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Research Article

CORRELATION AND PREVALENCE OF THYROID GLAND AND VITAMIN D IN DIFFERENT HUMAN AGE GROUPS Albulena Beadini¹, Sadi Bexheti¹, Sheqibe Beadini¹, Avdi Nazifi¹, Nexhbedin Beadini¹

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Abstract:

Research has found a link between Vitamin D deficiency and autoimmune thyroid diseases (AITD), which are Hashimoto's thyroiditis and Graves' disease. For example, one study found that the presence of vitamin D deficiency was significantly higher in patients with autoimmune thyroid disease, as compared to healthy patients (72 percent versus 31 percent, respectively). [12] Other research has found an association between vitamin D deficiency and the presence of anti-thyroid antibodies, hinting that vitamin D deficiency may be a trigger for the development of autoimmune thyroid disease. [8]

Lastly, early research suggests that vitamin D supplementation may help manage thyroid disease. For instance, one study demonstrated that antibodies in autoimmune thyroid disease significantly decreased as a result of taking vitamin D at 1,000 IU per day for one month. [15] Parathyroid gland is four small glands located behind thyroid gland. They are covered with connective tissue. The parathyroid gland are very vascular glands and they contain a capillary network. Parathyroid gland is formed by three types of cells. They secret parathyroid hormone (PTH). The PTH has important impact in regulation of the calcium and phosphate.

Vitamin D's main role is to regulate bone metabolism and calcium and phosphorus levels in the body, so it is not surprising if you generally associate vitamin D with keeping your bones strong and healthy. Over the past several years, though, other vitamin D roles have been examined, including its role in heart disease, cancer, and autoimmune conditions, like Hashimoto's and Graves' disease.

Keywords: vitamin D, autoimmune thyroid disease, parathormone, calcium, osteoporosis.

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INTRODUCTION:

Vitamin D is known as the "sunshine vitamin" because your body makes it after your skin is exposed to ultraviolet rays from the sun. Vitamin D can also be found in certain foods such as: Fatty fish like salmon, mackerel, tuna, trout, herring, and sardines. Cod liver oil, some dairy products (for example, milk, soy milk almond milk, and yogurt). Fortified ready-to-eat cereals, fortified orange juice, hard-boiled eggs.

A deficiency in vitamin D causes rickets in children and osteomalacia in adults. Rickets is rare now in the United States due to the fortification of milk, but osteomalacia remains a problem, especially due to its subtle symptoms of bone pain and muscle weakness. [7] According to the Institute of Medicine, vitamin D deficiency is defined as a level less than 30 nmol/L. while a vitamin D level greater than or equal to 50 nmol/L is considered sufficient. People with vitamin D levels between 30 nmol/L and 49 nmol/L are considered at risk for vitamin D deficiency. Keep in mind, there is no standard guideline regarding what an "optimal" vitamin D level is for a person with thyroid disease. It's possible that if you have autoimmune thyroid disease, your doctor may want your vitamin D level to be higher than 50 nmol/L, perhaps closer to 75 nmol/L. [10] There are multiple potential causes for vitamin D deficiency, but a big one has to do with low sunlight exposure, due in

large part to the frequent use of sun block to prevent skin cancer (a good measure, for sure), and the fact that we spend more time indoors on our phones and computers. [3] Diet too is an issue, considering there is not a whole lot of foods that contain vitamin D naturally. Most multivitamins do not contain enough vitamin D either—multivitamins typically have 400 IU vitamin D, but the recommend daily intake is around 600 IU for adults and 800 IU for adults over the age of 70.

Besides diet and low sunlight exposure, other causes of low vitamin D levels include:

- Gut malabsorption of vitamin D (for example, celiac disease or Crohn's disease)
- Increased breakdown of vitamin D (antiseizure medications)
- Impaired production of active form of vitamin D (liver or kidney disease)
- Decreased skin production of vitamin D (dark-skinned individuals)
- Sequestration of vitamin D in fatty tissue (obesity)

MATERIALS AND METHODS:

All cases included in this study were subjected to the followings:

- 1. Complete history taking
- 2. Complete clinical examination
- 3. Laboratory investigations, including
 - Routine investigations
 - Serum FT₃ (2.8-6.4 pmol/l) FT₄ (11.5 22.7 pmol/) and TSH for thyroid dysfunction patients with reference range (0.4- 4.0 μlU/ml) calcium (2.1-2.6 mmol/l) vitamin D (20-50ng/ml) parathormone (< 42 pg/ml)

	Ca ²⁺	TSH	FT4	FT3	Vitamin D	Parathormone
Normal range of the parameters	2.1-2.6 mmol/l	0.4-4.0 μIU/ml	11.5-22.7 pmol/l	2.8-6.4 pmol/l	20-50 ng/mL	< 42 pg/ml

Table.1. Normal level range of Ca^{2+,} TSH, FT₄, FT₃, vitamin D and parathormone

Veins blood procedure

When the patients have to do more analysis then the procedure is taking the veins blood and not the capillary blood.

MATERIALS:

Sterile needle syringe, sterile wound, 75% ethyl alcohol, rubber fixing connector.

PROCEDURE:

Vein puncture is the most common way to collect blood from adult patients. Collection takes place from a superficial vein in the upper limb, generally the median cubical vein; this vein is close to the skin and doesn't have many large nerves positioned close by. This reduces pain and discomfort for the patient.

Vein puncture can take place in a general medical practitioner's office and is often carried out by a trained phlebotomist or nurse. However, its commonality does not equate with it being the best way to collect a blood sample. Many patients find it inconvenient and worrisome. There are also risks related to the storage, transportation, and potential loss or contamination of the blood samples once they are collected. These same concerns also affect the suitability of arterial sampling.

Method for measuring the level of parathyroid hormone and vitamin D in blood samples

Vidas method is the apparatus by which the level of vitamin D and parathormone in blood serum are determined. This is a method of detecting IgG antibodies in human serum or plasma (EDTA) using ELFA (Enzymes Fluorescent Assay) technique.

The serological method (with immunoassay enzymes) is a fast method, with a very high sensitivity, non-invasive and not expensive.

Colorimetric method for determining calcium in the blood

When determining the level of calcium in the serum by the colorimetric method, it is necessary to work with two tubes: with one tube is determinate the analysis and with the other test tube is determinate the standard. The standard concentrations are 2 mmol/L while the measurement length for measuring absorbance of analysis and standard is 578 nm.

Statistical Analysis

Results were statistically analyzed by SPSS 11.5 for Windows. The mean and the standard deviation (SD) for all the variables were calculated. Analysis of variance F test (ANOVA) was used to compare the results of all examined cases in all studied groups. The correlations between serum vitamin D, calcium and TSH were presented by correlation coefficient (r2). Results considered significant or non-significant when P> or < 0.05, respectively.

RESULTS:

In this research the number of patients that have been analyzed is 100 patients, from which one 45 are females, 45 are males and 10 are control group of the patients. We have different age groups from 30-40 years old and the age group from 41-60 years old. This number of patients and their percentage will be shown by the table below.

Number of patients	Total number of the patients 100	45 % Male	45 % Female	10 % control patients
Age groups		30-40 years old and 41-60 year old	30-40 years old and 41- 60 year old	30-60 years old

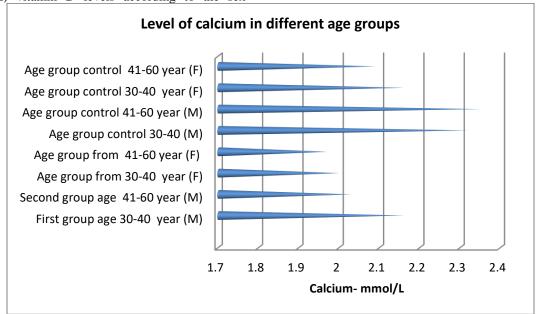
Table.2. Number of patients and their percentage (%) in different age groups

Parameters : Mean ± SD	Group I	Group II	t- value, p- value
Sex	22 M	20 M	
	23 F	25 F	p>0.05
Age (years)	$\textbf{30-40} \pm \textbf{6.29}$	$41-60 \pm 41-60$	t= - 0.379, <i>p</i> >0.05
Serum 25(OH)Vit D (ng/ml)	44.53 ± 14.91	14.79 ± 2.11	t= 11.13, <i>p</i> = 0.000
Serum Calcium (mmol/l)	10.37 ± 1.55	7.92 ± 1.77	t= 5.69, <i>p</i> = 0.000
Serum TSH (µlU/ml)	3.66 ± 0.91	6.92 ± 0.97	t = -13.38, p = 0.000
Serum FT ₃ (pg/ml)	2.94 ± 1.01	$\boldsymbol{1.08 \pm 1.02}$	t=4.78, p=0.000
Serum FT ₄ (ng/dl)	1.59 ± 0.30	0.64 ± 0.46	t=5.48, p=0.000
Parathormone PTH(pg/ml)	49.3 ± 1.20	1.70 ± 1.85	t= 4.20, p= 0.000

Table.3. Clinical characteristics of the participants used in the present stud	Table.3.	Clinical charac	cteristics of the	e participants u	ised in the p	resent studv
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By using t-test to compare between the two groups, serum 25(OH) vitamin D level was significantly lower in hypothyroid patients than in controls (t=-11.128, P =0.000) as illustrated in table 1. On comparing serum 25 (OH) vitamin D levels according to the sex

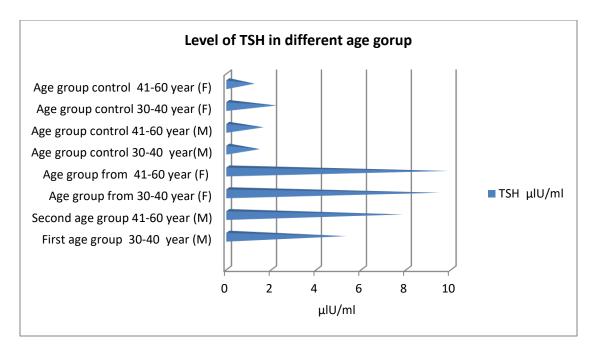
distribution, they were insignificantly decreased in females than those of male in controls and hypothyroid patients (t= -0.160, and t= -1.32, P >0.05) respectively.



Graph.1. Level of calcium in different age groups females and males

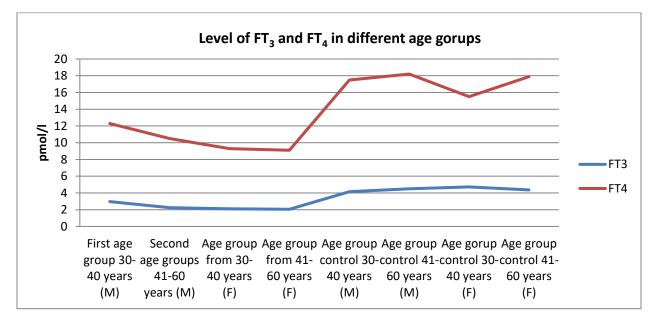
In the first graphic we have the level of calcium in different age groups in correlation with number of patients who are in the control group. This results show us the difference in the male patients and females about the level of calcium during the problems with hypothyroidism.

Calcium levels are lower in females than in males of the same age group.



Graph.2. Level of TSH in different age groups of females and males

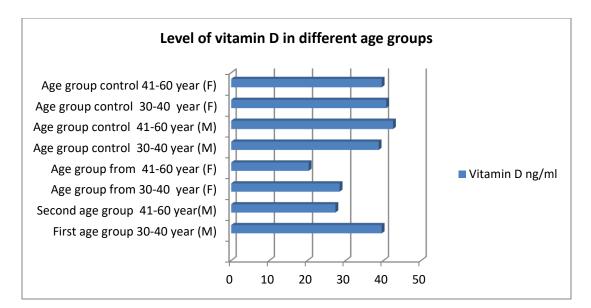
In the second graphic we have the prevalence of thyroid stimulate hormone in different age groups in female and male gender but the focus is on the age group from 30-40 years and the other group is 41-60 years. The level of TSH in the patients with hypothyroidism is increased in progressive way with decreasing the level of vitamin D and calcium in the blood of the researched patients.



Graph.3. Level of FT₃ and FT₄ in different age groups of females and males

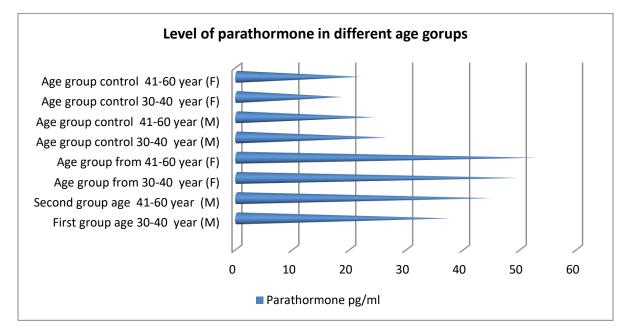
In the graphic above are described the values for level of FT_4 in different human age groups. The level of FT_4 in females with hypothyroidism is under level of normal range values.

In the chart above, we presented the data for FT_3 level in different age groups and different gender where from the results we see that the FT_3 level in hypothyroidism patients is in the limit of reference values or under reference values.



Graph.4. Level of vitamin D in different age groups of females and males

Vitamin D values are presented in different human ages, in females and males in the age groups 30-40 years and 41-60 years is lower compared to the male in the same age group and this correlates with low calcium levels in females compared with males.



Graph.6. Level of prathormone in different age groups of females and males

Patients with hypothyroidism have the highest level of parathyroid hormone compared to control patients both in men and women, in all age groups investigated.

DISCUSSION/CONCLUSION:

Vitamin D is known for its primary role in bone and mineral homeostasis, and it has been shown recently that its deficiency is associated with various diseases such as cardiovascular disease, cancer, infection, and adiposity as well as osteoporosis. Interestingly, it has been shown recently that vitamin D has potent immunomodulatory effects and plays important roles in the pathogenesis of autoimmune diseases. Serum concentration of 25(OH)D is the best indicator of vitamin D status. It reflects vitamin D produced cutaneously and that obtained from food and supplements and has a fairly long circulating half-life of 15 days. In contrast to 25(OH)D, circulating 1,25(OH)₂D is generally not a good indicator of vitamin D status because it has a short half-life of 15 hours and serum concentrations are closely regulated by parathyroid hormone, calcium, and phosphate (19). Levels of 1, 25(OH)₂D do not typically decrease until vitamin D deficiency is severe. (20-21) Therefore, in the present study we measured serum 25(OH)D rather than 1.25(OH)₂D to ensure we are getting more accurate results. 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 and those that yielded conflicting results. Byron Richards (2008) (35) studied the effect of vitamin D deficiency on thyroid gland in experimental study; he reported that a lack of vitamin D contributed to the possibility of low thyroid hormones. One of two mechanisms may explain the low levels of vitamin D in patients with hypothyroidism. First, the low levels of vitamin D may be due to poor absorption of vitamin D from the intestine. Second, the body may not activate vitamin D properly. Other articles have demonstrated that patients with Graves's disease also have low levels of

Supplementary Material

Vitamin D helps the intestines absorb calcium. However, the vitamin D must first be activated or "turned on" by parathyroid hormone (PTH). Once activated, vitamin D acts to greatly increase the amount of calcium that the intestines can absorb from food, sometimes by as much as two to four times. The body can either make its own vitamin D using a process that requires sunlight or obtain vitamin D directly from the diet (e.g. in fortified milk or vitamins). Many people across the world have vitamin D deficiency — experts estimate that one-third of Americans are vitamin D deficient.

For patients with vitamin D deficiency, it is difficult for the body to obtain calcium from the diet. This often leads to a rise in the PTH level, since the parathyroid glands must increase the PTH production in order to increase calcium levels by "stealing" it from the bones. Therefore, people with a normal blood calcium levels and a high PTH level may have secondary hyperparathyroidism, which means that the high PTH level is a normal response of healthy parathyroid's Vitamin D. (36) importantly, both vitamin D and thyroid hormone bind to similar receptors called steroid hormone receptors. A different gene in the Vitamin D receptor was shown to predispose people to autoimmune thyroid disease including Graves' disease and Hashimoto's thyroiditis.

Recent studies have demonstrated a role of vitamin D in Graves Disease (GD). First, Vitamin D related gene polymorphisms such as VDR gene and vitamin D binding protein gene are associated with GD. Second, Vitamin D deficiency modulates Graves' hyperthyroidism induced by thyrotropin receptor immunization in BALB/c mice. Third, Vitamin D analog inhibits inflammatory responses in human thyroid cells and T cells.

with Our results indicated that patients hypothyroidism suffered from hypovitaminosis D with hypocalcaemia. Moreover, the positive significant correlation between each of serum vitamin D and calcium with thyroid hormones and that negative significant correlation with TSH levels, suggested that deficiency of serum vitamin D and calcium levels were significantly associated with degree and severity of the hypothyroidism which encourage the advisability of vitamin D supplementation. Screening for Vitamin D deficiency and serum calcium levels recommended for all hypothyroid patients.

glands to another problem (like vitamin D deficiency or kidney failure).

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Appendix

IMMUNE ASSAY TEST- Immunoassays can be used to test for the presence of a specific antibody or a specific antigen in blood or other fluids

HYPOCALCAEMIA- Hypocalcaemia, also spelled hypocalcemia, is low calcium levels in the blood serum.

OSTEOPOROSIS- which literally means porous bone, is a disease in which the density and quality of bone are reduced. As bones become more porous and fragile, the risk of fracture is greatly increased. The loss of bone occurs silently and progressively.

OSTEOMALACIA- Osteomalacia may be caused by poor dietary intake or poor absorption of calcium and other minerals needed to harden bones. Osteomalacia is a characteristic feature of vitamin D deficiency in adults.