RESEARCH PAPER

Serum 25-Hydroxyvitamin D Levels and Disease Activity in Chronic Spontaneous Urticaria: A Multicentre Cross-Sectional Study from South India

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ABSTRACT

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Background. Chronic spontaneous urticaria (CSU) is a mast-cell–driven disorder in which an immunomodulatory role for vitamin D has been proposed. Data from Indian populations relating serum 25-hydroxyvitamin D [25(OH)D] to an objective measure of disease activity remain limited.

Objective. To examine the association between serum 25(OH)D and CSU disease activity, quantified by the seven-day Urticaria Activity Score (UAS7), and to determine whether it is independent of demographic, anthropometric and clinical covariates.

Methods. In this multicentre cross-sectional study, 150 adults with CSU across six centres in underwent standardized assessment, UAS7 scoring, and measurement of serum 25(OH)D and routine inflammatory markers. Associations were tested with Pearson and Spearman correlation, one-way ANOVA with Tukey post-hoc comparison, and multivariable linear regression.

Results. Mean age was 38.7 ± 11.2 years; 82 (54.7%) were women. Vitamin D deficiency (<20 ng/mL) was present in 70 (46.7%), insufficiency (20–29 ng/mL) in 62 (41.3%) and sufficiency (≥30 ng/mL) in 18 (12.0%). Serum 25(OH)D correlated inversely with UAS7 (Pearson $r = –0.55$; Spearman $\rho = –0.52$; both $p < 0.001$). Mean UAS7 fell stepwise across the deficient (26.2 ± 8.8), insufficient (20.6 ± 8.3) and sufficient (11.7 ± 7.0) groups (ANOVA $F = 23.1$, $p < 0.001$; all pairwise $p < 0.001$). In multivariable regression, each 1 ng/mL increase in 25(OH)D was independently associated with a 0.62-point lower UAS7 (95% CI –0.78 to –0.46, $p < 0.001$; adjusted $R^2 = 0.31$).

Conclusions. Lower serum 25(OH)D was independently associated with greater CSU disease activity in this South Indian cohort, supporting assessment of vitamin D status in CSU and motivating interventional trials of supplementation.

Keywords: Chronic Spontaneous Urticaria, Chronic Idiopathic Urticaria, Vitamin D, · 25-Hydroxyvitamin D, Urticaria Activity Score (UAS7).

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INTRODUCTION

Chronic spontaneous urticaria (CSU), historically termed chronic idiopathic urticaria, is defined by the recurrent appearance of wheals, angioedema, or both, on most days for six weeks or longer, in the absence of a consistent external eliciting trigger (1). It affects an estimated 0.5–1% of the population at any given time, occurs roughly twice as often in women, and carries a disease burden — sleep disruption, impaired daytime function and reduced quality of life — that is comparable to that of ischaemic heart disease (2,3). Although second-generation H1-antihistamines, up-dosed as required, remain first-line therapy, a substantial proportion of patients remain symptomatic, and the search for modifiable contributory factors is therefore of continuing clinical interest (4).

The pathophysiology of CSU centres on the cutaneous mast cell and its degranulation, with autoimmunity — including functional IgG autoantibodies to the high-affinity IgE receptor (FcεRIα) or to IgE itself — implicated in a proportion of patients (5,6). Against this background, vitamin D has attracted attention because 1,25-dihydroxyvitamin D and the vitamin D receptor are expressed throughout the innate and adaptive immune systems, where they promote regulatory T-cell activity, restrain T-helper-1 and T-helper-17 responses, and modulate mast-cell reactivity. These immunomodulatory properties provide a biological rationale for a link between low vitamin D status and heightened urticarial activity (7).

Vitamin D deficiency is highly prevalent across the Indian subcontinent despite abundant sunshine, owing to skin pigmentation, largely indoor occupations, conservative dress, vegetarian dietary patterns and limited food fortification (8). Several case-control studies have reported lower serum 25(OH)D in patients with chronic urticaria than in controls, and a small randomized study suggested symptomatic benefit from supplementation (9). However, relatively few studies have related 25(OH)D concentrations to a validated, objective measure of disease activity within an Indian population, and fewer still have examined whether any association is independent of confounders such as adiposity and disease duration (10).

We therefore conducted a multicentre cross-sectional study with two aims: to quantify the association between serum 25(OH)D and CSU disease activity as measured by UAS7; and to determine whether any such association persists after adjustment for demographic, anthropometric and clinical covariates. We hypothesized that lower serum 25(OH)D would be associated with higher UAS7, independent of these covariates.

MATERIALS AND METHODS

Study design and setting

This multicentre, cross-sectional observational study was conducted across six tertiary-care dermatology centres in South India, and is reported in accordance with the STROBE statement.

Participants

Consecutive adults aged 18–70 years with a clinical diagnosis of CSU of at least six weeks' duration were eligible. Exclusion criteria were inducible (physical) urticaria as the sole diagnosis, urticarial vasculitis, current systemic corticosteroid or immunosuppressive therapy, known chronic kidney or liver disease, granulomatous disease, malignancy, pregnancy or lactation, and recent vitamin D supplementation where it would confound baseline status. Prior supplementation and antihistamine regimen were recorded for adjustment rather than exclusion.

Variables and measurements

Clinical assessment. Standardized history and examination captured age, sex, residence (urban/rural), recruiting centre, CSU duration, presence of angioedema, personal history of atopy, personal or family history of autoimmune disease, smoking status, and self-reported daily sun exposure. Height and weight were measured and body-mass index (BMI) calculated as weight (kg) divided by height (m) squared.

Disease activity. Disease activity was quantified using the UAS7, the sum of once-daily patient-recorded scores over seven consecutive days, each day scoring the number of wheals (0–3) and pruritus intensity (0–3) for a weekly total of 0–42. Bands were defined as urticaria-free (0–6), well-controlled/mild (7–15), moderate (16–27) and severe (28–42).

Laboratory measurements. Fasting venous blood was drawn at enrolment. Serum total 25(OH)D was categorized, following Endocrine Society thresholds, as deficient (<20 ng/mL), insufficient (20–29 ng/mL) or sufficient (≥30 ng/mL). Supporting investigations comprised absolute eosinophil count, total serum IgE, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), thyroid-stimulating hormone (TSH) and albumin-corrected serum calcium.

Statistical analysis

Continuous variables are summarized as mean ± standard deviation and categorical variables as counts and percentages. The primary analysis tested the association between serum 25(OH)D and UAS7 using the Pearson correlation coefficient, with the Spearman rank coefficient reported as a distribution-free confirmation. UAS7 was compared across vitamin D status categories by one-way ANOVA

with Tukey's honestly-significant-difference test. Categorical associations were examined with the chi-square test. A multivariable linear regression model was fitted with UAS7 as the dependent variable and serum 25(OH)D, age, sex, BMI, disease duration, angioedema and autoimmune history as independent variables; coefficients are presented with 95% confidence intervals. A two-sided $p < 0.05$ was considered significant. Analyses were performed in Python (pandas, SciPy, statsmodels). A sample of 150 provides >99% power to detect a moderate correlation ($|r| = 0.30$) at $\alpha = 0.05$ and satisfies the events-per-variable requirement for the regression model.

Results

Participant characteristics

A total of 150 patients with CSU were analysed. Mean age was 38.7 ± 11.2 years (range 18–63) and 82 (54.7%) were women. Mean BMI was 24.7 ± 3.9 kg/m². Most were urban residents (104; 69.3%). Mean disease duration was 23.0 ± 15.0 months. Angioedema was reported by 52 (34.7%), atopy by 50 (33.3%) and autoimmune history by 13 (8.7%). Mean UAS7 was 22.1 ± 9.5 and mean serum 25(OH)D was 20.7 ± 8.4 ng/mL (Table 1).

Table 1: Baseline characteristics of the study population (N = 150).

Characteristic	Value
Age, years — mean ± SD	38.7 ± 11.2
Female sex, n (%)	82 (54.7)
BMI, kg/m² — mean ± SD	24.7 ± 3.9
Urban residence, n (%)	104 (69.3)
CSU duration, months — mean ± SD	23.0 ± 15.0
Angioedema present, n (%)	52 (34.7)
Atopy history, n (%)	50 (33.3)
Autoimmune history, n (%)	13 (8.7)
UAS7 score — mean ± SD	22.1 ± 9.5
Serum 25(OH)D, ng/mL — mean ± SD	20.7 ± 8.4
Vitamin D deficient (<20 ng/mL), n (%)	70 (46.7)
Vitamin D insufficient (20–29 ng/mL), n (%)	62 (41.3)
Vitamin D sufficient (≥30 ng/mL), n (%)	18 (12.0)

BMI, body-mass index; CSU, chronic spontaneous urticaria; UAS7, seven-day Urticaria Activity Score; 25(OH)D, 25-hydroxyvitamin D.

Serum 25(OH)D and disease activity

Serum 25(OH)D was moderately and significantly inversely correlated with UAS7 (Pearson r = –0.55, 95% CI –0.65 to –0.42, $p < 0.001$), confirmed by the Spearman coefficient ($\rho = –0.52$, $p < 0.001$). Higher vitamin D concentrations were consistently associated with lower measured urticarial activity across the observed range (Figure 1).

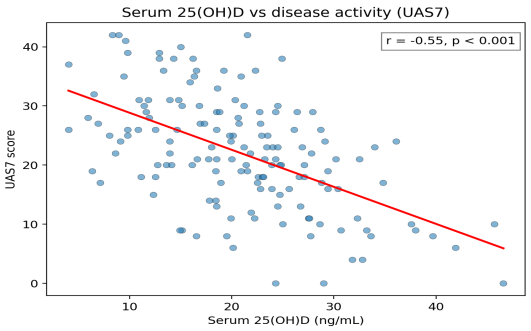

Figure 1. Scatterplot of serum 25(OH)D against UAS7. *Each point is one participant; the red line is the ordinary-least-squares fit. Pearson r = –0.55, p < 0.001.*

3.3 Disease activity across vitamin D status categories

Mean UAS7 decreased stepwise across worsening vitamin D status — 26.2 ± 8.8 (deficient), 20.6 ± 8.3 (insufficient) and 11.7 ± 7.0 (sufficient) (ANOVA $F = 23.1$, $p < 0.001$). All pairwise Tukey comparisons were significant: deficient vs insufficient (mean difference 5.5, $p < 0.001$), deficient vs sufficient (14.5, $p < 0.001$) and insufficient vs sufficient (8.9, $p < 0.001$) (Table 2, Figure 2). Reciprocally, mean serum 25(OH)D fell progressively across the mild, moderate and severe UAS7 bands (Figure 3).

Table 2: Disease activity and clinical features by vitamin D status.

Variable	Deficient (n=70)	Insufficient (n=62)	Sufficient (n=18)	p-value
Serum 25(OH)D, ng/mL	13.7 ± 4.2	24.3 ± 2.8	35.7 ± 5.0	<0.001
UAS7 score	26.2 ± 8.8	20.6 ± 8.3	11.7 ± 7.0	<0.001
Angioedema, n (%)	28 (40.0)	19 (30.6)	5 (27.8)	0.428

Values are mean ± SD unless stated. p from one-way ANOVA (continuous) or chi-square test (categorical). 25(OH)D, 25-hydroxyvitamin D; UAS7, seven-day Urticaria Activity Score.

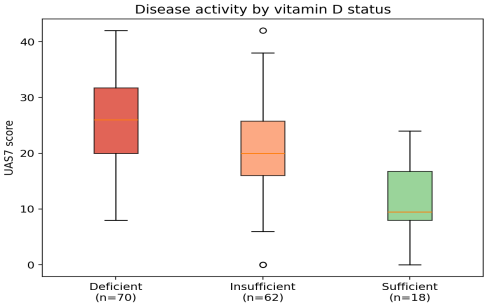

Figure 2: UAS7 by vitamin D status category. *Boxes show median and interquartile range; whiskers show range. ANOVA $p < 0.001$; all pairwise comparisons $p < 0.001$.*

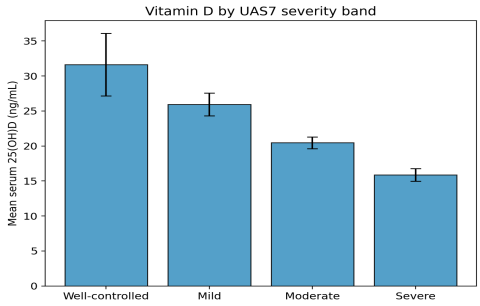

Figure 3: Mean serum 25(OH)D across UAS7 severity bands. *Error bars denote the standard error of the mean.*

3.4 Correlations with inflammatory markers

UAS7 was positively correlated with ESR (r = 0.61), CRP (r = 0.59) and absolute eosinophil count (r = 0.25); serum 25(OH)D was inversely correlated with ESR (r = –0.36), CRP (r = –0.26) and eosinophil count (r = –0.22) (all $p \leq 0.007$). No significant association was seen with age, BMI, disease duration, total IgE, TSH or corrected calcium (Table 3).

Table 3. Correlations of laboratory and clinical variables with serum 25(OH)D and UAS7.

Variable	r with 25(OH)D (p)	r with UAS7 (p)
ESR, mm/hr	–0.36 (<0.001)	+0.61 (<0.001)
CRP, mg/L	–0.26 (0.001)	+0.59 (<0.001)
Absolute eosinophil count	–0.22 (0.007)	+0.25 (0.002)
Total IgE, IU/mL	+0.06 (0.489)	–0.02 (0.820)
Age, years	–0.03 (0.758)	+0.04 (0.652)
BMI, kg/m²	+0.12 (0.142)	–0.03 (0.739)
CSU duration, months	–0.00 (0.985)	–0.01 (0.884)
TSH, mIU/L	–0.03 (0.703)	+0.08 (0.354)
Corrected calcium, mg/dL	+0.01 (0.937)	–0.02 (0.783)

r, Pearson correlation coefficient. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; TSH, thyroid-stimulating hormone.

Multivariable analysis

Serum 25(OH)D remained an independent predictor of UAS7 after adjustment: each 1 ng/mL increase was associated with a 0.62-point lower UAS7 (95% CI –0.78 to –0.46, $p < 0.001$). Angioedema was independently associated with a 3.8-point higher UAS7 (95% CI 1.1 to 6.6, p = 0.006), whereas age, sex, BMI, disease duration and autoimmune history were not significant. The model explained about 31% of the variance in UAS7 (adjusted $R^2 = 0.31$) (Table 4).

Table 4: Multivariable linear regression with UAS7 as the dependent variable.

Predictor	β	95% CI	p-value
Serum 25(OH)D (per ng/mL)	–0.62	–0.78 to –0.46	<0.001
Angioedema (present)	+3.83	1.10 to 6.56	0.006
Female sex	+1.01	–1.65 to 3.66	0.455
Age (per year)	–0.00	–0.12 to 0.11	0.965
BMI (per kg/m²)	+0.09	–0.24 to 0.43	0.585
CSU duration (per month)	–0.02	–0.11 to 0.07	0.672
Autoimmune history	+0.71	–3.86 to 5.27	0.760

β, unstandardized regression coefficient; CI, confidence interval; adjusted $R^2 = 0.31$.

Discussion

In this multicentre cross-sectional study of 150 South Indian adults with CSU, lower serum 25-hydroxyvitamin D was associated with greater disease activity (11). The inverse correlation with UAS7 was of moderate strength and highly significant, disease activity declined stepwise across the deficient, insufficient and sufficient categories, and the association persisted after adjustment for age, sex, adiposity, disease duration, angioedema and autoimmune history (12). Vitamin D status therefore behaved as an independent correlate of disease activity rather than a marker confounded by demographic or anthropometric factors.

These findings are concordant with earlier work reporting lower 25(OH)D in chronic urticaria and an inverse relationship with severity (13). The parallel correlations we observed — vitamin D falling, and UAS7 rising, with increasing ESR, CRP and eosinophil count — are consistent with the hypothesis that vitamin D insufficiency accompanies a more inflammatory phenotype, aligning with the recognized immunoregulatory actions of vitamin D on regulatory T cells, Th1/Th17 cytokines and mast-cell activation. The near-absence of any relationship with total IgE, TSH or serum calcium argues against a non-specific metabolic explanation (14).

The independent contribution of angioedema to higher UAS7 is clinically coherent, since concomitant angioedema marks a more active and burdensome course (15). That vitamin D retained its association after adjustment strengthens the case that the relationship is not merely a reflection of overall chronicity or body composition. Taken with the

earlier randomized observation that add-on high-dose vitamin D3 reduced urticaria symptom scores, our results provide a rationale — though not proof — for evaluating vitamin D repletion as an adjunct in patients with CSU and documented deficiency.

The high prevalence of hypovitaminosis D in this cohort (88% below the sufficiency threshold) mirrors the documented burden across India and underscores the low cost and wide availability of both measurement and supplementation (16). If a causal contribution were confirmed, correction of deficiency would represent a simple, inexpensive and safe adjunct to antihistamine therapy.

4.1 Strengths and limitations

Strengths include the multicentre design, the use of a validated and objective activity measure (UAS7), and multivariable adjustment for principal confounders. Limitations must be emphasized. The cross-sectional design precludes causal inference: reverse causation (more severe, housebound disease leading to less sun exposure and lower vitamin D) cannot be excluded. The absence of a non-urticarial control group limits interpretation of the deficiency prevalence. Season of sampling, dietary vitamin D intake and skin phototype were not fully modelled and may confound the association, and a single 25(OH)D measurement may not reflect long-term status.

Conclusion

In this South Indian cohort, lower serum 25-hydroxyvitamin D was independently associated with higher CSU disease activity, and vitamin D concentrations tracked inversely with systemic inflammatory markers. These observations support routine assessment of vitamin D status in patients with CSU and provide a rationale for randomized trials of supplementation as an adjunct to standard therapy.

REFERENCES

1. Grattan CEH, Sabroe RA, Greaves MW. Chronic urticaria. J Am Acad Dermatol. 2002;46(5):645–657
2. Kaplan AP. Chronic urticaria: pathogenesis and treatment. J Allergy Clin Immunol. 2004;114(3):465–474.
3. Zuberbier T, Asero R, Bindslev-Jensen C, et al. EAACI/GA²LEN/EDF/WAO guideline: definition, classification and diagnosis of urticaria. Allergy. 2009;64(10):1417–1426.
4. Zuberbier T, Asero R, Bindslev-Jensen C, et al. EAACI/GA²LEN/EDF/WAO guideline: management of urticaria. Allergy. 2009;64(10):1427–1443.
5. Mlynek A, Zalewska-Janowska A, Martus P, Staubach P, Zuberbier T, Maurer M. How to assess disease activity in patients with chronic urticaria? Allergy. 2008;63(6):777–780.
6. Kaplan AP, Greaves M. Pathogenesis of chronic urticaria. Clin Exp Allergy. 2009;39(6):777–787.
7. Maurer M, Weller K, Bindslev-Jensen C, et al. Unmet clinical needs in chronic spontaneous urticaria: a GA²LEN task force report. Allergy. 2011;66(3):317–330.
8. Greaves MW. Chronic idiopathic urticaria. Curr Opin Allergy Clin Immunol. 2003;3(5):363–368.
9. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357(3):266–281.
10. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911–1930.
11. Adorini L, Penna G. Control of autoimmune diseases by the vitamin D endocrine system. Nat Clin Pract Rheumatol. 2008;4(8):404–412.
12. Baeke F, Takiishi T, Korf H, Gysemans C, Mathieu C. Vitamin D: modulator of the immune system. Curr Opin Pharmacol. 2010;10(4):482–496.
13. Thorp WA, Goldner W, Meza J, Poole JA. Reduced vitamin D levels in adult subjects with chronic urticaria. J Allergy Clin Immunol. 2010;126(2):413.
14. Rorie A, Goldner WS, Lyden E, Poole JA. Beneficial role for supplemental vitamin D3 treatment in chronic urticaria: a randomized study. Ann Allergy Asthma Immunol. 2014;112(4):376–382.
15. Grzanka A, Machura E, Mazur B, et al. Relationship between vitamin D status and the inflammatory state in patients with chronic spontaneous urticaria. J Inflamm (Lond). 2014;11(1):2
16. Movahedi M, Tavakol M, Rahmani K, et al. Vitamin D deficiency in chronic idiopathic urticaria. Iran J Allergy Asthma Immunol. 2015;14(2):222–227