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# Vitamin D deficiency in patients with chronic and acute urticaria: A systematic review and meta-analysis

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To the editor:

Urticaria is an allergic disease that can be classified into acute and chronic form. Autoimmune responses are believed to contribute to the pathogenesis of chronic urticaria.[1] A vitamin D deficiency is associated with various autoimmune and allergic diseases, such as atopic dermatitis.[2] We attempted to meta-analyze current studies to elucidate the relationship between vitamin D deficiency and different types of urticaria in patients of different ages.

On November 30, 2017, we searched databases to include studies comparing the prevalence of vitamin D deficiency or vitamin D levels between patients with urticaria and controls. Odds ratio (OR) and standardized mean difference (SMD) were calculated using a random effects model.

Fourteen studies with 1655 patients with urticaria were included for analysis. The pooled prevalence of vitamin D deficiency was significantly higher in patients with urticaria than in the control group (OR = 4.456, 95% confidence interval [CI] = 2.261-8.782; Fig 1). Subgroup analysis revealed that the prevalence of vitamin D deficiency was significantly higher in patients with chronic urticaria than in the control group (OR = 5.723, 95% CI = 2.617-12.516) but similar difference was not observed in patients with acute urticaria (OR = 3.031, 95% CI = 0.706-13.022).

Random effects pooling of the 11 studies providing vitamin D levels revealed

that patients with urticaria had a significantly lower level of vitamin D than the control group (SMD = -1.211, 95% CI = -1.832 to -0.591; Fig 2). Subgroup analysis indicated that the vitamin D level was significantly lower in patients with chronic urticaria than in the control group (SMD = -1.067, 95% CI = -1.865 to -0.268) but the difference was not significant in patients with acute urticaria (SMD = -1.009, 95% CI = -2.314 to 0.296). The vitamin D level was significantly lower in adult patients with urticaria than the control group (SMD = -1.741, 95% CI = -3.472 to -0.010), whereas the difference was not significant in pediatric patients (SMD = -1.151, 95% CI = -3.725 to 1.424).

25-hydroxyvitamin D3 is converted by mast cells into metabolites that repress IgE-mediated mast cell activation.[3] Vitamin D enhances T regulatory cells, which contributes to the suppression of pro-allergic and autoimmune responses.[4,5] 1,25-dihydroxyvitamin D has been reported to suppress T helper (Th) 1 cytokine secretion, thereby inhibiting Th1-mediated autoimmune diseases.[5] 1,25-dihydroxyvitamin D also suppresses Th17 cells, an important trigger of autoimmune diseases.[5]

This study was limited by the significant heterogeneity of the included studies. Additionally, serum 25-hydroxyvitamin D levels are subject to many factors like comorbidity, sun exposure, and diet.

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In summary, compared with the control group, the prevalence of 25-hydroxyvitamin D deficiency was significantly higher and the level of 25-hydroxyvitamin D was significantly lower in patients with chronic urticaria but not in those with acute urticaria. The significantly reduced level of 25-hydroxyvitamin D was observed in adult patients but not in pediatric patients. However, the association of vitamin D deficiency with urticaria does not imply causation. Further studies are required to explore the role of vitamin D supplementation in treating urticaria.

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**Figure legends**

Figure 1. Forest plots. The forest plots showed that patients with urticaria had a significantly higher prevalence of 25-hydroxyvitamin D deficiency than those in the control group. (Odds ratio = 4.456, 95% confidence interval = 2.261-8.782, $I^2$ = 72.6%.)

Figure 2. Forest plots. The forest plots showed that patients with urticaria had a significantly lower level of 25-hydroxyvitamin D than those in the control group. (Standardized mean difference = -1.211, 95% confidence interval = -1.832 to -0.591, $I^2$ = 98.5%.) Std, Standardized.

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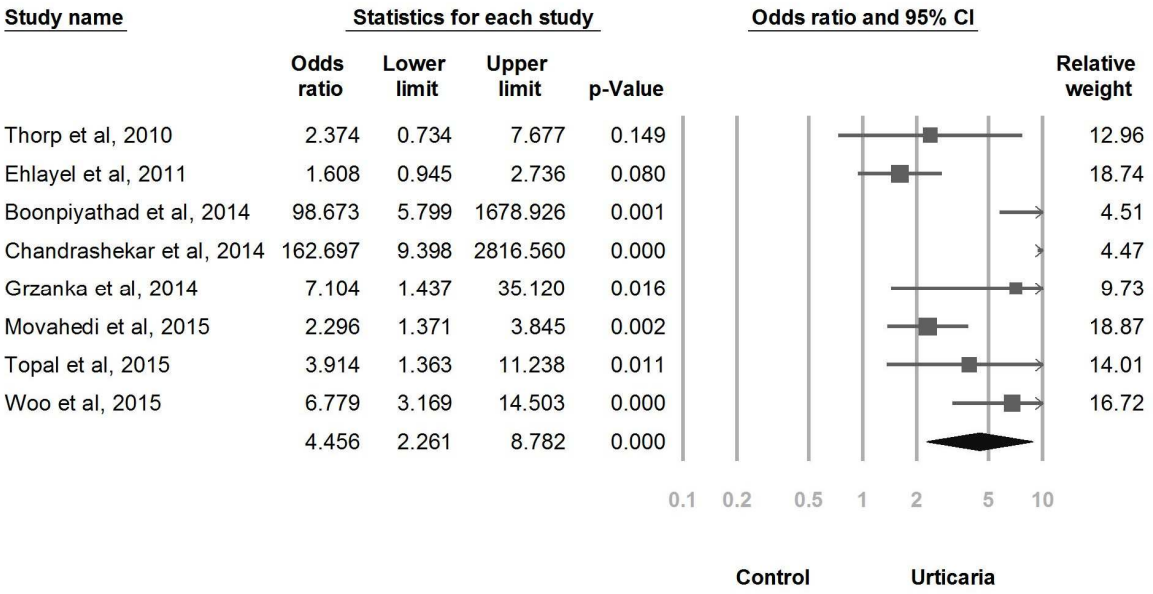


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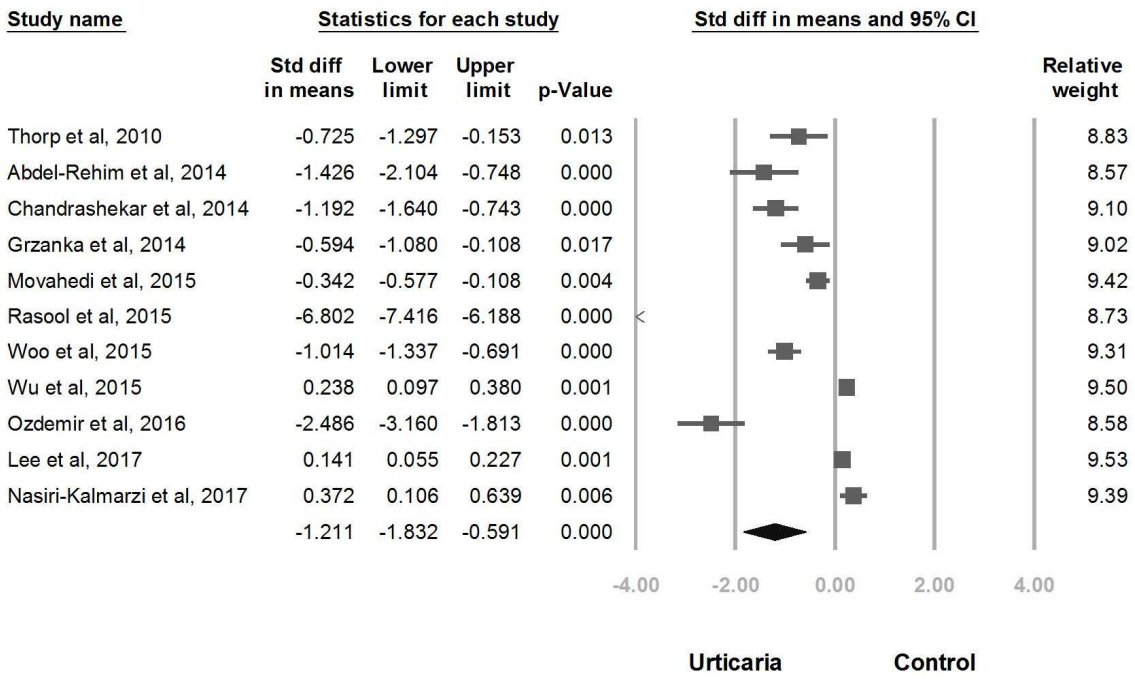


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