Original Article

Vitamin D Status in Hypothyroid Patients

Bhowmic R[1], Hasan MK[2], Bhuiyan MMU[3], Das UK[4], Siddiki MS[5], *Mubdi-Un-Naafi S[6], Chowdhury MFI[7]

Abstract

Vitamin D deficiency is a global health problem. It is estimated that about 25-50% of patients commonly encounter vitamin D deficiency in clinical practice. Recent studies show hypothyroid patients suffer from significantly low vitamin D level. As vitamin D and thyroid hormone act through steroid receptors, one can affect the other's action. Considering the scientific evidence, the study was aimed to assess the vitamin D level among the subjects with hypothyroidism. This hospital-based case-control study was conducted among 70 subjects including 35 cases and 35 controls at the Departments of Medicine and Endocrinology in Dhaka Medical College Hospital in 6 months duration following approval of this protocol. Data were collected by face to face interview, using a structured questionnaire and case record review. Hospital records including laboratory reports were also reviewed. Thirty-five cases and thirty-five control samples were screened for vitamin D levels. Data analysis was done using Statistical Package for Social Sciences (SPSS) version 23. Among the participants, 55 were female with a male-female ratio of 1: 3.67. The mean age was 44.6 ± 11.69 year. The highest number of patients were in between 41 to 55 year (41%). The majority of cases were from rural areas (67.0%). There was no significant differences in socio-demographic profiles between the cases and control groups (P >0.05). Hypovitaminosis D was found in 67% of cases. Among them 39.0% had mild insufficiency (20-29 ng/ml), 21.0% had moderate deficiency (10-19 ng/ml) and 7.0% had severe deficiency (< 10 ng/ml). The mean vitamin D level was 23.79 ± 8.1 ng/ml. Serum 25(OH)D level was markedly reduced in hypothyroid cases in comparison to the euthyroid control group [22.14 ± 8.02 and 26.22 ± 7.53 respectively); P < 0.005]. Data showed hypothyroid patient is likely to develop Hypovitaminosis D 3.37 times higher compared to a euthyroid patient (OR=3.37; 95% CI:1.644-9.7440; P=0.02). Moreover, this lower level is not associated with the difference in age, sex and occupation (P< 0.005). Hypovitaminosis D is associated with hypothyroidism with no variation in respect to age, sex and occupation. The hypovitaminosis D is significantly associated with hypothyroi- dism in the study population.

Keywords : *Hypovitaminosis D , hypothyroidism, euthyroid, serum TSH , serum 25(OH)D, vitamin D status*

1. Dr. Rajib Bhowmic, Assistant Registrar, Dept. of Medicine, Dhaka Medical College Hospital.
2. Mohammad Kamrul Hasan, Consultant (Medicine), OSD: DGHS, Deputation: Department of Gastroenterology, DMCH.
3. Dr. Md. Minhaj Uddin Bhuiyan, Registrar, Dept. of Medicine, Dhaka Medical College Hospital.
4. Dr. Uzzal Kanti Das, MD Internal medicine trainee (Non Residency), Chittagong Medical College Hospital
5. Dr. Md. Shahriar Siddiki, Medical Officer, Dept. of Medicine, Dhaka Medical College Hospital.
6. *Dr. Shah Mubdi-Un-Naafi, Assistant Surgeon, DGHS, Mohakhali, Dhaka. Attached: Upazila Health Complex, Gangachara, Rangpur, email: smnaafi@gmail.com
7. Professor Dr. Md. Faizul Islam Chowdhury, Professor of Medicine, Anwer Khan Modern Medical College

* For correspondence

INTRODUCTION

Vitamin D is called "the Sunshine Vitamin." Exposure to sunlight has been a significant source of Vitamin D in humans.[1] This fat-soluble steroid prohormone is mainly produced photochemically in the skin from 7-dehydro-cholesterol. [2] The ultraviolet light with a wavelength of 290–320 nm action makes Cholecalciferol (as denoted by Vitamin D) by acting on 7- dehydrocholesterol found in the skin of humans. After being made in the skin or ingested, vitamin D is transported to the liver from the kidney, where it is hydroxylated into 25-hydroxy vitamin, the primary circulating form of vitamin D.[3] Over the last few years, vitamin D has gained much attention.[4] Though initially thought to be uncommon, recent epidemiological data suggest that it is widespread. It was assumed that over a billion people worldwide are vitamin D deficient or insufficient.[5] Due to sufficient exposure to sunlight, Vitamin D deficiency is less common in tropical countries- this was the previous assumption.

Nevertheless, surprisingly, 80% of the population in South Asia suffers from vitamin D deficiency (<20 ng/mL), and almost 40% of them are severely deficient (<10 ng/mL).[6] In India, the prevalence rate is around 50-90%.[7]Goswami et al. evidenced that more than 90% of the healthy population has below-normal serum levels of 25-hydroxy Vitamin D (25(OH)D) with almost undetectable values during winter in India.[8] In Nepal, among adults, the prevalence is 73.7%.[3] In Bangladesh, most of the studies have focused on the children, and Ahmed AMS et al. showed 42·3 % insufficient, 31·2 % deficient and 3·4 % severely vitamin D deficiency in his study group.[9] On the other hand, the prevalence of vitamin D deficiency among women in the reproductive age group in Bangladesh is 81%.[10]

Vitamin D has been well-known for its role in bone metabolism and is an essential element for calcium and phosphate metabolism and skeletal health.[12] Deficiency in child cause rickets, whereas adult deficiency increases the propensity for osteoporosis.[12] In recent time, effects on extraskeletal tissue has also been observed.[13] Low Vitamin D level has been identified as a risk factor for diabetes mellitus, cancers, multiple sclerosis, atherosclerosis, infectious diseases, and other autoimmune diseases, including autoimmune thyroid diseases.[9,14,15] Several studies suggest that low levels of vitamin D have also been associated with autoimmune thyroid diseases like Hashimoto's thyroiditis and Graves' disease.[11,15-17] Moreover, impaired vitamin D signaling has been reported to encourage thyroid tumorigenesis.[16,17]

Vitamin D exerts its action through binding to vitamin D receptors (VDR) and activating VDR-responsive genes.[14] Initially thought to be vitamin D just affecting calcium homeostasis, researchers have shown that this steroid hormone works in more than 36 cell types with VDR, such as the thyroid gland; its role in regulating cell proliferation and differentiation has also been shown.[14,18] As both vitamin D and thyroid hormones act through steroid receptors; therefore, one may affect the action of another.[5] So, a lower level of vitamin D is likely to aggravate the systemic abnormalities associated with hypothyroidism.[18] The study was aimed to assess the vitamin D level among the subjects with hypothyroidism.

MATERIALS AND METHODS

This case-control study was conducted in the Departments of Medicine and Endocrinology in Dhaka Medical College Hospital. A total of 70 subjects were selected for the study; 35 were considered cases, and the rest 35 as control. Cases were diagnosed patients of hypothyroidism and control were healthy adult of similar age and sex. Hypothyroidism was defined as failure of the thyroid gland to produce sufficient thyroid hormone to meet the metabolic demands of the body. Symptoms of hypothyroidism include weight gain, cold intolerance, fatigue, dry skin, dry hair, menorrhagia, constipation, hoarseness, muscle aches and pain, depression, impotence, infertility.Signs of hypothyroidism include weight gain, hoarse voice, malar flush, periorbital edema, anemia, bradycardia, hypertension, delayed relaxation of deep tendon reflex, dermal myxedemaHypothyroidism is diagnosed if serum thyroid stimulating hormone (TSH) is >5.7 μU/mL (reference interval: 0.7-5.7 μU/mL) and free T4 (fT4) is <0.7 ng/dL (reference interval: 0.7-1.9 ng/dL).

Levels of vitamin D were categorized as:

- more than 30ng/ml is considered to be normal
- 20-29ng/ml (<50nmol/L) is insufficient
- less than 20ng/ml (<25nmol/L) is deficient
- less than 10ng/ml (12.5nmol/L) signifies severe deficiency.

Newly diagnosed patients with hypothyroidism and older than 13 years of age, both sexes, were included in the study as 'cases'. On the other hand, diagnosed patients with hypothyroidism on treatment or diagnosed with CKD, intestinal disease including Crohn's disease, cystic fibrosis and celiac disease, cholestatic liver disease, and strictly vegans were excluded from the study. Moreover, critically ill patients and pregnant women were also excluded. Informed written consent was taken from every patient. Ethical clearance was obtained from the ethical review committee of the Dhaka Medical College & Hospital. About 5ml of fasting sample was collected from each patient and control for testing of Serum T3, T4, TSH, and Vitamin D levels. Testing was done by ELISA using standard protocols. Besides this, socio-demographic parameters and duration of the illness were also recorded during the interview. Following the interview, collected data were recorded into the case-record form. Collected data were cleaned and cross-checked. Data were analysed using Statistical Package for Social Sciences (SPSS) version 23 for windows. Mean and the standard deviation (SD) for all the variables were calculated. Student's "t" test was performed to see the differences between mean values for each tested variable. Correlations between Vitamin D levels and TSH were shown by by correlation coefficient.

Odds Ratio was calculated to assess the strength of association between Vitamin D status and the Hypothyroidism. Results considered significant when $P < 0.05$.

RESULT

This study was done on 70 patients of either sex aged between 16 to 70 years of age. Thirty-five of these patients were considered the control group with normal thyroid levels. The other 35 cases were considered the case group who were newly diagnosed hypothyroid patients with increased serum TSH levels> 5.7 μU/ml.

Table I among the 70 evaluable patients, 55 were females, and 15 were males, with a male-female ratio of 1: 3.67. Among 70 studied cases, the mean age was 44.6 ± 11.69 years. Most of the patients were in-between 41 to 55 years (41%). The majority of cases were from rural areas (67%).

The socio-demographic profile was similar between both groups (P > 0.05).

Table I: Comparison of socio-demographic characteristics between case (35) and control (35) group (n=70)

Variable	Case group (Hypothyroid)	Control group (Euthyroid)	Total n (%)	p-value
Age group				
13-25 years	4	3	07 (10)	
26-40 years	8	9	17 (24)	0.791
41-55 years	16	13	29 (41)	
Above 55 years	7	10	17 (24)	
Sex				
(female)	29	26	55 (79)	0.382
Residence (Rural)	22	25	47 (67)	0.445
Monthly income				
< 15000 taka	12	16	28 (40)	
15000-40000 taka	17	15	32 (46)	0.578
> 40000 taka	6	4	10 (14)	
Academic qualification				
No formal education	6	8	14 (20)	
Primary	11	12	23 (33)	0.895
SSC	13	11	24 (34)	
HSC and above	5	4	09 (13)	

Table II shows serum 25(OH)D level was markedly reduced in hypothyroid cases compared to the euthyroid control group. T-test showed a significant decrease in vitamin D levels in hypothyroid patients (P-value < 0.005). The mean value of serum TSH and 25(OH)D in both groups are given

Table II: Comparison of the mean value of serum TSH and 25(OH)D in case and control group (n=70)

Study group	Case group (n=35) (Hypothyroid)	Control group (n=35) (Euthyroid)	Total (n=70)	p-value
Serum TSH value (Mean ± SD), μU/ml	10.89 ± 2.63	2.71 ± 0.98	6.81 ± 4.56	0.000
Serum 25(OH)D value (Mean ± SD), ng/ml	22.14 ± 8.02	26.22 ± 7.53	23.69 ± 8.1	0.032

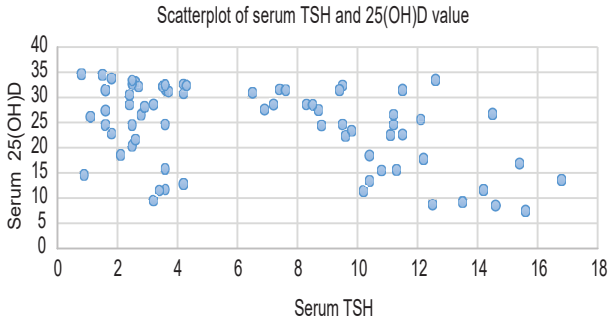

Figure 2. Scatterplot of serum TSH and 25 (OH) D value (n=70)

Figure-2 is a scatterplot of serum 25(OH)D and serum TSH of the studied cases (n=70) was done. Serum TSH values were plotted along with X-axis, and serum 25(OH)D values were plotted along Y-axis. It showed that serum 25(OH)D values decreased with the higher serum TSH values in most cases.

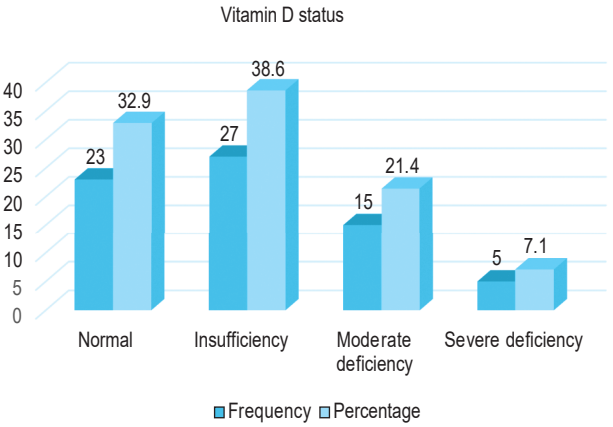

Figure 3. Vitamin D status of the cases according to serum 25 (OH) D level (n= 70)

Figure illustrate the Vitamin D status (assessed by serum 25(OH)D level) in both case and control groups. The mean value was 23.686 ± 8.1 ng/ml. Hypovitaminosis D was found in 67% of cases. Among them 39% had mild insufficiency (20-29 ng/ml), 21% had moderate deficiency (10-19 ng/ml) and 7% had severe deficiency (< 10 ng/ml). In 33% cases had normal value (≥ 30 ng/ml).

Table III shows socio-demographic profile of both case and control groups showed hypovitaminosis D was significantly found among elderly patients (P-value < 0.05). See details

Table III: Association of socio-demographic factors with hypovitaminosis D (n= 70)

Variable	Hypovitaminosis D (n= 47)	Normal Vit-D (n=23)	p value
Age group			
13-25 years	02	05	
26-40 years	10	07	0.041
41-55 years	21	08	
Above 55 years	14	03	
Sex (female)	39	16	0.199
Residence (Rural)	31	16	0.763
Monthly income			
< 15000 taka	19	09	
15000-40000 taka	22	10	0.871
> 40000 taka	06	04	
Academic qualification			
No formal education	10	04	
Primary	11	12	0.086
SSC	18	06	
HSC and above	08	01	

Table IV shows significant signs and symptoms observed in hypothyroid patients. Among the hypothyroid cases (n=35), fatigue (77%), cold intolerance (71%), and weight gain (69%) were more frequently found. Muscle pain was found in 65% of cases; on the contrary, muscle pain was present in 83% of cases (39 out of 47) of hypovitaminosis D

Table IV. Major signs and symptoms found among hypothyroid cases (n= 35)

Sign / symptom	Frequency	Percentage
Cold intolerance	25	71
Weight gain	24	69
Anorexia	22	63
Bradycardia	16	46
Delayed reflex	14	40
Fatigue	27	77
Muscle pain	23	65
Bone/joint pain	06	17

Table V shows in our study, hypovitaminosis D was more frequently found among the case group (hypothyroid cases) in comparison to the control group (euthyroid cases), and the result was statistically significant (χ^2 value = 5.245, P-value = 0.022, n = 70); shown

Table V. Association of hypovitaminosis D with hypothyroidism (n=70)

		Vitamin D status		Total	χ^2 value	p-value
		Hypovitaminosis D	**Normal vitamin D**			
Patient status	**Case group (hypothyroid)**	28	7	35	5.245	0.022
	Control group (euthyroid)	19	16	35		
Total		47	23	70		

DISCUSSION

Female predominance was observed in this study, which supports the study of Mehta M et al. in India, where female predominance was observed as out of 100 cases, 53 were female, and 47 were male[19]. Another study in a private medical college in Bangladesh by Hossain et al. Also found similar findings with female predominance where out of 212 patients, 73.6 % were female, and 26.4 % were male[20], which is identical to the results of this study.

Among 70 studied cases, the mean age was 44.6 ± 11.69 years between the case and control group. Most of the patients were in-between 41 to 55 years (41%). The majority of cases were from rural areas (67%), the monthly income of the majority, 46%, was 15000-40000 taka, and most of the respondents, 34%, had completed only SSC. The socio-demographic profile was similar between both groups (P > 0.05). Nevertheless, the socio-demographic profile of both case and control groups showed that hypovitaminosis D was significantly found among elderly patients (P-value < 0.05). A study about vitamin D levels in different socio-demographic populations in Bangladesh by Hossain et al. reported that the mean age of males was 49.7 (age range 18- 95) & females was 45.7 (range 18- 80). Regarding the level of education, 36.8% were graduate & post-graduate, level of education was not a strong determinant in that study, and occupation 61.7% of the study population was housewife, and socioeconomic status 85% were middle class[20]. Also, In other studies by Mehta M et al. [19]Koch et al.[21] Mackawy et al. [22] reported no relation or association between socio-demographic status and vitamin D and hypothyroidism. Benner et al.[23] also said no association between socio-demographic status and Vitamin D level and thyroid disease. Another study by Jääskeläinen et al.[24] among the adult population in mainland Finland reported a strong association between vitamin D level, age, and education level, which supports this study.

Among the hypothyroid cases (n=35), fatigue (77%), cold intolerance (71%), and weight gain (69%) were more frequently found. Muscle pain was found in 65% of cases; on the contrary, muscle pain was present in 83% of patients (39 out of 47) with hypovitaminosis D. In a study by Douchet et al.[25] reported clinical features were fatigue, weakness, mental slowness, drowsiness, chilliness, dry skin, constipation, deafness, depression, hoarseness, skin infiltration, anorexia, paleness, slowed reflexes, weight gain, cramps, snoring, paraesthesia, dizziness, bradycardia, disorientation. Out of these, fatigue and weakness were found in 50% of cases, and mental slowness, drowsiness, chilliness, dry skin, constipation, and deafness were found in % of the patients. In the young group, seven clinical signs were found in more than 50% of patients: fatigue, weakness, chilliness, paresthesia, weight gain, cramps, and depression. Seven other signs, mental slowness, dry skin, skin infiltration, drowsiness, constipation, dizziness, and slowed osteo-tendinous reflexes, were observed in more than 30% of patients. Some classical signs of hypothyroidism were not commonly observed. Another study by El-Shafie et al.[26] reported fatigue was the most typical symptom for 25%, followed by constipation which accounted for 20%. Rare symptoms such as dysarthria and dysphagia associated with a hoarse voice, and sleep apnea, all of which were localized in the oropharyngeal region, were observed in one patient. The patient had no goiter to explain these symptoms. Another rare presenting symptom was the swelling of the lower limbs, which was observed in another patient. Twenty-four patients (10 hypothyroid plus 14 subclinical hypothyroid) were asymptomatic, accounting for 38% of patients with hypothyroidism. Seven patients had only one symptom, and that was either constipation or fatigue. Three patients had two symptoms. Three had three symptoms, and one had four symptoms. Four patients had only one sign of hypothyroidism, either dry skin or the presence of a goiter. Only one patient had two signs. The remaining patients, i.e. 25 out of 30 patients with hypothyroidism, had no signs. Some classical signs of

hypothyroidism such as hoarseness of voice, hair loss, bradycardia, and confusion, were uncommon. These findings could be due to the place of study and inclusion criteria of the study population. Knutsen et al.[27] in a study of 572 patients reported that, in patients with nonspecific musculoskeletal pain, a total of 58% (334/572) patients had low vitamin D levels less than 50 nmol/L, which is supportive of the finding of this study.

Out of 70 patients, serum 25(OH)D level was markedly reduced in hypothyroid cases compared to the euthyroid control group. T-test showed a significant decrease in vitamin D levels in hypothyroid patients (P-value < 0.005). Mean value of serum TSH for case group (n=35) was 10.89 ± 2.63 and control group (n=35) was 2.71 ± 0.98, Mean value of serum 25(OH)D in case group (n=35) 22.14 ± 8.02 ng/ml, and control group (n=35) was 26.22 ± 7.53 ng/ml and for the total study population (n=70) mean value was 23.69 ± 8.1 ng/ml. In this study, hypovitaminosis D was more frequently found among the case group (hypothyroid cases) in comparison to the control group (euthyroid cases), and the result was statistically significant (χ^2 value = 5.245, P-value = 0.022, n = 70). A study by Khare et al. [28] reported that Vitamin D levels were found to be significantly lower in TPOAb-positive hypothyroid patients (both male and female) (10.66 ± 18.34 ng/dL), And Serum TSH was higher in TPOAb-positive hypothyroid females (13.67 ± 74.56). Another study in Korea among 304 patients by Shin et al.[29] reported lower levels of 25(OH)D3 (12.6±5.5) in patients with AITD hypothyroidism. These findings are supportive of the findings of this study. Another study by Kivity et al. [30] reported that vitamin D deficiency was significantly higher in patients with AITDs than in healthy individuals (72% versus 30.6%; P,0.001). Another study by Koch et al.[21] reported the mean value of vitamin D in subclinical hypothyroid patients (16.73±12.46 ng/ml) and overt hypothyroid (13.23±10.08 ng/ml) were remarkably lower than the euthyroid (29.07±19.01 ng/ml) with P value<0.05. A significant negative correlation analysis between vitamin D and TSH (r=-0.314, P<0.01) has been seen in Pearson's correlation. Vitamin D deficiency negatively correlates with TSH. In this study's result in the scatter plot, it can be seen that Vitamin D deficiency negatively correlates with TSH, similar to the study of Koch et al. Also, a study by Mackay et al. reported that Serum 25(OH) Vitamin D was significantly lower in hypothyroid patients than in controls (t=-11.128, P =0.000). Its level was insignificantly decreased in females than in male patients (t=- 1.32, P >0.05). Moreover, serum calcium levels were significantly decreased in hypothyroid patients compared to controls (t= -5.69, P = 0.000), which is somewhat similar to this study with small differences found due to study site, sample criteria, and study population.

CONCLUSIONS

Study finds that, women of the fourth decade were frequently affected with hypothyroidism compared to their male counterparts. Overall, hypovitaminosis of D was present in three-fifths of the patients. Hypovitaminosis D is significantly more common in hypothyroid patients than in controls. Therefore, it may be concluded that in this population, hypovitaminosis D is associated with hypothyroidism. However, a multi centre study with larger sample simple size is thus recommended.

REFERENCES

1. Zaman S, Hawlader MDH, Biswas A, Hasan M, Jahan M, Ahsan GU. High Prevalence of Vitamin D Deficiency among Bangladeshi Children: An Emerging Public Health Problem. Health, 2017; 9: 1680-1688.
2. MehtaM, Patel RK, Shah J. Vitamin D deficiency associated comorbidities - A study from Vadodara, India. IJRRMS 2012;2(4): 18-20.
3. Bhatta MP, Pandey BJ, Gurung KM, Nakarmi R, Gurung K, Gurung LB, et al.: Prevalence of vitamin D deficiency among adult population of Western Region of Nepal. International Journal of Medicine & Biomedical Sciences. 2016; 1(2):7-12.
4. Bhardwaj SH, Mishra B, Yadav S, Malik E, Jain A. Vitamin D levels correlated with hypothyroidism in Indian population: a pilot study. International Journal of Recent Scientific Research, 2014; 5(5):984-987.
5. Lohokare R, Gupta A, Jain A, Kothari V, Sarkar PD. A study of vitamin D levels in hypothyroid patients, a case control study in a tertiary care hospital of central India. National Journal of Medical and Dental Research, 2016; 4(2):89-92.
6. Arya V, Bhambri R, Godbole MM, Mithal A. Vitamin D Status and Its Relationship with Bone Mineral Density in Healthy Asian Indians. Osteoporosis International,2004; 15:56-61.

7. Harinarayan CV, Joshi SR. Vitamin D status in India-its implications and remedial measures. J. Assoc. Physicians. India, 2009;57:40-48.
8. Goswami R, Gupta N, Ray D, Singh N, Tomar N. Pattern of 25-hydroxy vitamin D response at short (2 month) and long (1 year) interval after 8 weeks of oral supplementation with cholecalciferol in Asian Indians with chronic hypovitaminosis D. British Journal of Nutrition, 2008;100: 526–529.
9. Ahmed AMS, Ahmed T, Long KZ, Magalhaes RJH, Hossain MI, Islam MM, et al. Prevalence and risk factors of vitamin D insufficiency and deficiency among 6–24-month-old underweight and normal-weight children living in an urban slum of Bangladesh. Public Health Nutrition, 2015:1-11.
10. Micka A. Vitamin D Status among Bangladeshi Women of Reproductive Age. 2009; Masters Theses 1911 - February 2014. 287. http://scholarworks.umass.edu/theses/287
11. Kim D. The Role of Vitamin D in Thyroid Diseases. Internatioal Journal of Molecular Science, 2017; 18: 1949-53.
12. 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; 63: 1-6.
13. 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. British Journal of Nutrition, 2009; 102:382–386.
14. Bhatta MP, Pandey BR, Lamichhane A, Bhatt P, Joshi M, Hamza Am, et al. Association of vitamin D deficiency with hypothyroidism in Nepalese population: a pilot study. International Journla of Advance Research, 2016; 4(12):710-718.
15. Sonawane S, Bora B, Shrikhande DW, Bansal S, Kumar P. Vitamin D Deficiency and its Association with Thyroid Diseases. International journal of contemporary research, 2017; 4(8): 1765-1767.
16. Muscogiuri G, Tirabassi G, Bizzaro G, Orio F, Paschou SA, Vryonidou A, et al. Vitamin D and thyroid disease: To D or not to D? Eur. J. Clin. Nutr. 2015; 69: 291–296.
17. Vondra K, Stárka L, Hampl R. Vitamin D and thyroid diseases. Physiol. Res, 2015; 64: S95–S100.
18. Koch N, Kaur J, Mittal A, Gupta A, Kaur IP, Agarwal S. Status of vitamin D levels in hypothyroid patients and its associations with TSH, T3 and T4 in north Indian population of Meerut, a cross sectional study. International Journal of Clinical Biochemistry and Research 2016;3(3):295-298.
19. Mehta M, Patel RK SJ. Vitamin D deficiency associated comorbidities - A study from Vadodara. IJRRMS. 2012;2(4):2–4
20. Hossain HT, Islam QT, Khandaker MAK, Ahasan HN. Study of serum vitamin D level in different socio-demographic population - A pilot study. J Med. 2018;19(1):22–9.
21. Koch N, Kaur J, Mittal A, Gupta A, Kaur IP, Agarwal S. Status of vitamin D levels in hypothyroid patients and its associations with TSH, T3 and T4 in north Indian population of Meerut, a cross sectional study. Int J Clin Biochem Res. 2016; 3(3):295.
22. Mackawy AMH, Al-Ayed BM, Al-Rashidi BM. Vitamin d deficiency and its association with thyroid disease. Int J Health Sci (Qassim). 2013;7(3):267–75.
23. Bener A, Ozdenkaya Y, Al-Hamaq AOAA, Barisik CC, Ozturk M. Low Vitamin D Deficiency Associated With Thyroid Disease Among Type 2 Diabetic Mellitus Patients. J Clin Med Res. 2018;10(9):707–14.
24. Jääskeläinen T, Knekt P, Marniemi J, Sares-Jäske L, Männistö S, Heliövaara M, et al. Vitamin D status is associated with sociodemographic factors, lifestyle and metabolic health. Eur J Nutr. 2013;52(2):513–25.
25. Doucet J, Trivalle C, Chassagne P, Perol M -B, Vuillermet P, Manchon N -D, et al. Does age play a role in clinical presentation of hypothyroidism? J Am Geriatr Soc. 1994;42(9):984–6.
26. El-Shafie KT. Clinical presentation of hypothyroidism. J Family Community Med. 2003; 10(1):55–8.
27. Knutsen KV, Brekke M, Gjelstad S, Lagerløv P. Vitamin D status in patients with musculoskeletal pain, fatigue and headache: A cross-sectional

descriptive study in a multi-ethnic general practice in Norway. Scand J Prim Health Care. 2010; 28(3):166–71.

28. Khare J, Reddy B, Nalla S, Srivastava P, Wadhwa J, Deb P. Vitamin D deficiency and its association with thyroid peroxidase antibodies positive hypothyroidism - Experience in a tertiary center in South India. Med J Dr DY Patil Univ. 2017; 10(4):355.
29. Shin DY, Kim KJ, Kim D, Hwang S, Lee EJ. Low serum vitamin D is associated with anti-thyroid peroxidase antibody in autoimmune thyroiditis. Yonsei Med J. 2014;55(2):476–81.
30. Kivity S, Agmon-Levin N, Zisappl M, Shapira Y, Nagy E V., Dankó K, et al. Vitamin D and autoimmune thyroid diseases. Cell Mol Immunol. 2011;8(3):243–7.