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STUDY OF VITAMIN D STATUS IN TYPE II DIABETES MELLITUS PATIENTS AND ITS CORRELATION TO THYROID FUNCTION: A CROSS SECTIONAL STUDY IN A TERTIARY HEALTH CARE CENTRE IN TRIPURA

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ABSTRACT **Background:** There has been a marked variance in the prevalence of Vitamin D deficiency in India. Limited evidence is available regarding the correlation of Vitamin D with thyroid hormones in patients with Type II Diabetes mellitus (T2DM).

Aims AND Objectives: To study the correlation of Vitamin D with thyroid hormones in patients with Type II Diabetes mellitus at tertiary health care in Tripura.

Materials And Methods: Hundred patients with T2DM diagnosed as per American Diabetes Association (ADA) were studied in across-sectional study which was conducted in the Department of Medicine at AGMC&GBP Hospital from January 2019 – June 2020. Blood tests were performed to estimate serum vitamin D level and thyroid profile and correlation was obtained with glycemic parameters.

Results: T2DM was more prevalent in the age group of 60-70 years with mean age being 55.28 years. Majority had (52%) hypothyroidism, 38% had had vitamin D deficiency and 13% had vitamin D insufficiency. Majority of the Vitamin D deficient patients TSH > 5 µIU/mL (31%). Linear regression analysis showed that inverse relationship between TSH and Vitamin D, HbA1c and Vitamin D. An equation of Vitamin D level estimation was derived as Vitamin D level = 28.48 – 0.81 * HbA1c level.

Conclusion: Prevalence of vitamin d deficiency is more prevalent among hypothyroid diabetics and the severity of the Vitamin D deficiency correlated with hypothyroid status.

KEYWORDS : hypothyroid, sunshine vitamin, deficiency, thyroid releasing hormone

INTRODUCTION

In a developing country like India marred by a plethora of infectious diseases, endocrine diseases are recently being researched to have an important bearing on the overall health of the people. Diabetes mellitus is a worldwide epidemic and currently, the most prevalent chronic illness in the world having a prevalence of around 9.3 % in the adult population. India alone has 69.1 million people afflicted with Diabetes mellitus. [1]

Type II diabetes mellitus and thyroid dysfunction are the emerging main threats in developing countries and impair the health and economic status. Type II DM increases the risk of coronary heart disease and thyroid dysfunction in the long-term. Type II DM and thyroid dysfunction are already the primary reasons for mortality and morbidity in most high-income and developing countries. [2]

Vitamin D deficiency has received special attention lately because of its high incidence and its implication in the genesis of multiple chronic illnesses. Vitamin D deficiency and Type II DM are usually recognized as a complication and risk for thyroid disease. Besides, high levels of TSH have been associated with lower Vitamin D levels. Moreover, suppressed levels of TSH have been associated with higher Vitamin D levels. Also, a linear association between TSH and Vitamin D has been noticed among Type II DM patients. Though higher levels of Vitamin D with suppressed TSH levels might be due to increased absorption of Vitamin D in hyperthyroid state. Metabolism of Vitamin D is also reciprocally regulated by thyroid hormones. Histological examination of the skin in hypothyroid patients has shown epidermal thinning and hyperkeratosis. Finally, the body may not activate vitamin D properly. [3] According to Krzewska et al, Hashimoto's thyroiditis and Graves' disease, are the most prevalent autoimmune diseases in patients with Diabetes mellitus. Their incidence is an estimated as 2–4-fold higher than those in the general population, with Hashimoto's thyroiditis the most common clinical form (14–28%). Familial clustering has been observed, suggesting a genetic predisposition. Various hypotheses of viral- and/or bacterial-induced pancreatic autoimmunity have been proposed; however, a definitive description of the autoimmune pathomechanism is still lacking. Recently, the association of vitamin D levels with thyroid disorders, particularly in Diabetic population has caught the attention of researchers across the world. [4]

There has been a marked variance in the prevalence of Vitamin D deficiency in a vast country like India. India also is a kaleidoscope of various races & ethnicity, a genetic predisposition for endocrine disorders shows significant diversity. There exist lacunae in the literature regarding the correlation of Vitamin D with thyroid hormones in patients with Type II Diabetes mellitus in North East India. Hence, the present study addresses the gap by studying the correlation of Vitamin D with thyroid hormones in patients with Type II Diabetes mellitus at tertiary health care in Tripura.

METHODOLOGY

Present cross-sectional study was conducted on 100 patients in the Department of Medicine at AGMC&GBP Hospital from January 2019 – June 2020 including either sex diagnosed with Type II Diabetes Mellitus.

A total of 100 patients with Type II DM who were diagnosed based on ADA criteria or who are taking treatment for Diabetes Mellitus attending AGMC &GBP HOSPITAL are included has to undergo Blood tests for determination of serum vitamin D Level i.e., 25 (OH) D by Fluorescent immunosorbent Assay through VIDAS, Thyroid Profile test by Fluorescent Immunosorbent Assay through VIDAS for the thyroid status and other blood examination for evaluation of type II Diabetes Mellitus. A detail History and Examination was done on these patients. Weight and height were measured to calculate BMI and each eligible study participants will have to undergo different laboratory investigation.

Informed written consent was obtained from every participant as per modified ICMR template, ensuring confidentiality while collecting and analyzing the data which was used for research purpose only. The application was placed before the Institutional Ethics Committee of Agartala Government Medical College for approval.

Biochemical examination was performed for fasting blood sugar, post-prandial blood sugar, glycosylated haemoglobin (HbA1c), fasting lipid profile, serum Vitamin D levels, serum urea, creatinine, and thyroid profile: FT3, FT4, TSH.

All patients with T2DM, aged more than 30 years irrespective of glucose control, treatment (OHA / INSULIN) and who gave consent to participate in the study were included.

Patients with Type I DM, gestational Diabetes, pancreatitis, chronic renal failure and diabetic nephropathy, acute illness (sepsis, acute myocardial infarction, severe heart failure, recent admission in the intensive care unit.), hepatic dysfunction, psychiatric illness, patient on treatment with drugs interfering with thyroid function (amiodarone, propranolol, corticosteroids, and oral contraceptives.), patient on

vitamin supplementation and those with any other endocrinopathies were excluded.

Diagnosis of Type II Diabetes was performed as per ADA Diagnosis Criteria [5] where a fasting plasma glucose (FPG) level of 126 mg/dL (7.0 mmol/L) or higher, *or* A 2-hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher during a 75-g oral glucose tolerance test (OGTT), *or* Random plasma glucose of 200 mg/dL (11.1 mmol/L) or higher in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, *or* A haemoglobin A1c (HbA1c) level of 6.5% (48 mmol/mol) or higher was consider as diabetes.

Subclinical Hypothyroidism was defined as elevated TSH (>5- 10 µIU/ml)with normal FT4 or FT3, overt Hypothyroidism as elevated TSH >10µIU/ml) with decrease T4 or FT4, subclinical Hyperthyroidism as decrease TSH with normal T3 or T4 levels and overt Hyperthyroidism as suppressed TSH and elevated T3 and T4.

The reference value of Vitamin D was considered as deficient (0- 20 ng / ml), insufficient (21-29 ng/ ml), sufficient (30 -100 ng / ml) and toxic (> 150 ng/ ml).

Data collected was analysed using the Statistical Package for the Social Sciences (SPSS Statistics for Windows, Version 25.0.) by frequency, percentage, mean, standard deviation, correlation, chi-square test, t-test. Chi-square test was used for categorical data and T-Test was used for measurable (continuous) data. Result obtained was discussed and correlated with the available literature and the conclusion will be drawn keeping in mind the limitation of the study.

RESULTS

Age ranged from 30 to 78 years. Mean age of the study group was 55.28 years. The highest number of subjects was from the age group of 60-70 years, followed by 50-60 years and 40-50 years. The lowest number of subjects was from 20-30 years.

Table 1: Baseline Demographic Characteristics Of Study

Variables	Sub variables	No of patients
Age (year)	20-30	2
	30-40	10
	40-50	22
	50-60	28
	60-70	30
	70-80	8
Sex	Male	65
	Female	35
Community	Bengali	58
	Indigenous	30
	Others	12
Locality	Urban	39
	Semi-urban	15
	Rural	46
Marital status	Married	74
	Unmarried	26

Table 2: Prevalence Of Hypothyroidism

Variables	< 0.25 µIU/ml	0.25 – 5 µIU/ml	> 5 µIU/ml
No. of subjects	9 (9%)	39 (39%)	52 (52%)

Among the study group, 52 (52%) patients had hypothyroidism. Out of 100 patients, 38 patients had vitamin D deficiency and 13 patients had vitamin insufficiency.

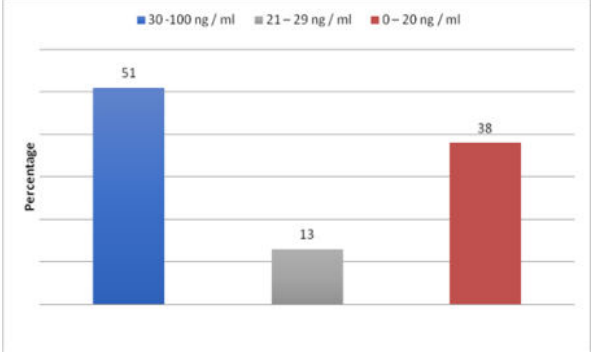

Figure 1: Distribution Of Patients According To Vitamin D Status

Table 3: Distribution of TSH with Vitamin D deficiency

Variables	TSH levels		
	< 0.25 µIU/ml	0.25 – 5 µIU/ml	> 5 µIU/ml
No. of subjects with Vitamin D Deficiency	1%	6%	31%

Among the vitamin D deficient patients of the study group (n=38), 1 (1%) subjects had TSH <0.25 µIU/ml, 6(6%) subjects had TSH between 0.25 – 5µIU/mL and 31 (31%) subjects had TSH > 5 µIU/mL. In our study, subjects with TSH < 0.25 µIU/ml had mean Vitamin D level of 34 ng /mL, subjects with TSH 0.25 – 5 µIU/ml had mean Vitamin D level of 28.36 ng /mL and subjects with TSH > 5 µIU/ml had mean Vitamin D level of 19.24 ng /mL. The student t-test was applied and p-value of 0.001 was derived indicating a statistically significant difference between the mean levels of vitamin D in these groups.

Further, subjects with TSH < 0.25 µIU/ml had mean HbA1c level of 6.55 %, subjects with TSH 0.25 – 5 µIU/ml had mean HbA1c level of 7.28 % and subjects with TSH TSH> 5 µIU/ml had mean HbA1c level of 9.1. The student t-test was applied and p-value of 0.023 was derived indicating a statistically significant difference between the mean levels of HbA1c in these groups.

In our study, subjects with Vitamin D level of 0 – 20 ng / ml had mean Ft4 of 9.54 Pmol / L, subjects with Vitamin D level of 21 – 29 ng / ml had mean Ft4 of 16.55 Pmol / L, subjects with Vitamin D level of 30 - 100 ng / ml had mean Ft4 of 23.25 Pmol / L.

In our study, total cholesterol was significantly higher in subjects with vitamin D levels of 0 – 20 ng/ml. Similarly, Triglyceride, LDL, VLDL was also found to be significantly higher in subjects with vitamin D levels of 0 – 20 ng/ml. In contrast, HDL was significantly lower in subjects with vitamin D levels of 0 – 20 ng/ml.

Table 4: Correlation Of Vitamin D And HbA1c

Variables	HbA1c levels			
	< 6 % (n=6)	6-9 % (n=73)	> 9 % (n=21)	P value
Mean Vitamin D levels	34.71	26.35	17.12	0.001

Mean Vitamin D levels in patients with HbA1c < 6 % was 34.71 ng / ml, in patients with HbA1c 6-9% was 26.35 ng / ml, in patients with HbA1c >9 %was17.12 ng / ml.

Table 5: Linear Regression: TSH And Vitamin D

Independent variable	Regression Coefficient	Intercept	SE	95 % CI	P-value
TSH	-0.86	27.47	11.17	- (0.354-1.12)	0.001
FT4	0.33	17.83	11.62	0.037 - 0.345	0.01
HbA1c	-0.81	28.48	11.73	-0.284 – 0.105	0.03

In linear regression derived between TSH as an independent variable and vitamin D as a dependent variable, Regression Coefficient of -0.86 was derived with Intercept of 27.47. The negative sign of Regression Coefficient indicated an inverse relationship between TSH and Vitamin D. An equation of Vitamin D level estimation was derived: Vitamin D level = 27.47 + -0.86 * TSH level. In linear regression derived between Ft4 as an independent variable and vitamin D as a dependent variable, Regression Coefficient of 0.33 was derived with Intercept of 17.83. An equation of Vitamin D level estimation was derived: Vitamin D level = 17.83 + 0.33 * FT4 level. In linear regression derived between HbA1c as an independent variable and vitamin D as a dependent variable, Regression Coefficient of -0.81was derived with Intercept of 28.48. The negative sign of Regression Coefficient indicated an inverse relationship between HbA1c and Vitamin D. An equation of Vitamin D level estimation was derived: Vitamin D level = 28.48 – 0.81 * HbA1c level.

DISCUSSION

Mild to moderate vitamin D insufficiency has been proposed as a risk factor for Type II diabetes. Higher plasma vitamin D is related to a lower risk for the development of diabetes mellitus in high-risk patients. Specific vitamin D receptor gene polymorphisms are related to components of the metabolic syndrome.

Moreover, vitamin D seems to affect glucose homeostasis, with vitamin D levels being inversely related to glycosylated haemoglobin levels in diabetes mellitus. Besides, vitamin D deficiency seems to be related to increased risk for the development of gestational diabetes mellitus.

In this context, our research studied the vitamin D status in Diabetic Mellitus Type II patients and its role in thyroid functions. Our study enrolled 100 patients with Diabetes mellitus Type II and hypothyroidism. Among them, age ranged from 27 years to 74 years. Majority of the patients were from the age group of 40-60 years. Though the prevalence of diabetes mellitus Type II increases with advancing age groups, our study had many patients from middle age. This is because of the representational bias (that is a greater number of patients in working age group access healthcare than the elderly population for treatment of Diabetes mellitus Type II on OPD basis).

There were 65 % male and 35 % female in our study. Bengalis constituted the majority, followed by the indigenous community. The majority were from the urban locality. The majority were married.

In our study, 62 (62%) patients had overt hypothyroidism and 38 (38%) subclinical hypothyroidism. Mean TSH among overt hypothyroidism was 14.7 + 3.4 mIU/L and among subclinical hypothyroidism was 8.43 + 2.1 mIU/L.

Coller and Huggins shown that surgical removal of parts of thyroid gland had an ameliorative effect on the restoration of glucose tolerance in hyperthyroid patients suffering from coexisting diabetes. [6] Brenta et al concluded a complex intertwining biochemical, genetic, and hormonal malfunctions mirroring the pathophysiological association. Thyroid hormones directly control insulin secretion. In hypothyroidism, there is a reduction in glucose-induced insulin secretion by beta cells, and the response of beta cells to glucose or catecholamine is increased in hyperthyroidism due to increased beta-cell mass. Moreover, insulin clearance is increased in thyrotoxicosis. [7]

Prevalence of hypothyroidism among those with Type II diabetes mellitus is significantly higher, ranging from 9.9 to 48%. In a study by Talwalkar et al, they found the prevalence of hypothyroidism among 20% of diabetics. [8] In a study by Akbar et al, the prevalence of thyroid dysfunction in Type II diabetes mellitus patients was reported to be 12.3% in Greece and 16% in Saudi Arabia. [9] This wide range of prevalence can be explained by the use of different definitions for TD diagnosis, depending on the presence of anti-thyroid peroxidase (anti-TPO), antithyroglobulin antibody (anti-TG), or both. Just as in the non-diabetic population, TD was found to be more common in females than in males with diabetes. TD is more common in Type II diabetes mellitus than in Type II diabetes mellitus patients, but the pathophysiology is more complex in Type II diabetes mellitus patients and has greater clinical implications.

In our study, in a subgroup analysis, hypothyroid patients on regular hypoglycaemic drugs (n=24) were compared with those who were not on treatment (n=27). Mean TSH in the treated group was 5.4+2.3 mIU/L and in the untreated group was 9.7+3.8 mIU/L and the difference was significant. Similar to our study, Cappelli et al evaluated the thyroid hormone profile by studying the interaction between metformin and circulating thyroid function parameters in patients who were started on metformin. [10] Study revealed baseline reduction of TSH level after 6 months. Similar findings were reported by Chen et al. [11]

In the present study, 38 patients had vitamin D deficiency and 13 patients who had vitamin D insufficiency. Further, vitamin D levels were found to be negatively correlated with glycosylated haemoglobin levels with a Pearson coefficient of – 0.48. The correlation persisted even after outliers were excluded. Lau et al have shown that vitamin D levels may be inversely related with glycosylated haemoglobin levels in gestational diabetes mellitus. Besides, it has been suggested that adequate vitamin D intake may be related to a lower risk for the development of gestational diabetes mellitus.[12] In a study by Kostoglou-Athanassiou et al, vitamin D levels were lower in the diabetes mellitus Type II patients than in the control group, being 19.26 ± 0.95 ng/ml and 25.49 ± 1.02 ng/ml, in the patient and control groups, respectively ($p < 0.001$). Vitamin D levels were found to be inversely associated with $HbA1_c$ levels in diabetic patients ($p = 0.008$, $r^2 = 0.058$, linear regression). [13] In a study by Heaney et al, an inverse association of insulin resistance with vitamin D levels was observed which was principally found at vitamin D levels between 16 and 36 ng/ml. [14]

In our study, there was a strong negative correlation between TSH and vitamin D levels with Pearson coefficient of -0.56, indicating higher the TSH, lower was the vitamin D levels. A similar positive correlation was also found between Free T3 and T4 with Vitamin D levels.In a study by Mackawy et al, 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 male patients (t=− 1.32, P >0.05). Moreover, serum calcium levels recorded a significant decrease in hypothyroid patients when compared to controls (t= −5.69, P = 0.000). The study concluded that patients with hypothyroidism suffered from hypovitaminosis D with hypocalcaemia that is significantly associated with the degree and severity of the hypothyroidism. [15] In a study by Talae et al on Vitamin D supplementation, after 12 weeks of intervention, compared to the placebo, vitamin D supplementation resulted in significant increases in serum 25-hydroxyvitamin D (+26.5 ± 11.6 vs. 0.0 ± 0.0 ng/mL, $P <$ 0.001) and calcium (+0.4 ± 0.7 vs. 0.1 ± 0.6 mg/dL, $P = 0.002$), and a significant decrease in serum thyroid-stimulating hormone (TSH) levels (−0.4 ± 0.6 vs. +0.1 ± 2.0 μIU/mL, $P = 0.02$). A trend towards a greater decrease in serum parathyroid hormone (PTH) levels was observed in the vitamin D group compared to the placebo group (−3.8 vs. +1.9, $P = 0.07$). We did not observe any significant changes in serum T3, T4, alkaline phosphatase (ALP) and albumin levels following supplementation of vitamin D compared with the placebo. [16] Kivity et al reported that the prevalence of vitamin D deficiency (< 25 nmol/L) was significantly higher in 50 patients with autoimmune thyroid diseases compared with 98 healthy individuals (72% vs. 30.6%; $p < 0.001$) as well as in 28 patients with hypothyroidism compared to 42 patients with non--autoimmune thyroid diseases (79% vs. 52%; $p < 0.05$). Vitamin D deficiency was also found to be correlated with the presence of anti-thyroid antibodies ($p = 0.01$), suggesting the involvement of vitamin D in the pathogenesis of autoimmune thyroid diseases. [17]

One of the 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. 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.

In our study, mean Vitamin D level was 28.36 ng /mL in patients with TSH 5 -10 μIU/mL and Vitamin D level of 19.24 ng /mL in patients with TSH > 10 μIU/mL. The difference between mean vitamin D levels was significant.In a study by *Konstantinos*et al, patients with Type II diabetes mellitus were older and more obese and had significantly lower vitamin D and higher TPO antibody titres compared to controls. Similarly, in our study, the majority of the patients were obese. Though our study did not have any control group, compared to a representative general population % of obese were high. [18] Similarly, our study also observed that majority of patients were either overweight or obese. This finding can be explained by the fact that obesity is one of the factors for causing insulin resistance. Added hypothyroidism further increased weight gain. Another behavioural aspect is that obese persons tend to go less out of the house and prefer to be sedentary. Hence, this adds to lack of exposure of sunlight and hence compounds the deficiency of vitamin D that's already prevalent in hypothyroid diabetics. In a study by Aljabri et al, they observed an association between vitamin D deficiency and TSH level among Type II Diabetes mellitus patients. Serum vitamin D level was significantly different among the study subgroups with the highest deficiency noted among patients with severe hypothyroidism. Along with TSH, age, gender, HbA1c were the independent predictors of vitamin D levels. Vitamin D deficiency was frequent in older patients, females and those who had higher HbA1c.[19] Bener et al also found a significant association between Vitamin D levels, TSH and HbA1c. Multivariable stepwise logistic regression analysis showed that TSH, HbA1c, BMI, family history of Type II Diabetes mellitus and family history of the thyroid were considered at higher risk as predictors of vitamin D deficiency among diabetic patients.[20]

Similarly, our study also observed that negative correlation between Vitamin D levels and TSH levels. Further, we noted that females had a higher prevalence of vitamin D deficiency compared to males.

In a study by Komisarenko et al, patients with Type II Diabetes mellitus in combination with autoimmune thyroiditis was studied. Though all patients had thyroid status after thyroid hormone replacement therapy, they observed that the prevalence of vitamin D deficiency was higher in the study group compared to the control group. This shows the probable lag between corrections to euthyroid

status and normalisation of vitamin D levels. However, as our study was a cross-sectional study, we did not assess the vitamin d deficiency after the attainment of thyroid status.[21]

When we compared the characteristics of patients with and without vitamin D deficiency, among those having hypothyroidism and Diabetes mellitus, we observed that former group were older, had higher BMI, had higher mean Hba1c, and had higher mean FBS and PPBS.

We compared vitamin D levels in patients with and without TPO antibody titre. We observed that in the former group, vitamin D levels was 17.21 ng /mL when compared to 22.51 ng /mL in the later. This points out the fact that the TPO antibody has a role in vitamin D deficiency.

Similarly, in a study by Chaudhary et al, from the data of 100 autoimmune thyroid patients (68 with thyroid-stimulating hormone [TSH] ≤10 mIU/L, 32 with TSH > 10 mIU/L), 93% had Vitamin D insufficiency. TPO-Ab titers were highest among patients in the lowest vitamin D quartile (P = 0.084). At 3 months follow-up, there was a significant fall in TPO-Ab in Group-1 (−46.73%) as compared to Group-2 (−16.6%) (P = 0.028).[22] The cross-sectional study by Goswami et alhas observed a weak inverse relationship between TPO-Ab and Vitamin D status. The study by Chaudhary et al also noted a weak inverse relationship between TPO-Ab and vitamin D levels, which approached statistical significance. [23]

Type II diabetes mellitus and thyroid diseases are highly correlated as the two commonest endocrinological medical conditions reported and linked with the vitamin D deficiency in general clinical practice. Vitamin D deficiency and Type II diabetes mellitus are usually recognized as a complication and risk for thyroid disease. Therefore, effective controls of vitamin D and Type II diabetes mellitus are essential to reduce the occurrence of thyroid diseases in the middle and elderly age group and may affect the quality of life. Additionally, a study has investigated the role of environmental and lifestyle factors. It is worth to note that the possible role of vitamin D insufficiency/ deficiency in the pathogenesis of both Type II diabetes mellitus and thyroid disease. However, vitamin D deficiency could be also secondary to these diseases. Oral anti-diabetic medications as well as therapeutic dietary restriction could affect vitamin D levels in patients with diabetes. Besides, thyroid dysfunction could also modify vitamin D intake, absorption or metabolism.

Present study is not devoid of limitation. Firstly, the sample might be partially biased we did not match case with control. Secondly, there were no cytological or histological results for hypothyroid cases.

CONCLUSION

Majority of the patients were from the age group of 40-60 years. Nearly 2/3 were males and 1/3 were females. Prevalence of hypothyroidism was 52%. Prevalence of vitamin D deficiency was 38 % and vitamin D insufficiency was 13%. Higher prevalence of vitamin D deficiency was probably because of a sedentary lifestyle and biochemical impact of hypothyroid status on vitamin D absorption. 31% of Diabetic patients had both vitamin D deficiency and hypothyroidism. Vitamin D levels were found to be negatively correlated with glycosylated haemoglobin levels indicating a linear association of the Vitamin D and Diabetes mellitus. Vitamin D levels were lower with higher TSH levels and vice-versa. Similarly, Vitamin D levels were lower with lower Free T3 and T4. Thus, our study reiterates that the prevalence of vitamin d deficiency is more prevalent among hypothyroid diabetics and the severity of the Vitamin D deficiency correlated with hypothyroid status.

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