Giardia lamblia assemblages and their correlation with the severity of diarrhea: A review article

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ABSTRACT

Background: *Giardia lamblia* is responsible for a range of clinical conditions, from asymptomatic to acute or chronic symptomatic forms. The genetic variability of *Giardia lamblia* raises the possibility of a relationship between its assemblages and the clinical severity of giardiasis. We conducted a review of the literature from 2001 to 2023 to explore the association between *G. lamblia* assemblages and the severity of diarrhea.

Material and Methods: A search was performed through databases of PubMed, WHO, Health Protection Agency, the UK and Centre of Disease Control USA websites and Medline. This search yielded 47 studies from 2001 to 2023 as only those articles providing information on the correlation between different assemblages of *G. lamblia* and the severity of the disease were included.

Results: Out of a total of 47 studies that were included, only 26 studies showed a meaningful comparison. 12 studies showed no difference between different *G. lamblia* assemblages and the severity of giardiasis, while 14 studies demonstrated the link between *G. lamblia* assemblage and the severity of the disease.

Conclusion: Numerous studies have attempted to identify the link between its assemblage profile and the symptoms it causes but with little success. However, the findings of these studies are contradictory and inconclusive, making it difficult to establish a clear association. However, the divergence in findings suggests that a definitive correlation cannot yet be established. To fully understand the link between assemblages and severe diarrhea, further molecular studies are needed, especially in large populations residing in endemic regions.

Keywords: Giardia lamblia, Diarrhea, Assemblages

BACKGROUND

Giardia duodenalis (syn. G. intestinalis, and G. lamblia) is an important cause of diarrhea (giardiasis) and a major public health concern worldwide. Around 250 million reported cases of diarrheal illness are caused by giardiasis globally. The estimated prevalence rate of G. lamblia in developing and developed countries is 70% and 2% respectively. Several factors such as environmental and socioeconomic factors, and personal hygiene habits account for the prevalence of G. lamblia infection. ^{2,3,4}

G. lamblia is a flagellated protist which belongs to the order Diplomonadida and most commonly detected

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protozoan parasite in the intestinal tract. G. lamblia isolates are categorized into seven assemblages (A-G), based on the characterization of the glutamate dehydrogenase, and small subunit triosephosphate isomerase genes. Only assemblages A and B infect humans and other hosts such as wild mammals, dogs, cats and other livestock. Type A G. lamblia is further divided into subtypes A-I and A-II. Isolation of both assemblages A and B from the individuals have been reported from Europe, Asia, Australia and North America. The true geographical distribution of different assemblages of this parasite with various communities remains less understood. Assemblage A is predominant in Europe^{6,7,8} while one study from Australia reported that 70% of children from a day-care center were infected with assemblage B.9 Water and foodborne transmission remains the main routes of G. lamblia. After ingestion of infected cysts from water or food, it is thought that protozoan causes direct damage to the microvilli of the duodenum and upper third of the jejunum which eventually leads to rapid turnover of the mucosal epithelium and changes in absorption and intestinal transit. The other possible route of transmission includes a person-to-person spread

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for instance in day-care settings, in mentally handicapped institutions and during sexual intercourse. Giardiasis is also linked with travel to endemic areas. 10,11

The clinical manifestations of giardiasis range from asymptomatic infection, acute self-limiting diarrheal illness, and chronic gastrointestinal symptoms with intermittent diarrhea to malabsorption. 12 The majority of infected individuals (60-80%) are asymptomatic. Subacute and chronic giardiasis probably leads to weight loss, growth retardation, decreased cognitive functions and poor performance at school in children. In addition, patients with giardiasis may present with cholecystitis and pancreatitis.¹³ Several extra-intestinal symptoms such as fever, urticaria, aphthous ulcers, polyarthritis, lymphadenopathy, maculopapular rash, geographic tongue and pulmonary infiltrates have previously been reported.¹⁴ The severity of giardiasis is associated with the virulence and pathogenicity of G. lamblia and host factors for example nutritional and developmental status, immune status and age. ¹ The possible association between the genotype of G. lamblia and the severity of the disease remains debatable. However, several studies have previously attempted to describe the possible association between different genotypes of G. lamblia and the severity of the disease. 15,16 This article aims to review the association between various Giardia lamblia genotypes and the degree of severity observed in cases of giardiasis.

MATERIAL AND METHODS

Several sources were used to access data for this review. A search was performed through databases of PubMed, WHO, Health Protection Agency, the UK and Centre of Disease Control USA websites and Medline with keywords *G. lamblia*, a correlation between Assemblages of *G. Lamblia* and severity of diarrhea. This search yielded 47 studies as of April 2023 as only those articles providing information on the correlation between different assemblages of *G. lamblia* and the severity of the disease were included.

RESULTS

Twenty-six studies which provided sufficient and useful information for a reasonable and meaningful comparison were included in this review. Of the 26 studies, 12 studies showed no difference between different *G. lamblia* assemblages and the severity of giardiasis as shown in Table-I, while 14 studies

demonstrated the link between G. lamblia assemblage and severity of disease as shown in Table-II. The studies that reported the absence of a significant association between G. lamblia assemblage and severity of illness were conducted in Albania, Brazil, Mexico, Turkey, Iran, Pakistan, India, Egypt, Cuba, England and Malaysia. In these studies, the authors investigated the possible association of G. lamblia genotype with the severity of diseases including the prevalence of genotypes, chronic diarrheal disease, presentation and markers of intestinal inflammation, nutritional status, environmental, socio-economic factors and G. lamblia infection. It was observed that children infected with Assemblage B shed more cysts than children with Assemblage A. Furthermore, children with diarrhea due to mixed assemblages shed more cysts than children with assemblages A or B alone.17

The studies that reported a significant association between G. lamblia assemblage and the severity of the disease were conducted in Spain, Bangladesh, India, Australia, Netherlands, Turkey, Ethiopia, KSA, Egypt, England, Iraq and Iran. A study from Spain showed a significant association of assemblage A with symptomatic giardiasis observed in < 5 years old patients.³² Two studies from Bangladesh^{15,34} showed a significant correlation between assemblage A and the severity of diarrhea. Higher DNA load was noted in assemblage B and was associated with asymptomatic patients.¹⁵ Ajjampur et al from India included 452 children with diarrhea in their study that showed assemblage A association with more diarrheal symptoms.³³A study conducted in Australia that included 353 children under five years of age showed assemblage A's significant association with severe giardiasis.16 In a study from the Netherlands, the researchers found that assemblage B was associated with persistent watery or profuse diarrhea while assemblage A was linked with intermittent diarrhea. The duration of diarrhea with assemblage B was also prolonged as compared to assemblage A.6 A study by Aydin et al in Turkey revealed Assemblage A identified in 17 symptomatic patients while Assemblage B caused diarrhea in three symptomatic patients.²⁸ A study from Ethiopia reported that assemblage B was associated with symptomatic infections such as diarrhea, abdominal pain and nausea in 12 of 13 cases.²⁹ In Saudi Arabia. patients infected with assemblage B were symptomatic, despite a low number of samples (n = 40). Two studies from different parts of Egypt showed variable results. EI

Basha *et al* reported clinical severity with Assemblage A, whereas, Ahmed NS *et al* observed more symptomatic cases with Assemblage B.^{38,39} Two studies

from Iraq and Iran reported the severity of symptoms associated with Assemblage B. 36,40

Table-I: Summary of the studies that observed no significant association between Giardia assemblage and the severity of diarrhea.

Author and year of publication	Study Location	Study population	Number of samples/PCR done	Assemblage	Statistically significant association
Cedillo-Rivera et al., 2003	Mexico City	Children and adults	26/26	A=21	None
				B = 1	
Berrilli et al., 2006	Albania	Children under 9	125/22	A=10	None
		years		B=12	
Kohli <i>et al.</i> , 2008	Brazil	Children	108/58	A=9	None
				B=43	
				Mixed A/B=6	
Breathnach AS et al., 2010	England	Children & adults	267/199	A=48	None
				B=145	
				Missed A/B=6	
Balcıoğlu, C et al., 2012	Turkey	Children & adults	63/54	A=38	None
				B=16	
Rafiei A et al., 2013	Iran	Children & adults	100/100	A=14	None
				B=27	
				Mixed A/B=59	
Tak et al., 2014	India	Children & adults	82/82	A=0	None
				B=82	
Choy HS et al., 2014	Malaysia	Children & adults	1252/138	A=69	None
				B=69	
Fahmy HM et al., 2015	Egypt	Children	96/75	A=21	None
				B=54	
Peubla LJ et al., 2017	Cuba	Children	45/36	A=4	
				B=19	
				Mixed A/B=13	
Kashinahanji et al., 2019	Iran	Children & adults	64/30	A=18	None
-				B=12	
Nawaz et al., 2020	Pakistan	Children	76/69	A=20	
				B=38	
				Mixed A/B=11	None

Table-II: Summary of the studies that observed a significant association between Giardia assemblage and the severity of diarrhea.

Author and year of publication	Study Location	Study population	Number of samples/ PCR done	Assemblage	Statistically significant association
Homan and Mank, 2001	Netherlands	Children & adults	18/18	A=9 B=9	Yes (B; severe diarrhea)
Read et al., 2002	Australia	Children under 5 years	36/23	A=7 B=16	Yes (A; severe diarrhea)
Aydin <i>et al.</i> , 2004	Turkey	Children & adults	56/56	A=20 B=30 Mixed A/B=6	Yes (A; severe diarrhea)
Haque et al., 2005	Bangladesh	Children & adults	322/304	A=36 B=247 Mixed A/B=16	Yes (A: severe diarrhea)
Gelanew et al., 2007	Ethiopia	Children & adults	80/59	A=31 B=13 Mixed A/B= 15	Yes (B: severe diarrhea)
Sahagun <i>et al.</i> , 2008	Spain	Children & adults	108/108	A II = 43 B=61 Mixed AII/B= 4	Yes (A: severe diarrhea)

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Ajjampur SS <i>et al.</i> , 2009	India	Children < 5 years	101/50	A=13 B=22	Yes (A: severe diarrhea)
Alam et al., 2011	Bangladesh	Children & adults	127/117	Mixed A/B=5 A=15 B=38	Yes (A: severe diarrhea)
Al-Mohammed., 2011	Kingdom of Saudi Arabia	Children	40/40	Mixed A/B=11 A=23 B=15 Mixed A/B=2	Yes (B: severe diarrhea)
Sarkari B <i>et al.</i> , 2012	Iran	Children & adults	205/172	A=158 B=6	Yes (A: severe diarrhea)
Minetti et al., 2105	England	Children & adults	247/239	Mixed A/B=8 A=82 B=158	Yes (B: severe diarrhea)
EI Basha <i>et al.</i> , 2016	Egypt	Children & adults	400/60	Mixed A/B=7 A=22 B=38	Yes (A: severe diarrhea)
Ahmed NS <i>et al.</i> , 2020	Egypt	Children & adults	100/93	A=30 B=37 Mixed A/B=26	Yes (B: severe diarrhea)
Al-Huchaimi <i>et al.</i> , 2020	Iraq	Children & Adults	75/75	A=22 B=53	Yes (A: severe diarrhea)

DISCUSSION

The review of the data on the association between the G. lamblia assemblage and the severity of giardiasis suggests that the correlation between the two is still not well described and is debatable. Data from studies from different parts of the world that investigated the correlation between G. lamblia assemblage and the severity of diarrheal illness were contradictory and inconsistent. The apparent discrepancies in the studies reviewed are reflected by the complex interaction between the parasite and the prevalence of genotypes, chronic diarrheal disease, clinical presentation, age and markers of intestinal inflammation, and nutritional, environmental, geographic and socio-economic factors. Sub-optimal sanitary conditions such as poor socioeconomic class, overcrowding conditions, limited access to clean drinking water, big family size and lack of knowledge about hygiene and cleanliness, travelling to the developing world, camping and caravanning are the established risk factors for the acquisition of the G. lamblia infection. 40 On the contrary, risk factors such as gender, low birth weight, maternal age at birth, family size, number of siblings and presence of animals or pets were not consistent with the severity of diarrhea. However, poor socioeconomic class and drinking municipality water were found to be associated with severe giardiasis.³² Furthermore, several other factors including children less than five years of age, the host's nutritional status, the host's immune response, virulence and pathogenicity of Giardia isolates, to a large extent,

influence both the susceptibility and severity of the diarrheal disease due to G lamblia.7,32 In this review, several studies did not show a significant association between Giardia assemblage and the severity of giardiasis apparently in healthy adults as the main study population. On the contrary, two studies reported a significant association between giardia assemblage A and the severity of illness in children. 15,16 It was not clear if this study population characteristic had a major impact on the presence or absence of a significant association between Giardia assemblage and disease. In one study, the researchers did not find any significant association between symptoms and the age, gender or geographical origin of patients.³⁰ In addition, Hollam-Delgado et al found that malnutrition was not a predisposing factor for giardiasis. Malnourished children infected with G. lamblia did not develop severe diarrhea in their study. 12

Studies from different regions of the world have revealed conflicting data on *Giardia* assemblages A and B. The question arises whether assemblage A or B alone or both are more linked with severe giardiasis. In India, Bangladesh, Australia and Turkey, genotypes A and AII were most associated with severe diarrhoea. 15,16, 29,30,32 Whilst assemblage B was more linked with watery and profuse diarrhea in the Netherlands and Ethiopia and assemblage A was linked with intermittent diarrhoea. 6,30 It is interesting to note that assemblage B was also associated with symptomatic patients. 29 It is difficult to ascertain from the above-mentioned studies which

giardia assemblage is most associated with the severity of giardiasis. These studies have several limitations such as a limited study population and a small number of G. lamblia isolates. Furthermore, these studies did not investigate the nutritional, immune status and the presence of the co-infections. We suggest that more patients with persistent diarrhea or with specific symptoms of giardiasis should be included in future molecular studies to determine the true association between the Giardia assemblage and the severity of the illness. Molecular-based studies from Australia, India, Italy, Ethiopia, and the United Kingdom have reported mixed infections from patients with G. lamblia. The mixed infection rate ranged from 2.0 to 25% in these studies and was found to be higher in developing nations. 16 41, 42, 43,44 Mixed infections (both assemblages A& B) are not uncommon and probably due to ingestion of sources such as water contaminated by sewage or slurry with heterogenous Giardia strains.⁴⁶ In this review, the mix assemblages rate ranged from 3.7% to 25% from Spain, Bangladesh, India and Ethiopia. 15,30,31, 32 These findings were consistent with the previous studies.46,47

In this review article, we have made an effort to determine the correlation between the severity of giardiasis and G. lamblia assemblage by examining various studies conducted worldwide. However, the findings of these studies are contradictory and inconclusive, making it difficult to establish a clear association.

CONCLUSION

Giardia lamblia is a common intestinal parasite. Numerous studies have attempted to identify the link between its assemblage profile and the symptoms it causes but with little success. However, the divergence in findings suggests that a definitive correlation cannot yet be established. This lack of correlation highlights the complexity of the relationship between G. lamblia and human health and underscores the need for further research in this area. To fully understand the link between assemblages and severe diarrhea, further molecular studies are needed, especially in large populations residing in endemic regions.

CONFLICT OF INTEREST

None

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Declared none

AUTHOR CONTRIBUTION:

Raja Nadeem Sajjad: Conceptualization, data acquisition and analysis and drafting

Mohammad Abdul Naeem: Critical revision of the manuscript

Kanwal Hassan Cheema: Data acquisition, analysis and final drafting of the manuscript

Afia Sarwar: Final proofreading of the manuscript

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