Original Article

Vitamin D status and TSH levels in pediatric non-autoimmune hypothyroidism: A case-control analysis

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ABSTRACT

The interplay between vitamin D (VD) and thyroid function is crucial, especially in pediatrics. Vitamin D deficiency (VDD) can significantly impact thyroid-stimulating hormone (TSH) levels, leading to potential health consequences. This study explores the essential role of VD in regulating thyroid function in children and highlights the clinical implications of VDD on pediatric thyroid health. A cross-sectional study was conducted on 102 children aged 3-18, selected from 2,503 patients referred to an endocrinology clinic. Participants were chosen based on specific inclusion criteria, excluding those with autoimmune thyroid disorders or recent medication use that could interfere with thyroid function. Data on demographic characteristics, thyroid function tests, and VD levels were collected. Statistical analysis was performed using binary logistic regression in IBM SPSS 24. The study population demonstrated significant VDD prevalence, with 63.7% of individuals falling below the recommended level. The mean VD level was found to be 27.66 ng/ml (standard deviation: 13.17 ng/ml). A significant positive correlation was observed between TSH levels and the odds of VDD. For each unit increase in TSH (mIU/L), the odds of deficiency increased by 70% (OR=1.70, CI 95%:1.19-2.43, p=0.003). However, no statistically significant associations were found between VDD and other demographic factors. This study demonstrates a significant positive correlation between VD status and TSH levels in pediatric patients with non-autoimmune hypothyroidism. The findings suggest that VDD may contribute to elevated TSH levels. Therefore, addressing VDD through supplementation may be a valuable adjunct therapy in the management of non-autoimmune hypothyroidism.

Keywords: Vitamin D, Thyroid stimulating hormone, TSH, Non-autoimmune hypothyroidism, children.

Introduction

Hypothyroidism, a condition characterized by insufficient thyroid hormone production, affects a significant portion of the global population. Prevalence rates range from 0.2% to 5.3% in Europe and 0.3% to 3.7% in the United States. Common symptoms include fatigue, cold intolerance, unexplained weight gain, and delayed puberty or growth in pediatric patients. Diagnosis of primary hypothyroidism involves measuring elevated blood thyroid-stimulating hormone (TSH) levels, indicating a compromised hypothalamic-pituitary-thyroid axis. Subclinical hypothyroidism, the early stage of thyroid dysfunction, is typically characterized by elevated TSH levels in the presence of normal thyroid hormone levels. Autoimmune hypothyroid disease (AITD), specifically Hashimoto's disease, is a common cause of hypothyroidism. However, other factors, such as iodine deficiency, genetic predispositions, neoplasms, or treatments like radiotherapy, surgery, or immune checkpoint inhibitors, can also contribute to the development of hypothyroidism [1-4]. Hypothyroidism in children can have significant and lasting consequences, including stunted development, challenges in behavior, and manifestations linked to Attention-Deficit/Hyperactivity Disorder (ADHD). Timely and accurate diagnosis and treatment are crucial to mitigate these adverse effects. Untreated or undertreated hypothyroidism in children can lead to severe neuropsychological deficits, cognitive impairments, and educational challenges, hindering their ability to achieve independence. The socioeconomic impact of

untreated hypothyroidism permeates both the individual and societal levels. [5]. Furthermore, the insidious onset of hypothyroidism symptoms often delays diagnosis, exacerbating its potential harm. Therefore, timely and comprehensive evaluation and management of thyroid disorders are essential for optimizing patient health. Hypothyroidism is a complicated aetiology that is impacted by a combination of lifestyle, environmental, and genetic variables. These variables include genetic variations, infections, drugs, neoplasms, the therapies they are connected with, and dietary condition. [1]. Vitamin D (VD), a pivotal nutrient, exerts diverse physiological functions through its receptors expressed in numerous organs. These functions encompass the regulation of ion homeostasis, immune responses, and cellular growth and differentiation [6, 7]. VD exerts its effects primarily through nuclear VD receptors, expressed in a wide range of human tissues and cells, comprising those within the endocrine system [8], which assumes a significant function in modulating the expression of more than 1,000 genes [9]. VD exerts its influence on thyroid hormone levels through multiple mechanisms. These mechanisms likely involve interactions with the hypothalamic-pituitary-thyroid axis and the regulation of thyroid hormone synthesis and metabolism [10]. Empirical investigations have provided compelling evidence of the direct influence of VD on type 2 iodothyronine deiodinase (DIO2), a key enzyme in the metabolic conversion of thyroxine (T4) to tri-iodothyronine (T3). In diabetic rats, VD supplementation has been shown to increase DIO2 expression in the brain and liver, leading to elevated levels of fT3 and decreased levels of fT4 [11].In addition, VD has been shown to suppress iodide uptake and TSH-stimulated adenylyl cyclase activity, suggesting a direct inhibitory effect on thyroid hormone synthesis. Conversely, VD administration has been observed to increase Thyrotropin-releasing hormone (TRH) induced TSH release in rat pituitary cells, indicating a potential central nervous system-mediated effect on thyroid hormone regulation. These findings collectively suggest that VD exerts both central and peripheral influences on the hypothalamic-pituitary-thyroid axis [10].

While numerous studies have investigated the relationship between VD and TSH levels, the majority have focused on adult populations or individuals with AITD [10]. Recent research suggests that factors unrelated to autoimmune dysfunction can also influence this association. To the present time, no investigations have been conducted that explicitly assess the influence of VD among pediatric populations with non-autoimmune thyroid diseases (NAITD).

Hypothyroidism in children presents a unique clinical and developmental profile, necessitating specialized pediatric research. While adult studies offer valuable insights, the distinct physiological and developmental characteristics of children demand tailored investigations. The potential for irreversible consequences, including cognitive impairment and growth retardation, in undetected or inadequately managed pediatric hypothyroidism underscores the urgency of research focused on this population. Such research is essential for optimizing diagnosis, treatment, and long-term outcomes, ultimately improving the quality of life for children affected by hypothyroidism [12]. According to the mentioned reasons, his investigation sought to analyze the correlation between VD concentrations and TSH levels in children diagnosed with NAITD. Furthermore, the investigation assessed the incidence of vitamin D deficiency (VDD) and its correlation with various demographic variables, encompassing sex, age, weight, height, body mass index (BMI), and seasonal variations.

Materials and Methods

Ethical Principles and Study Design

A cross-sectional investigation was undertaken comprising 2,503 pediatric subjects aged between 3 to 18 years, who visited the Pediatrics Metabolic and Endocrine Clinic located in Zanjan during the period spanning from January 2022 to May 2023. Following informed consent, 129 pediatric patients aged 3-18 years with a diagnosis of hypothyroidism were enrolled in the study. Inclusion criteria included no history of recent treatment with thyroid medications, oral contraceptive pills, anti-leptics, or glucocorticoids, as well as no history of other diseases that could affect thyroid function (e.g., diabetes, cancer, liver, heart, kidney) and conditions affecting VD synthesis (e.g., recent hospitalizations, immobility, limited movement). Patients were ineligible for inclusion in the study if they had incomplete medical records, were inaccessible during the study period, or if their parents refused to participate in data completion. Additionally, individuals were excluded from the study if they possessed a documented history of VD supplementation. or a positive anti-thyroid peroxidase (anti-TPO) antibody test following enrollment. The study flowchart is depicted in **Figure 2**.

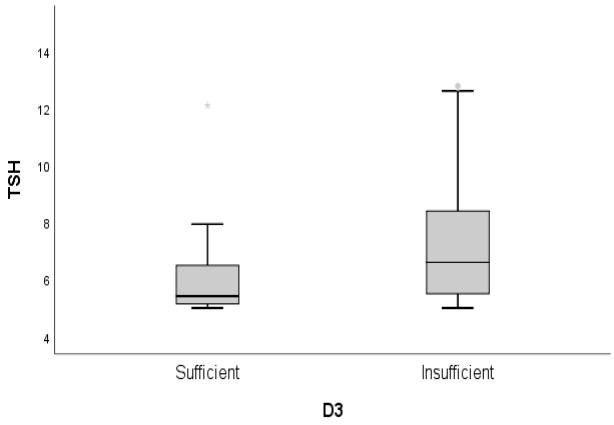

Figure 1. TSH level by vitamin D.

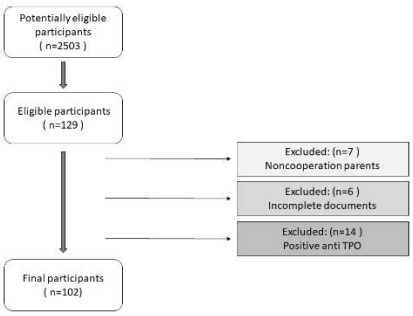

Figure 2. Study flow diagram.

The study was granted ethical approval (approval number IR.ZUMS.REC.1401.153) by the Ethics Committee of Zanjan University of Medical Sciences. All patient information was maintained in strict confidentiality, and the study did not impose any additional financial burden on the participants. Before the commencement of the study, documented informed consent was secured from all parents or legal guardians of the patients involved in the research.

Data Gathering and Outcome Variables

Demographic data, including gender and age, were extracted from the patient's medical records. Anthropometric measurements, such as weight in kilograms and height in centimeters, were collected at the time of the clinical consultation. The aforementioned data were later employed to compute the BMI through the conventional equation of weight (expressed in kilograms) divided by the square of height (measured in meters). Additionally, the sex of the pediatric subjects was determined depending on their physical phenotype. Age was calculated in months from the moment of birth until the time of the clinical appointment. The temporal date of the laboratory examinations was documented from the test requisition and subsequently classified into four distinct seasons. This information was obtained from the medical records of pediatric patients.

All laboratory assessments were performed laboratory situated at the Mousavi Hospital in Zanjan City. VD and TSH concentrations were quantified utilizing a chemiluminescent microparticle immunoassay (CMIA) employing Abbott Architect Reagent kits. The necessary data were obtained from the medical records of the final 102 patients incorporated into the study. A standardized data collection form was utilized to record relevant variables, encompassing age, sex, TSH level, VD level, height, weight, BMI, and the date of the assessments. The demographic information and laboratory results of the study participants are delineated in **Table 1**.

Table 1. Description of Season, weight, height, and BMI.

Variable	Category	Frequency	Percent
Season	**Spring**	31	30.4
	Summer	31	30.4
	Autumn	15	14.7
	Winter	25	24.5
Z score for height	**Z < -2**	8	7.8
	-2 < Z< 2	87	85.3
	Z > 2	7	6.9
Z score for weight	**Z < -2**	2	2.0
	-2 < Z< 2	84	82.4
	Z > 2	16	15.7
Z score for BMI	**Z < -2**	1	1.0
	-2 < Z< 2	79	77.5
	Z > 2	22	21.6

Multiple professional societies, including the American Association of Clinical Endocrinologists (AACE), Endocrine Society, International Osteoporosis Foundation, National Osteoporosis Foundation, and American Geriatric Society, have established guidelines for VD sufficiency. A VD level exceeding 30 nanograms per milliliter (ng/mL) is typically regarded as sufficient. Conversely, VDD is frequently characterized by a 25-hydroxy VD concentration falling below 20 ng/mL, while insufficiency is delineated as a concentration ranging between 21 and 29 ng/mL. In another definition, The AACE aligns with this definition, considering a VD level below 30 ng/mL as indicative of deficiency [13-15]. For the purposes of this study, VDD was defined as a serum concentration below 30 nanograms per milliliter, while a level above 30 ng/mL was considered sufficient. TSH levels were measured in milliunits per liter (mU/L) based on the initial laboratory requisition. A TSH level greater than 5 mU/L was classified as indicative of hypothyroidism, including both subclinical and primary hypothyroidism.

Data Analysis

The statistical studies were carried out utilising IBM SPSS version 24. While qualitative data were displayed as frequencies and percentages, quantitative variables were summarised by mean and standard deviation (SD). Given that the study population consisted of children, height, weight, and BMI were standardized using the Standard Deviation Score (SDS) formula and the 2000 Centers for Disease Control and Prevention (CDC) growth charts to account for age- and sex-specific norms. Z scores were calculated for weight, height, and BMI, and classified as less than -2 (below the 2nd percentile), between -2 and 2 (within the normal range), and greater than 2 (above the 98th percentile).

The normality of the data was assessed using the Shapiro-Wilk or Kolmogorov-Smirnov tests. To examine the relationship between VD status (deficient vs. sufficient) and other variables, independent t-tests were conducted for quantitative variables, and univariate and multivariate binary logistic regression analyses were performed for qualitative variables. The statistical significance level was set at 0.05.

Results and Discussion

A total of 102 participants were included in the study, with a mean age of 8.38 years (standard deviation [SD] = 2.90) and a range of 3.42 to 16.42 years. Females comprised 58 (56.9%) of the sample. The majority of participants (60.8%) were referred during the spring and summer months. Based on Z scores, most participants exhibited normal weight (82.4%), height (85.3%), and BMI (77.5%) **(Table 1)**. Moreover, The mean TSH level was 6.93 mU/L (SD = 2.53), ranging from 5.00 to 21.30 mU/L. The mean VD level was 27.65 ng/mL (SD = 13.17). Of the 102 participants, 3 (2.9%) had VD levels below 10 ng/mL, 26 (25.5%) had levels between 10 and 20 ng/mL, 36 (35.3%) had levels between 20 and 30 ng/mL, and 37 (36.3%) had levels above 30 ng/mL. Consequently, 36.3% had normal VD levels (> 30 ng/mL), while 63.7% exhibited VDD (< 30 ng/mL).

Figure 1 illustrates the distribution of TSH levels based on VDD and sufficiency. Children and adolescents with VDD exhibited lower TSH levels compared to those with sufficient VD. Binary logistic regression analysis revealed a significant association between TSH and VD, indicating that a one-unit increase in TSH (mU/L) was associated with a 70% increase in the odds of VDD (OR = 1.70, 95% CI: 1.19-2.43, P = 0.003). The findings of binary logistic regression studies evaluating the influence of height, weight, season, gender, age, and BMI on VDD are shown in **Table 2**. It was discovered that these variables had no relation to VDD.

Table 2. Univariate binary logistic regression to investigate effect variables on vitamin D status.

Variables	Category	Vitamin D level		P-value	OR (CI 95%)
		Sufficient	Insufficient		
Age	-	8.05 (2.70)	8.57 (3.02)	0.385	1.07 (0.92, 1.23)
Gender	Girl	21 (36.2)	37 (63.8)	0.987	1.02 (0.45, 2.27)
	Boy (Reverence)	16 (36.4)	28 (63.6)		
Season	Spring	11 (35.5)	20 (64.5)	0.345	1.68 (0.57, 4.92)
	Summer	9 (29.0)	22 (71.0)	0.148	2.26 (0.75, 6.80)
	Autumn	5 (33.3)	10 (66.7)	0.366	1.85 (0.49, 6.98)
	Winter (Reference)	12 (48.0)	13 (52.0)	-	-
Weight	Normal	32 (38.1)	52 (61.9)	0.411	0.62 (0.20, 1.92)
	Abnormal (Reference)	5 (27.8)	13 (72.2)	-	-
Height	Normal	31 (35.6)	56 (64.4)	0.745	1.20 (0.39, 3.70)
	Abnormal (Reference)	6 (40.0)	9 (60.0)	-	-
BMI	Normal	30 (38.0)	49 (62.0)	0.509	0.71 (0.26, 1.94)
	Abnormal (Reference)	7 (30.4)	16 (69.6)	-	-

Multivariate binary logistic regression was conducted to simultaneously assess the relationship between age, BMI, height, weight, season, gender, and TSH on VDD. After adjusting for all other variables, the adjusted OR for TSH remained significantly associated with VDD, with an OR of 1.78 (95% CI: 1.23-2.57).

This study investigated the relationship between VD status and thyroid function in children with NAITD. A notable inverse correlation was found between VD levels and TSH levels. VDD was prevalent in the study population, affecting 63.7% of patients. However, demographic factors such as sex, age, and BMI were not associated with VDD. These findings suggest that addressing VDD may be beneficial for improving thyroid function in this patient population.

The average concentration of VD in the study was determined to be 27.65 ng/ml, with a VDD prevalence rate of 63.7%This rate is consistent with previous studies conducted in nearby regions (54.9% and 51%) [16, 17] and aligns with a meta-analysis reporting a VDD rate of 61% in Iranian children under 18 [18]. Collectively, these findings suggest a heightened prevalence of VDD in hypothyroid pediatric patients compared to the general pediatric population in line with previous studies [19, 20]**.** Geographic factors, such as sunlight exposure and air pollution, may contribute to regional variations in VDD rates.

This investigation elucidated a negative correlation between VD levels and TSH concentrations in pediatric patients with NAITD, aligning with prior research demonstrating the positive effects of VD supplementation on thyroid function in AITD [20, 21]. A meta-analysis by Galusca *et al*. supported this association, reporting reductions in TSH levels and thyroid antibodies following VD supplementation [21]. Likewise, Metwalley *et al*. observed comparable outcomes in a study of children with AITD [20]. The present findings suggest a potential, yet intricate, relationship between VD and thyroid function that may extend beyond the specific population studied. While earlier research has largely emphasized the immunomodulatory effects of VD in AITD, the present investigation suggests that VD may exert an effect on TSH levels via multiple mechanisms. Nonetheless, additional research explicitly focused on our demographic is essential. A case-control study by Ahi *et al*. identified a link between adults with NAITD and VDD, supporting the notion of an underlying association [22]. A randomized clinical trial done by Pezeshki *et al*. revealed that VD supplementation led to a

significant reduction in TSH levels among adult patients with VDD and subclinical hypothyroidism [23]. Additionally, Zhou *et al*. documented a statistically notable inverse relationship between TSH concentrations and VD levels, consistent with our findings. Importantly, they ascribed this correlation to diminished sensitivity to thyroid hormones. [24]. Previous research by Jiang *et al*. and Waterhouse did not discover a significant inverse link between VD levels and TSH in paediatric patients with NAITD, in contrast to our study's findings [25, 26]. These discrepancies may be attributed to differences in baseline VD levels, study design, and intervention specifics. Furthermore, The studies conducted by Evliyaoğlu *et al*. and Gou *et al*. in younger pediatric populations exhibiting confounding variables factors highlight the necessity of including diverse populations and employing rigorous methodologies in anticipated studies to ensure the generalizability of findings [27, 28]. Recent studies suggest that VD may exert immunomodulatory effects on AITD through multiple mechanisms. These mechanisms encompass the modulation of dendritic cell-mediated T-cell activation, the inhibition of an exaggerated B-cell response, the preservation of an appropriate Th17/Treg cell balance, and the downregulation of human leukocyte antigen (HLA) class II gene expression within the thyroid. [29]. A supplementary study demonstrated that adequate VD status is associated with significant improvements in thyroid hormone levels and inflammatory markers [30]. Beyond its anti-inflammatory properties, VD has been shown to enhance antioxidant status and reduce oxidative stress. Further research in this area is warranted [31].

The current investigation did not establish a noteworthy correlation between the prevalence of VDD and either age or gender within the pediatric population. These results align with numerous preceding studies. [22, 32]. For example, Babaniamansour *et al*. observed a negative correlation between age and VD levels [16]. Additionally, Jazayeri *et al*. reported more frequent cases of VDD in Iranian girls compared to boys [18]. The diverse results documented in earlier research can be ascribed to cultural influences unique to the Iranian demographic, including disparities in clothing customs (e.g., the adoption of hijab) and varying sunlight exposure behaviors across genders and age categories [33]. Furthermore, restricted availability of public areas for exercise and insufficient involvement in both indoor and outdoor activities among females may exacerbate these inequalities.

Collectively, The present study demonstrated a positive association between elevated TSH levels and VDD in children. However, subsequent studies are required to determine the impact of VD supplementation on TSH levels, considering that the cross-sectional nature of this research restricts causal interpretation.

study limitations

The sample size of this study was constrained by the limited number of children with NAITD in Zanjan City. The study was further limited by incomplete medical records (n = 6) and parental refusal to participate in data completion (n = 7). Additionally, we were unable to collect data on the socioeconomic status, children's physical activity, sunscreen use, and supplement use.

Conclusion

VD plays a pivotal role in thyroid function, and individuals with NAITD often exhibit a higher prevalence of VDD, particularly those with elevated TSH levels. Addressing VDD may lead to a reduction in TSH levels, potentially reducing the long-term need for levothyroxine medication, frequent testing, and the risk of hypothyroid complications in children. Considering the essential function of thyroid hormones in the developmental and growth processes of children, alongside the notable prevalence of VDD among individuals with hypothyroidism and the possibility for VD to diminish TSH concentrations, it is advisable to provide supplementation of VD to pediatric patients diagnosed with hypothyroidism to mitigate VDD and decrease TSH levels. Further empirical investigation is necessitated to explore the correlation between VD levels and various thyroid laboratory metrics, as well as season, height, weight, and BMI within a more extensive demographic population. Additionally, clinical trials and studies on VD supplementation in children with NAITD are recommended.

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Conflict of interest: None

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Ethics statement: All research procedures were conducted in accordance with ethical standards and relevant institutional guidelines (approval number IR.ZUMS.REC.1401.153). Informed consent was obtained from all participants, and data was collected and analyzed anonymously to protect privacy.

References

1. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism. Nat Rev Dis Primers. 2022 May 19;8(1):30.
2. de Vries L, Bulvik S, Phillip M. Chronic autoimmune thyroiditis in children and adolescents: at presentation and during long-term follow-up. Arch Dis Child. 2009 Jan;94(1):33-7.

3. Hegedüs L, Bianco AC, Jonklaas J, Pearce SH, Weetman AP, Perros P. Primary hypothyroidism and quality of life. Nat Rev Endocrinol. 2022 Apr;18(4):230-242.
4. Jansen HI, Boelen A, Heijboer AC, Bruinstroop E, Fliers E. Hypothyroidism: The difficulty in attributing symptoms to their underlying cause. Front Endocrinol (Lausanne). 2023 Feb 6;14:1130661.
5. Feldt-Rasmussen U, Effraimidis G, Bliddal S, Klose M. Consequences of undertreatment of hypothyroidism. Endocrine. 2024 May;84(2):301-8.
6. Fang A, Zhao Y, Yang P, Zhang X, Giovannucci EL. Vitamin D and human health: evidence from Mendelian randomization studies. Eur J Epidemiol. 2024 May;39(5):467-90.
7. Janoušek J, Pilařová V, Macáková K, Nomura A, Veiga-Matos J, Silva DDD, et al. Vitamin D: sources, physiological role, biokinetics, deficiency, therapeutic use, toxicity, and overview of analytical methods for detection of vitamin D and its metabolites. Crit Rev Clin Lab Sci. 2022 Dec;59(8):517-54.
8. Taheriniya S, Arab A, Hadi A, Fadel A, Askari G. Vitamin D and thyroid disorders: a systematic review and Meta-analysis of observational studies. BMC Endocr Disord. 2021 Aug 21;21(1):171.
9. Voltan G, Cannito M, Ferrarese M, Ceccato F, Camozzi V. Vitamin D: An Overview of Gene Regulation, Ranging from Metabolism to Genomic Effects. Genes (Basel). 2023 Aug 25;14(9):1691.
10. Babić Leko M, Jureško I, Rozić I, Pleić N, Gunjača I, Zemunik T. Vitamin D and the Thyroid: A Critical Review of the Current Evidence. Int J Mol Sci. 2023 Feb 10;24(4):3586.
11. Alrefaie Z, Awad H. Effect of vitamin D3 on thyroid function and de-iodinase 2 expression in diabetic rats. Arch Physiol Biochem. 2015;121(5):206-9.
12. Rodriguez L, Dinauer C, Francis G. Treatment of hypothyroidism in infants, children and adolescents. Trends Endocrinol Metab. 2022 Jul;33(7):522-32.
13. Camacho PM, Petak SM, Binkley N, Clarke BL, Harris ST, Hurley DL, et al. American Association Of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2016--executive summary. Endocr Pract. 2016 Sep;22(9):1111-8.
14. Holick MF. The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. Rev Endocr Metab Disord. 2017 Jun;18(2):153-65.
15. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011 Jul;96(7):1911-30.
16. Babaniamansour S, Hematyar M, Babaniamansour P, Babaniamansour A, Aliniagerdroudbari E. The prevalence of vitamin D deficiency among one to six year old children of Tehran, Iran. J Kermanshah Univ Med Sci. 2019;23(4).
17. Rezaiee GA, Mojarrad M, Taghinezhad H, Zamaan J, Akbari TA, Sadegh H, et al. Frequency of vitamin D deficiency in the children below fifteen admitted to the 523 hospital, Urmia. 2019.
18. Jazayeri M, Moradi Y, Rasti A, Nakhjavani M, Kamali M, Baradaran HR. Prevalence of vitamin D deficiency in healthy Iranian children: A systematic review and meta-analysis. Med J Islam Repub Iran. 2018 Sep 8;32:83.
19. 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 Endocr Disord. 2021 Nov 12;21(1):224.
20. Metwalley KA, Farghaly HS, Sherief T, Hussein A. Vitamin D status in children and adolescents with autoimmune thyroiditis. J Endocrinol Invest. 2016 Jul;39(7):793-7.
21. Galuşca D, Popoviciu MS, Babeş EE, Vidican M, Zaha AA, Babeş VV, et al. Vitamin D Implications and Effect of Supplementation in Endocrine Disorders: Autoimmune Thyroid Disorders (Hashimoto's Disease and Grave's Disease), Diabetes Mellitus and Obesity. Medicina (Kaunas). 2022 Jan 27;58(2):194.
22. Ahi S, Dehdar MR, Hatami N. Vitamin D deficiency in non-autoimmune hypothyroidism: a case-control study. BMC Endocr Disord. 2020 Mar 20;20(1):41.
23. Pezeshki B, Ahmadi A, Karimi A. The Effect of Vitamin D Replacement on Patient with Subclinical Hypothyroidism: A Pilot Randomized Clinical Trial. Galen Med J. 2020 May 21;9:e1592.
24. Zhou L, Wang Y, Su J, An Y, Liu J, Wang G. Vitamin D Deficiency Is Associated with Impaired Sensitivity to Thyroid Hormones in Euthyroid Adults. Nutrients. 2023 Aug 24;15(17):3697.
25. Jiang H, Chen X, Qian X, Shao S. Effects of vitamin D treatment on thyroid function and autoimmunity markers in patients with Hashimoto's thyroiditis-A meta-analysis of randomized controlled trials. J Clin Pharm Ther. 2022 Jun;47(6):767-75.
26. Waterhouse M, Pham H, Rahman ST, Baxter C, Duarte Romero B, Armstrong BK, et al. The Effect of Vitamin D Supplementation on Hypothyroidism in the Randomized Controlled D-Health Trial. Thyroid. 2023 Nov;33(11):1302-10.
27. Evliyaoğlu O, Acar M, Özcabı B, Erginöz E, Bucak F, Ercan O, et al. Vitamin D Deficiency and Hashimoto's Thyroiditis in Children and Adolescents: a Critical Vitamin D Level for This Association? J Clin Res Pediatr Endocrinol. 2015 Jun;7(2):128-33.
28. Guo Y, Wu CY, Deng YH, Wu JL. Associations Between Serum 25-Hydroxyvitamin D Levels and Thyroid Function Parameters in Previously Healthy Children Aged 6 to 24

Months. Risk Manag Healthc Policy. 2020 Sep 21;13:1647-53.

29. Lebiedziński F, Lisowska KA. Impact of Vitamin D on Immunopathology of Hashimoto's Thyroiditis: From Theory to Practice. Nutrients. 2023 Jul 17;15(14):3174.
30. França R, Cordeiro A, Pereira SE, Saboya CJ, Ramalho A. The Effect of Vitamin D Adequacy on Thyroid Hormones and Inflammatory Markers after Bariatric Surgery. Metabolites. 2023 Apr 27;13(5):603.
31. Kubiak K, Szmidt MK, Kaluza J, Zylka A, Sicinska E. Do Dietary Supplements Affect Inflammation, Oxidative Stress, and Antioxidant Status in Adults with Hypothyroidism or Hashimoto's Disease?-A Systematic Review of Controlled Trials. Antioxidants (Basel). 2023 Sep 24;12(10):1798.
32. Chailurkit LO, Aekplakorn W, Ongphiphadhanakul B. High vitamin D status in younger individuals is associated with low circulating thyrotropin. Thyroid. 2013 Jan;23(1):25-30.
33. Hussain T, Eimal Latif AH, Malik S, Raza S, Saeed T, Salman Zahid A, et al. Vitamin D Deficiency and Associated Risk Factors in Muslim Housewives of Quetta, Pakistan: A Cross-Sectional Study. Cureus. 2021 Sep 1;13(9):e17643.