Original Paper

International Archives of Allergy and Immunology

Int Arch Allergy Immunol 2016;171:130–135
DOI: 10.1159/000450953

Received: May 26, 2016
Accepted after revision: September 20, 2016
Published online: December 2, 2016

# Parasitic Infections in Children with Chronic Spontaneous Urticaria

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**Key Words**
Abdominal pain · Children · Chronic spontaneous urticaria · Gastrointestinal symptoms · Parasite · Urticaria

**Abstract**
***Background:*** Parasites have been proposed to be an underlying cause of chronic spontaneous urticaria (CSU) in childhood, but a clear causal relationship between them has not been established. This study aimed to investigate the prevalence of parasitic infection-related CSU (PIRCSU) in children and to determine the factors associated with PIRCSU. ***Method:*** Data from 211 children with CSU were analyzed. Information on stool examination, antiparasitic medications received, and response to treatment was recorded. The disappearance of urticaria for more than 6 months is defined as remission, and remission of urticaria after antiparasitic treatment is defined as PIRCSU. ***Results:*** Parasites were detected in 21 (10%) patients. *Blastocystis hominis* was the most common parasite. After antiparasitic medication, all samples became normal; urticaria continued in 5, was reduced in 6, and disappeared in 10 patients. The latter 10 patients were considered as cases of PIRCSU (4.7%). The erythrocyte sedimentation rate was significantly higher in patients with PIRCSU than in those without [8.5 mm/h (3.5–14.5) vs. 2 (0–7), p = 0.011]. Gastrointestinal complaints were significantly more frequent in patients with PIRCSU than in those without. The occurrence of abdominal pain was a significant risk factor that increased the probability of PIRCSU [OR = 6.60, 95% CI = 1.35–32.23, p = 0.020]. ***Conclusion:*** Parasites may cause CSU even in nontropical countries, and remission may only be possible with the treatment of the parasitic infection. The occurrence of abdominal pain points to parasitic infection in patients with CSU. Therefore, we suggest that parasites should be investigated routinely, especially if the patient has gastrointestinal symptoms of CSU in childhood.



## Introduction

Chronic spontaneous urticaria (CSU), which is defined as the spontaneous and transient appearance of urticaria, angioedema, or both for more than 6 weeks, is a rare but often distressing allergic skin disorder in childhood [1]. Its estimated prevalence in children is 0.1–3% [2]. Data on the etiology of CSU in the pediatric age group are limited. The underlying etiology has been described

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in a small number of patients in a few studies [3]. To date, foods, infections, thyroid diseases, and autoimmunity have been shown to be etiologic factors [4–10]. Parasites have also been proposed to be an underlying factor of CSU, but a causal relationship between them has not been described in the literature. In fact, complete remission is required by elimination of the suspected factor to be the underlying cause of CSU. Although information on the prevalence of parasitic infections in CSU is available, data on the effect of its eradication in the natural course of urticaria are limited.

In a recent systematic review [11], the prevalence of parasitic infection in children with CSU and the efficacy of antiparasitic medication in CSU symptoms were found to have a wide range of 0–37.8 and 0–100%, respectively. Studies mentioned that parasitic infections in patients with CSU showed important differences in study design, inclusion criteria, and definition of disease or remission criteria. The relationship between parasitic infections and CSU remains unclear.

In the present study, we aimed to determine the effect of parasitic infection treatment on urticaria symptoms in patients with parasites in the stool and to investigate the prevalence of parasite-associated CSU in children in a large cohort. We also examined the factors related to parasitic infection-related CSU (PIRCSU).

## Method

*Study Population*

This study has both prospective and retrospective aspects. A total of 248 children who had been diagnosed with CSU at the Department of Pediatric Allergy, Hacettepe University School of Medicine, Ankara, Turkey, between 1992 and 2015 were enrolled. Among these patients, those who had been diagnosed between 2010 and 2015 were followed up and analyzed prospectively (n = 158), and those who had been diagnosed between 1992 and 2009 were analyzed retrospectively (n = 90). In total, 211 patients had stool examinations.

CSU was defined as the transient appearance of urticaria without a specific physical trigger for more than 6 weeks [1]. The daily or almost daily (>4 days/week) occurrence of urticaria symptoms was considered chronic persistent urticaria, and the occurrence of urticaria for 2–4 days a week was considered chronic recurrent urticaria [12]. Patients with inducible urticaria were excluded. The urticaria activity score 7 (UAS7) was calculated by the sum of the daily UASs for 7 consecutive days in patients according to the guideline [1].

The following demographic features were recorded: gender, age, duration of urticaria, UAS7 at admission, concomitant systemic symptoms other than urticaria or angioedema such as gastrointestinal complaints, accompanying allergic diseases including atopic dermatitis, allergic rhinitis, and asthma, chronic diseases other than allergic diseases and family history of allergic diseases.

Laboratory investigations included complete blood count, C-reactive protein, erythrocyte sedimentation rate (ESR), total IgE, C3 and C4 levels, free thyroxine and thyroid-stimulating hormone, thyroid autoantibodies (antithyroid peroxisomal antibody, antithyroglobulin antibody and anti-thyroid-stimulating hormone antibody), antinuclear antibody, anti-double-stranded DNA antibody and urine analysis.

Stool samples were obtained at admission. Samples were collected in clean plastic containers and then assessed within 30 min. Sampling was also performed by the sellotape method when suspicion of *Enterobius vermicularis* infection was present. Fresh stool samples were examined by a light microscope at ×100 and ×400 magnifications. Samples were also processed with a semiautomated system, FE-2 Intestinal Parasite Analysis Workstation, and then stained with iodine before assessment. Both methods were applied to the samples at the same time, and the detection of parasites in one of them was considered a positive result.

All patients were asked to answer a questionnaire about parasitic infection. This questionnaire included gastrointestinal symptoms (e.g. abdominal pain/cramp, diarrhea, mucus or blood in stool, anal pruritus and emesis), general symptoms (e.g. loss of appetite, fatigue, teeth grinding and fever) and previous detection of any parasite.

Patients who were found to have a parasite in the stool examination received parasite-directed treatments as indicated. Stool examination was repeated after treatment. If a parasite was again detected in the control stool examination, treatment was given until stool was cleared from the parasite. Response to the treatment was recorded.

A telephone interview was conducted to obtain information on the current status of symptoms in the participants. The disappearance of urticaria for more than 6 months was defined as remission, and remission of urticaria with negative stool examination after antiparasite treatment is considered PIRCSU. Patients with PIRCSU and non-PIRCSU were compared with each other according to the above-mentioned demographic, clinical, and laboratory characteristics.

A skin prick test was performed with common aeroallergens and common food allergens as indicated by history. Histamine (10 mg/ml of histamine phosphate) was used as the positive control, and 0.9% sterile saline was used as the negative control. The mean wheal diameter of the skin prick test ≥3 mm compared with the negative control was considered a positive result. Diagnosis of food allergy was made by oral food challenge tests with positivity of the skin prick test and/or specific IgE with the culprit food. Diagnosis of food additives was made with the disappearance of urticaria after 3 weeks of elimination diet and recurrence of urticaria with the addition of food additives in the diet.

An autologous serum skin test was performed as an intradermal skin test with 0.05 ml of sterile, fresh autologous serum and 0.9% sterile saline as the negative control. A skin prick test with histamine (10 mg/ml of histamine phosphate) was used as the positive control. The test was evaluated 30 min after injection, and it was considered a positive result if a wheal diameter of ≥1.5 mm was obtained compared with that of the saline solution [13].

*Statistical Analyses*

Data were analyzed using SPSS statistical software version 18.0 (SPSS Inc., Chicago, Ill., USA). The proportions in different groups were compared with the Pearson $\chi^2$ or Fisher's exact test where ap-

**Table 1.** Comparison of clinical and laboratory characteristics between patients with PIRCSU and non-PIRCSU

| Characteristics | PIRCSU (n = 10) | Non-PIRCSU (n = 201) | p |
|---|---|---|---|
| Girls | 4 (40) | 96 (47.8) | 0.631 |
| Age at admission, years | 7.4 [3.9–12.7] | 10.4 [6.9–13.2] | 0.188 |
| Age at symptom onset, years | 6.9 [3.4–11] | 9.2 [5–11.9] | 0.226 |
| Symptom duration, years | 0.5 [0.2–1] | 1 [0.3–2.5] | 0.112 |
| UAS7 at admission | 31.5 [22.8–42] | 28 [21–42] | 0.480 |
| Angioedema, % | 30 | 52.5 | 0.165 |
| Concomitant allergic disease, % | 20 | 16.9 | 0.800 |
| Concomitant symptoms, % | | | |
| Nausea/vomiting | 20 | 4 | 0.028 |
| Abdominal pain | 40 | 8 | 0.001 |
| Gastrointestinal symptoms | 40 | 11.2 | 0.010 |
| Laboratory findings | | | |
| Leukocyte count, n/mm$^3$ | 5,325 [7,905–9,525] | 7,840 [6,530–9,500] | 0.560 |
| Thrombocyte count, n/mm$^3$ | 253,000 [276,000–326,000] | 289,000 [250,250–352,750] | 0.708 |
| Peripheral eosinophil percentage | 2.3 [1.3–3.5] | 1.5 [0.8–2.6] | 0.180 |
| Total IgE, kU/l | 26.1 [12–169] | 66.8 [30.6–171] | 0.120 |
| ESR, mm/h | 8.5 [3.5–14.5] | 2 [0–7] | 0.011 |
| Autoantibody positivity, n | 4/7 (57.1) | 57/192 (29.7) | 0.122 |
| Autologous serum skin testing positivity, n | 1/3 (33.3) | 42/123 (34.1) | 0.977 |
| Skin prick test positivity, n | 1/6 (16.7) | 50/178 (28.1) | 0.539 |

Results are expressed as n (%) or median [interquartile range]. UAS7 = The sum of the daily urticaria activity score of 7 consecutive days.

propriate. All numeric variables were compared with Mann-Whitney U or Kruskal-Wallis tests where appropriate, and the results were given as median and interquartile ranges. The risk factors related to PIRCSU were determined by univariate and multivariate logistic regression analyses, and the results were given as odds ratio (OR) with a relevant 95% confidence interval (CI). A p value of less than 0.05 was considered statistically significant.

## Results

A total of 211 patients (187 chronic persistent urticaria and 24 chronic recurrent urticaria) were analyzed, and a parasite was detected in 21 (10%; 2 patients were in the retrospective arm and 19 in the prospective arm). The most common parasite was *Blastocystis hominis* in 12 samples, followed by *Giardia intestinalis* (n = 5), *Dientamoeba fragilis* (n = 3), *Enterobius vermicularis* (n = 3), and *Entamoeba* spp. (n = 1). All these patients had received antiparasitic medication as indicated. After the antiparasitic treatment for 10 days, stool examination became normal in all patients. Among the patients who had been given antiparasitic treatment, urticaria continued in 5, reduced in 6, and disappeared in 10 patients. In the follow-up, urticaria did not recur in these 10 patients, and they were considered cases of PIRCSU (4.7%). All patients with PIRCSU were in the prospective arm. The causative parasites were detected as *B. hominis* (n = 5), *G. intestinalis* (n = 4), and *D. fragilis* (n = 1).

Among the patients with non-PIRCSU, the etiology was identified in 8 patients (4%) as food allergy (n = 2), hypersensitivity to food additives (n = 3), pollen sensitization (n = 2), and Hashimoto thyroiditis (n = 1).

Comparison of the clinical and laboratory characteristics of patients with PIRCSU and those without is shown in table 1. Age at admission was slightly lower in patients with PIRCSU than in those without [7.4 years (3.9–12.7) vs. 10.4 (6.9–13.2), p = 0.118]. Duration of urticaria was shorter in patients with PIRCSU than in those without [0.5 years (0.2–1) vs. 1 (0.3–2.5) p = 0.112]. No differences were found among UAS7, angioedema or concomitant allergic diseases between the two groups. However, the prevalence of gastrointestinal symptoms was significantly higher in patients with PIRCSU than in those without (40 vs. 11.2%; p = 0.010). The most frequent gastrointestinal complaint was abdominal pain and nausea/vomiting (40 vs. 8%, p = 0.001, and 20 vs. 4%, p = 0.028,

**Table 2.** Univariate and multivariate factor analysis for PIRCSU

| | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | p | OR | 95% CI | p |
| Gender | 0.729 | 0.200–2.662 | 0.633 | | | |
| Age at admission | 0.893 | 0.770–1.035 | 0.133 | | | |
| Age at symptom onset | 0.910 | 0.785–1.056 | 0.215 | | | |
| Symptom duration | 0.706 | 0.404–1.233 | 0.221 | | | |
| UAS7 | 1.026 | 0.957–1.099 | 0.475 | | | |
| Angioedema | 0.388 | 0.097–1.542 | 0.179 | | | |
| Nausea/vomiting | 6.000 | 1.003–35.908 | 0.050 | | | |
| Abdominal pain | 7.667 | 1.852–31.738 | 0.005 | 6.600 | 1.352–32.226 | 0.020 |
| Allergic disease | 1.228 | 0.350–6.038 | 0.801 | | | |
| Eosinophilia | 1.095 | 0.807–1.486 | 0.559 | | | |
| Total IgE | 0.999 | 0.994–1.005 | 0.787 | | | |
| ESR | 1.062 | 0.988–1.140 | 0.101 | | | |
| CRP | 2.468 | 0.916–6.645 | 0.074 | | | |
| ASST | 0.964 | 0.085–10.945 | 0.977 | | | |
| Skin prick test positivity | 0.512 | 0.058–4.492 | 0.546 | | | |

UAS7 = The sum of the daily urticaria activity score of 7 consecutive days; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; ASST = autologous serum skin testing positivity.

respectively]. In laboratory investigations, although ESRs were within the normal limit in most patients, they significantly increased in patients with PIRCSU compared to those without [8.5 mm/h (3.5–14.5) vs. 2 (0–7), p = 0.011)].

According to the multivariate logistic regression analysis (table 2), abdominal pain was found to be a significant risk factor that increased the probability of PIRCSU (OR = 6.600, 95% CI = 1.352–32.226, p = 0.020).

## Discussion

In this study, we found a 4.7% prevalence of PIRCSU in childhood in a large cohort. A high prevalence of gastrointestinal symptoms was observed in these patients. Moreover, the inclusion of abdominal pain in the clinical history was found to be a significant risk factor for PIRCSU.

Several studies proposed parasites as etiologic factors of CSU in the pediatric age group. The prevalence of parasites in the stool examination, regardless of the treatment response, was reported as 2.4% by Kauppinen et al. [5], 2.5% by Du Toit [14], 2.7% by Sahiner et al. [9], 3.7% by Volonakis et al. [6], and 5.3% by Jirapongsananuruk et al. [8]. Similarly, in a systematic review of the underlying causes of chronic urticaria in childhood, 6 studies were assessed, and the prevalence of parasites was found to be 3.5% [15]. However, the type of parasites or the effects of parasitic infection treatment on CSU were established only in a few small studies with an improvement rate of urticaria of 0–2% after antiparasitic medication [8, 9]. In our study, the prevalence of parasites detected in stool in children with CSU was 10% and relevance with CSU was 4.7%. This ratio appears to be slightly higher than those in other studies. The prevalence of parasites may vary according to the geographic area and socioeconomic status or environmental sanitation conditions of a country. In 2 retrospective studies from our country, the prevalence of intestinal parasites in the general population was reported as 4 [16] and 5% [17], which are lower than that of our cohort. Previous studies showed that the prevalence of intestinal parasites in patients with allergic skin disorders including chronic urticaria was significantly higher than in healthy controls [18, 19]. This reason may explain the slightly higher prevalence of parasites in our cohort.

In the present study, most of the causative parasites were protozoa, and the most common were *B. hominis* and *G. intestinalis*. In a study comparing the prevalence of intestinal parasites among patients with allergic skin disorders such as chronic urticaria and healthy controls, the prevalence of *Giardia* spp. and *B. hominis* was significantly higher in patients than in the controls [18]. Similarly, these parasites were considered the most com-

mon parasites in CSU according to the results of the systematic review [11]. In our country, *B. hominis, G. intestinalis,* and *E. vermicularis* are prevalent during childhood [20].

The exact pathogenesis of parasites related to urticaria is still unclear. The proposed mechanism is the activation of skin mast cells leading to the release of histamine and other vasoactive mediators. This mechanism can be triggered by an interaction between a parasite-specific IgE and its high-affinity IgE receptors. It can also be triggered by the production of Th2 cytokines during parasitic infection, increased skin eosinophils, or activation of coagulation and the complement system [11]. Distinct mechanisms may be responsible for the diverse parasites. For example, the production of specific IgE against parasites has been shown for *Toxocara* [21] or *Anisakis simplex* [22]. Although some studies or case reports indicated high total IgE and/or parasite-specific IgE values in chronic urticaria patients infected with *Giardia* [23] or *B. hominis* [24], other studies reported no difference in total IgE levels between patients who had the same parasites and healthy controls [18]. In our cohort, total IgE levels did not differ from those of patients with PIRCSU or non-PIRCU.

Several pathophysiologic mechanisms of the induction of CSU by *B. hominis* have been proposed. For example, IgE-mediated allergic responses to parasite antigens were suggested in a few studies [25]. The significant oxidative stress caused by this protozoon was suggested as a predisposing factor of CSU [26]. Moreover, different subtypes were proposed to have distinct pathogenicity [27]. For example, the ameboid form was suggested to adhere strongly to gut epithelia and cause urticaria by an immune response to the antigens of the parasite surface [28]. Different factors, such as the parasite itself or the host, may play a role.

In this study, ESRs were within the normal limit in most of our participants, but patients with PIRCSU had significantly higher levels of ESR than those without. The ESR is a nonspecific measure of both acute and chronic inflammation. Chronic bacterial, viral or parasitic infections may induce an inflammatory response and increase ESR. Some studies showed high levels of ESR in a small proportion of patients with CSU. CSU itself is a chronic inflammatory condition of the skin that causes a slightly increased ESR.

Gastrointestinal symptoms, including nausea, vomiting, and abdominal pain, were frequent in the parasite-related group, but some of the patients with PIRCSU did not have any gastrointestinal symptoms. Intestinal parasites usually cause poorly localized abdominal pain and, although less frequently, diarrhea, nausea, vomiting, cramps, abdominal distention, flatulence, mucus or blood in stool, fatigue, and weight loss in patients while being sometimes asymptomatic [29]. Our results suggest that urticaria may be the only symptom of intestinal parasites.

Although some possible factors, such as concurrent gastrointestinal symptoms, previous parasitic infection, traveling abroad and unexplained peripheral eosinophilia may increase the risk of parasitic infection in a patient with CSU [11], specific risk factors associated with a parasite triggering CSU have not been established in publications to date. In the present study, we found for the first time that having abdominal pain increased the risk of PIRCSU. Recent guidelines recommend inquiring about gastric or intestinal complaints in patients with CSU [1] as supported by our data.

In conclusion, parasites may cause CSU, and remission may only be possible with the treatment of parasitic infection. The presence of abdominal pain may point to parasitic infection in patients with CSU. Therefore, we suggest that parasites should be investigated routinely as a causative factor of childhood CSU not only in tropical countries, but also in nontropical countries, especially if the patient has gastrointestinal symptoms.

## Statement of Ethics

The local ethics committee gave approval of this study.

## Disclosure Statement

All authors declare that there is no conflict of interest and no funding involved.

## References


1 Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica G, Church M, Ensina L, Giménez-Arnau A, Godse K: The EAACI/GA2LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. Allergy 2014;69:868–887.

2 Kaplan AP: Chronic urticaria and angioedema. N Engl J Med 2002;346:175–179.

3 Maurer M, Weller K, Bindslev-Jensen C, Giménez-Arnau A, Bousquet P, Bousquet J, Canonica G, Church M, Godse K, Grattan C: Unmet clinical needs in chronic spontaneous urticaria. A GA2LEN task force report. Allergy 2011;66:317–330.

4 Harris A, Twarog F, Geha R: Chronic urticaria in childhood: natural course and etiology. Ann Allergy 1983;51:161–165.
5 Kauppinen K, Juntunen K, Lanki H: Urticaria in children. Allergy 1984;39:469–472.
6 Volonakis M, Katsarou-Katsari A, Stratigos J: Etiologic factors in childhood chronic urticaria. Ann Allergy 1992;69:61–65.
7 Brunetti L, Francavilla R, Miniello VL, Platzer MH, Rizzi D, Lospalluti ML, Poulsen LK, Armenio L, Skov PS: High prevalence of autoimmune urticaria in children with chronic urticaria. J Allergy Clin Immunol 2004;114:922–927.
8 Jirapongsananuruk O, Pongpreuksa S, Sangacharoenkit P, Visitsunthorn N, Vichyanond P: Identification of the etiologies of chronic urticaria in children: a prospective study of 94 patients. Pediatr Allergy Immunol 2010;21:508–514.
9 Sahiner UM, Civelek E, Tuncer A, Yavuz ST, Karabulut E, Sackesen C, Sekerel BE: Chronic urticaria: etiology and natural course in children. Int Arch Allergy Immunol 2011;156:224–230.
10 Sackesen C, Sekerel BE, Orhan F, Kocabas CN, Tuncer A, Adalioglu G: The etiology of different forms of urticaria in childhood. Pediatr Dermatol 2004;21:102–108.
11 Kolkhir P, Balakirski G, Merk H, Olisova O, Maurer M: Chronic spontaneous urticaria and internal parasites – a systematic review. Allergy 2016;71:308–322.
12 Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, Zuberbier T, et al; World Health Organization, GA2LEN, AllerGen: Allergic rhinitis and its impact on asthma (ARIA) 2008 update (in collaboration with the world health organization, GA2LEN and AllerGen). Allergy 2008;63(suppl 86):8–160.
13 Konstantinou G, Asero R, Maurer M, Sabroe R, Schmid-Grendelmeier P, Grattan C: EAACI/GA2LEN task force consensus report: the autologous serum skin test in urticaria. Allergy 2009;64:1256–1268.
14 Du Toit G, Prescott R, Lawrence P, Johar A, Brown G, Weinberg EG, Motala C, Potter PC: Autoantibodies to the high-affinity IgE receptor in children with chronic urticaria. Ann Allergy Asthma Immunol 2006;96:341–344.
15 Caffarelli C, Cuomo B, Cardinale F, Barberi S, Dascola CP, Agostinis F, Franceschini F, Bernardini R: Aetiological factors associated with chronic urticaria in children: a systematic review. Acta Derm Venereol 2013;93:268–272.
16 Köksal F, Başlanti I, Samasti M: A retrospective evaluation of the prevalence of intestinal parasites in Istanbul, Turkey. Turkiye Parazitol Derg 2010;34:166–171.
17 Kırkoyun UH, Akgül O, Purisa S, Oner Y: Twenty-five years of intestinal parasite prevalence in Istanbul University, Istanbul Faculty of Medicine: a retrospective study (in Turkish). Turkiye Parazitol Derg 2014;38:97–101.
18 Giacometti A, Cirioni O, Antonicelli L, D'Amato G, Silvestri C, Del Prete MS, Scalise G: Prevalence of intestinal parasites among individuals with allergic skin diseases. J Parasitol 2003;89:490–492.
19 Zuel-Fakkar N, Abdel Hameed D, Hassanin O: Study of *Blastocystis hominis* isolates in urticaria: a case-control study. Clin Exp Dermatol 2011;36:908–910.
20 Yapici F, Sönmez TG, Arisoy ES: The distribution of intestinal parasites and their causative factors in children (in Turkish). Turkiye Parazitol Derg 2007;32:346–350.
21 Magnaval J-F, Faufingue J-H, Morassin B, Fabre R: Eosinophil cationic protein, specific IgE and IgG4 in human toxocariasis. J Helminthol 2006;80:417–423.
22 Gracia-Bara MT, Matheu V, Zubeldia JM, Rubio M, Ordoqui E, López-Sáez MP, Sierra Z, Tornero P, Baeza ML: *Anisakis simplex*-sensitized patients: should fish be excluded from their diet? Ann Allergy Asthma Immunol 2001;86:679–685.
23 Mahmoud M, Salem A, Rifaat M: Human giardiasis as an etiology of skin allergy: the role of adhesion molecules and interleukin-6. J Egyptian Soc Parasitol 2004;34:723–737.
24 Pasqui A, Savini E, Saletti M, Guzzo C, Puccetti L, Auteri A: Chronic urticaria and *Blastocystis hominis* infection. A case report. Eur Rev Med Pharmacol Sci 2004;8:117–120.
25 Hameed DMA, Hassanin OM, Zuel-Fakkar NM: Association of *Blastocystis hominis* genetic subtypes with urticaria. Parasitol Res 2011;108:553–560.
26 Chandramathi S, Suresh K, Shuba S, Mahmood A, Kuppusamy U: High levels of oxidative stress in rats infected with *Blastocystis hominis*. Parasitology 2010;137:605–611.
27 Clark CG: Extensive genetic diversity in *Blastocystis hominis*. Mol Biochem Parasitol 1997;87:79–83.
28 Valsecchi R, Leghissa P, Greco V: Cutaneous lesions in *Blastocystis hominis* infection. Acta Derm Venereol 2004;84:322–323.
29 Noyer CM, Brandt LJ: Parasitic infections of the gastrointestinal tract. Curr Gastroenterol Rep 1999;1:282–291.