Giardia duodenalis in Human Health: A Comprehensive Review of its Epidemiology, Transmission, Pathophysiology, Diagnostics, and Control Strategies

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Introduction and study aim: *Giardia duodenalis* is the entero-parasite cause of giardiasis, a diarrheal disease in both humans and animals. The article presents a summarized review of the epidemiology, transmission, pathophysiology, diagnosis, and control strategies of *G. duodenalis*. Given the limitations in the literature and information on giardiasis in developing countries, even though it continues to be a public health concern, this review aims to reassess and update the position of giardiasis. **Patients and Methods:** We searched Google Scholar, PubMed BMC, and Scopus using text keywords "*Giardia duodenalis* OR *Giardia lamblia* or *Giardia intestinalis* or intestinal protozoa or Giardiasis". **Results:** *Giardia duodenalis* infections are prevalent in inadequate sanitation, contaminated water sources, poor hygiene, impoverished and informal settlements, precisely in rural communities, and among immune-compromised individuals. Current primarily epidemiological studies of giardiasis rely more heavily on microscopic fecal inspection to determine prevalence, with less on species identification and genotype distribution by multi-locus genotyping and sequencing. To date, the illness has been discovered to be substantially linked to malnutrition, anemia, diarrhea, stunting, and wasting. Further, surveillance found that Giardia was concurrently present in animal settings, including domestic, wild, and pet animals, treated and untreated water, and tainted farm food. The information gathered is valuable to the corpus of knowledge on giardiasis, which helps manage the disease's effects around the world. **Conclusion:** Since giardiasis is associated with morbidities such as diarrhea, anemia, and malnutrition, improving disease control against giardiasis should be a top priority to promote the global agenda.

INTRODUCTION

Giardiasis is an enteric, parasitic disease caused by the flagellate protozoan *G. duodenalis* [1]. It is an intermittent or epidemic acute or chronic disease of domestic and aquatic animals, insects, wildlife, and humans [2–4]. The infection was, previously listed in the World Health Organization's Neglected Diseases Initiative due to its link to poverty [5]. It is the most recurrent intestinal food- and water-borne pathogen causing approximately 2 million cases and 200,000 abnormalities [6,7]. The tropical region bears three-quarters of this burden, with 100 cases per 100,000 people [8]. Furthermore, giardiasis accounts for several water-borne protozoan disease epidemics worldwide [9]. Infection rates in industrialized countries vary from 2-5%, with higher rates in low-income countries ranging from 15 to 50% [10].

In Sub-Saharan Africa [SSA], the prevalence ranges from 0.1% to 60% [11], with infection rates in Eastern Africa ranging from 4.0% in Rwanda to 17% in Kenya, 22.0% in Sudan, 45.0% in Uganda, 45.0% in Eritrea, and 36.0 in Ethiopia [9,12]. Infants, young children, international adoptees, elderly, immunocompromised, diabetic, and cystic fibrosis patients, and travelers are all at greater risk of giardiasis [13–16]. Studies have

reported high infection rates in children aged 10 in Busia County [17], and children aged 2-15 years from Bungoma and Kakamega Counties, Kenya [18,19].

Similarly, immunocompromised people are at a higher risk of giardiasis. For example, among cancer patients, the total weighted global prevalence of *G. duodenalis* infection was 7.0%, with 5.0% in Africa, 6.0% in Asia, 11.0% in Europe, 3.0% in North America, and 13.0% in South America [20]. Even though infants are at great risk of giardiasis, studies in Africa have shown that breastfed children are less likely to be infected [20–22]. Similarly, a higher proportion of giardiasis has been reported among HIV/AIDS patients, which is 1.2 times higher among antiretroviral treatment-naive persons [24]. Overall, giardiasis represents a significant infectious disease burden, with SSA nations bearing a higher proportion.

1.2. Risk factors of *Giardia duodenalis*

Giardiasis is extremely prevalent, especially in Africa. This is due to several factors including domestic animals, international travel to endemic regions, and ingestion of tainted food or water. In addition, poor sanitation, improper waste disposal, unhygienic practices, infants or young children, and immunosuppression are among the risk factors. Furthermore, close contact with giardiasis patients, animals [bovines, dogs, cats, poultry, and rodents], taking antibiotics, chronic gastrointestinal conditions, such as cystic fibrosis, and further increases acquisitions of infections [23–27]. Although this encourages a comprehensive and systematic strategy to reduce the burden, the knowledge of the risk factors in most low-income countries, particularly in rural regions is insufficient.

Giardia duodenalis has emerged as the most persistent intestinal parasite in humans, and some domestic and wild mammals globally [4]. Children are known to be more at risk of giardiasis than adults [30]. The risk of acquiring the disease is mostly associated with the socio-demographic, hygiene, nutritional, and immune status of the host as well as the strain of the parasite [31]. In most developed countries, the risk of infection is highly linked with the consumption of contaminated tap water, and fresh water and the movement of individuals from a non-endemic region to an endemic region as well as interaction with pet animals [32,33]. Additionally, a study conducted among children in New Zealand, revealed that changing nappies in children was associated with a high risk of giardiasis [33].

In low-income countries predominant risk factor associated with *G. duodenalis* infections is socio-demography. These include improper sanitation, bad personal hygiene, eating raw fruits and vegetables, and drinking contaminated tap water [31]. Concurring, in a study at Kolkata in India, there was a relationship between giardiasis and the socio-economic background of the study population [34] Their results showed that most of the diarrheal patients had lower socioeconomic status; the study population lived in the slums, so the disease condition could be highly associated with water and food-borne contaminations. Children whose ages were less than or equal to five years were most at risk for parasitic infections. Also, a cohort study in rural Egypt, results showed that *G. duodenalis* is more likely to occur in female infants as compared to male infants. Thus, the males had a lower number of symptomatic infections [35]. The reason provided was that some sociocultural and economic regulations could be operating in Egypt that keep male infants from encountering microbes in the environment. This includes the fact that males are given more attention and care than females. Similarly, a study in Busia County Kenya showed a high proportion of female gender among the cases, supporting the notion that the female gender, is more exposed to risk factors as compared to the male gender [17].

Several epidemiological studies have assessed the prominence of zoonotic spread in the manifestation of human giardiasis [36–38]. For instance, case-control studies of giardiasis in New Zealand didn't identify interaction with pets as a risk factor for children or adults, however, dealings with farm animals were linked with increased odds of infection for adults [39]. In agreement, with this finding, the infection prevalence of human giardiasis in New Zealand was 23% higher in rural areas than in urban areas. Likewise, farm visits were frequent among case patients, though, exposure to dogs, cats, horses, cattle, and sheep was not a significant risk factor in the UK and Kenya [40,41]. One case-control study in eastern England found an association of giardiasis with exposure to farm

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animals and pets, particularly pigs, dogs, and cats [42]. However, other studies in the United States, Canada, and the United Kingdom did not show an association between farm animals and giardiasis cases [38].

Other risk factors that predispose humans to giardiasis include season, co-infection, sex orientation, and immune status for instance among HIV-infected individuals [14,19,43,44]. Weak immune response as well as co-infection by other parasites and pathogenic bacteria increases morbidity and mortality [45]. In temperate countries, the infection is also higher during the winter season compared to summer [46,47].

1.3. Life cycle of *Giardia duodenalis*

Giardia duodenalis completes its life cycle in a single host with no intermediate hosts. Infection is transmitted through the fecal-oral route, through the ingestion of contaminated water, hands, or food. It can also be spread from person-to-person [anthroponotic], animal-to-person [antropozoonotic] or object-to-person [48]. Sexual transmission particularly among men who have sex with men [MSMs] via oral-anal, oral-genital, or anilingus with an infected partner has also been reported [49,50].

In humans, the *G. duodenalis* life cycle is split into two stages: 1] the trophozoite stage which exists freely in the small intestine [duodenum, jejunum, and ileum]; and 2] the cysts which are voided in feces into the environment for ingestion by a new host [51]. The infection begins with cyst ingestion, transit through the gastric acid stomach, and excystation in the duodenum. Excystation occurs within 5 minutes of the cyclist being exposed to bile, pancreatic enzymes, and the duodenum's alkaline pH [51]. Within 30 minutes of ingestion, two trophozoites emerge from each cyst via excystation in the duodenum. The trophozoites then firmly attach to the duodenal and proximal jejunal mucosa via a ventral adhesive disc or sucker in the presence of surface lectins or mechanically and multiply via binary fission. The trophozoites then enter the small intestines and multiply rapidly, doubling in 9-12 hours. The trophozoites then pass into large intestines, where they encyst and cluster throughout the intestines and caecum in the presence of neutral pH and bile salts [51].

Encystation occurs primarily in trophozoite clusters and begins with the appearance of encystation-specific secretory vesicles in the cytoplasm of trophozoites, followed by the production of cyst walls within 15 hours. The formation of a cyst begins with the shortening of the flagella, followed by condensation of the cytoplasm, and, finally, the secretion of a thick hyaline cyst wall. The encysted trophozoites then undergo nuclear division producing quadri-nucleated mature cysts. The cysts are the infective form of the parasite and are excreted in feces and the life cycle is repeated [51].

Infected persons shed 10^8 to 10^{10} cysts per day, with a minimum dose of 10 sufficient to cause infection [52]. The human host is infected after ingesting the cysts which then pass through the acidic stomach into the duodenum, where excystation occurs. Apart from excystation occurring in the presence of bile and the alkaline pH in the duodenum, it can also proceed in a neutral pH, thus individuals with hyperchlorhydria [or chlorhydria] are more susceptible to giardiasis [1].

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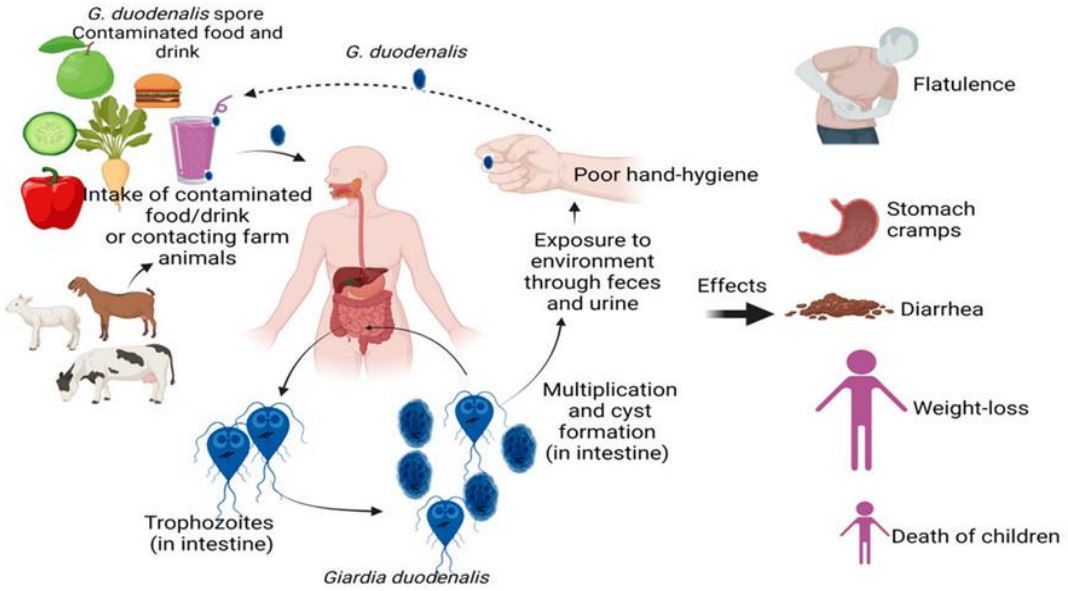

Figure (1). Giardia duodenalis life cycle. Quoted from

1.4. Pathogenesis of giardiasis

Pathogenesis is dependent on giardia parasite virulence and host susceptibility. Achlorhydria, hypogammaglobulinemia, trophozoite genotype, and attachment on the intestinal surface are factors influencing giardiasis severity [53]. Mechanisms of disease development include mechanical irritation leading to hyperemia and inflammation [mild illness], as well as, parasite-derived enterotoxins stimulating cytokine production and inducing the inflammatory response [51]. Damage to the endothelial brush border [blunting of the brush border and atrophy of villi], enterotoxins, immunologic reactions, increased permeability, altered gut motility, and fluid hypersecretion via increased adenylate cyclase activity are among the mechanisms of diarrhea and intestinal malabsorption in giardiasis [51].

Blunting of the brush border and villi atrophy are also implicated in fat malabsorption [greasy stool], folic acid, fat-soluble [ADEK; A, retinol; D, cholecalciferol; E, tocopherols; and K, phylloquinone] vitamin deficiency, iron, zinc deficiency sugar and carbohydrate fermentation by bacterial flora [gas production and flatulence]. In addition, infection results in electrolyte accumulation and causes increased water content in the intestinal lumen [51]. Giardia parasite has also been found to compete with the host for the zinc for synthesis of surface and flagella protein. Zinc deficiency may result in an immunosuppressive effect, hence increasing the susceptibility of infected patients to other gastrointestinal pathogens [54]. Furthermore, enterocytic injury mediated by activated host T lymphocytes and enterocyte apoptosis causes epithelial tight junction disruption, increasing intestinal permeability [55].

1.5. Pathophysiology of *Giardia duodenalis*

The pathophysiology of *G. duodenalis* infection largely results from enterocyte apoptosis, intestinal barrier dysfunction, activation of host lymphocytes, shortening of brush border microvilli with villous atrophy, disaccharidase deficiencies, small intestinal malabsorption, anion hypersecretion, and increased intestinal transit rates [51]. Alterations in intestinal permeability and malabsorption coincide with the peak of trophozoite colonization and cause significant derangements in intestinal barrier function [56,57]. Changes in apical tight junctions and apoptosis, as well as disruptions in F-actin, zonula-occludens-1, claudin-1, and alpha-actinin, have all been linked to increased intestinal permeability [58,59]. Malabsorption and maldigestion are caused by giardia-induced diffuse shortening of epithelial brush border

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microvilli via a lymphocyte-mediated mechanism, which impairs disaccharidase activities [51]. Further to that, murine model studies on the interactions between intestinal microbiota and *G. duodenalis* infections revealed that the parasite causes visceral hypersensitivity to intestinal luminal distensions, villus atrophy and crypt hyperplasia, mucosal intraepithelial lymphocyte, and mast cell proliferation, and promotes commensal bacterial translocation [60]. Furthermore, the intestinal microbiota promotes continuous giardia establishment, resulting in growth inhibition, by altering microbial host proteolysis co-metabolites [61].

Patients' hematological profiles are also altered as a result of *Giardia duodenalis* infection. Animal model studies of giardiasis in Mongolian gerbils revealed that cyst shedding was inversely correlated with mean corpuscular hemoglobin concentration [MCHC] [62]. Whereas, studies in male Albino rats infected with *G. lamblia* revealed decreased erythrocytes, Hb, MCHC, neutrophils, and monocytes, and elevated mean corpuscular volume [MCV] [63]. In human studies in Brazil, both relative and absolute numbers of eosinophils were elevated in adults with *G. duodenalis* infections [64]. Furthermore, the platelet count, platelet crit, mean platelet volume, platelet anisocytosis index, and large platelets were all reduced in *G. duodenalis* patients from Poland [65]. These findings suggest that *G. duodenalis* infections cause profound changes in the erythrocytic, leukocytic, and thrombocytic profiles.

Clinical chemistry analyses in Germany revealed elevated alanine transaminase [ALT] levels in giardiasis patients returning from the tropics and subtropics [66], as well as lower total serum cholesterol levels in giardiasis patients [67]. Furthermore, studies on soluble adhesion molecules in Egyptian giardiasis cases showed an increase in serum levels of soluble endothelial leucocyte adhesion molecule-1 [sELAM-1], which was related to the number of cysts in the stool [68]. As a result, clinical chemistry analysis can be used to determine the severity of infection.

In giardia infections, both innate and adaptive immunity influence the acquisition and progression of disease [69]. In addition, there is great variation in the outcome of giardia infections, ranging from self-limiting infection to re-infections and chronic infections, as well as, overt symptoms [severe cramps, nausea, and diarrhea] to severe disease [70]. Innate immunity to giardiasis includes colostrum components such as melatonin and cortisol which promote phagocyte giardiacidal effects [71,72]. Similarly, complement activation via the alternative, lectin, and classical pathways has been shown to control *G. duodenalis* trophozoites via mast cell recruitment and activation, as well as, through the membrane-attack complex lysis [71–73]. Adaptive immunity encompasses parasite-specific antibodies as well as T-cell-mediated responses. In Brazil, for example, children with *G. duodenalis* infection had higher levels of serum IgG and IgA antibody reactivity indexes, interferon [IFN]-γ levels, and serum and saliva nitric oxide derivatives [76]. Furthermore, symptomatic human giardiasis is associated with elevated serum IFN-γ, interleukin [IL]-2, IL-4, IL-10, IL-17, and IL-35 levels [77,78]. Additionally, elevated effector memory CD4+ T cells producing IL-17A have been detected in giardia-infected returning travelers in Germany [79]. These findings indicate that *G. duodenalis* infection induces protective antibody responses, as well as immune-modulatory pro-inflammatory and anti-inflammatory cytokine responses.

1.6. Pathology of giardiasis

Grossly, the parasite causes diffuse alterations and scattered white spots in the duodenum [80], while gastric giardiasis presents with atrophic gastritis and gastric mucosa metaplasia [81]. Furthermore, computed tomographic enterorrhaphy reveals hypotonic dilated small bowel loops and the capsule's delayed small bowel transit time on endoscopy [82]. Infection with *G. duodenalis* causes enterocyte damage and loss of the brush border of the epithelial cells lining the intestine, resulting in microvilli shortening and altered epithelial barrier function [83]. The variable blunting or atrophy of intestinal villi are examples of microscopic changes [82,84]. Similarly, fluorescent microscopy studies show that trophozoite infection causes epithelial tight junction disruption, enterocyte apoptosis, and necroptosis [85,86]. Likewise, electron microscopy studies in asymptomatic *G. duodenalis* infected children show increased mucoid coating of epithelial cells, infiltration of villi lumen with teardrop [pear or crescent] shaped binucleated parasites,

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branching and gaps in the microvilli, an increase in cytoplasmic dense bodies, and infiltration of lamina propria intercellular spaces with inflammatory cells, particularly lymphocytes and neutrophils [87]. Furthermore, histopathologic examinations of bowel biopsies from *G. duodenalis* stool-positive patients revealed mucosal abnormalities [inflammation, villous increase, intraepithelial lymphocytosis with prominent lymphoid aggregation, granulocytes in the lamina propria, and trophozoites in the terminal ileum] [88,89]. Thus, these pathologic features of Giardia-induced gastroenteritis reflect localized intestinal injury.

1.7. Clinical presentation of giardiasis

Following infection, the incubation period ranges from 1-2 weeks, with a mean of 9 days and emergence of symptoms varying from 3-10 weeks. However, most *G. duodenalis* infections remain asymptomatic with the rate of symptomatic infection ranging from 5-70% [51]. With encystation, the emerging trophozoites feed on mucus with the infection remaining asymptomatic [asymptomatic carriers or cyst passers] [90]. The trophozoites may also cause hyperemia and inflammation of the duodenal wall [duodenitis] leading to symptomatic infection. The typical symptoms of giardiasis include diarrhea or loose stools, malaise or weakness, foul-smelling stools, crampy abdominal pain or epigastric pain, weight loss, nausea, decreased appetite, greasy light-colored stools [steatorrhoea], bloating or distension, flatulence, vomiting, belching, fever, and constipation [51]. Severe symptoms include impaired pancreatic function [91], iron depletion, anemia, and vitamin B_{12} malabsorption. In addition, steatorrhea [92], includes long-term sequelae, such as irritable bowel syndrome, chronic fatigue, and impaired child growth and cognitive development [93]. A subset of patients progress to chronic diarrhea with foul-smelling stools, abdominal distention, and malodorous flatus; plus weight loss, fatigue, and failure to thrive in children [94]. Individuals with impaired immunity are at higher risk of developing severe giardiasis manifestations. For instance, giardiasis patients with Good's syndrome-associated hypoalbuminemia present with severe protein-losing enteropathy and severely low serum protein levels [95].

Giardiasis in patients with B cell deficiency-related agammaglobulinemia is often prolonged with malabsorption, villus flattening, pernicious anemia, and lymphoid nodular hyperplasia, while those with concurrent T cell deficiency experience intractable diarrhea [96]. Giardiasis in patients with concurrent immunodeficiency hypogammaglobulinemia or those with common variable immunodeficiency presenting with reduced IgA or switched memory B cell levels is likely to suffer chronic diarrhea or disease refractory to first-choice drugs, nitroimidazoles [97,98]. Moreover, *G. duodenalis* is a common protozoan opportunistic pathogen associated with diarrhea in HIV/AIDS [99,100]. Altogether, giardiasis patients with concomitant immunodeficiency are more likely to experience severe symptoms such as persistent diarrhea, anemia, steatorrhoea, malabsorption, hypoproteinemia, fat-soluble vitamin deficiency, jaundice, or biliary colic.

1.8. Prognosis of giardiasis

In immunocompetent individuals, giardiasis infection may heal without medication [101]. However, chronic infection may develop especially in immune-compromised individuals [102]. Children with persistent giardiasis are at risk for failure to thrive as well as more long-lasting sequelae such as growth stunting [103]. The majority of infected people are susceptible to lactose intolerance leading to symptoms that may mimic a chronic infection. In addition, some people experience post-infectious irritable bowel syndrome after the infection has cleared. Also, Giardiasis has been suspected in allergy cases [104]. This is thought to be due to its effect on intestinal permeability.

1.9. Diagnosis of Giardiasis

The diagnosis of giardiasis is supposed in patients presenting with subacute or chronic diarrhea accompanied by the typical symptoms of giardiasis. In low-resource settings, clinical presentations of patients have been largely used as diagnosis schemes. However, it has shown some limitations; for instance, some signs and symptoms are integrated with those of other protozoan parasites, hence confusing and unreliable [105]. As a result, direct stool examination and microscopy of fecal specimens is the "gold standard" for clinical diagnosis of giardiasis. Microscopy typically consists of wet

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[normal saline] preparation of fresh fecal samples detection of trophozoites and Lugol's iodine-fixed samples for cysts. Microscopic examination of one to three stool specimens can detect from 60% to >90% of infections, respectively [106], and can be increased by stool concentration methods, especially in persistent infections [107]. Microscopic identification, however, has low sensitivity in cases of a low number of cysts, is dependent on the expertise, intermittent cyst shedding may impair diagnosis and probable several stool samples may be needed over a week, and experience of the microscopist to differentiate between artifacts and giardia parasites in the fecal specimens [108]. Similarly, due to the inconsistency of trophozoite and cyst shedding in infected hosts, multiple samples must be studied over time, often one week [101].

Immunologic detection of stool antigens has a sensitivity similar to that of microscopy, as well as good specificity, and it is less labor-intensive, so in some settings, it is a good substitute for microscopy. Several antigen-antibody tests have been applied in detecting *G. duodenalis* infections these include enzyme immunoassays, and immunochromatographic rapid diagnostic tests [RDTs]. For instance, in the case of RDTs, the reported sensitivities were 48.2 to 85.7%, and 91.2 to 99.2% in stool samples of children admitted with severe acute malnutrition [SAM] and diarrhea in Kenya and Malawi, respectively [109]. However, these methods have low specificity, are expensive, and have low differentiation power, especially at the assemblage level.

Additional diagnostic methods such as endoscopic biopsy and duodenal content examination including the entero-test [string test] are valuable in rapid microscopic examination of the intestinal contents for trophozoites, and detection of other conditions causing diarrhea and malabsorption [110,111]. Lastly, *in vitro* culture of duodenal aspirates and other samples can be used for detecting the parasite but the process is arduous and erratic, hence not frequently used in clinical laboratory settings [112].

Detection of parasite DNA using PCR-based techniques offers greater sensitivity and specificity and can be effective in the diagnosis of asymptomatic infections. For example, a comparison of microscopy, copro-DNA using two PCR assays targeting topoisomerase gene loci [nested-PCR] and 18S-rDNA [conventional-PCR] gene loci in the detection of giardiasis indicated that both PCR assays have high specificity [100 and 96.9 %] and sensitivity [78.6 and 76.2 %] compared to microscopy, respectively [113]. Similarly, historical research using PCR-RFLPs genotyping at GDH, ssu rDNA, and β-gIardian [BG] gene loci, as well as sequencing, have demonstrated the efficiency and accuracy of the molecular assay [109–112].

2.9.1. Genotyping *Giardia duodenalis*

Genotyping techniques such as Polymerase chain reaction-restriction fragment lengthen polymerase [PCR-RFLPs] and DNA sequencing have been recognized as gold-standard diagnostic approaches, in the identification and differentiation of *G. duodenalis* at both assemblage and sub-assemblage levels [116,118]. These approaches exploit specific loci at β*g*, SSU-rDNA, *GDH*, and *TPI* genes loci. Regardless of the efficacy of these approaches, PCR-RFLPs at the GDH gene loci have shown a clear chromatogram and several double peak readings in both forward and reverse orientations, particularly for assemblage B [119], suggesting the possibility of mixed infection. The presence of heterogeneous sequences may be attributed to two nuclei, which are assumed to accumulate mutations and evolve independently, resulting in allelic sequence heterozygosity in assemblage B [120]. Furthermore, studies reveal that distinct genetic loci are targeted, and conflicting genotyping results might be achieved [121]. As a result of the substantial genetic variation among isolates in most indicators, new typing techniques for assemblage B may be required, using multiple loci approaches [122].

2.9.2. The glutamate dehydrogenase [*GDH*] and triosephosphate isomerase gene [TPI] gene

Glutamate dehydrogenase encoded by the glutamate dehydrogenase gene is key in the urea cycle, as it converts glutamate to -ketoglutarate in a reversible process [123]. Triosephosphate isomerase, which is encoded by the triosephosphate isomerase gene is involved in the reversible reaction for converting glyceraldehyde-3-phosphate and dihydroxyacetone phosphate in gluconeogenesis [124]. The GDH and TPI genes have been highly

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beneficial in genotyping *G. duodenalis* isolates due to their highly polymorphic. As a result, PCR-RFLPs and sequencing techniques at GDH and TPI gene loci have been applied in identifying *G. duodenalis* at both genotypes and sub-genotype levels. Thus, all eight assemblages [A-G] and mixed assemblages have been reported. Furthermore, sub-assemblages [AI, AII, AIII, BIII, and BIV] of A and B assemblages have been reported [117,125,126]. The success and accuracy of nested PCR-RFLPs for GDH and TPI gene loci genotyping have revealed inconsistent sensitivities. Previous investigations, for example, have demonstrated sensitivity between [53-95%] in varied contexts. This is largely due to the existence of fewer cysts, the nature of the primer, and the specificity of the restriction enzyme used [125,127,128].

2.9.3. Assemblages and sub-assemblages of *Giardia duodenalis*

Giardia duodenalis consists of eight assemblages [A-G] that are host-specific, with assemblages A and B, infecting both humans and animals [129]. For instance, assemblage A is frequently reported in livestock [cattle, water buffalo, sheep, goats, alpacas, and pigs] and companion animals [dogs, cats, and horses] [127–129]. In comparison, assemblage B is less frequently reported in livestock and companion animals, with only a few reports of infection of cattle, sheep, horses, dogs, cats, and rabbits [129]. Assemblage A, to a lesser extent, assemblage B are commonly found in wild animals, except beavers and muskrats, which seemingly have a high occurrence of assemblage A [133]. Other than A and B assemblages, C, D, E, F, and G, on the other hand, show significant host specificities and constrained host ranges [129]. For instance, assemblages C and D have been detected predominantly in dogs and other canines [foxes and coyotes], as well as canine-related animals [seals] [134]. In addition, assemblage E has been identified primarily in cloven-hoofed domestic mammals [cattle, water buffaloes, sheep, goats, and pigs], whereas, assemblages F and G have largely been detected in cats and rodents [135, 136]. However, with some exceptions to the host specificity, a mixed infection of assemblages C and D was reported in cats and humans. Similarly, assemblages D and E were also reported in pigs, cats, and humans [130,137,138]. Sub-assemblages of AI and AI have been commonly reported in animals with few cases in human isolates, suggesting anthropozoonotic transmission. Similarly, reports of AII assemblages, which are assumed to be human infections, in animals have also been discovered. While BIII and BIV sub-assemblages have both been found in human and animal isolates, however, BIV has been found more frequently in animals than in humans [139]. Suggesting, *G. duodenalis* is a versatile protozoan parasite with a wide range of hosts.

2.10. Prevention and control of giardiasis

Primary prevention of giardiasis involves evasion of acquiring the infection. The strategies of primary prevention include ensuring proper personal hygiene through hand washing with soap and water. Likewise, killing of cysts from water supplies by boiling and chlorination ensures safe drinking water and prevention of food and water contamination. Moreover washing fruits and vegetables with treated water before consumption is also an effective primary preventive method against giardia infections [19]. In addition, wearing protective clothing, e.g., boots during farm activities and protection against contact with domestic and wildlife, human and animal, as well as, control of potentially infected animals, such as rodents and cockroaches by covering food, habitat alteration and using rodenticides are effective primary preventive measures [140,141]. Furthermore, targeting the safe disposal of animal and human feces and proper handling of dung manure, dust control measures, proper sanitation, and sewage treatment can effectively prevent the transmission of giardiasis [142,143]. Besides, the direct primary preventive methods described above, exclusive breastfeeding of infants has been shown in Gabon and Egypt to effectively reduce the risk of having asymptomatic or symptomatic [mucus in stool, loss of appetite, and abdominal tenderness] giardiasis [144, 145].

Secondary prevention for giardiasis comprises effective diagnosis and treatment of cases as well as, infected domestic animals to reduce the number of cysts shedding into the environment, and mass treatment through expanded school and community-based programs with effective anti-giardia drugs. Benzimidazole [albendazole, mebendazole], quinacrine, and other 5-

nitroimidazoles, such as metronidazole, tinidazole, secnidazole, and ornidazole, are also useful in the treatment of the disease [146,147]. Due to its greater rates of parasitological cure, clinical efficacy, and lower side effects, several studies show that tinidazole is more beneficial for treating giardiasis than metronidazole or albendazole [148]. Although medication resistance is suggested by earlier research revealing an increasing problem with 5-nitroimidazole refractory giardiasis [149,150], the underlying mechanisms are still unknown. In addition, clinical studies showed that combination therapy with a 5-nitroimidazole [metronidazole, tinidazole, secnidazole, and ornidazole] and benzimidazole [albendazole, mebendazole], as well as quinacrine, is effective in treating refractory disease; however, it's unavailability and potential side effects prevent its widespread use [135–138]. Besides, to promote control of this parasitosis, it is important to keep a high index of suspicion and vigilance in finding cases at risk for infection. In addition, improving the provision of water, sanitation, and hygiene [WASH] initiatives, surveillance using more sensitive molecular detection methods in both human and zoonotic [domestic animals plus wildlife] transmission, and reporting are vital in reducing the burden of giardiasis [155].

While most infections are mild and self-limiting, some individuals may develop chronic or recurrent symptoms, leading to complications such as malnutrition, weight loss, and dehydration. Tertiary prevention strategies for reducing the development of complications and rehabilitation are effective in treating giardiasis. Prompt and adequate treatment can reduce the duration and severity of symptoms, prevent recurrence, and minimize the risk of complications. Nutritional support, such as vitamin and mineral supplementation and a high-calorie, high-protein diet, may be necessary to address the issues of nutritional deficiency. Also, adequate hydration, through oral rehydration therapy or intravenous fluids, can prevent or treat dehydration and its associated complications. Additionally, individuals with chronic or recurrent giardiasis should be closely monitored to ensure that their symptoms are adequately controlled. Education about the transmission of giardiasis, good hygiene practices, and appropriate food handling techniques can help prevent reinfection and reduce the risk of complications [156,157].

To date, there are no human vaccines against giardiasis infection. However, several vaccine candidates are in development. These candidate vaccines target different aspects of the Giardia parasite, including recombinant proteins, DNA vaccines, variant-specific surface proteins [VSP], cyst wall proteins [CWP], giardins, and enzymes [158,159]. Therefore, it is important to distinguish *G. duodenalis* assemblages and sub-assemblages and identify risk and clinical factors to effectively implement intervention strategies.

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HIGHLIGHTS

- *Giardia duodenalis* is the entero-parasite cause of giardiasis, a diarrheal disease in both humans and animals.
- Giardiasis is associated with morbidities such as diarrhea, anemia, and malnutrition.
- Improving disease control against giardiasis should be a top priority to promote the global agenda.

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