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Giardiasis of domestic animals and its zoonotic significance: A review

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Abstract

Giardiasis is the most common waterborne parasitic intestinal infection of both animals and humans worldwide, and it leads to significant morbidity and mortality in animals, particularly in young aged group like calves in the developing and developed world. It is a zoonotic infectious disease where animals are considered as sources of infection for humans through consumption of water and food contaminated with cysts of *Giardia*. *Giardia* species differ significantly in host range, with *G. duodenalis* having the broadest host range and greatest public health significance. *Giardia duodenalis* has eight different assemblages A through H. The disease Causes gastro intestinal disturbance, gall bladder colic and jaundice. Malabsorption and maldigestion mainly result from a diffuse shortening of epithelial microvillus. *Giardia duodenalis* (synonyms *intestinalis, lamblia*) is a flagellate binucleated protozoan, and it has two morphological forms: cysts and trophozoites. The life cycle of *Giardia* is direct, and the infective stage of the parasite, the cyst, is encysted when released into the feces and is immediately infectious. Trophozoites are pear-shaped, binucleate, multi-flagellated parasite forms and are the disease causing stage and colonize the upper small intestine, where they adhere to the epithelial surface and proliferate by binary fission. Infected animals, contaminated water and feed are main sources of infection. Age of animals, season of the year, area, housing, feeding, management practices are usually considered as risk factors for the occurrence of giardiasis. The infection can be transmitted by the fecal-oral route, or through contaminated food and water. To survive within the intestine, *Giardia* undergoes antigenic variation and few virulent factors have been identified to be responsible for the infection. These include ventral adhesive disc proteins and surface lectins, the four pairs of flagella which allow for movement and variant surface proteins. The clearance of *Giardia* from a host requires both innate and adaptive immunity effector mechanisms. The infection can be diagnosed by examining fecal specimens using different coproscopic techniques, serological tests and by molecular analysis. Restricting

animals from surface water during periods of high cyst shedding may reduce watershed contamination. Health education on personal and environmental hygiene would help in reducing the occurrence of the infection. This review work tries to gather information on giardiasis of domestic animals with respect to its epidemiology, host immune responses, pathophysiology, distribution and its public health importance.

Keywords: Giardiasis; *Giardia* assemblages; distribution; immune response; public health.

Introduction

Giardiasis is a diarrheal illness distributed throughout the world. It is caused by a flagellate protozoan parasite, *Giardia intestinalis* also known as *G. lamblia* and *G. duodenalis*. *Giardia* is a common cause of gastrointestinal disturbance in both high- and low-income countries (Hill and Nash, 2006). The synonyms of Giardiasis are Giardia enteritis, Lambliasis, lamblia intestinalis, beaver fever (Huang and White, 2006). *Giardia* is a ubiquitously distributed flagellate protozoon that inhabits the small intestine of its host. *Giardia* infection also affects the gall bladder of an adult cow (Degerli and Ozcelik, 2003). *G. bovis* (*G. duodenalis* assemblage E), *G. duodenalis* assemblage A and mixed infections of *G. duodenalis* assemblage A and *G. bovis* (*G. duodenalis* assemblage E) affect cattle especially calves (Geurden *et al*., 2012). *G. duodenalis* in livestock, particularly in cattle, is very common in this population and tends to infect younger calves leading to high prevalence of infection within herds.

Giardia infections are common in cattle and pet animals (Dogs and cats) (Armson *et al*., 2009). Dairy calves can excrete high number of the cyst of *Giardia*, and the disease in cattle is clinically important and can reduce the growth performance of ruminants. *Giardia duodenalis* assemblage E (*G.bovis)* is most prevalent in calves (Ralston *et al.,* 2003). Clinically, it is characterized by diarrhea, abdominal cramps, bloating, weight loss, and malabsorption. However, asymptomatic giardiasis occurs frequently, especially in developing countries (Hellard *et al*., 2000).

Direct transmission of *Giardia* between cattle and their handlers and indirect transmission through water ponds is possible. Giardiasis is zoonotic and zooanthroponosis. The major significance of giardiasis in veterinary medicine probably rests with its zoonotic potential although it has also been proposed as

a zooanthroponosis (Ehsan *et al*., 2015). Studies have reported between 45%-73% of calves 0-24 weeks of age having infections as well as infection rates as high as 100% (Winkworth *et al*., 2008). *Giardia*-infection in cattle is often subclinical or asymptomatic (Gillhuber *et al*., 2013); but when clinically occurs, the symptoms of giardial infection could include diarrhea, foul smelling stool, flatulence, loss of appetite, and emaciation in different proportions (Monis *et al*., 2009).

Giardiasis is considered to be an important zoonotic disease and animal reservoirs are believed to be cats, dogs, ruminants, and a variety of wild animals. Infections in domestic ruminants are of special concern because of the potential contamination of surface and ground waters through pasture run-offs and use of manure as a spray on fields. Outbreaks from waterborne giardiasis in humans have been attributed to pasture runoff leading to drinking water contamination. Morphological, protein, and DNA similarities among *Giardia* isolated from animals and humans have been demonstrated. The number of clinical reports and transmission studies suggest the possible zoonotic transmission of the *Giardia* parasite (Wolfe, 1992). The objective of this review work is therefore, to compile current information on giardiasis of domestic animals with regards to its epidemiology, host immune responses, pathophysiology, distribution and its public health importance

Etiology

Taxonomy of *Giardia*

Giardia is grouped under kingdom of protista, phylum of protozoa, subphylum of sarcomastigophora, class of mastigophora, order of Giardia, family of Giardia lamblia (Urquhart *et al.*, 1996). Currently, six *Giardia* species are recognized by most researchers. Among them, *G. agilis*, *G. ardeae*, *G. muris*, *G. microti*, and *G. psittaci* infect various animals, whereas *G. duodenalis* infects humans and many mammals (Upton and Zien, 1997). Thus, *Giardia* species differ significantly in host range, with *G. duodenalis* having the broadest host range and greatest public health significance (Yang *et al*., 2009). Cattle may be infected with *G. duodenalis*, which has synonyms of *G. intestinalis* and *G. lamblia*. *Giardia duodenalis* infects nearly all cattle at one time or another, and may cause diarrhea in calves older than 1 month. Although *G. duodenalis* is an important cause of diarrhea in people, and transmission from livestock has long been suspected, current genetic evidence suggests that cattle and people are infected by different subtypes (Olson *et al*., 2004).

The species names *G. duodenalis, G. intestinalis* and *G. lamblia* are used interchangeably in literature referring to the same organism. Both *G. duodenalis* and *G. intestinalis* are used in equal frequency in referring to the *Giradia* species infecting most mammals, including humans, their companion animals and livestock (Feng and Xiao, 2011).

Zoonotic (assemblages A and B) and Assemblage E are genotypes of *G. duodenalis* and *G. microti* (Yang *et al*., 2009). Assemblage A is frequently found in livestock (cattle, water buffalo, sheep, goats, alpacas, and pigs) and companion animals (dogs, cats, and horses). In comparison, assemblage B is less frequently reported from livestock and companion animals, with only a few reports of infection of cattle, sheep, horses, dogs, cats, and rabbits (Thompson *et al*., 2008). Assemblage A and to a lesser extent, assemblage B are commonly found in wild animals, with the exception of beavers and muskrats, which seemingly have a high occurrence of assemblage B.

The livestock-specific species *Giardia bovis* is the most frequently observed in cattle, however, the two zoonotic species *Giardia duodenalis* and *Giardia enterica* have also been found. Therefore, calves are thought to be of public health significance. *G. bovis*only affects cattle specially, calves (Gillhuber *et al.,* 2013). *G intestinG. duodenalis, G. lamblia)* can be subdivided based on molecular analysis into what are known as different genetic assemblages (A, B, C, D, E, F, G and H). Some of these assemblages can be classified even further into subtypes or genetic clusters (Groups I to IV) for example A-I, A-II, A-III, and A-IV. Each assemblage is capable of infecting certain species, and some assemblages are more commonly seen than others (Table1) (Feng and Xiao, 2011).

Phylogenetic analysis of a large set of nucleotide sequence data from the small subunit (SSU) rRNA gene and several housekeeping genes coding for glutamate dehydrogenase (gdh), ß-giardin (bg), elongation factor 1 alpha (ef1α) and triphosphate isomerase confirmed the genetic uniqueness of the assemblages A and B. Additional linages of *G. duodenalis* from animals were identified: assemblages C and D from dogs, assemblage E from artiodactyls, assemblage F from cats and assemblage G from rodents (Table 1).

There is sub structuring within assemblage A, which consists of mostly two subgroups or sub assebmblages AI and AII. The separation of subgroups AI and AII was initially made by allozyme analysis and is supported by phylogenetic analysis of assemblage A sequences at the *gdh* locus. The existence

of numerous subtypes related to subgroups AI and AII, however, made the separation of subgroup AI and AII less obvious at some other loci, such as *tpi* and *bg*. Recently, a third sub group within assemblage A, subgroup AIII, was identified and appears to be associated with wild hoofed animals. It has significant sequence difference from sub groups AI and AII at all loci examined so far.

Table *1.* Different genetic assemblages of *G. intestinalis*

Assemblages	Major species commonly infected
A-I	Humans and animals(Cats, dogs, livestock, Deer, Muskrats, Voles, Guinea pigs, Ferrets)
A-II	Humans (More common than A-I)
A-III and A-IV	Exclusively animals
B	Humans and animals (Livestock, chinchillas. Beavers, Marmosets, Rodents)
C and D	Dogs
E	Alpacas, cattle, goats, pigs, sheep
F	Cats
G	Rodents
H	Marine mammals

Source: (Feng *et al*., 2011)

Morphology

G. lamblia is bilaterally symmetrical like hexamita and possess eight flagella, six of which emerge as free flagella at intervals around the body. It is unique in possessing a large adhesive disc on the flat ventral surface of the body, which facilitates attachment to the epithelial cells of intestinal mucosa (Urquhart *et al.,* 1996) (Fig. 1). *G. duodenalis* (synonyms *intestinalis, lambilia*) is a flagellate binucleated protozoan. *G. lamblia* has two morphological forms: cysts and trophozoites. Trophozoites are pear-shaped, binucleate, multi-flagellated parasite having an adhesive disk on the ventral surface of the trophozoite (Buret *et al.,* 2005). Trophozoites resemble a pear or tear drop and measure 9-21 µm in length, 5-15 µm in width and 1-2 µm thickness (John *et al*., 2006). The trophozoite has two anteriorly placed nuclei and has four pairs of posteriorly directed flagella that aid in locomotion. Cysts are oval-shaped, thin-walled cyst that is 10 to 20 µm in length, 7-10 µm in width and 0.3-0.5 µm thickness (Huang and White, 2006).

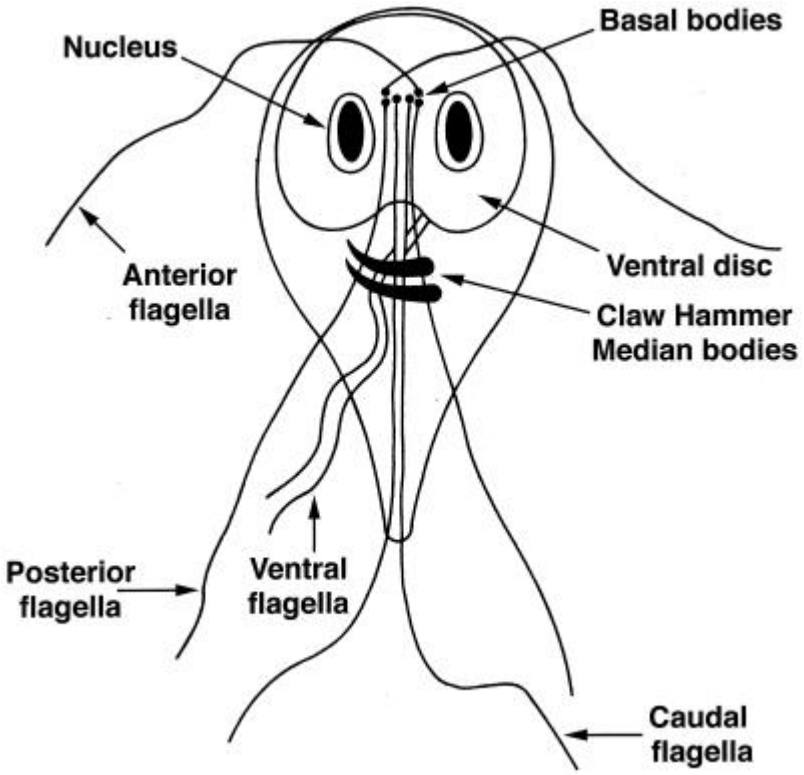

Figure 1. *Giardia lamblia* **trophozoite (Source: Faubert, 2000)**

Life cycle

G .duodenalis has a simple life cycle, which includes the dormant infective cyst released in the feces, each producing, upon exposure to gastric juices during ingestion, one tetranucleated short-lived excyzoite, which will divide twice to give rise to four diploid trophozoites. Trophozoites are the disease causing stage and colonize the upper small intestine, where they adhere to the epithelial surface and proliferate by binary fission (Muller *et al.,* 2008).

An adhesive disk on the ventral surface of the trophozoite facilitates attachment to the mucosal surface of the duodenum and jejunum, although the trophozoite does not invade the mucosal epithelium. Trophozoites that do not adhere to the small bowel move forward to the large intestine where they revert

to the infectious cyst form; conjugated bile salts appear to foster encystations (Buret, 2009).

The life cycle of *Giardia* is direct, and the infective stage of the parasite, the cyst, is encysted when released into the feces and is immediately infectious (Huang and White, 2006). Cysts remain infectious for months in cool, damp areas and rapidly accumulate in the environment. In soil, cyst infectivity is reduced by only 11% after 49 days at 4°C and is non-infective after 7 days at 25°C. In tap water, *Giardia* cysts are infectious for 56 days at 0°C to 4°C and 14 days at 20°C to 28°C. Similar results were obtained in lake water, with 56 days of survival at 0°C to 4°C or 6°C to 7°C and 28 days at 17°C to 20°C (Huang and White, 2006). Longer survival is noticed in river water, with 84 days of survival at 0°C to 4°C and 28 days at 20°C to 28°C (Huang and White, 2006). Cysts are the infectious form of the parasite; these can survive in moist environments for prolonged periods (Rendtorff, 1954). In seawater, *Giardia* cysts can survive for over 65 days at 4°C. Ingestion of 10 to 25 cysts can lead to giardiasis. When ingested by the host, cysts excyst in the duodenum, releasing the trophozoites (Erickson and Ortega, 2006). The latter trophozoites undergo repeated mitotic division and form environmentally resistant cysts in response to the stimulation of bile salts and other conditions. Cysts pass through the intestine in feces and are spread by contaminated water, food, fomites, and by direct physical contact (Erickson and Ortega, 2006) (Fig. 2).

Cysts are passed back into the environment in excreted feces; in the setting of diarrhea, trophozoites can also be found in the feces (Buret, 2009). A motile vegetative form (trophozoite) which resides in the small intestine and is responsible for disease manifestations and an infective resistant form (cyst) is responsible for transmission. The trophozoite is an aero tolerant anaerobe that requires glucose as a source of carbohydrate energy, and divides by longitudinal binary fission every 9 to 12 hours (Huang and White, 2006). The incubation period, which is the time from infection and manifestation of clinical signs is 7 to 14 days; however, the time from ingestion of the cysts to detection of the cysts may be longer than the incubation period (Leder and Weller, 2011).

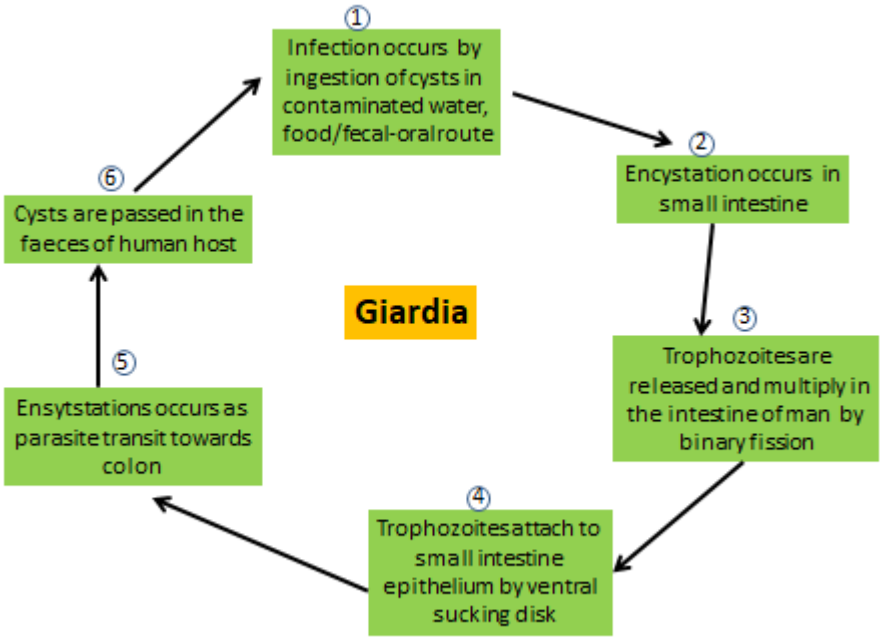

Figure 2. Life cycle of *Giardia intestinalis* (Muller *et al.,* 2008)

Epidemiology

An important aspect of the epidemiology of giardiasis is to understand the host range of different *Giardia* species and strains/genotypes, the potential for cross – species transmission and risk and environmental factors involved in the exposure of the pathogen. This is particularly important in determining the zoonotic potential of *Giardia* infections in domestic animals and in determining the human disease burden attributable to parasites of animal origin (Feng and Xiao, 2011).

Occurrence of giardiasis

Giardia infections occur worldwide (Krauss *et al*., 2003). Giardial infection is found in most continents and is identified in all of the common agricultural animals. A longitudinal studies of excretion patterns in grazing beef cattle,

feedlots cattle, dairy cattle, calves and foals show infection rates approaching 100% (Radostits *et al*., 2009). *G. lamblia* is one of the most commonly identified intestinal pathogens in humans and animals in the world (Xiao, 1994). Recent studies have identified domestic livestock (e.g., cattle, sheep, pigs, horses) as major hosts for this parasite. Calves become infected with *Giardia* at around 4 weeks of age and infections persist for over 120 days (Olson *et al*., 1997). In cattle, the occurrence of infection with *G. duodenalis* is higher in immature cattle than in adult animals. The highest risk of infection is seen in the pre-weaned age group (Minetti *et al*., 2012).

Source of infection of giardiasis

Young animals are the primary source of infection; infection being transmitted through the oral-fecal route. High excretion rates and excretion intensities in young animals result in the contamination of the environment and infection via fomites. The dam is also a source of infection for the young. Cross-infection from other species and infection from contaminated water and feed are other sources of infection. Epidemiological evidence suggests that domestic animals act as a reservoir for the parasite and serve as source of infection for humans (Radostits *et al*., 2009**)**.

Risk factors of Giardiasis

The parasite risk factors

The infectious dose of giardiasis is thought to be very small. *Giardia* is relatively resistant to environment and at 4 ^{o}C can survive for 11 weeks in water, 7 weeks in soil and 1 week in cattle feces. But, they do not survive in freezing. They are resistant to chlorination and extensive disinfection of the environment of calves does not prevent reinfection (Radostits *et al*., 2009).

Host risk factors

The age of the cattle probably contributed to the different infection rates observed (Feng and Xiao, 2011**)**. Age is a major determinant of infection; excretion rates are much higher in the young of all livestock species than in adults. Cysts excretion falls after weaning, but may persist intermittently into adulthood. Excretion rates in groups of calves are highest between 3 and 10 weeks of age with the number of cysts in feces highest at 1-6 weeks of age. The cyst

excretion levels varied considerably both within and between herds for all age of animals (Radostitis *et al.,* 2009). The prevalence of infection is varied according to the age group, with the highest prevalence of infection seen in preweaned animals followed by neonatal calves, post-weaned animals and adult cattle. The risk of *G. duodenalis* infection is significantly higher only in preweaned calves (Minetti *et al*., 2012).

Management risk factors

The prevalence of infection is higher in calves left with their dams to nurse colostrum than in calves removed from the dam at birth to individual housing and fed colostrums by nipple bottle (Radostitis *et al.,* 2009). There is a potential association between *G. duodenalis* infection and parameters relating to housing and production type. Prevalence of *G. duodenalis* varies according to production system; where an infection prevalence is high in suckler systems than infection prevalence in non-suckler systems (dairy, calf rearer or beef fattener). The prevalence of infection in housed animals is higher than that in cattle that are kept in outdoors or in mixed accommodation (Minetti *et al*., 2012). It is noted that the monthly distribution pattern of giardiasis in bovine is related to the temperature, humidity, the rainfall, season and area (Ayaz *et al*., 2008).

Mode of transmission of giardiasis

Giardia cysts are commonly excreted in the faeces. The organism is passed as multinucleated cysts in the faeces, where the flagella may be visible, and occasionally as trophozoites (Urquhart *et al*., 1996). Infection is acquired via the faecal-oral route**,** often through the ingestion of *Giardia* cysts from faecally-contaminated water. *G. lamblia* can be transmitted from person-to-person, animal-to-person, food borne or waterborne. Ingestion of as few as 10–25 cysts can cause illness (Hill and Nash, 2006).

Sexual behaviors that aid in transmission of *G. lamblia* include oral-anal, genital-anal, and digital anal contact. Contaminated soil and fomites can also contain infective cysts (Berger and Marr, 2006). It can be transmitted from person-to-person, especially persons with poor fecal-oral hygiene, causing epidemics (Huang and White, 2006).

The most common method of transmission in animals and humans is the fecal-oral route (Xiao, 1994). Disease outbreaks have most often been attributed to the waterborne method of transmission. It is believed that human effluent is the major source of water contamination, but certainly contamination of water with infected animal feces can lead to widespread infections in human and animals (Wallis *et al*., 1996). *Giardia* cysts are infectious at the time they are passed in feces (Olson *et al.,* 2004).

The high prevalence of infection in cattle reports that cattle shed cysts of zoonotic types that infect humans (Handley *et al*., 2000; Keulen *et al*., 2002). *Giardia* from cattle is potential zoonotic pathogen, and contact with their manure is believed to be the major risk factor for infection in humans (Olson *et al*., 2004). In cattle, direct transmission through the contamination of barns and/or pasture appears to be the principal mode of infection (Ruest *et al*., 1998).

Status of giardiasis

Global status of giardiasis

Giardia is the most common causes of protozoan diarrhea that lead to significant morbidity and mortality in the developing and developed world. Outbreaks of giardiasis are well documented worldwide. High infection rates for giardiasis are found in developing countries. The rates of infection are high in various Asian countries (Bangladesh, Cambodia, China, India, Indonesia, Laos, Malaysia, Nepal, Philippines, Thailand, Turkey, Saudi Arabia, and Vietnam), South America Cuba, Mexico, and Nicaragua, Argentina, Brazil, Colombia, and Peru, and Africa (Northern Africa, West Africa, and South Africa) (Wegayehu *et al*., 2013). *G. lamblia* is the most commonly identified intestinal parasite in the US as well as in Canada (Hill and Nash, 2009). The prevalence of cumulative infection is 73 to 100% in cattle in the world (Feng and Xiao, 2011) (Table 2).

Table 2. Global distribution of giardiasis in cattle

Country	Prevalence (%)	Reference
Turkey	3.7	Degerli and Ozcelik, 2003
Britain	36	McAllister *et al.*, 2005
Bangladesh	22	Ehsan *et al.*, 2015
Denmark	43.6	Feng and Xiao, 2011
Germany	38	Feng and Xiao, 2011
Iraq	30.6	Monis *et al.*, 2009
Italy	30.0	Feng and Xiao, 2011
Norway	49.0	Feng and Xiao, 2011
Ontario	64	McAllister *et al.*, 2005
Spain	26.6 to 30.1	Feng and Xiao, 2011
Canada	8.7 to 57.0	Feng and Xiao, 2011
United States	19.1 to 52.0	Feng and Xiao, 2011
Sweden	23	Bjorkman *et al.*, 2003
New Zealand	4.5 to 40.6	Feng and Xiao, 2011
Australia	58.0	Feng and Xiao, 2011

Status of giardiasis in Africa

In Africa, *Giardia* has been reported in several domesticated animal species including cattle, sheep, goats, farmed buffalo, horses, poultry (chicken and turkey), pigs, cultured tilapia (fish) and dogs (Di cristanziano *et al.*, 2014). However, the majority of research has been conducted in cattle.

Giardia duodenalis Assemblage E is the dominant species in ruminant livestock (cattle, farmed buffalo and goats) from the Central African Republic, Egypt, Rwanda, Tanzania and Uganda (Helmy *et al.*, 2014; Abdel-Moein and Saeed, 2016; Sabry *et al.*, 2009). Assemblage A (subtypes AI and AII) has been reported in goats, cattle, buffalos, ducks and chickens from Cote d'Ivoire, Egypt, Tanzania and Uganda and Assemblage B (BIV) and/or Assemblage A and B have been reported in goats, ducks and cattle from Cote d'Ivoire, and Tanzania (Sabry *et al.*, 2009; Helmy *et al.*, 2014; Abdel-Moein and Saeed, 2016) (Table 3).

Table 3. Prevalence and *Giardia duodenalis* assemblages reported in animals from Africa

Country	Animal spp	Prevalence (%)	Assemblage	Reference
Central Africa republic	Goat	11.1	E	Ignatius *et al.* (2012)
Cote d'voire	Dog	54.5	A	Berrilli *et al.* (2012)
	Goat	50	A, B	Berrilli *et al.* (2012)
	Chicken	58.1	A	Berrilli *et al.* (2012)
Egypt	Cattle	6.7	A	Helmy *et al.* (2014)
	Cattle	8.7	E	Abdel-Moein & Saeed, 2016
	Calves	30.8	A	Sabry *et al.* (2009)
Rwanda	Cattle	5.9	E	Hogan *et al.* (2014)
Tanzania	Zebu Cattle	21.1	A	Di Critanziano *et al.* (2014)
	Goats	22	E	Di Critanziano *et al.* *(*2014)
Uganda	Cattle(*Bos Taurus*)	10	A	Graczyk *et al.* (2002)

The status in Ethiopia

There are very few reports on the occurrence of *G. duodenalis* infection *(*Giardiasis) are available in domestic animals in Ethiopia. Outbreak of giardiasis was reported from cattle and human in Girar Jarso and Dera Districts of North Shewa Zone, Oromia Region, Ethiopia. (Wegayehu *et al*., 2013). The outbreak of *Giardia lamblia was also recorded in* Lante, Kolla Shelle, Dorze and Geressie kebeles of Gamo Gofa Zone, South Ethiopia. *Giardia lamblia (Giardia duodenalis)* infections have been reported from the lowland and highland areas of Gamo area **(**Wegayehu *et al*., 2013**).** Hailu *et al.* **(**2020) has reported 9.7 % prevalence of Giardia from dairy calves from southern Ethiopia (Arsi Negele, Shashemene and Hawassa dairy farms)**.** *Giardia lamblia (Giardia duodenalis)* infection has also been reported from Benishangul-Gumuz Region and South west Ethiopia (Jimma) (Eyasu *et al*., 2010; Mengistu *et al*., 2007) (Table 4).

Table 4. Prevalence of G. duodenalis species among cattle and human in Ethiopia

Study subjects	Study sites	Prevalence (%)	References
Cattle	Girar Jarso and Dera	2.3	Wegayehu *et al*., 2013
	Gamo Gofa zone	10.6	Teklu *et al*., 2013
Human	Girar Jarso and Dera	50	Wegayehu *et al*., 2013
	Benishangul Gumuz Region	26.6	Eyasu *et al*., 2010
	Jimma	47.7	Mengistu *et al*., 2007
Dairy calves	South Ethiopia	9.7	Hailu *et al*, 2020
Dairy calves	Central Ethiopia	9.6	Teklu *et al*., 2016

Pathology, virulence factors and host defense to giardiasis

Pathology of giardiasis

Animals and humans infected with *G. duodenalis* develop a broad range of clinical manifestations, ranging from an absence of symptoms to acute or chronic diarrheal disease with abdominal pain and nausea. Diarrheal symptoms mostly occur during the acute phase of the infection. The majority of *Giardia* infections are self-limiting, although reinfection and chronic infection can occur (Buret *et al*., 2015).

The pathophysiology of giardiasis is multifactorial and involves parasitic, host, dietary, and environmental factors, as well as immunological and non-immunological processes. The pathophysiology of acute diarrhea in giardiasis implicates increased rates of enterocyte apoptosis, a disruption of the intestinal barrier function, activation of host lymphocytes, CD8+ lymphocyte -mediated shortening of brush boarder microvilli with or without coinciding villous atrophy, disaccharidase deficiencies, small intestinal malabsorption, anion hypersecretion, and increased intestinal transit rates (Buret *et al*., 2015).

The small intestine is the site of the major structural and functional abnormalities associated with giardiasis. Mild or moderate partial villous atrophy or subtotal villous atrophy occurs in severe cases. An increase in crypt depth may be seen, and microvillus shortening or disruption may occur. Deficiencies in epithelial brush border enzymes, such as lactase, may develop (Buret, 2009).

Loss of epithelial barrier function is a result of *Giardia*-induced enterocyte apoptosis. These effects may facilitate the development of chronic enteric disorders, including inflammatory bowel disease, irritable bowel syndrome, and

allergies (Buret *et al.,* 2008). Reported changes are an increase in intraepithelial lymphocytes in the jejunum, with moderate to severe diffuse inflammation, crypt distortion and a reduction in villus to crypt ratio (Radostits *et al*., 2009).

In addition to duodenal involvement, the gall bladder may occasionally become parasitized by G. intestinalis. In such individuals, there may be associated gall bladder colic and jaundice, due to obstruction of the bile passages or irritation and edema (Buret *et al.,* 2015).

Pathogenic effects and virulence factors

Giardia lamblia causes infection of the small intestine, which leads to malabsorption and chronic diarrhea. In giardiasis, mucosal surface area per unit serosa area is decreased to 75% of control, as a result of which, epithelial resistance of giardiasis biopsy specimens is decreased. *G. lamblia* infection causes epithelial barrier dysfunction and increased epithelial apoptosis (Troeger *et al*., 2007).

Malabsorption and maldigestion mainly result from a diffuse shortening of epithelial microvillus and a loss of total epithelial brush border surface area, and diffuse microvillus shortening is mediated by activated host T- lymphocytes. This activation is secondary to *Giardia*- induced disruption of epithelial tight junctions, which in turn increases intestinal permeability. This parasite may breach the epithelial barrier by inducing enterocyte apoptosis. These effects may facilitate the development of other enteric disorders in infected patients. Recent observations indicate that host epithelial nitric oxide responses, as well as a newly discovered glucose-mediated cytoprotective mechanism, may represent effective modulators of the epithelial apoptosis induced by these parasites. Infection appears to cause diarrhoea via a combination of intestinal malabsorption and hyper secretion (Buret *et al*., 2008; Buret, 2009).

Clinical manifestations of giardiasis are quite variable, ranging from the absence of symptoms to acute or chronic diarrhea, dehydration, abdominal pain, nausea, vomiting, and weight loss (Robertson *et al*, 2010)). The severity of disease is probably determined by the interplay between the virulence of the parasite, the developmental, nutritional, and immunological status of the host, the nature of intestinal microflora, and the presence or absence of other co-pathogens. Although different *G. duodenalis* assemblages may produce different toxins or metabolic products that may contribute to their pathogenic-

ity, studies of the possible association between *G.duodenalis* assemblages and virulence (indicated by the likelihood of causing diarrhea and other clinical symptoms, as many *G. duodenalis* infections are asymptomatic) have thus far produced inconsistent results. Overall, *Giardia*-induced diffuse shortening of brush border microvilli causes small intestinal malabsorption due to impaired absorption of water, glucose, and electrolytes.

Giardia trophozoites undergo fundamental changes to survive outside the intestine of their host by differentiating into infective cysts. Encystation entails the synthesis, processing, transport, secretion and extracellular assembly of cyst wall components. To survive within the intestine, *Giardia* undergoes antigenic variation, a process by which the parasite continuously switches its major surface molecules, allowing the parasite to evade the host's immune response and produce chronic and recurrent infections (Lujan, 2011).

A few virulence factors have been suggested on the basis of their targeted effects (Ankarlev *et al*., 2010). For example, ventral adhesive disc proteins and surface lectins ensure appropriate attachment to enterocytes of the upper small intestine, while the four pairs of flagella allow for movement, and variant surface proteins help evade host IgA-directed clearance (Ankarlev *et al*., 2010).

Variant surface protein expression may also confer zoonotic infectivity to *Giardia* isolates. The arginine deiminase produced by the parasite deprives intestinal epithelial cells of arginine, thereby impairing intestinal epithelial proliferation and nitric oxide production (Stadelmann *et al*., 2013). Alpha-2 giardin appears to be an assemblage A-specific protein, but its role in host– parasite interactions remains obscure.

An unknown 58-kDa product released by *Giardia* trophozoites has been reported to induce anion hypersecretion and intestinal fluid accumulation by activating signal transduction pathways in host enterocytes (Stadelmann *et al*., 2013). However, parasite products directly involved in the pathogenesis of giardiasis remain largely unknown.

Host defense to *Giardia* infection

Although current knowledge regarding the mechanisms of immunity to *Giardia* is limited, several studies have produced significant advances in the

understanding of innate and adaptive host responses against the parasite (Faubert, 2000).

Innate and adaptive immune systems act in synchrony to control *Giardia* infection. Innate immune mechanisms are the first line of defense against *Giardia* colonization. The mucus layer on the intestine surface and peristaltic movements constitute mechanical barriers to *Giardia* attachment. Antimicrobial peptides (AMP) released by paneth and other cells can kill trophozoites (Faubert, 2000).

Gut microbiota have an anti-*Giardia* effect by competition, direct toxicity or modulating the immune response. Additionally, microbiota contributes to preserve gut integrity. Mast cells release pro-inflammatory cytokines such as IL-6; mast cell degranulation promotes peristalsis. Gut epithelial and immune cells produce nitric oxide (NO), which has a cytostatic effect on *Giardia* trophozoites, inhibits excystation/encystation processes and contributes to peristalsis (Faubert, 2000).

Mast cells take up antigens from the lumen of the gut by endocytosis into peyer patches (PP) to induce immune responses. Dendritic cells (DC) play a role as a 'connector' between innate and adaptive immunity. Dendritic cells are localized in lamina propria and peyer patches where they can recognize antigens. Dendritic cells also can expand their dendrites into the intestinal lumen to take up antigens (Faubert, 2000).

Dendritic cells ingest and process *Giardia* antigens for further presentation to naive T cells by MHC class II molecules (MHC-II). Activated T cells release a panel of cytokines, which modulate the anti-*Giardia* response. IL-6 released by mast cell, DC or T cells is an important modulator of B-cell maturation, and it induces antibody class switching to produce IgA. Plasma cells migrate to lamina propria to release IgA, which can inhibit *Giardia* attachment to intestinal epithelial cells. Th17 $CD4^+$ T cells are activated during early adaptive immunity against *Giardia,* and release cytokines such as IL-17, IL-21, IL-22, which play a pro-inflammatory role. Intra-epithelial lymphocytes (IEL) are mainly $CD8^+$ T cells and play a role in pathological damage of intestine during giardiasis (Faubert, 2000).

Public health significance of giardiasis

Giardiasis exerts a significant public health impact because of the high prevalence and disease burden of the infection, its propensity/inclination in causing major outbreaks and emergency responses, and its effects on growth and cognitive functions of infected children. Giardiasis is also a common disease in livestock and companion animals; thus, it is of veterinary health importance. In General, giardiasis is highly under reported for various reasons.

Infection rates for giardiasis in humans are generally lower in developed countries. Previous studies reported infection rates of 4.0% in Belgium (Geurden *et al.,* 2009), 1.5% in Germany (Sagebiel *et al*., 2009), 0.4% to 6.2% in Italy (Crotti *et al*., 2005, Giangaspero *et al*., 2007), 3.7% in Portugal (Almeida *et al*., 2006), 5.4% in Spain (Manzardo *et al*., 2008), 1.3% in the United Kingdom (Davies *et al*., 2009), 1.4% in the United States (Church *et al.,* 2010), 2.5% in South Korea (Huh *et al*., 2009), 1.6% to 7.6% in Australia, and 7.6% in New Zealand (Hellard *et al*., 2000).

Most of the surveys were conducted with asymptomatic children. The occurrence of giardiasis is probably higher in children with diarrhea. Thus, in the Nordic countries of Denmark, Finland, Norway, and Sweden, the infection rate of giardiasis was estimated to be 2.9% and 5.8% for asymptomatic and symptomatic persons, respectively (Horman *et al*., 2004).

A similar trend was seen in the Netherlands, with infection rates of 14.0% in patients with persistent diarrhea and 2.0% in asymptomatic subjects (Homan and Mank, 2001). Although *Giardia* is not considered an opportunistic pathogen in immunocompromised patients, the infection rates of giardiasis in HI infected people ranged from 3.5% to 6.2% in Italy before the introduction of highly active antiretroviral treatment (Giangaspero *et al*., 2007).

Relatively few *Giardia* genotyping studies have been conducted in Africa, however available reports reveal that five *G. duodenalis* assemblages (A, B, C, E and F) have been identified in humans. In Africa, Assemblage B was the most prevalent among typed samples (19.5– 100%) in 18 out of 28 studies reviewed (Ryan, 2017). Although many studies have reported that *Giardia* is not associated with severe diarrhea, one study reported that the prevalence of *G. duodenalis* Assemblage A was higher among children with vomiting and abdominal pain (Ignatius *et al*, 2012).

Assemblage C was detected in an adult immunocompromised male suffering from bladder cancer and diarrhoea in Egypt (Soliman *et al.* 2011) and Assemblage F was reported in six diarrhoeal and one asymptomatic individual in Ethiopia (Gelanew *et al.,* 2007). In that study, four of the identified Assemblage F isolates were mixed infections with Assemblage A. Assemblage E has been reported in humans in three separate studies in Egypt with a prevalence of up to 62.5% in one study population (Helmy *et al.,* 2014). Subtyping studies in Africa have identified sub assemblages AI, AII, BIII, BIV and various novel sub assemblages (Ryan, 2017).

Outbreaks of Giardiasis in humans

Although most cases occur sporadically, outbreaks of giardiasis are well documented. A review by Karanis *et al.,* 2007, indicated that there have been at least 132 reported waterborne outbreaks of giardiasis worldwide since 1954. Among them 104 were related to drinking water, 18 were related to recreational water and ten were related to foreign travel. The majority of the outbreaks were reported in North America and Europe because of better surveillance and reporting systems.

In addition, food-borne outbreaks of giardiasis linked to infected food handlers and food handlers who changed diapers of infected children prior to handling food have been reported (Hoffmann *et al*., 2007). Outbreaks resulting from person to person transmission in child care centers are also common (Ang, 2000). Few direct animals to human outbreaks have been documented.

Sources of infection for humans

Contaminated water

A review of waterborne disease outbreaks, between the years of 2004 and 2010, stated that *G. duodenalis* accounted for 70/199 (~35%) reported outbreaks of human disease due to waterborne protozoa within high-income countries (Baldursson and Karanis, 2011). It was however noted that the majority of the data in these studies was taken from higher income countries, as low-income countries often lack the necessary systems allowing surveillance capabilities. The real-world burden of waterborne disease outbreaks with *G. duodenalis* will remain unknown until global surveillance is implemented. Young children are often at the forefront of the effects of diarrhoeal-causing disease organisms, such as *G. duodenalis*, which can have a large impact on development.

Effective filtration and identification of the parasite from water samples is becoming significantly important to minimize the risk of water-borne outbreaks (Baldursson and Karanis, 2011).

Contaminated food

Salad items and vegetables have been often highlighted as a foodborne risk for giardiasis. Salad and vegetable items which are (a) improperly washed to remove cysts or (b) washed, but in contaminated water, and (c) poor food handler hygiene can lead to human giardiasis (De Lalla *et al.*, 1992).

Additional methods of foodborne giardiasis include infection via cold drinks (contaminated water frozen to make ice) (De Lalla *et al.,* 1992), shellfish which are contaminated with cysts (filter feeding shellfish can accumulate cysts within them) (Giangaspero *et al*., 2014).

Infected persons

Giardia duodenalis prevalence within the global human population varies between high- and low-income countries throughout the world, with infection estimates of between ~5 and ~20% respectively (Roxstrom-Lindquist *et al.,* 2006). Within the high-income countries, strict control and filtration of drinking water, as well as high-quality sanitation systems, prevent the disease being as prevalent as it is in poorer areas of the world (Roxstrom-Lindquist *et al.,* 2006).

Due to the cysts being infectious when excreted in feces, humans have the potential to pass on the pathogen to other humans either from direct contact or via transmission from contaminated sources, e.g. foods, most likely due to poor hygiene (Roxstrom-Lindquist *et al*., 2006).

Control and prevention

Treatment

Supportive treatment should be done; dehydration and electrolyte abnormalities should be treated symptomatically in humans (Handley, 1997).

Metronidazole, tinidazole, and furazolidone are effective drugs. Benzimidazoles (Fenbendazole, Mebendazole, Albendazole) have also been shown to be

effective in elimination of *Giardia lamblia (G. duodenalis)* in cattle (Handley, 1997). *Giardia* infections in agricultural animals have been successfully treated with Dimetridazole at a dose of 50mg/KgBW daily for 5 days (Radostits *et al*., 2009).

Preventive approach

Restricting cattle from surface water during periods of high shedding may reduce water shed contamination (McAllister *et al*., 2005). Cysts are relatively resistant to chlorination, but *Giardia* cysts in water can be inactivated with 4 mg/L of chlorine after 60 min at 5°C, at pH levels 6, 7 and 8. A chlorine concentration of 8 mg/L will inactivate *Giardia* cysts at pH 6 and 7 after contact for 10 min, and at pH 8 after 30 min. Also, at 25°C, *Giardia* cysts will be killed when exposed to 1.5 mg/L of chlorine for 10 minutes at pH 6. 6% H_2O_2 can be used as a surface disinfectant or in disinfection of spills. *Giardia* is inactivated by exposure to UV light (10 JM^{-2}). Cysts are also susceptible to boiling and freezing (Linden *et al*., 2002).

We can also decontaminate all wastes that contain or have come in contact with the infectious organism before disposing by autoclave, chemical disinfection, gamma irradiation, or incineration. The infectious agent should be stored in leak-proof containers that are appropriately labeled. Lab coat, gloves and eye protection must be used where there is a known or potential risk of exposure to splashes (Burnett *et al.,* 2009).

A *Giardia* vaccine (*Giardia*Vax®) is commercially available for dogs and cats but vaccine is not efficacious in preventing giardiasis or reducing cyst shedding in calves (Uehlinger *et al*., 2007).

G. duodenalis infection is widespread in varying magnitude among children and cattle. Significantly, higher prevalence of *G. duodenalis* is detected among children who have close contact with cattle than those who have no contact. This suggests that contact with cattle and their manure will be a risk factor for infection with this protozoan parasite. Therefore, molecular techniques are necessary to clarify the source of infection and transmission pattern of the parasites. Moreover, measures including health education on personal and environmental hygiene would help in reducing the prevalence of these parasites (Wegayehu *et al*., 2013).

Conclusions

Giardiasis is a protozoan infection affecting various domestic animals, wild animals and humans throughout the world. It has both zoonotic and veterinary importance. The causative agent, *Giardia doudenalis* has various assemblages with various host ranges. Transmission of the parasites usually occurs through fecal oral route from infected animals through cyst contaminated water and feed. The disease is very important in young animals, which are kept in confinements for instance in dairy farms, feedlots particularly in areas with poor hygiene. Various reports on the occurrence of giardiasis are available from developed countries however very few ones are reported from Ethiopia requiring attention to study its occurrence, epidemiology, transmission patterns of the parasite and its public significance. Giardiasis has both public health and veterinary significance being transmitted from infected animals to humans through drinking water, consumption of uncooked feed and through direct contact with infected animals. Detailed studies on the distribution and occurrence of giardiasis, pathogenic significance of *Giardia* and identification of circulating species/ genotypes of *Giardia* in domestic animals and humans in Ethiopia should be initiated.

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