Open Access

Original Article

Association of Chronic Urticaria with Decreased Vitamin D Levels in Female Patients visiting Tertiary Care Hospital in Pakistan

Sana Waqar Qureshi, Farid ur Rehman, Bilqees Fatima, Shamsa Kanwal, Sibqa Jamil

Fauji Foundation Hospital, Rawalpindi Pakistan

ABSTRACT

Objective: To evaluate association of chronic urticaria with decreased serum vitamin D levels in female patients.
Study Design: Comparative cross-sectional study.
Place and Duration of Study: Fauji Foundation Hospital, Rawalpindi Pakistan, from Jan 2020 to Jan 2021.
Methodology: Seventy female patients with chronic urticaria (Group-1) and 70 female age matched patients without urticaria (Group-2) were enrolled in the study by nonprobability sampling technique. Both groups were stratified into 3 age based groups: children (0-18 years), young adults (19-40 years) and middle aged (40-60 years). Inclusion criteria comprised of patients of either sex and of age less than 60 years showing urticarial symptoms at least twice a week for more than 6 weeks. Serum vitamin D level was evaluated by ELISA (enzyme linked immunosorbent assay). A deficiency in vitamin D was defined as serum 25-(OH)D concentrations <30 ng/mL.
Results: Out of 140 patients, 105(75%) had normal vitamin D levels (group 1=48(45.7%) & group-2=57(54.3%)) whereas 35(25%) were deficient; group 1=22(62.8%) & group 2=13(37.2%) (*p*-value =0.07). In the children group, 13 out of 15(86.6%) were sufficient whereas 2(13%) were deficient (*p*-value=0.17). In the young adults group, 40 out of 58(68.9%) were sufficient and 18(31%) were deficient (*p*-value=0.06). In the middle aged group, 52 out of 67(77.6%) were sufficient and 15(22%) were deficient (*p*-value=0.82).
Conclusion: There is no association of chronic urticaria with decreased serum vitamin D levels.

Keywords: Chronic Urtricaria, Urticaria Activity Score, Vitamin D.

How to Cite This Article: *Qureshi SW, Rehman F, Fatima B, Kanwal S, Jamil S. Association of Chronic Urticaria with Decreased Vitamin D Levels in Female Patients visiting Tertiary Care Hospital in Pakistan. Pak Armed Forces Med J 2025; 75(Suppl-2): S331-S334.*
DOI: https://doi.org/10.51253/pafmj.v75iSUPPL-2.7394

INTRODUCTION

Chronic urticaria is defined as episodes of recurrent hives, with or without angioedema, persisting for 6 weeks or longer.[1] According to a recent meta-analysis, point prevalence of chronic urticaria in the Asian population was higher (1.4%) than that in the Europe (0.5%) and Northern America (0.1%).[2] Etiology of chronic urticaria is extensive including drugs, food, food additives, chronic infections and infestations, systemic and autoimmune diseases,[3] etc. In spite of thorough laboratory investigations, 50% cases of chronic urticaria remain undiagnosed. In many cases, the etiology of chronic urticaria is multifactorial. This poses great difficulty for the clinician to treat these patients effectively as a number of clinical, chemical and serological workup is required to reach the root cause of chronic urticaria.[3] Vitamin D is a fat-soluble vitamin. It is synthesized in the skin from the nonenzymatic conversion of provitamin D3 to previtamin D3. Vitamin D is stored in the fat cells. In the blood, vitamin D circulates in the form of 25-hydroxyvitamin D3 (25[OH]D3). Measurement of (25[OH]D3) levels reflects solar and dietary exposure. Active form of vitamin D is 1,25-dihydroxyvitamin D (1,25[OH]2D) that is converted in the kidney.[4,5] Vitamin D exerts its immunomodulatory actions on both innate and adaptive immunity.[7] It influences allergic response by down regulating IgE-mediated mast cell activation.[6] It also influences autoimmune response by enhancing T regulatory cells and suppressing T helper (TH-1 and TH-17) cell mediated cytokine secretion.[6]

In all age groups worldwide, vitamin D deficiency is documented as a major health problem in both developed as well as underdeveloped countries.[4,7] Association of vitamin D deficiency with atopic diseases such as atopic dermatitis, allergic dermatitis and chronic urticaria has been studied recently showing conflicting results.[5,7,8] Vitamin D supplementation as an add on therapy at various dosages has also shown to improve urticaria activity score in recalcitrant cases.[9,10]

Correspondence: Dr Sana Waqar Qureshi, Fauji Foundation Hospital, Rawalpindi Pakistan
Received: 16 Sep 2021; revision received: 23 Dec 2021; accepted: 31 Dec 2021

The aim of this study was to assess whether a relation between chronic urticaria and deficiency of vitamin D exists in the Pakistani population as it has not been studied previously in this region and all studies done previously are international.[5,6,10] The rationale of this study was to increase evidence regarding association of reduced vitamin D levels and chronic urticaria. Results of this study would be helpful in revising current management guidelines of chronic urticaria and resultantly be beneficial for the patients.

METHODOLOGY

This Hospital-based comparative cross-sectional study was carried out at the Outpatient Department of Dermatology, Fauji Foundation Hospital, Rawalpindi Pakistan, from Jan to Dec 2020. Permission for this study was obtained from Hospital Ethical Committee Ref No.475/RC/FFH/RWP. Sample size was calculated by using WHO sample size calculator. Reference prevalence/population proportion was 1.4% [2] with 95% confidence interval and 5% margin of error. Non probability consecutive sampling technique was used to collect data. Purpose of the study was explained and informed written consent was taken from all the patients enrolled in the study. Seventy female patients with chronic urticaria (group-1) and 70 female age matched patients without urticaria (group-2) were enrolled. Both groups were further stratified into 3 age based groups: children (0-18 years), young adults (19-40years) and middle aged (40-60 years).

Inclusion Criteria: For Group-1 included patients of either sex having chronic urticaria showing urticarial symptoms at least twice a week for more than 6 weeks. Patients of age less than 60 years were included in this study, to avoid patients who had other age related comorbidities like deranged kidney function or osteo-porosis that could affect vitamin D levels and create a bias. Group-2 included patients who did not complain of having urticarial symptoms in the past 5 years.

Exclusion Criteria: Patients on vitamin D supplementation, systemic steroids, immuno-suppressant therapy, and other vitamin supplements in preceding 3 months. Pregnant and lactating mothers and patients having any chronic medical diseases disturbing bone mineralization homeostasis e.g. chronic renal failure, neoplastic disorders, chronic gastrointestinal malabsorption disorders were also excluded from the study.

Chronic urticaria was diagnosed on basis of detailed history and examination, with additional photographic evidence of weals, if available. Blood samples were taken from all the patients on OPD basis and were sent for analysis in the Hospital laboratory. Serum vitamin D levels were evaluated by ELISA. Tests were carried out free of cost and funding for the study was done by Fauji Foundation Hospital. A deficiency of vitamin D was defined as serum 25-(OH)D concentrations <30 ng/ml.[3]

Data was analysed using IBM Statistical Package for Social Sciences (SPSS version 20 for Windows). Fischer's exact test was used in the children group whereas chi square test was used in the young adults and middle aged groups. Overall association chronic urticaria and vitamin D levels was also assessed by chi Square test. Comparison of mean ages was done by t-test. The *p*-value≤0.05 was considered significant.

RESULTS

Total 140 patients were included in the study. Mean vitamin D levels in the group 1 were 43.91±23.89ng/ml whereas in group-2 was 57.23±31.52ng/ml.

105(75%) had normal vitamin D levels (group-1 = 48(45.7%) & group-2 = 57(54.3%)) whereas 35(25%) were deficient; group-1 = 22(62.8%) & group-2 = 13(37.2%) (*p*-value =0.07). In the children group, 13 out of 15(86.6%) were sufficient whereas 2(13%) were deficient (*p*-value=0.17). In the young adults group, 40 out of 58(68.9%) were sufficient and 18(31%) were deficient (*p*-value=0.06). In the middle aged group, 52 out of 67(77.6%) were sufficient and 15(22%) were deficient (*p*-value=0.82), shown in Table-I.

Table-I: Comparison of Group-1 and Group-2 in Terms of Normal and Vitamin D Deficient Patients with their Respective *p*-values

Age category	Group	Vitamin D levels		*p*-value
		Normal	Deficient	
Children	Group 1	6(8%)	2(3%)	0.17*
	Group 2	7(10%)	0(0%)	
Young	Group 1	16(22%)	12(17%)	0.06#
	Group 2	24(34%)	6(8%)	
Middle aged	Group 1	26(37%)	8(11%)	0.82#
	Group 2	26(38%)	7(10%)	
Overall	Group 1	48(68%)	22(31%)	0.07#
	Group 2	57(81%)	13(18%)	

**fisher's exact test #Chi square test*

The mean ages in groups 1 and 2 were 43.02±14.75 and 42.97±15.09 respectively (*p*-value =0.98). This showed that there was no statistically significant difference between various age categories

of the two groups and they were adequately matched. Results are tabulated in Table-II.

Table-II: Showing Mean Ages of Group 1 and Group 2

Group	Mean ages±SD	*p*-value
1	43.02±14.75	0.982
2	42.97±15.09	

DISCUSSION

The idea of conducting a comparative cross-sectional study was twofold; firstly, to find out association of chronic urticaria and vitamin D deficiency and secondly to assess the prevalence of vitamin D deficiency in the general population. There was no statistically significant difference between mean ages of group 1 and group 2. This shows that both groups were matched in terms of age. The fact that only females were enrolled in this study negates any possible gender bias between the two group as well. Results of our study showed no association of chronic urticaria and vitamin D deficiency.

Studies have shown variable results in the past. In a UK based study (2015) conducted by Wu *et al.*,[12] 282 patients with chronic urticaria were evaluated for nutritional deficiencies as compared to the general population. Serum vitamin D levels were normal in the chronic urticaria group. Moreover, Kim *et al.*,[13] conducted a study (2015) to assess vitamin D deficiency in patients of chronic urticaria, psoriasis and atopic dermatitis in Korean population. They found no association in chronic urticaria and psoriasis group and it was concluded that the impact of vitamin D in these dermatoses seem to be overestimated and a need of further study was suggested. Results of our study are consistent with the studies mentioned above.

A recent meta-analysis including 14 studies was conducted by Tsung-Yu *et al.*,[6] (2018). A total of 1655 patients of urticaria were included in this study for analysis. Vitamin D deficiency was prevalent significantly in the cases when compared to control groups. This deficiency was observed in adult cases only and not in pediatric patients.

In a recent regional study done in 2019, Rao Mudavath *et al.*,[14] compared 50 patients with chronic urticaria with 50 age and sex matched controls. Patients with chronic urticaria had significantly low serum vitamin D level when compared to control group. However, correlation between vitamin D deficiency and disease activity was not observed. Similar results were shown by several other studies conducted in South Asia.[3,9,15]

The literature regarding association of vitamin D and chronic urticaria shows mixed findings, majority of studies have described significant association of chronic urticaria with vitamin D deficiency, an inverse relationship between vitamin D levels and chronic urticaria severity and improvement in urticaria activity score with vitamin D supplementation.[16-18] However some studies, including ours have shown no association between the two.[12,13] Factors contributing to these results maybe the fact that families of veterans reporting to our hospital may have better medical facilities, more prompt diagnosis of nutritional deficiencies and easier access to treatment and supplementation than the general population of Pakistan (75% of both Group-1 and Group-2 had normal levels). Therefore, these results might not be a true reflection of the general population of Pakistan as multiple studies have shown high prevalence of vitamin D deficiency in the Pakistani population.[15]

Our study has helped in increasing evidence regarding association of vitamin D deficiency and chronic urticaria in the Pakistani population as no study was done previously in our region on this topic. Investigating vitamin D levels on routine basis in chronic urticaria cases may not be practical as its association is doubtful, however a trial of vitamin D supplementation in selective recalcitrant cases may be tried irrespective of its deficiency. It is recommended that further studies should be conducted on larger scale in order to confirm association of vitamin D levels with chronic urticaria before vitamin D supplementation can be added in the standard management guidelines of chronic urticaria.

AKNOWLEDGEMENT

We thank Dr. Waqar Ahmed Qureshi, Dr. Munir Akmal Lodhi, Dr. Samina Waqar, Dr. Tehmina Munir and Dr. Muhammad Almas Hashmi, for providing us all support required to carry out our study in the best possible manner.

LIMITATION OF STUDY

Only female patients could be enrolled in the study due to entitlement policy of the Hospital. Therefore, gender bias could not be avoided in our study. Other limitations of our study included a small sample size, single centred study and limited time period to carry out the study.

CONCLUSION

There is no association of chronic urticaria and vitamin D deficiency.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SWQ & FR: Data acquisition, data analysis, critical review, approval of the final version to be published.

BF & SK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SJ: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Yuan I, Katari P, Shaker M. Vitamin D treatment for chronic urticaria: a case report. J Med Case Reports 2019; 13: 193.
2. Fricke J, Ávila G, Keller T, Weller K, Lau S, Maurer M et al. Prevalence of chronic urticaria in children and adults across the globe: Systematic review with meta-analysis. Allergy. 2020; 75(2): 423-432.
3. Rather S, Keen A, Sajad P. Serum Levels of 25-hydroxyvitamin D in chronic urticaria and its association with disease activity: A case control study. Indian Dermatol Online J 2018; 9(3): 170-174.
4. Boonpiyathad T, Pradubpongsa P, Sangasapaviriya A. Vitamin d supplements improve urticaria symptoms and quality of life in chronic spontaneous urticaria patients: a prospective case-control study. Dermatoendocrinol 2014; 6(1): e29727.
5. Rosen CJ. Clinical practice. Vitamin D insufficiency. N Engl J Med 2011; 364(3): 248-254.
6. Tsai TY, Huang YC. Vitamin D deficiency in patients with chronic and acute urticaria: A systematic review and meta-analysis. J Am Acad Dermatol 2018; 79(3): 573-575.
7. Mitchell DM, Henao MP, Finkelstein JS, Burnett-Bowie SA. Prevalence and predictors of vitamin D deficiency in healthy adults. Endocr Pract 2012; 18(6): 914-923.
8. Quirk SK, Rainwater E, Shure AK, Agrawal DK. Vitamin D in atopic dermatitis, chronic urticaria and allergic contact dermatitis. Expert Rev Clin Immunol 2016; 12(8): 839-847.
9. Tuchinda P, Kulthanan K, Chularojanamontri L, Arunkajohnsak S, Sriussadaporn S. Relationship between vitamin D and chronic spontaneous urticaria: a systematic review. Clin Transl Allergy 2018; 8(1): 51-57.
10. Nabavizadeh SH, Alyasin S, Esmaeilzadeh H, Mosavat F, Ebrahimi N. The effect of vitamin D add-on therapy on the improvement of quality of life and clinical symptoms of patients with chronic spontaneous urticaria. Asian Pac J Allergy Immunol 2020.
11. 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.
12. Wu CH, Eren E, Ardern-Jones MR, Venter C. Association between micronutrient levels and chronic spontaneous urticaria. Biomed Res Int 2015; 926167.
13. Kim W, Kim JY, Park MY, Song M, Kim HS, Ko HC, et al. Vitamin D status and its relationship with disease severity/activity in patients with atopic dermatitis, psoriasis, and chronic idiopathic urticaria in Korea. Korean J Dermatol 2015; 53(3): 209-216.
14. Mudavath SR, Aruna C, Ramamurthy DVSB, Sridevi K, Senthil A, Kameti S. Evaluation of serum 25 hydroxy vitamin D levels in patients with chronic spontaneous urticaria: a hospital based cross sectional study in a tertiary care centre. J Pak Assoc Dermatol 2019; 29(3): 289-293.
15. Riaz H, Finlayson AE, Bashir S, Hussain S, Mahmood S, Malik F, et al. Prevalence of vitamin D deficiency in Pakistan and implications for the future. Expert Rev Clin Pharmacol. 2016; 9(2): 329-338.
16. Mohamed AA, Hussein MS, Salah EM, Eldemery A, Darwish MM, Ghaith DM, et al. Efficacy and safety of active vitamin D supplementation in chronic spontaneous urticaria patients. J Dermatolog Treat 2020; 13(1): 1-6.
17. Rorie A, Poole JA. Vitamin D supplementation: a potential booster for urticaria therapy. Expert Rev Clin Immunol. 2014; 10(1): 1269-1271.
18. Mony A, Chandrashekar L, Rajappa M, Munisamy M, Sahoo JP, Selvarajan S. Effect of vitamin D supplementation on clinical outcome and biochemical profile in South Indian population with vitamin D-deficient chronic urticarial - A randomized double-blind placebo controlled trial. Clin Chim Acta 2020; 504(1): 1-6.