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ORIGINAL PAPER

STUDY ON THE INCIDENCE OF BLASTOCYSTOSIS AMONG HOSPITALIZED PATIENTS WITH ACUTE AND CHRONIC SPONTANEOUS URTICARIA

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Abstract

Introduction. Blastocystosis is a zooantroponotic parasitic disease, caused by the anaerobic intestinal protozoan *Blastocystis sp.* The clinical presentation varies from asymptomatic to gastro-intestinal and/or allergic symptoms. Allergization during infection with *Blastocystis sp.* often presents with the development of acute or chronic spontaneous urticaria.
The objective of the study was to determine the incidence of blastocystosis among patients with acute and chronic spontaneous urticaria who were hospitalized in the Allergology Clinic of The University Hospital – Pleven, Bulgaria.
Material and methods. We retrospectively studied the rate of infection with *Blastocystis sp.* isolated from fecal samples from 1197 patients with urticaria and 1300 healthy individuals with no allergic symptoms, who were tested prophylactically for the presence of intestinal parasites.
Results. We determined that patients with urticaria had a statistically higher incidence of blastocystosis (9.6%), compared to healthy controls (1.2%) (p=0.001). The statistical analysis showed that the probability of being infected with *Blastocystis* is nearly 8 times higher

Résumé

Étude concernant la fréquence de la blastocystose dans le milieu hospitalier sur des patients porteurs d'une lésion urticaire spontanée aigüe ou chronique

Introduction. La blastocystose est une zoonose-maladie parasitaire, déclenchée par un protozoaire intestinal anaerobe *Blastocystis sp.* Le tableau clinique de la blastocystose est varié – parfois asymptomatique, pouvant se manifester soit par des signes gastro-intestinaux, soit par des symptômes allergiques, soit par une association des deux tableaux décrits au-dessus. Le processus allergique lié à la blastocystose se déclare souvent par l'apparition d'une lésion urticaire spontanée en forme aigüe ou chronique.
L'objectif de l'étude a été d'établir le pourcentage exact des patients contaminés par le *Blastocystis sp.* qui présentent une lésion urticaire aigüe ou chronique. Il s'agit de patients hospitalisés dans la Clinique Allergologique – Hôpital Universitaire de Pleven.
Materiel et méthodes. Études rétrospectives des coprocultures positives à *Blastocystis sp.* chez 1197 patients porteurs de signes de l'urticaire et 1300 sujets

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in patients with acute urticaria compared to the control group (OR = 7.806; p=0.001) and nearly 10 times higher in patients with chronic spontaneous urticaria (OR = 9.992; p=0.001).

Conclusions. Patients with acute or chronic spontaneous urticaria should be tested for intestinal parasites and those with a positive result for blastocystosis should be treated with antiparasitic drugs.

Keywords: *Blastocystis*, blastocystosis, urticaria, allergy.

List of abbreviations:
AU = acute urticaria
CSU = chronic spontaneous urticaria

sains sans pathologie allergique et sans pathologie parasitaire intestinale.

Résultats. Nous avons prouvé statistiquement une intensité plus élevée de Blastocystose chez les patients avec signes d'urticaire (9,6%) par rapport au groupe de contrôle de sujets sains (1,2 %) (p=0,001) et que la probabilité d'être infecté par *Blastocystis* est près de 8 fois plus élevée chez les patients souffrant d'urticaire aiguë par rapport au groupe contrôle (OR = 7,806; p=0,001) et près de 10 fois plus élevée chez les patients souffrant d'urticaire chronique spontanée. (OR =9,992; p= 0,001).

Conclusions. Les patients atteints d'urticaire spontanée aiguë ou chronique doivent subir un test de dépistage des parasites intestinaux et ceux dont le test de blastocystose est positif doivent être traités par des médicaments antiparasitaires.

Mots-clés: *Blastocystis*, blastocystose, urticaire, allergie

Introduction

The causative agent of blastocystosis is *Blastocystis sp.*, an anaerobic protozoan that parasitizes in the lumen of the large intestines in humans and animals[1]. The parasite has four morphological forms: vacuolar, granular, amoeboid and cyst form. Of them, the vacuolar form is the most commonly isolated from fecal samples[2]. Blastocystosis in humans can present as asymptomatic carriership or with either allergic or gastro-intestinal symptoms. The allergisation of people infected with *Blastocystis sp.* is common and usually presents with acute or chronic spontaneous urticaria[3, 4].

The objective of the study was to determine the incidence of infection with *Blastocystis sp.* among patients with acute and chronic spontaneous urticaria who were hospitalized in the Allergology Clinic of the University Hospital – Pleven, Bulgaria.

Materials and methods

The study covers a five-year period (2018-2023). The information was collected retrospectively from the medical records of 1197 hospitalized patients with acute urticaria (AU) or chronic spontaneous urticaria (CSU). All patients were tested for intestinal or tissue parasites in the parasitological laboratory of the University Hospital – Pleven, Bulgaria. The type of urticaria was determined based on the criteria of the international European Academy of Allergology and Clinical Immunology/ Global Asthma and Allergy European Network/ European Dermatology Forum/ Asia Pacific Association of Allergy, Asthma and Clinical Immunology (EAACI/GALEN/EDF / APAAACI)[2] guideline for the definition, classification, diagnosis, and management of urticaria[5].

For comparative analysis, we also retrospectively studied the incidence of infection with *Blastocystis sp.* in 1300 healthy individuals without allergic symptoms who were tested for intestinal parasites based on prophylactic indications.

The criteria for the diagnosis of blastocystosis was isolation of the vacuolar or granular form of *Blastocystis sp.* from fresh fecal samples, stained in a wet mound with Lugol's solution.

The data were processed with the software program SPSS, v.25 and EXCEL. All relationships, dependencies and differences between the studied groups were established at the significance level of the null hypothesis, $p<0.05$.

The study has been approved by the Committee of Scientific Ethics of Medical University – Pleven (Protocol № 88/27.11.2025).

Results

The type of allergic reaction and the demographic characteristics of the studied subjects are shown in Table 1.

Infection with *Blastocystis sp.* was found in 115 (9.6%) patients with urticaria. Among the control group of 1300 subjects, *Blastocystis sp.* was isolated from 15 of them (1.2%).

We determined that patients with urticaria had a significantly higher rate of infection with *Blastocystis*

Table 1. Distribution of subjects based on diagnosis, sex and age.

Type of allergic reaction	*Acute urticaria*	*Chronic spontaneous urticaria*	*Healthy controls*
	n (%)	*n* (%)	*n* (%)
Sex			
Male	154 (32.2%)	232 (32.3%)	427 (32.8%)
Female	325 (67.8%)	486 (67.7%)	873 (67.2%)
Total	*479 (100.0%)*	*718 (100.0%)*	*1300 (100.0%)*
Age Median (Min, Max)	51 (3, 82)	50 (3, 86)	40 (1, 82)

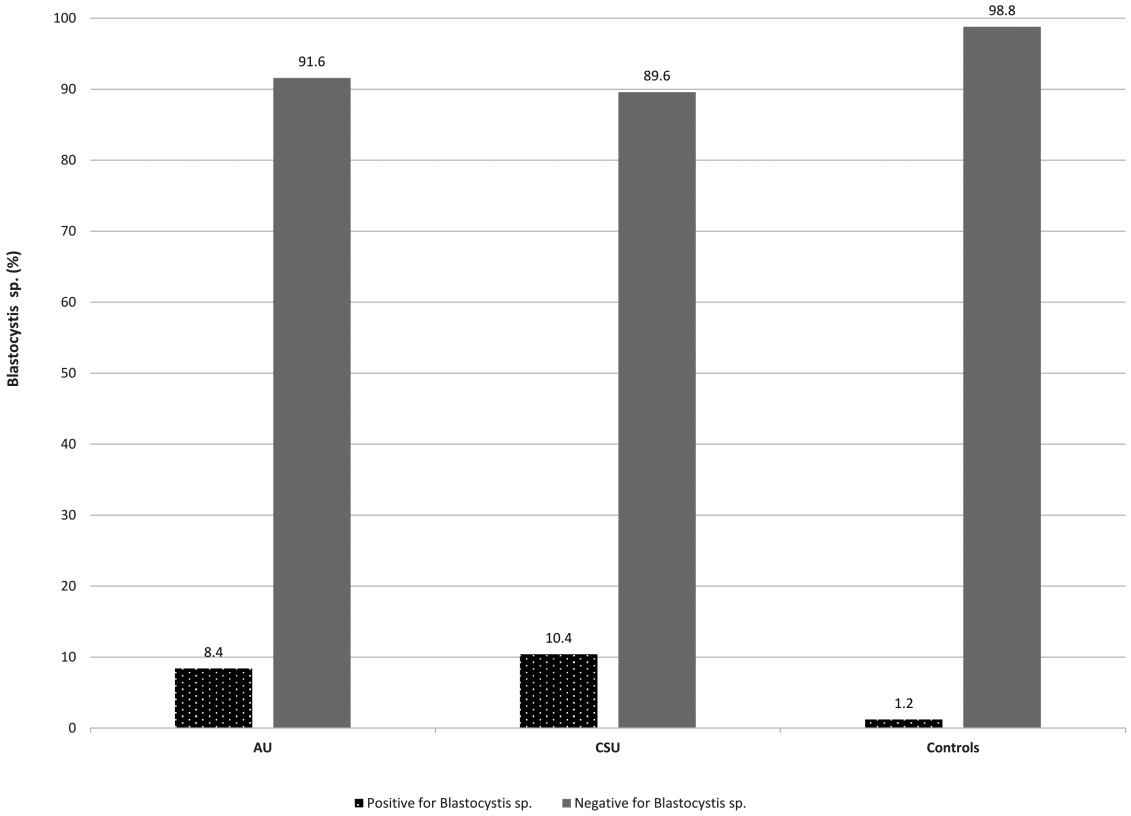


Figure 1. Frequency of blastocystosis in the compared groups (%)
(AU – acute urticaria; CSU – chronic spontaneous urticaria)

sp. than the healthy controls (χ^2=92.793, df=2, p=0.001, V=0.193).

Figure 1 shows the rate of infection with *Blastocystis sp.* among patients with AU and CSU and among the subjects from the control group. Out of 115 patients with urticaria who were positive for *Blastocystis sp.*, 40 (34.78%) had AU and 75 (65.22%) had CSU. The extent of infection with *Blastocystis sp.* was 8.4% in patients with AU and 10.4% among patients with CSU. There was no statistically significant difference in the infection rate based on the type of urticarial reaction (χ^2=1.452; df=1; p=0.228).

The age distribution of the 1197 patients with urticaria tested for blastocystosis was the following: 179 (14.95%) were in the 1-20 years of age group; 229 (19.13%) were in the group 21-40 years of age; 404 (33.75%) were patients between 41 and 60 years of age and 385 (32.16%) were in the age group 61-86 years old.

Among the patients with urticaria, the ones who were positive for *Blastocystis sp.* predominate in the age groups 41-60 (37.40%) and 61-86 (31.30%).

Figure 2 shows the extent of blastocystosis in patients with urticaria and healthy controls based on age.

The age stratification shows that the connection between age and the extent of infection is statistically significant in all age groups, except for the 61-86 years group (age 1-20 χ^2=16.463, df=2, p=0.001, V=0.193; age 21-40 – χ^2=38.069, df=2, p=0.001, V=0.246; age 41-60 – χ^2=57.161, df=2, p=0.001, V=0.249; age 61-68 – χ^2=2.398, df=2, p=0.301, V=0.069). The statistical analysis shows that age is a confounding factor.

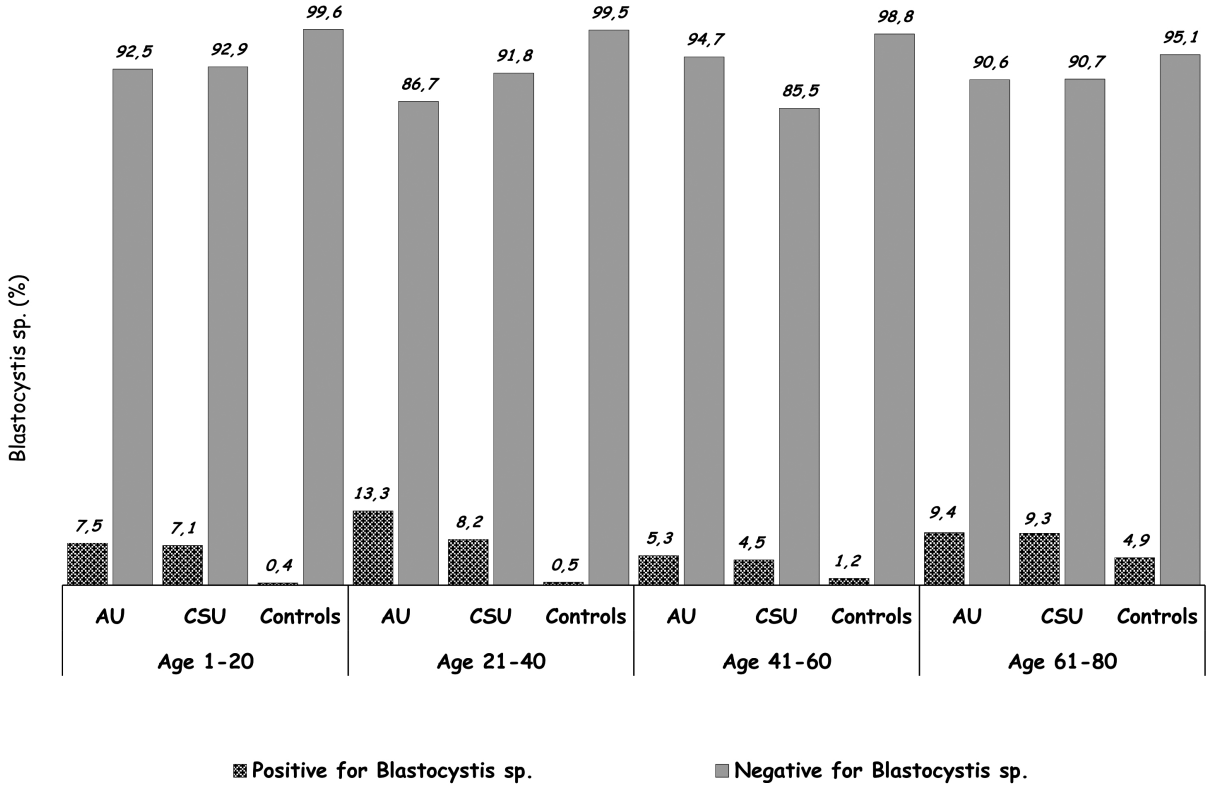


Figure 2. Frequency of infection with *Blastocystis sp.*in the compared groups – age stratification (%)
(AU – acute urticaria; CSU – chronic spontaneous urticaria)

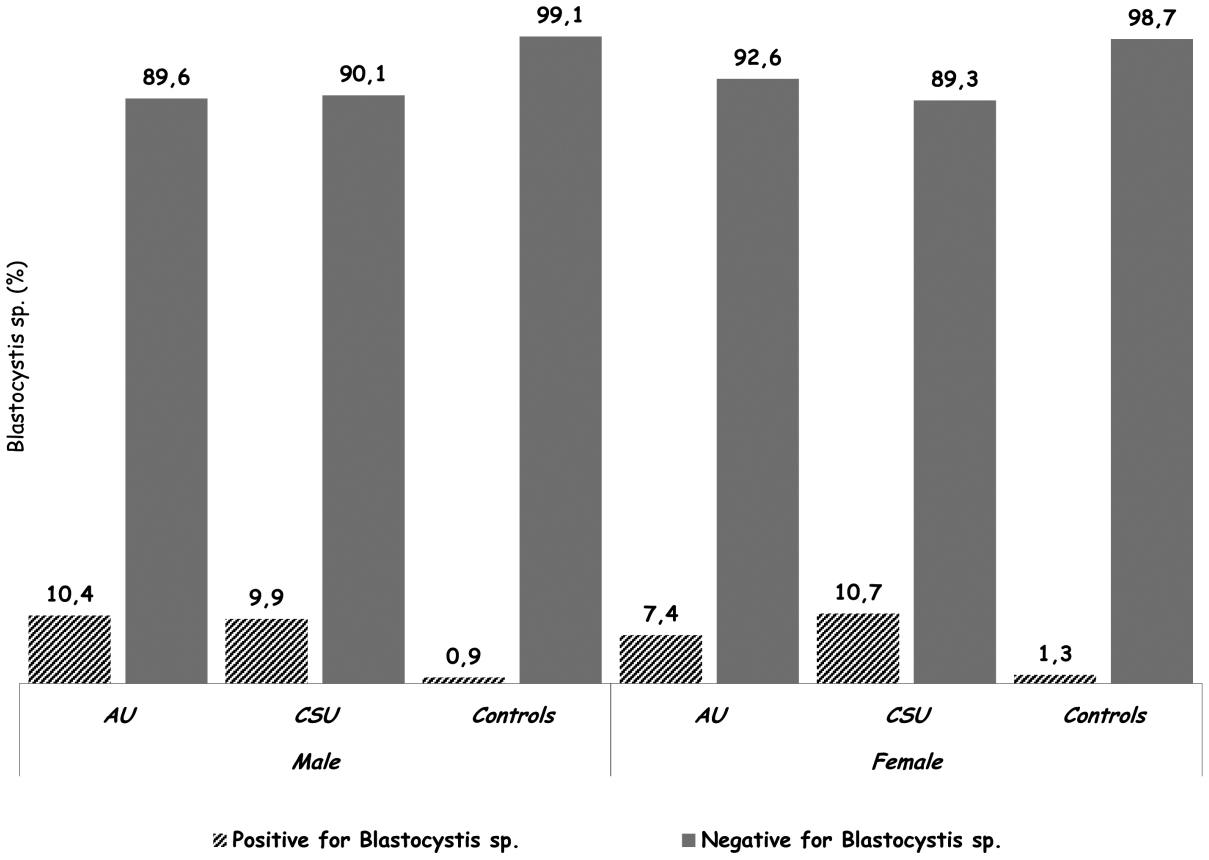


Figure 3. Frequency of infection with *Blastocystis* sp. in the compared groups – sex stratification (%)
(AU – acute urticaria; CSU – chronic spontaneous urticaria)

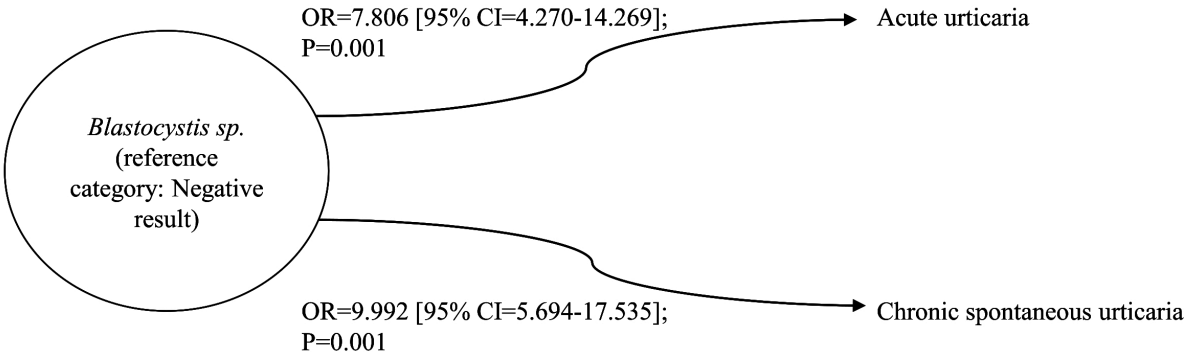


Figure 4. Results of the logistic regression analysis

Out of 1197 patients with acute and chronic spontaneous urticaria tested for *Blastocystis sp.*, 811 (67.75%) were female and 386 (32.25%) were male. Of the 115 patients with urticaria positive for blastocystosis, 66.1% were female and 33.9% were male. Despite the higher relative share of female patients infected with *Blastocystis sp.*, the extent of blastocystosis is higher in males (10.1%), compared to females (9.4%).

Figure 3 shows the rates of infection with *Blastocystis sp.*, based on the type of allergic reaction and sex.

Among patients with AU, males had a higher rate of blastocystosis (10.4%) than female patients (7.4%), while in CSU patients infected with *Blastocystis sp.* was more common in female individuals (10.7%), compared to males (9.9%).

Stratification based on gender showed that the connection between gender and infection with *Blastocystis sp.* is statistically significant: male – χ^2=34.050, df=2, p=0.001, V=0.205; female – χ^2=60.825, df=2, p=0.001, V=0.190). The analysis showed that gender is also a confounding factor.

Figure 4 presents a logistic regression model (singular multinomial regression), which shows the independent role of *Blastocystis sp.* in the etiology of allergic reactions.

The odds of urticaria patients being infected with *Blastocystis sp.* compared to the individuals from the control group is roughly 8 times higher in patients with AU (OR=7.806 95% CI=4.270-14.269; p=0.001) and roughly 10 times higher in patients with CSU – (OR=9.992 95% CI=5.694-17.535; p=0.001).

Discussion

Allergic diseases are caused by multiple factors and their development requires genetic predisposition towards hyperreaction to foreign antigens, as well as exposition to factors of the external environment (pollution, parasitic invasions, infections and other allergens)[6].

The exact mechanism and role of external factors in the pathogenesis of allergic diseases have not been fully elucidated. Since acute and chronic spontaneous urticaria often arise during the development of some parasitic diseases, different authors have been looking for a potential connection between allergic and parasitic diseases[7].

During the initial stages of research on *Blastocystis sp.* as a parasite and blastocystosis as a disease, clinically presented allergic symptoms were often associated with the intensity of colonization of the large intestine by the parasite. This also determined the therapeutic behavior of the physician in cases of blastocystosis with allergization[8].

There are multiple studies on the allergenic role of *Blastocystis sp.* Some consider that when the parasite comes into contact with the intestinal epithelium, its carbohydrate antigens stimulate the release of histamine liberating factors. This leads to degranulation of migrating mastocytes and basophils and leads to the development of acute urticaria[9]. According to other authors, the pathogenicity of *Blastocystis sp.* depends on local secretion of cysteine proteases by the parasite. These enzymes degrade the interepithelial space which increases intestinal permeability and stimulates cytokine release from T-lymphocytes[10,11].

Blastocystis sp. isolates from humans and animals show wide genetic diversity and are classified in 34 subtypes. Fourteen genotypes have been isolated from humans. It is generally considered that the differing clinical presentation of blastocystosis depends on the genetic diversity of the parasite[12].

The high frequency of isolation of a specific parasite among patients with specific symptoms could be an indirect sign that it is a cause of those symptoms. In our study, we found a statistically significant difference in the extent of blastocystosis between patients

with urticaria and healthy individuals, giving us reason to assume that infection with *Blastocystis sp.* is a co-factor for the development of allergic symptoms.

In the available literature, a similar high frequency of infection with *Blastocystis sp.* among patients with urticaria has been described by various authors. Aykur at al. report that 31.9% of patients with CSU they tested had blastocystosis[3]. Jafari et al. determined that 21.3% of patients with CSU had blastocystosis[13].

In several studies, the connection between blastocystosis and allergic skin symptoms has been confirmed due to the disappearance of urticaria after treatment with antiparasitic drugs[14,15]. Tuzer describes a decrease in the severity of urticaria and a drop in total serum IgE and peripheral eosinophilia in patients with blastocystosis and CSU treated with antiparasitic drugs and antihistamines, compared to patients only treated with antihistamines[16].

Analyzing the demographic characteristics of patients with urticaria infected with *Blastocystis sp.* in our study, we determined that most cases of blastocystosis were in the age groups 41-60 (37.40% of all cases) and 61-86 (31.30% of all cases) and that males were most likely to be infected – extent of blastocystosis of 10.1%. Similar data on the frequency of blastocystosis based on age and sex has been described in epidemiological studies by other authors around the world. Jinatham et al. determined that the age group 45 to 64 years has statistically the highest rate of *Blastocystis* infection[17]. Seyer et al. describe that 25.5% of people they studied between the ages of 40 and 59 had blastocystosis, however they did not find a statistically significant difference in the frequency of infection with *Blastocystis sp.* based on the age of the test subjects[18].

According to literature data, infection with *Blastocystis sp.* is more common in females[17,19]. This was not confirmed by our study among urticaria patients. The statistical analysis of demographic factors among patients with urticaria showed that both age and sex were confounding factors.

The logistic regression model determined that the risk of infection with *Blastocystis sp.* is almost 8 times higher in patients with AU and roughly 10 times higher in patients with CSU compared to healthy controls. We consider that the higher risk of infection with *Blastocystis sp.* and the high blastocystosis rate in patients with urticaria reflect the allergization potential of the parasite for the human host.

Conclusions

Patients with acute or chronic spontaneous urticaria should be tested for intestinal parasites and if positive for blastocystosis they should be treated with antiparasitic drugs.

Author Contributions

Conceptualization, L.S.S. and I.A.A.; methodology, I.A.A. and L.S.S.; software, L.S.S.; validation, I.A.A. and L.S.S.; formal analysis, L.S.S.; investigation, L.S.S and I.A.A.; resources, L.S.S.; data curation, L.S.S.; writing–original draft preparation, L.S.S.; writing–review and editing, L.S.S. and I.A.A.; visualization, L.S.S. and I.A.A.; supervision, I.A.A.; project administration, I.A.A. All the authors have read and agreed with the final version of the article.

Compliance with Ethics Requirements:

"The authors declare no conflict of interest regarding this article"

"The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study via standardized form"

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