



The effect of chronic giardiasis on cognitive functions and allergopathology in the pediatric population

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Abstract

Introduction: Giardiasis remains one of the most urgent parasitic infections in pediatric practice worldwide. The purpose of this retrospective cohort study was a comprehensive assessment of the clinical manifestations, risk factors, and long-term outcomes of giardiasis treatment in children.

Methods: The data of 500 patients aged 6-17 years were analyzed, formed into two groups comparable in basic parameters: the main group (250 children with verified giardiasis) and the control group (250 children without diagnosed invasion).

Results: The results of the study demonstrate that children with giardiasis before treatment had a significantly higher incidence of not only gastrointestinal symptoms, but also systemic manifestations. Asthenic syndrome was reported in 79.2% of patients, allergodermatoses in 49.6% versus 27.2%, and complaints of decreased concentration in 66.8% of children. A clear dependence of the risk of infection on social conditions was established: the main group was significantly dominated by children living in rural areas (58.0% versus 32.0%), using non-centralized water supply sources (52.8% versus 22.0%) and having contact with farm animals (47.2% versus 18.0%). Evaluation of long-term results 6, 12, and 24 months after successful eradication therapy showed rapid regression of gastrointestinal symptoms, but normalization of extra-intestinal manifestations was slower. 24 months after treatment, the prevalence of allergodermatoses was 28.0%, and complaints of decreased concentration were 20.0%, which was still higher than in the control group.

Conclusion: The data obtained indicate the need for an integrated approach to the management of patients with giardiasis, including long-term follow-up and targeted rehabilitation measures.

Keywords: Giardiasis, Children, Risk factors, Long-term consequences, Cognitive impairment, Rehabilitation

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Introduction

Giardiasis, an anthropozoonotic protozoal infection caused by intestinal protozoa *Giardia duodenalis* (synonyms: *G. intestinalis* and *G. lamblia*) retains the status of one of the most significant global issues in parasitology and pediatrics (1). Its high pathogenicity, prevalence, and ability to persist in the human body for a long period of time determine its continued relevance. Specialists are especially concerned about the vulnerability of the pediatric population, as the effects of this infection extend far beyond gastrointestinal symptoms and have a complex negative impact on physical, nutritional, and cognitive development (2, 3).

The pathogenesis of giardiasis is a complex, multifactorial process. After entering the gastrointestinal tract, resistant cysts reach the duodenum and jejunum under the influence of bile (4, 5). Trophozoites are released and adhere to the apical surface of enterocytes with the help of ventral attachment discs without penetrating the submucosal layer (6). This causes a cascade of destructive changes, including damage to the brush border of

enterocytes and disaccharidase deficiency, impaired absorption of fats, carbohydrates and fat-soluble vitamins, as well as triggering apoptosis and accelerating cell peeling, leading to villous atrophy, crypt hyperplasia and malabsorption syndrome (7-9). In addition to mechanical and enzymatic damage, the immunopathological response of the body plays an important role (10). *Giardia* antigens induce the activation of humoral and cellular immunity, but the parasite has sophisticated mechanisms to evade the immune response, including antigenic variation of surface proteins, which contribute to the chronicity of the process (11, 12).

The clinical picture of giardiasis is characterized by pronounced polymorphism, ranging from asymptomatic cyst formation, which is observed in a significant proportion of infected individuals, to severe manifestations (13). The acute phase, which is most typical of primary infection in children, is characterized by profuse, watery diarrhea with no blood admixture, severe flatulence, cramping pain in the epigastrium and mesogastrium, nausea, anorexia, and intoxication symptoms (14-16). However, in many cases,



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this stage goes unrecognized, and infection transforms into a chronic form (17). Chronic giardiasis poses the greatest challenge for pediatricians due to its nonspecific manifestations: chronic fatigue, irritability, emotional instability, headaches, sleep disturbances, slow weight gain, and growth, as well as persistent skin conditions such as dryness, keratosis, and atopic dermatitis (18-20).

Identification of risk groups is a cornerstone of epidemiological surveillance and prevention. The central place in high-risk groups is undoubtedly occupied by children, especially those of early and preschool age (1-6 years old), (21). Their vulnerability is determined by a complex of factors, including anatomical and physiological features of the gastrointestinal tract, reduced acidity of gastric juice, immaturity of local and systemic immunity, and, most importantly, active subject-practical behavior and lack of stable hygiene skills (22,23). High density of contacts in kindergartens and nurseries create ideal conditions for fecal-oral transmission (24).

Nevertheless, the risk of infection is extremely unevenly distributed among the child population and is determined by a number of environmental and social factors. Thus, for rural residents, especially in areas with developed personal animal husbandry, the main risk factors include non-centralized water supply systems (wells and springs), a high probability of faecal contamination of soil and water sources, as well as close contact with livestock and companion animals (25). In contrast, in large metropolitan areas with well-developed centralised water treatment systems, such as Moscow, the epidemiological profile is significantly different (26). Here, the main risk is shifted towards domestic contact-household transmission in conditions of crowding in preschool educational institutions and is also associated with socially disadvantaged families, where the level of hygiene culture remains low (27). Administrative centers of the regions of Russia, such as Vladikavkaz, often combine the features of urban and rural areas: along with organized children's groups there is a private sector with unorganized water supply and individual farms with livestock (Table 1).

Thus, a heterogeneous and diverse epidemiological landscape of giardiasis is being formed, where

urbanization is not an unambiguous protective factor, but rather mediates a shift in emphasis on transmission routes and risk factors (28). Therefore, conducting a comparative analysis of the incidence, clinical features, and long-term consequences of giardiasis among children living in areas with fundamentally different socioeconomic conditions is not only relevant but also necessary to develop targeted prevention and treatment strategies. The purpose of this study is to compare the incidence of *Giardia*, the structure of symptoms, and the course of disease after treatment among children in the metropolitan area (Moscow), in the administrative center (Vladikavkaz), and in rural settlements (North Ossetia-Alaniya).

Materials and Methods

To achieve above - mentioned goals, a retrospective cohort study was organized with the formation of two parallel comparison groups. The study was conducted in strict accordance with the principles of the Helsinki Declaration, and its protocol was approved by the ethics committee of the North Ossetian State Medical Academy (Vladikavkaz, Russia). Protocol No. 1278 dated 12/02/2023 was approved.

The study included medical records of children aged 6 to 17 years who were under dynamic supervision in children's polyclinics in Moscow, Vladikavkaz and rural settlements of the Republic of North Ossetia-Alania during the period from 2020 to 2023. The main group consisted of 250 children with a verified diagnosis of giardiasis established in the period between 2019 and 2021. The criteria for inclusion in this group were a positive result from microscopic examination of feces for *Giardia* cysts, or a positive immunochromatographic test for *Giardia* duodenalis antigens, as well as availability of full medical documentation including examination data prior to treatment and at different time points after treatment - 6, 12, and 24 months after therapy.

The control group consisted of 250 children, comparable in age and gender to the main group, who did not have a single case of giardiasis during the entire follow-up period. This was confirmed by at least three negative results from a parasitological examination, with an interval of one year

Table 1. Comparative epidemiological characteristics of giardiasis among children in various regions of the Russian Federation (according to data for 2020-2023)

Region and Type of Locality	Children Surveyed, n	Identified Giardiasis Cases, n	Infection Rate (%)	Presumed Leading Risk Factors and Epidemiological Features
Moscow (Metropolis)	35,200	1,408	4.0	High density of children's groups (preschools) as the main transmission focus; predominance of contact-household transmission; low risk of waterborne transmission due to centralized water treatment; presence of socially disadvantaged population groups.
Vladikavkaz (Administrative Center)	12,150	1,063	8.7	Mixed model: contact-household transmission in preschools combined with waterborne transmission in areas with non-centralized water supply; a significant proportion of the population keeps livestock in personal farmsteads, creating a risk of zoonotic transmission.
Rural Settlements of the Republic of North Ossetia-Alania	8,450	1,183	14.0	Clear predominance of waterborne transmission due to the use of wells and springs vulnerable to fecal contamination; widespread livestock keeping; traditional farming practices using organic fertilizers; less developed preschool infrastructure.

between them. The patients in the control group were randomly selected from a common database, using the random number method, and had the same exclusion criteria as the main group: the presence of chronic inflammatory bowel disease, celiac disease, malabsorption syndrome of different etiology, and severe somatic or neurological pathology, which could significantly affect the parameters assessed, such as academic performance and nutritional status.

The diagnosis of giardiasis was verified using a set of laboratory methods. Microscopic examination included triple microscopy of native and Lugol-stained fecal smears at intervals of 2–3 days. At the same time, immunochromatographic analysis was used to detect the specific *G. duodenalis* antigen in fecal samples using commercial test systems. To make a definitive diagnosis, at least two positive results were required, detected by either of the methods or by a combination of them. All patients in the main group received standard antiparasitic treatment in accordance with current clinical guidelines. The efficacy of the treatment was monitored 14–21 days after completion of the course by triple microscopic examination of feces and immunochromatography. Eradication of the parasite was confirmed by negative laboratory results.

For a retrospective analysis, the following data were collected from medical records and questionnaires: demographic data, including age, gender, residence and settlement type; anamnestic information on pets, contact with farm animals, and water supply sources; clinical manifestations prior to treatment, such as abdominal pain, dyspepsia, stool characteristics, asthenia, and skin allergies. Physical development and nutritional status parameters were also assessed based on anthropometric data and body mass index calculation; concomitant pathologies, particularly allergic diseases, were recorded; and the frequency of acute respiratory infections was noted. In children of school age, average annual grades were analyzed, and complaints from parents and teachers regarding decreased concentration and increased inattention were noted.

Statistical data processing was performed using the IBM SPSS Statistics v. 26.0 software package. Quantitative indicators were described using arithmetic mean and

standard deviation ($M \pm SD$). Qualitative variables are represented as absolute values and percentages. Quantitative indicators were compared between two independent groups using Student's t-test for normally distributed data and Mann-Whitney U-test for other distributions. The χ^2 criterion was used to compare qualitative features with the Yates correction, while paired Wilcoxon's test was used to assess changes within one group's dynamics. Statistical significance was established at $P < 0.05$ level.

Results

During the retrospective analysis, two groups were formed: the main group of children with verified giardiasis ($n = 250$) and the control group ($n = 250$). The groups were statistically comparable in basic demographic indicators: the average age in the main group was 8.2 ± 2.1 years, in the control group – 8.5 ± 2.3 years ($P > 0.05$). The gender distribution also had no significant differences: 52% of boys and 48% of girls in the main group, 49% in the control group and 51%, respectively ($P > 0.05$).

A comparative analysis of the data at the time of inclusion in the study revealed statistically significant differences between the main and control groups in a number of parameters (Table 2).

As can be seen from Table 2, abdominal pain (86.8% vs. 18.0%), asthenia symptoms (79.2% vs. 20.8%) and allergodermatoses (49.6% vs. 27.2%) were significantly more common in the main group. The rates of ARI were significantly higher in the group of children with giardiasis. They were also more likely to have a lag in physical development, lower academic performance at school, and complaints of decreased concentration.

The analysis of risk factors showed a clear relationship between living conditions and the likelihood of infection (Table 3).

Children from the main group were significantly more likely to live in rural areas, had contact with domestic and agricultural animals, and also used water from non-centralized sources (wells, springs) for drinking.

Assessment of the condition of children in the main group at 6, 12 and 24 months after successful eradication of *Giardia duodenalis* demonstrated positive dynamics in all analyzed parameters (Table 4).

Table 2. Comparative characteristics of the groups before treatment

Parameter	Study Group (n=250)	Control Group (n=250)	P-value
Abdominal syndrome, n (%)	217 (86.8%)	45 (18.0%)	<0.001
Asthenic syndrome, n (%)	198 (79.2%)	52 (20.8%)	<0.001
Allergodermatoses, n (%)	124 (49.6%)	68 (27.2%)	<0.001
Frequency of ARI (Acute Respiratory Infections) (episodes per year), $M \pm SD$	5.8 ± 1.5	3.9 ± 1.2	<0.01
Physical development delay (BMI (Body Mass Index) < 5th percentile), n (%)	42 (16.8%)	15 (6.0%)	<0.01
Average academic performance score (5-point scale), $M \pm SD$	3.7 ± 0.8	4.3 ± 0.5	<0.05
Complaints of attention deficit, n (%)	167 (66.8%)	75 (30.0%)	<0.001

The most pronounced positive dynamics was observed in relation to abdominal and asthenic syndromes. 6 months after treatment, the frequency of these symptoms decreased by more than three times. The frequency of allergodermatoses and ARI also decreased, but the normalization process was more gradual. After 24 months of follow-up, most children maintained a steady positive trend, although some indicators (for example, the prevalence of allergodermatoses and concentration complaints) were still higher than in the general population (control group), indicating long-term consequences of the invasion.

Discussion

The study revealed the complex effects of giardiasis infection on children's health and also demonstrated the dynamics of recovery after successful treatment. The results obtained allow a deeper understanding of the pathogenic mechanisms of *Giardia duodenalis* systemic effects on a developing organism.

The revealed high prevalence of abdominal syndrome (86.8%) and asthenia (79.2%) in the main group before treatment corresponds to classical concepts of chronic giardiasis (29-31). However, a significant predominance of allergen dermatoses in the same group (49.6% versus 27.2% in control) and higher incidence of acute respiratory infections indicate a systemic nature of invasion (32, 33). This can be explained by constant antigenic stimulation of immune system leading to formation of pro-inflammatory background, impaired immune regulation and potentiation of atopic reactions, reducing resistance to respiratory pathogens (34, 35).

The identified cognitive impairments deserve special

attention. A statistically significantly lower average academic performance score and a high prevalence of complaints of decreased concentration (66.8%) in children with giardiasis indicate that the effects of the infection go far beyond gastrointestinal symptoms (36, 37). The pathogenesis of these disorders is probably multifactorial and may be associated with chronic nutrient deficiency due to malabsorption syndrome, direct neurotoxic effects of parasite metabolites, as well as the effects of chronic asthenic syndrome on cognitive endurance and motivation (38). This aspect is extremely important for pediatric practice, as it allows us to consider giardiasis as one of the potential causes of school maladjustment.

The analysis of risk factors has convincingly demonstrated their leading role in the epidemiology of infection. Significant predominance in the main group of factors, such as living in rural areas (58.0% vs. 32.0%), use of water from non-centralized sources (52.8% vs 22.0%) and contact with farm animals (47.2% vs 18.0%) (39-41). These factors clearly indicate the dominance of aquatic and zoonotic transmission routes under these conditions, particularly the difference from predominantly residential contact routes in megacities (42-44).

The most significant data reflect the dynamics of condition after etiotropic therapy. Rapid regression of abdominal (86.8%-18%) and asthenic syndromes (79.2%-26%) during the first 6 months indicate that these symptoms are direct consequences of invasion and reversible when it is eliminated (45).

At the same time, analysis of long-term results revealed an important pattern: the normalization of a number of indicators was much slower and did not always reach the level of the control group even after 24 months. Therefore, the incidence of allergic dermatoses 2 years after treatment was 28.0%, which was still higher than in the control (27.2%), (46). A similar situation was observed with complaints about decreased concentration (20% vs. 30% in control). This suggested that chronic parasitic infection could initiate certain pathological immune and neurofunctional changes that persisted even after the parasite was eliminated. This finding was of key clinical significance, emphasizing the importance of not only timely diagnosis and treatment for giardiasis but

Table 3. Distribution of risk factors in the main and control groups

Risk Factor	Study Group (n=250)	Control Group (n=250)	P-value
Residence in rural areas, n (%)	145 (58.0%)	80 (32.0%)	<0.001
Ownership of domestic pets, n (%)	189 (75.6%)	135 (54.0%)	<0.01
Non-centralized water supply, n (%)	132 (52.8%)	55 (22.0%)	<0.001
Contact with farm animals, n (%)	118 (47.2%)	45 (18.0%)	<0.001

Table 4. Dynamics of clinical parameters in the main group after treatment (n=250)

Parameter	Before Treatment	After 6 Months	After 12 Months	After 24 Months
Abdominal syndrome, n (%)	217 (86.8%)	45 (18.0%)*	32 (12.8%)*	28 (11.2%)*
Asthenic syndrome, n (%)	198 (79.2%)	65 (26.0%)*	41 (16.4%)*	35 (14.0%)*
Allergodermatoses, n (%)	124 (49.6%)	95 (38.0%)*	75 (30.0%)*	70 (28.0%)*
Frequency of ARI (episodes per year), M±SD	5.8±1.5	4.5±1.3*	4.1±1.1*	4.0±1.0*
Physical development delay, n (%)	42 (16.8%)	35 (14.0%)	25 (10.0%)*	18 (7.2%)*
Average academic performance score, M±SD	3.7±0.8	4.0±0.6*	4.1±0.5*	4.2±0.5*
Complaints of attention deficit, n (%)	167 (66.8%)	85 (34.0%)*	58 (23.2%)*	50 (20.0%)*

Note: * — statistically significant differences compared to the indicator "Before treatment" ($P < 0.05$).

also long-term monitoring of convalescent patients with targeted rehabilitation programs (47-49).

The positive dynamics in terms of ARI frequency and physical development indicators, although pronounced, is also gradual. This confirms the concept of long-term impact of invasion on overall body resources. Thus, giardiasis in children should be considered a systemic disease with wide range of clinical manifestations. Despite etiotropic therapy leading to rapid regression of key symptoms, several consequences, particularly those affecting the immune system and cognitive function, may persist. Extended medical supervision and integrated rehabilitation are required (50-51).

Conclusion

The retrospective cohort study conducted made it possible to establish a significant negative impact of giardiasis on children's health. It identified key risk factors and analyzed the dynamics of recovery after treatment. The data obtained convincingly demonstrates that giardia in children should be considered a systemic disease and not just an intestinal infection. Before treatment, children with confirmed giardia were significantly more likely to experience not only gastrointestinal symptoms (86.8% had abdominal syndrome, compared to 18.0% in the control group) but also systemic manifestations, such as asthenic syndrome (79.2%), allergodermatoses (49.6%, compared to 27.2% in controls), and complaints of reduced concentration (66.8%). These findings indicate a complex negative effect of the invasion on the developing body.

The analysis of risk factors revealed a clear dependence of the probability of infection on social and living conditions. The main group was significantly dominated by children living in rural areas (58.0% vs. 32.0%), using non-centralized water supply sources (52.8% vs. 22.0%) and having contact with farm animals (47.2% vs 18.0), indicating the dominance of aquatic and zoonotic transmission routes in the studied regions.

The assessment of long-term treatment results showed multidirectional dynamics in recovery of various body functions. Fastest regression was observed with respect to gastrointestinal symptoms: already 6 months after treatment, prevalence of abdominal syndrome decreased to 18%. However, normalization of extraintestinal manifestations occurred more slowly: after 24 months, prevalence of allergodermatosis decreased to 28% and complaints about decreased concentration decreased to 20%, which were still higher than in the control group. This indicates that chronic parasitic infection can initiate long-term pathological changes that persist even after the pathogen has been eliminated.

Thus, the results obtained emphasize the need for an integrated approach to managing children with giardiasis. This includes not only timely etiotropic therapy but also long-term follow-up with targeted rehabilitation measures

aimed at correcting long-term consequences of infection. The significant association of the disease with specific social and household factors necessitates the development of differentiated prevention programs taking into account regional epidemiological characteristics.

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Authors' Contribution

All the authors participated equally in the organization of the experiment and the preparation of the manuscript

Competing Interests

The authors declare that there is no conflict of interest

Ethical Approval

The study was conducted in strict accordance with the principles of the Helsinki Declaration, and its protocol was approved by the ethics committee of the North Ossetian State Medical Academy (Vladikavkaz, Russia). Protocol No. 1278 dated 12/02/2023 was approved.

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