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Prevalence of Vitamin D Deficiency among Hypothyroid Patients in Benghazi Medical Center

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Abstract

Vitamin D is a steroid hormone introduced into the body through food, but major synthesis occurs through exposure of the skin to solar ultraviolet light. Vitamin D obtained from the skin or the diet is converted by the liver to 25(OH) vitamin D and is metabolized in the kidney to (1,25) dihydroxyvitaminD.The consequences of low vitamin D level is not only causing osteomalacia, but also found to increase risk of autoimmune thyroid disease. A different gene in the Vitamin D receptor was shown to predispose people to autoimmune thyroid disease including Graves' disease and Hashimoto's thyroiditis. Since hypothyroidism is a common endocrine problem in Benghazi, data on the effects of vitamin D supplementation on thyroid function in hypothyroid patients needs to be investigated.

***Keywords**: Hypothyroidism, Thyroid Stimulating Hormone (TSH), vitamin D*

INTRODUCTION

Hypothyroidism, also called underactive thyroid or low thyroid, is a disorder of the endocrine system, in which the thyroid gland does not produce enough thyroid hormone [1]. Hypothyroidism can cause a number of symptoms, such as poor ability to tolerate cold, a feeling of tiredness,constipation,depression, and weight gain. Sometimes, there may be swelling of the front part of the neck due to goiter [1].

The National Health and Nutrition Examination Survey (NHANES) found the prevalence of hypothyroidism in the general population to be about 3.7%, with higher prevalence of hypothyroidism in women than men [2].

Hypothyroidism is classified to (1) Primary hypothyroidism, which is the most common cause and mostly caused by the autoimmune destruction (Hashimoto thyroiditis), followed by radioiodine or surgical ablation for hyperthyroidism. Congenital hypothyroidism accounts for about 1 in 4500 live births [3]. (2) Secondary hypothyroidism, which is due to pituitary TSH deficiency, (3) tertiary hypothyroidism, which is due to hypothalamic TRH deficiency and (4) peripheral thyroid hormone resistance.

Vitamin D is a fat-soluble vitamin. In nature, it is present in very few foods such as vegetables like mushrooms; vitamin D_2 (ergocalciferols) and animals as fish, cod liver oil, fortified food, dairy products and egg yolk; vitamin D_3 (cholecalciferol) [4], or available as dietary supplements. Additionally, the body itself has the ability to produce vitamin D_3 when exposed to the UVB radiation from the sunlight. Vitamin D gotten from sun exposure, food, and supplements is biologically inert and must undergo hydroxylations in the body for activation. The first hydroxylation converts vitamin D to calcidiol (25-hydroxyvitamin D [25(OH) D]) in the liver, while the second forms the physiologically active calcitriol (1,25-dihydroxyvitamin D, $25(OH)_2$ D]) in the kidney [5] . Serum 25-hydroxyvitamin D (25(OH) D) is the commonly used biomarker of an individual's vitamin D status.

Recently, Vitamin D, which is required for normal development and mineralization of bone, as well as bone remodeling, has been recognized to be involved in various immune functions [6], and its deficiency has been shown to be associated with autoimmune diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), inflammatory bowel disease (IBD), multiple sclerosis (MS) and type 1 diabetes. Furthermore, vitamin D supplementation was found to prevent the onset and/or development of these autoimmune diseases [7,8]. Additionally, it was reported that patients with Hashimoto's thyroiditis had lower vitamin D levels [9,10]. The present study was aimed to investigate the relation between serum 25(OH) D and hypothyroidism in order to elucidate whether supplementation with vitamin D in the insufficient group affects these measures.

Methodology:

Study design: Cross sectional study was used to collect the data after Ethics Committee approval. One hundred patients of both sex and age range (20-65 years) were taken from the endocrine unit at the Benghazi Medical Center between July and October 2018.

Complete history of any medical or surgical problems from the patients was taken, in addition to the history of drug taken especially for (Corticosteroids, Anti-tuberculous, Anti-epileptic, and Lipid lowering drugs).

Quantitative determination of serum FT_4, TSH, and 25-OHD was performed using an enzyme linked immunosorbent assay (ELISA). Hypothyroidism was defined as a TSH level > 5 MIU/l and FT4< 50 nmol/l. While vitamin D deficiency was defined as a level of vitamin 25-OHD of <30 ng/ml and the level below 12ng/ml is considered as very severe deficiency for both men and women.

The study of sample size of 83 patients was calculated with an alpha error of <0.05.

Analysis of variance F test (ANOVA) was used to compare the results of all studied groups. The mean and the standard deviation (SD) and the range were calculated for all continuous variables. Student's *t*-test was used to compare the means of TSH and Vitamin D levels .Chi-square test was used to compare the prevalence of vitamin D deficiency among the hypothyroid patients Statistical analysis was performed using the software SPSS for Windows .

Results:

Out of (100) patients, 83 returned the filled questionnaire with a response rate of 83%. Regarding the age, it ranged between 20 and 65 years. The mean age among all participants was 48 years. The highest percentage (43.4%) of the study subjects was between 35-49 years old, while the lowest percentage (10.8 %) of the study subjects was 65+ years old (Figure 1)

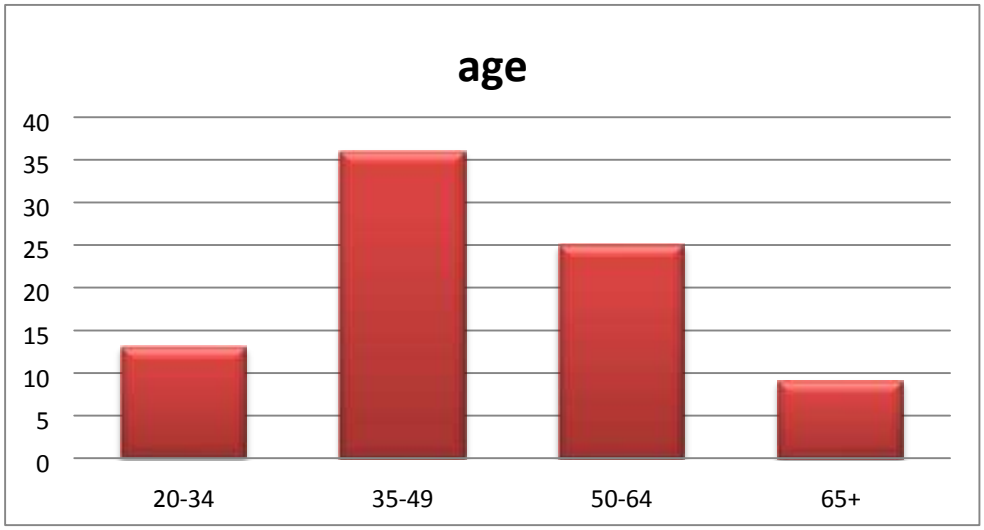

Figure 1: **Age distribution of hypothyroid patients (years).**

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In terms of gender, most of the samples (approximately 98%) of participants were females, whereas 2.02% of hypothyroid participant were males (Figure 2).

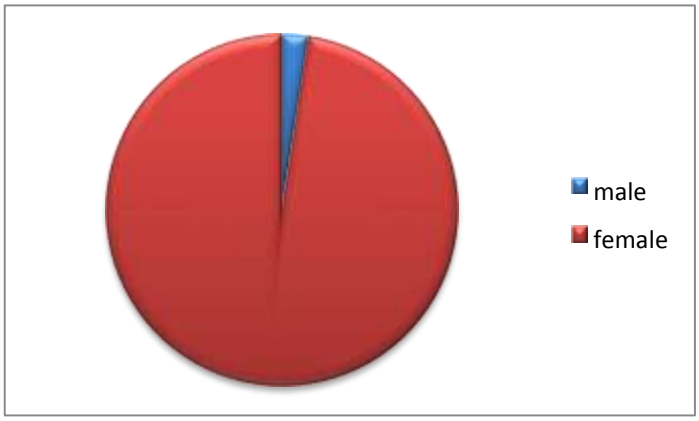

Figure 2: Sex distribution of hypothyroid patients.

It was found that the majority of hypothyroid patient had vitamin D deficiency (94%), whereas only (6%) had sufficient amount of vitamin D level. The Level of Vitamin D among hypothyroid patients was divided into deficient, insufficient and sufficient measured by percentage. The insufficient had the vast majority (48.2%), followed by deficient (45.8%). (Figure 3)

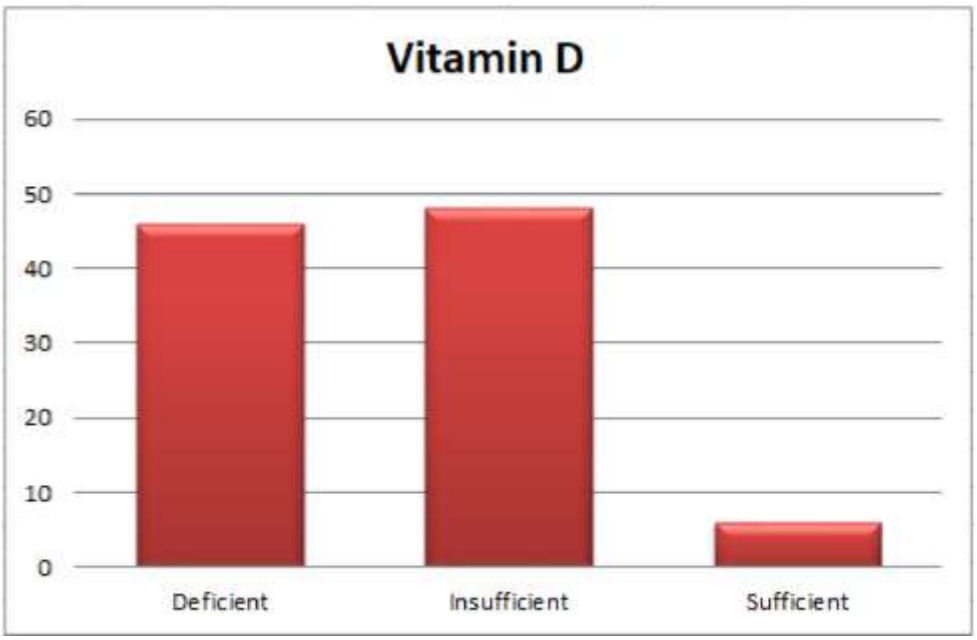

Figure 3: Vitamin D level among hypothyroid patents

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The study compared the level of vitamin D among controlled and uncontrolled hypothyroid patients. The uncontrolled participants are those patients who had hypothyroidism as a TSH level > 5 mU /l and FT4< 50 nmol/l. the uncontrolled group had the highest percentage (74.7%) of low vitamin D level (<30 ng/ml), whereas the controlled patients had a lower percentage (25.3%) of low vitamin D level (Figure 4).

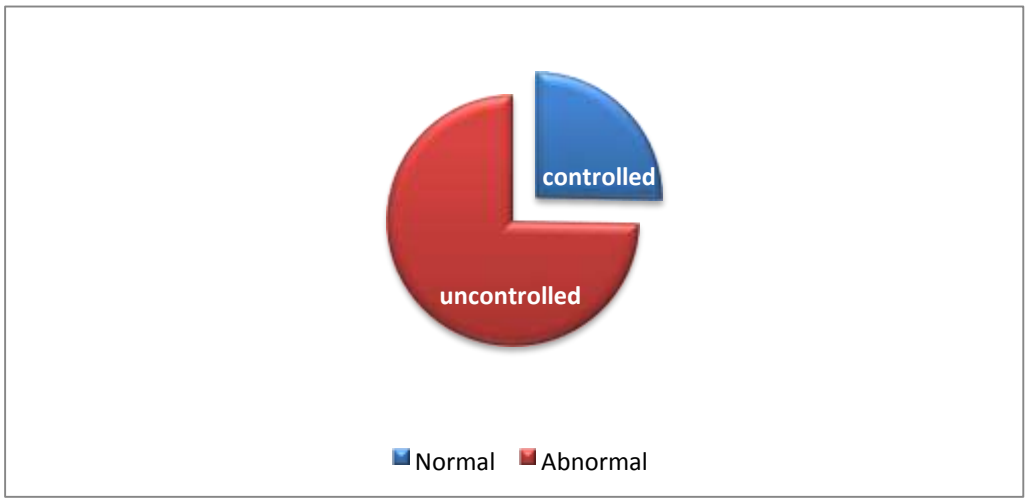

Figure 4: The percentage of vitamin D deficiency amonghypothroid patients

Treated=controlled Untreated=uncontrolled

The risk factors for vitamin D deficiency in our study were as follows; antiepileptic drugs (Carbamazepine and Phenytoin) (two patients) and Rifampin for treatment of tuberculosis (one patient).

Discussion:

This study was conducted in Benghazi city and included Libyan subjects who visited endocrine clinics at the Benghazi Medical Center, which considered as one of the largest referring hospitals for the eastern part of the country. All the participant in the study had primary hypothyroidism, which is the most common cause of hypothyroidism and mostly caused by the autoimmune destruction (Hashimoto thyroiditis) [11.12].

Vitamin D deficiency is a global problem throughout the world. It has been estimated that more than one billion people in the world have vitamin D deficiency or insufficiency [13]. In Libya, studies on vitamin D status in 2017 identified Vitamin D deficiency is common, especially in women of childbearing age and older age [14].

It has been recognized that vitamin D involved in various immune functions besides to its role in bone and muscle development Moreover, vitamin D deficiency has been shown to be associated with autoimmune diseases, including rheumatoid arthritis (RA), inflammatory bowel disease (IBD),

multiple sclerosis (MS) and type 1 diabetes (T1DM), and that vitamin D supplementation prevents the onset and/or development of these autoimmune[15].

Importantly, both vitamin D and thyroid hormone bind to similar receptors called steroid hormone receptors. Vitamin D mediates its effect through binding to vitamin D receptor (VDR), and activation of the VDR-responsive genes. While VDR gene polymorphism was found to associate with autoimmune thyroid diseases (AITDs) [16], a different gene in the vitamin D receptor was shown to predispose people to autoimmune thyroid disease including Graves' disease and Hashimoto's thyroiditis. Few studies have been conducted in order to find any significant association between the levels of vitamin D and hypothyroidism and to determine whether vitamin D deficiency involves in the pathogenesis of hypothyroidism or rather a consequence of the disease, however the results were conflicting.

Our results revealed that most of the hypothyroid patients (about 94%) had low vitamin D level. this was in accordance with a study performed in India by Idiculla et al in 2018 who demonstrated that there was a significantly higher proportion of severe vitamin D deficiency (<4.2 ng/dl) in hypothyroid group patients. This points to higher possibility of hypothyroidism in individuals deficient in vitamin D [17].

Furthermore, the Mackawy et al study concluded that the patients with hypothyroidism suffered from hypovitaminosis D and there was a significant positive correlation between serum level of vitamin D with thyroid hormones and a significant negative correlation with TSH levels and suggested that the deficiency of serum levels of vitamin D was significantly associated with the degree and severity of hypothyroidism [18]. They explained the association by the following factors. First, the lower levels of vitamin D may be due to the poor absorption of vitamin D from the intestine. Second, the body may not activate vitamin D properly [18].

Also, our result was in accordance with another study done by Byron Richards (2008) which, studied the effect of vitamin D deficiency on thyroid gland. The investigator reported that a lack of vitamin D contributed to the possibility of low thyroid hormones [19].

Besides, our result discovered that one of the hypothyroid patients had a history of tuberculosis which was treated by rifampicin. Tuberculosis (TB) remains a major worldwide health issue as the second most frequent cause of infection-related mortality [20,21]. Rifampin and isoniazid are used in treating tuberculosis (TB). The complex relationship between vitamin D and TB has long been recognized. Prior to the advent of antibiotics, sun exposure and

vitamin D supplements formed the primary treatment for the disease [22]. Vitamin D is a modulator of macrophage activity and enhances the production of the antimicrobial protein cathelicidin [23]. Vitamin D deficiency has been associated with increased susceptibility to TB infection or reactivation of latent TB infections [24]. Treatment with rifampin and isoniazid may also alter vitamin D status, as CYP3A4 is induced by rifampin and inhibited by isoniazid [25]. CYP3A4, a hepatic cytochrome P450 enzyme is involved in drug metabolism, and catabolism of Vit D via a similar pathway as CYP24A1 (an enzyme catalysing the hydroxylation steps of Vit D2 and Vit D3) [26]. Rifampicin causes an accelerated loss of Vitamin D due to increased clearance as it acts as an agonist to pregnane X receptor and inducing the activity of CYP3A4 and limiting the formation of active one alpha 25(OH)2D3 . Isoniazid causes impairment of 25hydroxylation leading to impaired Vit D action [27, 28].

On the other had our study also revealed that two of the hypothyroid patients who had vitamin D deficiency had a history of epilepsy and were treated by anti-epileptic drugs. Antiepileptics do affect the bone mineral metabolism adversely, as manifested by decreased vitamin D levels in serum of patients taking antiepileptic drugs [29]. Vitamin D and calcium supplementation have to be started with antiepileptic drugs therapy [30]. Phenytoin, phenobarbital and carbamazepine have been investigated for their influence on vitamin D metabolism [31]. The commonest theory is that antiepileptic drugs induce the cytochrome P450 enzymes in the liver and cause increased conversion of vitamin D to inactive metabolites. The inactive vitamin D results in decreased absorption of calcium in the intestines, leading to hypocalcaemia and increase in parathyroid hormone in circulation. The susceptibility of individuals to the effect of AED on vitamin D and bone metabolism may be influenced by some genetic factors [32].

Conclusion:

Vitamin D deficiency is common among hypothyroid Libyan patients living in Benghazi. This study regarding the prevalence of vitamin D deficiency among hypothyroid Libyan patients should be extended to measure vitamin D level among different ages and sexes and in all main cities within the country.

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