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Evaluation of vitamin d and key biomarkers in chronic urticaria patients

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Abstract
Background: Chronic urticaria is a persistent skin disorder characterized by recurrent hives and inflammation, often linked to immune dysregulation.
Aims of the study: Look into the possible role that blood vitamin D and key measures of inflammation play in the development of chronic urticaria.
Methodology: This case-control study was conducted at Al-Sader Teaching Hospital, Basrah, Iraq, from January to October 2024, with ethical approval from Basrah Medical College. It included 70 chronic urticaria patients and 70 healthy controls (aged 18-65 years). Exclusion criteria covered medication use affecting vitamin D, pregnancy, and chronic diseases. Blood samples were analyzed for CBC, CRP, and vitamin D using advanced laboratory equipment. Vitamin D levels were measured via the COBAS® e411 immunoassay, while CRP and hematological parameters were assessed using COBAS® INTEGRA 400 PLUS and Sysmex XN-330.
Result: There were no significant differences in gender and age distribution between chronic urticaria patients and controls. However, vitamin D levels were significantly lower in patients (17.01±5.85 ng/mL) than in controls (30.27±8.87 ng/mL, $p<0.05$). CRP and MPV levels were significantly higher in patients, while basophil count was lower ($p<0.05$). A negative correlation was found between vitamin D and both CRP (r =-0.419) and MPV (r =-0.452), suggesting an association between vitamin D deficiency and inflammation in chronic urticaria.
Conclusions: Chronic urticaria patients showed significantly lower vitamin D levels and higher CRP and MPV, indicating increased inflammation. Vitamin D deficiency may contribute to immune dysregulation, enhancing inflammatory responses. The negative correlation suggests vitamin D's potential role in modulating inflammation, making supplementation a possible therapeutic approach.

Keywords: Chronic urticaria, vitamin D deficiency, Inflammation, C-reactive protein (CRP), mean platelet volume (MPV), immune dysregulation

Introduction

Urticaria, derived from the Latin word urtica (meaning "to burn"), commonly referred to as hives, is a skin condition characterized by red, raised, and itchy wheals, often accompanied by angioedema. Wheals are red and swollen, and their sizes range from a few millimeters to a few centimeters [1]. Usually, they have a center area that is swollen and surrounded by redness. They also frequently have a burning feeling or itching. Most of the time, these blisters go away in one to twenty-four hours. When someone has angioedema, the inflammation may spread deeper into the dermis, causing swelling that hurts instead of just irritating the skin. Angioedema most often happens on the face, especially around the eyes and around the mouth. It can take up to 72 hours to go away and it can also happen to the hands, feet, and private parts [2]. It is thought that between 0.5% and 5% of the general population has chronic urticaria. It happens more often in women and is very hard on people who have it. It gets in the way of their daily lives, lowers their quality of life, and is often linked to mental illnesses like sadness and anxiety [3]. Chronic urticaria (CU) is categorized based on its aetiology into chronic spontaneous urticaria (CSU), where no specific cause is identified, and chronic induced urticaria (CIU), which is triggered by various physical or environmental stimuli [4]. Numerous potential causes have been proposed for chronic urticaria, with autoimmunity being considered one of the most common underlying factors.

Several autoimmune and endocrine disorders have been associated with the condition, including coeliac disease, systemic lupus erythematosus, cryoglobulinemia, juvenile rheumatoid arthritis, and autoimmune thyroid diseases such as Graves' disease [5]. Vitamin D is a fat-soluble vitamin that comes in two forms: D2 (ergocalciferol) and D3 (cholecalciferol). It is taken in by the body through food and air. It has been shown that some mushrooms, like button and shiitake mushrooms, contain vitamin D2. Vitamin D3 can be found in foods like halibut, mackerel, eel, salmon, beef liver, and egg whites [6]. The skin is the only part of the body that makes vitamin D3. UVB light (wavelength: 290-315 nm) changes 7-dehydrocholesterol into previtamin D3 in the skin. Vitamin D3 is then made from previtamin D3. 25-hydroxyvitamin D (25(OH)D) is the main vitamin D molecule that is found in blood and is often used to check vitamin D levels. Vitamin D2 and D3 from food and vitamin D3 from skin photobiosynthesis are the first things that the liver enzyme 25-hydroxylase (CYP2R1) makes. Vitamin D is changed in the kidneys by an enzyme called 1-alpha hydroxylase made by CYP27B1 gene. This enzyme changes 25(OH)D into 1,25(OH)2D, which is the most biologically active form of vitamin D [7, 8]. A lack of vitamin D is widely seen as a worldwide problem right now. The main reason many people don't get enough vitamin D is that they don't realize that modest sun contact is they main source of vitamin D for most people. Many foods that have been added to with vitamin D don't meet an adult or baby's vitamin D needs, and there aren't many foods that naturally have vitamin D. Several things affect vitamin D levels, such as where you live, the season, your race, and the usual test result for adequate, insufficient, and normal vitamin D. In 2008, it was thought that about a billion people did not get enough vitamin D. This number is almost certainly higher now [9]. Lack of vitamin D can cause rickets in babies and make osteoporosis, osteopenia, and fractures worse in people. A lack of vitamin D has been linked to a higher chance of virus diseases, autoimmune disorders, high blood pressure, and common cancers [10]. In order to keep chemical balance, you need vitamin D. Its main job is to keep bones healthy, but it also helps the skin's immune system by connecting with special receptors on epithelial cells and immune cells like mast cells, monocytes, macrophages, T cells, B cells, and dendritic cells [11]. Vitamin D boosts the natural immune system's ability to fight off microbes by encouraging the production of antibacterial peptides like human β-defensin and cathelicidin [12]. In a lab experiment, it was shown that T cells in the adaptive immune system can be triggered to express CYP27B1. This enzyme changes D3 into its active form, (1,25(OH)2D), at amounts similar to those found in living organisms when serum is not present [13]. Biomarkers are measurable indicators that can be used to assess normal biological processes, disease states, or responses to therapeutic interventions [14]. With the increasing use of genomic screening in modern biology, researchers have been able to identify molecular targets in the field of urticaria, offering potential biomarkers for diagnosis, treatment, and prognosis, thereby expanding the range of possible treatment strategies. In recent years, research has focused on understanding the mechanisms behind chronic urticaria, especially chronic spontaneous urticaria (CSU), and identifying mediators that can serve as biomarkers for disease severity, prognosis, and treatment response [15]. C-reactive protein (CRP) is a pentameric protein produced by the liver, whose levels rise in response to inflammation. As an acute-phase reactant, CRP is primarily induced by interleukin-6 (IL-6), which stimulates the gene responsible for its transcription during inflammatory and infectious processes. CRP has protective properties, such as reducing neutrophil-mediated damage to lung tissue in alveolitis. It also exhibits both pro-inflammatory and anti-inflammatory effects. By binding to various substances like phosphocholine, phospholipids, and fibronectin, CRP helps identify and remove pathogens and damaged cells, promoting the clearance of apoptotic cells and foreign invaders through the classical complement pathway and phagocytic cells. However, CRP can also exacerbate tissue injury in autoimmune conditions by activating the complement system and triggering inflammatory cytokine release [15, 16]. Mean platelet volume (MPV) is a reliable marker for assessing platelet activity and function. It is commonly measured in complete blood count tests to estimate platelet size and volume. Platelet size and volume are influenced by bone marrow production. Platelets play a key role in the inflammatory processes associated with CU (30). During inflammation, platelet counts often rise, but their volume may either decrease or increase [16]. MPV has been recognized as an inflammatory marker in various diseases, including rheumatoid arthritis (RA), acute rheumatic fever (ARF), familial Mediterranean fever (FMF), and cystic fibrosis (CF) [16, 17]. The human body contains various types of white blood cells, one of which is basophils. These cells are the least abundant among mammals, making up less than 1% of the white blood cells in circulation. Basophils are produced in the bone marrow and are an important part of the immune system. Basophils are also referred to as granulocytes. The granules within these cells contain various chemicals that influence the activity of other cells and biological substances. Notable substances like heparin, histamine, and other inflammatory mediators are stored in the granules of basophils [18]. High basophil count or basophilia occurs in many conditions like hypothyroidism, chronic inflammation, myeloproliferative disorders and cancer. On the opposite, low levels of basophils (basopenia) can be seen in allergic reactions, acute infection, hyperthyroidism and long-term steroid therapy, chemotherapy, or radiation therapy [19].

Methodology

This case-control study was conducted at Al-Sader Teaching Hospital's dermatology outpatient clinic in Basrah, Iraq, from January 2024 to October 2024, following approval by the Research Ethics Committee at Basrah Medical College and Basrah health directorate. The study included 70 patients diagnosed with chronic urticaria (lasting more than six weeks) and 70 healthy controls, with participants aged 18-65 years of both genders. Exclusion criteria encompassed individuals using medications or supplements that could alter vitamin D levels (such as corticosteroids, anticonvulsants, and anti-tuberculosis drugs), pregnant and breastfeeding women, and those with liver disease, chronic kidney disease, malabsorption disorders, or cancer. After confirming eligibility, participants underwent interviews to collect demographic data and assess symptoms using a structured questionnaire (Appendix 1). Blood samples were collected for laboratory analysis, including complete blood count (CBC) with differential, C-reactive protein (CRP), and vitamin D levels. A total of 6 mL of whole blood was

drawn, with 3 mL placed in a serum separator tube for CRP and vitamin D analysis, left to clot at room temperature, centrifuged at 3000 RPM for 10 minutes, and stored at 2-8°C before transfer to a private laboratory. The remaining 3 mL, placed in an EDTA tube, was analyzed for CBC in the hematology unit on the same day. The study utilized the Nuve centrifuge (Turkey), COBAS® INTEGRA 400 PLUS analyzer, COBAS® e411 analyzer (Roche Diagnostics, Germany), and Sysmex XN-330 Hematology Analyzer. Vitamin D levels were quantified using the COBAS® e411 immunoassay analyzer with Electro ChemiLuminescence (ECL) technology, employing the Vitamin D total II kit, which remained stable for 56 days at 2-8°C and 28 days on the analyzer. CRP levels were determined via a particle-enhanced immunoturbidimetric assay using the COBAS® INTEGRA 400 PLUS analyzer, where CRP agglutinated with latex particles coated with monoclonal anti-CRP antibodies, with stability maintained for 12 weeks after loading. Mean platelet volume (MPV) and basophil counts were measured using the Sysmex XN-330 Hematology Analyzer, employing Fluorescence Flow Cytometry and DC impedance with hydrodynamic focusing. All reagents were stored refrigerated and remained stable for 12 weeks on the analyzer.

Statistical analysis

IBM SPSS (statistics Package for the Social Sciences) 64-bit MS Windows version 29 was used to do the statistics study. For numbers, the mean and standard deviation were used. When there were category factors, percentages were used. For factors that are not parametric, the Kruskal-Wallis test and the Mann-Whitney U test were used. As a way to compare the vitamin D, CRP, MPV, and basophils counts between the case and control groups, Mann Whitney U was used. Spearman correlation coefficients were used to look into the link between all the factors in both the control group and the case group.

Ethical approval

The study was okay with the human ethics committee from College of Medicine and Basrah Health directorate. Everyone who took part in the study was told about it and had to fill out a permission form. In addition, the patient was told that his information would be kept secret.

Results

Demographic Characteristics of Study Participants

The results showed no statistically significant differences between the patient group and the control group with regard to gender and age distribution. The percentage of females in the patient group was 68.6% compared to 62.9% in the control group, while the percentage of males was 31.4% and 37.1%, respectively, with no significant difference between the two groups (P=0.476, χ^2=0.507). As for the mean age, it was 34.65±13.62 years in the patient group compared to 32.09±14.14 years in the control group, and the difference between them was not statistically significant (P=0.350, t=0.934).

Table 1: Comparison of Gender Distribution and Age Between Cases and Controls

		Control n(%)	Case n(%)	χ2	P value
Gender	Female	44(62.9)	48(68.6)	0.507a	0.476
	Male	26(37.1)	22(31.4)		
Age	Mean (SD) Years	32.09(14.14)	34.65(13.62)	0.934 b	0.350

χ2=a: chi square test, b: Maan Whitney U test

Comparison of Biomarker Levels Between Cases and Controls

Vitamin D levels were much lower in people with chronic urticaria than in the control group. The average amount in the chronic urticaria group was 17.01±5.85 ng/mL, while it was 30.27±8.87 ng/ml in the control group. The difference was statistically significant (p<0.05, Z =-8.559). C-reactive protein (CRP) levels also increased significantly in the patient group, with an average of 9.74±10.42 mg/L compared to 1.86±1.19 mg/L in the control group (p<0.05, Z = 8.453). The mean platelet volume (MPV) for the patient group was 11.52±1.10 femtoliters, which was significantly higher than the MPV for the control group, which was 9.75±0.66 femtoliters (p<0.05, Z = 7.868). On the other hand, total basophil count (BBC) was lower in the patient group (0.019±0.008 × 10^3/µL) compared to the control group (0.03±0.02 × 10^3/µL), with a significant difference (p<0.05, Z =-4.148).

Table 2: Vitamin D, CRP, MPV, and Basophil Count in Study Groups

Variable	Group	Mean (SD)	Median (IQR)	Z value	p value
Vit.D Level ng/mL	Control	30.27(8.87)	28.3(8.78)	-8.559	<0.05
	Case	17.01 (5.85)	17.65(8.03)		
CRP Level mg/L	Control	1.86(1.19)	1.4(2)	8.453	<0.05
	Case	9.74(10.42)	6.95(6.5)		
MPV Level fL	Control	9.75(0.66)	9.7(1)	7.868	<0.05
	Case	11.521(1.10)	11.85(1.1)		
Basophils count 10^3/uL	Control	0.03(0.02)	0.02(0.01)	-4.148	<0.05
	Case	0.019(0.008)	0.02(0.02)		

Correlation Matrix of Age and Biomarker Levels in Cases and Controls

The correlation analysis showed that there was a strong positive relationship between age and both CRP levels (r = 0.534, p<0.01) and mean platelet volume (MPV) (r = 0.436, p<0.01) in the control group. However, there was a weak and insignificant relationship between age and vitamin D and basophil levels. In the patient group, there was a negative relationship between vitamin D and both CRP levels (r =-0.419, p<0.01) and MPV levels (r =-0.452, p<0.01). This means that low vitamin D may be linked to high levels of these inflammatory markers. In addition, there

was a negative correlation between basophil count and CRP levels (r =-0.447, p<0.01) and MPV (r =-0.316, p<0.01) in the patient group, which may reflect the role of these cells in regulating the inflammatory response in chronic urticaria.

Table 3: Relationship between Age, Vitamin D, CRP, MPV, and Basophil Count

Group		Age	Vit.D Level	CRP Level	MPV Level	Basophils count
Control	Age	1				
	Vit.D Level	0.262*	1			
	CRP Level	0.534**	0.164	1		
	MPV Level	0.436**	-0.012	0.427**	1	
	Basophils count	0.059	0.188	-0.373**	0.063	1
Case	Age	1				
	Vit.D Level	-0.13	1			
	CRP Level	0.079	-0.419**	1		
	MPV Level	0.061	-0.452**	0.321**	1	
	Basophils count	-0.062	0.427**	-0.447**	-0.316**	1

* Significant at 0.05 ** significant at 0.01

Discussion

Chronic urticaria is a skin disease that makes a person unable to do many things and makes many parts of their life worse. Several studies were done to look into the link between vitamin D and chronic hives. The immune system is affected by vitamin D because it stops dendritic cells and monocytes from making certain hormones. This means that vitamin D shortage is less likely to be the cause of this functional impairment. This leads to an imbalance of regulatory T-cell cytokine production and raises the level of circulatory pro-inflammatory cytokines which may worsen the symptoms in patients with chronic urticaria [20]. We observed that most patients in our study were female, with an average age of 32.09 years. According to the literature, chronic spontaneous urticaria can affect individuals across various age groups, but it is most prevalent in young women, typically between the ages of 20 and 40 [21]. This aligns with the demographic characteristics seen in our patient sample.

The present study found that patients with chronic urticaria had significantly lower serum 25-(OH) D3 levels (p<0.05) compared to healthy controls. Similarly, numerous earlier studies have demonstrated a positive correlation between chronic urticaria and low serum vitamin D levels. Wang *et al*. did a meta-analysis that showed people with hives had lower amounts of vitamin D in their blood than people who were not allergic [23]. The data was then split into two subgroups based on vitamin D levels: those who did not get enough and those who did not get enough. By looking at each cluster separately, we found that chronic urticaria was linked to vitamin D shortage, not insufficiency. Therefore, extreme vitamin D depletion, especially at very low levels (<20 ng/mL), might serve as an extra sign for autoimmune urticaria [22]. It was found in a study by Grzanka *et al*. in Poland that people with chronic spontaneous urticaria had significantly lower median serum vitamin D levels than healthy people. The middle number was 26 ng/mL and the highest number was 31 ng/mL (P = 0.02). Vitamin D insufficiency was much more common in the urticaria group than in the healthy controls, which was in line with these results (P = 0.02) [20]. In the same way, Chandrashekar *et al*. did study in India and found that the mean 25(OH)D levels of the group with recurrent spontaneous urticaria were much lower than those in the control group. The average values for the first group were 13 ng/mL and for the second group they were 24 ng/mL (p<0.001) [23]. Thorp *et al*., on the other hand, found that there wasn't a big difference between the two groups in the percentage of people who were vitamin D deficient (described as 25-OHD < 30 ng/mL). 48% (12 out of 25) of the people in the chronic urticaria group had it, while only 28% (7 out of 25) in the control group did (p = 0.24) [24]. The reason for this discrepancy remains uncertain and may be influenced by factors such as differences in control group characteristics, seasons of blood sampling, geographic regions, lifestyle and cutoff value for vitamin D deficiency used in each study. There is also evidence that blood 25(OH)D levels are often lower in Middle Eastern countries compared to the US and Europe [25]. Serum 25(OH)D levels are lower in people with urticaria, as shown by our results and those of Wang *et al*. [22] and Grzanka *et al*. [20]. It's still not clear whether this decrease is a risk factor or a sign of disease activity, and it's also not clear what causes it. We saw a link between blood 25(OH)D levels and CRP levels, which is a sign of how active urticaria is. This is true even though some studies show that lower 25(OH)D levels are linked to more severe or active inflammatory diseases [27]. This association, however, was very small (P= 0.164), which is in line with what Abdel-Rehim *et al*. found. The relationship between biomarkers might be important for understanding how urticaria starts, and looking at the relationship between various biomarkers in the same patient might help with prognosis [26]. Because CRP is a strong activator of the classical cascade of complement, it may cause or worsen inflammatory lesions in some situations. The findings of the previous studies by Magen *et al*., and Kasperska *et al*., are consistent with the current study results which declares a high level of CRP in patients with chronic urticaria in comparison to control [28]. Our results suggest that chronic urticaria may be a type of immune-mediated inflammatory disease. This is because the high CRP levels we saw in our study suggest that a systemic inflammatory process may be involved in how it works [29]. Previous studies have shown that CU is marked by high levels of proinflammatory cytokines in the blood and immune system abnormalities. This is linked to a systemic inflammatory profile and T cells secreting cytokines in the wrong way [29]. MPV is a measure of platelet size that shows how well and how often platelets are activated. Kolkhir *et al*. showed that people with chronic urticaria had higher amounts of MPV than people who were not allergic [6]. The present study also found a significant difference (p>0.05) in MPV levels between cases and controls, which is in line with this result. In addition, our findings were also similar to those of Cohen *et al*., with elevated MPV being the most frequently observed laboratory abnormality in chronic urticaria patients, among 12,778 individuals with chronic urticaria

who were involved in their study, 3,552 showed increased MPV levels. Specifically, 31% of women and 23% of men had significantly higher MPV compared to control subjects [29]. Furthermore, Chandrashekar *et al*. reported that patients with chronic urticaria showed significantly higher mean platelet volume and platelet distribution width compared to controls. The observed variation in platelet size could suggest a direct involvement of activated platelet mediators in urticaria, or it might simply be a sign of bone marrow stimulation due to heightened systemic inflammation [29]. It was found that MPV levels were linked to CRP levels, which suggests that the inflammatory features in chronic urticaria (CU) are likely the same. This is because mast cells becoming active causing CRP levels to rise, which is followed by an inflammatory reaction [32]. This means that the inflammatory state and platelet activity are linked in the development of CU. There was a positive relationship found between CRP and MPV in this study, which means that higher MPV levels were linked to higher CRP levels. The results of this study are similar to those of earlier research by Confino-Cohen *et al*. [33]. IgE is needed for basophils to play a key role in the development of chronic allergic inflammation of the skin. According to John A. Eckman *et al*. [34], people who have chronic urticaria (CU) have changed basophil IgE receptor activity. The results of this study showed that the basophil numbers of CU patients were very different from those in the control group. For example, peripheral basophil numbers were much lower in people in the CU compared to controls ($p<0.05$). A lot of studies have found that CU patients have low levels of basophils in their peripheral blood. Researchers Rauber *et al*. also found that people with chronic urticaria (CU) have fewer peripheral basophils and these cells don't work as well as they should [33].

In the study conducted by Grattan *et al*. [34], some urticaria patients showed an absence of detectable basophils when analyzed by both granule staining and flow cytometry, which utilized surface immunophenotyping to identify these cells. This dual-method absence implies that these patients likely experience true basopenia (an actual deficiency in basophil count) rather than just a detection issue related to degranulated or altered basophils. The findings indicate that basophil depletion may be an inherent characteristic in some individuals with urticaria, potentially contributing to or reflecting specific immune dysfunctions associated with the disease. We think that this complete lack of basophils could help us learn a lot about the immune system and possible disease processes in these patients. One possible reason for the lower amount of basophils in CU is that these cells are actively recruited into damaged epidermis. This result is similar to what Grattan *et al*. found in a previous study [35].

Conclusion

Chronic urticaria patients exhibited significantly lower vitamin D levels and higher CRP and MPV, indicating increased systemic inflammation. Vitamin D plays a crucial role in immune regulation by modulating T-cell responses and reducing pro-inflammatory cytokine production. Its deficiency may lead to heightened immune activation, contributing to chronic inflammation and disease severity. The negative correlation between vitamin D and inflammatory markers suggests a potential protective role. These findings highlight the importance of assessing vitamin D status and considering supplementation as a supportive therapeutic strategy.

References

1. Simpson JA. The Oxford English Dictionary. Oxford: Clarendon Press; 1989.
2. Ghosh S, Kundu S. Step by Step: Urticaria & Angioedema Management. London: JP Medical Ltd; 2016.
3. Deacock SJ. An approach to the patient with urticaria. Clinical & Experimental Immunology. 2008;153(2):151-161.
4. Pozderac I, Lugović-Mihić L, Artuković M, Stipić-Marković A, Kuna M, Ferček I. Chronic inducible urticaria: classification and prominent features of physical and non-physical types. Children. 2020;3(1):9-23.
5. Bansal S, Hayman GR. Graves disease associated with chronic idiopathic urticaria: 2 case reports. Journal of Investigational Allergology & Clinical Immunology. 2009;19(1):54-56.
6. Kolkhir P, Giménez-Arnau AM, Kulthanan K, Peter J, Metz M, Maurer M. Urticaria. Nature Reviews Disease Primers. 2022;8(1):1-17.
7. Black AK. Physical and cholinergic urticarias. In: Kaplan AP, editor. *Urticaria and Angioedema*. New York: Informa Healthcare; 2009. p. 181-204.
8. Clifford J, Rosen MD. Vitamin D insufficiency. New England Journal of Medicine. 2011;364(3):248-254.
9. Ko JA, Lee BH, Lee JS, Park HJ. Effect of UV-B exposure on the concentration of vitamin D2 in sliced shiitake mushroom (*Lentinus edodes*) and white button mushroom (*Agaricus bisporus*). Journal of Agricultural and Food Chemistry. 2008;56(10):3671-3674.
10. Ringe JD, Kipshoven C. Vitamin D-insufficiency: an estimate of the situation in Germany. Dermato-Endocrinology. 2012;4(1):72-80.
11. DeLuca HF, Cantorna MT. Vitamin D: its role and uses in immunology. The FASEB Journal. 2001;15(14):2579-2585.
12. Hata TR, Kotol P, Boguniewicz M, Taylor P, Paik A, Jackson M, *et al*. History of eczema herpeticum is associated with the inability to induce human β-defensin (HBD)-2, HBD-3 and cathelicidin in the skin of patients with atopic dermatitis. British Journal of Dermatology. 2010;163(3):659-661.
13. Kongsbak M, von Essen MR, Levring TB, Schjerling P, Woetmann A, Ødum N, *et al*. Vitamin D-binding protein controls T cell responses to vitamin D. BMC Immunology. 2014;15(1):1-13.
14. Working GBD. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clinical Pharmacology & Therapeutics. 2001;69(3):89-95.
15. Kolkhir P, Altrichter S, Hawro T, Maurer M. C-reactive protein is linked to disease activity, impact, and response to treatment in patients with chronic spontaneous urticaria. Allergy. 2018;73(4):940-948.
16. Heymann WR. Chronic urticaria and angioedema associated with thyroid autoimmunity: review and therapeutic implications. Journal of the American Academy of Dermatology. 1999;40(2):229-232.
17. Sert A, Aypar E, Odabas D. Mean platelet volume in acute rheumatic fever. Platelets. 2013;24(5):378-382.

18. Kastl BC, Pohlman LM. Basophils, mast cells, and their disorders. In: Weiss DJ, Wardrop KJ, editors. Schalm's Veterinary Hematology. 6th ed. Ames: Wiley-Blackwell; 2022. p. 373-380.
19. Orum MH. Basophil count, percentage of basophil and basophil lymphocyte ratio in psychiatry practice: current approaches and future directions. Journal of Contemporary Medicine. 2020;10(2):295-296.
20. Grzanka A, Machura E, Mazur B, Misiolek M, Jochem J, Kasperski J, *et al*. Relationship between vitamin D status and the inflammatory state in patients with chronic spontaneous urticaria. Journal of Inflammation. 2014;11(1):1-5.
21. Naaman S, Sussman G. Chronic idiopathic urticaria: treatment with omalizumab. Skin Therapy Letter. 2014;19(6):1-4.
22. Wang X, Li X, Shen Y. The association between serum vitamin D levels and urticaria: a meta-analysis of observational studies. Giornale Italiano di Dermatologia e Venereologia. 2017;153(3):389-395.
23. Chandrashekar L, Rajappa M, Munisamy M, Ananthanarayanan PH, Thappa DM, Arumugam B. 25-hydroxy vitamin D levels in chronic urticaria and its correlation with disease severity from a tertiary care centre in South India. Clinical Chemistry and Laboratory Medicine. 2014;52(6):e115-e118.
24. Thorp WA, Goldner W, Meza J, Poole JA, Hata T, Gallo R. Reduced vitamin D levels in adult subjects with chronic urticaria. Journal of Allergy and Clinical Immunology. 2010;125(2 Suppl):AB30.
25. Grant WB, Fakhoury HMA, Karras SN, Al Anouti F, Bhattoa HP. Variations in 25-hydroxyvitamin D in countries from the Middle East and Europe: the roles of UVB exposure and diet. Nutrients. 2019;11(9):2065-2083.
26. Abdel-Rehim AS, Sheha DS, Mohamed NA. Vitamin D level among Egyptian patients with chronic spontaneous urticaria and its relation to severity of the disease. Egyptian Journal of Immunology. 2014;21(2):85-90.
27. Kasperska-Zajac A. Acute-phase response in chronic urticaria. Journal of the European Academy of Dermatology and Venereology. 2012;26(6):665-672.
28. Bingham III CO. Immunomodulatory approaches to the management of chronic urticaria: an immune-mediated inflammatory disease. Current Allergy and Asthma Reports. 2008;8(4):277-287.
29. Chandrashekar L, Rajappa M, Sundar I, Munisamy M, Ananthanarayanan PH, Thappa DM, *et al*. Platelet activation in chronic urticaria and its correlation with disease severity. Platelets. 2014;25(3):162-165.
30. Kasperska-Zajac A, Sztylc J, Machura E, Jop G. Plasma IL-6 concentration correlates with clinical disease activity and serum C-reactive protein concentration in chronic urticaria patients. Clinical & Experimental Allergy. 2011;41(10):1386-1391.
31. Magen E, Mishal J, Zeldin Y, Schlesinger M, editors. Clinical and laboratory features of antihistamine-resistant chronic idiopathic urticaria. In: Proceedings of the 2011 Annual Meeting of the American Academy of Allergy Asthma & Immunology. Rhode Island: Oceanside Publications; 2011. p. 1-4.
32. Eckman JA, Hamilton RG, Gober LM, Sterba PM, Saini SS. Basophil phenotypes in chronic idiopathic urticaria in relation to disease activity and autoantibodies. Journal of Investigative Dermatology. 2008;128(8):1956-1963.
33. Rauber MM, Pickert J, Holiangu L, Möbs C, Pfützner W. Functional and phenotypic analysis of basophils allows determining distinct subtypes in patients with chronic urticaria. Allergy. 2017;72(12):1904-1911.
34. Grattan CEH, Walpole D, Francis DM, Nill MI, Dootson G, Edler S, *et al*. Flow cytometric analysis of basophil numbers in chronic urticaria: basopenia is related to serum histamine releasing activity. Clinical & Experimental Allergy. 1997;27(12):1417-1424.
35. Grattan CEH, Dawn G, Gibbs S, Francis DM. Blood basophil numbers in chronic ordinary urticaria and healthy controls: diurnal variation, influence of loratadine and prednisolone and relationship to disease activity. Clinical & Experimental Allergy. 2003;33(3):337-341.