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Biochemistry

STUDY OF THYROID PROFILE AND ITS ASSOCIATION WITH GLYCEMIC CONTROL IN TYPE II DIABETES MELLITUS

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ABSTRACT Diabetes mellitus is a considered as a group of metabolic disorders characterised by defective regulation of carbohydrate, lipid and protein metabolism. Amid the two types of diabetes, type II is linked with insulin resistance. Insulin and thyroid hormone metabolism can result in functional abnormalities of one another. Therefore, the present study was undertaken in a tertiary care hospital over a period of one and half years with the aim to assess the changes in thyroid profiles of patients with type II diabetes mellitus and to correlate their levels with glycated haemoglobin. Results of the study indicated that mean serum T3 and T4 levels were reduced in diabetic patients while mean serum TSH was increased. T3 levels correlated negatively with glycated haemoglobin whilst TSH correlated positively. Further 33% patients had hypothyroidism among 100 cases indicating hypothyroidism as the most common thyroid dysfunction in type II diabetics.

KEYWORDS : Diabetes mellitus, Insulin, Hypothyroidism, Glycated haemoglobin

INTRODUCTION:

"Living with diabetes is like living with a tiger, if you look after it and never turn your back on it, you can live with a tiger. If you neglect it, it will pounce on you."[1] Diabetes mellitus is not a single disease entity but rather a group of metabolic disorders characterised by defective regulation of carbohydrate, lipid and proteins causing hyperglycaemia and negative nitrogen balance.[2] Prevalence of diabetes mellitus is rising at alarming rate all over the world. There are 382 million people living with diabetes mellitus and majority of them are in 40-59 age group.[3] WHO has declared India as 'Diabetic capital of the world'.[4]

Diabetes mellitus and thyroid dysfunction are the most common endocrine diseases seen in adult population.[5] Insulin or thyroid hormones metabolism can result in functional abnormalities of one another. Because of the strong link between diabetes and thyroid diseases, American Diabetic Association (ADA) has proposed that people with diabetes must be checked periodically for thyroid dysfunction.[6] Glycemic control may get affected by the presence of thyroid dysfunction. In hypothyroidism, there are wide ranging changes in carbohydrate metabolism.

Detection of thyroid abnormality in type II diabetics depending on the clinical symptoms only can be problematic. Poor glycemic control can produce symptoms resembling hyperthyroidism like weight loss in spite of increased appetite and weakness. On the other hand, in severe diabetic nephropathy, patients may have oedema, fatigue, pallor and weight gain which can be mistaken for hypothyroidism.[7] Hence the study was undertaken to assess the changes in thyroid profile in type II diabetes mellitus patients.

MATERIAL & METHODS:

The present study was conducted in a tertiary care hospital over a period of one and half years in department of Biochemistry after approval of institutional ethics committee.

Selection of Study population: Patients were selected from those attending the OPD of Medicine department and admitted in wards. 100 patients were taken as cases and 100 healthy age matched and gender matched volunteers were taken as controls.

Sample size calculation: From the study of Pasupathi P et al[8]

- Biochemical parameter of serum T_4
- SD_1 in type II diabetes cases= 10.56
- SD_2 in controls= 8.21
- Difference in means of serum T_4 in two groups=2.35
- α error = 5%
- β error = 0.10
- Power = 90%
- Minimum sample size needed in in each arm = 50

Sample size calculated using Power and sample size version 3.0 software

Study design: Hospital based cross sectional study with comparison groups.

Inclusion criteria:

1. Patients and healthy volunteers willing to enter the study in the age group 30 to 59 years
2. All type II diabetes mellitus patients irrespective of glucose control
3. All type II diabetes mellitus patients irrespective of treatment

Exclusion criteria:

1. Study subjects less than 30 years and more than 59 years
2. Type I diabetes mellitus patients
3. Gestational diabetes mellitus patients
4. Patients with Pancreatitis
5. All those with proven thyroid disorder and on treatment
6. Pregnant and lactating women
7. Patients with renal failure, acute myocardial infarction, chronic diarrhoea
8. Patients on diuretics, aminoglycosides, vitamins and minerals supplementation

Sample collection: 6 ml venous blood from antecubital vein was drawn after taking all the aseptic precautions. 3 ml sample was transferred to plain bulb from that serum was separated by centrifugation after coagulation which was used for estimation of Thyroid profile. 2 ml blood was transferred to EDTA bulb and after centrifugation; plasma separated from it was used for estimation of Glycated haemoglobin. 1 ml sample was transferred to Fluoride bulb which was used for estimation of blood sugar. All the samples were estimated on the same day. Haemolysed samples were discarded.

Method of estimation:-

PARAMETER	METHOD OF ESTIMATION	EQUIPMENT
Plasma glucose	Enzymatic GOD-POD method[8]	Erba XL-300 Autoanalyser
Glycosylated haemoglobin	Ion exchange resin method[9]	Erba XL-300 Autoanalyser

Thyroid profile	ELISA[10,11,12]	LISA plus microplate ELISA reader

Statistical analysis:

- All the demographic and biochemical parameters were expressed as Mean±SD
- Unpaired t test was used for comparison between cases and controls
- Pearson's correlation coefficient was calculated to assess the correlation
- p value<0.05 was considered statistically significant and p<0.001 was considered as highly significant
- Software GRAPH PAD Prism version 6.0 was used for analysis

RESULTS:

TABLE No: 1

Table showing age wise distribution of study subjects

Age in years	Cases		Controls		p Value
	n	%	n	%	
30 to 40	14	14	15	15	
41 to 50	42	42	43	43	
51 to 59	44	44	42	42	
Total	**100**	**100**	**100**	**100**	
Mean Age	**49.52 ± 9.1**		**48.23 ± 9.3**		**0.826**

The above table shows age distribution in cases and controls. There was no statistical difference between the mean age of cases and controls. (p value= 0.826)`

TABLE No: 2

Table showing values of fasting plasma glucose and HbA1C in the study subjects

Parameter	Cases (n=100) Mean SD	Controls (n=100) Mean SD	p Value
Fasting blood glucose (mg/dL)	177.2 55.10	94.66 10.15	p= 0.0001
HbA1C (%)	8.38 1.6	4.89 0.37	p= 0.0001

p<0.001= highly significant

Above table shows the comparison of mean fasting plasma glucose levels and glycated haemoglobin in between type II diabetes mellitus cases and healthy controls. Both the values are significantly higher in cases compared to controls.

TABLE No: 3

Table showing comparison of Thyroid profile in the study subjects

Parameter	Cases (n=100) Mean SD	Controls (n=100) Mean SD	p Value
Serum T_3 (ng/ml)	0.95 0.23	1.31 0.26	p=0.0001
Serum T_4 (µg/dL)	6.91 2.01	8.97 2.04	p=0.0001
Serum TSH (mIU/ml)	4.98 1.96	3.36 1.6	p=0.0001

p<0.001= highly significant

Table No 3 shows the comparison of mean serum T_3, T_4 and TSH values between type II diabetes mellitus cases and healthy controls. On comparison it was found that mean serum T_3 and T_4 levels were decreased highly significantly in cases compared to controls while mean serum TSH levels were increased highly significantly in cases as compared to the controls.

TABLE No: 4

Table showing distribution of type II diabetes mellitus patients according to their Thyroid

Thyroid Status	Number (n)	Percentage (%)
Hypothyroidism	33	33
Hyperthyroidism	4	4
Euthyroidism	63	63

The above table shows the distribution of type II diabetes mellitus patients in case groups according to their thyroid status. 63% patients out of 100 were having euthyroid status. 33% patients were detected as having hypothyroidism and 4% patients were found to have hyperthyroidism. Thus in our study, most common thyroid abnormality detected was hypothyroidism.

TABLE No: 5

Table showing correlation between Thyroid profile and HbA1C in type II diabetes mellitus patients

Parameter	HbA_{1C}
Serum T_3	r= - 0.4397 p= 0.0001
Serum T_4	r= 0.0088 p= 0.9301
Serum TSH	r= 0.3333 p= 0.0007

p<0.001= highly significant

The above table shows the correlation between the mean serum T_3, T_4 and TSH with HbA_{1C} in type II diabetes patients. From the above table it was found that a statistically significant negative correlation was observed between mean serum T_3 and HbA_{1C} and significant positive correlation was found between mean serum TSH and HbA_{1C}. While no correlation was observed between serum T_4 and HbA_{1C}.

DISCUSSION-

Our study was carried out in a tertiary care medical institute over a period of one and half years with the prime objective to assess the changes in thyroid profile of type II diabetes mellitus patients and to find out the correlation between thyroid profile and glycemic control.

From the results obtained from the study, it was found that mean plasma glucose, glycated haemoglobin and serum TSH levels were increased highly significantly in cases as compared to healthy controls while serum T_3 and T_4 values were reduced highly significantly in cases compared to controls. A significant negative correlation was observed between mean serum T_3 and HbA_{1C} while a significant positive correlation was obtained between serum TSH and HbA_{1C}. The findings of our study correlated well with the studies conducted by **Uppal V et al[13], Anita Devi M et al[14] and Rai S et al[15].**

Thyroid hormones and insulin both are intimately involved in cellular metabolism and can affect the function of each other. Decreased levels of thyroid hormones may be due to presence of thyroid hormone binding inhibitor (THBI) in diabetes mellitus patients. THBI inhibit the enzyme 5 - deiodinase which is required for peripheral conversion of T_4 to T_3. It has also been shown in several studies that in diabetics there is dysfunction of hypothalamo- pituitary axis which can adversely affect regulation of thyroid gland and may lead to thyroid dysfunction.[14]

Apart from these reasons, abnormal thyroid hormones can also be attributed to various medications such as insulin or oral hypoglycaemic drugs. Insulin suppresses T_3 levels by inhibiting peripheral conversion of T_4 to T_3.[16,17] On the other hand, some of the oral hypoglycaemic agents are known to supress the levels of free T_4 and T_3, while rising the levels of TSH.[16]

In our study, hypothyroidism was found to be the most frequent thyroid abnormality in type II diabetes mellitus patients (33%). Our observations are in agreement with the reports of **Suzuki et al[18]** and **Smithson MJ[19]**.

Further in our study, a negative correlation was obtained between serum T_3 and HbA_{1C} while a positive correlation was obtained between serum TSH and HbA_{1C}. These results matched with the results obtained in the studies of **Uppal V et al[13]** and Bilic-**Komarica E et al[20]**.

CONCLUSION:

Thyroid dysfunction is common among type II diabetes patients which can produce significant metabolic disturbances. Failure to recognise thyroid dysfunction may be a primary cause of poor management in type II diabetics. Therefore it is necessary to perform routine assay of thyroid hormones in type II diabetes mellitus patients particularly in patients with poor glycemic control so that early detection and treatment of thyroid dysfunction may have a positive impact on glycemic control as well as type II diabetes management.

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