%) had acute appendicitis and peri-appendicitis with extensive neutrophilic infiltrate and focal perforation. The other 3 cases (1.5%) had lymphoid hyperplasia and patchy eosinophilic infiltrate in the appendiceal wall. The worms were located in the lumen of all of the positive cases without wall invasion. Schistosoma ova surrounded by granulomatous reaction were detected in 2 cases (1%) showing extensive wall fibrosis and marked luminal narrowing, see table (3) and figures (4 &5). Of all the investigated cases, 23 of them (11.5%) showed focal perforation of the appendiceal wall, 85 (42.5%) had edematous wall, 35 (17.5%) accompanied with fibroled wall and the remaining 57 cases (28.5%) were grossly and histologically normal, see figure (6).
Table (1): Distribution of the parasitic infections among investigated patients

<table>
<thead>
<tr>
<th>Stool Analysis</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>80</td>
<td>40.0%</td>
</tr>
<tr>
<td>Positive</td>
<td>120</td>
<td>60.0%</td>
</tr>
<tr>
<td><em>E. histolytica</em></td>
<td>43</td>
<td>21.5%</td>
</tr>
<tr>
<td><em>E. vermicularis</em></td>
<td>15</td>
<td>7.5%</td>
</tr>
<tr>
<td><em>Fasciola sp.</em></td>
<td>2</td>
<td>1.0%</td>
</tr>
<tr>
<td><em>G. lamblia</em></td>
<td>10</td>
<td>5.0%</td>
</tr>
<tr>
<td><em>S. mansoni</em></td>
<td>7</td>
<td>3.5%</td>
</tr>
<tr>
<td><em>T. trichura</em></td>
<td>1</td>
<td>0.5%</td>
</tr>
<tr>
<td><em>A. lumbricoides</em></td>
<td>19</td>
<td>9.5%</td>
</tr>
<tr>
<td><em>Taenia sp.</em></td>
<td>2</td>
<td>1.0%</td>
</tr>
<tr>
<td>Mixed infection</td>
<td>21</td>
<td>10.5%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>200</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table (2): Results of CBC examination

<table>
<thead>
<tr>
<th></th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Leucocytosis:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>33</td>
<td>16.5%</td>
</tr>
<tr>
<td>Present</td>
<td>167</td>
<td>83.5%</td>
</tr>
<tr>
<td><strong>Eosinophilia:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>160</td>
<td>80.0%</td>
</tr>
<tr>
<td>Present</td>
<td>40</td>
<td>20.0%</td>
</tr>
<tr>
<td><strong>Anemia:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>157</td>
<td>78.5%</td>
</tr>
<tr>
<td>Present</td>
<td>43</td>
<td>21.5%</td>
</tr>
</tbody>
</table>

Table (3) : Distribution of histopathological examination of appendices

<table>
<thead>
<tr>
<th>Inflammatory changes</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>7</td>
<td>5%</td>
</tr>
<tr>
<td>Positive</td>
<td>13</td>
<td>5%</td>
</tr>
<tr>
<td>Parasitic infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>94</td>
<td>0%</td>
</tr>
<tr>
<td>Positive</td>
<td>5</td>
<td>0%</td>
</tr>
<tr>
<td><em>E. vermicularis</em></td>
<td>1</td>
<td>0%</td>
</tr>
<tr>
<td><em>Schistosoma sp</em></td>
<td>2</td>
<td>0%</td>
</tr>
</tbody>
</table>
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**Figure (1):** Distribution of the parasitic infections among investigated patients

**Figure (2):** Results of CBC examination

**Figure (3):** Distribution of parasitic infection among examined cases
Figure (4): Light photo micrograph of high-power view showing markedly edematous submucosa (red arrow), infestation with fresh (yellow arrow) and calcified bilharzial ova (black arrow), and marked inflammatory infiltrate (blue arrow) (H&E X 360)

Figure (5): Light photo micrograph of medium-power view showing marked edema and inflammatory cellular infiltrate (blue arrow) and 3 parasites (*E. vermiculais*) invading mucosa and surrounded by clear zone “parasitophorus vacuole” (black arrows) (H&E X 235).

Figure (6): Distribution of histopathological examination
DISCUSSION

Appendicitis is the most common acute surgical circumstance of the abdomen and appendectomy is one of the most common surgical operations worldwide. It is commonly associated with obstruction (50-80% of cases), usually due to a fecalith, gallstone, tumor, presence of *Enterobius vermicularis* and diffuse lymphoid hyperplasia. Obstruction causes increased intraluminal pressure, collapse of draining veins, ischemia, mucosal injury and ulceration, bacterial overgrowth which lead to more edema and more ischemia. However, not all cases show clear evidence of lumen obstruction.

The current study was performed on two hundred patients suffering from acute appendicitis attending the General Surgery Departments at Al-Hussein and Sayed Galal University Hospitals. Out of them 126 (63%) were males and 74 (37%) were females. The male: female ratio was (1.7:1) which coincided with that obtained by Yabanoglu et al.,*12* (1.6:1) and Yildirim et al.,*13* (1.7:1). In contrast, Helmy et al.,*14* and Zakaria et al.,*15* reported that the male: female ratio among patients previously diagnosed with appendicitis in Cairo was (1:2) and (1:1.2), respectively.

Features of acute suppurative appendicitis were observed in 143 (71.5%) cases, of which, 98 (49%) had luminal obstruction by fecalith and 45 (22.5%) had patent lumen. Non suppurative appendicitis were presented in 57 cases (28.5%) which included lymphoid hyperplasia in 21 cases (10.5%) and neuronal hyperplasia in 6 cases (3%) as well as granulomatous appendicitis with features consistent with appendiceal Crohn’s disease (CD) in 30 cases (15%) which coincided with that obtained by Yabanoglu et al.,*12* and Dorfman et al.,*3*. Of all the investigated cases, 23 of them (11.5%) showed focal perforation of the appendiceal wall, 85 (42.5%) had edematous wall, 35 (17.5%) accompanied with fibrosed wall and the remaining 57 cases (28.5%) were grossly and histologically normal.

Parasitic infection was detected in 6 appendectomy specimens (3%). The presence of *E. vermicularis* worms and their eggs were observed in 4 cases (2%). *Schistosoma* ova were also detected in 2 cases (1%). These results are coincided with that obtained by Yabanoglu et al.,*12* who reported that among 1159 operated patients as acute appendicitis, parasitic infections were seen in 17 (1.4%) patients where *E. vermicularis* was determined in 15 cases (88.2%) and *E. histolytica* in 2 cases (11.7%) of them. Moreover Zakaria et al.,*15* reported that the ratio was 5.5% and the parasitic infections were (51.1%) enterobaisis, (9.1%) schistosomiasis, (26.1%) ascariasis, (8%) trichuriasis, and (5.7%) taeniasis.

In India, Jada et al.,*16* detected a wide spectrum of parasitic infections (32%) in one hundred surgically removed appendices which included *A. lumbricoides* (18%), *E. vermicularis* (6%), *A. duodenale* (4%), *T. colubriformis* (1%) and *T. trichiura* (1%).

In Egypt, Hedya et al.,*17* reported that the retrospective study of appendectomies revealed 11 out of 251 (4.38%) having parasitic infections distributed as *E. vermicularis* (1.59%), *A. lumbricoides* (0.79%), *Schistosoma* sp. eggs (1.19%) and amoebiasis (0.79%).

Also, Abdellatif et al.,*18* reported that out of 100, surgically removed appendices in Minia University Hospital the presented parasites were *E. vermicularis* (3%), bilharzial granulomas (3%) as well as *A. lumbricoides, A. duodenale* and *H. nana* (1% for each).

In another study in Cairo city, Helmy et al.,*14* reported that parasites were detected in 14.8% of surgically removed appendices.

The present identification of *E. vermicularis* worms in 2% of cases coincided with reported results by Arca et al.,*19* in USA and Ramezani and Dehghani.,*20* (2.9%) in Iranian population. In Turkey, several studies recorded the presence of *E. vermicularis* in 3.15% of surgically removed appendices from a Turkish population while in Nepal, *E. vermicularis* was identified in 1.62% of Nepalese patients with clinically diagnosed appendicitis.

The wide range of these percentages indicates that the association between *E. vermicularis* and appendicitis differs from country to another. This can be explained on the basis that parasitic diseases
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affect four billion individuals worldwide, especially in communities that have lower hygiene, sanitation, socio economic status, and education as well as living conditions.

According to stool analysis, 120 cases (60%) were identified as having one or more of the following parasites, E. histolytica (21.5%), G. lamblia (5.0%), S. mansoni (3.5%), E. vermicularis (7.5%), Fasciola (1.0%), T. trichura (0.5%), Taenia specie (1.0%) A. lumbricoïdes (9.5%) and mixed infection (10.5%). This agrees with Mousa et al. 23 and Bayoumy et al. 24 who detected high prevalence rate of parasitic infection in Egyptian patients reaching 67%. At the same time these results agreed, with a study in Kenya recorded by Obala et al.25 (52.3%) and a study in Ethiopia recorded by Abate et al.26. On the other hand these results are higher than that recorded by Abed et al., 27 in Qalubia Governorate (24.7%), Deepesh et al. 28 in India (16.8%) and Kheirandish et al. 29 in Iran. Also these results were higher than Ibrahim, 30 who reported that the prevalence of parasitic infection among Egyptian patients in El-Minia Governorate villages in Upper Egypt was 39.3%. However, the present results were less than that reported in Upper Egypt by El-Masry et al. 31 who reported that the prevalence of parasitic infections among Egyptian patients in rural area in Sohag Governorate villages were 88.5%. These differences could be attributed to the locations of the studies, the season of the year of the study was carried out and the method of stool analysis.

The high prevalence of parasitic infections in the present study suggested a generally low standard of living and poor environmental sanitation in the study area and confirmed that intestinal parasitic infection was a common problem in Egypt.

Among the infected 120 cases, 26 (21.7%) of them had anemia, 108 (90%) had leucocytosis and 40 (33.3%) had eosinophilia. There was statistically significant increase in leucocytosis and oesinophilia as regards stool analysis (P < 0.05). The ratio of eosinophilia was lower than that obtained by Meeusen and Balic, 32 who found that 81% of helminthic infections associated with eosinophilia. Also, Demirci, 33 who found that 63% of parasite infected patients had eosinophilia. This difference because in the present study some parasites that detected in the stool live in intestine only without migration to body tissues.

CONCLUSION
It can be concluded that infections of the appendix by schistosomiasis and enterobiasis are important agents in the pathogenesis of appendicitis in Egypt. Differential diagnosis of parasitic infections as etiology of acute appendicitis should be in mind and this attention can save patients from a negative laparotomy and morbidity and even mortality. Detection and treatment of intestinal parasites should be done regularly to avoid future complications that may necessitate surgical interference.

REFERENCES


