

## A commentary on: Vitamin D deficiency in non-autoimmune hypothyroidism; a case-control study

Salma Ahi

Research Center for Noncommunicable Diseases, Jahrom University of Medical Sciences, Jahrom, Iran

### Article Info

#### Article Notes

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#### \*Correspondence:

\*Dr. Salma Ahi, Research Center for Noncommunicable Diseases, Jahrom University of Medical Sciences, Jahrom, Iran; Email: salmaahi.61@gmail.com.

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We have recently published an article entitled “**Vitamin D deficiency in non-autoimmune hypothyroidism; a case-control study**”, investigating the role of vitamin D in Autoimmune hypothyroidism and non-Autoimmune hypothyroidism. Different from previous studies, this study directed comparing vitamin D levels between autoimmune and non-autoimmune hypothyroid patients<sup>1</sup>; in our knowledge it was the first study emphasizing the Vitamin D association in the non-autoimmune form of the disease, having a large-scale study design, reusing a separate control group for comparison of autoimmune and non-autoimmune hypothyroid subjects<sup>2</sup>. The association of vitamin D deficiency with autoimmune diseases has been well studied<sup>3-16</sup>; although the association of vitamin D in thyroid autoimmune diseases was obviously reflected in previous studies, the role of vitamin D in non-autoimmune thyroid diseases, negative antibodies hypothyroidism and hyperthyroidism, is unclear.

Our previous case-control study focused on a total of 1138 participants including new cases and previously diagnosed patients undergoing levothyroxine treatment (n=633), nonimmune hypothyroid patients (n=305), and healthy control subjects (n=200). Significantly higher 25OHD levels of healthy control population than hypothyroid participants regardless of autoimmunity is a key finding in this field that needs more studies to differentiate the cause and mechanism. No significant differences in 25OHD levels that were observed between immune and nonimmune hypothyroid participants also remind other clues of the thyroid and vitamin D relationship aside from autoimmunity. Hence this study findings, new aspects of vitamin D and thyroid disease correlation have been marked that; vitamin D deficiency not only impresses the immune system but also affects the thyroid gland function directly<sup>1</sup>. Investigation of vitamin D's association in non-autoimmune hypothyroidism is the innovation view of this study and indicates it unique, up to now. Limitations of the study were: various duration of disease in participants, the effect of disease course, and treatment dose in this relation, which should be in mind for future studies.

In the literature review, there were few studies comparing vitamin D levels or status of immune and non-immune hypothyroid patients with controls or versus each other. Christopher et al. study on 50 autoimmune and 50 non-auto-immune subjects indicated a lower level of vitamin D in autoimmune hypothyroid patients<sup>17</sup>. Our study results demonstrated a considerably lower level of vitamin D in both Hashimoto's immune and non-immune thyroiditis compared with healthy controls ( $P < 0.05$ ). But there wasn't any difference

between immune and non-immune hypothyroid groups. Christopher et al. didn't make any comparison with healthy normal subjects. Their vitamin D deficiency cut off criteria were considered below 20 ng/ml as well as our study. But no information was addressed about the season of vitamin D assessment.

The status of vitamin D deficiency was compared between immune and non-immune hypothyroid patients in the study of Shaye Kivity et al.<sup>3</sup> they study revealed a higher rate of vitamin D deficiency in immune thyroiditis. The cut off ranged that was considered as the vitamin D deficiency in their study was 10; while we used 20 ng/dl as our cut off. Clinical judgment and comparison of studies according to different definitions of vitamin D deficiency, is difficult. Shaye Kivity et al. was the only study taking healthy control groups into account for comparisons; While their study sample size was very low. Also, they report higher rate of vitamin D deficiency in immune than non-immune hypothyroid patients; in contrary to ours.

Comparison of immune and non-immune hypothyroidism by Jaideep Khare et al. didn't include the control group, so conclusion about the possible role of the vitamin D in non-autoimmune hypothyroidism would not be judicable<sup>18</sup>. Dong Yeob Shin's study, comparing the same groups of immune and non-immune, hadn't a healthy euthyroid group in study design, too<sup>19</sup>.

In pathophysiological view, Vitamin D plays a key role in the prevention of inflammatory, infectious and autoimmune diseases by interfering in macrophages-TCD8-TCD4 and B cells function<sup>20,21</sup>, progression of DM1, SLE, RA and IBD in vitamin D deficiency is considered recently<sup>22,23</sup>. Also, an increase in the incidence rate of Hashimoto thyroiditis might be related to vitamin D deficiency<sup>24</sup>, low 25OHD have recently been associated with autoimmune thyroid disorders: Hashimoto thyroiditis, Graves' disease, and post-partum thyroiditis, as well as thyroid cancer<sup>25,26</sup>. Limited articles in controversy, declared no relationship between

Hashimoto and vitamin D deficiency, despite the significant positive association of TpoAb and vitamin D in males; also none of the studied females, as the most prevalent part of Hashimoto thyroiditis population, is vitamin D deficient<sup>27</sup>. Around the other article, it's more acceptable to record no association between Hashimoto thyroiditis and vitamin D insufficiency, not deficiency<sup>17</sup>.

Role of vitamin D deficiency in hypothyroidism aside from cause is a novel challenge, vitamin D role in non-immune thyroid diseases, hasn't been studied before; the relationship between thyroid autoantibodies and vitamin D, as well as patients' thyroid status, opens a new door in nowadays practice.

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Pub year	Limitation	Conclusion	Vit D cut off	Study by
2019	No control euthyroid group	Lower vit D level in immune cases	20ng/dl	Christopher
2011	With control group but small sample size	A higher rate of vit D deficiency in immune thyroiditis	10g/dl	Kivity
2017	No control euthyroid group	Patients with TPOAb positivity have more significant 25(OH)D3 deficiency	20ng/dl	Khare
2015	Lack of sun exposure, socioeconomic data, no control euthyroid group	Low serum 25(OH)D is related to the presence of TgAb in females	20ng/dl	Wang x
2014	No control euthyroid group	Vit D level is affecting the presence of TPOAb in AITDs	9.3ng/ml RIA	Shin
2016	None of female participants are vitamin d deficient	No relationship between Hashimoto and vit D deficiency	20ng/dl	Yasmeh
2016	No control euthyroid group, but vitamin D sufficient control	Vitamin D deficiency was significantly associated with AT in the elderly	20ng/dl	Muscogiuri
2015	No control euthyroid group	Vitamin D deficiency is associated with HT in children and adolescents	20ng/dl	Evllyaoğlu
2016	No control euthyroid group	Vitamin D insufficiency was associated with AITD and HT, especially overt hypothyroidism	Insuff<75nmol/lit	KIM

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