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PREVALENCE OF THYROID DYSFUNCTION IN TYPE 2 DIABETES MELLITUS PATIENTS IN SAHARANPUR, UTTAR PRADESH, INDIA.

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ABSTRACT

ORIGINAL RESEARCH ARTICLE

As per World Health Organization (WHO) data - India, China and USA are among the top three countries with a high number of diabetic populations. In 2015 there were about 69.2 million patients (7.8%) affected with type 2 diabetes mellitus in India. Thyroid dysfunction was more common in type 2 diabetes mellitus subjects as compared to non-diabetics. Both diseases influence each other in several ways. Treatment of diabetic patient becomes very difficult when both thyroid disorder and diabetes mellitus exist together. Present study is designed to estimate the prevalence of thyroid dysfunction in type 2 diabetes mellitus subjects along with other biochemical parameters. Among the diabetic group 109 patients and 120 patients in control group were found to be euthyroid. Higher prevalence of thyroid dysfunction was found in patients with type 2 diabetes mellitus, 19.26% patients in Group I and 9.77% patients in Group II were found to have thyroid dysfunction. A routine assessment of thyroid function test should be performed for patients with type 2 diabetes mellitus.

INTRODUCTION:

Diabetes mellitus is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia resulting from the diverse group of etiology such as environmental and genetic factors acting simultaneously or jointly.[1–3]

As per World Health Organization (WHO) data - India, China and USA are among the top three countries with a high number of diabetic populations.[4] While the number of type 2 diabetes mellitus (T2 DM) patients in China increased from 20.4 million in 1980 to 102.9 million in 2014, there have been also similar trends of increase in diabetics in India. India had about 50.8 million people with type 2 diabetes mellitus in 2010 which has increased in 2015 to 69.2 million people (7.8%). Latest Indian studies have shown a rapid conversion of impaired glucose tolerance to diabetes mellitus in the southern states of India, where the prevalence of diabetes mellitus among adults has reached to

approximately 20% in urban populations and 10% in rural populations[5].

Thyroid disorders have been known to occur more frequently in diabetic population than expected. This study is aimed to assess thyroid dysfunction among the type 2 diabetes mellitus subjects as compared to non-diabetics. Both diseases influence each other in several ways. Diabetes mellitus influences thyroid functions at two sites (a) Hypothalamic control of thyroid stimulating hormone (TSH) release (b) Conversion of T4 to T3 at peripheral tissue level.[6,7] Uncontrolled diabetes mellitus leading to hyperglycemia causes reduction in hepatic concentration of deiodinase and decreased serum triiodothyronine (T3), increased reverse T3 and low, normal or high thyroxine (T4) levels. In contrast hyperthyroidism stimulates hepatic glycogenolysis and glucose absorption that can aggravates hyperglycemia[8].

Hyperthyroidism leads to hyperglycemia. In hyperthyroidism, the half-life of circulating plasma insulin is decreased because of two reasons: (a) Increased rate of degradation of circulating plasma insulin (b) increased release of biologically inactive insulin precursors. In untreated subjects of hyperthyroidism there is reduced C-peptide to proinsulin ratio that reflects an underlying defect in proinsulin processing.[9]

Saharanpur is an area in Uttar Pradesh of Northern India which lies near to foothill regions of Himalayan mountain range. Goiter is very common in these foothill regions. Diabetes mellitus is such a disease which can be treated and adequately managed to prevent its future complications. Control of hyperglycemia in type 2 diabetes mellitus patients becomes too difficult when both thyroid disorder and diabetes mellitus exist together.

The main objective of the present study is to estimate prevalence of thyroid dysfunction in type 2 diabetes mellitus subjects and to compare some biochemical and clinical variables between these diabetic and normal healthy subjects.

MATERIALS AND METHODS:

The present study was conducted in Saharanpur district over a period of 24 months from January 2015 to December 2016. Subjects were selected from the patients visiting the outpatient department and those admitted in Medicine ward in S.M.M.H. Medical College, Saharanpur (U.P.). Inclusion and exclusion criteria were laid down for the selection of subjects.

Inclusion Criteria

- Patients diagnosed with type 2 diabetes mellitus as per American Diabetic Association (ADA) criteria.
- Patients were from either gender of the age group of 40-80 years.
- Patients without any prior history of thyroid disorders.

Exclusion Criteria

- Patients diagnosed with type 1 diabetes mellitus and gestational diabetes.
- Patients reported with prior history of thyroid dysfunction or taking medications that interfere with thyroid functions.
- Patients below 40 years and above 80 years of age.

All the selected patients were informed about the procedure and its expected outcomes. Duly signed written consent was taken from all the patients.

Measurement

The measurement of biochemical parameters was done with the standard laboratory procedure. Following parameters were monitored of all the selected patients.

Body Mass Index (BMI), Fasting Blood Sugar, 2 hours post prandial blood sugar. T_3 and T_4 were estimated by Chemi Luminescence Immunoassay (CLIA) and thyroid stimulating hormone (TSH) by Ultra-Sensitive CLIA method. Blood sugar was estimated by GOD-POD (Glucose Oxidase - Peroxidase) method; Lipid profile analyzed as – total cholesterol (TC) by CHOD-PAP method, triglyceride (TG) by Amino-4-Antipyrine method.[10,11]

Triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein

(LDL), very low-density lipoprotein (VLDL) were also measured.

PROCEDURE

At the assessment visit all type 2 diabetic subjects and normal healthy subjects underwent clinical and laboratory evaluation. The baseline characteristics of type 2 diabetic patients and normal healthy subjects were noted as per the standard questionnaire. The following clinical variables were assessed in both cases and controls: age (years), gender, duration of diabetes mellitus (years), weight, height, BMI, treatment modality of diabetic subject and diabetic subjects performing self-monitoring of blood glucose (SMBG). The diabetic subjects were also counselled for Self-Monitoring of Blood Glucose (SMBG) at their first and subsequent follow up visits.

Classification for detection of thyroid dysfunction was based on following criteria:

- Normal- When total T_3, total T_4 and TSH were in the normal range (i.e., TSH = 0.35–5.50 µIU/ml; Total T_4 = 5.01–12.45 µg/dl; Total T_3 = 0.60–1.81 ng/ml)
- Primary Hypothyroidism– when TSH is more than 5.50 µIU/ml and T_3, T_4 less than normal.[12]
- Primary Hyperthyroidism– when TSH is less than 0.35 µIU/ml and T_3, T_4 more than normal.
- Subclinical Hypothyroidism– when TSH is more than 5.50 µIU/ml and T_3, T_4 is within normal range.
- Subclinical Hyperthyroidism– when TSH is less than 0.35 µIU/ml and T_3, T_4 is within normal range.[13]

Statistical analysis

The result obtained and expressed in Mean ± SD. Comparison was done using student's t-test. $p < 0.05$ at 95% confidence intervals with 5% level of significance and data analyzed by using GraphPad Software.

RESULTS:

Selection of patients and demographic distribution

The present study was conducted over a period of 24 months from January 2015 to December 2016. Total 135 type 2 diabetes mellitus subjects were recruited in Group I, which comprised of 48 males and 87 females.

Total 133 healthy subjects comprising of 76 males and 57 females were enrolled in Group II to serve as the control group. The demographic distribution of the selected subjects is given in the Table 1.

Table 1: Demographic distribution of subjects of Group I and Group II

Age Group (Yrs.)	Group I			Group II		
	Total	Males	Females	Total	Males	Females
40-50	50*	09	41	63*	31	32
50-60	41*	17	24	30*	19	11
60-70	26*	12	14	26*	16	10
70-80	18*	10	08	14*	10	04
Total	135	48	87	133	76	57

* P> 0.05, No Significant difference

Female preponderance was observed in Group I; however no statistically significant difference was observed. A decreased number of patients were observed at higher ages. Maximum patients were from age 40-50 years in both groups i.e. 50 and 63 in Group I and Group II respectively. 18 patients in Group I and 14 patients in Group II were reported from the age 70-80 years. Also, no statistically significant difference was observed in the total number of patients in both groups in each age bracket. It justifies the uniqueness and unbiased distribution of patients among the groups.

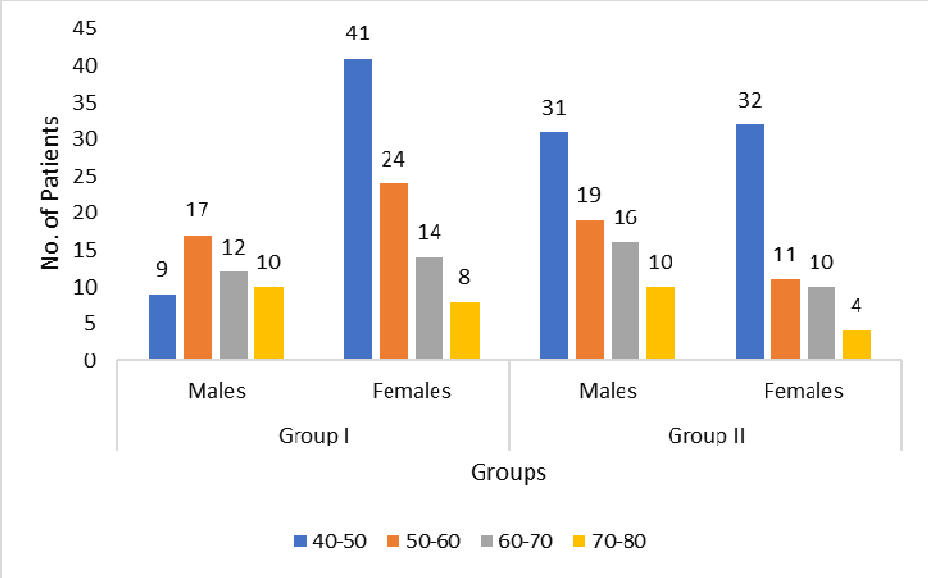

Fig 1: Demographic distribution of subjects in both groups.

Among the diabetic group of 135 patients 89% were taking oral hypoglycemic agent, 3% were taking insulin and 8% patients were taking both treatment modalities.

Biochemical Profile

Patients of both groups were subjected to investigation of biochemical parameters. The results are tabulated in Table 2.

Table 2: Comparison of clinical and biochemical parameters among both groups

Parameters	Group I	Group II	P value
BMI (kg/m^2)	25.08±5.11	23.99±3.56	0.0430
TG (mg%)	167.85±69.75	132.53±48.91	0.0001
LDL (mg%)	111.78±29.78	96.30±29.12	0.0001
VLDL (mg%)	32.61±12.71	26.43±9.76	0.0001

Data is represented as Mean±SD
P<0.05, Significant difference

Statistically significant difference was found between mean BMI, TG, LDL and VLDL values of the diabetic patients and healthy subjects. It suggests that there is no interference of such biochemical parameters in the pathogenesis of thyroid dysfunction.

Thyroid function test parameters and thyroid dysfunction

The mean T3 value was found to be 2.02±10.91 ng/ml among the diabetic group and 1.03±0.26 ng/ml among the healthy subjects respectively. T4 of both the groups were found 8.34±2.40 µg/dl and 8.5±1.62 µg/dl respectively. TSH values were found to be 3.24±3.58 µIU/ml in Group I as compared to 4.17±3.51 µIU/ml in Group II.

Table 3: Comparison of thyroid function test parameters among both groups

Parameters	Group I	Group II	P value
T3 (ng/ml)	2.02± 10.91	1.03 ± 0.26	0.2928
T4 (µg/dl)	8.34 ± 2.40	8.5 ± 1.62	0.5214
TSH (µIU/ml)	3.24 ± 3.58	4.17 ± 3.51	0.0320*

P<0.05, significant difference

Table 4: Comparison of thyroid dysfunction among both groups

Thyroid status	Group I			Group II		
	Subclinical	Overt	Total	Subclinical	Overt	Total
Hypothyroidism	10	10	20	07	04	11
Hyperthyroidism	05	01	06	01	01	02

Total of 109 patients among the diabetic group and 120 patients in control groups were found to be euthyroid. Higher prevalence of thyroid dysfunction was found in patients with type 2 diabetes mellitus, 19.26% patients in Group I and 9.77% patients in Group II were found to have thyroid dysfunction. Among the patients in Group I, 14.81% patients were diagnosed with Hypothyroidism and 4.44% patients were found to have hyperthyroidism.

Whereas among the subjects of control group 8.27% subjects were diagnosed with Hypothyroidism and 1.5% subjects were found to have hyperthyroidism.

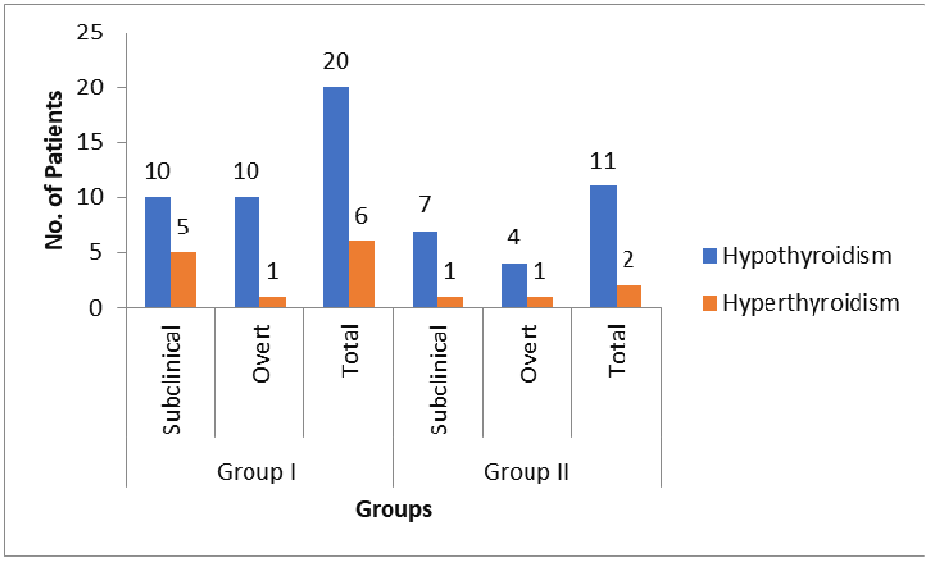

Fig 2: Comparison of thyroid dysfunction among both groups

DISCUSSION:

In the present study the clinical and mean biochemical parameters like BMI, TG, LDL and VLDL were found to be statistically significantly different. The findings are similar with the findings of Laakso M. et al., who reported that BMI and diabetes mellitus had a statistically significant interaction (analysis of variance) with respect to HDL and HDL2 cholesterol and LDL, VLDL and triglycerides concentrations, indicating that the effects of obesity on lipids and lipoproteins were more severe in patients with diabetes than in non-diabetic subjects.[14]

Both hyperthyroidism and hypothyroidism have been associated with insulin resistance which has been reported to be the major cause of impaired glucose metabolism in T2DM. The state-of-art evidence suggests a pivotal role of insulin resistance in underlining the relation between T2DM and thyroid dysfunction.[15]

Thyroid disorders can have a major impact on glucose control and untreated thyroid disorders affect the management of

diabetic patients. Consequently, a systematic approach to thyroid testing in patients with diabetes is recommended.[16]

The prevalence of thyroid dysfunction among Greek diabetic patients is 12.3%. Diabetic women were more frequently affected than men. Presence of thyroid dysfunction was associated with lower levels of LDL-cholesterol concentrations.[17]

In women with type 2 diabetes mellitus without known thyroid disease, subclinical hypothyroidism is a common but incidental finding. The routine screening of thyroid function in type 2 diabetes is questionable.[18]

The present study is also in accordance with the reported findings as the prevalence of thyroid dysfunction was found to be higher in the patients with type 2 diabetes mellitus.

From the findings of the present study it can be concluded that out of the total 135 diabetic patients 48 comprised of males and 87 comprised of females. There was preponderance of female diabetic subjects (64.44%). The highest number of male diabetics (12.59%) belonged to 50-60 years of age group while female diabetics (30.37%) belonged to 40-50 years of age group. The prevalence of thyroid dysfunction (Hypothyroidism and Hyperthyroidism) was higher in diabetic subjects (19.26%) as compared to control group subjects (9.77%). In diabetic subjects with hypothyroidism 07.41% subjects had subclinical and 07.41% diabetic subjects had overt hypothyroidism.

CONCLUSION:

Thyroid dysfunction is more common among type 2 diabetes mellitus patients. Undiagnosed thyroid dysfunction may be an important reason for uncontrolled blood sugar in some cases of type 2 diabetes mellitus. All type 2 diabetes mellitus patients must undergo routine screening for thyroid function tests during the workup of disease.

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