

Evaluation of IL-17 as an Inflammatory Marker in Patients with Hypothyroidism and Low Vitamin D Levels

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ABSTRACT

Hypothyroidism is defined as the inability of the thyroid gland to produce sufficient hormones. Interleukin-17 (IL-17) plays a crucial role in the development of hypothyroidism by promoting inflammation and modulating immune responses. This study aimed to evaluate the concentration of certain cytokines, including IL-17, and the low serum vitamin D levels in Iraqis with hypothyroidism. The study included 65 male and female participants (58.4% female and 41.5% male) aged 25–57 years, as well as 30 healthy individuals of varying ages. After a 12–14 hour fast, blood samples were collected to assess serum IL-17 levels using an ELISA assay. The results revealed an increased concentration of interleukin-17 in patients (13.53 ± 3.05) compared to the control group (10.31 ± 1.06). Vitamin D levels were also significantly decreased in patients (15.4 ± 2.15), suggesting that vitamin D deficiency may contribute to the elevated interleukin-17 levels, as pro-inflammatory cytokines are believed to play a role in the mechanism of hypothyroidism. The results also showed a significant increase in FT3, FT4 levels, with a mean serum FT3 level of 4.12 ± 0.31 pmol/L in patients and 3.21 ± 1.05 pmol/L in healthy individuals. While mean serum free thyroid hormone (FT4) level in patients was 3.61 ± 1.17 pmol/L, compared with 2.06 ± 2.42 pmol/L in healthy individuals. A significant increase in thyroid-stimulating hormone (TSH) concentration were also observed., while the mean thyroid-stimulating hormone (TSH) level in patients was 9.20 ± 0.30 mIU/L, compared with 0.42 ± 0.56 mIU/L in healthy individuals.

Key words: pro-inflammatory cytokines, IL-17, IL-6, Hypothyroidism, vitamin D

INTRODUCTION

Hypothyroidism is one of the most common endocrine disorders and can be described as a condition in which thyroid-stimulating hormone (TSH) levels are high and thyroxine (T3/T4) levels are low. These disorders affect various body systems, such as metabolism, the heart, the nervous system, and the immune system, and can be fatal [1]. Inflammatory cells, such as lymphocytes and thyroid follicular cells, produce cytokines, and an individual's health status can influence the resulting immune response. In hypothyroidism, type I helper T cells (Th1) predominate, whereas in autoimmune thyroiditis and in a healthy thyroid, the immune response is mixed between Th1 and Th2 cells [2, 3]. Furthermore, cytokines can directly interfere with thyroid follicular cell function and immune responses, which may be a key factor in cytokine-induced thyroid dysfunction [4]. Elevated levels of interleukin-17, a key cytokine in the helper T cell 17 (Th17) pathway, promote inflammation and tissue damage in the thyroid gland [5]. Vitamin D deficiency can also increase Th17 cell differentiation and suppress regulatory T cells (Tregs), exacerbating immune dysfunctions [6]. A growing body of evidence suggests a strong association between vitamin D deficiency and the prevalence and severity of hypothyroidism [7, 8]. Individuals with hypothyroidism show lower blood levels of vitamin D compared to healthy individuals, and this decrease is typically associated with levels of thyroid-stimulating hormone (TSH) and free thyroxine (FT4) [9]. This suggests that vitamin D may play a direct role in influencing thyroid hormone synthesis and act as an immune regulator, protecting thyroid follicular cells from immune damage. Vitamin D (1,25-dihydroxyvitamin D3) significantly affects the immune system [10]. Therefore, this study aimed to evaluate the concentration of IL-17, and vitamin D and their relationship with the severity of hypothyroidism,

MATERIAL AND METHODS

Study subjects

The models used in the current study were collected from an outpatient clinic in Baghdad. Hospital/Medical City and included 65 patients of both sexes, aged 25 to 57 years, between June and August 2025. These patients were clinically diagnosed with hypothyroidism. An additional 30 healthy individuals of varying ages were also included. After fasting for 12–14 hours, venous

blood samples (5 mL) were drawn from each participant in the hypothyroidism and control groups.

Collection of blood samples and Biochemical analysis

All demographic information, clinical outcomes, and medication history were recorded throughout the evaluation period. Sterile 10 mL syringes were used to withdraw 5 mL of blood via venipuncture from patients with hypothyroidism. A collection tube containing a coagulation inducer and a gelatinous medium was used to collect the withdrawn blood. This tube was used to separate the serum. The blood was allowed to coagulate for 10 to 15 minutes, after which the serum was separated and centrifuged at 3000 rpm for three assays. These assays included determining T3, T4, and TSH levels, measuring vitamin D levels, and measuring serum levels of cytokines, such as interleukin-17, using BioSource ELISA kits [11].

Statistical Analysis

SPSS (Standard Statistical Application, version 24) was used for all calculations and to detect the effect of the differential groups (control and patients) in this study. Data are represented as mean $\pm$ SD, where statistical significance is defined as a p-value < 0.05 and high statistical significance as a p-value < 0.01 [12].

RESULTS AND DISCUSSION

In this study, samples were collected from individuals with hypothyroidism, aged between 28 and 57 years. However, only 58.4% of the study sample were female, while 41.5% were male. As shown in Figure 1.

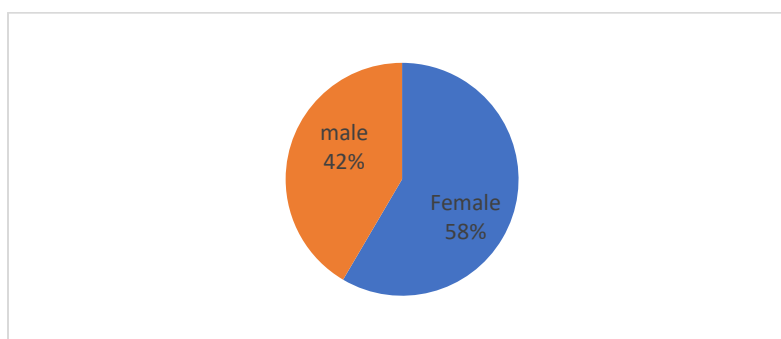


Figure 1. The proportion of impacted women in comparison to men.

This may be due to the stimulation of the immune system by estrogen (particularly 17β -estradiol), which promotes B cell survival and stimulates the production of autoantibodies, while testosterone suppresses the immune system in males [13,14]. This estrogenic immune stimulation leads to an increased level of thyroid autoantibody production, which causes these antibodies to attack the thyroid gland, the most common cause of hypothyroidism [15].

Statistical analysis, as shown in Table 1, revealed a significant increase ($P \leq 0.05$) in serum free triiodothyronine (FT3) levels compared with healthy controls. Specifically, serum FT3 levels in patients were 4.12 ± 0.31 pmol/L, whereas in healthy individuals it was 3.21 ± 1.05 pmol/L, the results revealed a decrease in free thyroxine hormone (FT4) levels, with serum levels in patients being (3.61 ± 1.17) pmol/L compared to (2.06 ± 2.42) pmol/L in healthy individuals. Conversely, a significant increase in serum thyroid-stimulating hormone (TSH) levels was recorded in patients (9.20 ± 0.30) mIU/L compared to (0.42 ± 0.56) mIU/L in healthy individuals.

Table 1. The concentration of level thyroid hormones FT3, FT4, TSH in patients with Hypothyroidism and control by pmol/L and mIU/L

parameter	Patients N=65	Controls N=30	P-value
Ft3(pmol/L)	4.12 ± 0.31	3.21 ± 1.05	$P < 0.05^*$
Ft4(pmol/L)	3.61 ± 1.17	2.06 ± 2.42	$P < 0.05^*$
TSH (mIU/L)	9.20 ± 0.30	0.42 ± 0.56	$P < 0.05^*$

*** $P < 0.05$ considered significant**

The current study demonstrated a significant increase in thyroid-stimulating hormone (TSH), thyroxine (T4), and triiodothyronine (T3) levels in hypothyroid patients compared to the control group and healthy individuals, this contrasts with the findings of other studies [16, 17]. The TSH results are consistent with those of Ali et al., who observed elevated TSH levels in hypothyroid patients [18], Elevated thyroid-stimulating hormone (TSH) levels are a common diagnostic feature of this disease, particularly in individuals over 40 years of age, with women being seven times more likely to develop it than men. Disruption of thyroid function and activation of the

feedback mechanism between the hypothalamus, pituitary gland, and thyroid gland leads to increased thyroid stimulation and, consequently, increased hormone production in tissues, particularly TSH production from the pituitary gland [2][1]. While significant elevations in free thyroid hormone levels (FT3 and FT4) are attributed to several factors, including disease stage and thyroid hormone replacement therapy, elevated FT3 and FT4 levels may also be due to functional thyroid hormone resistance syndrome. In this syndrome, body tissues and cells resist the absorption of these hormones due to defects in peripheral receptors resulting from mutations in the thyroid hormone receptor (TR α or TR β), ultimately leading to elevated hormone levels. [19] Previous studies have shown that some hypothyroid patients receiving levothyroxine treatment may exhibit elevated levels of free thyroid hormone in the blood, despite their continued elevated TSH levels [20]. As shown in Figure 2, a statistically significant decrease ($P < 0.05$) in serum 25-hydroxyvitamin D [25(OH)D] levels were observed in patients with primary hypothyroidism (15.4 ± 2.15 ng/mL) compared to the healthy control group (18.10 ± 10.21 ng/mL).

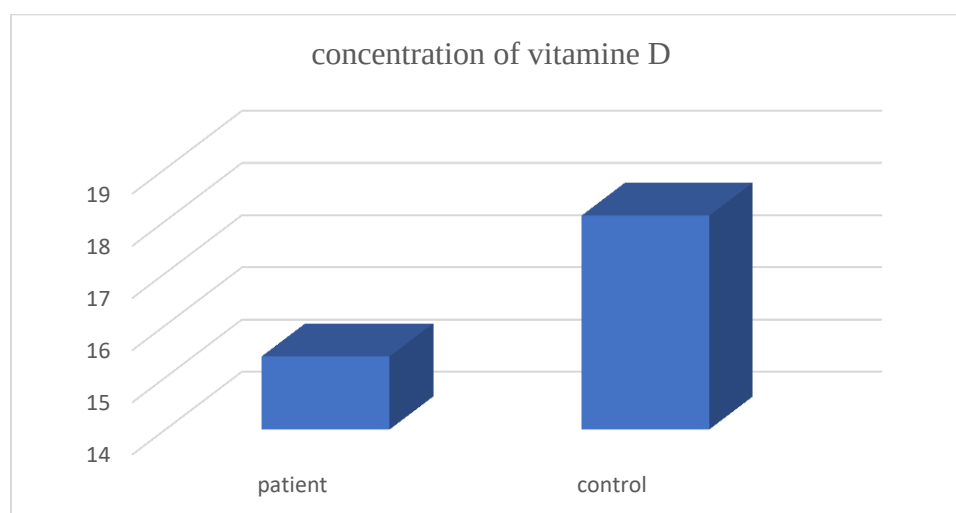


Figure 2. The concentration of vitamin D in patients and healthy by ng/mL.

Our results are consistent with a study conducted in Erbil, Iraq, which investigated the relationship between vitamin D deficiency and elevated TSH levels [9]. Several studies have demonstrated an association between vitamin D deficiency and hypothyroidism, with hypothyroid patients often suffering from vitamin D deficiency [21]. Vitamin D is known to

contribute to thyroid function, and its deficiency can lead to dysfunction in the T4-to-T3 conversion pathway [22]. Vitamin D is known to contribute to thyroid function, and its deficiency can lead to a disruption in the T4-to-T3 conversion pathway [23]. This severe vitamin D deficiency may be a consequence of the general metabolic slowdown caused by hypothyroidism. Hypothyroidism primarily affects gastrointestinal motility and reduces the expression of mucosal transporters, negatively impacting the absorption of lipophilic vitamins, including cholecalciferol, by intestinal cells [24]. Thyroid hormones are also key inducers of hepatic 25-hydroxylase and renal 1-alpha-hydroxylase enzymes. Thus, hypothyroidism significantly reduces the metabolic conversion of vitamin D to its biologically active form, 1,25(OH)₂D [25]. In contrast, this relationship follows a two-way path through the autoimmune axis. In addition, vitamin D acts as a major immune modulator, inhibiting the proliferation of Th1/Th17 lymphocytes and preventing the synthesis of pro-inflammatory cytokines. This leads to a significant deficiency in vitamin D levels, which is reflected in impaired immune tolerance. This, in turn, leads to the activation of autoreactive B cells and accelerates the destruction of thyroid follicle cells by autoantibodies, which is clinically manifested as hypothyroidism [26].

It was found that immunological, inflammatory, and cytokine indices differed significantly between hypothyroid patients and healthy individuals, as shown in Table 2 and Figure 3, the mean concentration of interleukin-17 (IL-17) in patients was significantly higher (13.53 ± 3.05) pg/mL than in the healthy group (10.31 ± 1.06) pg/mL, and this difference was statistically significant at a probability level of $P \leq 0.05^*$.

Table 2. Concentration of IL-17 in patients with Hypothyroidisms and Control

parameter	Patients N=65	Controls N=30	P-value
IL-17	13.53 ± 3.05	10.31 ± 1.06	$P < 0.05^*$

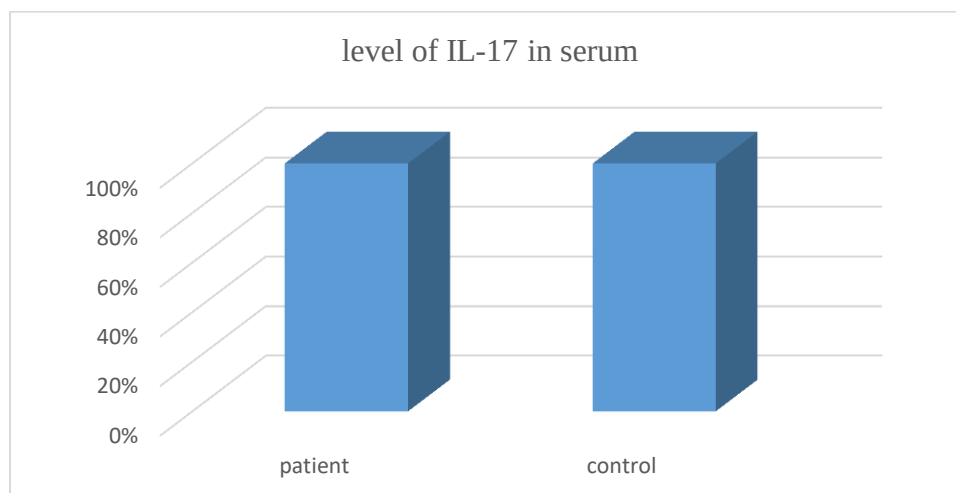


Figure 3. The concentration of IL-17 in hypothyroidism's patient and control.

The marked increase in interleukin-17 (IL-17) levels in hypothyroid patients is consistent with the findings of Lu *et al.*, who reported a significant rise in IL-17 levels in patients.[27] However, Ali *et al.* [18] found no substantial differences in IL-17 levels among patients, which contradicts our current findings. Helper T cells 17 (Th17) produce pro-inflammatory cytokines, including interleukin-17 (IL-17), which is a crucial step in inducing inflammatory processes by causing inflammation in tissues through neutrophil polarization and amplifying thyroid injury by stimulating the immune response.[28] These cells play a role in the persistence of inflammation within thyroid tissue. Interleukin-17 stimulates thyroid epithelial cells and fibroblasts to produce more inflammatory mediators (such as interleukin-6 and interleukin-8), leading to increased polarization of immune cells and destruction of thyroid cells (lingual thyroids) [30]. Studies have shown a correlation between localized expression of interleukin-17 in thyroid tissue and the degree of fibrosis, ultimately leading to the loss of the gland's functional capacity to produce hormones. Some research also indicates that serum levels of interleukin-17 are markedly elevated in the early stages of Hashimoto's thyroiditis (when thyroid function is normal) and may decline relatively as the disease progresses to overt hypothyroidism due to the destruction of most of the thyroid tissue [31]. Furthermore, Lu *et al.* [27] found that interleukin-17 may sometimes inhibit immune stimulation by increasing the release of inflammatory cytokines and other chemokines, leading to thyroid tissue destruction. Interleukin-17 is known to induce the NF- κ B pathway, leading to apoptosis and the release of further inflammatory cytokines [24]. A strong association was found between vitamin D deficiency and elevated levels of interleukin-17 in patients with

hypothyroidism, as demonstrated by the results reported in the Erbil study (2025), which shows that vitamin D acts as a strong immune modulator, inhibiting the differentiation of T cells into Th17 cells, and thus reducing the production of interleukin-17. Its deficiency leads to the loss of this immune effect, allowing for elevated levels of interleukin-17 and exacerbating the immune attack on the thyroid gland [9].

Conclusions

The study confirmed a link between hypothyroidism, increased concentration of thyroid hormones (FT3 and FT4), and elevated TSH levels, consistent with our understanding of the negative feedback system. The study also demonstrated a significant decrease in vitamin D levels in hypothyroid patients, as well as a correlation between vitamin D deficiency, inflammatory markers (IL-17), and hypothyroidism. This information helps to clarify the complexity of the disease.

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