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Association Between Thyroid Disorder and Vitamin D among Yemeni Patients

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Abstract: Background: Vitamin D deficiency is a global health concern, with implications for a variety of disorders. However, its role in thyroid illnesses is not yet fully recognized. Hypothyroidism is a frequent condition in which the thyroid does not produce and release sufficient thyroid hormone into the bloodstream. It is considered primary hypothyroidism. Autoimmune damage causes about half of primary hypothyroidism cases, while other aetiologies or exposures cause the remaining half. **Objectives:** This research investigates the relationship between thyroid disorders and vitamin D levels in Yemeni patients residing in Sana'a city. **Methods:** In this cross-sectional study, data regarding the thyroid gland, patient sex, and results collected from various laboratories were analyzed. The study population consisted of approximately 378 patients diagnosed with thyroid gland disorders and vitamin D deficiency, who were treated at Alulaqi Specialized Medical Laboratory and the Central National Laboratory. **Result:** The study comprised 378 individuals with thyroid gland disorders; the majority were adult females, followed by elderly females (55–87 years old), and a small percentage were females (7–12 years old), the youngest of whom had the illness at a lower frequency. In terms of vitamin levels, the highest number of participants had vitamin D, followed by TSH, while T3 had the fewest participants, followed by T4. Also, there were no significant links found between the averages of the measured parameters (T4, T3, TSH, and Vitamin D) and sex among the people who were studied (P values of 0.279, 0.426, 0.170, and 0.065, respectively). **Conclusions:** it can be concluded that Vitamin D did not appear to be associated with thyroid problems in this investigation of Yemeni patients.

Keywords: Thyroid disorders; Vitamin D and Yemeni patients; TSH

Introduction

Calcitriol, the active form of vitamin D, exhibits a strong binding affinity for the intracellular vitamin D receptor (VDR), which interacts with response elements of target genes to mediate its effects. The musculoskeletal system recognizes calcitriol as a vital hormone. In recent years, the extra skeletal effects of $1,25(OH)_2D$ have garnered significant research interest, particularly following the identification of vitamin D receptors in nearly all tissue types.[1,2] Calcitriol exhibits antiproliferative and pro differentiating effects in thyroid tumorigenesis, while its role in modulating the immune system is significant in autoimmune thyroid disease (AITD). This review will briefly present the role of vitamin D in relation to thyroid function, including hypo- and hyperthyroidism. Mackawy, AlAyed, and Al-Rashidi found an association between hypothyroidism and hypovitaminosis D in

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their study of 30 patients and 30 controls. Serum 25(OH)D levels were measured at 14.8 and 44.5 ng/ml, revealing a negative correlation between TSH and calcidiol, with r = −0.59.[3] A hypothesis suggesting a protective effect of vitamin D against non-cutaneous cancers has been proposed.[4] Vitamin D deficiency, indicated by suboptimal calcidiol concentrations, is considered a significant risk factor for cancer .[5] Several reports indicate that there are no significant differences in vitamin D status between patients with thyroid cancers and control groups. Laney and colleagues observed that 25(OH)D concentrations below 30 ng/ml did not differ among three groups: 45 thyroid cancer patients in remission, 24 patients with active thyroid cancer, and 42 patients with thyroid nodules. The prevalence of vitamin D deficiency in these groups was notably higher (48–58%) compared to healthy controls in a previous study conducted at the same institution (32%) .[6] The effects of calcitriol are influenced by VDR, and the polymorphic variants of VDR have been studied to a limited extent in relation to thyroid cancer. Bozkurt and colleagues reported correlations between 25(OH)D concentrations and thyroid volume (r=0.15), anti-TPO levels (r=−0.36), and anti-TG levels (r=−0.34) in the context of vitamin D status and Hashimoto's thyroiditis. In the study, 180 euthyroid patients with Hashimoto's thyroiditis, 180 newly diagnosed Hashimoto's thyroiditis subjects, and 180 healthy controls were enrolled. Calcidiol levels below 10 ng/ml were observed in 48.3%, 35%, and 20.5% of subjects, respectively. [7] The prevalence of vitamin D deficiency was significantly greater in children with HT (n=78) compared to healthy controls (n=74), specifically 73% versus 17.6%. There is an inverse correlation between patients' calcidiol concentrations and anti-TPO levels (r=−0.3) [8] Mansournia et al. enrolled 41 hypothyroid HT patients and 45 healthy controls, finding an inverse association between 25(OH)D concentration and HT risk; the ratio of geometric means of calcidiol concentrations for patients to controls was 0.66.[9]A study by Zhang, Liang, and Xie found that the vitamin D status in 35 Graves' disease (GD) patients with anti-TSH-receptor antibodies (TRABs) was significantly lower compared to 35 seronegative GD patients and 70 healthy controls. 25(OH)D concentrations below 20 ng/ml were observed in approximately 65%, 20%, and 17% of subjects, respectively. An inverse correlation was observed between TRAB titer and 25(OH)D level, with a correlation coefficient of r=−0.5.[10] Krysiak, Kowalska, and Okopień investigated four groups of non-lactating women: hypothyroid (n=14) and euthyroid (n=14) subjects with postpartum thyroiditis, participants with non-autoimmune hypothyroidism (n=16), and a euthyroid group without thyroid autoimmunity (n=15). Serum 25(OH)D levels were lower in people with thyroiditis compared to other people. Women who were hypothyroid had lower levels than women who were euthyroid (mean values for the four groups were 18, 30, 38, and 53 ng/ml). There was also a link between the levels of anti-TPO and anti-TG antibodies and calcidiol, with r coefficients ranging from -0.22 to -0.34. People who had hypothyroidism were given L-thyroxine, but only people who had postpartum thyroiditis saw their calcidiol levels rise. Thyroid function got better in both groups that needed treatment, though. Researchers discovered a link between the amount of 25(OH)D in the blood after thyroxine treatment and the number of antibodies. The relationship was r=-0.3 for anti-TPO and r=-0.2 for anti-TG. The authors point out some major problems with their results, such as the small size of the sample and the fact that there weren't any big differences in the amounts of calcidiol in the different groups when the season of sample collection was taken into account.[11]

Methods

Study Design

The study employed a cross-sectional design and was carried out at the Alulaqi specialized medical laboratory and the Central National Laboratory in Sana'a city. It involved approximately 378 patients diagnosed with thyroid gland disorders and vitamin D deficiency during their visits to these laboratories from November 2021 to March 2022.

Data Collection and Sample Size

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We collected the data from 378 Yemeni patients at the Alulaqi specialized medical laboratory and the Central National Laboratory in Sanaa. We obtained age, gender, nationality, thyroid function test (TFT), and serum 25(OH)D levels.

Statistical Methodology

The categorical data were summarized through frequency and percentages, while the continuous data were summarized using mean and standard deviation. For continuous variables, an independent test was used to see if there was a difference in the average between the two groups. For categorical variables, the chi-square test of association was used. When the two groups were compared, patients with an odds ratio and a 95% confidence interval (CI) had a higher chance of not getting enough vitamin D and having hypothyroidism. Pearson's correlation coefficient r was calculated to determine the strength of the relationship between TSH and other laboratory parameters. Statistical tests were deemed significant if the p-value was below 0.05. Furthermore, a box plot was drawn to compare the descriptive statistics of vitamin D3 (25(OH)D) between the two groups. Log transformation was applied to vitamin D3 values for simplification and enhanced understanding. A bar graph was created to illustrate the frequency differences among the groups. All analyses were conducted using version 25 of the Statistical Package for the Social Sciences.

Results

Table 1 presents the sociodemographic characteristics of participants. The majority of participants were female (289, 76.5%), with the highest age group being 30-39 years (104, 27.5%), followed by the 20-29 years age group (93, 24.6%) and the 40-49 years age group (91, 24.1%). Conversely, the male participants constituted a smaller proportion (89, 23.5%), with the least represented age group being under 20 years (24, 6.3%), followed by those aged 50 years or older (66, 17.5%).

Table 1. The Sociodemographic characteristics of The Studied Participants.

Variable		N	%
Age	**Between 20-29 year**	93	24.6
	Between 30-39 year	104	27.5
	Between 40-49 year	91	24.1
	More than or equal to 50 year	66	17.5
	Less than 20 year	24	6.3
Sex groups	**Male**	89	23.5
	Female	289	76.5

Table 2 displays the average values of the measured parameters among the participants in the study. Vitamin D had the highest number of participants (378) with a mean standard deviation of 19.02631, followed by TSH (376) with a mean SD of 2.2927 ± 3.35957. In contrast, T3 had the fewest participants (242) with a mean SD of 2.7575 ± 1.52048, and T4 had the fewest participants (263) with a mean SD of 1.1969 ± 1.38329.

Table 2. Mean of the measured parameters among The Studied Participants.

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Test	N	Mean	SD
T4	263	1.1969	1.38329
T3	242	2.7575	1.52048
TSH	376	2.2927	3.35957
Vitamin D	378	22.8025	19.02631

Table 3 shows that the People aged 20 to 29 show the widest range of T4, T3, and TSH levels. This is shown by their high average standard deviation values: T4 is 1.1261 with a standard deviation of 0.95232, T3 is 2.7471 with a standard deviation of 1.23472, and TSH is 2.5965 with a standard deviation of 1.59579. This may indicate that hormonal levels exhibit greater variability or reduced stability during this age range. Furthermore, the age groups under 20 years and 50 years or older exhibit higher mean vitamin D levels than the other age groups. Nonetheless, these groups exhibit elevated variability (SD), indicating a broad spectrum of vitamin D levels among individuals. The variations in mean levels and standard deviation across age groups indicate that age may affect the levels of T4, T3, TSH, and Vitamin D. The variability observed within each age group, particularly among individuals aged 20–29, suggests that individual differences and additional factors, such as lifestyle, diet, and health conditions, may significantly influence these measurements.

Table 3. The Relationship between mean of the measured parameters and age among the studied participants.

Test	Less than 20 year		Between 20-29 year		Between 30-39 year		Between 40-49 year		≥50 year	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
T4	1.1261	.95232	1.3510	2.38966	1.0591	.48181	1.0893	.64321	1.3173	1.04367
T3	2.7471	1.23472	2.9070	2.56955	2.8597	.76213	2.6508	.83998	2.5398	1.00943
TSH	2.5965	1.59579	2.5048	5.92887	2.0258	1.73725	2.1986	1.71157	2.4310	2.33867
Vit-D	27.3267	20.93761	18.9975*	16.08218	23.8708	21.57299	20.8387*	14.66139	27.5433*	22.02252

*. Correlation is significant at the 0.05 level (2-tailed).

With P values of 0.279, 0.426, 0.170, and 0.065, Table 4 shows that there were no significant relationships between the studied participants' sex and the means of the measured parameters (T4, T3, TSH, and Vitamin D).

Table 4. The Relationship between mean of the measured parameters and sex among the studied participants.

Test	Male			Female			P value
	N	Mean	SD	N	Mean	SD	

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T4	47	1.0781	.45386	216	1.2227	1.51128	.279
T3	43	2.8086	.85321	199	2.7465	1.63059	.426
TSH	87	1.9474	1.41499	289	2.3967	3.74853	.170
Vitamin D	89	23.3390	14.90163	289	22.6373	20.14699	.065

Table 5 indicates significant relationships between T4 and the measured parameters (T3 and TSH), with P values of 0.000 for both. However, a P value of 0.628 indicated no significant relationship with vitamin D. Similarly, T3 showed significant relationships with T4 and TSH, both with P values of 0.000, while the relationship with vitamin D was not significant, with a P value of 0.539. TSH also demonstrated significant relationships with T4 and T3, both having P values of 0.000, yet the relationship with vitamin D was not significant, with a P value of 0.403. Overall, the relationships between vitamin D and the measured parameters (T4, T3, TSH) were not significant, with P values of 0.628, 0.539, and 0.403, respectively.

Table 5. The Relationship between the measured parameters among the studied participants.

Test	**T4**		**T3**		**TSH**		**Vitamin D**	
	R	P value	r	P value	r	P value	R	P value
T4	1	.000	.636**	.000	.763**	.000	-.030	.628
T3	.636**	.000	1	.000	.701**	.000	-.040	.539
TSH	.763**	.000	.701**	.000	1	.000	.043	.403
Vitamin D	-.030	.628	-.040	.539	.043	.403	1	0.403

**. Correlation is significant at the 0.01 level (2-tailed).

Discussions

Vitamin D is a crucial nutrient for maintaining bone health. Higher bone mineral density in the elderly can decrease fracture risk, achievable through pharmacological and dietary interventions.[12] A normal euthyroid state is essential for the maintenance of adult bone structure and strength .[13] Currently, there is a lack of information regarding the impact of vitamin D treatment on thyroid morphology and function in relation to osteoporosis. This study found that females were the predominant participants, which aligns with the findings of a previous study.[14]

The recent study demonstrated no significant relationships among TSH, T4, and vitamin D. This finding fits with others that say serum T4 and TSH levels stay the same. [15] but it goes against other studies that say iodide trapping and thyroid hormone production change. [16,17] The new study showed that there were no significant differences in TSH, T3, T4, and Vitamin D levels between men and women. This is similar to what another study.[14] found. The recent study demonstrated significant relationships between TSH, T4, and T3. This finding is consistent with another study that indicated significant relationships between T3 and T4, but no significant relationship between T3 and TSH.[14]

Conclusion

The majority of participants in this study were female, primarily within the age range of 30-39 years, followed by those aged 20-29 years and then 40-49 years. Conversely, the least represented

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groups were male participants under 20 years and those aged 50 years or older. In terms of vitamin levels, the highest number of participants had vitamin D, followed by TSH, while T3 had the fewest participants, followed by T4. Also, there were no significant links found between the averages of the measured parameters (T4, T3, TSH, and Vitamin D) and sex among the people who were studied (P values of 0.279, 0.426, 0.170, and 0.065, respectively).

Authors contribution: A: prepared the manuscript, results . B: participated in the methodology , references.

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Institutional Review Board: This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Intuitional Review Board in the Ethics Committee of the Faculty of Medicine and Health Science, Sanaa university, Yemen (Research code: REC-32-2023).

Human Ethics and consent to participate: the study was conducted according to the guidelines of the declaration of Helsinki and approved by the Ethics committee of the Faculty of Medicine and Health Science, Yemen university, Yemen. (Research code: REC-32-2023).

Consent to participate: informed consent was obtained from all individuals participants included in the study.

Consent to publish: patients signed informed consent regarding publishing their data to the journal.

Data availability: all data included in the manuscript are available upon request.

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Conflict of interest: The authors of this study do not report any conflict of interest.

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