Association between vitamin D status and subclinical hypothyroidism

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Abstract

Aims and Objectives: The purpose of this study is to investigate the relation between Vitamin D levels and sub-clinical hypothyroidism and the effect of Vitamin D supplementation on treatment outcome.

Design: A retrospective cohort file-based study.

Method: In this study, the relation between Vitamin D level and subclinical hypothyroidism and the effect of Vitamin D supplementation on patients with subclinical hypothyroidism were evaluated where 30 patients were diagnosed with subclinical hypothyroidism followed up in Armed forces hospital southern region, KSA was included through electronic files revision.

Results: The mean age was 41.6 +/- 12.4 years among the study group. Twenty-seven patients (90%) had their thyroid function test normalized after Vitamin D correction, while the rest had their TSH level improved from the baseline level. The presence of thyroid peroxidase antibodies (TPO) antibodies was found to be inversely related to TSH level after correction of Vitamin D level, and all patients who were negative for TPO 19 (100%) had their Thyroid Stimulating Hormone (TSH) level normalized after Vitamin D correction. In comparison, 3 (27.3%) of TPO-positive patients had subclinical hypothyroidism despite vitamin D correction.

Conclusion: Vitamin D deficiency is inversely related to TSH, and TPO status and correction of Vitamin D deficiency in patients with subclinical hypothyroidism can normalize the thyroid function. Further studies are needed to establish the relationship between Vitamin D deficiency and subclinical hypothyroidism.

Keywords

Subclinical hypothyroidism, Vitamin D, Thyroid-stimulating hormone, Thyroid peroxidase antibodies

Imprint


Introduction

Vitamin D is a fat-soluble vitamin established to have systemic effects (1, 2). Its deficiency has been recognized as contributing factor for diabetes mellitus (3, 4), malignancies (5), multiple sclerosis (6), atherosclerosis (7), infectious diseases (8), and other autoimmune diseases (9,10), including autoimmune thyroid disease. Vitamin D exerts its effects through vitamin D receptors and regulates corresponding genes (11). Vitamin D receptors are located in different tissues such as the thyroid, pancreas, and cardiac tissues, indicating their role in the function of these organs (12). Both vitamin D and thyroid hormone receptors are steroid receptors. They have a similar response to vitamin D and thyroid hormone; respectively, thus low vitamin D is expected to worsen systemic abnormalities associated with hypothyroidism (13, 14). The relationship between vitamin D status, thyroid antibodies, and thyroid function remains controversial and requires more investigation (15).

Autoimmune thyroid disease (AITD) is among the most common organ-specific autoimmune disorders. Despite inconclusive results, many studies have addressed the risk of developing AITD in patients with Vitamin D receptors (VDR) polymorphism. A meta-analysis of eight studies concludes a significant association between AITD patients with VDR polymorphism (15).

Kivity et al. (16) demonstrated the relation between vitamin D deficiency and autoimmune thyroid disease, and hypothyroidism. Bozkurt et al. Reported a suggestion of the significant role of vitamin D deficiency in the development of hypothyroidism or progression to hypothyroidism (17). Additionally, there is an inverse relationship between vitamin and anti-thyroglobulin levels in females (18). This study aims to evaluate the relation between vitamin D level and subclinical hypothyroidism and the effect of vitamin D supplementation on treatment outcome.
Materials and method

Patient and Public Involvement

The selected patients’ data were revised during the study period after obtaining the ethical committee and managerial approval. No, patients were not involved in the recruitment or any other study protocol procedures. Only their medical history was used to analyse the main research question of the reported study.

Study Population

This retrospective study was conducted at Armed forces hospital southern region, KSA from May 2017 to March 2020, where all the patients presented with subclinical hypothyroidism aged 18-65 years were included. Our exclusion criteria were patients with overt hypothyroidism, post total thyroidectomy, another autoimmune disease, pregnancy, lactation, bone abnormalities, and those aged above 65 years.

Data collection

The primary investigator collected data from patients' files using a constructed structured data collection. Electronic files of patients who were diagnosed with subclinical hypothyroidism and Vitamin D deficiency, had taken Vitamin D supplementation and did not receive thyroid replacement therapy were selected, reviewed for demographic data, diagnosis, past medical and surgical history, thyroxin replacement therapy, thyroid function test with a reference range of (TSH = 0.38-5.60 μIU/ml), TPO antibodies and Vitamin D level results pre and post Vitamin D supplementation. Vitamin D deficiency was defined as serum 25(OH)D of less than 20 ng/ml.

Statistical Analysis

The results were analysed using Statistical Package for Social Sciences (SPSS 22 for Windows). Descriptive statistics were computed in frequency and percentage for categorical data, the state of central tendency measures (arithmetic mean), and measures of dispersion (standard deviation and range) for continuous variables. To test the significance of differences paired t-test was used. Pearson correlation was used to determine the association between variables. Differences were considered statistically significant when the p-value was less than 0.05 (p<0.05).

The research ethics committee approved the research methods and protocols of Armed Forces Hospital.

Results

Of the 30 patients included, 93% were female, and only 7% were males. Sample distribution according to age showed that 36.7% of the patients were aged between 45 to 55 years (Mean age: 41.6+/−12.4). Regarding Vitamin D level at the time of diagnosis, 27 (90%) patients had vitamin D deficiency while 3 (10%) patients had vitamin D insufficiency. TPO status distribution revealed that 63% of patients were antibody positive, and the Distribution of sample according to TSH level after vitamin D correction showed that 27 (90%) patients had normalized thyroid function test and only three patients had vitamin D level above 20 and TSH more than 5.6 with no response as shown in table 1.

<table>
<thead>
<tr>
<th>TSH level</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 5.6</td>
<td>27</td>
<td>90</td>
</tr>
<tr>
<td>greater than 5.6</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>100</td>
</tr>
</tbody>
</table>

Regarding the status of vitamin D level after supplementation, the analysis showed that 12 patients (40%) reached the sufficient level (above 30 IU/ml), 15 patients were between 20-30 IU/ml who were considered still at insufficiency level, and 3 (10%) patients had their vitamin D levels under 20 IU/ml. In one patient (3.3%), vitamin D level improved from 11.7 to 19.6 IU/ml (borderline), and TSH improved from 6.1 to 1.9. In two other patients, the vitamin D levels were 9.4 and 9.3, and their TSH were 2.6 and 0.7, while their vitamin D levels after correction were 19.3 and 18.3, respectively, table 2. Variation of the duration of the treatment of vitamin D replacement ranged from 2 months to 6 months, as presented in table 3. Correlation between TPO and TSH after correction of Vitamin D level showed that all patients who were negative for TPO 19 (100%) had their TSH level normalized after Vitamin D correction. Eight (72.7%) TPO-positive patients normalized their TSH level after Vitamin D correction. In comparison, 3 (27.3%) TPO-positive patients did not improve subclinical hypothyroidism despite Vitamin D correction as listed in table 4, p<0.05. Correlation between TSH level and vitamin D after correction showed that 27 (90%) patients normalized their TSH level after Vitamin D correction. However, three of these patients (27.3%) remained vitamin D deficient, as displayed in table 5.
Table 2
Distribution of sample according to Vitamin D level after supplementation:

<table>
<thead>
<tr>
<th>Vitamin D level</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 20</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Between 20 and 30</td>
<td>15</td>
<td>50</td>
</tr>
<tr>
<td>Above 30</td>
<td>12</td>
<td>40</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 3
Correlation between TSH level and vitamin D after correction:

<table>
<thead>
<tr>
<th>Vitamin D level</th>
<th>Less than 5.6</th>
<th>More than 5.6</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 20</td>
<td>(2) 7.4%</td>
<td>(0) 0.0%</td>
<td>(2) 6.7%</td>
</tr>
<tr>
<td>More than 20</td>
<td>(25) 92.6%</td>
<td>(3) 100.0%</td>
<td>(28) 93.3%</td>
</tr>
<tr>
<td>Total</td>
<td>(11) 100%</td>
<td>(3) 100.0%</td>
<td>(30) 100.0%</td>
</tr>
</tbody>
</table>

Table 4
Correlation between TPO and TSH after correction of Vitamin D level:

<table>
<thead>
<tr>
<th>TPO status</th>
<th>less than 5.6</th>
<th>more than 5.6</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>(8) 72.7%</td>
<td>(3) 27.3%</td>
<td>(11) 100%</td>
</tr>
<tr>
<td>Negative</td>
<td>(19) 100.0%</td>
<td>(0) 0.0%</td>
<td>(19) 100%</td>
</tr>
<tr>
<td>Total</td>
<td>(27) 90.0%</td>
<td>(3) 10.0%</td>
<td>(30) 100%</td>
</tr>
</tbody>
</table>

Table 5
Correlation between TSH level and Vitamin D in Negative TPO

<table>
<thead>
<tr>
<th>Vitamin D levels</th>
<th>less than 5.6</th>
<th>more than 5.6</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 20</td>
<td>(0) 0.0%</td>
<td>(0) 0.0%</td>
<td>(0) 0.0%</td>
</tr>
<tr>
<td>Between 20 -30</td>
<td>(9) 100%</td>
<td>(0) 0.0%</td>
<td>(9) 100%</td>
</tr>
<tr>
<td>Above 30</td>
<td>(10) 100%</td>
<td>(0) 0.0%</td>
<td>(10) 100%</td>
</tr>
<tr>
<td>Total</td>
<td>(19) 100%</td>
<td>(0) 0.0%</td>
<td>(19) 100%</td>
</tr>
</tbody>
</table>

Discussion

This study reported that Vitamin D deficiency and subclinical hypothyroidism are more common in females 93% than males 7%, which is parallel with other studies (19, 20). We selected 30 patients with subclinical hypothyroidism where 27 patients (90%) had vitamin D deficiency while three patients (10%) had vitamin D insufficiency. After Vitamin D supplementation, we observed that 27 patients (90%) had normalized thyroid function tests, and only three patients had vitamin D levels above 20 and TSH more than 5.6, with no response. In this study, we didn’t look for the cause of hypothyroidism, which might be directly related to vitamin D low levels as reported by Byron Richard et al. In an experimental study, there was a possible association between hypothyroidism and Vitamin D deficiency had been reported (21). However, we observed a significant inverse relation between Vitamin D level and hypothyroidism reported in previous studies highlighting the correlation between low vitamin D levels and autoimmune thyroiditis and Hashimoto’s thyroiditis (16, 22, 23). Furthermore, in many experimental studies, Vitamin D supplementations have been shown to prevent autoimmune thyroiditis by preventing the production of thyroid antibodies (24, 25). After correcting Vitamin D levels, we reported an inverse correlation between TPO and TSH. Moreover, it was also seen that there might be difficulty in the discipline of Vitamin D deficiency in patients with positive TPO. A study by Shin et al. reported a lower 25(OH)D3 in TPO-positive patients (26). An open-label randomized control trial by Chaudhary, Dutta (27) showed that supplementation of vitamin D among patients with autoimmune thyroid disorders could reduce TPO titers. Given the small sample size, further research with a larger sample size and control group is required to study the relationship between Vitamin D supplementation, TPO antibody status, and subclinical hypothyroidism. Our study could not establish the direct connection of Vitamin D deficiencies because TPO antibody measurement was not done. Furthermore, the period of supplementation and dose was not uniform in all the patients since this was a retrospective study.

Conclusion and Limitation

Vitamin D deficiency is inversely related to TSH and TPO, and correction of vitamin D deficiency in patients with subclinical hypothyroidism can normalize thyroid function. Further research is needed to establish the relationship between Vitamin D deficiency and subclinical hypothyroidism and understand the underlying molecular mechanism. This retrospective cohort study is a that measured vitamin D deficiency and underline diseases in males and females. Standard protocols were applied to report the patient participation in this study. However, further investigation is required to gain more reliable and results on collection of big data size. In addition, this study was carried out in limited time because of unavailability of designated participants and lack of funding bodies.

Acknowledgments

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wards this research study. We are also very grateful to onsite doctors and general physicians who have actively participated in this study in compiling and prescribing patient data.

Authors’ contribution
Jaber Alfaifi: Principal investigator, drafted initial proposal and conducted the main procedures of the study. Drafted manuscript
Waleed Abdalrazig Dosogi Elzain: Conducted clinical assessment and analyzes the data obtained
Saeed Mohamed Alshahrani: Assisted collection of the data and drafting of manuscript
Khalid Tahir Ibrahim Mohamed Soliman: Data analysis and discussion of the results obtained
Hasan Korairi: Literature review and discussion of the results obtained
Ahmed Yousef Abouelyazid: approved final draft of the manuscript, methodology and final results obtained.

Ethical Approval
Ethical approval was taken from Research Ethics Committee, Armed forced Hospital, South Region, Kingdom of Saudi Arabia with the registration number AFHSRMREC/2019/INT MEDICINE/425

Ethical declaration
The study was conducted in accordance to the STROBE guidelines. Consent was taken from the selected patients before starting this study.

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Conflict of interest
The authors declare no conflict of interest, financial or otherwise.

Consent for Publication
The authors agree to the final version submitted in the journal.

References: