



The Relationship between Chronic Spontaneous Urticaria and Intestinal Infestation in Iraqi Patient

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Abstract

Background

Chronic urticaria is classified as urticaria which is triggered by specific stimulants or developed without stimulants which is named as chronic spontaneous urticaria. The cause of chronic spontaneous urticaria cannot be defined in about 90% of the cases. This study aimed to evaluate the association between chronic spontaneous urticaria and intestinal infestation in Iraqi patient.

Patients & Methods:

A cross sectional study was done in the department of dermatology and venereology at Salah Al-Deen General Hospital with some cases at private clinic. The study was carried out during 1st October 2021 to 30th April 2022. Target population were patients with chronic spontaneous urticarial. Sample of 21 patients with chronic spontaneous urticaria was studied. The data collected through questionnaire by direct interview and laboratory investigation of general stool examination, eosinophil cell percentage and Erythrocyte sedimentation rate.

Results:

About (76.19%) of the patient aged ≤ 18 years, and (23.81%) aged > 18 years. Male patient were (38 %) and female patient were (62%), Concomitant angioedema was found among (57.1 %) of the cases, and (42.9%) had no angioedema. Intestinal infestation was found among (14.3%) of the cases of CSU, while (85.7%) had no parasitic infestation. Intestinal symptoms among those with intestinal infestation was significantly higher than those without infestation: Vomiting (66.7%), Nausea 2(66.7%), Diarrhea found among (33.3%), abdominal pain (66.7%) and bloating found among 1(33.3%) of those with Intestinal infestation. The mean Eosinophil percentage was significantly higher among those with intestinal infestation (2.57 ± 1.14), than those without infestation (1.37 ± 0.59). The mean ESR level was significantly higher among those with intestinal infestation among those with intestinal infestation (17.67 ± 8.14), than those without (8.32 ± 3.31). Giardia found among (33.3%) of the cases and found among (33.3%) in combination with E.Coli, Ecoli alone found among (33.3%).

Conclusions

There is relationship between intestinal infestation and CSU, therefore in any case of CSU the intestinal infestation should be rolled out and treatment should be prescribed if intestinal infestation proved.

Keywords: Chronic Urticaria & Intestinal Infestation in Iraqi Patient, Relationship between Urticaria and Intestinal Infestation

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Blastocystis has been found to be associated with symptoms such as abdominal pain, diarrhea, nausea, vomiting, bloating, anorexia and urticaria, as can be detected in people without any gastrointestinal complaints [10].

Patient and Method

Formal consent was taken from each patient after full explanation about the nature of the present study and an ethical approval was obtained from the Scientific Ethical Committee of Tikrit University-College of Medicine included in the study. Both groups informed about the study aims and informed about the results of their tests. A convenient ample of (21) patients CSU were selected from the out-patient in the department of dermatology and venereology of Salah Al-Deen General Hospital, as well as some cases from private clinic. And this study is a cross sectional study. The control group was 21 person without CSU selected from the dermatology outpatient. This study was carried out for a period of six months, from October 2021 to 30th April 2022. Data collected through: A- Direct interview with the patient using structured questionnaire:formed by the researcher and reviewed by supervisor, it consist of: demographic information. Disease related questions e.g : if any provoking agents, duration of the disease, family history of the disease, presence of angioedema, Gastrointestinal symptoms (nausea , vomiting, diarrhea , bloating abdominal pain). Laboratory investigation: general stool examination:One or more consecutive fresh stool samples done for all patients and control group. Blood test: Laboratory investigations included complete blood count, erythrocyte sedimentation rate (ESR). Inclusion criteria were the following; patient with CSU at any age were included in the study without known causes and having only urticarial plaques persistent more than six weeks. Exclusion criteria were the following; patients with known possible causes of chronic urticaria like; suspicious drug usage and signs of infection, patients with high stress.

Introduction:

Urticaria, is also called hives, is a most prevalent dermatologic disorder characterized by erythematous, edematous and itchy plaques that involve skin and mucous membranes&is divided into acute and chronic. Acute urticaria, thatpersist less than six weeks is mostly triggered by medications, foods, infections, stress, or insect venom [1,2]. Chronic urticaria (CU) is defined as the presence of recurrent urticaria, with or without angioedema, for a period of six weeks or longer. Chronic urticaria is classified as urticaria which is triggered by specific stimulants or developed without stimulants which is named as chronic spontaneous urticaria (CSU). The incidence of CSU is between 0.5% and 1.5% in the population. The cause of CSU cannot be defined in about 90% of the cases. Autoimmunity, food intolerance and infections such as intestinal parasitic infections (IPI) are suggested to be some of the causes of CSU [4]. In 1949, a case report about CSU had been published which IPI had been blamed as the cause of CSU. In this report *G. duodenalis*and urticaria of unknown origin had been detected together after which IPI was successfully treated by the specific parasitic therapy [8]. Since then, the relation between CSU and IPI have been being studied [5]. Intestinal parasitic infections continue to be important as being a common health problem especially in developing countries. Low socioeconomic status, poor hygiene and crowded living conditions increase the risk of parasitic infections. It is estimated that IPI affects more than one billion people worldwide. Thehighly prevalent intestinal helminths have been reported as *Ascaris lumbricoides*, *Trichuris trichiura*, *Necator americanus*, *Ancylostoma duodenale* and *Strongyloidesstercoralis*, intestinal protozoa as *Blastocystis sp.*, *G. duodenalis*, *Dientamoeba fragilis* and *Entamoeba spp.* [5,9]. Recently, *Blastocystis* is the most common intestinal protozoon found in human stool specimens but its clinical importance and pathogenicity is still controversial.



Results

Twenty one patient with CSU was analyzed, the age distribution show that 16(76.19%) were aged ≤ 18 years, and 5(23.81%) aged > 18 years, compared with 15(71.4%), and 6(28.6%) of the controls respectively, this relation was statistically not significant P value > 0.05 , as shown in figure1.

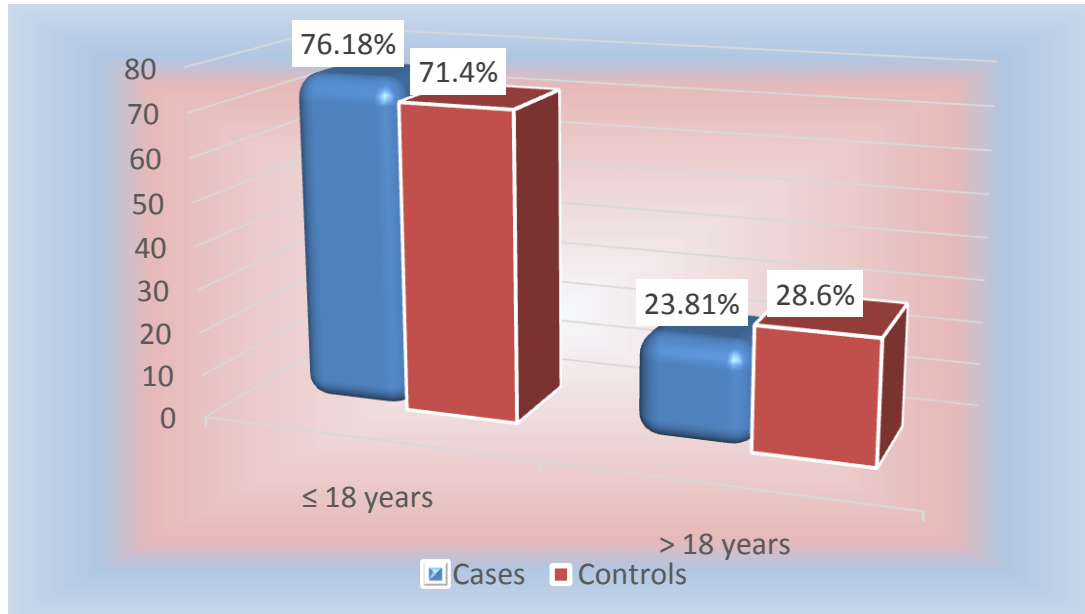


Figure 1. The Age Distribution Of the Cases Of CSU and Controls

The cases distribution according to the sex show that male patient were 8(38 %) and female patient were 13(62%), as shown in figure 2.

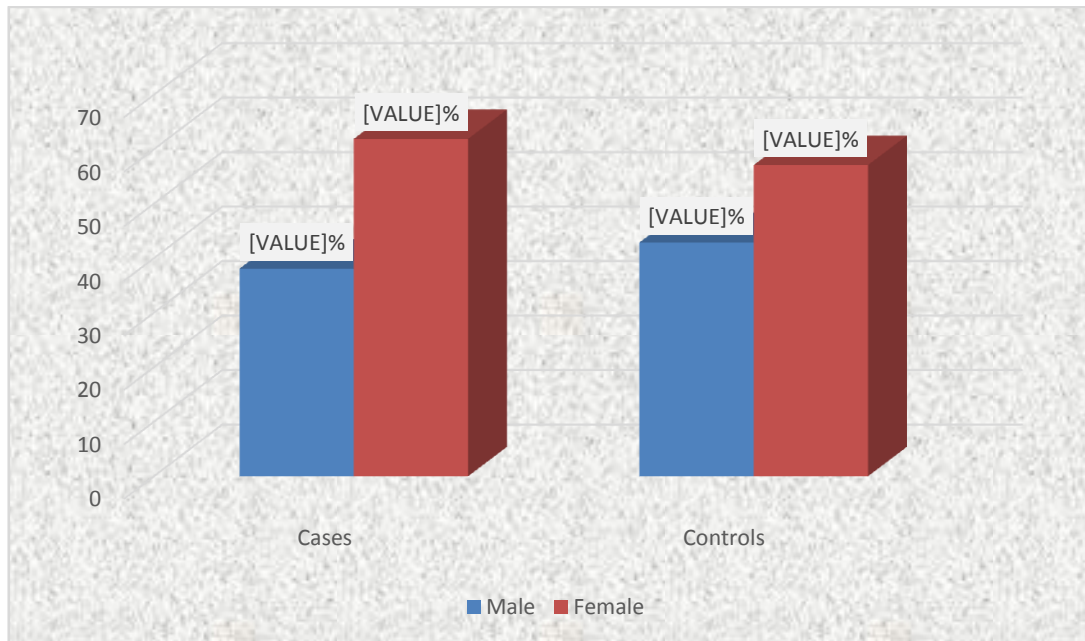


Figure 2. The Sex Distribution Of Cases Of CSU and Controls

Concomitant angioedema was found among 12(57.1 %) of the cases, and 9(42.9%) had no angioedema, as shown in figure 3

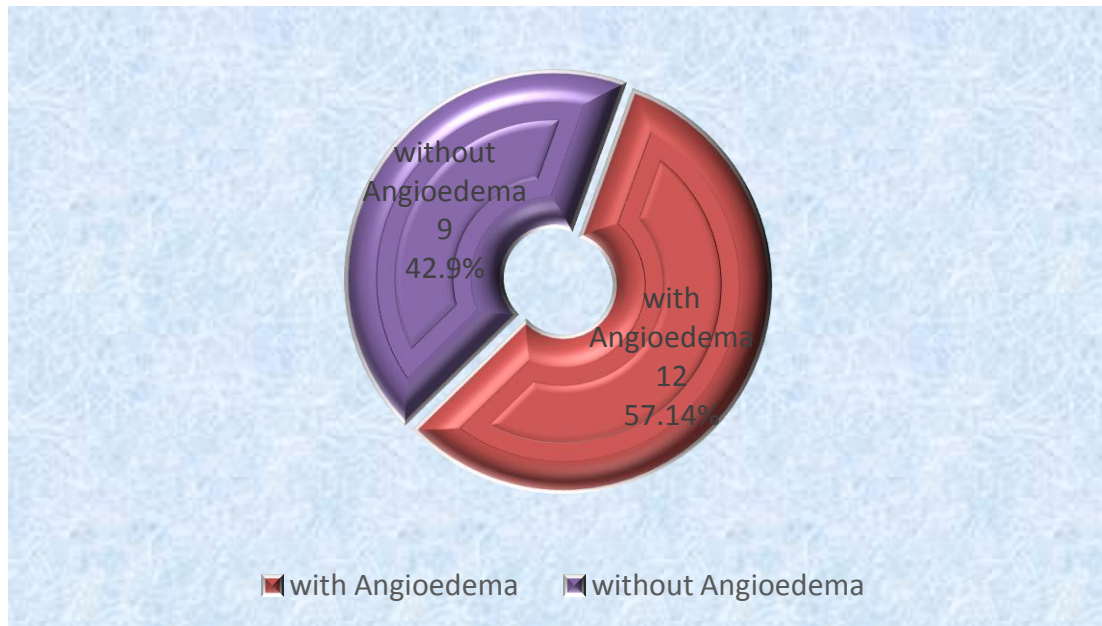


Figure 3. The Concomitant Angioedema Among CSU Cases

Intestinal infestation was found among 3(14.3%) of the cases of CSU, while 18(85.7%) had no parasitic infestation, in comparison to 2(9.5%), 19(90.5%) of the controls respectively, this relation was statistically not significant ($\chi^2= 0.23$, $df=1$, P value > 0.05) as shown in figure 4.

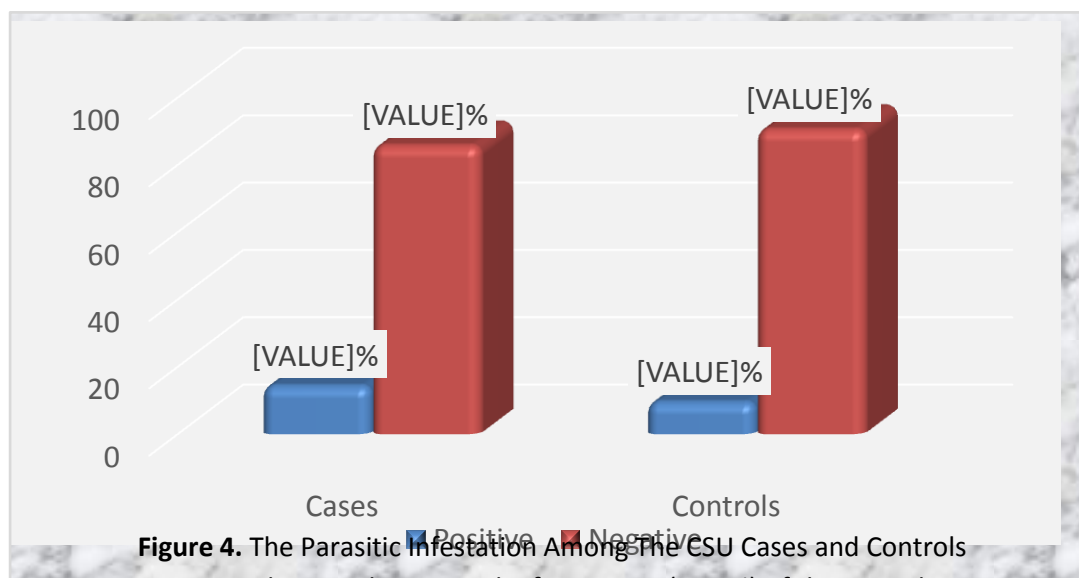


Figure 4. The Parasitic Infestation Among The CSU Cases and Controls

Among cases those with intestinal infestation; 2(66.7%) of them aged ≤ 18 years, and 1(33.3%) aged > 18 years, and those without intestinal infestation 14(77.8%) of them aged ≤ 18 years, and 4(22.2%) aged > 18 years, among controls those with intestinal infestation; 1(50%) of them aged ≤ 18 years, and 1(50%) aged > 18 years, and those without intestinal infestation 14(73.7%) of them aged ≤ 18 years, and 5(26.3%) aged > 18 years, this relation was not statistically significant, as shown in table 1.

Table 1. Distribution of Cases and controls According to Intestinal Infestation & Age

Age	Intestinal infestation among cases				Intestinal infestation among controls			
	Positive		Negative		Positive		Negative	
	Frequency	%	Frequency	%	Frequency	%	Frequency	%

≤18 years	2	66.7%	14	77.8%	1	50%	14	73.7%
> 18 years	1	33.3%	4	22.2%	1	50%	5	26.3%
Total	3	100 %	18	100 %	2	100%	19	100%

$\chi^2=0.8$, $df=3$, P value > 0.05 not significant

Among cases of CSU those with intestinal infestation 1(33.3%) of them had angioedema in comparison to 11(61.1%) of those without intestinal infestation, this relation was statistically not significant, as shown in table 2.

Table 2. Distribution of Cases According to Intestinal Infestation & Angioedema.

Angioedema	Intestinal infestation			
	Positive		Negative	
	Frequency	%	Frequency	%
Yes	1	33.30%	11	61.10%
No	2	66.70%	7	38.90%
Total	3	100.00%	18	100.00%

$\chi^2=0.81$, $df=1$, P value > 0.05 not significant

Vomiting found among 2(66.7%) of those with Intestinal infestation in comparison to 1(5.6%) of those without intestinal infestation, this relation was statistically significant. nausea found among 2(66.7%)of those with Intestinal infestation in comparison to 2(11.1%) of those without intestinal infestation, this relation was statistically significant. Diarrhea found among 1(33.3%)of those with Intestinal infestation in comparison to 0(0%) of those without intestinal infestation, this relation was statistically significant. abdominal pain found among 2(66.7%)of those with Intestinal infestation in comparison to 1(5.6%) of those without intestinal infestation, this relation was statistically significant. Bloating found among 1(33.3%) of those with Intestinal infestation in comparison to 1(6.5%) of those without intestinal infestation, this relation was statistically not significant. As shown in table 3.

Table3. Distribution of CSU According To Intestinal Infestation and GIT Symptoms.

Gastrointestinal symptoms	Intestinal infestation				P value
	Positive		Negative		
	Frequency	%	Frequency	%	
Vomiting	2	66.70%	1	5.60%	<0.05 S
Nausea	2	66.70%	2	11.10%	<0.05 S
Diarrhea	1	33.30%	0	0.00%	<0.05 S
Abdominal Pain	2	66.70%	1	5.60%	<0.05 S
Bloating	1	33.30%	1	5.60%	> 0.05 NS

The mean Leukocyte count among those with intestinal infestation was (7.27±1.56n/mm³), in comparison of (8.15±1.09 n/mm³) among those without infestation, and healthy controls(5.89 ± 2.3 n/mm³), this relation was statistically significant. The mean



Eosinophil percentage among those with intestinal infestation was (2.57±1.14), in comparison of (1.37±0.59) among those without infestation, and healthy controls (1.1 ± 0.9), this relation was statistically significant. The mean ESR level among those with intestinal infestation was (17.67± 8.14), in comparison of (8.32 ± 3.31) among those without infestation, and (5.9 ± 2.5) among healthy controls, this relation was statistically significant.as shown in table 4.

Table 4. Distribution of CSU According To Intestinal Infestation and healthy controls And Laboratory Results.

Laboratory results	Intestinal infestation				Healthy control		P value
	Positive		Negative		Mean	SD	
	Mean	SD	Mean	SD			
Leukocyte count, n/mm³	7.27	1.56	8.15	1.09	5.89	2.3	< 0.05 NS
Eosinophil percentage	2.57	1.14	1.37	0.59	1.1	0.9	< 0.05 S
ESR mm/h	17.67	8.14	8.32	3.31	5.9	2.5	< 0.05 S

Giardia found among 1(4.76%) of the cases of CSU and found among 1(4.7%) in combination with *E.Coli*, *Ecoli* alone found among 1(4.7%), in comparison to control group *Giardia* found among 1(4.76%) of the control group and found among 1(4.7%) in combination with *E.Coli*, as shown in table 5.

Table 5. The Distribution of Cases of CSU and Controls According To Intestinal Infestation And General Stool Examination Results

general stool examination results	Cases		Control	
	Frequency	%	Frequency	%
Negative	18	85.71	19	90.48
Giardia lamblia	1	4.76	1	4.76
Giardia lamblia+ E coli	1	4.76	1	4.76
E Coli	1	4.76	0	0.00
Total	21	100.00	21	100.00

$\chi^2=1.01$, $df=3$, P value > 0.05 not significant

found in a study in Korea by Kim BR et al 2018 that the highest prevalence rates at 0–9 years (50%). CSU as itself limiting disease it may persist into adulthood in a sizable population, adding to other age-related comorbidities. [12] In this study female patient affected more than male gender (62%), (38 %) respectively. This

Discussion

The common age group was ≤ 18 years (76.19%) while those aged > 18 years was (23.81%). This goes with what found Weller K et al 2022 in Germany, [68] that CSU has a higher incidence in younger patients than oldest age group (81%) under 18 years, and with what



(34%), inappetence (45%), diarrhea (23%), weight loss (29%), the alternation diarrhea-constipation (12%), nausea (17%).^[17]

The mean Eosinophil percentage was significantly higher among those with intestinal infestation (2.57 ± 1.14), than those without infestation (1.37 ± 0.59). This goes with Vezir S et al^[72] 2019 found that the median value of eosinophil percentages in peripheral blood smears were 2% (0.7-3.6%) in the pediatric patient group^[15]. The mean ESR level was significantly higher among those with intestinal infestation among those with intestinal infestation (17.67 ± 8.14), than those without (8.32 ± 3.31). some studies like Erdem Y et al found that High ESR found among 24.1% of the patients,^[18] while Akarsu et al. reported high ESR in 50% of patients.^[19]

Giardia found among (33.3%) of the cases and found among (33.3%) in combination with E.Coli, Ecoli alone found among (33.3%), the Giardia lamblia (also called G. intestinalis or G. duodenalis), this goes with Siddiqui MH et al 2018 who found that (20%) of the patient with CSU had Giardia Lambilia.^[16] Vezir S et al 2019 found that Blastocystis sp. was the most prevalent parasite Blastocystis sp. (17.1%), G.lambilia (1.3%) and Entamoeba coli (1.3%).^[15] In a prospective study held in Thailand, in 92 pediatric patients with CSU, parasitic infections were diagnosed in 5.4% of the patients and Blastocystis sp., D. fragilis and G. duodenalis were detected^[20].

In a study held in Turkey, parasitic infections had been detected in 38.8% of the CSU patients and 11.1% of control group of which the difference between the groups was statistically significant.^[21]

In this study, Blastocystis sp. and G. duodenalis were the most common detected parasites. Some studies reported

goes with Kim BR et al 2018 who found CSU higher in women than men (1:1.39 and 1:1.34, respectively)^[12].

Concomitant angioedema was found among (57.1 %) of the patients, this goes with . Zhong H, et al 2014 found that (38%) of patient with CSU had angioedema^[13]. Concomitant angioedema non- significantly found more among those without intestinal infestation (61.1%) than those with intestinal infestation (33.3%). This goes with Yilmaz EA et al 2016 who found non- significant differences were found among patient with and without angioedema (52.6%) , (30%) respectively .^[14] Intestinal infestation was found among (14.3%) of the cases of CSU, this goes with Yilmaz EA et al 2016 who found parasites infestation detected among (10%) of the children affected by CSU,^[14] and found intestinal infestation among (10%) .

Intestinal infestation found among (66.7%) of those aged ≤ 18 years, and (33.3%) of those aged > 18 years. This goes with Vezir S et al found that intestinal parasites were detected in 22.3% among children and in 18.4% of the adults with CSU^[15]. In this study we found that intestinal symptoms among those with intestinal infestation was significantly higher than those without infestation: vomiting (66.7%), nausea (66.7%), diarrhea found among (33.3%) , abdominal pain (66.7%) and bloating (33.3%). This goes with Siddiqui MH et al 2018 found that (57%) denied any gastrointestinal symptoms during the entire course of the urticarial, (43%) having varying levels of diarrhoea, abdominal discomfort, flatulence, anorexia and foul smelling bulky stools.^[16] Another study by Nedelcuță M et al in Romania 2019 found that children with skin disorders and giardiasis had the following digestive symptoms : pain

of intestinal mucosa, endocrine, metabolic mechanisms, and neurological transmission^[33]. Pundir P et al 2019 found that the differences between the patients affected by E.coli and had CSU and the healthy control group were mainly in the membrane transport and metabolic pathway. According to the pathogenesis of CSU, it was assumed metabolic products corresponding to abnormal gut microbiota might enter the blood as quorum-sensing molecules (QSMs) through the interaction with Mas-related G-protein coupled receptor member X2 (MRGPRX2) to activate mast cells and promote the occurrence of urticarial^[34].

Conclusions

There is relationship between intestinal infestation and CSU, therefore in any case of CSU the intestinal infestation should be rolled out and treatment should be prescribed if intestinal infestation proved.

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that urticaria may disappear in the patients with parasitic infection after specific treatment for the parasite^[22]. In a study, 16 CSU patients with IPI were treated with anti-parasitic therapy and 43.7% of them had regression in urticaria symptoms^[23]. Vezir S et al reported caseation of symptoms of CSU in 57.1% of the pediatric group and 60% of the adult group.^[15]

The difference between type of the prevalence and type of parasites among these studies may be related to the population differences or differences in times of stool examination and use of PCR in detection of some microorganisms. prevalence data of *Blastocystis* sp., may depend on detection methods, especially direct-light microscopy (DLM) of fecal smears versus polymerase chain reaction (PCR) assays.^[24]

The results of various published reports reveal a clear relationship between Giardial infection and allergy. Khan et al 2010 from Pakistan^[25]. and de Andrade CM et al 2019 from Brazil^[26]. ,Nedelcuță M et al 2019 in Romania^[27] and Brandt Oet al 2022 in south Africa^[28] *Giardia lamblia* elicits both a cellular and humoral immune response, inducing cytokines such as tumour necrosis factor (TNF), interferon (IFN)- γ , and interleukin (IL)-17,^[29] as well as nitric oxide (NO), production of anti giardial IgA antibodies, and intestinal mastocytosis.^[30] not find the significant differences in *E. coli* and *Salmonella* between CSU patients and controls^[31]. Lu T et al 2019 found that the microbial composition was significantly different between CU patients and controls; they pointed out that *Escherichia coli* is a pathogenic strain in CU^[32].

Previous studies reported that gut microbiota could affect human immune response through structural modification



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