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Evaluation of Serum Ferritin and Vitamin D and Their Correlation with TSH in Hypothyroid Patients in Basrah City

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Abstract

Objective*: The study was designed to estimate the serum Vitamin D3 and ferritin levels and their correlation with TSH level in hypothyroid patients.*

Patients and Methods*: This is a case control study in which sixty two hypothyroid patients and another age and sex -matched healthy individuals were included. . Serum Ferritin, Vitamin D3 (vit D) and thyroid stimulating hormone (TSH), were measured for all participants. Statistical analysis for the collected data was done using SPSS software with appropriate statistical tests.*

Results*: On comparing the two groups, serum Vit D level and Ferritin was significantly decreased in hypothyroid patients than that in the controls, P value < 0.001 and < 0.01 respectively. Significant negative correlation was found between serum Vit D level (r= -0.43, P<0.05) and serum Ferritin (r= -0.78 ,p <0.01) with TSH where low levels of Vit D and ferritin were found in hypothyroidism.*

Introduction

Thyroid hormones production occurs in the thyroid follicles, which are the functional unit of the thyroid gland. They are essential for the proper operation of physiological systems .Through feedback mechanisms; the hypothalamus-pituitary-thyroid axis (HPT) regulates the synthesis of thyroid hormones. Via this mechanism, the hypothalamus produces thyrotropin-releasing hormone (TRH) in response to a reduction in thyroid hormone levels. TRH stimulates anterior pituitary to secrete Thyroid stimulating hormone (TSH) which acts on thyroid gland to enhance the synthesis of Thyroid hormone in the thyrocytes (1). In order for thyroid hormones to be synthesized, iodide is actively taken up via the sodium/iodide symporter (NIS). After oxidization of iodide, it is quickly associated with thyroglobulin (TG) in a process called Organification. This process is catalyzed by thyroid peroxidase enzyme (TPO) in the presence of hydrogen peroxidase resulting in the formation of mono- and diiodotyrosines (MIT, DIT). In the subsequent coupling reaction, , two iodotyrosines are coupled to form either thyroxine (T4) or triiodothyronine (T3) .

Thyroid gland produces T4 to T3 in a ratio of 14:1 (2), however, in the tissue, the majority of T4 transforms to

T3. The enzymes mediate this transformation are type 1 and type 2 iodothyronine deiodinases(3) . In the plasma, The majority of thyroid hormones are attached to plasma proteins in a bound form and only (fT4 and fT3) that are unbound or free form are available for cellular uptake.

Vitamin D is classified as a fat-soluble secosteroid present naturally in five forms (vitamin D1–D5). For humans, vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol) are the two forms of vitamin D that are most significant. Only 5–10% of vitamin D is obtained from food (vitamins D2 and D3), with the majority being produced in the skin following exposure to sunshine (vitamin D3)(4). When skin comes into contact with sunlight, 7-dehydrocholesterol is converted to vitamin D3. Then 25-hydroxylase converts vitamin D3 in the liver to form 25-hydroxyvitamin D (25(OH) D), sometimes referred to as calcidiol or calcifediol. The kidneys produce 1,25-dihydroxyvitamin D3, commonly referred to as calcitriol, 1,25-dihydroxycholecalciferol, or 1α,25-dihydroxyvitamin D3, from 25(OH)D through the activity of the enzyme 1α-hydroxylase, which is encoded by the CYP27B1 gene(5). This is the active form of vitamin D3, while serum 25(OH)D levels are the primary indicator of vitamin D status.

The modulation of calcium and phosphate concentrations is the primary function of calcitriol, the active form of vitamin D3. Intestinal and renal absorption of calcium and phosphate in addition to bone mineralization is enhanced by calcitriol(4). Moreover, calcitriol is engaged in immunological, neuromuscular, and cell growth control. Also, it demonstrates an immunosuppressive and anticancer effects (5, 6). Calcitriol binds to the nuclear receptor superfamily for vitamin D (VDR). Following this interaction, VDR travels to the nucleus, dimerizes with the retinoid X receptor (RXR), and binds to vitamin D response elements found in DNA (7). More than a thousand genes have their expression regulated by VDR(8) present in nearly every tissue(9).

The relationship between thyroid hormones and iron is bidirectional. Iron is an essential nutrient required for various physiological functions. Iron deficiency (ID) is a widespread nutritional disorder worldwide, affecting about two billion people, mainly pregnant women and women of childbearing age(10). Iron is essential for Hemoglobin production, and for other proteins and enzymes that produce energy and support cellular activity. Iron insufficiency may have detrimental effects on the thyroid gland, particularly on the thyroid peroxidase enzyme's activity (11). Moreover, around 5% of the population has anemia from ID, which is a common comorbidity in people with thyroid dysfunction(12). Previous studies reported that ID might be a major factor in the etiology of thyroid dysfunction. They observed a significant incidence of ID in individuals suffering from thyroid conditions. both overt and subclinical hypothyroidism are associated with anemia and adding iron to thyroxine therapy improves both conditions compared to thyroxine therapy alone (13). On the other hand ,Thyroid hormone affect erythrocyte proliferation directly by increase the proliferation of erythrocyte precursors and indirectly by decreasing enhance production of erythropoietin(14, 15).

The aim of the present study is to evaluate the association between vit D , ferritin and TSH in hypothyroid patients in Basrah city.

Patients and Methods

This is a case control study in which sixty two hypothyroid patients and another 62 age and sex –matched healthy individuals were included. . Serum Ferritin, Vitamin D3 and thyroid stimulating hormone (TSH), were measured for all participants. The applicable principles for acceptable clinical practices were taken into consideration and the study was authorized by the institutional ethics committee.

Study population

Random patient selection was done using predetermined inclusion and exclusion criteria. The study included participants who fulfilled the following requirements. Patients with hypothyroidism (TSH level greater than 5.0 mIU/L) who have not taken calcium and vitamin D supplements. Subjects who had a history of thyroid disease other than hypothyroidism were not included in our study.

Clinical and biochemical assessment

Following an overnight fast, blood samples were taken from each participant in the morning. When drawing blood, the appropriate aseptic and antiseptic procedures were followed. Three milliliters of drawn blood were placed into a in a plane collection tube. Blood was placed in a rack and left to clot for at least half an hour at room temperature. After that, it was centrifuged for 10 minutes at 2000 rpm. The chemiluminescence immunoassay method was used to measure serum levels of vitamin D, iron, and TSH.

Statistical Analysis

SPSS version 14.0 was utilized for data analysis in order to evaluate the study's results.

RESULTS

Sixty two patients (20 males and 42 females) were included in this study, their age ranged from 15 to 65 years. Patients were divided into four age groups. There were 11 people (17.4%) in the first group aged 15 to 20.years;1 male and 10 female. 24 people (38.7%) In the second age group aged 20 to 30 years; 13 females and 11 males. The third group included twenty patients (32.2%) ;5 males and 15 females aged 30 to 45. The last group aged 45 years to 65 years included 7 patiens (11.2%) ; 4 females and 3 males, Table 1 and Figure 1.

Table 1: Age and sex distribution of hypothyroid patients

Age groups (years)	Frequency (%)	Female	Male
15-20	11 (17.4)	10	1
20-30	24 (38.7)	13	11
30-45	20 (32.2)	15	5
45-65	7(11.2)	4	3
Total	62 (100)	15	7

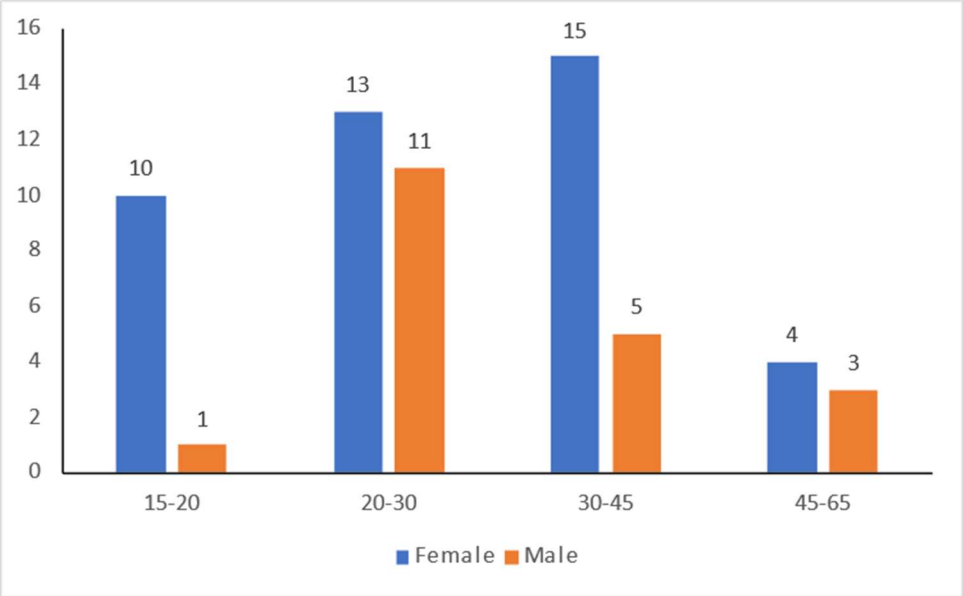

Figure 1: Distribution of hypothyroid patients into age groups

There was no significant difference in mean age of hypothyroid patients (45.1±18 years) and the control group (42.6±9.2 years), *P value* > 0.05. There were 42 (68%) female patients and 20 (32%) male patients, yet the difference was not significant with control, *P value* > 0.05, table 2.

Table 2: Demographic characteristics of the patient and the control groups

Parameter	**Healthy control**	**hypothyroid patients**	**t-value**
	Mean ± SD	Mean ± SD	**p value**
Age	42.6±9.2	45.1±18	0.97
			0.33
Sex	38F (61%)	42F (68%)	> 0.05
	24M (39%)	20M (32%)	

The mean serum vitamin D was 13.52 ng/ml and 20.06 ng/ml in the in the hypothyroid group and control group respectively. Vit D was significantly lower in hypothyroid group compared to the control, *P value* < 0.001). Also, there was significant decrease in serum Ferritin level, *p value* <0.01. TSH levels were significantly elevated in Hypothyroid patients, *P value* < 0.001, table 3, figure 2.

Table 3: comparison of a serum vit D , Ferritin and thyroid profile between the patient and control groups

Parameter	**Healthy control**	**hypothyroid patients**	**t-value**
	Mean ± SD	Mean ± SD	**p value**
Serum Vit D	20.06±2.66	13.522±3.23	-1.130

nM/L			0.001
Serum ferritin µM/L	67.15±1.01	25.74±1.23	-5.816 0.01
Serum TSH miU/L	3.65±0.35	15.009±1.15	1.052 0.000

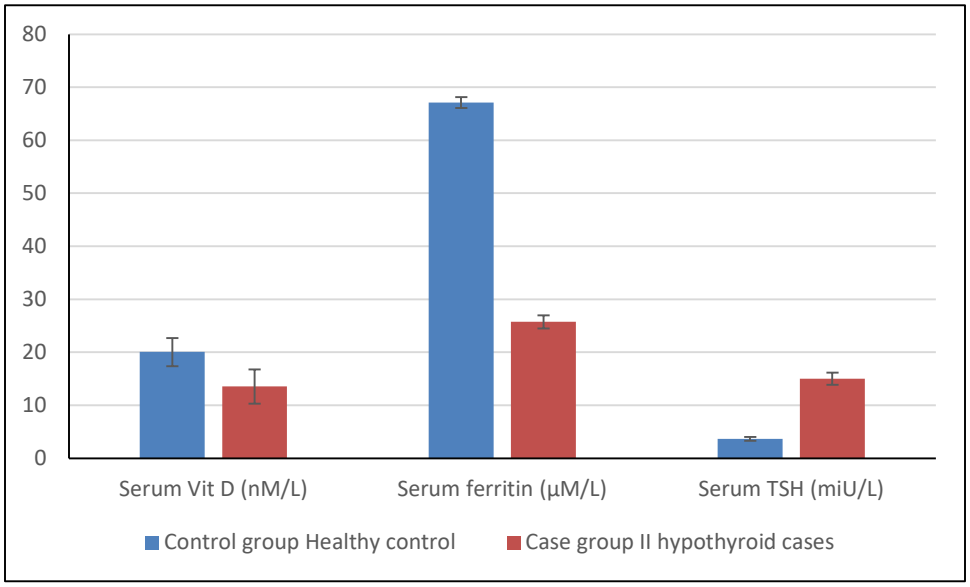

Figure 2: comparison of a serum vit D, Ferritin and thyroid profile between the patient and control groups

In the hypothyroid group, however, there were no significant differences in the vitamin D, ferritin and TSH level between the male and female patients (*P value* 0.38 , 0.37 and 0.291 respectively), table 4, figure 3.

Table 4: Serum Vt D, Ferritin and TSH level in female and male patients group

	Hypothyroid cases		
Parameter	Female	Male	t-value p value
Serum Vit D nM/L	13.57±2.34	13.59±1.32	1.087 0.38
Serum ferritin µM/L	25.74±1.23	25.23±1.42	0.954 0.370
Serum TSH miU/L	15.08±3.15	15.12±2.21	1.130 0.291

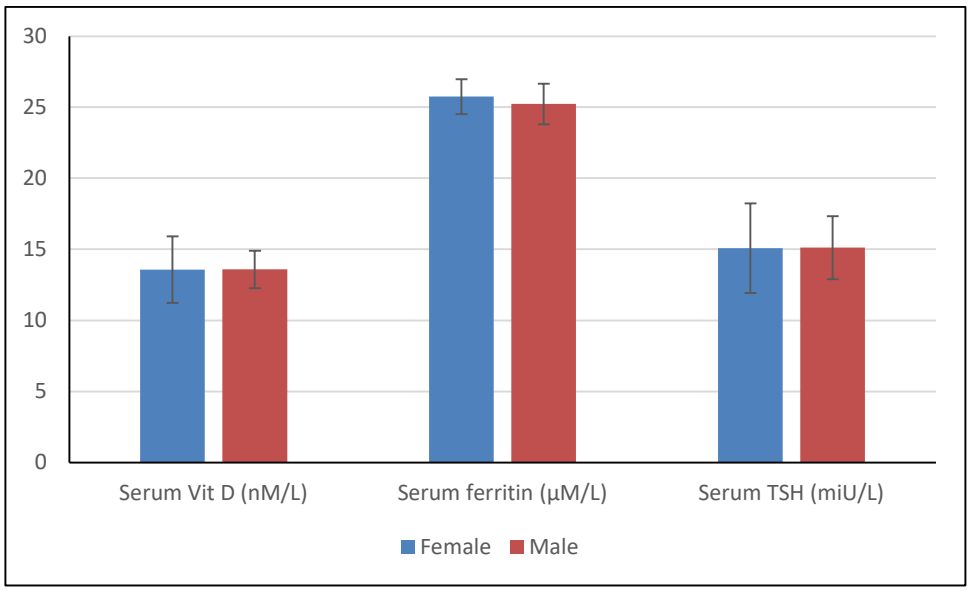

Figure 3: Serum Vit D, ferritin, and TSH in hypothyroid patients.

Lastly, There was significant negative correlation between Vit D levels and Ferritin with TSH level in hypothyroid group (r= -0.43, P<0.05) and (r= -0.78 ,p <0.01), respectively; hence hypothyroid patients had both vitamin D and iron deficiency table 5. Also, Serum vit D and serum ferritin showed a positive correlation in both the case and the control groups, however it was not significant (r= 0.328, P= 0.09).

Table 5 : Correlation of Serum vit D and ferritin with TSH level in hypothyroid patients

	Hypothyroid patients		
	TSH		
	Correlation coefficient (r)	**P value**	**Conclusion**
Vit D	-0.43	<0.05	Significant
Ferritin	-0.78	<0.01	Significant

DISCUSSION

In this study, the majority of hypothyroid patients were females aged between 20 and 45 years. This result was close to other previous studies conducted in other nations including Arab countries (16-18) , however, other studies reported that the highest prevalence of hypothyroid disease was observed in individuals aged ≥60 years(19).

Hypothyroid patients in this study showed a significantly higher mean of TSH levels than the control group (p<0.01) with a cut off level of TSH >5 mIU/L. These finding were consistent with other study group(20) ,however, other study reported a lower TSH value around 7 mU/L in hypothyroid patients (21). Different study

design and inclusion criteria could lead to these variations in the TSH result. For instance, the tests in this study were conducted for newly diagnosed in addition to the known cases of hypothyroidism.

The current investigation revealed that the mean vitamin D levels in the patients group were considerably lower than that in the control group ($p<0.01$). Several studies from other nations have corroborated this conclusion (21, 22) Additionally, there were no appreciable variations in vitamin D levels between females and males in concordance with other previous studies (21) (23) . On the contrary, Zahid Naeem. et al found that the mean serum vitamin D level in males was much higher than females considering that males work more outdoor than females and have high chances of sun exposure (24).

There was a significant negative correlation between serum vitamin D and TSH ($p<0.01$). several reports showed a comparable relationship between TSH and vitamin D (20). Vitamin D deficiency is considered a risk factor for the development of many thyroid disorders, including autoimmune thyroid diseases and thyroid cancer. Also, a study on rat pituitary cells has showed that calcitriol administration increases TRH-induced TSH release which indicates a permissive or regulatory role of vitamin D in the normal pituitary gland (25). While some studies did not find a correlation between vit D and thyroid hormones(26)or thyroid antibodies (27), Many other studies have reported a negative association between anti-thyroid antibodies and vit D levels (28-30) , For instance, an epidemiological survey conducted in china revealed that vitamin D deficiency was positively associated with thyroid autoantibody, and vitamin D deficiency seems to be involved in Hashimoto thyroiditis pathological mechanism (31). Also , Genetic studies have found that polymorphisms in VDR and other genes involved in vitamin D signaling are associated with an increased risk of autoimmune thyroid diseases(32, 33).

In this study, patients mean ferritin levels were substantially lower than that in the control group ($p<0.01$). This result is in line with other studies findings (20, 34) .Also , there was a strong negative correlation between serum iron and TSH ($p<0.01$). Similar results were obtained by Eftekhari et al.(35). While Tienboon et al found that normal thyroid function was preserved in children with iron deficiency anemia, , 3 of 9 children had minor abnormalities of hypothalamic-pituitary function(36). The relationship of thyroid hormones and serum Ferritin and their impact on each other is bidirectional. These observation can be explained by the effect of thyroid hormone on erythrocytes proliferation; thyroid hormones increase the proliferation of erythrocyte precursors indirectly by increase the production of erythropoietin (14) , and directly by induction of erythropoiesis via a thyroid receptor mechanism (TRα) (15). On the other hand , ID might affects hypothalamic–pituitary–thyroid axis leading to decrease thyroid hormone secretion and the response to TSH stimulation (12). Furthermore, studies on animals showed that ID can interfere with the activity of thyroxine deiodinase and reduce the conversion of T4 to T3 (37).

Our study revealed that adult hypothyroid patients especially females had iron and vitamin D deficiency. Also, In the newly diagnosed hypothyroid patients, serum iron and vitamin D levels were significantly dropped. According to this study, women in the Basrah who were between the ages of 15 and 45 were more likely to acquire hypothyroidism and, at the same time, iron and vitamin D insufficiency.

As a result, starting in early adulthood, hypothyroid female patients could have issues related to iron and vitamin D. Female hypothyroid patients may exhibit osteoporotic alterations as a result of vitamin D insufficiency. These modifications weren't assessed as the scope of this investigation was restricted to examining the relationship between vitamin D and iron deficits in hypothyroidism. Determining the pathophysiological mechanism of this association need to be more clarified in future studies.

Conclusions

This study examined the vitamin D and serum ferritin status in hypothyroid patients aged (15–65 years old) in Basrah city , Iraq. It may be inferred that the hypothyroid patients, including both male and female individuals, could also have a bi-deficiency of iron and vitamin D. Thus, iron and vitamin D tests are advisable to be checked with the routine thyroid function test examinations in hypothyroid patients. Hence, it is possible to identify vitamin D and iron deficiencies early on and provide supplements to stop the progression of the disease -related conditions like osteoporosis and iron deficiency anemia.

References

1. Fekete C, Lechan RM. Central regulation of hypothalamic-pituitary-thyroid axis under physiological and pathophysiological conditions. Endocrine reviews. 2014;35(2):159-94.
2. Dayan CM, Panicker V. Novel insights into thyroid hormones from the study of common genetic variation. Nature reviews Endocrinology. 2009;5(4):211-8.
3. Bianco AC, Kim BW. Deiodinases: implications of the local control of thyroid hormone action. The Journal of clinical investigation. 2006;116(10):2571-9.
4. Hoermann R, Midgley JE, Larisch R, Dietrich JW. Relational Stability in the Expression of Normality, Variation, and Control of Thyroid Function. Frontiers in endocrinology. 2016;7:142.
5. Antonelli A, Ferrari SM, Corrado A, Di Domenicantonio A, Fallahi P. Autoimmune thyroid disorders. Autoimmunity reviews. 2015;14(2):174-80.
6. Baeke F, Takiishi T, Korf H, Gysemans C, Mathieu C. Vitamin D: modulator of the immune system. Current opinion in pharmacology. 2010;10(4):482-96.
7. Barsony J, Prufer K. Vitamin D receptor and retinoid X receptor interactions in motion. Vitamins and hormones. 2002;65:345-76.
8. Carlberg C. Vitamin D and Its Target Genes. Nutrients. 2022;14(7).
9. Stocklin E, Eggersdorfer M. Vitamin D, an essential nutrient with versatile functions in nearly all organs. International journal for vitamin and nutrition research Internationale Zeitschrift fur Vitamin- und Ernahrungsforschung Journal international de vitaminologie et de nutrition. 2013;83(2):92-100.
10. Pasricha S-R, Tye-Din J, Muckenthaler MU, Swinkels DW. Iron deficiency. The Lancet. 2021;397(10270):233-48.
11. Zimmermann MB, Kohrle J. The impact of iron and selenium deficiencies on iodine and thyroid metabolism: biochemistry and relevance to public health. Thyroid : official journal of the American Thyroid Association. 2002;12(10):867-78.
12. Garofalo V, Condorelli RA, Cannarella R, Aversa A, Calogero AE, La Vignera S. Relationship between Iron Deficiency and Thyroid Function: A Systematic Review and Meta-Analysis. Nutrients. 2023;15(22).
13. Soliman AT, De Sanctis V, Yassin M, Wagdy M, Soliman N. Chronic anemia and thyroid function.

Acta bio-medica : Atenei Parmensis. 2017;88(1):119-27.

14. Ahmed SS, Mohammed AA. Effects of thyroid dysfunction on hematological parameters: Case controlled study. Annals of medicine and surgery. 2020;57:52-5.

15. Golde DW, Bersch N, Chopra IJ, Cline MJ. Thyroid hormones stimulate erythropoiesis in vitro. British journal of haematology. 1977;37(2):173-7.

16. Ajlouni KM, Khawaja N, El-Khateeb M, Batieha A, Farahid O. The prevalence of thyroid dysfunction in Jordan: a national population-based survey. BMC Endocrine Disorders. 2022;22(1):253.

17. Wani FA, Thirunavukkarasu A, Alrashed H, Alblwan AS, Alfuhigi YM, Dilli M, et al. Evaluation of Age and Gender-Related Patterns in Clinical Features and Hematological Findings Among Hypothyroidism Patients in the Al-Jouf Region of Saudi Arabia: A Hospital-Based Study. Cureus. 2024;16(3):e56161.

18. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. Indian journal of endocrinology and metabolism. 2013;17(4):647-52.

19. Zhang X, Wang X, Hu H, Qu H, Xu Y, Li Q. Prevalence and Trends of Thyroid Disease Among Adults, 1999-2018. Endocrine Practice. 2023;29(11):875-80.

20. Dr. Busi Karunanand PK, Dr. Abhishek Gaurav DSKB. A STUDY ON SERUM VITAMIN D AND FERRITIN LEVELS IN FEMALES DIAGNOSED WITH HYPOTHYROIDISM. Obstetrics and Gynaecology Forum. 2024;34(3s):2233-7.

21. Mackawy AM, Al-Ayed BM, Al-Rashidi BM. Vitamin d deficiency and its association with thyroid disease. International journal of health sciences. 2013;7(3):267-75.

22. Appunni S, Rubens M, Ramamoorthy V, Saxena A, Tonse R, Veledar E, et al. Association between vitamin D deficiency and hypothyroidism: results from the National Health and Nutrition Examination Survey (NHANES) 2007–2012. BMC Endocrine Disorders. 2021;21(1):224.

23. Lippi G, Montagnana M, Meschi T, Borghi L. Vitamin D concentration and deficiency across different ages and genders. Aging clinical and experimental research. 2012;24(5):548-51.

24. Naeem Z, Almohaimeed A, Sharaf FK, Ismail H, Shaukat F, Inam SB. Vitamin D status among population of Qassim Region, Saudi Arabia. International journal of health sciences. 2011;5(2):116-24.

25. D'Emden MC, Wark JD. 1,25-Dihydroxyvitamin D3 enhances thyrotropin releasing hormone induced thyrotropin secretion in normal pituitary cells. Endocrinology. 1987;121(3):1192-4.

26. Zhou P, Cai J, Markowitz M. Absence of a relationship between thyroid hormones and vitamin D levels. Journal of Pediatric Endocrinology and Metabolism. 2016;29(6):703-7.

27. Zhang Q, Wang Z, Sun M, Cao M, Zhu Z, Fu Q, et al. Association of high vitamin d status with low circulating thyroid-stimulating hormone independent of thyroid hormone levels in middle-aged and elderly males. International journal of endocrinology. 2014;2014:631819.

28. Goswami R, Marwaha RK, Gupta N, Tandon N, Sreenivas V, Tomar N, et al. Prevalence of vitamin D deficiency and its relationship with thyroid autoimmunity in Asian Indians: a community-based survey. The British journal of nutrition. 2009;102(3):382-6.

29. Zaidman VE, Maceiras M, Lazzati JM, Kutasz EP, D'Isa G, Chilleli C, et al. High prevalence of anti-thyroid antibodies associated with a low vitamin D status in a pediatric cohort. Clinical chemistry and laboratory medicine. 2014;52(6):e119-22.

30. Kim C-Y, Lee YJ, Choi J-H, Lee SY, Lee HY, Jeong DH, et al. The Association between Low Vitamin D Status and Autoimmune Thyroid Disease in Korean Premenopausal Women: The 6th Korea National Health and Nutrition Examination Survey, 2013–2014. Korean J Fam Med. 2019;40(5):323-8.

31. Fang F, Chai Y, Wei H, Wang K, Tan L, Zhang W, et al. Vitamin D deficiency is associated with thyroid autoimmunity: results from an epidemiological survey in Tianjin, China. Endocrine. 2021;73(2):447-54.

32. Meng S, He S-t, Jiang W-j, Xiao L, Li D-f, Xu J, et al. Genetic susceptibility to autoimmune thyroid diseases in a Chinese Han population: Role of vitamin D receptor gene polymorphisms. Annales d'Endocrinologie. 2015;76(6):684-9.

33. Inoue N, Watanabe M, Ishido N, Katsumata Y, Kagawa T, Hidaka Y, et al. The functional polymorphisms of VDR, GC and CYP2R1 are involved in the pathogenesis of autoimmune thyroid diseases. Clinical and Experimental Immunology. 2014;178(2):262-9.

34. V Durga Prasad ES, G V Ramana. Assessment of Iron, Ferritin, TIBC and LDH levels a cross sectional study in Hypothyroid patients. Int J Clin Biochem Res. 2020;7(4):458-60.

35. Eftekhari MH, Keshavarz SA, Jalali M, Elguero E, Eshraghian MR, Simondon KB. The relationship between iron status and thyroid hormone concentration in iron-deficient adolescent Iranian girls. Asia Pacific journal of clinical nutrition. 2006;15(1):50-5.

36. Tienboon P, Unachak K. Iron deficiency anaemia in childhood and thyroid function. Asia Pacific journal of clinical nutrition. 2003;12(2):198-202.

37. Brigham DE, Beard JL. Effect of thyroid hormone replacement in iron-deficient rats. The American journal of physiology. 1995;269(5 Pt 2):R1140-7.