

The Pathogenesis of Giardia Intestinalis

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Abstract. *Giardia intestinalis* infection leads to intestinal cell damage and loss of the brush border of the intestinal epithelium, resulting in shortened microvilli and impaired epithelial barrier function. Watery diarrhoea, diarrhoea, nausea, abdominal pain, vomiting, and weight loss are all symptoms of this pathological alteration. Most infections are asymptomatic. Malnutrition absorption is the most common symptom of *Giardia intestinalis* infection. To treat *Giardia intestinalis*, several medications with good efficacy are employed, but the dose regimen is not always ideal, and the evolution of drug resistance is beginning to cast doubt on their clinical worth. In addition, some of these drugs can produce side effects that cause discomfort and make it difficult for patients to adhere to treatment. *Giardia intestinalis* is an important zoonotic parasite that causes diarrhoea in humans and many mammals. In recent years, its pathogenesis, including structural proteins and excretion of *Giardia intestinalis*, surface antigen variants, and the role of *Giardia intestinalis* in the small intestine, has been extensively studied. This article discusses this issue and lists the risks of *Giardia intestinalis* to the human intestine and the various diseases it can cause.

Keywords: Gastrointestinal disease, *Giardia intestinalis*, Parasite.

1. Introduction

Giardia intestinalis, or *Giardia* for short, is a protozoan parasite found in the human intestine and in many mammals that causes giardiasis, a disease with a focus on diarrhoea [1]. The disease is widely spread worldwide and has been present or occurring worldwide since the 1970s. It is currently ranked as one of the top 10 parasitic diseases threatening human health. WHO estimates that approximately 1-30% of the world population is infected with *Giardia*, with prevalence rates of 0.4-7.5% in populations of industrialized countries and 8-30% in populations of developing countries. A study of 8,685 dog and 4,214 cat faecal samples from seven European countries showed that 24.8% and 20.3% of the samples were positive for *Giardia intestinalis*, a parasite that can be transmitted between humans and pets. Thus, *Giardia intestinalis* is an important parasite for humans and animals. It is generally believed that *Giardia* can attach to the epithelial surface of the small intestine through flagellated ventral suckers, directly damaging the intestinal mucosa and causing shortening, thickening and even atrophy of the intestinal epithelium micro vibrations, thus affecting nutrient absorption and causing diarrhoea; however, the actual mechanism by which *Giardia* causes diarrhoea is still unclear. In order to better understand the pathogenic role of *Giardia intestinalis*, this paper reviews the progress of research on its cytoskeletal proteins and excretion, surface antigens and their role in the host small intestine.

2. Giardia Cell Stock Proteins And Excretory Secretions

2.1. Giardia Intestinalis

Giardia intestinalis has a highly developed cytoskeletal system, consisting of microtubules, microfilaments, and cytoskeletal proteins. Recent studies have confirmed that the cytoskeletal proteins of *Giardia* are closely related to its pathogenicity. Among the many proteins involved in the composition of the cytoskeleton, the cytoskeletal proteins specific to *Giardia intestinalis* are one of the main components. In 1983, the concept of Giardin was first introduced by Crossley [2]. And it is now divided into four main groups: α - Giardin, β - Giardin, γ - Giardin, and δ - Giardin.

In recent years, the cellular localisation and function of α -amylase has been studied in detail. Peattie first isolated a 33 kDa protein by SDS-PAGE and prepared a polyclonal antiserum using this protein as antigen [3]. Later, Wenman used the same method to confirm the distribution in the earthworm plasma membrane, and Feliziani demonstrated by immunohistochemical analysis that the Giardin-a-1 protein is mainly distributed in the cytoplasmic membrane of trophozoites [4]. And identified 14 additional α -Giardin genes (α -4, α -5, α -6, α -8 to α -13 and α -15 to α -19) by scanning the Giardia genome [5]; studies on the cellular localisation of the α -Giardin family also showed that α -3, α -5 and α -17 are distributed in the ventral suckers; α -15 and α -16 are distributed along the cell membrane; α -1, α -7.1. The remaining eight species (α -1, α -2, α -6, α -7.2 The remaining eight species (α -1, α -2, α -6, α -7.2, α -7.3, α -9, α -10, α -14) were mainly distributed in the cytoplasm, flagella or cell membrane of suckers, as they were overexpressed after transfection of trophozoites with recombinant vectors [3, 6]. In recent years, polyclonal antibodies to the Giardia-specific α -4 peptide have been produced and cellular immunohistochemistry studies have been performed [7]. Giardin α -4 was found to be mainly distributed in the flagellate fraction of trophoblastic cells and it was hypothesised that it might be involved in the motility and infection process of Giardia. Kim used a similar approach to localise Giardin α -11 and showed that it was mainly distributed in the basal body of small encrusting and preflagellated worms [8].

β -Giardin is the only giardin that has been shown to share a structural domain with skeletal muscle hypo crystallin [9]. Skeletal muscle hypo crystallin has been shown to be closely linked to filament fibre formation and function. Crossley found that β -giardin is able to assemble into 2.5 nm microfilaments and, in addition, forms auxotrophic plasma ultra-structures of ventral suckers. Feliziani generated monoclonal antibodies against β -giardin and studied its localisation, finding a predominant distribution at the suction site. Subsequently, Macarisin demonstrated its distribution on the dorsal surface of suckers using confocal laser microscopy. Jimenez identified different amino acid sequences of β -Giardia intestinalis in different strains treated with albendazole, suggesting that albendazole resistance is related to β -giardin. γ -giardin is a 38 kDa protein located mainly on the suckers of Giardia trophozoites. Giardia intestinalis is a 31 kDa protein identified by Elmendorf Jenkins prepared a specific antiserum to study its localisation and showed that δ -giardin was predominantly localised to Giardia intestinalis suckers and that reaction of the antiserum with the worm reduced the adsorption capacity of the worm, suggesting that δ -giardin is involved in the process of adsorption of suckers to the small intestinal mucosa [10].

The life cycle of Giardia intestinalis (Figure 1) consists of three parts. The cyst becomes a trophozoite, the trophozoite multiplies asexually and the trophozoite returns to the cyst form. Giardia cysts are an infectious stage. The hard wall of the cyst allows it to resist decomposition in an acidic environment. When a cyst is swallowed, it migrates to the small intestine where it undergoes the process of exocytosis, i.e., the transformation of the cyst into a trophozoite. This process is initiated when the environment changes from a low pH to a natural pH. The optimum pH for the efflux process is pH 4.0. Once released, the trophozoite undergoes asexual multiplication, also called binary longitudinal fission. After multiplication, the trophozoites begin to absorb nutrients from the host. During this period, not all people show symptoms. When a Giardia cyst moves into the large intestine, it undergoes encystation, which is the opposite of excystation. Encystation is the process of transformation of trophozoites into Giardia cysts and takes place in the rectum. During this process, metabolism begins to slow down as the cells close and enter a resting state. Eventually, the cysts are eliminated with the host's feces [11].

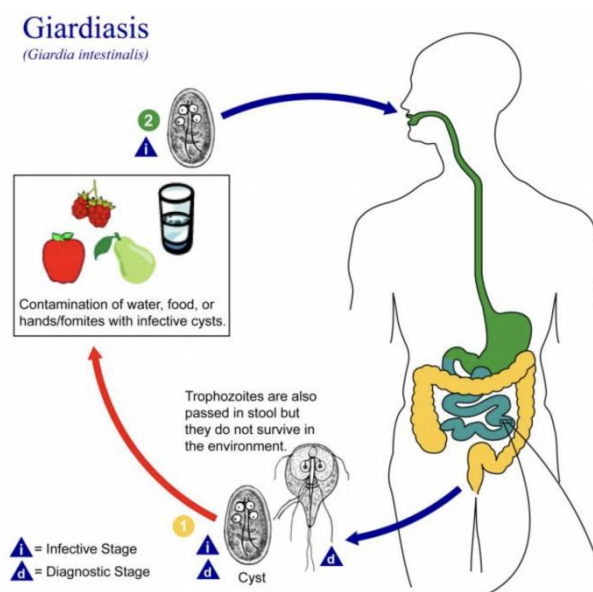


Figure 1. Life cycle of *Giardia intestinalis*

2.2. Model *Giardia Intestinalis* Of Pathogenesis

When modelling pathophysiology, consider the three most common clinical symptoms of infection: (a) asymptomatic infection, (b) acute self-limiting diarrhoea, and (c) persistent diarrhoea with intestinal malabsorption (Figure 2). The host must be infected with a relatively avirulent strain, that there is no significant virulence factor, or that the host's immune and possibly non-immune defence mechanisms are fully functional to control the parasite population and the subclinical infection in the case of asymptomatic transmission. It's unclear whether transmission has to start with acute diarrhoea or if it might be clinically quiet for the entire period of transmission. Acute gastroenteritis has a prognosis duration of about 7-10 days. This is in line with the long time it takes for parasites to colonize and establish an infection, as well as the slow rate at which parasites multiply. This is clearly distinct from acute bacterial diarrhoea caused by enterotoxigenic *Escherichia coli* (ETEC), which typically appears within 1-2 days of the organism's consumption. ETEC is produced in much less time and also rapidly releases protein-secreting enterotoxins. In cases of *Giardia intestinalis*, the time of onset of symptoms coincides with the undetectable activity of enterotoxins in vivo [12]. This period prior to symptom onset should coincide with the involvement of immunopathogenesis.

In the case of chronic infection, malabsorption, a multifactorial process may be involved, including mucosal and ductal events. Lack of radiation to the body can cause progressive disruption of epithelial structure and function, and there is evidence that the severity of intestinal malabsorption is significantly connected with the level of villi shortening and crypt hyperplasia. Intestinal fat malabsorption activates the "brakes" of the ileum and leads to a slowing of intestinal transit, which favours long-term bacterial colonisation. In the case of prolonged uncontrolled infection, the parasite population can be expected to increase progressively, so that the number of trophozoites is sufficient to significantly influence luminal hydrolase activity and eventually lead to a biological decrease in the salt concentration of the luminal bile [13]. This leads to a destructive cycle of malabsorption that can only be broken by the use of antiarrhythmics.

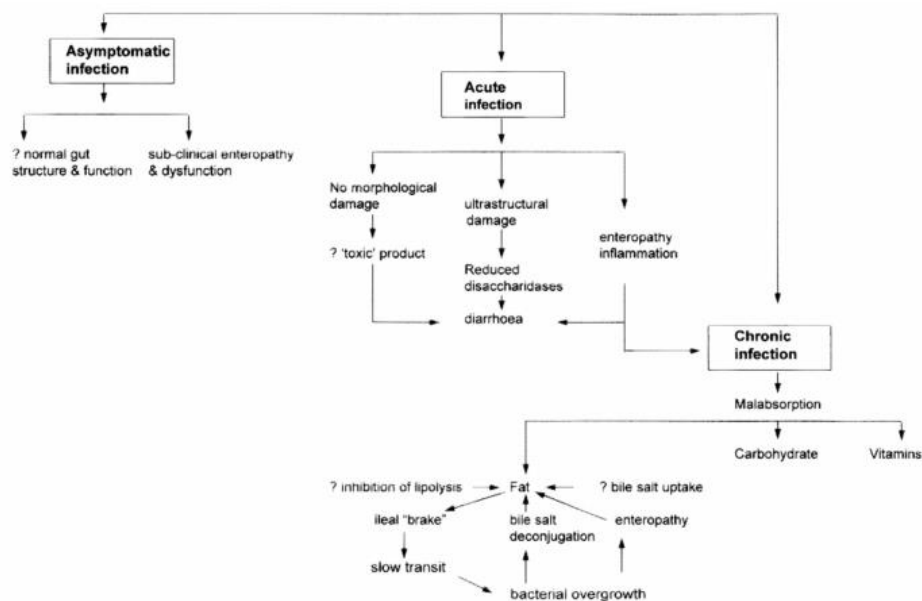


Figure 2. Model of pathogenesis of *Giardia intestinalis*

2.3. Excretory Secretions

Several *Giardia* excretions may be involved in host pathogenesis, including metabolic enzymes released by *Giardia*, soluble substances of different sizes and unknown cysteine proteases. *Giardia* has been found to release arginine deaminase (ADI) and ornithine carboxyltransferase (OTC), both of which may be involved in the metabolism of L-arginine, a nutrient that is the preferred energy source of the growth and reproductive stages of *Giardia* [14]. Although a single molecule of L-arginine produces one molecule of ATP, *Giardia intestinalis* uses this pathway to obtain ATP more rapidly than the glycolytic pathway [15]. L-arginine is a precursor of nitric oxide (NO) and produces NO and L-citrulline in the presence of nitric oxide synthase (NOS). NO production by small intestinal epithelial cells inhibits growth, cyst formation and decapsulation of *Giardia* [15]. By depleting the large intestine of L-arginine, *Giardia* inhibits the proliferation of intestinal epithelial cells on the one hand and indirectly inhibits the production of NO by epithelial cells on the other, whereas the NO content of small intestinal cells is important for regulating water absorption/excretion, which may be important for *Giardia* diarrhoea [16].

2.4. *Giardia* Surface Antigen Variants

Giardia surface antigen variation has been found to aid in immune evasion and the establishment of chronic infection. The phenomenon of *Giardia* surface antigen variation was first discovered during in vitro culture, as different *Giardia* populations cultured in vitro secrete proteins with different antigenicity into the culture medium, and specific monoclonal antibodies recognizing a surface antigen molecule can only bind to individual *Giardia* cells in the same population. Further studies revealed that antigenic variation in *Giardia* also occurs during infection in humans and experimental animals [17]. *Giardia* surface antigens mutate once in about 6.5 to 13.5 generations depending on the isolate, producing another antigenic molecule. Nash reported that the pathogenicity of *Giardia* surface antigen varies between strains and between clones expressing different surface antigens within the same strain, e.g., the GS strain is highly pathogenic, with all 10 volunteers infected with this strain's acquiring infection and showing clinical symptoms [17]. In addition, two different clones of the GS strain were used to infect the volunteers, and four of the volunteers who received the clone with a surface antigen of 72 kDa were infected, while only one of the 13 volunteers who received the clone with a surface antigen of 200 kDa was infected.

3. Effect Of Giardia On The Host Intestine

3.1. Giardia Soluble Mediators Disrupt Intestinal Cell Functions

Apoptosis, also known as programmed cell death, is an important regulatory mechanism for maintaining a normal internal environment in the body and essential for maintaining the stability of the intestinal epithelium. Activation of the precursor's caspase 3 and caspase 9, expression of the pro-apoptotic Bax and the anti-apoptotic down-regulating factor Bcl-2, and hydrolysis of the polyad-ribose polymerase PARP play important roles in the initiation of apoptosis in Giardia. Under normal conditions, intestinal epithelial cell apoptosis does not affect the integrity of the intestinal mucosa, but pathogenic microorganisms in the gut can induce intestinal epithelial cell apoptosis, thereby impairing intestinal barrier function and increasing the expression of apoptotic genes in Giardia-treated CaCO-2 cells [18]. Apoptosis was significantly increased in intestinal epithelial cells condensed with Giardia intestinalis. In patients with chronic Giardia, apoptosis of intestinal epithelial cells is induced by an exogenous apoptotic pathway mediated by the MorT3 receptor.

Soluble and diffusible substances that disrupt intestinal function may induce more extensive and profound pathological changes in giardia than the close interaction between trophozoites and gastrointestinal epithelial cells. To investigate whether the secretory behaviour of Giardia virulence factors leads to changes in intestinal epithelial cells, short-circuit currents (Isc) were measured in continuously polarized epithelial cells without additives, in CaCo2 cultured with duodenum or in a clear dilution (1:1000) with Giardia [19]. Further experiments showed that two experimental conditions stimulated the major ISC inhibitors basolateral amPC (10 μ M forskolin ISC) and activated calcium (basolateral UTP administration) 100 μ M), both in co-culture with jadi for 24 h and in diluted jadi supernatant. The CFTR chloride channel inhibitor GlyH101 (50 M) and the calcium-activated chloride channel inhibitor DIDS (100 M) were applied to the top of the test chamber to discover which ion channels were impacted. The activation of the CFTR chloride channel, which was blocked by GlyH101, was the main cause of the field-stimulated ISS. Because calcium-activated chloride channels were blocked by DIDS, calcium-activated ISS was mostly attributable to their activation [19].

3.2. Structural Disruption And Dysfunction Of The Intestinal Epithelium

Disruption of dense structures has been reported to lead to increased intestinal permeability in a variety of gastrointestinal and intestinal disorders, such as disruption of ZO-1 protein, claudin protein and skeletal f -actin can lead to increased intestinal epithelial permeability, resulting in intestinal epithelial barrier dysfunction [20]. Giardia-mediated increases in intestinal epithelial permeability are caused by alterations in the intestinal epithelial intercellular junction complex. Increased intestinal epithelial permeability in chronic Giardia patients is associated with reduced levels of claudin-1 protein [20]. Buret demonstrated that Giardia disrupts ZO-1 protein in tight junctions and increases intestinal epithelial cell permeability. Teoh showed that Giardia-induced intestinal epithelial cell damage is associated with f-actin and α -actin rearrangements and that their protein rearrangement allows Scott to further show that Giardia intestinalis-induced ZO-1 and f-actin rearrangements occur in a myosin light chain kinase-dependent manner. A recent study found that inhibition of caspase-3 prevented its disruption of ZO-1 protein in tight junctions, suggesting that Giardia intestinalis can induce apoptosis of intestinal epithelial cells and lead to intestinal barrier dysfunction [20].

In summary, Giardia intestinalis can cause host diarrhoea through mechanisms such as shortening of the microvillous brush border, causing indigestion and impaired absorption, increased intestinal transit rate and excessive anion secretion [21]. These mechanisms are closely related to Giardia-mediated caspase-dependent cellular regulation and disruption of intestinal epithelial tight junctions.

4. Ecology And Epidemiology

4.1. Giardia in Fresh Produce, Seafood, And Environmental Waters

Giardia intestinalis is a parasite that causes worldwide epidemics of water- and food-borne diarrhoea. Its water-borne transmission, in particular, is of considerable epidemiological importance in terms of parasites and continues to be a serious public health issue. *Giardia intestinalis* is known to exist in eight genotypes, ranging from A to H, with genotypes A and B causing human infection. IGCC VII has undertaken various investigations on *Giardia intestinalis* detection in water samples. This study examined surface water matrices from Europe (Austria, Serbia) and Korea and discovered a high prevalence of the parasite, as well as the dissemination of numerous combinations, including A and B. Loop-mediated isothermal amplification (LAMP) was utilized to detect *Giardia intestinalis* in a variety of matrices in another study [22]. Foodborne epidemics of *Giardia* have been difficult to document to date, owing to technological limitations and the fact that the envelope is more susceptible to environmental conditions (e.g., drying), which may restrict the possibility for transmission through food. Because fresh produce is one of the potential causes of foodborne infections, the studies presented at IGCC VII focused on a variety of vegetables, including sprouts, herbs, and fruits. The necessity for more standardisation and cost reduction of immunomagnetic separation technologies for the recovery of *Giardia* cysts from food matrices was noted during IGCC VII [22]. Filter-feeding molluscs, such as oysters, are thought to be a possible source of *Giardia* for humans. According to a study published in IGCC VII, frequent food contamination resulted in an infectious A pool for humans. The subject of whether cysts in food matrices can infect humans has not been well investigated [23].

4.2. Zoonotic Giardiasis

For many years, scientists have been interested in *Giardia*'s zoonotic potential, and molecular methods are now frequently employed to isolate genotypes from agricultural, domestic, and wild animals. At the 7th IGCC meeting, a number of intriguing findings were presented. Using beta-*Giardia* markers and SSU rRNA, a large-scale investigation in Scotland discovered high to moderate incidence of *Giardia* in cattle, sheep, rabbits, rodents, and deer, as well as zoonotic and host-specific combinations in all of these species. Multilogues genotypes from animals and people, as well as various combinations of A isolates, were compared to a newly devised highly polymorphic typing scheme, and its validity was proven in an Italian investigation. *Giardia intestinalis* isolates from lambs were typed and identified using two markers in an Algerian investigation. Finally, a study of nonhuman primates in captivity verified the significant incidence of *Giardia* in these animals, with the B strain being the most common [24].

Wild rodents were the topic of two Italian research. The first investigation found a significant incidence of *Giardia intestinalis* in coronary porcupines, but the isolates were not molecularly identified. The presence of *Giardia intestinalis* in captive voles was confirmed in the second investigation, corroborating the hypothesis that wild animals frequently exhibit host-specific, non-zoonotic species or aggregation [24]. The prevalence of many infections and intricate interactions with the microbiota confound interpretation of *Giardia intestinalis* pathogenic role in domestic animals, according to a synopsis of the clinical relevance and public health implications of *Giardia intestinalis* in domestic animals. Another study found no link between *Giardia intestinalis* aggregates and clinical symptoms, emphasizing the importance of taking co-infections and gut flora into account.

4.3. Human Epidemiology

At 35 levels, the IGCC VII verified country disparities in *Giardia intestinalis* molecular epidemiology. In most research, B combinations were shown to be more common in low-income and high-income locations, as well as in different age groups. The prevalence of BIV sub combinations in Europe, the first detection of C and F combinations in people in Europe, and the frequent occurrence of mixed infections were among the findings of these investigations. The methods utilized

in these investigations vary, with some depending on a single marker and others using genotyping at numerous locations. This makes it difficult to compare investigations and necessitates the standardization of molecular methods.

5. Pathologies

5.1. Giardia-Host Interactions And Disease

In 2006, *Giardia* was added to the World Health Organization's Neglected Diseases Programme, and it is now known to cause serious morbidity in young children. In regions where intestinal disease is frequent worldwide, *Giardia*-infected youngsters appear to be protected from diarrhoea, according to recent observations, for unknown reasons. Individuals may be infected with numerous germs that cause diarrhoea at the same time in nations with poor sanitation and inadequate water purification systems. *Giardia* infection can result in severe acute illness and serious post-infection sequelae, such as functional gastrointestinal disorders including irritable bowel syndrome [25]. Indeed, a link has recently been established between *Giardia* and the development of intestinal hypersensitivity following infection, which is linked to the breakdown of intestinal barrier function during the acute phase of infection. The parasite's pathophysiology is unknown, but its effects can be felt in places far from its active colonization, such as joints, eyes, and the central nervous system. Recent findings, such as those given at the 7th IGCC meeting, indicate that parasite-host interactions, co-infected gut pathophysiology, and host diet all play a role in clinical disease outcomes. The molecular pathophysiological pathways of *Giardia* are, however, yet unknown. Similarly, whether the recurrence of *Giardia intestinalis* after a patient has been treated with medicine indicates reinfection or parasite resistance is unknown. Recent advances in 'histological' approaches have begun to identify new pathogenic processes, as detailed below [25].

5.2. Immune Responses In Giardia Intestinalis

Giardia intestinalis does not generally infect healthy mucosal tissue, yet new research suggests that this could happen in the lab. Because of the parasite's robust anti-inflammatory activity, which appears to be caused by its cysteine protease, this infection displays no symptoms of local inflammation. Significant progress has been made in our understanding of *Giardia intestinalis* innate and adaptive immunity in recent years, particularly the role of variant-specific surface proteins (VSPs) and antigenic variations in chronic infection in complicated animal models like the Mongolian gerbil. *Giardia intestinalis* can elicit Th1, Th2, and Th17 immune responses in mature hosts infected with *Giardia intestinalis*, and new findings reveal that pancreatic rennin mast cell protease-4 modulates intestinal cytokine production in *Giardia intestinalis*-infected mice. Infection triggers a powerful protective and adaptive immunological response in humans and animals, with CD4⁺ T lymphocyte-mediated IgA synthesis playing a key role [26]. According to recent findings from IGCC VII, local increases in the number of Th17 and Treg cells in the lamina propria and Peyer's patches of the mouse small intestine boost infection resistance. Another study observed an increase in the number of IL-17A positive cells in Peyer's patches and the epithelial lumen of infected animals, supporting this notion. Interestingly, the altered duodenal mucosal lymphocytes were maintained for several months after infection in human patients. Consistent with previous observations, these reports also reveal that CD8⁺ T cells are not involved in immune protection; instead, in *Giardia intestinalis*, CD8⁺ T cells are responsible for microbial and dysaccharidase epithelial damage; serum gamma interferon levels are also elevated in infected patients or mice, an observation consistent with a possible role for macrophages in mediating, rather than directly controlling, infection. *Giardia intestinalis* has also been demonstrated to modify macrophage pro-inflammatory signaling by cleaving the p65RelA component of the nuclear transcription factor kappa b. Experiments in human intestinal epithelial cells revealed that the zinc finger protein tristriploin (TTP), which encodes the rna-binding protein, is involved in post-transcriptional cytokine production and attenuation by suppressing ERK1/2 and

P38 phosphorylation. Interestingly, mice previously infected with *Giardia intestinalis* appear to modulate the immune response to another parasite, *Toxoplasma gondii*.

5.3. The Pathogenesis of *Giardia*

Giardia actively interacts with the gut surface during the acute phase of infection, producing epithelial injury, mucus layer degradation, and gut flora dysbiosis [26]. The involvement of *Giardia* excretion and secretion products, as well as the host immunological response, play a role in these effects, which can occur at the site of infection and beyond. *Giardia* cysteine proteases appear to play a critical role in the parasite's interaction with host intestinal epithelial cells, as well as the resulting microbiota imbalance. Intricate experiments in a mouse model system proved that *Giardia* infection affects gut flora, paving the path for more research into the microbiota's interaction with *Giardia*. IGCC VII also explains why clinical symptoms in *Giardia* can manifest in such a variety of ways. In fact, *Giardia*'s cysteine protease cleaves pro-inflammatory mediators, reducing the pathophysiology of intestinal lesions induced by co-infection adhesion and eliminating intestinal pathogenesis caused by severe inflammatory diarrhoea. The method involves the activation of NLRP3 inflammatory vesicles, which activates -defensins and epithelial antimicrobial peptides of intestinal trefoil factor 3. Experiments with the non-mucus-producing Hu-Tu-80 human intestinal cell line revealed noteworthy alterations in mucus protein MUC2 and mRNA MUC5AC levels when the cells were exposed to *Giardia duodenalis* trophozoites, indicating the parasite's pathogenic function in intestinal mucus physiology [27].

Giardia intestinalis may also cause disease through influencing the host's lipid metabolism by changing lipid transporters. The polymorphic arginine deaminase of *Giardia duodenalis*, which is required for the parasite's arginine metabolism, could be another virulence and immune avoidance component for this parasite. *Giardia intestinalis* was linked to intestinal epithelial cell injury in a sample of Brazilian infants, as demonstrated by increased intestinal fatty acid binding proteins, increased plasma IL-17 and IL-10 levels, and decreased plasma IL-8 and IL-5 levels [27]. *Giardia intestinalis* trophozoites damage the epithelial barrier of the human Hu-Tu-80 cell line under a hypoxic environment, accompanied by changes in cellular protein kinases, which could give a new cellular model for such investigations. *Giardia intestinalis* enolase damages host intestinal epithelial cells via an apoptosis-inducing factor, resulting in host intestinal epithelial cell necrosis. The role of *Giardia* microcysts in pathogenesis is being investigated right now. The findings suggest that research into the pathophysiology of epithelial failure could be extremely beneficial for the usage of human tissues similar to the small intestine. Patients with symptomatic or subclinical illness had higher serum levels of serotonin, a key modulator of intestinal motility and a functional indication of intestinal hypersensitivity in irritable bowel syndrome, according to a study at IGCC VII [27].

6. Conclusion

Several complex factors may be involved in the pathogenesis of *Giardia intestinalis*, primarily *Giardia intestinalis*, excretory secretions and *Giardia intestinalis* surface antigen variants, as well as apoptosis of the intestinal epithelium induced by *Giardia intestinalis*, leading to structural destruction and dysfunction of the intestinal epithelium. *Giardia intestinalis* is a common parasitic protozoan parasite of human and animal origin that causes *Giardia intestinalis* and is classified by the World Health Organization as one of the top 10 parasitic diseases for human health. However, the pathogenesis of *Giardia intestinalis* diarrhoea is unclear and may be related to: (1) Cytoskeletal proteins: The trophozoite of *Giardia intestinalis* is an important feeding and reproductive stage with a complex cytoskeletal system consisting of four pairs of flagella (anterior, caudal, ventral and posterior lateral flagella), ventral and intermediate suckers. The flagellum is a unique component of the cytoskeleton of flagellates. There are four classes of *giardia*, α -, β -, γ - and γ -flagellates, which have been reported to be closely associated with their pathogenicity. A variety of complex factors may be involved in the pathogenesis of *Giardia*, including primarily *Giardia intestinalis*, *Giardia*

intestinal secretions, antigenic surface variants and Giardia-induced apoptosis of intestinal epithelial cells, leading to structural disruption and dysfunction of the intestinal epithelium. The specific mechanisms underlying many of these aspects are not known, e.g., how homologous VSP RNAs are identified in the RNA interference pathway that regulates Giardia intestinalis VSP expression and whether other mechanisms are involved in this process. The main pathways of worm-induced apoptosis in intestinal epithelial cells, whether Giardia intestinalis-induced apoptosis in intestinal epithelial cells is related to AIF, and which major nutrients are associated with structural damage and dysfunction in the intestinal epithelium remain to be investigated. Future research should focus on the main Giardia intestinalis pathogenicity factors and the links between them in order to identify the main Giardia intestinalis pathogenicity factors and provide an important scientific basis for the development of drugs and vaccines against Giardia intestinalis.

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