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Abstract

Type 2 diabetes mellitus (T2DM) is a significant public health concern. Menopausal women often encounter it as a result of the aging and ovarian effects. This study's objective was to evaluate vitamin D3, clinical indicators, and metabolic hormones in menopausal women with hypothyroidism who also had diabetes. The study was done during the period of (JULY 2024 to SEPTEMPER 2024) on (45) hypothyroidism diabetic women in Baghdad Teaching Hospital, Baghdad, Iraq, compared with (45) control their ages were about (35–54) years. The results show that the BMI level increase in patients with hypothyroidism compared with the control group. Patients with hypothyroidism showed a significant decreased in D3, TT3, TT4, ca, and ALP in contrast to the control group, but a significant increase in TSH, FBS, and HbA1c. It is possible to draw the conclusion that a Vitamin D3 deficiency can interfere with symptoms of hypothyroidism, such as fatigue and muscle weakness. When thyroid hormones are under-secreted, this can lead to disturbances in vitamin and mineral metabolism, increasing the likelihood of vitamin D3 deficiency in postmenopausal women.

Keywords: Vitamin D3, Hypothyroidism, Diabetes mellitus, Menopausal women

1. Introduction

Type 2 diabetes mellitus (T2DM) is a significant public health concern. Menopausal women often encounter it as a result of the aging and ovarian effects [1, 2]. In addition to lowering bone mineral density (BMD) and raising the risk of fracture, the decrease in endogenous estrogens can also cause phenotypic, metabolic, and biochemical alterations that can predispose to the development of type 2 diabetes, both individually and in combination with aging [3, 4]. Weight gain, hypertension, visceral fat accumulation, glucose homeostasis impairment, and a decrease in muscle mass and strength are all linked to the menopause transition, It is necessary to add that a number of abnormalities in beta cell islets and insulin secretion (i.e., increased amyloid deposition and decreased amylin secretion, impaired insulin secretion pulsatility, decreased insulin sensitivity of pancreatic beta-cells to insulin tropic gut hormones, and diminished insulin response to non-glucose stimuli such as arginine) increase physical activity and decrease insulin secretion. Each of these is a significant risk factor for type 2 diabetes [5–7].

The frequency of thyroid disorders is five to ten times higher in women than in males, and they mostly affect women. Furthermore, the majority of thyroid conditions become more common as people age. Therefore, postmenopausal and older women are more likely to experience thyroid gland autoimmunity, hypothyroidism, nodular goitre, and malignancy [8]. Hypothyroidism is the underactivity of the thyroid glands.

The thyroid gland's ability to function is subsequently diminished. Middle-aged women are most likely to have hypothyroidism. Women are experiencing menopause during this period [9]. During

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menopause, estrogen levels drop dramatically. Many of the symptoms of menopause are brought on by this. Function of the thyroid may also be impacted by estrogen levels. In a 2011 peer-reviewed study, researchers looked at how estrogen levels affect thyroid receptors. Thyroid hormones can penetrate cells due to molecules known as thyroid receptors. Researchers discovered that thyroid diseases could result from estrogen levels influencing thyroid function [10]. In addition to its crucial function in maintaining calcium and phosphate homeostasis, vitamin D may be a key modulator of autoimmunity [11, 12]. and sensitivity to insulin [13]. It is believed that vitamin D favors the Th2 immune response phenotype over the Th1 acting via immune cells that express the vitamin D receptor (VDR-) [14]. This study's objective was to evaluate vitamin D3, clinical indicators, and metabolic hormones in menopausal women with hypothyroidism who also had diabetes.

2. Material and method

The study was done during the period of (JULY 2024 to SEPTEMPER 2024) on (45) hypothyroidism diabetic women in Baghdad Teaching Hospital /Baghdad/Iraq, compared with (45) control their ages were about (35–54) years. Information about each patient was collected, including their height, weight, age, and body mass index (BMI). Serum fasting blood sugar (S.FBS) is measured using automated Cobas instrumental procedures. glycoselated hemoglobin (HbA1c), thyroid function test [total triiodothyronin (TT3), tetraiodothyronin (TT4), thyroid estimation hormone (TSH), vitamin D3, Alkaline Phosphates (ALP) and Calcium (Ca) were estimated.

2.1. Study design

The current study is an observational case-control study that was conducted at Baghdad Teaching Hospital, Baghdad, Iraq, from July to September 2024. Participants enrolled in the current work were divided into two groups: 45 women who diagnosed with comorbid hypothyroidism and type 2 diabetes mellitus (T2DM) (considered as a case group) and 45 age and gender-matched healthy subjects (considered as a control group). The study targeted to assess the biochemical markers, thyroid function, and metabolic parameters in case group in comparison with controls. Data were collected cross-sectionally during a single clinical encounter.

2.2. Participants and sampling

- Case Group: Women aged 35–54 years with confirmed diagnoses of primary hypothyroidism (elevated TSH, reduced FT4) and T2DM (fasting blood glucose $\geq$ 126 mg/dL or HbA1c $\geq$ 6.5%) were recruited from the hospital's endocrinology clinic.
- Control Group: Age-matched ($\pm$3 years) healthy women with no history of thyroid dysfunction, diabetes, or chronic metabolic disorders were enrolled. Controls were selected from outpatient departments during routine health screenings.

2.3. Inclusion and exclusion criteria

2.3.1. Inclusion (cases):

- Confirmed hypothyroidism (TSH > 4.5 mIU/L, TT4 < 5.0 μg/dL) and T2DM (HbA1c $\geq$6.5%).
- Stable thyroid medication (levothyroxine) for $\geq$3 months.

2.3.2. Exclusion (all):

- Pregnancy, thyroid carcinoma, or secondary hypothyroidism.
- Chronic kidney/liver disease, malignancy, or recent vitamin D/calcium supplementation ($\leq$3 months).
- Acute infections or corticosteroid use.

2.4. Grouping and clinical data collection

Participants were divided into groups after confirmation of the diagnoses via laboratory tests and clinical evaluation. Anthropometric data, including height, weight and BMI were assessed using standardized protocols and the BMI was calculated as weight (kg)/height (m^2).

2.5. Laboratory methods

Fasting venous blood samples were collected between 8:00–10:00 AM after a 12-hour fast. Serum was separated via centrifugation (3,000 rpm, 15 min) and analyzed using the following methods:

1. ***Fasting Blood Sugar (FBS):*** Enzymatic colorimetry (glucose oxidase method; Cobas c501 analyzer, Roche Diagnostics).
2. ***Glycated Hemoglobin (HbA1c):*** High-performance liquid chromatography (HPLC; Bio-Rad D-10 system).
3. ***Thyroid Function Tests:***
   - TSH, Total T3 (TT3), Total T4 (TT4): Electrochemiluminescence immunoassay (ECLIA; Cobas e411 analyzer, Roche Diagnostics).
4. ***Vitamin D3 (25-OH-D):*** Chemiluminescent microparticle immunoassay (CMIA; Abbott Architect i2000).

5. ***Alkaline Phosphatase (ALP) and Calcium (Ca):*** Colorimetric assays (Cobas c501 analyzer).

All assays followed manufacturer protocols, with intra- and inter-assay CVs <5%. Internal quality controls and calibrators were used for accuracy.

2.6. Statistical analysis

Version 22 of the SPSS software (SPSS, Chicago, IL, USA) is utilized to store data and to perform the required analytical analysis. All data were expressed as mean ± standard deviation (SD). The independent t-test (independent-samples t-test) was used for the statistical analysis to compare the patients' group with controls, with $P < 0.05$ serving as the lower limit of significance. Additionally, chi-square test were used to assess the difference in the age distribution in the studied groups considering $p < 0.05$ as a significant diference.

2.7. Ethical approval

Approval was obtained from the Scientific and Ethical Committee in the College of Medicine, Mustansiriyah University (approval number: MOG 227 in June 13, 2024). Patients' consent to participate in the current study was obtained verbally.

3. Result and discussion

The results of the age distribution analysis between the patients and control groups are illustrated in Table 1 which showed that the patients group, 36.0% (n = 11) of participants were aged 35–44 years, while 64.0% (n = 34) were aged 45–54 years. For the Control group, 56.0% (n = 24) fell within the 35–44 age range, and 44.0% (n = 21) were in the 45–54 age range. A chi-square test revealed no statistically significant difference in age distribution between the groups ($\chi^2 = 0.33$, $p = 0.56$).

Hypothyroidism particularly affects women and the elderly. Women are 8-9 times more likely to hypothyroidism compared to men [15]. Hormonal changes during menopause can exacerbate these risks. Regardless of sex, the elderly are further more at risk [16]. The incidence of hypothyroidism in postmenopausal women was calculated in the study's sample which include 90 female patients which showed that 17% of them had hypothyroidism. Hypothyroidism is linked to a number of symptoms, including age at menopause, BMI, TSH, T3 and T4, fatigue, cramping in the muscles, depression, weight gain, cold sensitivity, and difficulty sleeping [17].

Table 1. Distribution of the studied groups according to age range groups (years).

		Study Groups	
		Hypo	Control
Age range (Years)			
(35–44)	N	11	24
	%	36.0%	56.0%
(45–54)	N	34	21
	%	64.0%	44.0%
Total	N	45	45
	%	100.0%	100.0%
Chi-sequare		0.33	
P-value		0.56	

Table 2. Comparative the mean levels of BMI (Kg/m^2) between cases and control.

Parameters	Study Groups	Mean	SD	P-value	Signs.
BMI (Kg/m^2)	Hypo	29.59	2.99	≤0.0001	H.S
	Control	25.77	3.44		

In the Table 2, the results show that the BMI level (kg/m2) increase in patients with hypothyroidism (29.59 ± 2.9) compared with the control group (25.77 ± 3.4), it was highly statically significant with a p-valu of $0.0001 < 0.01$.

Studies examining the association between hypothyroidism and obesity have traditionally used a baseline group drawn from obese patients whose thyroid hormone levels were measured. Obese patients had greater rates of hypothyroidism than the general population in a number of these investigations [18–20]. In light of these results, some researchers have proposed that slight thyroid malfunction may be a contributing reason to notable weight fluctuations, which may serve as a risk factor for overweight and obesity [21]. According to our current research, in consistent with previously published researches, obesity can be considered as a risk factor for hypothyroidism, showing that people with greater BMI are more likely to develop hypothyroidism and that weight loss is crucial for lowering the risk of hypothyroidism [22].

In hypothyroidism patients, serum TSH levels increase when thyroid hormones secretion (T3, T4) is insufficient [23]. There were significant differences in mean serum levels of TSH, TT3, and TT4 between hypothyroidism patients, and control group as in Table 3.

In this context vitamin D deficiency causes decreased calcium absorption as well as an increase in parathyroid hormone, which in turn causes decreased bone mass and calcium reabsorption from bone [24]. In a study of postmenopausal Indian women, blood calcium levels in the patient group were considerably lower than those in the control group. The bone

Table 3. Mean levels of thyroid hormones in cases comparing with control.

Parameters	Study Groups	Mean	SD	P-value	Sig
TT3 (nmol/l)	Hypo Control	0.81 1.98	0.15 0.32	≤0.0001	H.S
TT4 (nmol/l)	Hypo Control	49.34 96.12	10.62 14.79	≤0.0001	H.S
TSH (uIU/ml)	Hypo Control	17.85 2.63	8.49 1.62	≤0.0001	H.S

Table 4. The levels of S. Ca, S.ALP and s.D3 in cases comparing with controls.

Parameters	Study Groups	Mean	SD	P-value	Sig
S. Ca (mg/dl)	Hypo Control	4.73 7.90	0.41 0.71	≤0.0001	H.S
S. ALP (U/l)	Hypo Control	46.63 91.56	6.70 8.59	≤0.0001	H.S
S. D3 (ng/ml)	Hypo Control	10.72 33.08	2.31 3.25	≤0.0001	H.S

Table 5. The levels of FBG (mg/dl) and HbA1C (%) in cases comparing with controls.

Parameters	Study Groups	Mean	SD	P-value	Sig
FBG (mg/dl)	Hypo Control	182.52 85.60	55.79 4.37	≤0.0001	H.S
HbA1c (%)	Hypo Control	7.80 4.78	1.89 0.36	≤0.0001	H.S

markers assessed in the previous study were calcium, phosphorus, and alkaline phosphatase serum levels. And the results of the previous research showed that the patient group had considerably greater serum levels of phosphorus and alkaline phosphatase than the control group [25]. Furthermore, the relationship between bone density and serum calcium levels in Indian women before and after menopause was investigated; in postmenopausal women, the findings indicated a significant link [26].

Bone fractures and reduced bone density in postmenopausal women with osteoporosis have been linked to vitamin D deficiency [27]. Previous study showed that the amount and density of bone minerals in the hip and lumbar vertebrae (L1-L4) were significantly correlate with vitamin D levels, [28] but this previous findings to appear clearly in the women subjected to the present study in that the majority of them with a good health even those who experienced low levels of vitamin D.

The present study showed that about 49% of diabetic patients enrolled in the present study showed a vitamin D deficiency (Tables 4 and 5) (VDD). Furthermore, reduced concentrations of 25-hydroxyvitamin D (25-OHD) have been associated with elevated TSH levels and also the higher levels of 25-hydroxyvitamin D (25-OHD) have been associated with lower levels of TSH. Additionally, it has been demonstrated that in those with T2DM, TSH and 25-OHD levels are inversely correlated. Additionally, the metabolism of 25-OHD is reciprocally regulated by thyroid hormone [29]. The development and increased risk of thyroid disease are known to be influenced by vitamin D deficiency and type 2 diabetic mellitus (T2DM). Therefore, effective strategies to control vitamin D and type 2 diabetes are essential to reducing the incidence of thyroid conditions in middle-aged people, which may have an effect on their general health [30, 31]. Since T2DM and thyroid disorders are the most frequently reported endocrinological conditions linked to vitamin D deficiency in routine clinical practice, there is a strong correlation between the two conditions. Additionally, Numerous risk factors, such as iodine availability and shortage, BMI, age, gender, smoking status, genetic factors, impaired fasting glucose, and diabetes mellitus, have been linked to thyroid volume in another research [32]. It is crucial to recognize that thyroid disease and diabetes mellitus (DM) may both be influenced by vitamin D shortage or insufficiency [14]. Vitamin D levels in diabetics may be affected by the application of oral diabetes drugs and compliance with therapeutic dietary restrictions [33]. Moreover, vitamin D intake, absorption, or metabolism may be changed by thyroid dysfunction [34]

4. Conclusion

It was concluded that Vitamin D3 deficiency can interfere with symptoms of hypothyroidism, such as fatigue and muscle weakness. When thyroid hormones are under-secreted, this can lead to disturbances in vitamins and minerals metabolism, increasing the likelihood of vitamin D3 deficiency in postmenopausal women.

Disclosure

The authors have no conflict of interest and the work was not supported or funded by any drug company.

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