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ASSESSMENT OF THYROID FUNCTION TEST IN OBESE WITH DIABETES MELLITUS PATIENTS: A HOSPITAL BASED STUDY IN NORTH INDIA

Biochemistry

Gunjan Kumar Mandal — Ph.D. Student, Department of Biochemistry, MMIMSR, Mullana, Ambala, Haryana, India.

Dr. Suvarna Prasad* — Professor & Head, Department of Biochemistry, MMIMSR, Mullana, Ambala, Haryana, India. *Corresponding Author

Dr. B. K. Agrawal — Professor & Head, Department of Medicine, MMIMSR, Mullana, Ambala, Haryana, India.

ABSTRACT

Background and Objective: Several patients with Type 2 Diabetes Mellitus (T2DM) are obese. Altered thyroid hormone status has been described in obese with Diabetes Mellitus (DM) patients.

Methods: The study includes 100 obese with diabetes mellitus (DM) patients as a case and 100 healthy volunteers as a control. Thyroid profile was assayed in obese with DM patients.

Results: In our study it was noted that thyroid dysfunction was prevalent in 42 patients out of 100 patients included of which 12 patients were hypothyroidism, 7 patients were hyperthyroidism, 22 patients were subclinical hypothyroidism and 1 patients were subclinical hyperthyroidism.

Interpretation and Conclusion: The study advocates that screening should be recommended for all obese with DM patients to rule out thyroid dysfunction.

KEYWORDS

Body mass index, Diabetes Mellitus, Metabolic syndrome, Obese, Thyroid profile.

INTRODUCTION:

Accumulation of body fat in an irregular or excessive manner is defined as Obesity [1]. It is represented by enlarged adipose tissue from the positive energy calculation in the connection intake against calories expenses has a multifactorial etiology. [2,3] Since the middle of 1970 the prevalence of obesity has raised. [4] It is a chief reason of prematurity death between middle age adult. [5] It is one of the 5 components of the metabolic syndrome. It is related through multiple co morbidities, raised mortality and can take important part in the progression of metabolic syndrome. [6]

In many countries obesity epidemic is a chief threat to health. [7] A World Wide health problem is considered to Obesity and its occurrence is known to raise gradually and considerably all over the World. [8] It cause change in thyroid hormones, i.e. raised thyroid hormone levels, raised Thyroid stimulating hormone (TSH), with no consequence on Triiodothyronine (T3) and Thyroxine (T4) or raised in TSH and T3 with no consequence on T4. On the other hand, due to result of slow metabolism Subclinical hypothyroidism can lead to obesity. [9] Several studies have reported that due to decrease in weight in obesity have reported a low level of serum TSH and T3 levels. [10]

In general population hypothyroidism appears to be associated with obesity and in people with raised in body mass. [11] TSH concentration have been shown to be positively associated with Body mass index (BMI) and fat accumulation. In a Cohort of older Australian, obesity has been shown to be a significant predictor of overt hypothyroidism. [12]

Due to thyroid dysfunction an obvious influence of body mass, overt hypothyroidism is related with a raise in body mass, which is mainly caused by oedema, where as hyperthyroidism result in a decrease in weight, mostly due to catabolic effects on muscle and adipose tissue. [13]

In relation to obesity earlier information investigate functional and morphological alterations of the thyroid gland. TSH level was significantly positively associated with waist circumference and BMI in **Ayturk S et al.** study. [14] FT3 was positively associated with waist circumference and T4 did not show relationship with metabolic parameters in a **Gutch M et al.** study. [9] Subclinical hypothyroidism was related with overweight and obese status in a cohort of adolescent and children. [15]

Several study has reported that obese females patients have shown an association among decreased thyroid function and raised body weight. [16] Insulin resistant, hyperlipidemia and obesity has been found to be associated with subclinical hypothyroidism. [17] Weight and thyroid cancer show a borderline positive relationship among body mass index and the risk of cancer, in thyroidology study. [18]

In obese people, FT3 and also in a few studies FT4 in serum tends to be increased. [19] Increase BMI values are related with an increased number of comorbidities, such as hypertension, cardiovascular disease, obstructive sleep apnea, dyslipidemia, type 2 diabetes, insulin resistance, osteoarthritis and cholelithiasis. [6]

Diabetes mellitus (DM) is a chronic disorder that can alter protein, carbohydrate and fat metabolism. It is caused by absence of insulin secretion due to defects in insulin uptake in the peripheral tissue or either the progressive or marked in ability of the β- Langerhans islet cells of the pancreas to produce insulin. It is generally classified as type 1 and type 2 diabetes. [20] Up to 86% of patients with type 2 diabetes mellitus (T2DM) have metabolic syndrome. [21]

Several patients with T2DM are obese. [22] Both obesity and T2DM are severe health concern. It is clear that fat distribution is significant to the risk for developing T2DM, with central adiposity conferring the huge risk. Waist circumference is a positive predictor for consequent development of T2DM. The relationship between obesity with T2DM is established well when comparing odd ratios for progress of T2DM according to BMI range. **Nauyen and Colleagues** explore the connection among obesity and T2DM in a US adult population based on finding from the National Health and Nutrition Examination study in 1999-2006. A survey done among 21,205 adults, 2894 adults (13.6%) had T2DM. Among those with T2DM 80.3% were overweight and 49.1% were obese and the prevalence of T2DM rising according to severity of obesity. [23]

In DM patients thyroid dysfunction has been commonly encountered. The clinical correlation among DM and thyroid functions is becoming more broadly documented with hypothyroidism among DM patients. [24] Patients with DM, altered thyroid hormone status has been described in **S. Shabnam** study. [25]

Two sites of thyroid function was appears to be influence by DM. Ist sites at the stage of hypothalamic control of TSH liberate and 2nd sites at peripheral tissue by converting T4 to T3. Increase in blood sugar cause decrease in hepatic concentration of T4-5 deiodinase, decrease serum concentration of T3, raised level reverse T3 and decrease, normal or high level of T4. Thyroid hormone control metabolism and diabetes can alter metabolism. [26]

The aim of our study was to assess the correlation and association of thyroid function in obese with diabetes mellitus patients.

MATERIALAND METHODS

The study was done in the department of biochemistry in collaboration with Department of Medicine, Maharishi Markandeshwar institute of Medical Sciences and Research, Mullana, Ambala, Haryana, India. 100 obese with DM patients as a case and 100 healthy volunteers as a control, were randomly selected and were included in this study and they were subjected to detailed Medical history, General and Systemic Physical examination with prior consent of the patient after which they were subjected to Thyroid Function tests and other appropriate and related tests. The results of which were statistically analyzed.

Obesity is define as when BMI $\geq$ 25kg/m^2 for both genders based on the World Health Organization Asian Pacific guideline with or without abdominal Obesity.[27]

BODY MASS INDEX (BMI) will be determined by the formula:
BMI = Weight (kg)/Height^2 (m^2)

Criteria for the diagnosis of diabetes mellitus.[28]

- Fasting plasma glucose $\geq$ 126 mg/dl. Fasting is defined as no caloric intake for at least 8 hours.

OR

- 2 hours plasma glucose $\geq$ 200 mg/dl during an oral glucose tolerance test.

OR

- Patients with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose $\geq$ 200 mg/dl.

INCLUSION CRITERIA:

100 obese with DM patients.
100 healthy volunteers.

EXCLUSION CRITERIA

(1) Patients not willing to participate in the study.
(2) Patients who are below age 20.
(3) Pregnant women
(4) Presence of goiter or known thyroid disease.
(5) Patients with medical syndrome associated with obesity.
(6) Patients with family history of thyroid diseases.
(7) Patients on drugs known to cause Hypothyroidism (Propranolol, Iopanoic Acid, Iodide, Amiodarone, Salicylates, Phenytoin, Glucocorticoids, Lithium, Amphetamines, Sertraline, Aminogluthetimide, Dopamine, Somatostatin, Octreotide, Interleukins, Heroin)
(8) Patients with cirrhosis of liver
(9) Patients with Heart failure

Sample collection: Fasting blood samples were collected for estimation of thyroid profile and lipid profile of cases and control. Thyroid profile was done by chemiluminescent micro particle immunoassay method. Lipid profile – Total cholesterol (TC) cholesterol-oxidase, triglyceride (TGL) glycerol oxidase - peroxidase, High density lipoprotein (HDL) enzymatic assay, Low density lipoprotein (LDL), very low density lipoprotein VLDL friedewald's calculation method.

Statistical analysis:

For statistical analysis SPSS 20 software was used and data were expressed as the mean and standard deviation. Student's t test was used for analysis of statistical significance. Significance was considered for all tests ($p<0.05$).

RESULTS

In our study total number of patients were 200 out of which 100 were obese with DM as a case and 100 were healthy volunteers as a control. In case 32 patients were males and 68 patients were females and in control 24 were males and 76 were females.

In our study the mean age of the studied subject was 54.59±9.42 years and in control was 44.49±11.56 years. Mean weight of the studies subjects was 72.03±6.27 kg and in control was 53.87±8.06 kg, with a BMI of studies subjects was 27.21±1.81 kg/m^2 and in control was 20.76±2.40 kg/m^2 and mean waist circumference was 105.2 cm and in control was 81.7±5.38 cm.

Table-1: Thyroid status of the case with respect to control.

	EUTHYROID	HYPOTHYROIDISM	HYPERTHYROIDISM	SUB CLINICAL HYPOTHYROIDISM	SUB CLINICAL HYPERTHYROIDISM
CASE	58	12	7	22	1
CONTROL	98	0	0	2	0

Our study shows that in 100 obese with DM patients, 58 were euthyroid, 12 patients were hypothyroidism, 7 patients were hyperthyroidism, 22 patients were subclinical hypothyroidism and 1 patients were subclinical hyperthyroidism. 2 patients were subclinical hypothyroidism out of 100 patients in control groups.

Table-2: Mean values of thyroid profile in obese with DM patients with respect to control

Parameters	Mean & STDEV		Standard Error		P-value
	Case	Control	Case	Control	
T3	1.25±1.27	1.0±0.30	0.127	0.030	0.05
T4	7.36±3.52	7.34±1.55	0.352	0.155	0.95
TSH	7.15±12.71	2.24±1.19	1.27	0.119	0.000
FT3	2.71±0.75	2.97±0.39	0.075	0.039	0.003
FT4	1.21±0.61	1.20±0.25	0.061	0.025	0.88

In our study T3 level in obese with DM patients were 1.25±1.27 and in control were 1.0±0.30 ($p< 0.05$). T4 level in case were 7.36±3.52 and in control were 7.34±1.55 ($p< 0.95$). TSH level in case were 7.15±12.71 and in control were 2.24±1.19 ($p< 0.000$). FT3 level in case were 2.71±0.75 and in control were 2.97±0.39 ($p< 0.003$). FT4 level were 1.21±0.61 and in control were 1.20±0.25 ($p<0.88$).

Table -3: Mean values of FBS, PPBS and lipid profile in obese with DM patients with respect to control.

Parameters	Mean & STDEV		Standard Error		P-value
	Case	Control	Case	Control	
FBS	175.27±54.64	81.02±6.64	5.464	0.664	1.148
PPBS	278.32±96.17	105.37±12.17	9.617	1.217	8.299
TC	171.47±31.55	161.51±18.03	3.155	1.803	0.007
TGL	151.87±84.99	129.79±15.87	0.499	1.587	0.01
HDL	41.45±9.37	39.16±6.64	0.937	0.664	0.04
LDL	101.38±29.44	96.39±18.70	2.944	1.870	0.15
VLDL	29.12±10.61	25.95±3.17	1.061	0.317	0.004

In our study Fasting blood sugar (FBS) level in obese with DM patients were 175.27±54.64 and in control were 81.02±6.64 ($p< 1.148$). Postprandial blood sugar (PPBS) level in case were 278.32±96.17 and in control were 105.37±12.17 ($p< 8.299$). TC level in case were 171.47±31.55 and in control were 161.51($p< 0.007$). TGL level in case were 151.87±84.99 and in control were 129.79±15.87 ($p<0.01$). HDL level in case were 41.45±9.37 and in control were 39.16±6.64 ($p<0.04$). LDL level in case were 101.38±29.44 and in control were 96.39±18.70 ($p<0.15$). VLDL level in case were 29.12±10.61 and in control were 25.95±3.17 ($p<0.004$).

DISCUSSION:

In our study it was noted that thyroid dysfunction was prevalent in 42 patients out of 100 patients included of which 12 patients were hypothyroidism, 7 patients were hyperthyroidism, 22 patients were subclinical hypothyroidism and 1 patients were subclinical hyperthyroidism.

Thyroid dysfunction was predominantly seen in females (27) compare to males (15).

In our study thyroid dysfunction was mostly seen in 41 to 60 years age groups patients. Obese with DM patients have higher in age (54.59±9.42) as compare to control (44.49±11.56) groups. Patients older than 40 years of age was positively related with subclinical hypothyroidism with obesity, in a cross sectional population based study.[13] **Proces et al.** survey, originate that beside known factors such as age and drugs, thyroid function can be altered in obese and DM patients.[29]

Obese with DM patients have higher BMI (27.21±1.81) as compared to control (20.76±2.40) groups in our studies. Obese with DM patients have higher waist circumference (105.2±9.53) as compared to control (81.7±5.38) groups in our studies. An elevated TSH levels was found

in morbidly obese women (BMI > 40 kg/m^2) than other with moderate obesity (BMI < 40 kg/m^2) and TSH levels were positively associated with BMI in euthyroid subject. Study advocate that in overweight persons with normal thyroid function the serum TSH levels and the grade of obesity were positively correlated.[30] In a **Agarwal P et al.** study Free triiodothyronine (FT3) was positively associated with waist circumference.[31]

In a French **Monica** cohort study demonstrate a considerably elevated body mass, low HDL cholesterol, waist girth in females than in males.[32] Obesity causes raise in TSH and T3 with no effect on T4 in **Stichel et al., Reinehr et al.,** and **Kiortsis et al.** study.[33] A moderate raise in total T3 or free T3 levels has been reported in obese subjects in a **De Pergola et al.** study. A latest study show that a higher rate of subclinical hypothyroidism in a morbid obese patients.[12]

In our study a significant association between serum cholesterol and obese with DM subjects (p< 0.007) was found. Triglyceride (p< 0.01), High density lipoprotein (HDL) (p< 0.04) and very low density lipoprotein (p< 0.004) was also significantly associated with obese with DM subjects. Our study show that obese with diabetes mellitus patients have high triglyceride (151.87±84.99) level compare to control (129.79±15.87) groups. So obese with DM patients have higher risk for developing metabolic syndrome.

We can't find any association between Low density lipoprotein and obese with DM subjects. **Vikhe V et al.** study show that in diabetes patients shows significantly elevated serum levels of cholesterol, triglyceride, LDL, VLDL, and lower level of high density lipoprotein as compared to non diabetic patients. **Sawant et al.** study found similar results. Considerably lower level of T3, T4, and elevated levels of TSH in diabetic group is similar to the result observed in Punjabi people of North India.[34]

CONCLUSION

Our study has determined that screening should be recommended for all obese with diabetes patients to rule out thyroid dysfunction. Obese with diabetes can lead to metabolic syndrome, which further lead to cardiovascular disease. So to prevent from cardiovascular disease overweight and diabetes should be controlled.

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