INTRODUCTION

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A parasite is an organism that lives in or on, and takes its nourishment from another organism. [1] The intestinal parasite is a parasite that lives in the gastrointestinal tract. The intestinal parasites include both helminthes and protozoa. Helminthes are worms such as tapeworms, pinworms and roundworms. All these worms can live, but typically not reproduce, inside the human intestine.[2]

In contrast to worms, which are composed of many cells, protozoa are single celled organisms that can multiply inside the body. Examples of protozoa that live in the intestinal tract are *Giardia lamblia* and *Cryptosporidium*.[2]

Parasitic infestation occurs when a parasite inhabit another organism in numbers or quantities large enough to be harmful or threatening.[1]

Worldwide, the children aged 6-12 years represent a big sector of population (about 25% of total population). They are considered as one of the vulnerable groups of population. They are more liable to communicable diseases including parasitic infestations which are attributed mainly to their low level of immunity and lack of awareness of health practices.[3]

Parasitic infestations have a high prevalence rates throughout the world and it's estimated that more than three billion people are infected with intestinal parasites in the world in 2009.[4] They are more common and severe in school children in poorer communities and pose a serious threat on the physical and cognitive development of children. Almost 70% of the disease burden of intestinal parasitic infestation in whole population is estimated to be preventable by treating school children alone.[5]

Types of intestinal parasites

Several types of intestinal parasites have been found, which find their way into the human body via multiple exposure routes. [6] Although the worms are almost similar in form, they can cause varying illnesses and are treated with different medicines.[7]

The first type is roundworm (nematodes) which usually resides in the small intestine and enters the body through ingestion with contaminated food or water, unwashed hands and contact with contaminated objects. [8] The most commonly isolated nematodes are *Ascaris lumbricoids*, hookworm and pinworm. [9] Pinworm and some of the roundworms that parasitize the human intestinal tract, and that on occasion may be present in the feces, are large enough to be seen with naked eye. Adult pinworms measure about 1 cm in length and *Ascaris lumbricoides* may attain lengths of 30 cm or more. [10]

Ascaris lumbricoides is transmitted to humans by ingestion of embryonated eggs, [11] while hookworm is transmitted to humans by invasion of the filariform larva through the intact skin, where it migrates to the lungs, and then breaks out into alveolar capillaries, up the trachea and into the pharynx, then swallowed into the small intestine.[12]

The adult hookworms inhabit most commonly in the caecum,[12] while the adult pinworms inhabit caecum, appendix and adjacent portions of the ascending colon. [13]The female pinworm migrates down the colon to put its eggs onto the peri-anal and perineal skin and then dies causing peri-anal itching, the infection occurs by direct fecal or auto-infection, exposure to viable eggs on soil, bed linen and other environmental objects.[13] Children who suck their fingers are more likely to be infected. It has been suggested that retro-infection may occur after hatching on the anal mucosa.[14]


Fig. (1): *Ascaris* worm may reach 16 inches in length as shown.[10]

The second type is tapeworm (cestodes): which lives in the intestine and enters the body through eating raw or undercooked beef.[15] The most commonly isolated cestodes are *Taenia saginata, Taenia solium* and *Hymenolipes nana*.[15] The adult tapeworm lives only in the small intestine of humans.[15]

Cattle are the intermediate host for *T. saginata*, while pigs are the intermediate host for *T. solium*, which is the most important human tapeworm, because it is the only intestinal parasite responsible for human cysticercosis. [16] Its importance resides in the capacity of the embryos to traverse the intestinal wall and lodge in muscle masses or in the brain, where they develop into larval stage of the parasite.[17] Human neurocysticercosis is the most serious disease caused by this parasite.[18]

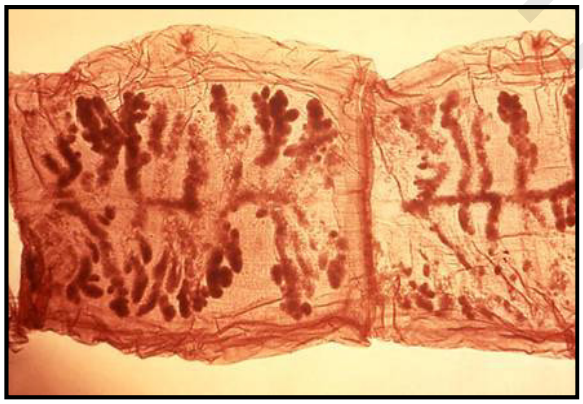
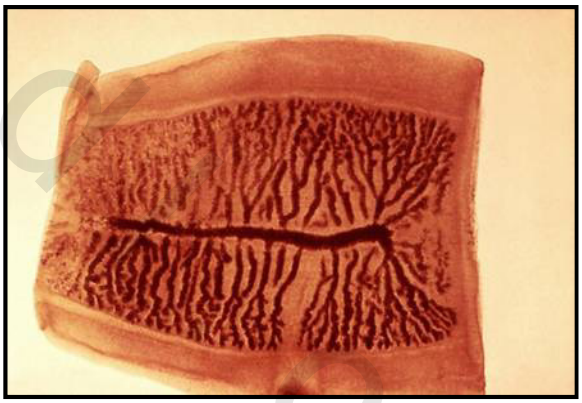

Fig. (2): Segment of *T. solium.*[15]

Fig. (3): Segment of *T. saginata*.[15]

The third type is flukes (trematodes): they enter the human body through ingestion of their metacircaria.[19] The most common examples are Fasciola (plants are the intermediate host) and Paragonimus (crayfish are the intermediate host).[20]

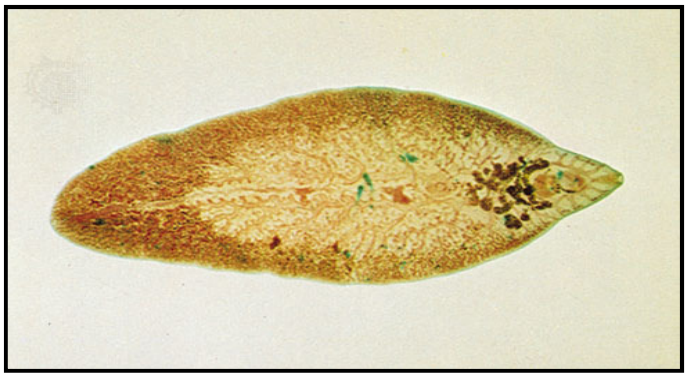

Fig. (4): *Fasciola hepatica.*[20]

The fourth type is protozoa which live in the intestine, bladder, rectum, liver, spleen, lungs or veins.[21] The quadrinucleate cyst, the infectious form of the parasite, is resistant to chlorination and gastric acidity.[22] Infection occurs due to fecal-oral spread with focally contaminated food or water. Excystation of the cysts occurs in the intestine where the cyst forms eight trophozoites which can colonize or invade the large bowel.[23] Hepatic abscess may occur by *Entamoeba histolytica* due to migration of the organism via the portal vein.[24]

Disruption of the intestinal surface by protozoal infestation can reduce the body's ability to absorb nutrients from food passing through the intestine, if not absorbed, nutrients remain in the intestinal tract, where they may contribute to diarrhea, cramps, and gas associated with protozoa infestation. The protozoa may cause food to move more quickly through the intestine, which can contribute to diarrhea. [25]

The most common types of protozoa which infest humans are Entamoeba histolytica and Giardia lamblia.[26]

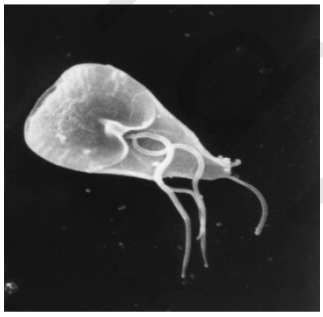

Fig. (5): *Giardia* cyst.[26]

Magnitude of the problem

Globally, the neglected intestinal parasitic infestations such as soil-transmitted helminthes and protozoa infections have been recognized as one of the most significant causes of illnesses and diseases specially in developing communities.[27] In 2004, the average prevalence rate of intestinal parasitic infestations among children was estimated to be 50% in developed world and almost 95% in developing countries.[28]

Of these illnesses, infections by soil-transmitted helminthes have been increasingly recognized as an important public health problem and most prevalent form of intestinal parasitic infestations.[29] Soil-transmitted helminthes infestations caused by *Ascaris lumbricoids, Trichuris trichura* and hookworm (Necator *americanus* and *Anchylostoma doudenale*) are most significant in poor people.[30]

Worldwide, *Ascaris lumbricoides*, *Trichuris trichura* and hookworm were estimated to infect 1.4, 1 and 1.2 billion people respectively in 2001, representing about 25% of the world's population. [31] On the other hand, the prevalence of *Giardia lamblia* ranges from 2%-7% in developed countries and 20%-60% in developing countries in the same year.[32] Calculations in 2002 were suggested that more than 800 million children were infected with *Ascaris*, 550 million children by *Trichuris trichura* and 700 million children by hookworm worldwide.[33]

Approximately one third of children all over the world were infected with at least one species of soil-transmitted helminthes in 2006,[34] and resulting in up to 65000 deaths among children annually.[35] As regard *Ascaris* infection, there is an increased risk of intestinal obstruction with increasing worm burdens and these occur in 3-5% of cases with *Ascaris* infection in endemic countries. This complication is associated with mortality of 17% of cases of intestinal obstruction due to *Ascaris* infection.[36]

Schistosomiasis is one of the world's major health problems. In 2003, the world health organization estimated that at least 110 million children in 74 countries were infected and at least 300 million more at risk.[37] In endemic areas, the highest prevalence and intensity of infection occurs in 10-12 years of age.[38] *S. mansoni* is endemic through Africa and Middle East.[39]

With regards to intestinal protozoal infections, giardiasis caused by *Giardia doudenalis*, is the most predominant protozoa infection affecting approximately 200 million people worldwide in 2004, half of them were children.[40] In the USA in 2000, *Giardia* was found in 4-7% of the examined stool specimens of school children, and it causes as many as 2.5 million infections per year.[41] In developing regions, over 60% of children become infected with *Giardia lamblia.*[42]

Although many of children infected with *Giardia lamblia* are asymptomatic, they can introduce the organism to family members and contribute to high endemic rates in the community.[43]

Amoebiasis caused by *Entamoeba histolytica* is another important pathogenic protozoon affecting approximately 90 million children in 2005 worldwide, of whom 20000 to 50000 children succumbed to death annually.[44] The largest burden of disease caused by *E. histolytica* infection was in Central and South America, Africa and India.[45]

Metastatic foci of infection such as amebic liver abscess were found to be equally distributed among boys and girls. The severity of the disease increases among children, pregnant women and malnourished persons.[46]

The opportunistic protozoa, *Cryptosporidium sp.* has also emerged as an important cause of diarrheal illnesses worldwide particularly in young children and immunocompromised patients with a prevalence of 4% among children in developed countries and 3-4 times more frequent in developing countries.[47]

It was found that 56% of malnourished children in Ethiopia were infested with one or more intestinal parasites in the year 2009.[48] Seventy-eight percent of malnourished children were infected with intestinal parasites in Mexico in2004.[49] Severe anemia was found in 29% of children infected with hookworm in sub-Saharan Africa in *2009*.[50] Also, it was found that high prevalence of both malnutrition and anemia were observed in intestinally infested children in Zanzibar in the year 2008 (50% and 75% respectively).[51] Parasitic infections affect the mortality and quality of life of school-aged children.[52]

In Egypt, several surveys had been done to determine the prevalence of intestinal parasitic infestations among children. One of these surveys was in 2004 in a rural area in Souhag; the overall percentage of intestinal parasitic infestations among school children was 38.5%.[53] Another survey had been done in 2001 in Malamis village in Lower Egypt and revealed that 31.9% of school children were infected by intestinal parasites.[54] In 2003, another survey had been done in Tamouh village in Lower Egypt, which revealed that 60.2% of school children were infected with one or more intestinal parasites.[55] In a rural area of Qalubia, another survey had been done in 2003 that revealed that 40.4% of children aged 5-11 years in this area were infected with intestinal parasites.[56]

Risk factors of intestinal parasitic infestations in children

The set of environmental, social and behavioral predictors of intestinal parasitic infestations are not always consistent across studies, crowding, poor education of mothers, open defecation, inadequate water supply, poverty, poor nutritional status, use of human biosolids for fertilizers and irrigation, neglecting hand washing before eating, pig ownership and consumption of raw pork and raw water plants are often reported among infected school children.[57]

As one example, in India, a survey of households on tea plantations and revealed five significant risk factors of *Ascaris* prevalence: age (children), house-hold crowding (more than 6 people per household), outdoor defecation, ownership of pigs and low level of education.[58]

In general, the associated risk factors of intestinal parasitic infestations among children are classified into main four groups which are environmental, sanitary, socioeconomic and behavioral risk factors.[59]

Environmental factors were related to living background. Living in the rural regions itself is considered as a major risk factor of intestinal parasitic infestations. It could be attributed to the other risk factors (sanitary, socioeconomic and behavioral factors).[60]

Sanitary risk factors: Contaminated water is a common source of infection by many intestinal parasites.[8] *Giardia* is one of the most common agents identified in water-borne outbreaks of diarrhea. [61] Several factors contribute to frequency of water-transmitted disease. First, *Giardia* is widely distributed in both humans and other mammalian species, allowing for frequent contamination of surface water supplies. Second, the cyst form of *Giardia* can survive for weeks in cold fresh water. Third, *Giardia* cysts are relatively resistant to chlorination alone. And fourth, only a few parasites are necessary to establish infection.[62] The presence of piped water significantly reduces the risk of infection as in schistosomiasis and giardiasis.[63]

Living in a region with poor sanitation where egg-infested feces contaminate public water sources, often from a lack of available latrines, is the major risk factor for many parasitic infestations as in flukes, *E. histolytica, Giardia* and *A. lumbricoides.*[64] Pica is important mode of transmission in many parasitic infestations as in intestinal nematodes, as a fecal-oral transmission on unwashed hands.[65]

Unsafe sewage disposal is also an important risk factor of parasitic infestations; this may contaminate the water source.[66] In 2006, Turkish researchers have reported that the prevalence of parasitic infections was found to be elevated among villages with insufficient infrastructure for both clean drinking water and sewage system.[67]

Socioeconomic risk factors: Transmission of intestinal parasitic infections is known to be easier in crowding families.[68] Many researchers have shown that parasitic infections were found to be more common in children sharing rooms, which could be due to negative hygienic attitude of the children.[69] Several researchers have demonstrated firm relationship between parasitosis and lack of education of the parents, lack of regular job of the fathers and lack of social security of the family.[70] Lower socio-economic status is also a risk factor for intestinal parasitic infestations. The effect of socioeconomic status on risk of infectious diseases in general, and parasitic infestations in particular, is complex in nature and could be attributed to several other factors such as lack of access to clean water, poor hygienic environment, lack of access to education and overcrowded conditions.[71]

Behavioral risk factors: eating with unwashed hands is a direct method for fecal-oral route of transmission of many types of intestinal parasites as in *E. vermicularis, A. lumbricoides* and protozoa infections.[72] Pinworm induces peri-anal itching promoting auto-infection if the child won't wash his/her hands before eating.[13] Through eating unwashed vegetables or fruits, *Fasciola* can be transmitted to humans.[19] Walking barefoot is an important risk factor of intestinal helminthes infestation especially in hookworm infestation, so, control of hookworm requires individuals to wear appropriate foot wear.[12] Also, biting hand fingers and sucking thumb are behaviors contribute in intestinal parasite transmission.[73]

In the urban community, the risk factors included having pools of water, sewage around houses, not wearing shoes, not attending school, having mothers with 4-8 years of education, and having mothers below 35 years of age.[74]

In Egypt, screening visits were performed on 650 school children aged 5-15 years over a one-year period (2008-2009) in the Nahya Village, Giza Governorate. The findings of the study showed that severe malnutrition, poverty, poor education of parents, poor hygiene, lack of access to potable water and hot and humid tropical climate are the factors associated with intestinal parasitic infections.[75]

Clinical manifestations of intestinal parasitic infestations in children

Clinical manifestations of intestinal parasites in children can range from asymptomatic to many,[76] which can be classified into general, gastrointestinal and extra-intestinal manifestations.

Asymptomatic colonization is a common presentation of *E. histolytica* infection. The children that are found to be colonized with *E. histolytica* are at risk for the future development of invasive disease months to even years later and should be treated.[77]

In general manifestations, weight loss is a common clinical manifestation; it represents 44% of children infested with *E. histolytica.* [78] Its most probably due to malnutrition associated with parasitic infestations. [79] However, in many developing countries, a new form of malnutrition is emerging- obesity. Among school children living on Pacific Islands where *Ascaris*, *Trichuris* and hookworm are endemic, helminthes-infected children had a significantly higher risk of elevated body mass index, an indicator of overweight.[80]

Low grade fever is a manifestation representing 8% of children infested with protozoa.[81] Katayama fever is a form of acute schistosomiasis which occurs when worms become mature and begin to lay eggs; it's characterized by spiking fever with chills, myalgia, headache, fatigue and cough. [82]

Iron deficiency has a strong association with impaired school performance and is common in children with high intensity hookworm infection due to the hookworms taking up blood meals; this feeding is associated with a blood loss. The impact of anemia is clearly dependent on the nutrition of the host and his iron reserves.[83]

Gastrointestinal manifestations: diarrhea is the most common manifestation in intestinal parasitic infestations among children**;** [84] it represents 93% of the children infested with *E. histolytica* and 25-50% of those with *G. lamblia*.[85] The hallmark of giardiasis is the duration of diarrhea which lasts for 7-10 days. This feature combined with weight loss help distinguish giardiasis from most viral and bacterial etiologies of diarrhea, which usually have shorter durations of illness.[86] Intermittent diarrhea which alternate with constipation is the most common symptom of intestinal involvement with *Schistosoma mansoni*.[87]

Diarrhea that contains visible mucous and blood, what is called dysentery, is a common presentation in children with *amoebiasis (*representing 94% of them).[88] Severe form of intestinal involvement of *S. mansoni* may leads to colonic polyposis and frank schistosomal dysentery which intern lead to protein-losing enteropathy, hypokalemia and severe dehydration.[89] Trichuris dysentery syndrome occurs with heavy *Trichuris* infection and characterized by chronic diarrhea, anemia and growth retardation.[90]

Abdominal pain is a major symptom in most intestinal parasitic infestations, representing about 35% of the children infested with *E. histolytica*, 40% of those with *S. mansoni* and most of children with flukes. It may be associated with rebound tenderness in children with amoebic colitis.[91-94]

Constipation, gases and bloating can also arise due to the worms' obstruction of certain vital digestive organs as colon and upper intestine.[95] Anorexia or polyphagia may also occur.[96]

Extra intestinal manifestations as urticaria, which occurs in about 5%of infected children with *Giardia*,[97] it's possible that allergic manifestations occur because of passage across an injured gut of food or other allergens.[98] In a small percentage of children with schistomiasis, an immediate itching and urticaria is seen at the site of cercarial penetration, often referred to schistosome dermatitis, it may progress into popular lesions that can persist for 3-7 days, what is called swimmer itch.[99]

In pinworm infestation, most infestations are asymptomatic but children often present with pruritis ani and perineal pruritis. Symptoms are typically worse at night and may produce insomnia and restlessness. Heavily infected children may develop blood loss, poor concentration, emotional disturbance and enuresis. In girls, vulval vaginitis, acute urinary tract infection, enuresis and incontinence are associated with infection.[100]

Hepatomegaly is a common feature in flukes and schistosomal infections. It's commonly develops 6months to 2 years after initial infection with *S. mansoni*. Hepatic enlargement is diffuse and not tender.[101]

Less common, but possible symptoms include blisters that appear on mouth or lips, increased runny nose, asthma and nervousness.[102]

Intestinal helminthes and cognitive function: Intestinal helminthes have been identified as a major source of chronic ill-health, compromising the growth potential and intellectual achievement of children throughout the world. This association was first suggested by a study early in the twentieth century that demonstrated a correlation between

helminthes infection and the educational achievement of school children. Children with hookworm infection and, to a lesser extent, *Ascaris,* developed more slowly at school and had a significant deficit in the grades achieved. In the subsequent 85 years, many other studies have attempted to relate failure in educational achievement with helminthes infection. The literature is complicated by different measures of school achievement and different methods of assessing cognitive function.[103] Another studies in 9-12 years old children in Jamaica found a positive correlation between helminthes infection and academic achievement. Also the level of school absenteeism was related to intensity of infection in these children.[104]

Complications of intestinal parasitic infestations in children

As parasitic infestations build up over time, many of the health problems caused by these worms become chronic. The worms can cause malnutrition as they rob the body of food- either by reducing appetite, or by preventing food from being absorbed properly once it has been eaten. Children with chronic worm infestations and large number of worms may become stunted and underweight.[105]

Heavy infections with roundworm can cause bowel obstruction.[106] Intestinal worms- especially hookworm- can contribute to anemia by causing intestinal bleeding and thus loss of blood.[107] The larger the number of worms, the more likely they are to make a person ill. Chronic infections can lead to long- term retardation of mental and physical development and, in very severe infections, even death.[108] The long-term presence of parasites may contribute to the development of food allergies.[109]

The most important complication in cestode infestations is clinical syndrome called cysticercosis. It's the larval stage (metacestode) of *Taenia solium* that produces cysticercosis. Three sites are preferred targets for cysticerci: the nervous system, the muscle and the eye. By far the most frequent and most important form of human cysticercosis is neurocysticercosis. The disease is endemic in the developing world. The clinical manifestations of cysticercosis depend to a great extent on the location of the parasites; parenchymal cysticercosis induces epilepsy in most cases. When the number of parasites is large, mental disturbances or focal neurological symptoms may be present. Giant cysticerci may induce a tumor-like picture.[110]

Diagnosis of intestinal parasitic infestations

Diagnosis of parasitic infestations can be often suspected from history of prolonged bloating or diarrhea[111] and can be confirmed by the following tests:

a. Ova and parasites test of the stool, the test is often false negative so three stool samples from three different days should be tested.[112] In *E. histolytica* infestations, microscopic examination of stool for *E. histolytica* cysts and trophozoites is very insensitive. Antigen detection is more sensitive than microscopy and is specific for *E. histolytica* infection.[113]
b. Occult blood in the stool may be revealed.[114]
c. Blood tests often reveal elevated eosinophils and IgE, and lowered hemoglobin level.[115]
d. The diagnosis of *E. vermicularis* depends on acquiring samples from the perianal skin. This can be achieved by the application of a strip of adhesive tape to the anus and then sticking it to a microscope slide.[116]
e. Neuroimaging studies, magnetic resonance imaging (MRI) and computed tomography (CT) are irreplaceable studies for proper diagnosis and characterization of neurocysticercosis.[110]

Preventive measures of intestinal parasitic infestations in children

In general, for prevention of the intestinal parasitic infestations, the plan of prevention must stress on interference with the route of transmission or break the life cycle of the parasite as use of safe and adequate water supply, improvement of environmental sanitation and practicing good sanitation and hygiene habits.[117]

In particular, prevention and control of amebiasis requires interruption of the feco-oral spread of the infectious cyst stage of the parasite by improved hygiene, sanitation and water treatment.[118] Another example regarding the prevention of giardiasis, which requires the proper disposal of human waste, the provision of portable water in community setting, and feco-oral hygiene for individuals.[119] Because of the relative resistance of *Giardia* to halogenations, chlorination alone may not be sufficient to render water safe for drinking. Therefore, when communities use water from streams, rivers, lakes or reservoirs, the water should be processed by flocculation, then sedimentation, filtration and finally chlorination.[120]

Several measures can be taken to interfere with the life cycle of taeniasis/cysticercosis. The most important and affordable is public education on the life cycle of the parasite to implement simple measures aimed at preventing infection, such as proper disposal of human feces whenever feasible, the routine freezing of pork, proper cooking of pork at > 70^{o}C, identification and treatment of taenia carrier, confinement of pigs, and preventing irrigation of vegetables with water contaminated with human feces.[121]

Prevention and control of hookworm requires individuals to wear appropriate foot wear, especially when working in the fields, as occupational exposure is thought to be an important risk factor for infection in working children.[122]

Vaccination against schistosomiasis has been under active investigation for over three decades. Most vaccines have been targeted toward prevention of infection. More recently, investigators have worked toward developing a vaccine that would minimize end-organ damage by inducing a modification in the immune response to eggs.[123]