

Review article

Helminthiasis in India and Recent Trends in Treatment Modalities among Pregnant Women

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Abstract:

Helminthes are multicellular organisms that infecting very large number of humans and cause a broad range of diseases. Over 1 billion people are infected with filarial nematodes, flukes and tapeworms. They are even a greater problem in domestic animals. Many drugs, which are directed against a number of different targets, are available to treat helminthic infections. In the developing world, the main goal is control of infection, with elimination of most parasites controlling disease symptoms and decreasing the transmission of infection. In other cases, complete elimination of parasites is the goal of therapy, although this goal can be challenging with certain helminthic infections, due to both limited efficacy of drugs and frequent reinfection after therapy in some endemic areas.¹

Keywords: Anemia, Pruritus, Cysticercos, Pregnancy.

Introduction:

The helminthes (from the Greek meaning "worm") are higher, multicellular organisms possessing three germ layers and exhibit a bilateral symmetry. It originally meant to refer to only intestinal worms, but also includes tissue parasites as well as many free-living species. These are metazoa.²

Global distribution and prevalence^{10, 14, 28}

Global distribution includes wide numbers like more than 1.5 billion people, or 24% of the world's population, are infected with soil-transmitted helminthic infections. Helminthic infections are widely distributed in tropical and subtropical areas, with the high numbers of infection occurring in sub-Saharan Africa, the Americas, China and East Asia.

Over 270 million children of preschool-age and over 600 million school-age children live in areas where these parasites are highly transmitted, and are in

constant need of treatment and preventive interventions.

Causes of helminthiasis:

The primary cause of is the result of transmission. This transmission is of an infectious disease. Some subtypes of this disease are contagious which spread easily between people, while other subtypes are infectious that are transmitted by a pathogenic organism.

Epidemiology:

Worm infestations (helminthiasis) is one of the major global public health problems which affects more than 1 billion people all over the world, its prevalence being highest in tropical regions, the rate of simultaneous infection with more than one type of helminthes is common eg. roundworm & hookworm. Some other factors like poverty, illiteracy, lack of adequate sanitary facilities and of pure water supply, besides environmental conditions peculiar to tropics,

, eradication of this problem concerning helminthes infestation is very difficult.²

Classification³

Helminths are classified into 2 major phylla:

1. *Phyllum Nemahelminthes*-Nematodes (Intestinal and Somatic)
2. *Phyllum Platyhelminthes*: Cestodes and Trematodes (Flat worms)

TABLE 1: The major helminthic infections and provides a guide to the drug of choice and alternative drugs for each infection.

HELMINTH	COMMON NAME	DRUG OF CHOICE	ALTERNATE DRUGS
1.NEMATODES (INTESTINAL)			
<i>Ascaris lumbricoides</i>	Roundworm	Albendazole Mebendazole	Pyrantelpamoate Piperazine
<i>Ancylostoma Duodenale</i>	Hookworm	Albendazole Mebendazole	Pyrantelpamoate Thiabendazole
<i>Enterobius Vermicularis</i>	Pinworm	Albendazole Mebendazole	Pyrantelpamoate Piperazine
<i>Trichuris Trichura</i>	Whipworm	Mebendazole	Albendazole Thiabendazole
<i>Strongyloides Stercoralis</i>	Threadworm	Ivermectin	Thiabendazole Albendazole
<i>Trichinella Spiralis</i>	Pork Roundworm	Albendazole	Thiabendazole Mebendazole
2.NEMATODES (SOMATIC)			
<i>Wucheria Bancrofti</i>	Lymphatic filarial worm	Diethylcarbamazine Ivermectin	Ivermectin
<i>Onchocerca Volvulus</i>	Oculodermal filarial worm	Ivermectin	Diethylcarbamazine
<i>Dracuncula Medinensis</i>	Guinea worm	Metronidazole	Mebendazole
3.CESTODES			
<i>Taenia Saginata</i>	Beef Tapeworm	Praziquantel	Niclosamide
<i>Taenia Solium</i>	Pork tapeworm	Praziquantel	Niclosamide
<i>Cysticercus Cellulose</i>	Larva of taenia solium	Albendazole	Praziquantel
<i>Diphyllobothrium Latum</i>	Fish Tapeworm	Praziquantel	Niclosamide
<i>Hymenolepsis Nana</i>	Dwarf Tapeworm	Praziquantel	Niclosamide
<i>Echinococcus Granulosus</i>	Hydatid Larva	Albendazole	Mebendazole

4.TREMATODES			
Schistosoma hematobium	Blood Flukes	Praziquantel	Metrifonate
Schistosoma Mansoni	Blood Flukes		Oxamniquine
Schistosoma Japonicum	Blood Flukes		--
FLUKES			
Fasciola Hepatica	Liver Fluke	Praziquantel	Niclosamide
Clonorchis Sinensis	Chinese liver fluke		
Fasciola Busci	GastoIntestinal fluke		
Paragonimus Skrjamini	Lung Fluke		

TABLE 2A⁴: Lists of Morphological patterns of various phyla:

CHARACTER	CESTODE	TREMATODE	NEMATODE
Shape	Tape-like	Leaf-like	Cylindrical and elongated
Segmentation of the body	Segmented	Unsegmented	Unsegmented
Sexes	Hermaphrodite (Monoecious)	Hermaphrodite except schistosoma species	Separate (diecious)
Cephalic ends	Has suckers (some species have hooks)	Has suckers,doesnot have hooks	Both suckers and hooks are absent
Alimentary anal canal	Absent	Present, Incomplete (no anus)	Present,complete
Coelom (body cavity)	Absent	Absent	Present

TABLE 2B⁴: Difference between Taenia Saginata and Solium

PARTS	TAENIA SAGINATA	TAENIA SOLIUM
1. Scolex	4 suckers, no hooks, rhomboid	4 suckers, rostellum with hooks, globular
2. Mature segment	Ovary:2 large lobes Testes:Small follicular, 300-400	Ovary:2large and 1 small lobe Testes:small follicular, 150-200
3. Gravid segment	Uterine branches: 15 – 30 [more than 13] present on each side, vaginal sphincter PRESENT.	Uterine branches: 7-12 (upto13) on each side, vaginal sphincter ABSENT.
4. Egg	Acid-fast~	Non-acid fast

~ Using Ziehl - Nielsen technique

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TABLE 3^{1, 2, and 4}: CLINICAL FEATURES & DIAGNOSIS OF HELMINTHES [See Table-3]

WORM	TRANSMISSION	CLINICAL PICTURE AND DIAGNOSIS	COMPLICATION	TREATMENT OF COMPLICATION
Ascaris (Roundworm)	Oral	Non productive cough, substernal discomfort and dyspnea, fever, eosinophilic pneumonia-LOEFFLERS PNEUMONIA Dx: eosinophilia, eggs in faecal sample	Small intestinal obstruction	Bowel rest and removing source of obstruction. Exploratory Laprotomy.
Ancylostoma and Necator (hookworm)	Percutaneous	Cutaneous larva migrans-larvae produce pruritic maculopapular dermatitis. They migrate and produce serpiginous itchy traits in subcutaneous tissue. Dx: Microcytic hypochromic anemia.	Iron deficiency anaemia, malnutrition from protein loss.	Iron supplements and in severe cases blood transfusion. Parenteral nutrition
Enterobius Vermicularis (pinworm)	Oral	Perianal pruritis Dx: Perianal swab method NIH swab	Rarely vulvo-vaginitis, salphingitis and peritoneal granulomas	Anti-TB drugs and surgical approach.
Trichuris trichura (whipworm)	Oral	Trichuriasis -abdominal pain, bloody or mucoid diarrheoa Dx: Barrel shaped eggs in faeces.	Haemorrhagiccoliticaemia, malnutrition and growth retardation.	Steroid therapy. Iron supplements and in severe cases blood transfusion. Parenteral nutrition
Strongyloides (Threadworm)	Percutaneous autoinfection	Urticaria, larva currents migrans. Larva produce pruritic, raised erythematous lesion. Dx: Rhabditiform larvae in faeces.	Duodenitis, hyperinfection in immunocompromised patients.	Supportive therapy e.g. Intravenous, blood transfusion, mechanical ventilation. Pruritic dermal manifestations

				antihistaminics. Wheezing – beta agonist, leukotriene's.
Wuchereria Bancrofti or Brugiamalayi (Lymphatic filariasis)	Mosquito vector	Elephantiasis-non-pitting edema (brawny edema), filarial fever Dx: Microfilaria in blood, serology, antigen capture	Lymphangiomas of scrotum and spermatic retroperitoneal lymphadenitis.	Combination of steroids, anti-inflammatory. Single dose Ivermectin Surgical excision.
Onchocerca volvulus (river blindness)	Black fly vector	Itchiness, persistent skin nodules, leopard skin-loose hypo/ hyperpigmented. Dx: skin nodules in adults, microfilaria in skin biopsy(snips).	Punctate and sclerosing keratitis, iridocyclitis.	Penetrating keratoplasty Glucocorticoid, steroids, cycloplegics like atropine & homatropine. Antimetabolites like methotrexate. Mectizan treatment has beneficial effects.
Onchocerca Loa(eyeworm)	Horse fly vector	Allergic reactions from swellings called calabar swellings. Worms migrate to subconjunctival tissue (African eye worm) Dx: blood examination for microfilaria, eosinophilia.	Nephropathy, encephalopathy, cardiomyopathy	Angiotensin converting enzyme 1 inhibitor.
Dracuncula medinensis <i>(ERADICATED)</i>	Cyclops vector	Rash, diarrhea, nausea, dizziness, blister, ulcer Dx: Larvae can be demonstrated in exposure to water. ELISA.	Abscess, cellulitis, tetany.	Removal of worms: 1.Surgical removal 2. Forced parturition.
Taenia saginata (beef tapeworm)	Raw beef	Vague abdominal discomfort, nausea, weakness, weight loss Dx: Protoglotids or eggs in feces. Perianal swab method(NIH swab)	Appendicitis, Intestinal obstruction.	Appendectomy Median laparotomy Mechanical eradication of taenia.

		Cellophane swab method.		
Taenia solium(pork tapeworm)	Raw pork	Abdominal discomfort and bowel disturbances. Human cysticercosis-produces palpable nodules in subcutaneous tissue and cystic nodules in muscle. Dx: CT-more sensitive in identifying calcified lesions. CSF studies-increased proteins, reduced sugar and pleocytosis. MRI-in detecting small cystic lesions.	Neurological manifestations seizures and focal neurological deficits develop due to inflammation and production of space occupying lesions (SOLs) hydrocephalus and increased intracranial tension.	Anticonvulsants, Steroid therapy. Ventricular shunt.
Cysticercus cellulose	Larvae of taenia solium	Same as above	Same as above	Same as above
Diphyllobothrium Latum	Fish tapeworm	Asymptomatic Dx: Megaloblastic anaemia, detection of characteristic eggs.	Intestinal obstruction, cholangitis.	Laparotomy
Hymenolepis nana	Dwarf tapeworm	Anorexia, abdominal pain, diarrhoea Dx: finding eggs in faeces.	-	-
Echinococcus granulosus	Hydatid larva	Hydatid cyst disease. Common site of localization is LIVER(65%) followed by lung(25)% Abdominal pain/palpable swelling Leakage of hydatid fluid-fever, pruritis, urticaria. Dx: Eosinophilia X-ray or Ultrasound studies Serology diagnosis achieved with Indirect Haemagglutination test, Fluorescent antibody test -	Obstructive jaundice CNS-SOLs Heart-conduction defects and pericarditis.	Cystectomy

		Immuno Electrophoresis & ELISA. Detection of antibodies against Ag 5(arc 5) is most specific.		
Schistosoma hematobium	Blood fluke	Urinary Schistosomiasis/ Bilhaziasis. Cerarial dermatitis- Swimmer stitch, fever, cough, lymphadenopathy, liver and spleen enlargement- Katayama fever, dysuria. Dx: haematuria, schistosomahematobium in urine. Tests: 'Cercarian-Huller' reaction, IHA, IFA, ELISA, RIA.	Hydroureter, Hydronephrosis, Squamous cell carcinoma of bladder.	Urethral, Cauterization ureteral stent placement.
Schistosoma Mansoni	Blood fluke	Intestinal bilharziasis (schistosomal dysentery, schistosomiasis Mansoni). Eggs deposited in the sigmoido-rectal plexus symptoms mainly related to large intestine. Dx: Characteristic eggs found in faeces. Proctoscopic Biopsy is useful.	Hepato-splenomegaly and portal hypertension.	Variceal bleeding- Propranolol, Isosorbide mononitrate. TIPS (transjugular intrahepatic portosystemic shunting)
Schistosoma japonicum	Blood fluke	Oriental schistosomiasis/ Katayama disease. Dysentery intermittently for many years. Chronic illness-liver involved-periportal cirrhosis- SYMMERS PIPE-STEM FIBROSIS develops. Dx: Characteristic eggs found in the faeces.	Esophageal varices, gastrointestinal bleeding and splenomegaly. Space occupying lesion, granuloma.	Variceal bleeding- propranolol, Isosorbide mononitrate. TIPS (transjugular intrahepatic portosystemic shunting). Active variceal bleeding- vasoactive drugs somatostatin, ooctretotide.
Fasciola hepatica	Liver fluke	Liver produce fascioliasis-fever, hepatomegaly, abdominal pain.	Cholecystitis, Cholelithiasis.	Cholecystectomy.

		Dx: eosinophilia, operculated eggs in faeces. Enterotest-demonstration of eggs in duodenum. ELISA, gel-diffusion test.		
Clonorchissinensis	Chinese liver fluke	Causes clonorchiasis. Early stages-fever, epigastric pain, diarrhoea, tender hepatomegaly. Heavy infection-cholangitis, biliary cirrhosis & obstructive jaundice. Dx: Operculated eggs in faeces or bile.	Malignant changes in bile duct, liver and pancreas.	Tumours can be fully resected Liver transplantation Adjuvant chemotherapy and radiation therapy.
Fasciola buski	Giant intestinal fluke	Causes fasciolopsiasis - ulcerations and local inflammation at site of attachment. Diarrhoea, fever & abdominal pain. Dx: Characteristic operculated eggs in faeces.	Ascites and Anasarca.	Salt restriction, diuretics (Spironolactone), paracentesis, TIPS & peritoneovenous shunt.
Paragonimus westermani/ Skrjamini	Lung fluke	Causes paragonimiasis. Early stages – fever, hepatosplenomegaly, cough, pleural effusion, and pneumothorax result due to migrating worms. Dx: Eggs in sputum / faeces. X-ray – “SOAP BUBBLE “ calcification Serological tests – CFT & IHA.	Brain involvement serious complication. Presents as jacksonian epilepsy or SOLs.	Avoid alcohol, caffeine, plenty of rest. Anticonvulsant medications: Carbamazepine, Phenytoin, Fosphenytoin, Phenobarbitone, gabapentine.

Helminthic treatment in pregnancy: ^{1,2,6}

Intestinal helminthes infections occurring during pregnancy are associated with adverse outcomes that includes conditions like low birth weight and prenatal mortality. Pregnant women are at high risk of nutritional deficiencies caused by helminthic infection. There are various studies showing reduction in severity of infection and reduction of anaemia with the help of deworming and iron supplementations among pregnant women and this has also lead to positive birth outcomes. Most common is Hookworm which is contracted directly through the soles of feet, usually around open areas of defecation and latrines, when people do not wear shoes or do not cover foods. Schistosomiasis is highly contracted by swimming or wading in contaminated water².

Immune response during pregnancy and during chronic helminthes infections shift toward Type 2 immunity.^(1,3-6) There occurs an activation and also expansion of CD4+Th2 cells (including eosinophils, mast cells, basophils and the antibody isotypes IgG1, IgG4 and IgE). Moreover, there is production of cytokines such as IL ^(4, 5, 9, 10, 13, 20) and levels of TGF-beta increases. Furthermore, there is an increased activation and expansion of cytotoxic CD8+T cells, NK cells, neutrophils and macrophages during infection particularly with intracellular pathogens ^(4,13). Hence, helminthic infections during pregnancy

lead to a weaker response to the infections and require strong Th1 immune response¹.

Drugs like Albendazole a benzimidazole can be used in pregnancy to treat intestinal roundworms, like *Ancylostoma duodenale*, *Necator Americanus*, *Ascaris Lumbricoides*. Ivermectin an anthelmintic medication, is a gamma-aminobutyric acid (GABA) agonist metabolized by the liver (cytochrome P₄₅₀ 3A4) is used to treat invasive roundworms such as *Strongyloides Stercoralis*, *Onchocerca Volvulus*, *Wuchereria Bancrofti* and *Loa Loa*⁶.

Another effective drug Metronidazole is a Nitromidazole derivative used as an antimicrobial agent for anaerobic infections as well as for treatment of intestinal protozoa, such as *Giardia*⁶.

Diethylcarbamazine (DEC) can be used to treat disease caused by trematodes, including lymphatic filariasis; however a very close monitoring is required in areas with overlapping onchocerciasis and loasis⁶.

Praziquantel which again can be given in pregnancy but caution is required and is better avoided in pregnancy as it is metabolized by the liver and has drug-drug interactions with cytochrome P₄₅₀ inducers such as Rifampicin. In pregnancy if required it is used to treat infection with invasive flatworms such as Schistosomiasis and Intestinal flatworms such as *Taenia solium*.

TABLE 4²: Percentage of pregnant women responding to the following drugs :

DRUGS	RESPONSE OF PREGNANT WOMEN TO THESE DRUGS
Albendazole	7%
Ivermectin	6%
Metronidazole	7%
Diethylcarbamazine	3%
Praziquantel	77%

Drugs contraindicated in pregnancy^{1,2,6}:

1. Praziquantel

MOA: Increased muscular activity followed by contraction and paralysis of the worms.

Causes ABORTION.

2. Pyrantel Pamoate

MOA: Depolarising neuromuscular blocking agent causing paralysis of worms.

3. Piperazine

MOA: Blocks acetylcholine at myoneuronal junction causing flaccid paralysis of worms.

4. Metrifonate is a OrganoPhosporus compound

MOA: Cholinesterase inhibition.

5. Mebendazole is TERATOGENIC Causes Convulsions in infants.

NOTE : If pregnant women need deworming it can be done after delivery. Deworming in pregnancy need not be an urgent decision.

Conclusion:

Helminthiasis is a leading cause of anaemia in India especially in children and women, of reproductive age group. Major way of averting this Deadly infection is by deworming method carried out in highly sensitive age group in children and women every 6 months. Also, good sanitation and hygiene methods in cooking, eating, washing hands is important in prevention of helminthiasis especially roundworm and hookworm.

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