**INTERNATIONAL JOURNAL OF HEALTH & MEDICAL RESEARCH**

ISSN(print): 2833-213X, ISSN(online): 2833-2148

Volume 03 Issue 06 June 2024

DOI : 10.58806/ijhmr.2024.v3i06n28

Page No. 429-432

# Giardiasis: Diagnosis, Pathogenesis and Treatment

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**ABSTRACT:** Giardiasis has become a worldwide health problem and it is the most frequent cause of diarrhea in both pediatric and adults' patients. Ingestion of cysts directly or indirectly via the fecal-oral route is the main mode of transmission. The laboratory diagnosis of Giardia spp. primarily relies on identifying microscopic cysts or trophozoites in stool samples. Additionally, various immunological assays and molecular methods are available for diagnosing giardiasis. The infection stimulates the immune system, leading to increased production of immunoglobulins and cytokines. Generally, metronidazole, nitazoxanide and tinidazole are the preferred drugs for treating giardiasis. This review summarizes existing literature on giardiasis, covering diagnosis, pathogenesis, management, and treatment.

## 1. INTRODUCTION

Giardiasis is brought about by the protozoal parasitic Giardia lamblia, (synonyms G. duodenalis; G. intestinalis). Giardia lamblia is one of the most common protozoal parasites with flagella that infect human gut. The life cycle of Giardia species is a simple process that involves two distinct forms: the active trophozoite and the cyst. Transmission occurs via the fecal-oral pathway, either by direct or indirect intake of infected cysts. The duration of time between consumption and the onset of symptoms ranges from 9 to 15 days. The symptoms of this condition can range significantly, from being asymptomatic to experiencing abrupt watery diarrhea, nausea, epigastric discomfort, and weight loss (Ryan & Cacciò, 2013).

Giardiasis is a highly prevalent disease that has a global distribution and can affect individuals of all age groups, including both children and adults. This is a major contributor to the occurrence of diarrhea transmitted by water and food, as well as outbreaks in childcare facilities and cases of diarrhea among travelers. Infection with Giardia is more prevalent in countries that are considered to be undeveloped, with over 200 million cases being diagnosed annually around the world. Since 2004, the World Health Organization has classified giardia as a category of sickness that is not being adequately addressed. In industrialized regions, the infection incidence among children who are asymptomatic ranges from 1% to 8%, but in less developed countries, the infection rate can vary anywhere from 8% to 30%. Giardiasis is more likely to be found in people who have diarrhea, as its prevalence is higher in those individuals (Hooshyar et al., 2019; Leung et al., 2019).

The estimated incidence of giardiasis in the United States is around 1.19 million cases, however the majority of cases go unreported due to the presence of asymptomatic carriers. The Centers for Disease Control and Prevention (CDC) recorded over fifteen thousand cases in 2012. The demographic group most impacted was youngsters between the ages of 0 and 4, with the greatest proportion of cases observed in the northwestern region of the United States. The increased frequency found in northern states may be attributed to disparities in state-level surveillance systems rather than a genuine increase in incidence. The incidence of giardiasis reaches its highest point during the late summer and early fall, which corresponds with a rise in outdoor water-related activities (Zajaczkowski et al., 2018).

Common risk factors for giardiasis infection include children attending daycare, childcare workers, persons living in institutions, tourists visiting locations where the infection is prevalent, ingestion of water that is polluted or used for recreational purposes, and those with weakened immune systems. Diarrhea is the most common symptom in acute cases, affecting 90% of symptomatic patients. Additionally, 70% to 75% of symptomatic individuals suffer from abdominal cramping, flatulence, and bloating. Chronic giardiasis is marked by persistent anorexia, malaise, nausea, weight loss, and diarrhea. Post-infection lactase deficiency is also a common occurrence (Halliez & Buret, 2013).

This review highlights the previously published information about giardiasis, including: diagnosis, pathogenesis, management and treatment.

## DIAGNOSIS

Conventional microscopy, when used in combination with stool concentration methods, should continue to be used in normal medical laboratories since they are cost-effective and have a high level of sensitivity. It is recommended to utilize immunological assays and molecular approaches as additional testing to the standard strategy (Hooshyar et al., 2019).

This approach is regarded to be the most accurate way for diagnosing giardiasis since it involves the microscopic identification of Giardia species in fecal samples. It is possible to recognize cysts and trophozoites with the use of this approach. The sensitivity of microscopy is dependent on the utilization of either direct or concentration processes, the quantity of fecal samples that are studied, and the level of expertise of the individuals who are involved (Soares & Tasca, 2016). Giardia trophozoites have nuclei and a fully formed cytoskeleton, but they do not have mitochondria, peroxisomes, or components for oxidative phosphorylation. The organisms possess an endomembrane system that exhibits certain characteristics of the Golgi complex and endoplasmic reticulum. This system becomes more noticeable throughout the process of encystation (Adam, 2001).

Fecal concentration is a standard procedure recommended for enhancing the detection of Giardia cysts, especially those that may be overlooked in direct smear wet mounts. These methods are designed to isolate protozoan cysts and helminth eggs from excessive fecal debris. Parasitological laboratories commonly utilize flotation and sedimentation techniques for concentration. Zinc sulfate is widely recommended as the optimal saturated solution for detecting Giardia cysts (Smith and Mank 2011).

Over the past three decades, numerous antibody and antigen detection methods have been developed and employed for immunodiagnosis of giardiasis. However, immunodiagnosis still plays a supplementary role alongside stool microscopy tests in diagnosing the condition. Immunodiagnostic methods used to detect Giardia spp. involve immunoassay techniques, such as ELISA, to identify antibodies, as well as methods specifically designed to detect Giardia intestinalis antigens in human fecal samples (Heyworth, 2014).

The identification of fecal antigens in formalin-preserved and fresh stool samples has been accomplished through the utilization of a number of immunoassay techniques. These techniques include enzyme-linked immunosorbent assays (ELISAs) and rapid antigen detection tests (RDTs), as well as non-enzymatic immunochromatographic (II) assays. The sensitivity of these methods is considered to be comparable to or even higher than that of microscopy when it comes to fecal testing. Various commercially available kits employ enzyme-linked immunosorbent assays (ELISAs) to identify antigens of Giardia intestinalis in fecal samples. Immunoassay kits have been created to identify Giardia and Cryptosporidium, or Giardia spp., Cryptosporidium, and Entamoeba species antigens together in fecal samples (Hooshyar et al., 2019).

## PATHOGENESIS

The life cycle of Giardia is simple, encompassing just two stages: Trophozoite, which is the active feeding stage residing freely in the human small intestine; and Cyst, the dormant and resilient stage that is passed into the environment. In the colon, Giardia forms cysts that are excreted. These cysts are oval-shaped, have thick walls, and exhibit high resistance. Juvenile cysts typically have two nuclei, while mature cysts have four nuclei, measuring between 8 and 14 micrometers in length (Dunn and Juergens, 2024).

Intermediate hosts are not required in the Giardia life cycle. When cysts are ingested through contaminated water or food, they pass into the stomach and duodenum. Here, exposure to gastric acid and pancreatic enzymes triggers excystation. Trophozoites can emerge in the duodenum within minutes of infection and quickly multiply in the small intestine. Encystation takes place as the trophozoites reach the large intestine, where neutral pH and secondary bile components facilitate the process. Cysts are then excreted into the environment, restarting the cycle (Hanevik et al., 2007).

The precise mechanism underlying the symptoms of giardiasis is not fully understood. Trophozoites are able to cling to the intestinal epithelium because they are equipped with a ventral disk that permits them to do so. These protozoa are thought to have the potential to break connections between epithelial cells in the small intestine and interfere with brush border enzymes, according to the hypothesis of the researchers. Individuals who are infected may notice changes in the motility of their gastrointestinal tract as a consequence. Protozoa are also responsible for the production of thiol proteinases and lectins, both of which have the potential to cause damage to cells. All of these processes, when combined, can result in increased permeability and make it more difficult for carbs to be absorbed (Leung et al., 2019).

It has been observed that no single cytokine is essential for controlling infections. Several studies have demonstrated that animals lacking gamma interferon (IFN-γ), interleukin-4 (IL-4), interleukin-4 receptor-alpha (IL-4Rα), and STAT-6 are capable of efficiently managing G. lamblia infections in a manner that is comparable to that of wild-type mice. Giardia infections are characterized by a substantial generation of anti-parasite IgA antibodies, and this phenomenon demonstrates itself in both human and animal models. An extensive proportion of these antibodies are directed against isoforms of the variant-specific surface protein (VSP), which is a protein that is rich in cysteine and coats the surface of the parasite (Singer & Nash, 2000; Singer, 2016). Research by Singer (2015) It has been demonstrated that immune responses that are dependent on CD4+ T cells often result in the elimination of parasites within a few weeks after infection in the majority of instances. Although CD4+ T lymphocytes play a significant role in the elimination of parasites in mice models of giardiasis, neither gamma interferon (IFN-γ) nor interleukin-4 (IL-4) are required for

the process of removing parasites. Hadi et al. (2022) noted elevated levels of IL-17 and IL-35 in patients with giardiasis, suggesting the significant role of interleukins in activating the immune system during intestinal inflammation.

The outlook for patients diagnosed with giardiasis is generally positive since most infections resolve on their own. The mortality risk associated with giardiasis is low, although infants or malnourished children with severe dehydration may face a slightly higher risk. Several antibiotics are effective in reducing the duration of illness, although instances of drug resistance have been documented in clinical settings. Without treatment, giardiasis can persist for weeks as the parasite continues to be shed in the stool, increasing the risk of reinfection. Possible complications include weight loss, deficiency in disaccharidases, stunted growth, and malabsorption (Dizdar et al., 2007).

## TREATMENT

The majority of people with giardiasis are generally non-toxic and may need oral rehydration for the first restoration of fluids. In instances of extreme severity, the administration of intravenous (IV) fluids may be required. It is crucial to manage fluid and electrolyte balance properly, especially in cases of significant diarrheal fluid losses. The standard treatment for giardiasis involves antibiotic therapy. Metronidazole, tinidazole, and nitazoxanide are commonly recommended as first-line treatments. However, resistance to these medications has been increasing in recent years. Therefore, there is an urgent need to identify new molecular targets for antigiardial drugs. (Leung et al., 2019).

Research indicates that once-daily dosing of metronidazole could be as effective. Caution is warranted when administering metronidazole to pregnant women, particularly in the first trimester, due to potential risks of cleft lip formation. Patients should be advised to avoid alcohol consumption to prevent the disulfiram-like reaction, which can cause symptoms such as flushing, headaches, and nausea. Metronidazole is considered safe for use in children, with a typical recommended dose ranging from 30 mg/kg to 50 mg/kg per day, divided into three doses. It is recommended to treat children who present with failure to thrive, acute or chronic diarrhea, malabsorption, or other gastrointestinal symptoms when Giardia organisms have been identified. (Youn et al., 2009).

Other treatment options for giardiasis include paromomycin, albendazole, mebendazole, nitazoxanide, and tinidazole. Paromomycin, which has limited absorption into the bloodstream, might be considered safe for pregnant patients in the first trimester. The effectiveness of therapy for giardiasis is uncertain due to contradictory findings. According to a systematic study, albendazole has been found to be equally effective as metronidazole, but with a lower incidence of side effects. It is advisable to switch to a medicine from a different class if patients persist in experiencing symptoms after treatment (Escobedo et al., 2018).

## CONCLUSIONS

The parasite Giardia lamblia, which is responsible for causing giardiasis, has a simple life cycle that consists of two forms: the active trophozoite and the cystic form. A prevalent cause of diarrhea in people of all ages, this disease is found all over the world and has a widespread distribution. Ingestion of cysts, either directly or indirectly, is the means by which it is transmitted through the fecal-oral pathway. The identification of minute cysts or trophozoites in stool samples is often the method that is utilized for the diagnosis of this ailment. However, immunological testing and molecular approaches are other viable potential methods. Elevated levels of IL-17 and IL-35 are often observed during giardiasis, suggesting their role in immune defense against this intestinal infection. Metronidazole, nitazoxanide and tinidazole, are the preferred medications for treating giardiasis**.**

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