A Study on Prevalence of Thyroid Dysfunction and Dyslipidaemia in Type 2 Diabetes Mellitus in a Tertiary Care Hospital - Kottayam, Kerala

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ABSTRACT

BACKGROUND

It has been noted of the interdependence and impact of diabetes mellitus and thyroid dysfunction on each other. Prevalence of thyroid dysfunction was found to be higher in individuals with diabetes mellitus. Most commonly associated thyroid dysfunction in diabetes was hypothyroidism. Hyperthyroidism can precipitate complications in diabetes mellitus. The purpose of this study was to assess the prevalence of thyroid dysfunction and dyslipidaemia in type 2 diabetes mellitus patients.

METHODS

This cross-sectional study included a total number of 100 type-2 diabetic patients aged >15 years. All the patients were evaluated for thyroid dysfunction and dyslipidaemia by estimating triiodothyronine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) and lipid profile [total cholesterol (TC), triglycerides (TGA-c), high density lipoprotein (HDL-C), low density lipoprotein (LDL-C)].The correlation of prevalence of thyroid disorder with gender distribution, age distribution, HbA1C, duration of diabetes, family history of thyroid disorder, body mass index (BMI), usage of oral hypoglycaemic agents (OHA's) and insulin and dyslipidaemia was carried out. The observations and interpretations were recorded and results obtained were statistically analysed. This study was conducted from December 2018 to November 2019 at Government Medical College, Kottayam, Kerala.

RESULTS

The study revealed a high prevalence (26 %) of thyroid disorders in patients with type 2 diabetes mellitus (T2DM), most common being hypothyroidism (20 %) which was further found to be more in females, patients with uncontrolled diabetes i.e. HbA1C values ≥ 8.7 or patients on OHA and patients with BMI > 25. High prevalence of dyslipidaemia in diabetics (62 %) was observed; of which 51 % had hypertriglyceridaemia, 49 % had decreased HDL-C, 47 % had hyper cholesterolaemia and 43 % had increased LDL-C. Only 30.6 % diabetics with dyslipidaemia had thyroid dysfunction.

CONCLUSIONS

Screening of thyroid dysfunction should be done in all diabetic patients especially in patients with poor glycaemic control as micro vascular complications were commonly observed in this group of patients with dual endocrine disorders. There is a high prevalence of dyslipidaemia in diabetics.

KEYWORDS

Diabetes Mellitus, Thyroid Dysfunction, Dyslipidemia

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DOI: 10.18410/jebmh/2021/630

How to Cite This Article:
Thankappan PK. A study on prevalence of thyroid dysfunction and dyslipidaemia in type 2 diabetes mellitus in a tertiary care hospital - Kottayam, Kerala. J Evid Based Med Healthc 2021;8(40):3477-3482. DOI: 10.18410/jebmh/2021/630

Submission 26-08-2021,
Peer Review 02-09-2021,
Acceptance 30-09-2021,
Published 04-10-2021.

BACKGROUND

Diabetes mellitus and thyroid dysfunction are two of the most commonly encountered endocrine diseases in clinical practice. The incidence of thyroid dysfunction is found to be higher in diabetic individuals when compared to general population. A great number of studies suggest a combination of biochemical, inherited, and endocrine defects leading to this interdependence. Thyroid hormones are involved in metabolism, energy distribution and insulin sensitivity. Diabetes affects the responsiveness of TSH to thyrotropin-releasing hormone (TRH) and cause low T3. It is said that correction of abnormal thyroid status in diabetic individuals will correct the blood glucose levels and decrease cardiac and other complications, improving general health.

Type 2 DM is a non-communicable disease (NCD) prevalent across the globe with an increasing incidence in all socioeconomic groups. Diabetes is characterized by a chronic hyperglycaemic state in conjunction with other metabolic derangements. If untreated, it may cause complications like coronary artery disease (CAD), end stage renal disease, cerebrovascular accident (CVA), retinopathy and many others.

In the most recent estimate for the United States (2012), the Centre for Disease Control and Prevention (CDC) estimated that 9.3 % of the population had diabetes (~28 % of the individuals with diabetes were undiagnosed; globally, it is estimated that 50 % of individuals may be undiagnosed). In individuals age > 65years, the prevalence of DM was 26.9 %. Worldwide, most individuals with diabetes are between the ages of 40 and 59 years.[1]

Diabetes mellitus is a common endocrine disorder rising in India and has reached approximately 20 % in urban populations and approximately 10 % in rural population.[2] On long term, it is associated with vascular complications which are responsible for increased morbidity and mortality among diabetic subjects.[3] New addition to these complications is the thyroid dysfunction which is indicated by the recent studies.[4,5]

Objectives

1. To study the levels of thyroid hormones in T2DM.
2. To study the lipid profile (TC, LDL, HDL and triglycerides), fasting blood glucose and glycosylated haemoglobin in type 2 diabetes mellitus
3. To study the association between thyroid dysfunction and dyslipidaemia in diabetics.

METHODS

The present study is a cross sectional study conducted from December 2018 to November 2019. A total of 100 diabetic patients attending diabetic clinic, Department of Medicine, Government Medical College, Kottayam were included in the study by simple random sampling. Patient data includes demographic parameters like age, sex, previous or current treatment (OHA/insulin), duration of diabetes and risk factors were evaluated for:

- Glycaemic parameters: Random blood sugar (RBS), fasting blood sugar (FBS), post-prandial blood sugar (PPBS), HbA1c.
- Thyroid function test (TSH, T3, T4)
- Lipid profile (total cholesterol, LDL, HDL, triglycerides)
- Renal function tests, 2D echocardiography (ECG), ultrasound abdomen and ophthalmologic evaluation.

Method of Collection of Data

The data was collected by reviewing patient's medical records and further information and testing of glycemic parameters (FBS, PPBS, HbA1c), blood urea and serum creatinine, thyroid function test (TSH,T3,T4) and lipid parameters (total cholesterol, HDL-C, LDL-C, triglycerides), 2D echocardiography, ophthalmologic evaluation (fundus examination), ultrasound abdomen.

a) Estimation of serum glucose by glucose oxidase-peroxidase method. ADA guidelines for diabetes diagnosis:
   1. FPG ≥ 126 mg/dL (7.0 mmol/L)
   2. 2-hr PG ≥ 200 mg/dL (11.1 mmol/L) during OGTT (75-g)
   3. A1C ≥ 6.5 %(48 mmol/mol)
   4. Random PG ≥ 200 mg/dL (11.1 mmol/L)

b) Estimation of TSH, T3 and T4 by enzyme linked immunosorbent assay (ELISA): Normal range of:
   1. TSH: 0.35 - 5.5 µIU/ml
   2. T3: 0.58 - 1.59 pg/ml
   3. T4: 3.5 - 12.6 ng/dl
   4. fT3: 1.71 - 3.71 pg/ml
   5. fT4: 0.89 - 1.76 ng/dl

c) Estimation of glycosylated haemoglobin (HbA1c) by ion exchange method.

d) Triglycerides measured by enzymatic method; LDL, HDL by direct method.

Patients will be diagnosed based on ATP III classification of LDL, total and HDL cholesterol (mg/dl).

Inclusion Criteria

All patients with type 2 diabetes mellitus newly diagnosed or already on treatment (OHA/Insulin)

Exclusion Criteria

1. Patients with type 1 diabetes mellitus
2. Gestational diabetes mellitus
3. Pancreatitis
4. Steroid induced diabetes

5. Patients with chronic kidney disease and those taking drugs (anti-arrhythmics and lithium) that can affect thyroid disease.
6. Patients with pre-existing thyroid disease.

Data Analysis

Data was coded and entered in Microsoft Excel and IBM Statistical Package for Social Sciences (SPSS) version 22. Statistical test like chi square test and independent sample test were used. A p value < 0.05 was considered statistically significant.

Study Procedure

Detailed history was obtained from each patient and was entered in the proforma. Then, complete clinical examination including ophthalmological evaluation, ultrasound examination and echocardiography was also done. Data and investigation results were entered in proforma and analysed.

RESULTS

In the present study, out of 100 diabetic patients, 37 % were in the age group of 35 - 50 years, 39 % were in the group of 51 - 60 years and 24 % were in the age group of > 60 years. Mean age of study population was 54.62 ± 9.15 years. Among the patients, 55 were males and 45 were females. Regarding management of diabetics, 64 % patients were on OHA, 18 % patients were on insulin and remaining 18 % were newly detected and not on any medications.

Among diabetics, most common symptom of hypothyroidism was found to be tiredness and weakness (40 %) followed by constipation (12 %) and dry skin (10 %). Most common symptom of hyperthyroidism in diabetics was found to be fatigue and weakness (37 %) followed by polyuria. In the present study, out of 26 diabetic patients who had thyroid dysfunction, 4 patients had evidence of thyroid gland enlargement.

Most common sign of hypothyroidism in diabetics was found to be dry coarse skin (12 %), bradycardia (11 %) and pedal oedema (11 %). Most common sign of hyperthyroidism in diabetics was found to be tremor (2 %). Study revealed 99 % had poorly controlled fasting blood sugars and 72 % had poorly controlled postprandial blood sugars levels respectively. 2 % of diabetics had fair control of HbA1c.

Out of 100 % diabetic patients, 26 % had thyroid dysfunction. Most common thyroid dysfunction being overt hypothyroidism (11 %) followed by subclinical hypothyroidism (9 %), sick euthyroid syndrome (5 %) and 1 % overt hyperthyroidism.

Out of 26 diabetic patients with thyroid dysfunction, 14 (53 %) were on OHA, 6 (23.1 %) were on insulin and remaining 6 (23 %) were not on any medications. Out of 100 type-2 diabetics, 62 % had dyslipidaemia. Most common dyslipidaemia was hypertriglyceridaemia (51 %), followed by decreased HDL-C (49 %) and hypercholesterolemia (47 %) and increased LDL-C (43 %). Study shows that diabetic patients with HBA1c >8.7 had higher prevalence of thyroid dysfunction compared to diabetics with HBA1c < 8.7 and it is statistically significant. Among diabetics, females (19 %) had higher prevalence of thyroid dysfunction compared to males (7 %) and it was statistically significant.

Variable		Frequency	Percent
BMI	Normal	34	34.0
	Over weight	34	34.0
	Class I obesity	30	30.0
	Class II obesity	1	1.0
	Class IV obesity	1	1.0
WHR	Abnormal	50	50.0
	Normal	50	50.0

Table 1. Anthropometry among the Diabetic Patients

Variable		Frequency	Percent
Thyroid dysfunction	Present	26	26.0
	Absent	74	74.0
Thyroid status	Normal	74	74.0
	Overt hyperthyroidism	1	1.0
	Overt hypothyroidism	11	11.0
	Sick euthyroid syndrome	5	5.0
	Subclinical hypothyroidism	9	9.0

Table 2. Thyroid Profile among the Diabetic Patients (n = 100)

Variable		Thyroid Dysfunction		P Value
		Present	Absent	
BMI	Normal (n = 34)	6 (17.6)	28 (82.4)	0.32
	Over weight (n = 34)	13 (38.2)	21 (61.8)	
	Class I obesity (n = 30)	7 (23.3)	23 (76.7)	
	Class II obesity (n = 1)	0 (0.0)	1 (100.0)	
	Class IV obesity (n = 1)	0 (0.0)	1 (100.0)	
HbA1c group	Diabetes (n = 98)	26 (26.5)	72 (73.5)	0.397
	Pre-diabetes (n = 2)	0 (0.0)	2 (100.0)	

Table 3. BMI and HbA1c Levels Versus Thyroid Dysfunction

Lipid Parameters		Frequency	Percent
Dyslipidaemia	Present	62	62.0
	Absent	38	38.0
Cholesterol	Desirable	53	53.0
	Borderline high	29	29.0
	High	18	18.0
Triglycerides	Normal	49	49.0
	Borderline high	30	30.0
	High	21	21.0
HDL	High	51	51.0
	Low	49	49.0
LDL	Optimal	57	57.0
	Above optimal	17	17.0
	Borderline high	15	15.0
	High	10	10.0
	Very high	1	1.0

Table 4. Lipid Profile among the Diabetic Patients (n = 100)

Variables	Thyroid Dysfunction Present Mean ± SD	Absent Mean ± SD	T statistic	P Value
Parameters				
Age	54.46 ± 10.93	54.68 ± 8.52	-0.091	0.928
Duration of DM	4.46 ± 4.57	3.3 ± 3.16	1.202	0.238
BMI	27.71 ± 3.15	27.46 ± 5.17	0.281	0.78
Glycaemic indices				
HBA1c	8.77 ± 1.52	8.03 ± 1.73	2.065	0.044
FBS	197.85 ± 52.95	199.14± 55.82	-0.105	0.917
PPBS	227.58 ± 36.28	240.3 ± 67.75	-1.198	0.234
Lipid indices				
Cholesterol	204.12 ± 45.99	192.54± 52.78	1.061	0.294
TGA	185.35 ± 85.34	157.9 ± 55.87	1.529	0.136
HDL	39.06 ± 12.92	38.22 ± 8.36	0.31	0.759
LDL	109.81 ± 46.41	102.97± 32.39	0.694	0.493

Table 5. Comparison of Glycemic and Lipid Indices among Two Groups of Thyroid Profile

Majority of the patients with thyroid dysfunction were in the age group of 31 - 60 years (20 %) and remaining 6 % were above 60 years of age. No relationship was found between duration of diabetes and the presence of thyroid dysfunction.

Most common diabetic complication in patients with TD was found to be retinopathy (19 %) and nephropathy (17 %) followed by coronary artery disease (8 %) and neuropathy. Prevalence of dyslipidaemia was found to be higher in diabetics within the age group of 50 - 60 years (75.8 %). Out of 62 diabetic patients with dyslipidaemia, 38 had diabetes of duration < 5 years, 11 had diabetes duration of 6 - 10 years, 11 were newly detected diabetics and 2 had diabetes duration of > 10 years. Out of 71 diabetic patients with complications of diabetes, 48 (67.6 %) had dyslipidaemia compared to 23 (32.4 %) who did not have dyslipidaemia. Diabetic patients who were overweight and obese had higher prevalence of dyslipidaemia and it was statistically significant. Out of 62 diabetic patients with dyslipidaemia, 19 (30.64 %) had thyroid dysfunction (TD) compared to 43 (69.4 %) who don't have TD.

From the above (Table 5), we can conclude that diabetic patients with HBA1c > 8.7 had higher prevalence of thyroid dysfunction compared to diabetics with HBA1c < 8.7 and it was statistically significant.

Variable		Thyroid Dysfunction		P Value
		Present	Absent	
Dyslipidaemia	Yes (n = 62)	19 (30.6)	43 (69.4)	0.176
	No (n = 38)	7 (18.4)	31 (81.6)	
	Total (n = 100)	**26 (26.0)**	**74 (74.0)**	

Table 6. Dyslipidaemia versus Thyroid Dysfunction among Diabetic Patients

DISCUSSION

The association between diabetes and thyroid dysfunction has been known for decades (Hecht and Gershberg,[6] 1968; Gray et al. 1979, Feely and Isles, 1979). Most of the investigators who have studied the prevalence of thyroid disease in diabetic patients have focused on type 1 diabetes, due to the autoimmune nature of this disorder (Feely and Isles, 1979, Abrams et al. 1996,[7] Fernandez-Castañ et al. 1999,[8] Franzese et al. 2000 Kordonouri et al. 2002).

Thyroid Status	General Population	Present Study	P Value
Thyroid dysfunction	6 %	26 %	0.0001145
Hypothyroidism	10 %	11 %	0.8176
SC-Hypo	4.3 %	9 %	0.1825
Hyperthyroidism	1 %	1 %	➢ 0.5
SC-Hyper	1 %	0 %	➢ 0.5
SES	-	5 %	

Table 7. Prevalence of TD in our Study Compared to General Population

Contrary to type 1 diabetes, studies in patients with type 2 diabetes (T2DM) have been remarkably scarce. In the seventies, Gray et al. (1979) found an elevation of thyrotrophic (TSH) in 6 % of patients with T2DM. Thus among thyroid dysfunction, maximum prevalence was found to be of hypothyroidism (20 %) whereas hyperthyroidism (1 %) was least found. Our results are in concordance with results of Diez et al. (2011)[9], Raghuwanshi et al.[10](2015), Pasupathi et al.[11] C.E.J Udoing et al. Ravi Shankar et al.[12] LalooDemitrost et al.[13]

In the present study, the prevalence of thyroid dysfunction was high (26 %) compared to general population (6 %) and it was statistically significant (P value < 0.05). Most common thyroid dysfunction in our study was hypothyroidism (11 %) followed by subclinical hypothyroidism (9 %) and hyperthyroidism (1 %). There was two-fold increased risk of subclinical hypothyroidism in type 2 diabetics compared to general population in our study, though it was not statistically significant. Many different studies have been performed globally to ascertain this relationship and the clear reason for this co-existence is not well known.

In this study, the prevalence of thyroid disorders was more in females as compared to males (19 % vs. 7 %) which when evaluated statistically was significant (Table 14). Our results are consistent with studies of Perros et al. (1995), Diez et al. (2011), Ravishankar et al. (2013),[12] Raghuwanshi et al. (2015)[10] and Ghazali et al. which also showed higher prevalence of TD in females compared to males. Thus prevalence of thyroid disorder in diabetic patients is strongly influenced by female gender.

Thyroid diseases are more prevalent in females. The knowledge of the relationship between sex and thyroid disease is becoming important for the epidemiological study of aging population. Aging has been proposed to trigger for the development of autoimmune phenomena resulting in the production of both organ and non-organ specific auto antibodies. Studies on the relationship between sex and thyroid autoimmunity in elderly subjects have shown that the age-related prevalence of anti- thyroid auto antibodies is greater in women > 60 years of age.

Thyroid Dysfunction in Type-2 Diabetics in Relation to Age

Although some studies have found that the prevalence of thyroid dysfunction increased with age (Hollowell et al. 2002; Chubb et al. 2005; Ravishankar et al.[12] 2013; Jain G et al. 2013;). We found no significant relationship between the presence of thyroid dysfunction and the age in this sample of diabetic patients.

Thyroid Dysfunction in Type-2 Diabetics in Relation to Type of Medications Used

- In patients with poorly controlled T2DM, the prevalence of thyroid dysfunction was higher in patients on insulin in comparison with those receiving oral agents (Celanietal 1994[5]). However, we did not find a higher prevalence of thyroid dysfunction in patients on insulin in comparison with patients treated by oral hypoglycaemic agents or diet.
- Patients on metformin have been associated with a significant reduction in serum TSH in diabetic patients with primary hypothyroidism both with thyroxin therapy and untreated (Cappelli et al. 2009). This

study showed that patients on metformin therapy had higher prevalence of thyroid dysfunction than those with other OHA.

Correlation of Prevalence of TD with HbA1c Levels

In our study, out of 100 diabetic patients, the prevalence of thyroid disorder was found to be more in patients with HbA1c ≥ 8.7 ± 1.52 as compared to patients with HbA1c < 8.7.This difference was highly significant statistically (Table 12). Our results were comparable with the previously conducted studies where Schlienger JL et al. observed that patients with poorly controlled diabetes i.e. HbA1c ≥12 were having low T3 levels, Bazrafshan HR et al. found significant positive correlation between HbA1c and TSH levels, Ardekani MA et al. found HbA1c significantly higher in diabetic patients having thyroid disorder as compared to euthyroid patients. (8.9 ± 1.99 vs. 7.1 ± 1.02) Thus prevalence of thyroid disorder was more in patients with HbA1c ≥ 8.7 i.e. in patients having poorly controlled diabetes.

TD and Duration of T2DM

Out of 26 diabetic patients who had TD, 6 (23.07 %) were newly detected diabetics, 12 (46.1 %) had duration of diabetes ≤ 5years, 1 (3.84 %) had duration of diabetes for 5 -10 years, 7 (26.9 %) had duration of diabetes for 6 - 10 years. However, this difference when evaluated statistically was not significant. Thus, we found that prevalence of thyroid disorder was not significantly affected with duration of diabetes. Our results are in concordance with Diez JJ et al.[9] who also found no significant relationship between presence of thyroid dysfunction and duration of diabetes.

Family History of DM and TD

In our study, out of 26 diabetic patients who had thyroid dysfunction, 20 (76.92 %) had no family history of thyroid disorder and 6 (23.07 %) had family history of thyroid disorder. In this study, the prevalence of thyroid disorder was found to be more in patients who had no family history of thyroid disorder. Pimenta WP et al. and Schroner Z et al. found higher frequency of thyroid disorder with family history of thyroid disorder. The difference observed in our study and above mentioned studies could be due to the reason that in these studies both types of diabetes mellitus (type 1 and 2) were studied but in our study only patients with type 2 diabetes mellitus were included.

TD Versus BMI

In our study, out of 26 diabetic patients who had thyroid disorder, 6 (23.07 %) had BMI < 25, 13 (50 %) had BMI between 25 - 30 and 7 (26.92 %) had BMI >25. Thus, the prevalence of thyroid disorder was found to be more in patients who had BMI > 25. This data when evaluated statistically was insignificant. The findings of our study are similar to the studies by Papazafiropoulou A et al.[4] and Process et al. who also found prevalence of thyroid disorder to be significantly more in patients who had higher BMI.

Association between TD and Dyslipidaemia

Subclinical hypothyroidism in patients with T2DM has been related to the presence of dyslipidaemia (Wang et al. 2009) and diabetic nephropathy (Chen et al. 2007[14]). However, our data suggested that in type 2 diabetics, the presence of dyslipidaemia and chronic diabetic macro- and micro vascular complications had no correlation with thyroid hormone level.[15] These findings are in agreement with those reported by Chubb et al. (2005), who found that there was no association between subclinical hypothyroidism in diabetic women and the presence of cardiac disease, blood pressure, modality of anti-diabetic treatment, HbA1c and lipid profile.

Dyslipidaemia in T2DM

In the present study, the incidence of dyslipidaemia was seen in 62 % of the patients. Increased triglycerides in 51 %, LDL in 43 % and cholesterol in 47 %, decreased HDL in 49 % of patients.

- In a study conducted in Nigeria, the incidence of dyslipidaemia was seen in 89 % of the patients. Increased LDL was noted in 74 %, triglycerides in 13 %, total cholesterol in 42 %, decreased HDL in 53 % of patients.
- In Indian study, Udawat et al. the incidence of dyslipidaemia was seen in 89 % of the patients. Increased LDL was noted in 73 %, decreased HDL in 58 % of patients.

This study reveals that dyslipidaemia is a very common association of type 2 diabetes mellitus, and culprit of majority diabetic related cardiovascular mortality. Since it is reversible, early detection and treatment at the earliest will definitely reduce mortality and morbidity and improves the quality of life. Up till there is no clear consensus on the practice of screening tests for thyroid dysfunction in people with diabetes. Some clinical guidelines recommend an evaluation at the time of diagnosis (AACE, 2000), while others recommend periodic assessments in patients at risk (Ladenson et al., 2000).

Data of the literature is not sufficient to support the recommendation or recommendation against the screening for thyroid dysfunction in T2D. This study is in favour of the detection of thyroid dysfunction in diabetic patients, based on the high prevalence found and the potential morbidity associated to untreated hypothyroidism and hyperthyroidism.

CONCLUSIONS

In this study, there is high prevalence of TD (26 %), as most of the diabetic patients attending our hospital were already under medical care and screened with high index of suspicion. No association was found between the duration

of diabetes and the presence of thyroid dysfunction in this study, as majority of diabetic patients (76 %) in the present study had duration of diabetes < 5 years. From the above study, it is clearly evident that dyslipidaemia (hypertriglyceridemia) is a very common association of type 2 diabetes mellitus (62 %), and culprit of majority diabetic related cardiovascular mortality. Since it is reversible, early detection and treatment at the earliest will definitely reduce mortality and morbidity and improve the quality of life. No association was found between dyslipidaemia and risk of thyroid dysfunction in this study.

Limitations of the Study

Our TSH-based screening cannot detect hypothyroidism or hyperthyroidism secondary to pituitary disease.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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