Section: Biochemistry

Research

INVESTIGATION OF THYROID PROFILE AND VITAMIN D LEVELS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract

Background: Non-communicable illness is a pressing public health issue in India, resulting in a significant rise in both death and morbidity. Out of them, Type-2 diabetic mellitus (T2DM) and hypertension are seeing a significant rise. Type 2 diabetes mellitus (T2DM) elevates the likelihood of developing thyroid dysfunction over an extended period of time. Type 2 diabetes mellitus (T2DM) and hypothyroidism are the leading causes of death and illness in both affluent and poor nations. **Aim:** Investigation of Thyroid Profile and Vitamin D Levels in Patients with Type 2 Diabetes Mellitus. **Materials and Methods:** This research used a case-control design, using a sample of 100 individuals from Department of Biochemistry, Rajshree Medical Research Institute diagnosed with type 2 diabetes and 100 individuals without diabetes. The venous blood sample was obtained, and the serum was separated and kept at a temperature of -70 °C until it could be examined. The commercially available kit was used to quantify the vitamin D metabolite, serum 25-hydroxyvitamin D (25OHD). Thyroid function was evaluated by quantifying thyroid stimulating hormone (TSH), free-T3 (FT3), and free-T4 (FT4) levels using immunochemoluminescent tests performed by an automated instrument. **Result:** The clinical biochemistry values for individuals with type 2 diabetes mellitus (T2DM) showed lower levels of vitamin D ($P < 0.001$), calcium ($P < 0.001$), magnesium ($P < 0.001$), potassium ($P = 0.01$), phosphorous ($P < 0.001$), fasting blood glucose ($P < 0.001$), cholesterol ($P < 0.001$), HbA1c ($P < 0.001$), high-density lipoprotein (HDL) cholesterol ($P < 0.001$), low-density lipoprotein (LDL) cholesterol ($P = 0.003$), albumin ($P < 0.001$), triglycerides ($P = 0.002$), systolic blood pressure (SBP) ($P < 0.001$), and diastolic blood pressure (DBP) ($P < 0.001$), as well as lower levels of TSH ($P < 0.001$), triiodothyronine (T3) ($P < 0.001$), and thyroxine (T4) ($P < 0.001$) compared to control subjects. These differences were statistically significant ($P < 0.001$). **Conclusion:** There is a significant correlation between vitamin D insufficiency and the prevalence of thyroid problems in people with T2DM. This research demonstrates a correlation between the rise in thyroid illnesses and the growth in metabolic syndrome, vitamin D insufficiency, HbA1C levels, diabetes, and obesity.

INTRODUCTION

Thyroid dysfunction, diabetes mellitus, and vitamin D insufficiency have a high prevalence worldwide, including in India. As to the worldwide diabetes federation, the global population of individuals with diabetes is projected to rise from 415 million to 642 million by 2040. Among them, India is estimated to have 69.1 million diabetes patients.[1] Furthermore, research has shown that around 42 million individuals in India are afflicted with thyroid disorders.[2] Subclinical hypothyroidism is a common thyroid problem that affects 3-15% of the adult population. Over time, a significant proportion of people develop this condition. Subclinical hypothyroidism has a conversion rate of 4.3 to 8% to overt hypothyroidism, particularly among the adult population with a high propensity.[3–6] Conversely, there is a global rise in vitamin D insufficiency, with a prevalence of 80-90%. Despite this, it remains the most often overlooked and treatable dietary deficit worldwide.[7,8] The relationship between vitamin D insufficiency and numerous illnesses, such as cancer, cardiovascular disorders, autoimmune diseases, endocrine diseases, and metabolic diseases, is receiving significant attention.[9,10] Vitamin D acts as an immunomodulator, and a lack of it may impact autoimmune thyroid disease. Subclinical hypothyroidism is characterised by elevated levels of TSH and normal levels of T3 and T4. It is often an early stage of hypothyroidism and is frequently caused by chronic autoimmune thyroiditis. Over time, this condition may progress to overt hypothyroidism, with an annual conversion rate of 4.3-8%. Multiple publications have documented positive connections between vitamin D insufficiency and thyroid dysfunction in individuals with type 2 diabetes mellitus.[9] Clinical practise has documented the correlation between vitamin D insufficiency and thyroid illnesses, which are the most prevalent endocrinological medical problems.[10] Impairments in pancreatic β-cell function, insulin sensitivity, and systemic inflammation are some of the variables that contribute to the development of T2DM. The primary hazards in both developed and developing nations are Type 2 Diabetes Mellitus and hypothyroidism. T2DM heightens the long-term susceptibility to thyroid dysfunction.[11] T2DM and hypothyroidism are the leading causes of death and illness in both affluent and developing nations.[12] The purpose of our research was to investigate the potential correlation between reduced levels of vitamin D and the prevalence of thyroid illness. This research is a cross-sectional case-control analysis that investigated the levels of 25(OH)D in individuals with thyroid conditions, both with T2DM and in a control group.

MATERIALS AND METHODS

This research used a case-control approach. The research included individuals aged 20 to 63 who were admitted to our hospital. This research used a case-control design, using a sample of 100 individuals from Department of Biochemistry, Rajshree Medical Research Institute diagnosed with type 2 diabetes and 100 individuals without diabetes (control participants). The current investigation obtained ethical clearance from the institution, and patients provided informed written permission prior to commencement. Patients were classified as having DM if they had a documented history of DM and were presently using any oral drugs for diabetes. The World Health Organisation (WHO) and the International Diabetes Federation (IDF) define the diagnosis of DM as having a fasting venous blood glucose (FBG) concentration of 7.0 mmol/L or higher and/or a postprandial blood glucose (PPG) concentration higher than 11.1 mmol/L. A participant was assigned to the control group (consisting of individuals without diabetes) if their fasting blood glucose (FBG) level was below 7.0 mmol/L (126 mg/dL), their glycosylated haemoglobin (HbA1c) level was below 48 mmol/mol (6.5%), and they did not disclose taking any prescription diabetic drugs. The following variables were also examined: FBG, serum cholesterol, serum triglycerides, HDL, LDL, PPG, HbA1c, VLDL, blood urea, and serum creatinine.

Methodology

The venous blood sample was obtained, and the serum was separated and kept at a temperature of -70 °C until it could be examined. The commercially available kit was used to quantify the vitamin D metabolite, serum 25-hydroxyvitamin D (25OHD). The processed samples were then analysed using the competitive binding radioimmunoassay (RIA) method. The subjects were categorised into two distinct classifications: 1) Insufficient levels of Vitamin D, with a 25(OH)D concentration below 20 ng/mL; 2) Adequate levels of Vitamin D, with a 25(OH)D concentration over 20 ng/mL, as recommended by Bener et al,[10] Mazokopakis and Kotsiris,[13], and Holick et al.[14] Thyroid function was evaluated by quantifying thyroid stimulating hormone (TSH), free-T3 (FT3), and free-T4 (FT4) levels using immunochemoluminescent tests performed by an automated instrument. The measurement of TSH was conducted using an immunoassay technique. The assessment of FT3 and FT4 is crucial in the diagnosis of thyroid diseases, since the levels of these hormones are influenced by changes in binding protein concentrations. Accurate assessment of hormone concentration is crucial for free thyroid hormone measurement, especially in the face of substantial variance. Patients with thyroid nodules larger than 1.00 cm were recommended to have a fine needle aspiration biopsy of the thyroid. This research included several criteria, including socio-demographic characteristics, lifestyle behaviours, and biochemical test findings. Patients were classified as physically active if they engaged in walking or cycling for a duration exceeding 30 minutes per day.

Statistical Analysis

Analysed data was processed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows, Version 25.0). The statistical significance of differences in mean values between two continuous variables was assessed using the Student's t-test for normally distributed data and the Mann-Whitney test for non-normally distributed data. The chi-square and Fisher's exact tests are used to determine significant differences between two or more category groups. A multivariate logistic regression analysis was conducted to forecast the risk variables associated with the occurrence of thyroid nodules. A significance threshold of 0.05 was used.

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RESULTS

Table 1 displays the socio-demographic and clinical characteristics of the T2DM patients and control participants that were examined. Statistically significant disparities were seen between those with T2DM and those without the condition in terms of BMI, physical activity, family history of diabetes, hypertension, and family history of thyroid nodules. [Table 1]

Table 2 displays the first clinical biochemistry data for both T2DM and control individuals. The clinical biochemistry values for individuals with type 2 diabetes mellitus (T2DM) showed lower levels of vitamin D (P < 0.001), calcium (P < 0.001), magnesium (P < 0.001), potassium (P = 0.01), phosphorous (P < 0.001), fasting blood glucose (P < 0.001), cholesterol (P < 0.001), HbA1c (P < 0.001), high-density lipoprotein (HDL) cholesterol (P < 0.001), low-density lipoprotein (LDL) cholesterol (P = 0.003), albumin (P < 0.001), triglycerides (P = 0.002), systolic blood pressure (SBP) (P < 0.001), and diastolic blood pressure (DBP) (P < 0.001), as well as lower levels of TSH (P < 0.001), triiodothyronine (T3) (P < 0.001), and thyroxine (T4) (P < 0.001) compared to control subjects. These differences were statistically significant (P < 0.001). [Table 2]

Table 3 gives multivariable stepwise logistic regression analysis of independent predictors for the presence of thyroid nodules. TSH mIU/L (OR: 5.03, 95% CI: 2.99 – 6.06, P = 0.01), HbA1c (OR: 4.02, 95% CI: 3.11 – 5.19, P = 0. 01), vitamin D deficiency (OR: 3.29 95% CI: 1.99 – 6.71, P =0.01), SBP (mm Hg) (OR: 3.11, 95% CI: 1.89 – 4.06, P = 0.01), family history of T2DM (OR: 2.52, 95% CI: 1.77 – 4.36, P = 0.001), BMI (OR: 2.39, 95% CI: 1.59 - 3.87, P = 0.002), serum calcium level (mmol/L) (P = 0.006), and family history of thyroid (P = 0.01) were considered at higher risk as predictors of thyroid among T2DM patients. [Table 3]

Table 1: Basic profile of the participants.

	T2DM =100		**Control =100**		**P value**
Gender	Number	Percentage	Number	Percentage	
Male	34	34	33	33	0.31
Female	66	66	67	67	
Age groups (in years)					
below 25	10	10	11	11	
25-35	16	16	18	18	0.54
35-45	25	25	24	24	
45-55	20	20	22	22	
above 55	29	29	25	25	
Family history of DM					
Yes	15	15	6	6	0.001
No	85	85	94	94	
BMI (kg/m^2)					
Normal (< 25 kg/m^2)	25	25	32	32	
Overweight (29 - 30 kg/m$^{2)}$	45	45	43	43	0.02
Obese (> 30 kg/m^2)	30	30	25	25	
Physical activity					
Yes	25	25	30	30	0.04
No	75	75	70	70	
Hypertension					
Yes	20	20	12	12	0.003
No	80	80	88	88	

Table 2: Biochemical parameter.

Parameter	**T2DM =100**		**Control =100**		
	Mean	**Sd**	**Mean**	**Sd**	**P value**
Vitamin D (ng/mL)	18.03	2.36	24.06	3.96	0.001
Hemoglobin (g/dL)	12.15	2.48	13.45	1.87	0.14
Magnesium (mmol/L)	0.81	0.06	0.93	0.22	< 0.001
Potassium (mmol/L)	3.45	0.34	3.82	0.44	< 0.001
Calcium (mmol/L)	1.59	0.39	1.77	0.39	0.001
Phosphorous (mmol/L)	1.51	0.44	1.63	0.41	0.041
Creatinine (mmol/L)	69.63	4.58	68.06	4.89	0.11
Fasting blood glucose (mmol/L)	7.52	1.25	6.49	1.64	< 0.001
HbA1C (mmol/L)	7.45	1.11	5.36	1.03	< 0.001
Cholesterol (mmol/L)	4.72	0.98	4.28	0.63	< 0.001
HDL (mmol/L)	0.97	0.11	1.21	0.28	0.43
LDL (mmol/L)	1.65	0.45	1.56	0.54	0.003
Albumin (mmol/L)	42.26	2.65	40.09	3.61	< 0.001
Bilirubin (mmol/L)	7.02	1.09	6.99 ± 2.54	1.74	0.01
Triglyceride (mmol/L)	1.69	0.87	1.61	0.77	< 0.001
Uric acid (mmol/L)	281 .47	8.36	265.58	7.96	< 0.001
Systolic blood pressure (mm Hg)	129.78	5.58	125.98	5.33	0.007

Diastolic blood pressure (mm Hg)	78.52	4.39	76.05	4.06	0.003
Thyroid stimulating hormone (TSH)	2.61	0.78	2.29	0.55	< 0.001
T3	1.91	0.69	1.61	0.36	< 0.001
T4	1.21	0.48	0.96	0.21	< 0.001

Table 3: Multivariate Logistic Regression Analysis.

Independent variables	Adjusted odds ratio (95% Confidence interval)	P value
TSH, mIU/L	5.03(2.99 – 6.06)	0.01
HbA1C (mmol/L)	4.02(3.11 – 5.19)	0.01
Vitamin D deficiency	3.29(1.99 – 6.71)	0.01
Systolic blood pressure, mm Hg	3.11(1.89 – 4.06)	0.01
Family history of T2DM	2.52(1.77 – 4.36)	0.01
BMI (kg/m^2)	2.39(1.59 – 3.87)	0.002
Serum calcium level (mmol/L)	2.01(1.44 – 3.05)	0.006
Family history of thyroid	1.84(1.22 – 3.04)	0.01

DISCUSSION

Diabetes mellitus is a global pandemic and now the most widespread chronic disease in the world, affecting around 9% of the adult population. Furthermore, VDD has garnered significant scrutiny recently due to its elevated prevalence and its involvement in the development of other chronic diseases. VDD and T2DM are well acknowledged as a comorbidity and susceptibility factor for thyroid disease.[15] The present research discovered that vitamin D deficiency (VDD) is prevalent among individuals with diabetes, with a prevalence rate of 49%. Furthermore, elevated levels of TSH have been linked to decreased levels of 25-hydroxyvitamin D (25-OHD). Furthermore, decreased levels of TSH have been linked to elevated levels of 25-hydroxyvitamin D (25-OHD). Furthermore, a direct correlation has been shown between TSH and 25-OHD levels in individuals with type 2 diabetes mellitus. Higher levels of 25-OHD with suppressed TSH levels may be attributed to enhanced absorption of 25-OHD in a hyperthyroid condition. The metabolism of 25-OHD is likewise controlled in a reciprocal manner by thyroid hormones. Examination of the skin in individuals with hypothyroidism has shown a reduction in the thickness of the outer layer of the skin (epidermis) and an excessive accumulation of keratin (hyperkeratosis). Consequently, the body may have difficulties in effectively utilising vitamin D.[16] The present research included a matched case-control design to investigate the correlation between vitamin D and thyroid illness in individuals with T2DM. The presence of low levels of vitamin D has been shown to be associated with elevated levels of thyroid antibodies in both adults and adolescents.[17-19] This aligns with the present findings of the research. Additionally, vitamin D insufficiency and type 2 diabetes mellitus (T2DM) are well acknowledged as factors that contribute to the development and increased likelihood of thyroid illness. Hence, it is crucial to implement efficient measures to regulate vitamin D and T2DM in order to decrease the prevalence of thyroid disorders among individuals in the middle age bracket, which might potentially impact their overall well-being. In addition, the present study found that individuals with T2DM had a greater frequency and bigger size of thyroid nodules, which aligns with earlier research indicating a favourable association between insulin resistance and thyroid nodule size. The current investigation revealed a significant disparity in average vitamin D levels between those with thyroid nodules, who exhibited a deficit, and those without thyroid nodules, who had sufficient levels of vitamin D. This is consistent with the findings of the earlier cited research.[17,18] T2DM and thyroid illnesses have a strong correlation, since they are the most often reported endocrinological medical problems that are associated with vitamin D insufficiency in general clinical practise. Moreover, other studies have shown a correlation between thyroid volume and various risk factors, including iodine shortage and supply, BMI, age, gender, smoking status, hereditary variables, impaired fasting glucose, and diabetes mellitus.[18-20] In addition, a research has examined the influence of environmental and lifestyle variables. It is important to acknowledge that vitamin D insufficiency/deficiency may have a role in the development of both diabetes mellitus (DM) and thyroid illness. However, it is possible for vitamin D insufficiency to potentially be a result of these disorders. The use of oral anti-diabetic drugs and adherence to therapeutic dietary restriction may have an impact on the vitamin D levels of individuals with diabetes. Furthermore, thyroid dysfunction has the potential to alter the intake, absorption, or metabolism of vitamin D. Several recent studies have identified several risk factors for thyroid cancer, such as iodine deficiency, environmental variables, genetic factors, family history of diabetes mellitus and hypertension, and lifestyle factors.[21] Given the current investigation into the intricate relationship between vitamin D and thyroid autoimmunity in the setting of T2DM, our data findings provide confirmation for the hypothesis put out in this research. The incidence of thyroid cancer has been increasing at a faster rate compared to other types of cancer throughout time. This may be attributed to the rise in obesity, diabetes, and sedentary lifestyle, which increase the risk of developing thyroid cancer.[22,23] The findings of our study align with earlier research, specifically indicating that there is a correlation between vitamin D insufficiency and a higher likelihood of developing thyroid illness in individuals with type 2 diabetes mellitus.[24] Moreover, the heightened susceptibility to thyroid cancer in individuals with diabetes may be associated with other variables such as elevated HbA1C and metabolic syndrome, triglyceride levels, obesity, dietary habits, and lifestyle choices. Individuals who are obese have a much higher risk, 10 times greater, of acquiring diabetes. Additionally, obesity is linked to an elevated risk of thyroid cancer.[24] The results of our study showed a notable occurrence of thyroid disorders among individuals with type 2 diabetes mellitus (T2DM) as compared to the control group. This study validates prior research findings on the association between vitamin D insufficiency and thyroid illnesses in diabetic patients within the Turkish population. Additionally, it highlights the frequency of thyroid problems in patients with type 2 diabetes, a topic that has been inadequately explored in other studies.[17] The research has several merits, although it also presents some shortcomings. The current investigation has many constraints. Firstly, the sample may exhibit partial bias, which is suboptimal for a matched case and control research. This is because there is a potential for selection bias as the individuals were chosen from patients who sought treatment at a tertiary hospital. Another constraint relates to the absence of data about the frequency of thyroid tests in our research sample. Finally, there were no cytological or histological findings for either nodule. The primary benefits of this research lie in its extensive participant pool and the comprehensive dataset including many risk factor variables, including TSH, T3, T4, body weight, physical activity, smoking, food, BMI, family history of diabetes, hypertension, and thyroid. Moreover, the differentiation between the T2DM participants and the control group was established by evaluating fasting blood glucose and HbA1c levels, ensuring a definitive separation between the two groups.

CONCLUSION

There is a significant correlation between vitamin D insufficiency and the prevalence of thyroid problems in people with T2DM. This research demonstrates a correlation between the rise in thyroid illnesses and the growth in metabolic syndrome, vitamin D insufficiency, HbA1C levels, diabetes, and obesity. While it is evident that the incidence of thyroid cancer has been increasing at a faster rate compared to other types of cancer, this may be attributed to factors such as the rise in obesity, diabetes, and sedentary lifestyle.

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