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Original Article

Hospital-based cross-sectional study to assess Vitamin D levels in patients of chronic spontaneous urticaria and its relation to severity of disease activity

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ABSTRACT

Objectives: The aim of this study was to assess and evaluate Vitamin D levels in CSU cases and compare with controls and to determine a correlation if any between Vitamin D levels and severity of CSU.

Material and Methods: A hospital-based case–control study of 130 cases and 130 controls was done. The assessment of severity of CSU was done using Urticaria Activity Score (UAS7). Laboratory investigations including Vitamin D levels were done in both groups.

Results: Mean serum Vitamin D levels in cases and controls were 14.29 ng/ml and 28.8 ng/ml, respectively. Ninety-nine (76.2%) cases had deficient levels, 25 had insufficient levels, and six had normal levels. In controls, 63 had normal serum Vitamin D levels, 46 had insufficient, and 21 (16.1%) had deficient levels ($t = -13.2340$; $P < 0.001$). Cases with Vitamin D levels <10 ng/ml, 10–20 ng/ml, 20–30 ng/ml, and >30 ng/ml had mean UAS score of 18, 15.17, 7.28, and 6.67, respectively.

Conclusion: In this study, deficient Vitamin D levels were more commonly seen in cases as compared to controls and correlated inversely with the severity of disease as measured by UAS7. Vitamin D might be one among the multiple factors involved in etiopathogenesis/exacerbation of CSU or may be an outcome of the disease process. Adding Vitamin D supplements may improve clinical outcome in patients of CSU and reduce use of corticosteroids and immunosuppressive.

Keywords: Chronic spontaneous urticaria, Chronic urticaria, Vitamin D

INTRODUCTION

Urticaria is a transient, circumscribed, pruritic swelling of the dermis.[1] It can be seen in association with angioedema which involves edema of the lower dermal and subcutaneous tissue. Angioedema can involve the mucous membranes taking up to 72 h for resolution. Chronic urticaria (CU) is defined as occurrence of wheals with or without angioedema for 6 or more weeks.[2] It has been reported in 0.1–3% of population with women reporting twice the prevalence.[3]

The pathogenesis of CU is yet to be fully characterized. Postulated mechanisms include immunological and genetic polymorphisms in histamine-related genes,[4] the direct effect of urticants,[5] infections,[6] drugs,[7] and pseudo allergens.[8] Chronic spontaneous urticaria (CSU) skin lesions show induction of multiple cells including mast cells, neutrophils, basophils, T lymphocytes, and eosinophils.[9] Various new mechanisms and exacerbating factors are being evaluated for their role in CU/CSU. One such factor being evaluated is Vitamin D.

The contribution of Vitamin D as an immune regulator was first determined with detection of its receptors on peripheral blood mononuclear cells. Since then Vitamin D has also been found to have effects on helper as well as regulatory subsets of T-cells, B-cells, and dendritic cells.[10] The effect of Vitamin D in innate immunity is mediated through stimulating chemotactic and phagocytic action of immune cells, activating transcription of antimicrobial molecules defensin β2 and cathelicidin.[11]

This study aimed to detect serum Vitamin D deficiency in CSU and its correlation with urticaria severity. It may add to ascertain the association of Vitamin D levels with urticaria considering the different geographical areas, topographic variation, and UV index along with different cultural habits and clothing in this region.

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MATERIAL AND METHODS

This study was undertaken after receiving approval from the Ethics Committee. It was a hospital-based case–control study involving 130 cases and 130 controls. Clinically, diagnosed cases of CU of any age and sex, duration (>6 weeks), and severity attending the Out-Patient Department of Dermatology from November 2018 to October 2019 were evaluated as cases.

Exclusion criteria comprised physical urticarias, patients with urticarial lesions lasting more than 24 h, patients with urticaria caused by infection, patients with history of urticaria caused by food/drug, patients with autoimmune disease, alcoholic, GI problems, skeletal disorders, renal disease, metabolic disorders including calcium, patients who received steroids, bisphosphonates, barbiturates, phototherapy, sulfasalazine, in the previous 3 months, Vitamin D supplementation, pregnancy, lactation, and patients who refused to give consent.

The control group was age- and gender-matched with cases. Detailed history, general physical, and systemic examination were performed. Clinical assessment of CSU was done on basis of Urticaria Activity Score (UAS7).

Routine investigations including complete blood profile, renal and liver function tests were done in all cases. Thyroid profile and blood sugar fasting were done to exclude thyroid and diabetes. Serum calcium and 25 (OH) Vitamin D were determined in both study groups.

On the basis of Vitamin D levels, patients were grouped as follows: <10 ng/ml: Severe Vitamin D deficiency, 10–20 ng/ml: Deficient levels, 20–30 ng/ml: Insufficient levels, and ≥30 ng/ml: Normal levels.

Statistical analysis

The collected data were analyzed with computer software Microsoft Excel and Statistical Package for the Social Science version 21.0. Reporting of data was done as mean ± standard deviation for quantitative variables and as proportions for qualitative variables. Unpaired "*t*"-test was used to test statistical difference between two group mean values and Chi-square test/Fisher's exact test was used to compare qualitative data. For determining statistical significance between more than two groups, analysis of variance was used. The correlation between mean Vitamin D level and duration, UAS7, gender, residence, and angioedema was examined using Pearson correlation and Spearman correlation.

RESULTS

The mean age in case and control was 29 ± 13.02 years and 29 ± 12.21 years. Forty-nine out of the total 130 cases and controls were female. The mean disease duration was 15.15 ± 1.60 months. Out of the total 130 cases, 62 (47.69%) patients gave a history of angioedema. Rural population dominated the study in both groups with 81 rural cases (62.31%) and 83 rural controls (63.85%). Urban population comprised 49 cases (37.69%) and 47 controls (36.15%) ($P = 0.797$).

Mean serum calcium levels in male cases were 9.16 ± 0.36 mg/dl and male controls were 9.25 ± 0.39 mg/dl. Mean serum calcium levels in female cases were 9.15 ± 0.32 mg/dl and female controls were 9.19 ± 0.34 mg/dl ($P = 0.538$) [Table 1].

Mean value of serum Vitamin D in cases was 14.29 ng/ml, while, in controls, it was 28.8 ng/ml. In cases, 99 patients had deficient (76.2%) serum Vitamin D levels, 25 (19.2%) had insufficient and 6 (4.6%) had normal levels. In controls, 63 patients had normal (48.5%) serum Vitamin D levels, followed by 46 (35.4%) with insufficient levels and 21 (16.1%) with deficient levels ($t = -13.2340$; $P < 0.001$) [Figure 1]. Mean serum Vitamin D level in female cases was 14.17 ng/ml and in male cases was 14.50 ng/ml ($P = 0.820$).

Mean value of Vitamin D in patients with angioedema was 14.19 mg/dl, while, in patients without angioedema, it was 14.38 mg/dl ($P = 0.890$).

Cases with disease duration fewer than 6 months had mean serum Vitamin D levels of 14.55 ng/ml. Mean Vitamin D levels in disease duration of 6 months–1 year, 1 year–3 years, and more than 3 years were 14.77 ng/ml, 13.31ng/ml, and 14.17ng/ml, respectively ($P = 0.8890$) [Table 2].

Cases with Vitamin D levels lower than 10 ng/ml had a mean UAS score of 18, with Vitamin D levels 10–20 ng/ml had mean UAS of 15.17, with levels 20–30 ng/ml had mean UAS of 7.28, and those with serum Vitamin D levels greater than 30 ng/ml had mean UAS score of 6.67 ($P < 0.001$) [Table 3]. The correlation between serum Vitamin D and urticaria activity as determined by UAS7 depicted that with decrease in serum Vitamin D levels disease activity increased. Interpretation was highly significant ($r = -0.538$, $P < 0.001$).

DISCUSSION

Vitamin D insufficiency is emerging as an important nutritional concern. The connection between autoimmune diseases such as diabetes mellitus, multiple sclerosis, lupus erythematosus, rheumatoid arthritis, vitiligo, psoriasis, inflammatory bowel disease, and Vitamin D deficiency[12] has led to increase in research concerning Vitamin D, health, and diseases. Data from animal and human studies have shown favorable immune related effects of Vitamin D supplementation.[11]

In this present study, we tried to review serum Vitamin D levels in patients of CSU and their relation to disease severity. Out of the total 130 cases in this study, 99 patients (76.2%) had deficient Vitamin D levels, 25 patients (19.2%) had insufficient levels, and six patients (4.6%) had normal Vitamin D levels. This was in disparity with the 130 controls, in whom 21 (16.1%) had deficient levels, 46 (35.4%) had insufficient levels, and 63 (48.5%) had normal Vitamin D levels. These findings are in accordance with various past studies, where association of serum Vitamin D levels with CSU has been

Table 1: Features of case and controls

	Case	Control
Total Number of patients	130	130
Mean age (years)	29±13.02	29±12.21
Gender (M/F)	81/49	81/49
Mean serum calcium	M: 9.16±0.36 mg/dl F: 9.15±0.32 mg/dl	M: 9.25±0.39 mg/dl F: 9.19±0.34 mg/dl

Table 2: Association of serum vitamin D with variables

Variable	Mean Vitamin D
Gender (*P*=0.820)	
Male	14.50 ng/ml
Female	14.17 ng/ml
Disease duration (*P*=0.8890)	
<6 Months	14.55 ng/ml
6 Months–1 Year	14.77 ng/ml
1–3 Years	13.31 ng/ml
>3 Years	14.17 ng/ml
Angioedema (*P*=0.890)	
Present	14.19 mg/dl
Absent	14.38 mg/dl

Table 3: Vitamin D levels and UAS7

Vitamin D levels (ng/ml) (r=−0.538, *P*<0.001)	Mean UAS7 score
<10	18
10–20	15.17
20–30	7.28
>30	6.67

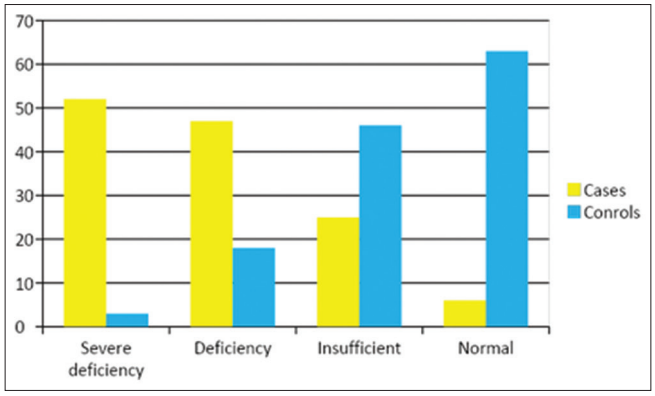

Figure 1: Bar chart showing distribution of cases and controls according to serum Vitamin D levels.

studied.[13-16] Contrasting results with no difference in levels between patients and controls have also been reported.[17,18]

The association of Vitamin D levels with UAS7 was found to be significant with a negative correlation between the two ($P < 0.001$) (r= −0.538). Supportive findings were obtained in previously done studies[19,20] wherein serum Vitamin D levels were found to have a negative correlation with UAS. In contrast to these few studies[21,22] have shown no association of DLQI scores and UAS7 with serum Vitamin D levels.

As seen in previous studies[20,23], this study also supported lack of association between Vitamin D levels and gender. Considerably lower levels of Vitamin D in females as compared to males have also been documented[19,24], possibly attributed to biological and behavioral differences.

No significant association of Vitamin D levels with disease duration has been seen as supported by previous studies.[13,25]

Various studies are available supporting the supplementation of Vitamin D in CSU[21] with significant improvement seen in DLQI scores and UAS7 in Vitamin D supplemented group. Around 70% of patients[26] have shown clearance of symptoms with Vitamin D supplementation. We did supplement our patients with Vitamin D, but our follow-up of patients was insufficient and inadequate to draw any conclusion.

Limitations

The sample size was small. Subjective score of pruritus and UAS7 was used. Seasonal variation of Vitamin D was not assessed. Follow-up of patients to evaluate the therapeutic role of Vitamin D supplementation could not be done.

CONCLUSION

In our study of assessing serum Vitamin D levels in CSU, it was found that Vitamin D deficiency is more common in cases of CSU as compared to controls. Furthermore, Vitamin D levels are inversely correlated with the severity of disease as measured by UAS7. However, no significant association was seen with duration of disease and the presence of angioedema. Vitamin D may be one of the factors involved in etiopathogenesis or exacerbation of CSU or may be an outcome of the disease process. Adding Vitamin D supplements may improve the clinical outcome in patients with CSU and may reduce use of corticosteroids and immunosuppressives. Clinical studies confirming role of Vitamin D as a therapeutic agent in CSU are required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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