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RESEARCH ARTICLE

Colonic *Trichuris trichiura* infection presenting as iron deficiency anemia in adult population, in an endemic area, Kashmir (India).

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Abstract

Background: *Trichuris trichiura* infection causing abdominal symptoms with iron deficiency anemia is common in children but presentation as occult blood loss with iron deficiency anemia in adults is infrequent.

Aim: To define the role of colonic *Trichuris trichiura* in causing iron deficiency anemia in adult population.

Methods: A total of 160 consecutive adult patients of undefined iron deficiency anemia underwent upper and lower gastrointestinal endoscopy. Those having colonic trichuriasis were treated with mebendazole 100 mg BD for 5 days and followed for 24 weeks for improvement in hemoglobin.64 multislice CT enterography, jejunal biopsy and anti endomysial antibody estimation were done to rule out small bowel and celiac disease in these patients.

Results: Upper and lower gastrointestinal endoscopy revealed positive findings in 87/160 (54.3%).Thirty two patients had colonic trichuriasis, mean (SD) age 49± 13.5 years. None of these patients had any abdominal symptoms. *Trichuris trichiura* involved caecum in 8(25%), caecum and ascending colon in 23(71.8%), caecum, ascending colon and transverse colon in 1 patient (3.1%).Colonoscopy revealed hemorrhages at the site of attachment of worm with erythema, edema, and erosions. Nineteen (52.8%) patients had positive fecal occult blood. Colonic biopsy revealed eosinophilic infiltration in 10/32(31.2%) patients. Repeat colonoscopy at 4 weeks revealed eradication of infection and resolution of colitis. The mean (SD) hemoglobin level at baseline, 6, 12, 18 and 24 weeks was [9.1± 0.6], [11.1±1.6 P=0.02], [11.6±1.5 P= 0.001], [11.7± 1.5 P=0.02], [12.4± 1.7 P= 0.02] gm/dl respectively.

Conclusions: Colonic trichuriasis manifests as iron deficiency anemia in adults in endemic zone.

Introduction

Iron deficiency anemia (IDA) is commonly seen in adult men and post-menopausal women with a frequency of 2-5% and represents 4-13% of all referrals for outpatient GI (gastro intestinal) clinics (McIntyre and Long 1993; Sayer and Long 1993). Patients with undefined IDA with or without fecal occult blood test (FOBT) positivity

undergo upper gastrointestinal endoscopy and ileo-colonoscopy to rule out gastrointestinal tract lesions that may cause chronic blood loss (Savides and Jensen 2010). In patients over 50 years, the most common cause of IDA is chronic gastrointestinal bleeding due to non-parasitic causes, such as gastric ulcers, duodenal ulcers or gastrointestinal cancers (Goddard et al., 2011).

IDA in adult men due to dietary causes is uncommon and in such patients other causes of IDA should be looked at (Ania et al.,1997;Rockeyand Cello1993).Gastric and duodenal biopsies are taken to rule out *H.pylori* gastropathy and celiac disease as they are known to present solely as IDA (Xin-Hua Qu et al., 2010; Baccini et al., 2006). In case of negative investigations, small bowel is evaluated for a possible bleeding lesion with capsule endoscopy or CT enterography followed by small bowel enteroscopy if a lesion is detected on capsule endoscopy or CT enterography (Bermejo and Garcia-López2009).

It is our frequent observation to find the presence of Trichuris trichiura (TT) on colonoscopy while evaluating GI cause of IDA. TT infection is associated with features of colitis in the form of erythema, edema, erosions and hemorrhages at the site of worm infestation. TT as a cause of IDA has been reported earlier especially in children (Darawan et al., 2005;Ramdath et al., 1995) but data regarding its prevalence and presentation as IDA with or without occult GI bleed in adults is scarce (Khuroo et al 2010). Among the intestinal parasitic infections, helminth infections are the most common on the Indian sub-continent. Kashmir (India) is an endemic zone for intestinal helminthes especially *Ascaris lumbricoides, Trichuris trichiura* and *Enterobius vermicularis.*

In Kashmir Valley, the prevalence rate of ascariasis and trichuriasis among school children is 75.3% and 26.4% respectively. (Wani et al., 2007a; Wani et al., 2007b) Majority of patients with TT infections are asymptomatic, however heavy infections are associated with symptoms of rectal prolapse, mucoid diarrhea and occasional bleeding, a combination called "Trichuris dysentery syndrome (TDS)" with associated mental retardation. (WHO 1997; Bundy et al., 1997;Stephenson et al.,2000; Callender et al., 1993; Cooper et al., 1990).

The aim of the present study was to assess the prevalence and the role played by colonic TT, among cases of IDA in adult population, who were referred for GI evaluation and to see the effect of eradication of TT on hemoglobin levels and to establish whether IDA was attributed to presence of TT infection.

Material and Methods

Subject population: From March 2008 to May 2012 adult males (above 18 years) and post-menopausal females of undefined IDA with or without FOBT positivity were evaluated for possible GI cause of IDA. Proper written consent was taken for the study and approval was taken from ethics committee of the institute.

Methods: Patients of hypochromic microcytic anemia with iron deficiency were subjected to detailed history and physical examination to exclude other causes with special emphasis on history of drug intake especially aspirin, non-steroidal anti-inflammatory drugs (NSAID), anti-coagulants, family history of bleeding disorder, post-menopausal bleeding or any other systemic disease. Baseline hemoglobin (Hb) estimation was done and these patients were further subjected to stool examination to look for ova of parasites or cysts. The stool samples were processed using Kato-Katz thick smear technique. This was followed by FOBT, upper GI endoscopy with gastric biopsy, rapid urease test (RUT) for H. pylori and jejunal biopsy. Ileo-colonoscopy was done if upper GI endoscopy was negative.

Patients who had TT infection with associated colitis were subjected to colonic biopsies at the site of worm infestation. Biopsies were also stained for acid fast bacilli (AFB) and tissue subjected to polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* (MTB).

Patients who had TT infection were further evaluated for small bowel disease before giving treatment for TT infection to rule out concomitant small bowel disease, because TT infection could be an incidental finding keeping in view the endemic zone for parasite infestation. Small bowel evaluation was done by using 64 multi-slice CT enterography (Scott et al., 2006; Sodhi et al., 2012). Anti endomysial antibody estimation was done in case the above investigations were negative, to rule out celiac disease (Bhatnagar and Tandon 2006).

Mebendazole Treatment: Patients with TT infection were treated with tablet mebendazole 100 mg twice a day for 5 days and sent home with proper hygiene advice regarding prevention of re-infection. Repeat stool examination was done to look for eradication of TT. Check colonoscopy was done at 4 weeks to look for the eradication of TT infection and healing of colitis. On follow up hemoglobin levels were monitored at 6, 12, 18 and 24weeks to look for response to therapy.

Statistical analysis: All data were recorded as the mean ± SD. P value <0.05 was considered statistically significant. All statistical analysis was performed with the statistical package for social sciences (SPSS 10) Chicago, USA software.

Results

From March 2008 to May 2011, 160 patients with IDA were evaluated by upper GI endoscopy and ileo-colonoscopy. Base line characteristics of these patients are shown in (Table 1).Upper GI endoscopy and ileo-colonoscopy revealed positive findings in 87/160 (54.3%) patients.TT infection was the most common finding seen in 36 (22.5%) patients followed by carcinoma stomach in16 (10%). Duodenal ascariasis was seen in 2 patients, of whom one had underlying gastric ulcer and the other had *H. pylori* associated antral gastritis. The other findings are shown in (Table 2). Stool examination revealed ova of TT in 26/160(16.25%), *Ascaris lumbricoides* in 64/160(40%) and 2 patients had cysts of *Giardia lamblia*. In 73 (45.6%) patients, etiology of anemia was not ascertained by upper GI endoscopy and ileo-colonoscopy.

Thirty-six (22.5%) patients revealed TT infection on colonoscopy; four had associated lesions which included carcinoma colon (1 patient), solitary rectal ulcer (1 patient), ileal gastrointestinal stromal tumour (1 patient), and jejunal adenocarcinoma (1 patient). Finally there were 32 patients who were treated with mebendazole to see the effect of treatment on hemoglobin levels (Fig 1).Characteristics of these patients are shown in (Table 3)

Among 32 patients of TT infection, mean (SD) hemoglobin level was 9.1(6.1) gm/dl. Peripheral blood eosinophil count was normal in 27 patients while as 5 patients had mild eosinophilia (7-9%). Stool examination revealed ova of TT and *Ascaris* in 26/32(81.2%) of patients and only *Ascaris* in 8(25%) of patients. Eight (25%) patients had cecal involvement, 23(71.8%) involved cecum and ascending colon and one (3.1%) affected cecum, ascending colon and transverse colon. (Figure 2 a, b, c, d). The associated mucosal changes included hemorrhages at the site of attachment of anterior end of TT with features of surrounding colitis in the form of erythema, edema, erosions and hemorrhages Colonic biopsy revealed nonspecific colitis in all patients with infiltration of mucosa with lymphocytes, plasma cells and eosinophilic infiltration in 10/32(31.2%) patients. None of the biopsy revealed any granuloma, AFB, cryptitis, crypt abscess or atrophy. Tissue PCR for MTB was negative in all patients. Jejunal biopsies revealed nonspecific findings and anti endomysial antibody was negative in all patients. Stool examination at 6 and 18 weeks were negative for ova of TT however ova of *Ascaris* were seen in 4/32(12.5%) at 18 weeks. Repeat colonoscopy performed in 28 patients at 4 weeks, revealed eradication of TT infection and resolution of associated colitis.

There was significant and progressive increase in hemoglobin between baseline values and those estimated at week 6, 12, 18 and 24 weeks (Table 3). Two patients on follow up had persistent anemia. These patients had capsule endoscopy done subsequently, which was normal. Both these patients were put on iron therapy and responded with improvement in hemoglobin level at week 24.

Table1: Base line characteristics of patients of iron deficiency anemia (n=160).

S.No.	Parameters	No. (%)
1.	Age, mean (SD)*	46.5(17.4)
2.	Sex, males.	87(54.3)
3.	Serum Iron (ug/dl) means (SD*)	33.7(26.1)
	TIBC (ug/dl)	480 (36)
	Serum ferritin (ug/l)	12(3)
	Transferrin saturation	13(6)
4.	Hemoglobin (g/dl) mean (SD)*	7.3(1.9)
5.	Mean cell volume (MCV) mean (SD)*.	71.2(5.7)
6.	FOBT Positivity	44(27.5)

SD*: Standard Deviation; FOBT: Fecal Occult Blood Test; TIBC: Total iron binding capacity

Table 2: Outcome of patients of iron deficiency anemia following upper GI endoscopy and ileo colonoscopy (n =160).

S. No.	Parameters	No. (%)
1.	Duodenal ulcer	2(1.2)
2.	Gastric ulcer	4(2.5)
3.	Gastritis with *Helicobacter pylori*	7(4.3)
4.	Gastritis without *Helicobacter pylori*	3(1.8)
5.	Carcinoma stomach	16 (10)
6.	Carcinoma colon	10 (6.2)
7.	Angiodysplasia (cecum)	3(1.8)
8.	Chronic ulcerative colitis	3(1.8)
9.	Polyposis coli.	2(1.2)
10.	*Trichuris trichiura*	34(21.2)
11.	Duodenal adenocarcinoma	1(0.6)
12	Solitary rectal ulcer with *Trichuris trichiura*	1(0.6)
13	Carcinoma colon with *Trichuris trichiura*	1(0.

Table 3: Characteristics of patients of *Trichuris trichiura* infection with iron deficiency anemia (n=32).

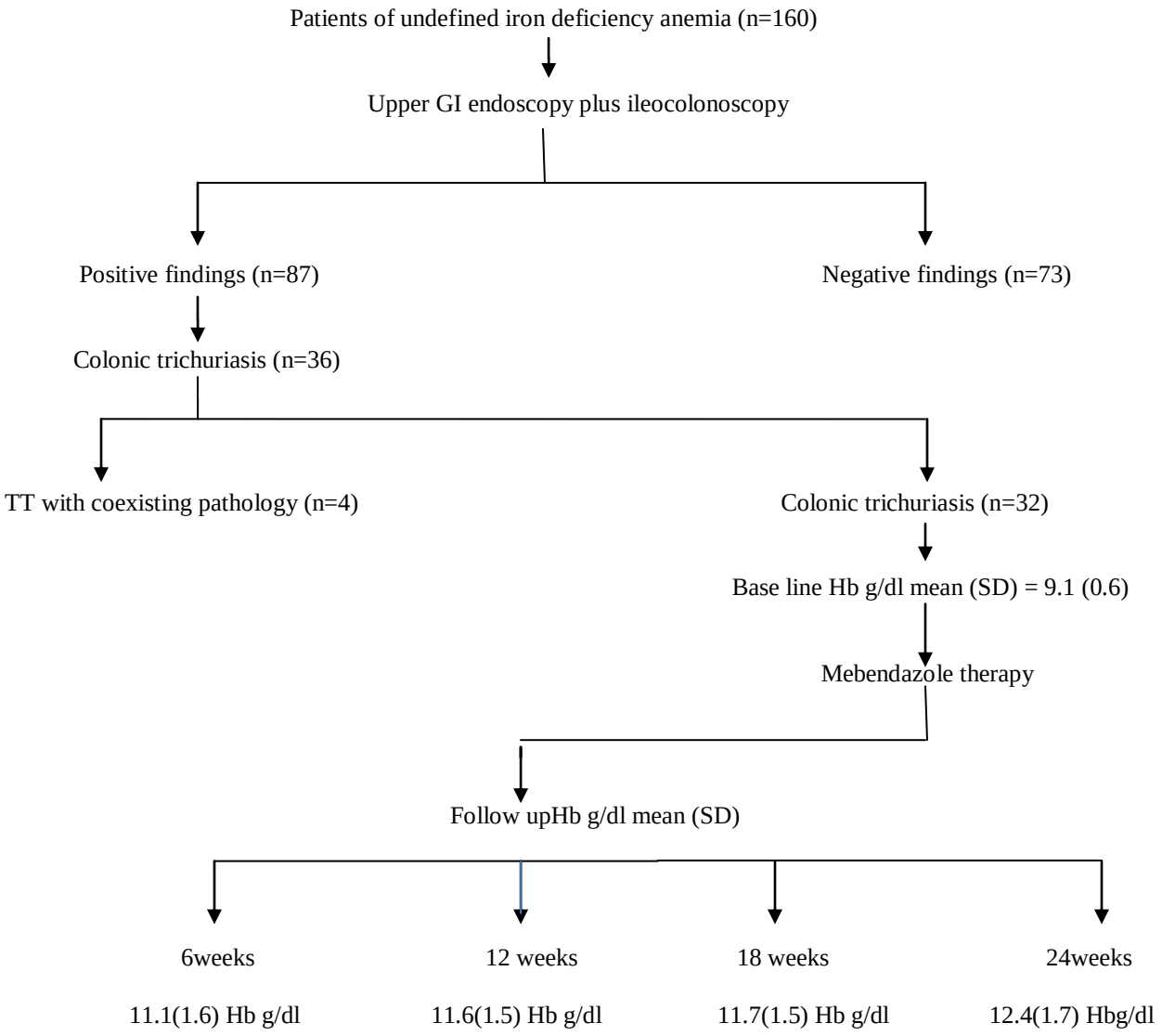
S.No.	Parameters	No. (%)
1.	Age, mean (SD*)	49 (13.5)
2.	Sex, males.	20 (62.5)
3.	Rural	22 (68.7)
4.	Hemoglobin (g/dl) mean (SD*)	9.1(6.1)
5.	Peripheral eosinophil count.	5 (15.6)
6.	Mean cell volume (fL) mean (SD*).	78.4(5.2)
7.	Fecal Occult Blood Test Positivity	19 (52.8)
8	Stool for ova of *Trichuris trichiura*	26(81.2)
9	Stool for ova of *Trichuris trichiura* plus *Ascaris*	8 (25)
10	Distribution of *Trichuris trichiura* infection	
	Cecum	8(25)
	Cecum and ascending colon	23(71.8)
	Cecum, ascending colon, transverse colon	1(3.1)

SD*: Standard Deviation; fL: Femtoliters

Table 4: Effect of Mebendazole therapy on hemoglobin in patients of colonic *Trichuris trichiura* infection.

Duration	Mean (SD) Hb g/dl	P Value
Baseline	9.1(0.6)	
6 weeks (n=32)	11.1(1.6)	0.02
12 weeks (n=32)	11.6(1.5)	0.001
18 weeks (n=28)	11.7(1.5)	0.02
24 weeks (n=26)	12.4(1.7)	0.02

Figure 1: Algorithm describing outcome of treatment of patients with iron deficiency anemia.



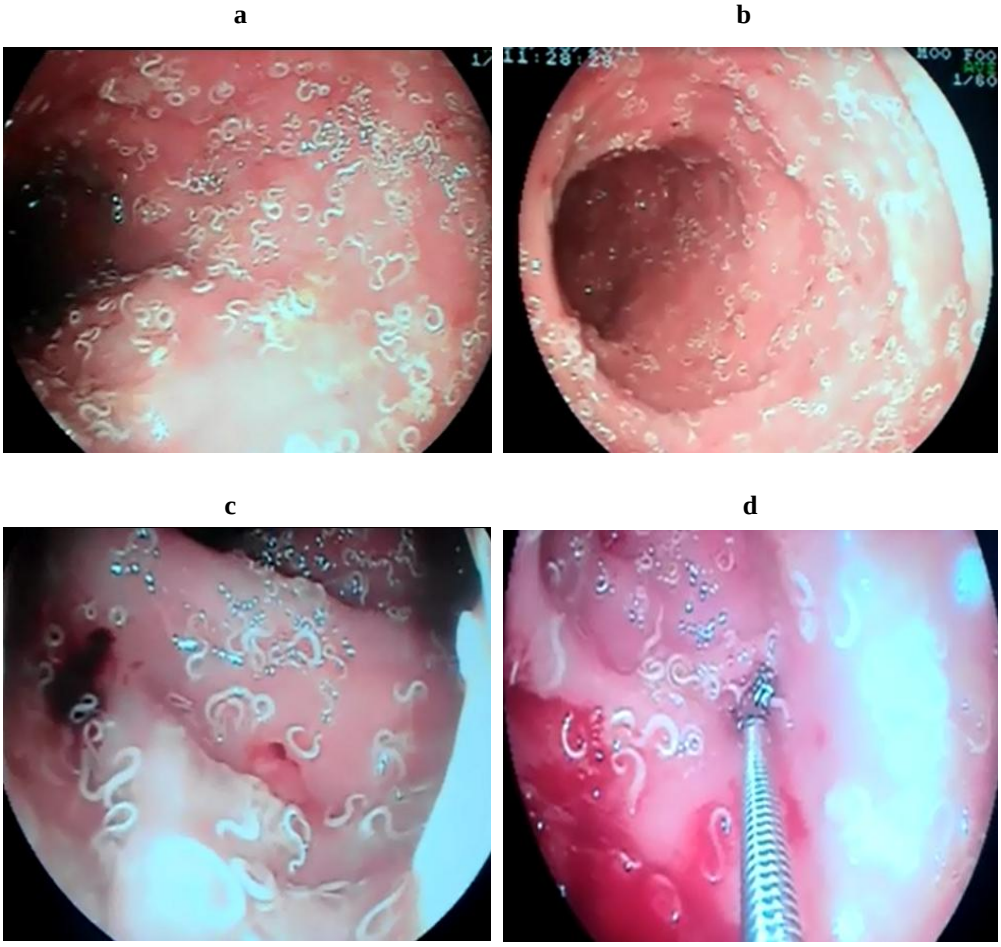
SD: Standard deviation

Discussion

This study reveals that TT infection is common finding while evaluating GI causes of IDA in Kashmir province which is an endemic zone for various parasitic infections (Wani et al., 2007a; Khuroo 1996) and can manifest as IDA with occult GI blood loss without abdominal symptoms and also highlights the link between IDA and TT infection, as there was significant improvement in hemoglobin levels after eradication of TT with mebendazole therapy.

In this study we evaluated 160 cases of IDA in adult male and post-menopausal female population. Upper GI endoscopy and ileo colonoscopy revealed positive findings in 87/160 (54.3%) patients.TT infection was the most common finding, seen in 36(22.5%) patients, followed by carcinoma stomach. Stool examination revealed ova of TT in only 26/32(81.2%) patients. This could be due to day-to-day variation in helminth egg excretion and single stool examination, although sensitivity estimates of the Kato-Katz technique for one stool sample were 96.9% and 91.4% for *A. lumbricoids* and TT, respectively (Tarafder et al., 2010).

Figure 2 (a, b, c, d)**:** Colonoscopic images of colonic *Trichuris trichiura*



Among 36 cases of TT infection with IDA, FOBT positivity was seen in 19(52.8%) patients suggesting asymptomatic occult blood loss. TT related colitis was seen in the form of erythema, edema and superficial ulceration with fresh blood at the site of worm infestations. In some patients there were multiple TT burrowing through the mucosa near the ulcers. Despite presence of colitis these patients did not have GI symptoms.

Mebendazole effectively eradicated TT infection with subsequent resolution of colitis in all patients which was evidenced by stool examination and repeat colonoscopy 4 weeks after the treatment. Overall there was significant and progressive rise in hemoglobin level at 6, 12, 18 and 24 weeks following eradication of TT infection. Improvement in anemia indicates that iron deficiency could be sole manifestation of TT infection in adult population.

This study reveals that in adult population, TT infection with associated colitis can cause severe IDA due to asymptomatic occult blood loss, as was seen in19 (52.7%) patients who had FOBT positivity. In this study we did not see any clinical feature suggesting TDS which is reported mainly in children despite the fact that these patients had TT infection with TT associated colitis. There are no large studies regarding TT infection with TT associated colitis presenting as occult blood loss with IDA in adult population. In an earlier study, in the same endemic zone, Khuroo et al (2010), reported 10 patients of TDS among 80 cases of IDA. Nine out of these 10 patients were asymptomatic while as only one had abdominal symptoms with hematochezia and concluded that severe TT infection should be considered as a differential diagnosis of progressive chronic iron deficiency and occult blood loss. Although TDS is a well-known entity mainly described in children with heavy work load, its occurrence in adults is not common, rather these patients have asymptomatic colitis which adds to occult blood loss, besides TT infection leading to iron deficiency.

We excluded other GI causes of anemia by imaging the small bowel, anti endomysial antibody estimation and jejunal biopsy which was negative in all these patients except two cases: one of small bowel gastro intestinal stromal tumor (GIST) and the other one of jejunal adenocarcinoma which were diagnosed by 64 slice multiphase CT enterography. TT infection should be kept as a possible cause during GI evaluation of iron deficiency anemia and treated first before subjecting these patients to battery of tests like capsule endoscopy and CT enterography.

TT lives preferentially in cecum, although in heavy infections it can be seen throughout colon and rectum. The adult parasite leads both an intracellular and an extra cellular existence with anterior end embedded in epithelial tunnels within the intestinal mucosa and posterior end located in the lumen. Inflammation at the site of attachment from large number of TT results in colitis. Long standing colitis produces a clinical disorder that resembles inflammatory bowel disease including chronic abdominal pain and diarrhea as well as sequelae of impaired growth (Crompton 1998).

In our study 19/36 (52.7 %) patients of TT infection were positive for FOBT. The data regarding FOBT positivity in relation to colonic trichuriasis is scanty. Previous studies reveal that there is no co relation between light TT infection and FOBT positivity, using guaiac test, (Raj 1999) however this could be due to relatively low sensitivity and specificity of this conventional test. Immunochemical tests for FOBT detection have been demonstrated to be more sensitive and specific than the traditional technique (Allison et al., 1996).

In TT infection the severity of mechanical damage to epithelium of the colon is apparently related to worm burden. Adult worms are embedded in the colonic mucosa with their piercing stylets and feed on host blood (Layrisse 1967). Blood loss is further compounded by associated severe colitis. The amount of fecal blood loss from TT is about 5 micro liter per worm/day which is 6-10 times and 30-50 time less than with *Necator americanus* and *Ancyclostoma duodenale* respectively (Sanjur and Nesheim 1992).The association between TT infection with decreased hemoglobin concentration and IDA is evidenced when infection intensifies greater than 5000 eggs per gram and 10000 eggs /gm of stool respectively (Elliott 2006)

In summary this study revealed that TT infection with TT associated colitis is a common finding among patients of IDA referred for GI evaluation in endemic zone of TT and can solely manifest as severe IDA for which eradication of parasite relieves their anemia. This is in contrast to children where heavy infections can present as TDS. Severe colonic TT infection should be kept as a possible cause while evaluating GI causes of IDA especially in an endemic zone. These patients should be treated first to look for improvement in their anemia before they are subjected to other battery of tests. The best way to prevent TT infection is by improving personal hygiene such as washing hands and by proper disposal of human feces, avoiding fecal contamination of food, avoiding crops fertilized with night soil.

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