

**Original Research Article****A Descriptive Study of Vitamin D Deficiency in Chronic Urticaria and Its Possible Role in Pathogenesis**

Authors

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Kaviarasan PK**Abstract**

Background: Chronic urticaria, though is not lethal, it significantly affects the quality of life of patients. The cause is idiopathic in 55% and autoimmune in 45% of chronic urticaria cases. Role of vitamin D3 in various immune mediated skin diseases like vitiligo, atopic dermatitis and psoriasis has been already explored and well established. It is now known that chronic urticaria is often triggered by autoimmune reactions, since vitamin D plays an important role in innate and adaptive immunity, it is more likely to be associated with chronic urticaria

Aim: The purpose of the present study was to evaluate the serum vitamin D3 levels and other clinical characteristics in patients of chronic urticaria.

Method: This is a descriptive study which was performed in about 36 subjects with chronic urticaria who attended the outpatient Department of Dermatology in a tertiary care centre. Serum vitamin D3 levels were measured and stratified into vitamin D deficiency, insufficiency and sufficiency as per standard reference range and compared with healthy controls to ascertain the relationship between vitamin D status and chronic urticaria.

Results: Serum vitamin D3 level was significantly lower in chronic urticaria subjects as compared with the healthy controls. The prevalence of vitamin D deficiency (<30 ng/ml) was significantly higher in patients with chronic urticaria.

Conclusion: The present study showed a strong positive correlation between vitamin D deficiency and chronic urticaria. This study also warrants that each subject with chronic urticaria should be screened for serum vitamin D3 levels before initiating treatment.

Keywords: Chronic urticaria, vitamin deficiency, VDR receptors, immunomodulatory, 5D pruritus score, Autologous Serum Skin Test (ASST).

Introduction

Urticaria more commonly known as “hives” is a prevalent disorder that affects between 15-25% of the population at some point in their lifetime¹. Chronic urticaria is defined as the presence of evanescent wheals which occur for greater than 6 weeks without an identifiable trigger¹. The cause remains idiopathic in 55% and autoimmune in 45% of cases with circulating histamine releasing antibodies against high affinity IgE receptor or IgE.

Vitamin D is known to have modulatory effects on dendritic cells and monocytes, and the functional impairment of these cells interferes with the production of various cytokines. The impaired function of various immunocytes due to low vitamin D levels might lead to increase of circulating pro-inflammatory cytokines and imbalance of regulatory T-cell cytokine production, which cause worsening of chronic urticaria².

Method

This study is a descriptive study which was performed in about 36 study subjects with chronic urticaria with duration more than 6 weeks who attended the outpatient Department of Dermatology in a tertiary care centre. A detailed written and informed consent was obtained from all the participants and ethical clearance was sought from the institutional ethical committee. Along with the 36 study subjects, an equal number of sex and age-matched healthy volunteers from hospital visitors with no history of urticaria was chosen as the control group. For each patient, a complete medical history, detailed physical and cutaneous examination was done and a questionnaire regarding the characteristics of the disease and exacerbating factors was taken. Routine baseline investigations including complete blood count, urine analysis, ESR, C-reactive protein, serum IgE Helicobacter pylori antibody serology, thyroid function tests were done for all the study subjects. In addition autologous serum skin test (ASST) were

performed. Urticarial activity in study subjects were assessed using 5D pruritus score - a multidimensional questionnaire which includes five domains namely degree, duration, direction, disability and distribution of pruritus per 24 hours with minimum score <8 to maximum score of >25.

Investigations specific to our study like serum 1-25 (OH) vitamin (vitaminD3) levels were measured in all the study subjects and healthy controls using Chemiluminescent immunoassay technique (CLIA). Values less than 20 ng/mL were considered as vitamin D deficient, between 20 ng/mL and 30 ng/mL as vitamin D insufficiency, and values more than 30 ng/mL were categorized as sufficient.

Inclusion Criteria

Patients aged 14-60 years of either sex, with persistent signs and symptoms of urticaria (itching and wheals) for more than 6 weeks.

Exclusion Criteria

Children, Pregnant, Lactating mothers, immunocompromised individuals, subjects with acute urticaria were excluded from the study.

Statistical Analysis

Statistical analysis was performed using IBM SPSS statistics version 20 for windows. The baseline characteristics in the study groups were analysed using ANOVA with 95% confidence interval for mean and the results were expressed in mean \pm standard deviation. Independent sample 't' test was used to compare the mean serum vitamin D3 levels between the study group and healthy control group. Analysis was carried out at 5% level of significance and $p < 0.05$ was considered as significant.

Results

A total of 36 study subjects were enrolled in the present study. Overall there was no significant difference in age of chronic urticaria subjects (Mean years \pm SD 35.806 \pm 12.7365) versus healthy controls (Mean years \pm SD 36.763 \pm 12.7365) and patients were predominantly female (52.8%) versus males (47.2%). Mean duration of urticaria

in months was 15.500±19.699. Mean serum IgE in chronic urticaria subjects was 643.186 ±683 compared to healthy controls (54.333±533). ASST was found positive in 44.4 % of study subjects. Helicobacter pylori association was found to be

11.11% among chronic urticaria subjects. Hypothyroidism association was found to be 13.388 % among the study subjects. Mean 5D pruritus score were higher in vitamin D Deficiency study subjects.

Table1: Clinical characteristics of patients and controls

Characteristics	Chronic urticaria subjects (n=36)	Healthy controls (n=36)	Significance P<0.05
Age in months	35.806±12.7365	36.763±12.7365	Not significant
Gender M :F	17:19	18:18	Not significant
Mean serum IgE	643.186 ±683	(54.333±533).	Significant
Mean5D Pruritus score	16.700 ± 1.5347	-	-

Serum Vitamin D3 Level

Mean ± SEM Vit D3 was found to be 21.52 ± 1.428ng/ml in chronic urticaria subjects versus 27.17 ± 1.677ng/ml in healthy controls was proved to be statistically significant by independent paired ‘t’ test. (tab.2, fig.1). Low

levels of vitamin D levels were observed in 83.4% of study subjects compared to healthy controls (66.6%) (tab.3). Females with chronic urticaria had predominantly lower levels of vitamin D (50%) when compared to males (33.33%) (Tab.4 fig.2)

Table 2: Independent paired ‘t’ test

Mean Serum VitD3 Levels	Study subjects	Healthy Controls	t value	p value
	21.52±1.428	27.17±1.677	-2.57	0.012

Fig 1

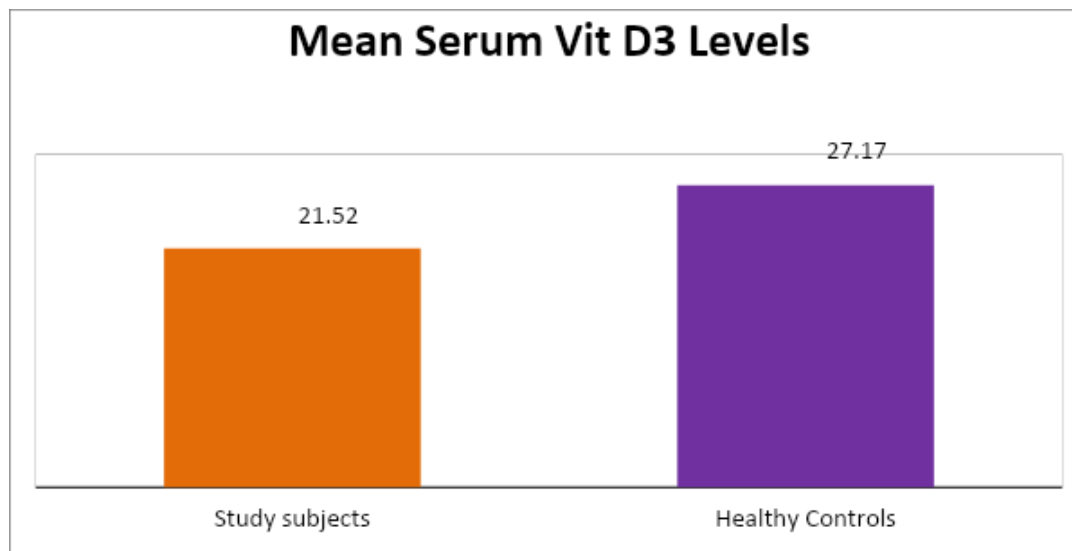


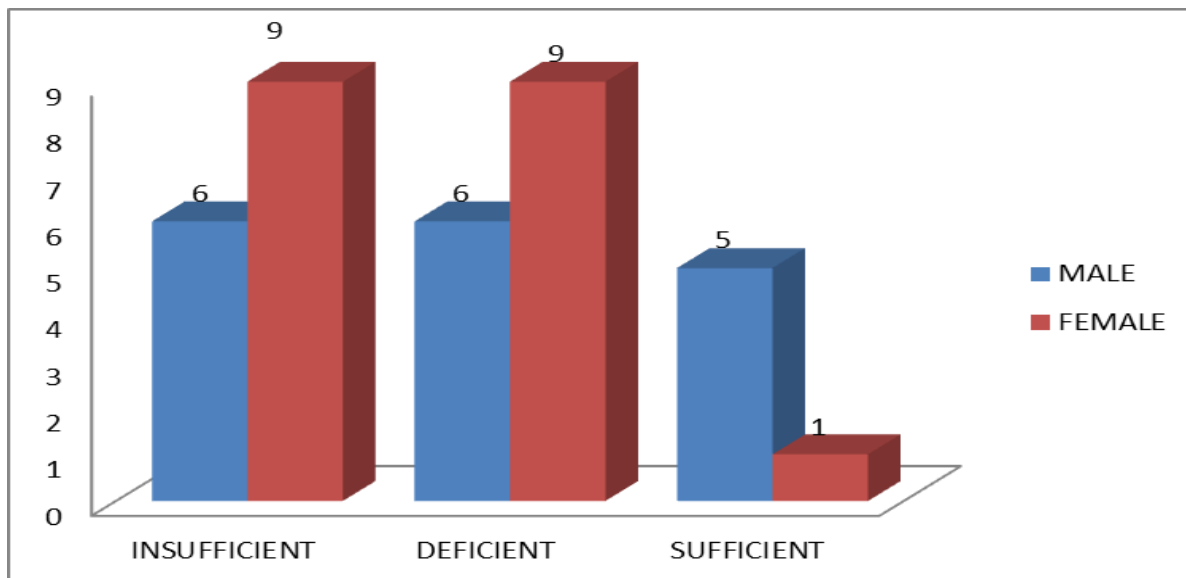
Table 3: Vitamin D status in patients and controls

Vitamin D3 Levels	Study subjects	Healthy controls
Vitamin D deficiency	15 (41.66%)	8 (22.22%)
Vitamin D insufficiency	15(41.66%)	16 (44.44%)
Vitamin D Sufficiency	6 (16.66%)	12 (33.33)

Table 4: Serum vitamin D3 Levels among gender in study subjects

VITAMIN D LEVELS	MALE	FEMALE
Insufficient	6 (16.66%)	9 (25%)
Deficient	6 (16.66%)	9 (25%)
Sufficient	5 (13.88%)	1 (2.77%)
Total	17 (47.22%)	19 (52.77%)

Fig.2



Discussion

Chronic urticaria, a heterogenous group of skin disease with diverse etiological factors, at times the cause is almost not found, which severely debilitates the day to day activities of the individuals. However in 40 % of cases, chronic urticaria is found to be autoimmune in nature with circulating autoantibodies against IgE and its receptors signifies the role of vitamin D as a immunomodulator in the pathogenesis of chronic urticaria.

Role of Vitamin D3 In the pathogenesis of chronic urticaria

Vitamin D can exert immunomodulatory actions in both innate and adaptive immunity primarily by modifying vitamin D receptors (VDR) receptors on mast cells, inhibiting mast cell differentiation and inducing mast cell apoptosis thereby reducing the recurrent episodes of urticaria³.

Mast cells express VDR and respond to 1-25(OH)₂D₃. Mechanism of action for 1-25(OH)₂D₃ in inhibiting mast cell activity is by means of down-regulating mast cell development, differentiation, and eventually function via VDR,

inhibition of IL3, which is a crucial cytokine involved in mast cell survival, proliferation and maturation, induction of apoptosis of bone marrow mast cell precursors ,inhibits the release of inflammatory mediators by bone marrow mast cells stimulated by FcεRI cross-linking.⁴

Calcitriol also plays a role in mast cell activation and produces interleukin 10 (IL-10) without causing degranulation. Calcitriol maintains mast cell stability and reduces histamine production. Generated IL-10 will inhibit the production of immunoglobulin E-dependent pro-inflammatory mediators. Mediators will reduce leukotriene C4 involved in eosinophil activation process.⁵

Hence, low vitamin D levels might lead to increase of circulating pro-inflammatory cytokines and imbalance of regulatory T-cell cytokine production, which cause worsening of chronic urticaria.

Vitamin D is considered now as a marker for chronic inflammatory disease, but also for the acute phase of inflammation it could be suspected that low vitamin D levels among patients initially presenting with acute urticaria may provide a

marker for predicting higher probability to progression to the chronic form.²

In our study, the mean age in the study group was found to be 35.806 ± 12.7365 vs 36.763 ± 12.7365 . This is similar to previous study done by Chandrasekar et al.⁶ In our study, chronic urticaria patients were predominantly females (52.8%) versus males (47.2%). This female preponderance in chronic urticaria subjects in our study was very similar to previous studies done by Chandrasekar et al.⁶ and Andy Rorie et al. Mean duration of chronic urticaria in our study was found to be 36.00 ± 15.50 which is similar to previous study done by Nazila Ariaee et al. Mean serum IgE in chronic urticaria subject was found to be 643.186 ± 683 compared to healthy controls (54.33 ± 533). This is similar to study done by Kamini CR et al.⁷ ASST was found to be positive in 44.4% of the study subjects. This is similar to study done by Bajaj et al.⁸

Our study showed a strong positive correlation between vitamin D deficiency and chronic urticaria. This is similar to previous studies by Rather et al. who showed a significant reduction in the levels of vitamin D3 in patients with CSU as compared to healthy control, Wu et al. showed that the majority of people with urticaria (54.6%) had vitamin D levels below normal limits, Chandrashekar et al. proved Significant lower vitamin D levels among chronic urticaria patients and controls, Rasool et al. (Randomized case-control study) showed Low serum 25(OH)D levels in 91% of CSU patients and 64% of the healthy subjects.⁹

Limitations of the study

Our study had a small sample size. Further large scale studies are needed to replicate this association. Since Hypovitaminosis D has been recently established in healthy Indian population, low serum vitamin D levels in most of our chronic urticaria subjects is whether due to inadequate diet, less sunlight exposure, pattern of clothing is unclear. Furthermore studies are needed to

evaluate the etiopathogenesis of vitamin D and the association in chronic urticaria.

Conclusion

The present study showed significantly reduced vitamin D3 levels in chronic urticaria subjects compared to healthy controls and explained the possible role of vitamin D3 as an immunomodulator in the pathogenesis of chronic urticaria. This study also warrants that each subject with chronic urticaria should be screened for serum vitamin D3 levels before starting a treatment.

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