

ASSOCIATION BETWEEN VITAMIN D DEFICIENCY AND HYPOTHYROIDISM AMONG PATIENTS WITH CHRONIC HYPOTHYROIDISM ATTENDING AND AT AL-MARJ CITY ,LIBYA : A RETROSPECTIVE STUDY.

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Abstract—The relationship between vitamin D and thyroid diseases has attracted a lot of attention, although the evidence remains conflicting. To address this, we conducted a retrospective study during the period from January to May 2023. This exploratory study included 477 adult patients with chronic hypothyroidism attending and registered at Al-Marj Hospital for the treatment of diabetes and endocrinology, with 436 females and 41 males, as well as 100 healthy control subjects. All participants were tested for thyroid function, including TSH, T3, and T4, and biomarker tests such as vitamin D, calcium levels, RFT, cholesterol, and TG. The results showed that vitamin D deficiency is prevalent among hypothyroid individuals. Additionally, significant positive correlations were observed between serum vitamin D and calcium levels, as well as thyroid hormones. Our findings suggest that hypothyroid individuals should be tested for low serum calcium and vitamin D deficiency. Serum 25(OH) vitamin D was significantly lower in hypothyroid patients than in controls ($t = -11.128$, $P = 0.000$), with no significant gender-based differences in vitamin D levels ($t = -1.32$, $P > 0.05$). Conclusion: Our findings showed that the vitamin D deficiency is present in hypothyroid individuals; additionally, there are significant positive correlations between serum vitamin D and calcium levels and thyroid hormones. All hypothyroid individuals should undergo testing for low serum calcium levels and vitamin D insufficiency.

Keywords: hypothyroidism, biomarker, deficiency, Al-Marj.

I Introduction

Vitamin D deficiency and hypothyroidism are two common and widespread health issues with significant implications for global health. The thyroid, responsible for regulating critical functions such as metabolism, growth, and development, is highly influenced by the levels of various nutrients, including Vitamin D. Hypothyroidism, defined as an underproduction of thyroid hormones

(primarily thyroxine), can lead to a wide range of clinical symptoms, such as fatigue, weight gain, depression,

and cold intolerance(1).Its prevalence is rising worldwide, with autoimmune diseases like Hashimoto's thyroiditis being a leading cause of chronic hypothyroidism (2).Vitamin D, a fat-soluble vitamin, is synthesized in the skin in response to sunlight and can also be obtained through dietary sources. It plays a crucial role in maintaining bone health, immune function, and reducing inflammation. A growing body of evidence has highlighted the importance of Vitamin D beyond its classical role in bone metabolism, with several studies suggesting an association between low Vitamin D levels and an increased risk of autoimmune diseases, including hypothyroidism (3;4).While the relationship between Vitamin D deficiency and hypothyroidism has been suggested, the exact nature of this association remains unclear, and the findings across various studies have been inconsistent. Some studies have reported a higher prevalence of Vitamin D deficiency in patients with hypothyroidism, particularly those with autoimmune thyroiditis (5), while other studies have found no significant link between the two conditions (6). Despite this inconsistency, there is a growing hypothesis that Vitamin D deficiency may contribute to the development or exacerbation of hypothyroidism by modulating immune responses and thyroid function (3).The autoimmune nature of chronic hypothyroidism, particularly in cases like Hashimoto's thyroiditis, suggests that immune dysregulation could be an important mechanism linking Vitamin D deficiency with thyroid dysfunction. Vitamin D is known to play a pivotal role in immune modulation by regulating the activity of immune cells like T-cells and dendritic cells, which are involved in the autoimmune processes underlying hypothyroidism (7).Furthermore, Vitamin D receptors (VDR) are present on thyroid cells,

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indicating a direct interaction between Vitamin D and thyroid function, which may influence thyroid hormone production or the immune response that leads to thyroid destruction in autoimmune hypothyroidism (8).

The aim of the study was to investigate the relationship between the incidence rate of subclinical hypothyroidism and vitamin D (VitD) levels. Investigate the association between thyroid function indicators such as TSH (thyroid stimulating hormone), T3 (triiodothyronine), and T4 (thyroxine) and serum vitamin D levels.

II. Materials and Methods

a) A. Study population and design

A retrospective study was performed during period from January to May 2023. This exploratory study included 477 adult patients with chronic hypothyroidism attending and registered at Al-Marj Hospital for the treatment of diabetes and endocrinology, females 436 higher than males 41 with and 100 adult healthy subjects used as control group 50 % females and 50% males. All participants were tested for thyroid function including TSH, T3, T4 and biomarker test such as Serum vitamin D (25-OH), calcium levels, RFT, Cholesterol, TG. Vitamin D deficiency was designated at levels lower than 20 ng/ml.

b) B. Sociodemographic data collection

Clinical data were collected from the patient's medical records.

c) C. Laboratory measurements

The serum samples were stored at -80°C , avoiding repeated freeze-thaw cycles. Hormonal analysis Thyroid hormones (TSH, T3 and T4) and were evaluated in all participants. Biochemical analysis: The estimation of transaminases (Ca^{++} , Urea, Creatinine, AST, ALT, Cholesterol and T.G) was done by Reitman and Frankel. Statistical analysis The statistical analysis was performed using spss version 22 (All data were analyzed with non-parametric statistics).

III. Results

Table(1) showed total number recruited was 477 suffering from hypothyroidism, the mean age of all participants was 50.8 ± 14 years, and 436 patients (91.45%) were female and 41 (8.6%) were male. which attending the attending and registered at Al-Marj Hospital for the treatment of diabetes and endocrinology and 100 adult healthy subjects used as control group 50 % females and 50% males during period from January to May 2023. The mean TSH among hypothyroidism in the study participants were (2.4 ± 3 mIU/L) and Total T4 (93.9 ± 27.8) while Total T3 mean was (1.7 ± 0.4) respectively. and the mean of TSH among healthy subjects (2.7 ± 3) and total T4 (99.7 ± 30) while total T3 mean was (1.1 ± 0.3) respectively.

The range according to 5% to 95% percentile for TSH, Total T4, Total T3 were ($0.88-5.52$ mIU/L), ($61.6-181.2$), ($1.02-3.2$) respectively. There was no significant difference between vit-D groups in terms of age, gender, TSH, T4, T4, AST, ALT, Urea, Creatinine (table 2). Table(3) Moreover, serum calcium levels recorded a significant decrease in hypothyroid patients when compared to controls ($t = -5.69$, $P = 0.000$).

Table (1). The percentage of the patients in the sample according to gender

Gender	Hypothyroidism (%)	Mean age $\pm$ SD	Control Group (%)	Mean age $\pm$ SD
Females	436 (91.45%)	(52.1 ± 16.6)	50(50%)	(42 ± 9)
Males	41 (8.6%)	(50.7 ± 14)	50(50%)	(35 ± 19)
Total	477 (100%)	(50.8 ± 14)	100(100%)	(40 ± 7)

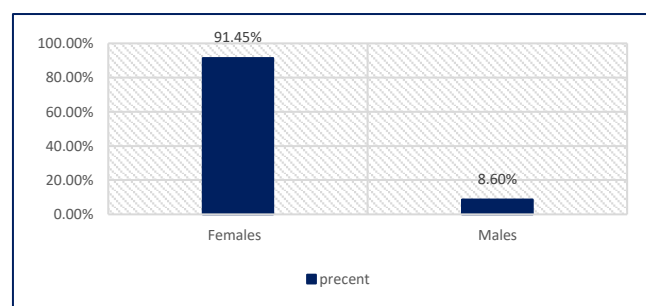


Figure 1. The percentage of the patients in the sample according to gender

Table 2 Illustrate the Descriptive statistics of the study sample.

Parameters : Mean $\pm$ SD	Mean	Std. Deviation	Range 5%-95%	N
Age	50.8	14	-	477
Hypothyroidism			-	477
Serum TSH (mIU/L)	2.4	3	0.88-5.52	477
Serum T3 (pg/ml)	1.7	0.4	1.02--3.2	477
Serum T4 (ng/dl)	93.9	27.8	61.6--181.2	477
Healthy subjects				
Serum TSH (mIU/L)	2.7 $\pm$ 3	3	0.88-5.52	100

Serum T3 (pg/ml)	T3	1.1 +/- 0.3	0.3	1.02--3.2	100
Serum T4 (ng/dl)		99.7+/- 30		61.6-- 181.2	100

Table (3) Mean± SD of serum 25(OH) vit D, Calcium and TSH levels in hypothyroid patients ..

Parameters : Mean ± SD	Mean± SD Hypothyroidism	Mean± SD Control group	Range 5%- 95%	N
Serum 25(OH)Vit D (ng/ml)	17.2± 4.6		-	577
Calcium levels (mg/dl)	7.56±0.66	9.90 ± 1.55	-	577
Wight	84.3± 8.712	80.6 ± 5.712	-	577
Urea	25.68±6.133	22.4± 6.2	Up to 45	577
Creatinine	0.75 ± 0.1891		0.5 -1.1	577
ALT	30.06 ±6.57		Up to 40	577
AST	21.53±8.078		Up to 40	577
Cholesterol	157±33.3		<200	577
T.G	118.1±29.2		< 150	577

IV. Discussion

Our findings indicated that female patients and controls had lower serum vitamin D levels compared to male patients and controls, although this difference was not statistically significant. Consistent with our results, previous studies have reported no significant difference in serum 25(OH)D levels between males and females.(9; 10) .Furthermore, our study revealed that serum levels of vitamin D and calcium were significantly lower in hypothyroid patients compared to the controls. We observed a significant positive correlation between vitamin D and calcium levels in both groups. Additionally, serum levels of vitamin D and calcium showed a negative correlation with TSH levels. These findings align with the results of (3) Zhao et al. (2018), who conducted a meta-analysis and found that vitamin D deficiency is more prevalent in individuals with hypothyroidism, especially those with Hashimoto's thyroiditis, the most common form of autoimmune hypothyroidism. Our study supports these findings, suggesting that vitamin D deficiency may exacerbate autoimmune processes and worsen the clinical progression of hypothyroidism. The lack of a significant difference in vitamin D levels between male and female hypothyroid patients in our study ($P > 0.05$) contrasts with some studies reporting gender-based differences in vitamin D levels, particularly in relation to thyroid function. For instance, some studies (5) have observed that females with hypothyroidism tend to have lower levels of vitamin D compared to males, potentially due to hormonal differences and lifestyle factors such as sunlight exposure and dietary habits. The comparison between hypothyroid patients and a healthy control group in our study, which showed significantly lower serum 25(OH) vitamin D levels in hypothyroid patients, supports the idea that vitamin D deficiency is more

pronounced in individuals with thyroid dysfunction. This finding is consistent with other research, such as Berk et al. (2015), who found similar results in their study, where patients with hypothyroidism had significantly lower vitamin D levels than healthy controls. This strengthens the hypothesis that vitamin D deficiency could contribute to thyroid dysfunction. Furthermore, other studies have also suggested a bidirectional relationship between vitamin D and thyroid function, particularly in individuals with autoimmune thyroid diseases (7) We also observed a significant difference.

in serum calcium levels between the studied groups, with lower levels found in hypothyroid patients. Although calcium levels were insignificantly lower in female patients compared to male patients, our study supports the notion that thyroid dysfunction may influence calcium metabolism. In contrast, a study conducted by [11] observed significant changes in ionized calcium (the physiologically active form) but no change in total calcium, indicating that thyroid dysfunction may specifically affect the active form of calcium, while overall calcium concentration remains unchanged. Regarding thyroid function markers, the mean TSH, T4, and T3 levels in our study were consistent with established reference ranges. Specifically, TSH levels were elevated in hypothyroid patients compared to healthy controls, which aligns with findings from [6], who reported similar thyroid function changes in their cohort. Likewise, T4 and T3 levels were lower in hypothyroid patients, which further supports the diagnosis of hypothyroidism and is consistent with findings from other studies, including [5]. Our study's reference ranges for TSH (0.88–5.52 mIU/L), T4 (61.6–181.2 nmol/L), and T3 (1.02–3.2 nmol/L) are consistent with literature values (Biondi, 2010), confirming the accurate measurement of thyroid function markers. Finally, we examined markers of liver (AST, ALT) and renal function (urea, creatinine) and found no significant difference across the vitamin D groups. This is consistent with (3;12) Zhao et al. (2018), who reported no significant effect of vitamin D status on liver or kidney function in patients with thyroid disease, suggesting that vitamin D deficiency primarily impacts thyroid function rather than liver or kidney function in this retrospective study.

Limitations

While the results of this study align with many previous studies, there are several limitations that should be taken into account. First, the retrospective design of the study limits our ability to establish causal relationships between vitamin D deficiency and hypothyroidism. Longitudinal studies would be more effective in determining the long-term effects of vitamin D supplementation on thyroid function. Another limitation is the potential impact of seasonal variation on vitamin D levels. Since data were collected from January to May, seasonal fluctuations in vitamin D levels,

particularly lower levels during the winter months due to reduced sunlight exposure, may have influenced the results. This factor may not

have been fully accounted for in the analysis and could affect the generalizability of the findings.

Conclusion

Our findings showed that the vitamin D deficiency present in hypothyroid individuals. Additionally, the significant positive correlations between serum vitamin D and calcium levels and thyroid hormones. All hypothyroid individuals should undergo testing for low serum calcium levels and vitamin D insufficiency.

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