

Clinico-epidemiological spectrum of strongyloidiasis in India: Review of 166 cases

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ABSTRACT

Strongyloidiasis is frequently asymptomatic but can cause disseminated disease and variable presentations. Diagnosis is often delayed or misdirected either due to poor degree of clinical suspicion or clinical imitation of other gastrointestinal conditions. This infection is not infrequent and several cases from all over India have been reported barring few states from central India. We reviewed 166 cases published in English literature from India; from 2001 till 2018 including 2 recent cases from our institute. The mean age of presentation was 35 years with male female ratio of 2.8:1. The duration of disease at the time of presentation varied from 15 days to 10 years. Most important predisposing factor identified in the study was HIV (13.3%) and steroid therapy (6.6%). Most common modality of diagnosis was by stool microscopy (69.3%). Radiological investigations were ordered in 33.7% patients before stool microscopy. Ivermectin was the most common treatment regimen with cure rate of 97.6%. Better awareness and early clinical suspicion of the disease with stool microscopy and adequate therapy are necessary to improve the outcome. Strongyloidiasis is rather widely prevalent infection with variable symptomatology and calls for a close coordination from family physicians and microbiologists.

Keywords: Contrast enhanced computed tomography, gastrointestinal, Human immunodeficiency virus, India, strongyloidiasis, ultrasonography

Introduction

Strongyloides stercoralis, a soil transmitted helminth, occurs worldwide. Clinical manifestations range from asymptomatic eosinophilia in the immunocompetent host to disseminated disease and septic shock in immunocompromised host. It is endemic in rural areas of tropical and subtropical regions. It also occurs sporadically in temperate areas (Appalachia and southern Europe).^[1,2] In developed nations such as United States, the highest rates of infection are among residents of the southeastern states.^[3,4] While from India, there are few scattered case studies, which have

reported localized involvement to disseminated strongyloidiasis.^[5,6] Most of these patients undergo many radiological investigations before a diagnosis of strongyloidiasis is made. A very few case series describing the clinical manifestations, therapy, and outcome are available from India. We herein report two cases from our institute and review those reported in the Indian literature to provide the descriptive data on the epidemiology, clinical features, therapeutic regimen practiced, and outcome of the disease.

Case 1

A 62-years-old Indian woman hailing from Rishikesh housewife by occupation living in crowded settings, presented to emergency with complaints of recurrent vomiting for last 7 months. Frequency of vomiting increased gradually from 2–3 episodes per day to 10–12 episodes during the course of illness hampering her daily life. Her general hygiene was very poor. On blood investigations, her counts were within normal limits, but there

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was no eosinophilia. Ultrasonography (USG) abdomen revealed ill-defined circumferential hypo-echoic wall thickening of pylorus causing luminal narrowing with dilated proximal stomach. No improvement in patient's condition was observed after initial conservative management. Upper gastrointestinal endoscopy was done which showed antrum mucosal atrophy with edematous mucosa in pylorus and duodenum. Biopsy revealed normal histology. Contrast enhanced computed tomography (CECT) abdomen showed diffused symmetric circumferential wall thickening involving antrum of the stomach and duodenum with no proximal dilatation [Figure 1]. CECT thorax revealed calcified fibrothorax likely due to chronic right sided empyema. After all these investigations, stool and sputum microscopy were done. Rhabditiform larvae and adult worm of *Strongyloides stercoralis* were seen in stool wet mount [Video 1]. Rhabditiform

larvae were seen in sputum wet mount [Figure 2]. After this, the patient was given one dose of ivermectin 10 mg and albendazole 400 mg. After 3 days of therapy, patient improved clinically and was discharged.

Case 2

A 35-year-old psoriatic female from Haridwar, on steroids admitted with complaint of abdominal pain, diarrhea, vomiting for 5 days associated with fever. Patient gave history of one episode of melaena. She also had right sided pleural effusion and maculopapular rashes over abdomen. There was hepatomegaly on ultrasound abdomen. The patient condition did not improve after initial conservative management. Other routine investigations were normal. Investigations such as CECT and endoscopy were planned but could not be performed as patient could not afford them. Later, microscopy was done for the stool sample which revealed rhabditiform larvae of *Strongyloides stercoralis* [Figure 3]. Patient improved on ivermectin and albendazole treatment and was discharged after 3 days of therapy. Patient was lost to follow up.

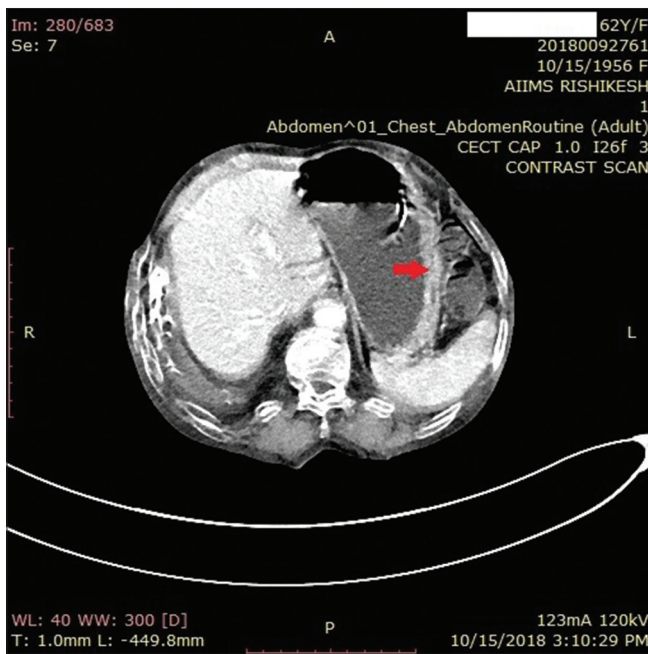


Figure 1: Contrast enhanced computed tomography abdomen showed diffused symmetric circumferential wall thickening involving antrum of the stomach and duodenum with no proximal dilatation



Figure 3: Stool microscopy showing *Strongyloides* larvae



Figure 2: Rhabditiform larvae in sputum wet mount

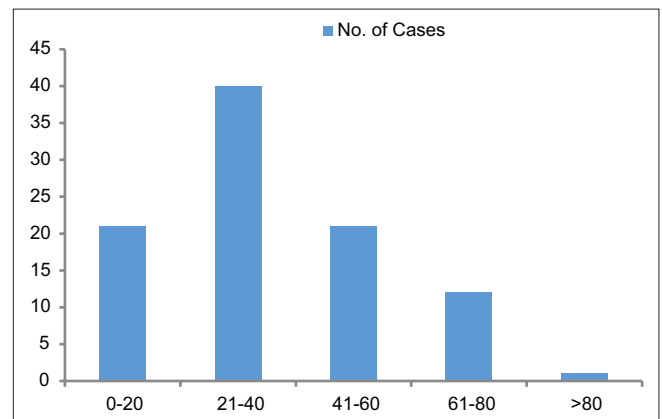


Figure 4: Distribution of cases among different age group

“*Stercoralis India*,” “*Rhabditiform larvae India*,” “*Disseminated Strongyloidiasis India*.” Only cases from English literature were reviewed. Reference lists of retrieved articles were checked to detect additional articles missed by this search strategy.

Data analysis

Data on demographic characteristics, geographical location, clinical presentation, and clinical manifestations along with the duration, diagnostic modality, treatment given, and outcome were noted for each case. If the information on the resident state of the patient was unavailable, the institute from where the study had been reported was considered. Cases were considered as “immunocompromised” in which an underlying disease or predisposing factor was mentioned and as “immunocompetent” in which no such predisposing condition and negative Human immunodeficiency virus (HIV) serology was mentioned. Cases were identified as having hyperinfection syndrome or disseminated strongyloidiasis as reported in studies. The data are presented as frequencies and percentages or mean and standard deviation (SD).

Results

Studies and cases

Our literature search for the period of 2001 to 2018 yielded 61 studies with 164 cases.^[5-65] In addition to these, two recent cases from our institute were also included. Hence, a total of 166 cases were evaluated. The maximum number of cases was reported from Delhi in 2017 and contained data collected over a period of one and half decade. Another retrospective study

from Vellore spanning over 7 years reported *Strongyloides stercoralis* larvae detection in 2,309 stool samples.

Age and gender

The mean age at presentation was 36.37 years ± 19.50 (range 2- to 90-year old, data available for 95/166 cases). The information regarding the gender was available for 95 patients, out of whom, 70 (73.6%) were males and 25 (26.4%) were females. The male to female ratio was 2.8:1. Most of the patients infected with Strongyloidiasis were from age group of 21–40 years of age [Figure 4].

Geographical location

The highest number of cases was reported from Delhi (36). Out of these 36 cases, 30 cases have been reported from a tertiary level referral hospital.^[14] Next in order are Assam (17), Maharashtra (17), Karnataka (16), Tamil Nadu (12), Uttar Pradesh (9), Odisha (5), Andhra Pradesh (4), Kerala (3), Jammu and Kashmir (3), Uttarakhand (3), Rajasthan (3), Manipur (2), West Bengal, Punjab, Chandigarh, and Gujarat (1 case each) [Figure 5].

Risk factors and underlying diseases

Of 166 cases, 43 (data available for 78/116 cases) had a history of underlying immunosuppression in the form of HIV, steroid therapy, human Tcell-lymphotropic virus (HTLV), and malignancy. Several other underlying conditions have also been reported as shown [Figure 6]. Interestingly, few studies from different parts of India, such as Udaipur, Assam, Manipur, and Chennai, have also showed presence of *S. Stercoralis* larvae in stool samples of asymptomatic school going children of rural and tribal population. The prevalence ranged from 0.09% to 6%.^[31,38,59,63]

Duration of disease

Duration of the symptoms ranged from as 15 days to 10 years (mean 9.5 months, data available for 64/166 cases).

Clinical presentation

Most common clinical presentation was acute diarrhea in 47 cases (61%, data available for 77 cases) followed by cough

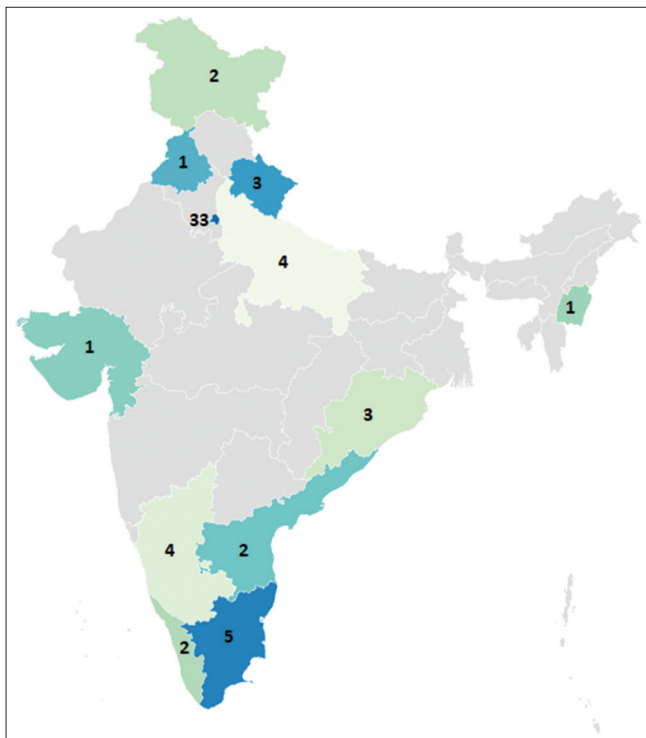


Figure 5: Distribution of cases among different geographical locations

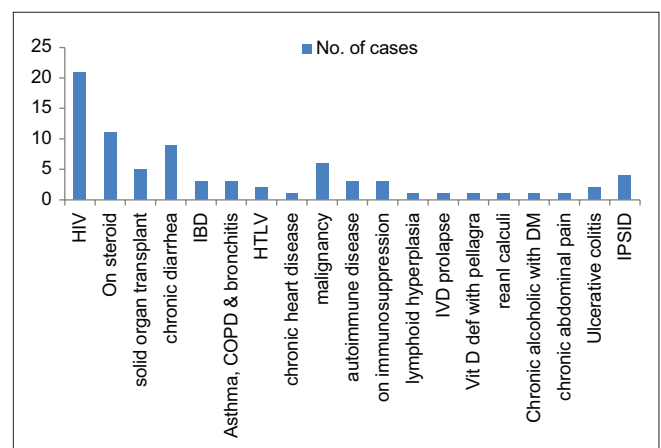


Figure 6: Risk factors/underlying conditions

and respiratory symptoms in 20 (25.9%). Other 10 cases had vague symptomatology ranging from abdominal pain, bloating, generalized weakness, and purpuric rashes.

Diagnostic modality

The most common diagnostic modality used was stool microscopy (115/160; 69.3%) followed by duodenal biopsy (22/98; 22.4%), sputum microscopy (12/98; 12%), and cytology (5/98; 5%) of body fluids. Other samples from which parasite was detected were cervical biopsy and gastric aspirate in occasional cases.

All the samples which detected Strongyloidiasis mostly found the larva (rhabditiform/filariform); however, eggs were also detected along with larva in stool (3), duodenal biopsy (5), and sputum (1). Adult worm was found in two cases of duodenal biopsy.

Before stool microscopy was done, 56 (33.7%) out of 166 cases had undergone investigations, such as Chest X-ray (9.6%), plain X-ray (1.8%), CECT (5.4%), endoscopy (7.2%), USG abdomen (6.6%), ECHO (0.6%), and ECG (2.4%).

Therapeutic regimen

Therapeutic regimen followed was available for 98 cases. Forty-two cases (42/98; 42.8%) were treated with ivermectin alone with a cure rate of 97.6% (41/42). Nine cases (9.1%) treated with combination of ivermectin and albendazole giving cure rate of 88.8% (8/9). Five cases ((5.1%) treated with combination of ivermectin and thiabendazole with cure rate of 100% (5/5). Thirty-six cases (36.7%) were treated with Albendazole alone with cure rate of 100% (36/36). Combination of albendazole plus thiabendazole and thiabendazole plus mebendazole was used in one patient each, both of whom expired due to comorbid conditions.

Outcome

The documentation of outcome of infection was available for 102 cases. The outcome was described as cure in 90 cases. Mortality was seen in 12 cases. Mortality in disseminated strongyloidiasis was 44.4% (4/9), whereas it was 8.3% (1/12) in hyperinfection syndrome.

Discussion

This study gives gestalt on epidemiology, clinical manifestations, diagnostic modalities, treatment regimen, and outcome of strongyloidiasis in India.^[1,5,6,15-52,66-71] Following the first report in 1876 in stool sample of French soldiers with diarrhea returning home from expeditions in Indo-china region, the disease has been infrequently reported.^[66] This is a review on Indian studies from 2001 onward, which includes mostly case reports and retrospective studies. Few prospective studies have reported Strongyloides infection from Manipur, Assam, Udaipur, and Chennai.

In India, maximum cases have been reported from Delhi (21.6%), but it was a retrospective study from a single tertiary level referral

center where patients from all over the country are referred spanning over a period of 15 years. Next highest cases were from Assam (10.2%). To the best of our knowledge this is first comprehensive review on strongyloidiasis in India [Figure 5]. Our study highlights that this disease is prevalent in close to 10 states with different weather conditions. Internationally, the existing information suggests that *S. stercoralis* infections affect between 10% and 40% of the population in many tropical and subtropical countries. Brazil and Thailand are *S. stercoralis* endemic countries where reliable and consistent data on infection is available and the infection rate is estimated to be 10.8%. European studies principally focused on refugees, immigrants and travelers to endemic countries where the adjusted prevalence is close 12.7%, whereas in the United States, it ranges from 6% to 45% depending on the population screened. In neighboring country, Nepal, it is estimated to be 5.8%. Little information is available from countries with the largest populations, namely, China and India.^[1,72] Our study tries to address that concern, but further prospective community-based cross-sectional studies with participation of family physicians are needed to quantify infection rates.

The review found the disease to be more prevalent in males 21–40 years, with an overall male to female ratio of 3:1. This is in concordance with a study from Thailand.^[44] Infections in children and adolescents have also been reported. The most common manifestations are waxing and waning gastrointestinal, cutaneous, or pulmonary symptoms that persist for years; others may have eosinophilia without any symptoms. Most Strongyloides infections manifest as asymptomatic peripheral blood eosinophilia that varies from 350 to 450/ μL .^[73] In this study, most common clinical presentation was acute diarrhea. The predisposing factors are an important indication for suspecting infection with Strongyloides. The most common being HIV infection and steroid therapy followed by HTLV infection, chronic alcoholism, malignancy, immunosuppressive therapy, and chronic diarrhea, which is in concordance with data elsewhere.^[1,74]

In its typical life cycle, *Strongyloides* travels from the skin to the lungs and then to the gastrointestinal (GI) tract of its host. In hyperinfection, there is increase in number of worms migrating through different stages of standard lifecycle. While in disseminated disease there is presence of parasites out-side of the traditional life cycle (i.e. in organs other than the skin, GI tract, or lungs). Filariform larvae may enter arterial circulation and lodge in various organs such as lymph node, pericardium, pancreas, liver, kidneys, and brain.^[75,76] The vague clinical presentation of Strongyloidiasis delays clinical suspicion leading to hyperinfection and disseminated Strongyloidiasis. Therefore, persistent and vague gastrointestinal, cutaneous or pulmonary symptoms along with underlying predisposing conditions and prolonged duration of illness should arouse suspicion for this parasitic infection.^[77] In our review, mortality due to disseminated strongyloidiasis (44%) was higher as compared with hyperinfection syndrome (8.3%), which is in contrast with studies elsewhere.^[78] However, accurate and timely diagnosis of strongyloidiasis is essential, to prevent

hyperinfection and disseminated Strongyloidiasis both of which have poor outcome.^[77-79]

Laboratory diagnosis of strongyloidiasis involves demonstration of larvae in stool using the wet mount method. “Figures 2 and 3” Sensitivity of a single direct fecal microscopic examination is said to be less than 30% and it increases to 70% if three fecal specimens are screened.^[76] The chances of finding larvae increases only after collecting and observing more than seven samples from each suspected patient; applying stool concentration techniques together with other advanced laboratory techniques. Ironically, most of these patients underwent many expensive investigations before a diagnosis of strongyloidiasis could be made mainly using stool microscopy. In our review also, 56 patients (33.7%) had undergone investigations such as chest X-ray (9.6%), plain X-ray (1.8%), CECT (5.4%), endoscopy (7.2%), USG abdomen (6.6%), ECHO (0.6%), and ECG (2.4%), although role of these investigations in determining the extent of disease cannot be undermined. Stool microscopy is a simple, rapid, and inexpensive investigation ironically done quite late in the course of disease. Larva is most detected morphological form but rarely eggs may be found in sputum sample obtained from patients with hyperinfection syndrome.^[77]

Ivermectin is the treatment of choice for the condition, its efficacy is more than other drugs used to treat this condition.^[78,79] In our study also, ivermectin was the most common treatment regimen with cure rate of 97%. Moreover, ivermectin is well tolerated and has less adverse effects than benzimidazole group of drugs.^[78] However, other antihelminthic drugs like albendazole, mebendazole, and thiabendazole have also been prescribed in combination for disseminated and hyperinfection with successful cure.^[74]

Prevalence in asymptomatic school going children and tribal population ranging from 0.09% to 6% highlights the importance of national deworming day conducted on February 10, initiated by Ministry of health and family welfare, Government of India, in 2015 which has covered 26.68 crore children by February 2018.^[80] Moreover several villages in India are open defecation free as a result of toilet being constructed under “Swachh Bharta Abhiyan” which will further contribute to the cause.^[81] In conclusion, strongyloidiasis is widely prevalent in India. Patients presenting with vague gastrointestinal symptoms, on steroid therapy, HIV infection should have their multiple stool examined for parasites. Strongyloidiasis is a highly underreported infection requiring further research with close coordination between microbiologists and family physicians.^[82]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for images and other clinical information to be reported in the journal. The patient understands that name and initials will not

be published, and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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