RESEARCH ARTICLE

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Investigation of Urinary Findings in Urticaria Patients

¹Department of Dermatology and Venereology, Near East University Faculty of Medicine, Nicosia, North Cyprus

Abstract

BACKGROUND/AIMS: Urticaria is a common disease in the population which presents with wheals, angioedema or both. There are many stimuli in the etiopathogenesis of urticaria and infections are considered among the first triggers.

MATERIALS AND METHODS: The urinalysis results of patients were reported and the relationship between these findings and both laboratory and clinical spectrum was presented.

RESULTS: In the urinalysis results of the patients, bacteriuria was found in 100 (42.6%), pyuria in 69 (29.4%) and pyuria and bacteriuria in 60 (25.5%). Ninety-one (91%) of those patients with bacteriuria (p=0.000), 65 (94%) of those patients with pyuria (p=0.000), and 59 (98.3%) of those patients with bacteriuria and pyuria were female (p=0.000). Also, the leukocyte values of those patients with bacteriuria were significantly higher than those without bacteriuria (p=0.041). For the group of patients with pyuria, the leukocyte and neutrophil values were significantly higher than for those without pyuria (p=0.006; p=0.036, respectively). Lastly, the leukocyte values of those patients with bacteriuria and pyuria were significantly higher than those without bacteriuria and pyuria (p=0.013).

CONCLUSION: In female patients with a diagnosis of urticaria, the rates of bacteriuria and/or pyuria were found to be significantly high, and there was also a statistically significant high mean leukocyte value in those patients with bacteriuria and/or pyuria, suggesting that inflammation in the urinary tract may be an important stimulus in its etiology.

Keywords: Urticaria, bacteriuria, pyuria, urinalysis, angioedema

INTRODUCTION

Urticaria is a common disease in the population, which presents with wheals, angioedema or both. Urticaria develops due to edema in the superficial dermis and suddenly appears clinically and then spontaneously disappears within the same day. Angioedema develops due to edema in the deep dermis, subcutaneous tissue or mucous membranes. 1 Coexistence with angioedema is observed in approximately half of the cases of urticaria.² If urticaria and/or angioedema attacks last less than 6 weeks, it is called acute urticaria, while if it lasts longer

than 6 weeks and there are at least two attacks per week, it is called chronic urticaria.³ Acute urticaria is observed in 20% of the population and chronic urticaria is observed in 5% of the population.4 1-30% of acute urticaria patients can progress to chronic urticaria. According to the mechanism of urticaria formation, it is divided into two groups, as either spontaneous urticaria or inducible urticaria.1

Acute urticaria etiology includes 40% acute infections and 10% drug intolerance.2 Cystitis and tonsillitis are the most common bacterial infections associated with acute urticarial. Also various viral and parasitic

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ORCID IDs of the authors: D.M. 0000-0001-6615-1483; S.M. 0000-0002-8774-1965; N.S. 0000-0003-2468-6118.



Address for Correspondence: Didem Mullaaziz E-mail: didem mullaaziz@vahoo.com **ORCID ID:** orcid.org/0000-0001-6615-1483

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²Department of Mathematics, Near East University Faculty of Arts and Sciences, Nicosia, North Cyprus

agents have been associated with acute urticaria.⁵ There are many reports regarding the benefits of eliminating infectious processes.⁶ It has been reported that *Helicobacter pylori* infection of the gastrointestinal tract, bacterial infections of the nasopharynx (recurrent sinusitis and tonsillitis), dental sepsis, urinary tract infections, and cutaneous fungal infections are associated with chronic urticaria which needs be treated in these patients.⁷⁻⁹ In this study, we aimed to investigate the association between urinalysis, laboratory findings and the clinical spectrum of patients with acute and chronic urticaria.

MATERIALS AND METHODS

Retrospectively, all patients over the age of 18 with a diagnosis of urticaria who were followed up in our outpatient clinic between January, 2017 and January, 2020 were included in this study. Ethical approval was obtained from the Ethical Committee of the Near East University Hospital for the study (approval number: 2021/90-1326). Pregnant women, female patients who were in the menstrual period at the time of admission, and patients who described genital discharge were not included in this study. The patients were questioned regarding age, gender, duration of urticaria, presence of angioedema accompanying urticaria, systemic diseases, drug usage in the previous two weeks, a history of infection in the previous two weeks, a history of chronic infection, the presence of atopy, the presence of dermographism, and the presence of dysuria. Regarding laboratory findings, hemogram, high-sensitivity C-reactive protein (hs-CRP), total immunoglobulin E (IgE) levels, and urinalysis results were obtained and the urine culture results of those patients with bacteriuria were also obtained. Leukocyte, neutrophil, lymphocyte, eosinophil, neutrophil lymphocyte ratio values and biochemically hs-CRP and total IgE levels in the hemogram were reported numerically. The presence of pyuria was accepted as a polymorphonuclear leukocyte count >10 white blood cells/high power field (WBC/HPF) in the urine. Leukocyte esterase positivity and bacteriuria in urine were evaluated as positive or negative. The urine culture results of those patients with bacteriuria were obtained. Cases with significant levels of squamous epithelial cells (≥15/HPF) in urine samples were not included in this study because they were considered to be contaminated.

Statistical Analysis

The data analysis was carried out using SPSS version 23.0 (IBM SPSS Corp.; Armonk, NY, USA). Independent samples t-test was used to compare the two groups. Also, frequencies and percentages were obtained for the qualitative variables and the chi-square test was used to determine statistical significance for categorical variables. In this study, p-values ≤0.05 were considered statistically significant.

RESULTS

Our study included a total of 235 urticaria patients, where 157 (66.8%) were female and 78 (33.2%) were male. The patients were aged between 18 and 74 years and their mean age was 31.6 ± 12.8 years [mean \pm standard deviation (SD)]. The duration of the disease was 1 day to 20 years. The patients were further categorized as either acute or chronic urticarial. One hundred and fifty-nine (67.7%) of the patients (1.13 ±0.09 weeks) (mean \pm SD) were diagnosed as acute urticaria, and 76 (32.3%) (85.02 ±18.07 weeks) (mean \pm SD) as chronic urticaria. Isolated urticaria was detected in 48 (20.4%) of the patients included

in this study, and urticaria and angioedema were detected in 187 (79.6%) of them. 58 (24.7%) of the patients had atopy history and 27 (11.5%) had dermographism. 23 of the patients (9.8%) had a history of accompanying systemic disease, 16 of the patients (6.8%) had thyroiditis and 7 (3%) had anemia.

Infection history in the previous two weeks was determined in 54 (23%) of the patients included in this study. A significant relationship was found between the history of infection in the previous two weeks and the acute urticaria and chronic urticaria patient groups ($\chi^2=12.031$, p=0.001). The distribution of infection was dental infection in 1 patient, pilonidal sinus infection in 1 patient, and upper respiratory tract infection in 52 patients. 47 (87%) of the patients with a positive history of infection were diagnosed with acute urticaria, and 7 (13%) of them were diagnosed with chronic urticaria. In addition, 66 patients (28.0%) had a history of medicinal drug use within the previous two weeks, 38 patients (16.2%) were using non-steroidal anti-inflammatory drugs, 27 patients (11.5%) were using antibiotics and 1 patient (0.4%) was using antidepressants. A significant relationship was found between the groups with acute urticaria and chronic urticaria in terms of medicinal drug use within the previous two weeks (χ^2 =4.242, p=0.045). Fifty-one (77.6%) of the patients who had a history of medicinal drug use within the previous two weeks were diagnosed with acute urticaria, and 15 (22.4%) were diagnosed with chronic urticaria. In the urinalysis results of the patients included in this study, bacteriuria was found in 100 (42.6%), pyuria in 69 (29.4%), and pyuria with bacteriuria in 60 (25.5%). In 3 (3%) patients with bacteriuria, positive urine culture was detected, with Escherichia coli being found in 2 patients and Serratia marcescens in 1 patient. Leukocyte esterase positivity was detected only in 2 (2%) patients with bacteriuria.

Bacteriuria existence was determined in 67 patients (67%) with acute urticaria, and 33 patients (33%) with chronic urticaria. There was no significant association between the acute urticaria and chronic urticaria patient groups in terms of of bacteriuria existence (χ^2 =0.035, p=0.888). 46 of the patients (66.7%) with pyuria were diagnosed with acute urticaria, and 23 (33.3%) of them were diagnosed with chronic urticaria. In the comparison of pyuria existence, there was no significant association between the two groups (χ^2 =0.044, p=0.879). Fourty of the patients (66.7%) with bacteriuria and pyuria coexistence were diagnosed with acute urticaria, and 20 (33.3%) of them were diagnosed with chronic urticaria. Bacteriuria and pyuria coexistence were compared in the two patient groups and no significant association was found $(y^2=0.036, p=0.874)$ (Table 1). In addition, there was a significant association between those patients with bacteriuria and those patients who had pyuria (χ^2 =80.538, p=0.000), as 60 (60%) of the patients with bacteriuria had pyuria simultaneously.

Regarding gender, the results were statistically significantly higher in female patients than male patients due to the evaluation of bacteriuria (91%) and pyuria (94%) existence separately, and bacteriuria and pyuria coexistence (98.3%) (p=0.001) (Table 1).

Twenty-three (23%) of the patients with bacteriuria had a history of atopy, and no significant association was found between bacteriuria and atopy history (χ^2 =0.265, p=0.607). No statistically significant association was found between bacteriuria and dermographism (χ^2 =1.079, p=0.299). Dermographism was found in 14 (14%) patients with bacteriuria. Atopy history was present in 13 (18.8%) of the patients with pyuria, and no

significant association was found between pyuria and atopy history (χ^2 =1.792, p=0.245). Dermographism was found in 9 (13%) of the patients with pyuria, and no significant association was found between pyuria and dermographism (χ^2 =0.232, p=0.656). There was atopy in 12 (20%) of the patients with bacteriuria and pyuria coexistence, and no significant association was found between bacteriuria and pyuria coexistence and atopy history (χ^2 =0.950, p=0.388). In addition, dermographism was present in 8 (13.3%) of the patients with bacteriuria and pyuria coexistence, and no statistically significant association was found between bacteriuria and pyuria coexistence and dermographism (χ^2 =0.269, p=0.641) (Table 1).

Dysuria was described in 12 (5.1%) of the total number of patients included in this study, 10 (10%) of the patients with bacteriuria, 7 (10.1%) of the patients with pyuria, and 7 (11.7%) of the patients with bacteriuria and pyuria coexistence. A significant association was found between bacteriuria and dysuria (χ^2 =8.603, p=0.003), where 10 (10%) of the patients with bacteriuria had dysuria simultaneously. There was a significant association between pyuria and dysuria (χ^2 =5.118, p=0.044), where 7 (10.1%) of the patients with pyuria had dysuria concurrently (Table 1). A significant association was found between bacteriuria and pyuria coexistence and dysuria (χ^2 =7.156, p=0.014), as 7 (11.7%) of the patients with bacteriuria and pyuria coexistence had dysuria at the same time.

When the laboratory results of the patient groups with bacteriuria and/ or pyuria were examined, there was no significant difference between the groups in terms of the values of lymphocyte, eosinophil, neutrophil lymphocyte ratio, hs-CRP, and total-IgE since all p-values >0.05, as can be seen in Table 2.

On the other hand, there was a significant difference in the leukocyte value between the patient groups with bacteriuria (p=0.041). There was no significant difference in the neutrophil value between those patient groups with or without bacteriuria (p=0.112). There was a significant difference in the neutrophil (p=0.036) values between those patients with or without pyuria and also there was a significant difference in the leukocyte values between the patient groups with pyuria (p=0.006). Also, there was a significant difference in the leukocyte (p=0.013) values between those patients with and those without the coexistence of bacteriuria and pyuria, as seen in Table 2.

DISCUSSION

Urticaria is a skin disease which significantly impairs quality of life, especially when it becomes chronic. In the literature, the approximate rates of the urticaria cases were 40% urticaria, 40% urticaria and angioedema simultaneously, and 20% isolated angioedema.⁴ In our study, the rate of cases was found to be higher than in the literature, as isolated urticaria was identified in 48 (20.4%) of the patients, and urticaria and angioedema simultaneously were detected in 187 (79.6%) of them. In studies, acute urticaria is observed equally in both genders in the young age group, but chronic urticaria is more common in middle-aged women.⁴ In our study, there was a female dominance as 157 (66.8%) of the cases were female in the acute and chronic urticaria groups.

Urticaria can develop idiopathically, however, in chronic urticaria patients, the risk of accompanying autoimmune diseases, such as thyroid diseases, type 1 diabetes, systemic lupus erythematosus and rheumatoid arthritis is quite high.^{4,7} In our study, thyroiditis (6.8%) and anemia (3%) were present as chronic systemic diseases accompanying urticaria cases.

While medicinal drugs may be the primary cause of acute urticaria, they are also observed as a triggering or exacerbating cause in chronic urticaria. Drug-related urticaria is particularly observed in association with nonsteroidal anti-inflammatories and antibiotics.² It was reported in one study that urticaria and angioedema are the most common clinical manifestations among hypersensitivity reactions due to the use of nonsteroidal anti-inflammatory drugs.¹⁰ In our study, 66 (28.0%) of the patients had a history of drug usage within the previous two weeks, and 51 (77.6%) of them were diagnosed with acute urticaria. Compatible with the literature, in our study, 38 patients (16.2%) were using non-steroidal anti-inflammatory drugs while 27 patients (11.5%) were using antibiotics at the time they were diagnosed with urticaria.

Although the relationship between acute urticaria and infection has been explained more clearly, it is also suggested that infections in chronic urticaria play a triggering and exacerbating role in the course of the disease rather than being the primary cause.^{5,7} In our study, a significant relationship was found between the history of infection within the previous two weeks and both acute urticaria and chronic urticaria patients (χ^2 =12.031, p=0.001). 54 (23%) of the patients had a history of infection within the previous two weeks; specifically, there

		Patients with bacteriuria			Patients with pyuria			Patients with bacteriuria and pyuria		
		χ²	р		χ²	р		χ²	р	
C	Female	91 (91%)	45.044	0.001	65 (94%)	22.050	0.001	59 (98.3%)	26 110	0.001
Gender	Male	9 (9%)	45.941	0.001	4 (6%)	33.058	0.001	1 (1.7%)	36.110	0.001
D	Acute	67 (67%)	0.025	0.000	46 (66.7%)	0.044	0.070	40 (66,7%)	0.036	0.074
Duration	Chronic	33 (33%)	0.035	0.888	23 (33.3%)	0.044	0.879	20 (33.3%)	0.036	0.874
Angioedema		19 (39.6%)	0.218	0.641	16 (33.3%)	0.459	0.484	15 (31.25%)	1.037	0.308
Atopy		23 (23%)	0.265	0.607	13 (18.8%)	1.792	0.245	12 (20%)	0.950	0.388
Dermographis	n	14 (14%)	1.079	0.299	9 (13%)	0.232	0.656	8 (13.3%)	0.269	0.641
Dysuria		10 (10%)	8.603	0.003	7 (10.1%)	5.118	0.044	7 (11.7%)	7.156	0.014

Patients without bacteriuria M (SD) 5.78 (3.54) 2.06 (0.92) 0.19 (0.91)	_										
M (SD) 5.78 (3.54) 2.06 (0.92) 0.19 (0.91)				Patients without pyuria	Patients with pyuria			Patients without bacteriuria and pyuria	Patients with bacteriuria and pyuria		
5.78 (3.54) 2.06 (0.92) 0.19 (0.91)			d	M (SD)		٠	d	M (SD)		+	ď
2.06 (0.92) 0.19 (0.91)		-1.60	0.112	5.78 (3.50)	6.87 (3.71)	-2.11	0.036	5.85 (3.51)	6.83 (3.76)	-1.81	0.071
0.19 (0.91)		-1.36	0.174	2.06 (0.87)	2.30 (0.94)	-1.84	0.068	2.07 (0.88)	2.30 (0.93)	-1.73	0.085
		1.09	0.327	0.18 (0.83)	0.09 (0.14)	0.84	0.402	0.17 (0.80)	0.10 (0.15)	99.0	0.508
Neutrophil lymphocyte 3.49 (3.29) 3.77 (3.92) ratio		-0.56	0.574	3.53 (3.66)	3.80 (3.47)	-0.51	0.611	3.62 (3.74)	3.60 (3.18)	0.03	0.973
hs-CRP (mg/dL) 0.56 (0.87) 0.59 (0.94)		-0.28	0.783	0.58 (0.92)	0.55 (0.86)	0.178	0.859	0.58 (0.92)	0.54 (0.86)	0.34	0.735
Leukocyte (10³/uL) 8.56 (3.86) 9.60 (3.66)		-2.06	0.041*	8.55 (3.73)	10.05 (3.80)	-2.748	0.006*	8.63 (3.71)	10.06 (3.89)	-2.50	0.013*
Total IgE (IU/mL) 137.84 (65.63) 150.67 (98.25)		-0.42	0.672	140.32 (53.89)	150.48 (99.77)	-0.30	0.767	137.75 (47.79)	159.49 (31.95)	-0.61	0.544

was a history of dental infection in 1 patient, pilonidal sinus infection in 1 patient, and upper respiratory tract infection in 52 patients. Forty-seven (87%) of the patients with a history of infection within the previous two weeks were diagnosed with acute urticaria, and 7 (13%) of them were diagnosed with chronic urticaria.

Asymptomatic bacteriuria is defined as the presence of bacteria in properly collected urine samples of patients without signs of urinary tract infection, with or without pyuria. It is especially detected in the elderly and in females and treatment is not recommended, except for some special conditions. 11 Although the predominant consensus is that asymptomatic bacteriuria is a local organ-specific condition, there are opinions that it stimulates a generalized immune response.¹² In our study, the existence of bacteriuria and pyuria in female patients were significantly higher than in male patients. It is reported that the prevalence of urinary tract infections is significantly higher in women than in men until the age of 60 years and older. 13 Some of the reasons for urinary tract infections in women may be the shorter distance between the urethra and the anus, frequent coitus and the use of spermicides.¹⁴ Therefore, it is understandable that women have urticaria more frequently than men as urinary infections are seen more frequently in women and they are known to be a triggering factor.

The gold standard for the diagnosis of urinary tract infection is the detection of the pathogen by the urine culture method, accompanied by clinical symptoms. Pyuria (leukocyturia) describes an increase in the number of polymorphonuclear leukocytes in the urine (usually >10 WBC/HPF) or leukocyte esterase positivity. The presence of pyuria is an indicator of genitourinary system infection, but it is not an absolute indicator for urinary tract infection and does not require treatment. However, the absence of pyuria excludes urinary tract infection.⁹

Reports have shown that urinary tract infection is a trigger in acute and chronic urticaria and urticarial complaints regressed after the treatment of the urinary tract infection with antibiotics.^{5,15} Zotter et al. 16 reported that, in patients with hereditary angioedema with C1-inhibitor deficiency, the frequency and number of attacks were higher in those patients with bacteriuria compared to those without bacteriuria. Kadhim et al.9 reported that urinary tract infections were found at a significantly higher rate in urticaria patients compared with the control group in their study. There was also a statistically significant relationship between urticaria and both pyuria and positive urine culture, and they reported pyuria in 19.8% of urticaria patients and positive in urine culture in 8.2% of them. Additionally, it was reported that 32.6% of the patients with pyuria and 28.9% of the patients with urine culture were asymptomatic. In our study, the presence of pyuria was detected in 69 (29.4%) of the urticaria patients and a positive urine culture result was found in 3% of those patients with bacteriuria. In addition, dysuria was determined in 7 (10.1%) patients with pyuria and dysuria was determined in 2 (66.7%) out of 3 patients with positive urine culture results. A significant relationship was found between bacteriuria and the presence of dysuria (χ^2 =8.603, p=0.003), and 10 (10%) patients with bacteriuria had dysuria at the same time. There was a significant relationship between pyuria and dysuria (χ^2 =5.118, p=0.044), where 7 (10.1%) of the patients with pyuria had dysuria simultaneously. A significant relationship was found between bacteriuria and pyuria association and dysuria (χ^2 =7.156, p=0.014), as 7 (11.7%) of the patients with bacteriuria and pyuria had dysuria as well.

The leukocyte values of those patients with bacteriuria were significantly higher than those without bacteriuria. For the group of patients with pyuria, the leukocyte and neutrophil values of those patients with pyuria were significantly higher than those without pyuria. Also, the leukocyte values of those patients with bacteriuria and pyuria were significantly higher than those without bacteriuria and pyuria (Table 2). For these reasons, our study supports the hypothesis that pyuria and/or bacteriuria may play a role in the etiology of urticaria by triggering an inflammatory response.

CONCLUSION

In order to define the role and importance of bacteriuria and/or pyuria in the etiology of urticaria, it is clear that studies with larger numbers of cases and controls are needed. Especially in female patients diagnosed with urticaria, the rates of bacteriuria and/or pyuria were found to be significantly higher, and the statistically significantly higher number of leukocytes in patients with bacteriuria and/or pyuria suggests that inflammation in the urinary tract may be an important stimulus in the etiology of urticaria. These results may pave the way for studies to be conducted to evaluate the urticaria treatment response rates with urinary infection treatments to be given to urticaria patients with bacteriuria and/or pyuria.

MAIN POINTS

- Although the etiopathogenesis has not been clearly explained, many infections are reported as being triggering factors for urticaria.
- Studies have shown that urinary tract infection is a triggering factor in urticaria and that urticaria complaints regress after urinary tract infection treatment.
- According to the findings of this study, it is suggested that asymptomatic bacteriuria and/or pyuria may also be a significant triggering factor for urticaria.

ETHICS

Ethics Committee Approval: Ethical approval was obtained from the Ethical Committee of the Near East University Hospital for the study (approval number: 2021/90-1326).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: D.M., Design: D.M., Data Collection and/or Processing: D.M., S.M., N.S., Analysis and/or Interpretation: D.M., S.M., N.S., Literature Search: D.M., S.M., N.S., Writing: D.M. S.M.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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