



The Prevalence of *Blastocystis* Infection in Pediatric Patients with Malignancy: A Single-Center Study in Ahvaz, Iran

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Abstract

Background: *Blastocystis* spp. is known as one of the few intestinal parasites, prevalent in more than 5% and 30 - 60% of the population in industrialized and developing countries, respectively. In this respect, immunocompromised individuals, such as patients undergoing chemotherapy or those with malignancies, are at risk of the clinical symptoms of *Blastocystis* infection; however, the given condition is often self-limiting in healthy individuals.

Objectives: The current study aimed at evaluating the prevalence of *Blastocystis* infection in children with malignancies receiving chemo drugs.

Methods: The current descriptive, cross-sectional study was conducted on 52 stool specimens collected from patients with cancer admitted to the Oncology Ward of Shahid Baqaei 2 Hospital, Ahvaz, Iran, for six months. A standardized questionnaire was filled out for all cases. Each specimen was also prepared using direct smear, the Lugol iodine staining, and the formalin-ether condensation method.

Results: *Blastocystis* spp. was detected in 21.1% of the cases among them, 11.5% demonstrated gastrointestinal symptoms; therefore, a significant relationship was observed between *Blastocystis* infection and gastrointestinal symptoms.

Conclusion: Patients undergoing chemotherapy should be screened for opportunistic parasitic infections such as *Blastocystis* to avoid potentially life-threatening outcomes. Besides, further studies are required to identify the subtypes of *Blastocystis*.

Keywords: *Blastocystis*, Children with Cancer, Chemotherapy, Immunocompromised Individuals

1. Background

Infectious diseases, especially opportunistic ones, are significant complications among immunocompromised patients (1). *Blastocystis* is the most common single-celled opportunistic parasite found in humans and a wide range of animal stool specimens. The *Blastocystis* infection prevalence in humans varies from 0.5% to 30% in the industrialized and 30% to 76% in developing countries (2, 3). In a study in Tehran, Iran, the parasitic infection prevalence was 32.5% in primary immunodeficiency, 25.9% in cancer, and 28% in organ transplanted groups. The prevalence of *B. hominis* infection in patients with primary immunodeficiency disorders (PIDs) was 16.2%. *Blastocystis hominis* causes the most prevalent intestinal parasitic infection in patients with cancer (22.3%) (4). Many *Blastocystis* spp. carriers are asymptomatic, and the term infection is often used for those manifesting pathological symp-

toms (5). This infection is generally self-limiting, and fecal-oral is the main route of transmission due to poor hygiene, close contact with infected animals, and consumption of contaminated food or water, resulting in a wide range of prevalence in different types (6, 7). Nevertheless, the non-specific gastrointestinal symptoms of *Blastocystis* infection- e.g. diarrhea, abdominal pain, flatulence, nausea, vomiting, constipation, weight loss, or fatigue, lead to a poor understanding of its pathogenesis (8). A large rising trend in the incidence of cancers is projected in the following years, and the best existing treatment is chemotherapy. Although chemotherapy improves survival rate and quality of life in patients, it is associated with long-term changes in immunological parameters, etc. (9). The clinical manifestations of *Blastocystis* infection are more highlighted among patients with immunodeficiency and cancer compared with healthy individuals since such people have quantitative or qualitative changes in their im-

mune responses that prevent it from functioning effectively. Self-limiting diarrhea caused by *Blastocystis* infection in healthy individuals can manifest as severe diarrhea in immunocompromised patients and cause complications such as weight loss, anorexia, malabsorption syndrome, fever, and abdominal pain (10-14).

Many symptoms in patients with PIDs could be mimics parasitic infestation-e.g., fever, and diarrhea; therefore, the diagnosis of parasitic infections varies across clinical signs and symptoms.

2. Objectives

The current study aimed at investigating the prevalence of *Blastocystis* infection in pediatric patients with malignancy admitted to the Oncology Ward of Baqaei 2 Hospital in Ahvaz, Iran.

3. Methods

The current descriptive, cross-sectional study was conducted on 52 stool specimens collected from children with cancer admitted to the Baqaei 2 Hospital from April to October 2019 after obtaining signed informed consent. The study protocol was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences. Collected samples were examined by light microscopy using Lugol-stained smears at 100× and 400× magnifications to detect *Blastocystis*. A direct saline smear was prepared for each patient with trichrome staining and then examined by light microscopy. The specimens were screened using the formalin-ether condensation method, and the results were transferred into the questionnaire.

The duration of the first chemotherapy course in all the patients ranged from six months to three years (with a mean of one year), and they were treated with combinations of chemo drugs (Table 1). Neutropenia was also observed in 2% of the patients; 11% were treated with antifungal drugs and antibiotics. Supportive therapy included a three-day course of metronidazole. The interval between sampling and the last session of chemotherapy was 1 - 2 days. However, 41 (78.8%) patients were in the maintenance phase of treatment. To determine the prevalence of *Blastocystis* infection, a standardized questionnaire, comprised of demographic information, type of cancer, gastrointestinal symptoms (such as stomachache, cramps, nausea, vomiting, and diarrhea), stool appearance (color and consistency), and the stool test result, was designed and completed. Finally, the data were analyzed by SPSS software, and the Chi-square test was used for qualitative variables.

4. Results

In the current study, 52 stool specimens were obtained from children with cancer. According to the study findings, 28 (53.8%) patients were male, and 24 (46.2%) females. The prevalence of *Blastocystis* infection was 21. % (n = 11) in the studied patients. Based on Lugol-stained smears, *Blastocystis* was detected in 10 positive children with cancer (19%). The formalin-ether concentration technique detected 11 positive cases (21%). The trichrome-stained smear detected 11 positive cases (21%). The age range of the patients was from four months to 16 years, classified into four groups of ≤ 1 year [n = 8 (15.4%)], 1 - 5 years [n = 18 (34.6%)], 6 - 10 years [n = 12 (23%)], and 11 - 16 years [n = 14 (27%)] (Tables 2 and 3).

The obtained results indicated no statistically significant differences in gender, age, and prevalence of *Blastocystis* infection among the subjects ($P < 0.05$). The results also highlighted that among 52 children with cancer, 11 were infected with *Blastocystis* spp. among which six (11.5%) had gastrointestinal symptoms, including stomachache, cramps, nausea, vomiting, and diarrhea. The correlation between the type of cancer and gastrointestinal symptoms in patients with *Blastocystis* infection is shown in Table 4.

Statistical analysis revealed a significant relationship between *Blastocystis* infection and gastrointestinal symptoms ($P < 0.05$).

5. Discussion

Blastocystis is an anaerobic and zoonotic micro-eukaryote with a global distribution, generally found in the large intestine of the human and a wide range of vertebrates (10), as reported by Alexief more than 100 years ago (15). Since the asymptomatic carriers of *Blastocystis* spp. are common, its pathogenicity remained uncertain (2). Numerous digestive and non-digestive symptoms, such as diarrhea, abdominal pain, nausea, fatigue, constipation, flatulence, vomiting (11), cutaneous disorders, and chronic or acute urticaria, are attributed to *Blastocystis* infection (16). *Blastocystis* spp. can produce large quantities of proteases, hydrolases, and protease inhibitors, contributing to its pathophysiology. Instant serine protease can further result in stomachache, muscle contractions, and broad-spectrum pains (12). Cysteine protease can also cleave human secretory immunoglobulin A (IgA) and promote mucosal adhesion of pathogens (17). Many reports considered *Blastocystis* spp. as opportunistic pathogens in immunocompromised patients; therefore, their clinical symptoms are more intense (18). At the early stages of chemotherapy, a few cases colonized

Table 1. Types of Chemotherapy for Acute Myeloid Leukemia, Acute Lymphocytic Leukemia, Neuroblastoma, and Ewing Sarcoma

Type of Cancer	Chemotherapy
AML	Cytarabine + daunomycin
ALL	Vincristine, daunorubicin, cytarabine, L-asparaginase, mercaptopurine, methotrexate, cyclophosphamide, prednisone, dexamethasone, nelarabine
Neuroblastoma	Carboplatin, cyclophosphamide, doxorubicin, etoposide
Ewing sarcoma	Doxorubicin, cyclophosphamide, ifosfamide, vincristine, etoposide

Table 2. Demographic Characteristics of Children with Cancer

Demographic Characteristics	No. (%)
Gender	
Male	28 (53.8)
Female	24 (46.2)
Age group (y)	
≤ 1	8 (15.4)
1 - 5	18 (34.6)
6 - 10	12 (23)
11 - 16	14 (27)
Total	52

Table 3. The Prevalence of *Blastocystis* Infection in Children with Cancer

Demographic Characteristics	The Prevalence of <i>Blastocystis</i> Infection, No. (%)
Gender	
Male	7 (13.4)
Female	4 (7.7)
Age group	
≤ 1	1 (1.9)
1 - 5	2 (3.8)
6 - 10	5 (9.6)
11 - 16	3 (5.7)
Total	11

Table 4. Types of Cancer and Gastrointestinal Symptoms in Patients with *Blastocystis* Infection

No.	Type of Cancer	Gastrointestinal Symptom
1	AML	Diarrhea
2	ALL	Abdominal pain
3	ALL	Fever, vomiting
4	Neuroblastoma	Diarrhea
5	Ewing sarcoma	Diarrhea

with *Blastocystis* spp. are undetectable. The immune system of patients is compromised during chemotherapy,

and consequently, the parasitic disease develops and diminishes the effect of chemo drugs, and accordingly, cancer progresses (19). Among unicellular infections in immunocompromised individuals, *Blastocystis* is the most common one. The findings of the present study showed that the prevalence of *Blastocystis* infection was 21% (n = 11) in children with cancer, among which 11.5% had gastrointestinal symptoms; therefore, there was a significant relationship between *Blastocystis* infection and gastrointestinal symptoms. According to Hafeez-Abdel et al., the prevalence of *Blastocystis* infection in children with immunodeficiency was 12.1% in Egypt. Uysal et al., reported that 23. % of patients with common variable immune deficiency were infected with *Blastocystis* spp. in Turkey (20, 21). The data in the present study were also confirmed by Idris et al., reporting that 54.8% of 42 immunocompromised children with diarrhea were infected with *Blastocystis* spp. in Indonesia (22). Lack of significant differences in gender, age, and *Blastocystis* spp. infection among the patients was another finding of the present study; however, Ozlem Years et al., obtained quite different results. They noted that the prevalence of *Blastocystis* infection was higher in male patients than females, and interestingly, the rate of gastrointestinal symptoms was not significantly different between infected and non-infected cases (23). Moe et al., found an age-related susceptibility to *Blastocystis* infection in immunocompetent BALB/c mice. In the concerned investigation, juvenile mice were more susceptible than adult cases, and eight-week-old adult mice were resistant to *Blastocystis* infection (24). This difference might be related to various *Blastocystis* strains, the issue needs molecular studies. During chemotherapy, the risk of parasitic infections is minimized due to particular conditions, including lifestyle, diet, and environment; therefore, it can be claimed that it is the opportunity for opportunistic pathogens to invade and cause clinical problems (25). Fontanet believed that there was no significant difference in the prevalence of parasitic infections among people with and without immunodeficiency. On the other hand, in some studies, such as the one by Escobedo and Nunez, the prevalence of *Blastocystis*

infection was reported higher in immunocompromised patients compared with healthy individuals (25). Under such circumstances, person-to-person was the main route of transmission. The limitation of the present study was the relatively small sample size.

5.1. Conclusion

Patients undergoing chemotherapy should be screened for opportunistic parasitic infections such as *Blastocystis* spp. to avoid potentially life-threatening outcomes, prevent person-to-person transmission, and help to improve patient responses to treatment. Further studies are required to identify the subtypes of *Blastocystis*.

Footnotes

Authors' Contribution: Study concept and design: Roya Salehi Kahish; analysis and interpretation of data: Shokofeh Hadadi, Arash Alghasi, and Marziyeh Abbasi Nasab; drafting of the manuscript: Ayda Mafakher and Shokofeh Hadadi; critical revision of the manuscript for important intellectual content: Arash Alghasi, Mohammadreza Mahmoudian Sani, Roya Salehi Kahish, and Shokofeh Hadadi; statistical analysis: Marziyeh Abbasi Nasab and Ayda Mafakher.

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Informed Consent: Written informed consent was taken from the parents of the participants before enrollment.

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