Giardiasis in Man: Review and Updates

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Abstract. Giardia lamblia (known as G. duodenalis or G. intestinalis) is a microscopic flagellated organism. This protozoan parasite was described for the first time by van Leeuwenhoek in 1681 followed by Lambl in 1859. Giardia is one of the most common causes of diarrhea, with 280 million cases per year. It is included in the “Neglected Tropical Diseases” of the World Health Organization. The organism has two life forms; motile flagellated trophozoite, and a non-motile cyst. The mode of transmission is through ingestion of viable cysts from water, food and by faecal–oral route from person-to-person. Giardia infection may result in clinical aspects that range from the asymptomatic cyst passer state to acute or chronic diarrhea, malabsorption and failure to thrive. The reference method for giardiasis diagnosis is by microscopic detection of the diagnostic stages in faecal samples. Detection of coproantigen of Giardia by enzyme-linked immunosorbent assay or direct immunofluorescence may be helpful. Additionally, molecular techniques are able to detect and identify the parasite in stool. Duodenal biopsy and aspirate could be a useful tool in diagnosis. Human Giardia infections are unlikely to be ever eradicated, and thus, chemotherapy and other methods of control of the disease will always be required.

Keywords: Giardiasis, Giardia, Diagnosis, Intestinal parasites.
Historical Introduction

*Giardia lamblia* (Syn. *G. duodenalis* and *G. intestinalis*) is one of the causative agents of enteroparasitic diseases in the world, with high significant risk for travellers[1].

*Giardia duodenalis* was the first protozoan parasite of man to be discovered when in 1681 the Dutch lens maker, Antonie van Leeuwenhoek, observed the parasite in his own stools using a simple self-constructed microscope[2,3]. In 1859, Vilem Lambl, from whom *Giardia* obtained one of its names, rediscovered the parasite in children's stools, but it was not until the twentieth century that convincing evidence was presented that the clinical syndrome of persistent diarrhea, colicky abdominal pain, abdominal distension, a feeling of bloating often associated with nausea, vomiting, and loss of appetite were attributed to *Giardia* parasites[3].

Epidemiology

*Giardia* is one of the most common causes of diarrhea, with 280 million cases per year. Because of its influence on socioeconomic status and on domesticated animals like sheep and cattle, mainly in poor hygienic countries, Giardiasis is included among “Neglected Tropical Diseases” of the WHO[1,4].

The principal hosts of *Giardia* are humans, livestock, dogs, cats and some species of wild or marine mammals[5].

It is known that giardiasis occur more in children than adults. Prevalence of the disease is influenced by several factors such as social, economical, climatic and environmental[6].

In endemic areas of giardiasis, the infection is more common in children below 10 years of age than those above 10 years, and it decreases with age due to acquired immunity and decrease the exposure to *Giardia* cyst. Higher prevalence of *Giardia* infection is associated with overcrowding, high population density, low-income, lack of water and sewerage services[7].
Occupations may be one of the most important risk factors for giardiasis for example; irrigation and sewage workers are highly affected than others due to their exposure to *Giardia* cysts. In nursery schools and other situations where young children are grouped together, the incidence of *Giardia* infection is high\(^8\). Recent studies were conducted in Saudi Arabia revealed that prevalence of *Giardia* in food handlers in Jeddah and Makkah were 4.6% and 1.98%, respectively\(^9,10\).

**Taxonomy**

Species, *lamblia* of the genus *Giardia*, is under the family *Hexamitidae*; the order *Diplomonadida*; the class *Zoomastigophora* and the phylum *Sarcomastigophora*. There are wide genetic divergences in *Giardia* isolates. Human strains were grouped into the major assemblages A and B\(^11\).

**Morphology**

*Giardia* organism has two life forms; a motile flagellated trophozoite and a non-motile cyst form (Figs. 1, 2). These forms lack mitochondria, peroxisomes and a typical Golgi apparatus, which are common in higher eukaryotes\(^12\). The trophozoite form ranges in size between 10-20 X 5-15 µm. This tear drop-shaped form propels with four pairs of flagella. The most prominent feature of the trophozoite is the ventral sucking disk that helps *Giardia* to attach to intestinal epithelial cells. There are two nuclei, which on stained preparations give the characteristic face-like appearance. There are also two longitudinal axonemes, and two slightly curved coma-shaped bodies called parabasal (median) bodies. The trophozoites reproduce by binary fission\(^12,13\). The cysts are usually oval in shape with four nuclei usually located at one end, fibril axonemes, and parabasal bodies. The cyst forms measure 11-14 X 7-10 µm\(^14\).
Fig. 1. Labeled diagrams of *Giardia* cyst (a); and trophozoite (b).

Fig. 2. Trichrome stained smear of *Giardia* cyst (a) at different focuses showing the four nuclei; and trophozoites (b) from ventral and lateral view (x 100).

Many studies reported outbreaks among travelers and campers or due to lack of sanitation\[^{[8,15,16]}\]. Waterborne outbreaks were related to untreated water, chlorinated water or municipal water supplies\[^{[17,18]}\].
Person-to-person contact is usually common in small children in nursery centers, human in custodial institutions and male homosexuals due to low fecal-oral hygiene\cite{19}.

The prevalence of 20-50\% has been recorded among young children in several countries\cite{19,20}. Those children are usually asymptomatic and able to spread the parasite to their family and the surrounding community.

Transmission of *Giardia* through food is becoming an increasingly notable mode for transmission of this disease\cite{21}. Non-biting flies have been incriminated in contaminating food and dissemination of the disease through mechanical transmission of the infective stage\cite{22}.

High incidence of *Giardia* is increased in areas of close contact between animals and human inhabitants because of the high chance for direct or indirect disease transmission\cite{3,5,23}. Coprophagia in animals increases the autoinfection and dissemination of the disease resulting in high risk for their exposure to infective *Giardia* cysts in fecal matters\cite{4}.

**Life Cycle**

*Giardia* is characterized by its simple life cycle, which begins by ingestion of the quadrinucleated cysts in contaminated food, drink or by fecal-oral route. Cysts resist the acidity of the stomach and their walls are dissolved in duodenum. Each cyst gives rise to two trophozoites, which multiply by longitudinal binary fission. These trophozoites live freely or attached to small intestinal epithelium by their ventral sucking disks, without invading the mucosal tissue. Encystation occurs mainly in the large intestine, and the cysts pass out in the stool. These cysts remain viable and infective for months in cold water or humid conditions\cite{14}.

**Clinical Features**
*Giardia* infection may result in clinical aspects that range from the asymptomatic cyst passer to acute or chronic diarrhea, malabsorption and failure to thrive\[^{24}\]. There are many reasons for this variability in clinical features; such as the immunity of the patient during infection, the ingested cyst number, previous history of exposure, the strain of *Giardia* and its virulence as well as the age of the host beside other factors\[^{25}\].

The incubation period of acute diarrhea is 1-2 weeks. Symptoms of the acute phase can include nausea, anorexia, fever, chills, and a sudden onset of explosive, foul-smelling diarrhea. Stools may have increased amounts of fecal fat and mucus, but no blood is present. Fat absorption may be disrupted because of the presence of trophozoites coating the mucosal lining\[^{26}\].

The presence of anorexia, nausea probably contribute to the important finding of weight lost, which occurs in over 50\% of patients by the time they present to a physician. On average, persons suffering from *Giardia* may lose up to 4 kg\[^{23}\]. The symptoms gradually withdraw within two to four weeks because of the production of secretory IgA, IgG antibodies\[^{27}\]. Chronic giardiasis may develop after acute manifestations resolve. There may be evidence for malabsorption of fat, vitamins A and B12, protein, D-xylose, iron and lactose\[^{6}\]. Deficiency of lactase is common, and persists for several weeks after therapy. All patients should be instructed to avoid lactose containing products during this recovery period, so that recurrent diarrhea will not be confused with relapse of infection\[^{28}\].

Failure to thrive in children is associated with symptomatic giardiasis\[^{29}\] with significantly lower weight-for-age and lower height-for-age than asymptomatic giardiasis\[^{30}\].

Extra intestinal manifestations of *Giardia* have been described. These include urticaria in about 5\% of infected persons, biliary tract disease and rarely a reactive arthritis\[^{31}\]. Achlorhydric patients may be associated with gastric giardiasis\[^{32}\].
In some successfully treated cases, the abdominal symptoms continued two years after elimination of the parasite, but the cause remains unexplained\textsuperscript{[33]}.

**Laboratory Diagnosis**

Laboratory diagnosis is recommended for patients suffering from persistent diarrhea, workers dealing with water and food as well as people travelling to endemic regions.

Throughout the years, the standard golden method for intestinal giardiasis diagnosis has been the microscopic stool examination for trophozoites and cysts\textsuperscript{[28]}. In order to achieve sensitivity more than 90\%, multiple samples of stool should be collected in three successive days\textsuperscript{[34]}. A saline wet mount of a fresh, unpreserved liquid or fatty stool may reveal motile trophozoites with "falling leaf" motility. Formed and hard stools usually contain only cysts. Both trophozoites and cysts are more easily detected by mixing the sample with iodine, which will stain them brown and highlight the diagnostic characters. However, in case of light infection, direct smear examination might end up showing false negative diagnosis\textsuperscript{[9]}.

To increase the chances of isolation of cyst stage but not trophozoite, concentration techniques could be used. These techniques start with larger amount of stool in comparison to the direct smears. Ritchie (formal ether) technique is one of the best sedimentation concentration techniques\textsuperscript{[6]}. Flotation concentration techniques are alternative methods for cyst detection\textsuperscript{[35]}.

Permanent staining such as trichrome or iron hematoxylin stain can be used with preserved or unpreserved specimens to enhance the appearance of the diagnostic features for trophozoites and cysts in blue, green and purple to red colour\textsuperscript{[9,56]}.
Examination of duodenal aspirate is used occasionally for detection of *Giardia* trophozoites. Duodenal biopsy using endoscopy, duodenal contents using string test (Entero test) also applicable for recovering the flagellates. The obtained material could be examined as a wet preparation for motility, stained and/or cultivated in a suitable culture medium.

Nowadays, many rapid immunochromatographic assays are commercially available to detect the parasite antigens in the stool specimens. These kits can be performed quickly without the need for work effort or technical expertise. However, variations in sensitivity and specificity between several studies were observed. These variations could be due to the lack of standardized reagents and the close relationship between many intestinal protozoa.

Serological tests are used to detect antibodies, although they are not particularly helpful in diagnosing luminal parasite. It is difficult to distinguish acute versus chronic or resolved infection by serology. A recent study, which was conducted in Egypt to evaluate direct immunofluorescence (DIF) against the routine microscopy, suggested that microscopic examination is reliable as a first choice test. Though, DIF is recommended in clinically diagnosed cases with negative microscopy. Some of serological methods are mainly applied in cases of outbreaks, screening and for epidemiological purposes.

In recent years, polymerase chain reaction (PCR) and the real time PCR are considered the advanced molecular based techniques in diagnosis of *Giardia*. In PCR technique, a specified DNA fragment from the complex parasite DNA can be amplified to give rise to many millions of copies of the target DNA molecule. The PCR end product then viualized by electrophoretical separation depending on their size in agarose gels. This technique is sensitive, specific, and applied for detection and genotyping of the parasite. However, these tools are costly, need expertise, and mainly applied in research rather than in routine parasitic diagnosis.
Other advanced techniques have been tried for identification of *Giardia* parasite such as fluorescent in situ hybridization (FISH), but with less suitability\[45\].

Additionally, in recent time, several researches are going on developing innovative approaches utilizing nanomaterials to detect infectious pathogens including *Giardia*\[46\].

Radiological examinations are usually not helpful in *Giardia* diagnosis. They are non-specific and demonstrate increased bowel transit time and irregular thickening of small bowel folds\[28,47\].

**Treatment**

The choice drug in giardiasis treatment is *metronidazole* in a dose of 250 mg three times daily for one week. In pregnancy, the alternative drug is paromomycin in a dose of 500 mg every eight hours for five to ten days especially in the first trimester. Tinidazole in an easy dose of 2g in adults has a high cure rate (90–98%). Furazolidone can be used also instead of metronidazole, but it requires administration every six hours for ten days. Nitazoxanide in a dose of 500 mg twice daily for three days is effective in treatment of refractory HIV-infected patients\[24,48\].

**Prevention and Control**

The important line of defense against giardiasis transmission is hygiene procedures. This include hand washing after defecation and before eating, protection of food from flies, washing of fresh vegetables, fruits before eating as well as feces must not be used as fertilizer\[49\].

Improved sanitation measures can be effective in controlling the person-to-person spread of infection. Travelers are advised to avoid drinking from local water supplies when travelling to foreign countries and to limit intake to bottled water. Iodine disinfection of
drinking water as well as the use of filtration systems may serve to allow the decontamination of water sources\textsuperscript{[14]}. In developing countries, water-treatment systems seem to be unavailable; therefore, boiling the water before drinking is recommended\textsuperscript{[50]}. In order to decrease venereal route of giardiasis, the patients should be advised to avoid unhygienic sexual activities\textsuperscript{[19]}. Attention should be given to the animals living with or close to man as they could be a source for direct infection or indirect contamination of water-catchment areas\textsuperscript{[4]}.

It is recommended that treatment is not only for proven cases of giardiasis, but also for cyst passer carrier persons especially food handlers as they carry the risk of transmission of infection to others\textsuperscript{[6,10,25]}.  

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الجيارديا في الإنسان: استعراض وآخر التحديثات

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الجيارديا (المعروفة باسم الجيارديا الإنتاعيرشية أو الجيارديا المعوية) هو سوطي مجهري. وقد وصف هذا الطفيلي وحيد الخلية لأول مرة، فأن يويهوك في عام ١٨٨١م، وبعد ذلك لامب في عام ١٨٥٩م. يعتبر طفيلي الجيارديا أحد المسببات الأكثر شيوعا للاصلال، شملة ٢٨٠ مليون حالة سنويا. يتم تضمينه في "الأمراض المهملة في المناطق الحارة" التابعة لمنظمة الصحة العالمية. هذا الكائن يتواجد بأحد طورين؛ متحرك باستخدام السوط (تروفووزويت)، ومتحوصل غير متحرك (الطور المتحوصل).

طريقة إنتقال العدوى عن طريق ابتلاع الطور المتحوصل الحي من الماء والغذاء الملوث أو أي نتائج بالبراز يصل إلى الفم من شخص إلى شخص. الإصابة بالجيارديا قد يؤدي إلى جوانب سلبية تتراوح من حالات بدون أعراض (حاملين للطور المتحوصل) إلى الإصابات الحادة أو المزمن، وسوء الأتمتص، والفشل في النمو. الطريقة
المرجعية لتشخيص الجيارديا هو من خلال الكشف المجهري للأطوار التشخيصية في عينات البراز. الكشف عن مولد المضاد الجيارديا (أنتيجين) قد يكون بواسطة DIF أو ELISA. بالإضافة إلى ذلك، فتقنيات الأحياء الجزيئية قادرة على كشف وتحديد الطفيلي في البراز. خزعة الإثني عشر وكذلك النضح يمكن أن تكون أداة مفيدة في تشخيص المرض. عدوى الجيارديا البشرية من غير المرجح أن يتم القضاء عليها كلياً، وبالتالي سوف تكون هناك حاجة دائماً للعلاج بالأدوية وغيرها من طرق السيطرة على المرض.