

Serum Vitamin D Level in Patients with Chronic Urticaria

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Original Article

ABSTRACT

Background: Chronic urticaria is defined as episodes of urticaria or angioedema or both for more than 6 weeks. Its pathology remains unclear for most of the cases. The role of vitamin D in various chronic dermatological and systemic diseases such as malignancies, infectious diseases, autoimmune diseases and allergic disease, including atopic dermatitis and asthma, has been a matter of great interest however limited data are available on the status of vitamin D level in patients with chronic urticaria.. **Objective:** to evaluate the level of vitamin D in patients with chronic urticaria and compare it with serum level of vitamin D in healthy controls. **Patients and Methods:** This observational cross-sectional study was conducted from December 2020 to March 2021 in Sulaymaniyah teaching center for dermatological diseases, attempted to find an association between serum level of Vitamin D and chronic urticaria. **Results:** Eighty candidates (40 patients with chronic urticaria and 40 healthy controls) were enrolled in this study, majority were females (54 females) and (26 males), their age ranged between 18 and 72 years. A significant relationship was found between the level of vitamin D and chronic urticaria. The mean level of vitamin D in patient group was 16.12 ± 6.81 , while for the control group the mean was 27.79 ± 14.37 . The calculated P value was (<0.001) that showed a statistically significant difference of vitamin D level between the two groups.. **Conclusion:** Patients suffering from chronic urticaria have significant lower level of vitamin D in comparison to healthy controls.

Keywords: Urticaria, chronic, pathophysiology, Vitamin D, autoantibodies, immunoglobulin, cytokines

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1. INTRODUCTION

Urticaria is a vascular reaction of the skin characterized by the appearance of wheals, associated with severe itching, stinging, or pricking sensations. These wheals are caused by localized edema ⁽¹⁾ Angioedema swellings occur deeper in the dermis and in the subcutaneous or submucosal tissue. ⁽²⁾ Chronic urticaria that persist for more than 6 weeks can be grouped as “nonacute” or “chronic” urticaria. ⁽³⁾

The pathophysiology of chronic urticaria is not well-understood, but it may involve the dysregulation of intracellular signaling pathways within mast cells and basophils that lead to defects in trafficking or function of these cells ⁽⁴⁾. Moreover, it involves the development of autoantibodies to immunoglobulin E (IgE) on both mast cells and basophils ⁽⁵⁾.

In addition, increased levels of circulating pro-inflammatory cytokines, such as tumor necrosis factor- α , interleukin (IL)-1, IL-6, and IL-12 have been observed in patients with chronic urticaria ⁽⁶⁾. Vitamin D, a fat-soluble vitamin, exists in two forms: D2 (ergocalciferol) and D3 (cholecalciferol). Vitamins D2 and D3 from diets and vitamin D3 from skin photobiosynthesis are initially metabolized by the liver enzyme 25-hydroxylase (CYP2R1) to 25-hydroxy- vitamin D (25(OH)D), the major circulating metabolite which is commonly used for evaluation of status. The 25(OH)D is metabolized in the kidneys by the enzyme 25-hydroxyvitamin D-1 α -hydroxylase (CYP27B1) to 1,25-dihydroxyvitamin D (1,25(OH)₂D), the most biologically active form of vitamin D ⁽⁷⁾. Vitamin D can exert several immunomodulatory actions in both innate and adaptive immunity primarily by affecting its nuclear vitamin D receptor (nVDR) and plasma membrane receptors (mVDR) on epithelial cells, mast cells, monocytes, macrophages, T-cells, B-cells, and dendritic cells ^(8,9). Vitamin D inhibits production of IL-1, IL-6, IL-12, IL-23, interferon- γ (IFN- γ), and regulated on activation, normal T cell expressed and secreted (RANTES) ^(8,9,10). Vitamin D enhances intercellular adhesion molecule 3 (ICAM-3) expression in mast cells which can result in modulation of proliferation, apoptosis, differentiation, function, cytokine production of mast cells in addition to their adhesion to matrix components ⁽¹¹⁾. Furthermore, vitamin D contributes to the conversion of CD4+ T cells to regulatory T cells. T regulatory cells, which have been shown to play a role in the suppression of pro-allergic mechanisms ⁽¹²⁾. The role of vitamin D in various chronic diseases such as malignancies, infectious diseases, autoimmune diseases and allergic disease, including atopic dermatitis and asthma, has been a

matter of great interest⁽¹³⁾. In view of these points we tried to find a relationship between level of vitamin D and chronic urticaria.

2. PATIENTS and METHODS

This observational cross-sectional study was conducted (from December 2020 to March 2021) in (Sulaymaniyah teaching center for dermatological diseases) in Iraq - Kurdistan region - Sulaymaniyah governorate, attempted to find an association between serum level of vitamin D and chronic urticaria.

Eighty patients were enrolled in this study their age range was (18-72) years, the majority (54) were females and 26 were males. Forty of them were suffering from urticarial lesions at least twice weekly for more than 6 weeks (patient group) and forty of them randomly selected, who were healthy and had no previous history of urticaria (control group).

The exclusion criteria for the patient group:

1. Patients suffering from urticaria for less than 6 weeks.
2. Patients taking vitamin D supplement in the past 6 weeks.
3. Patients suffering from renal or hepatic failure.
4. Patients suffering from malabsorption syndrome.
5. Taking vitamin D supplement in the past 6 weeks.

A verbal consent was obtained from all patients who participated in this study, approved by (Kurdistan board for medical specialties) ethical committee.

History and clinical examination was performed, fully detailed questionnaire was obtained from the patients and control and serum sample of each patient was assessed for vitamin D level in different governmental and private laboratories by ELISA technique (using Cobas e601 by Roche), according to the device manual the vitamin D reference ranges were (Deficiency : < 20 ng/ml , Insufficiency: 20-29 ng/ml , Sufficiency : 30-100 ng/ml).

The obtained data was analyzed by using SPSS version 22. The statistical significance of differences in patient groups was assessed by Chi-square test. Continuous variables were expressed as mean± SD. P value less than 0.05 was considered statistically significant.

3. RESULTS

In the current study, 80 patients (54 female and 26 male), their age ranges from 18 to 72 years were included with mean age of 38.73 ± 14.55 in patient group and 41.23 ± 15.49 in the control group. In patient group 18 of them (45%) experienced symptoms of chronic urticaria on daily basis, 14 of them (35%) had 4-6 attacks per week and 8 patients (20%) of them had 2-3 attacks per week. The Mean BMI \pm SD in patient group was 26.35 ± 3.29 and in the control group was 28.28 ± 6.46 . Majority (92.5%) of patients' group didn't have family history of urticaria (**Table 1**).

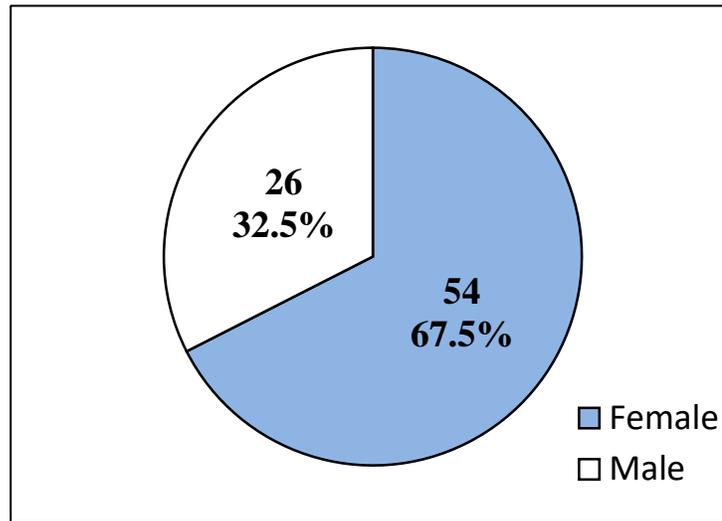


Figure 1. Gender distribution of the studied group

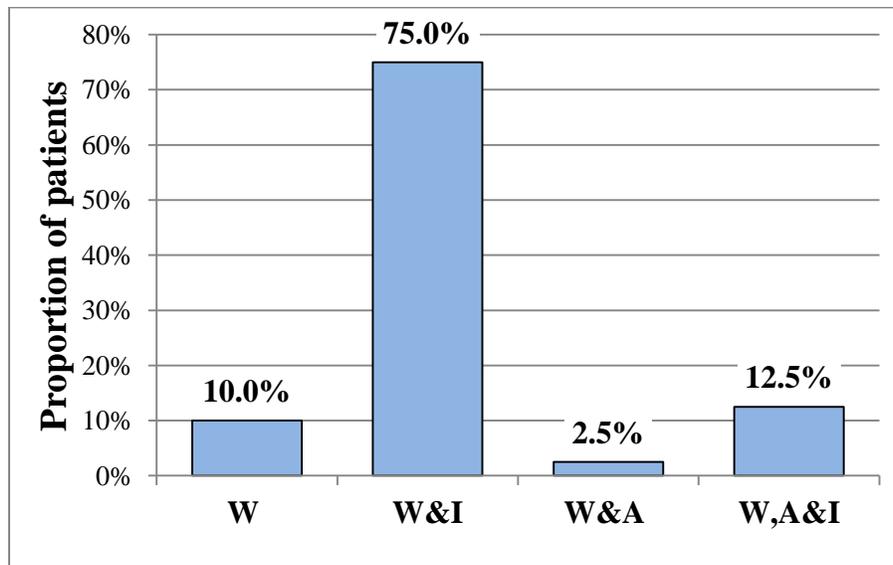


Figure 2. Distribution of Symptom among patients' group (W: Wheels. I: Itching, A: Angioedema.)

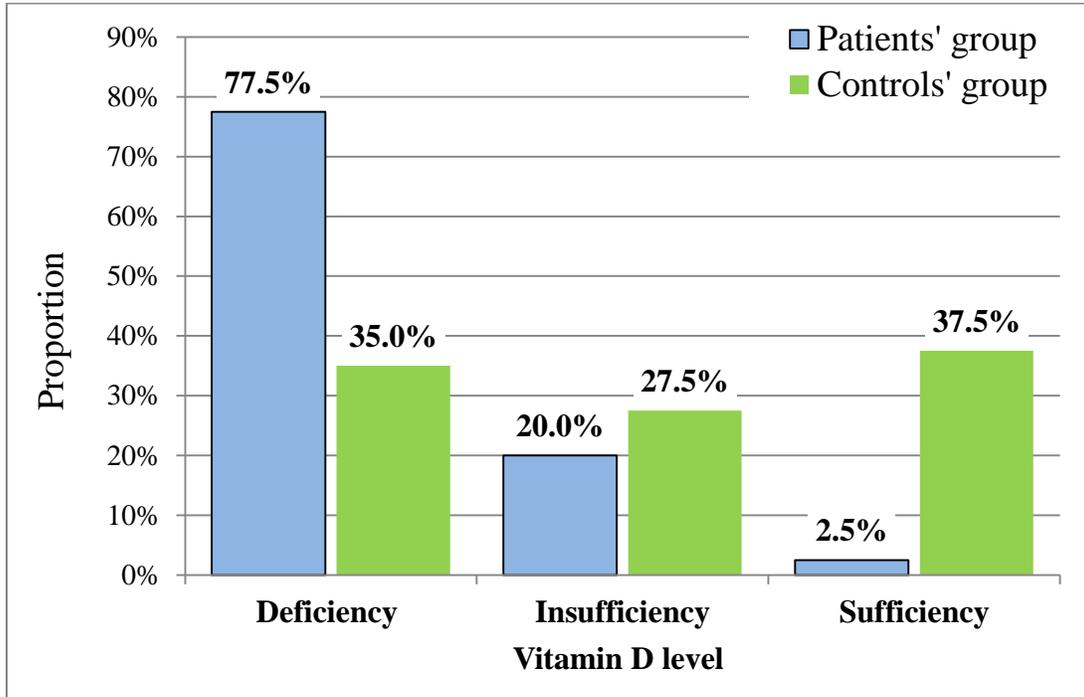


Figure 3. Bar-Chart for comparison of serum vitamin D levels of patient and controls according to reference ranges. (Deficiency <20 ng/mL, Insufficiency 20-29 ng/mL, Sufficiency 30-100 ng/mL)

Table 1. Serum Vitamin D levels in patient and controls' group

Vitamin D level	Patient group	Control group	P. value
Mean	16.12	27.79	< 0.001
SD	6.81	14.37	

4. DISCUSSION

Vitamin D deficiency is a major public health problem worldwide in all age groups⁽¹⁴⁾. In the current study there is a significant relationship between the level of vitamin D and chronic urticaria. In patients with chronic urticaria, (77.5%) of them, compared to only (35%) of control group had vitamin D deficiency while the vitamin D level of only 2.5% of the patient group and 37.5% of the control group was sufficient. The mean \pm SD level of vitamin D in patient group was 16.12 ± 6.81 , while for the control group the mean \pm SD was 27.79 ± 14.37 , this shows that the vitamin D level in patients with chronic urticaria is much less than of the control group, in addition to the calculated P value (<0.001) that shows a statistically significant deference of vitamin D level between patient and control group. These results are coinciding with the results of Yu Ri Woo et al⁽¹⁵⁾, where the serum 25-(OH)D₃ levels were significantly lower in the chronic urticaria group (11.86 ± 7.16 ng/ml; mean \pm SD) compared with the healthy controls (20.77 ± 9.74 ng/ml, $p < 0.001$). In patient group 49% of them had critically low vitamin D, 39% of them had vitamin D deficiency, 10% of them had vitamin D insufficiency and only 2% of them had vitamin D sufficiency. While regarding the control group, (8%) were grouped as having critically low vitamin D, (45%) as vitamin D deficient, (27%) as vitamin D insufficient and (20%) as being vitamin D sufficient.

We observed that the means level of vitamin D, were higher in both patient and control group compared with You Ri Woo et al⁽¹⁵⁾ results, it could be due to more sunny seasons in Iraq, so there is more sun exposure in our population. These results are also coinciding with Marzieh Tavakol et al⁽¹⁶⁾, Patients with chronic urticaria significantly showed lower levels of vitamin D in comparison with the control group and the p value was ($p = 0.005$).

Also our results were coinciding with Throp WA et al⁽¹⁷⁾, where vitamin D levels were significantly reduced in patient group compared with controls. The (Mean \pm SD) vitamin D was 29.4 ng/mL (± 13.4) for patient group versus 39.6 ng/mL (± 14.7) for controls with a P value of (0.016). And also coincided with Alicja Grzanka et al⁽¹⁸⁾, their results were as follows : serum vitamin D concentration was significantly lower in chronic urticaria patient group as compared with the control group (median: 26.0 vs. 31.1 ng/ml, with a p -value = 0.017). And also coincided with Rather S. et al⁽¹⁹⁾ in, the mean vitamin D levels of chronic

urticaria patients was 19.6 ± 6.9 ng/mL, whereas in control group, the mean level was 38.5 ± 6.7 . The difference in vitamin D levels between the two groups was statistically significant ($P < 0.001$). However our results contradicted Wu et al⁽²⁰⁾ where VitaminD levels were higher in the chronic urticaria patients than in the general UK population (mean vitamin D \pm SD, 51.4 ± 27.03 versus 45.4 ± 24.84 nmol/L; $P = 0.001$, may be due to the patient and the control group were not from the same region with a long distance between the two regions, this is reported by Elina Hyppönen and Chris Power⁽²¹⁾.

5. CONCLUSIONS

Patients suffering from chronic urticaria have significant lower level of vitamin D in comparison to healthy controls

Ethical Clearance: Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 for ethical issues of researches involving humans, informed consent obtained from all patients. Data and privacy of patients were kept confidentially.

Conflict of interest: Authors declared none

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