ORIGINAL ARTICLE

Comparative Study of Thyroid Hormone Levels in Type I & Type II Diabetes Mellitus

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Abstract

Background: *Diabetes Mellitus (DM) is a chronic disorder in which there is impaired metabolism of carbohydrate leading to development of various complications. DM is due to lack of insulin secretion by pancrease leading to hyperglycemia & metabolic derangement. It is leading cause of both mortality & morbidity.* ***Aims :*** *To evaluate & assess thyroid hormones (T_3, T_4, TSH) as most suitable parameter for prognosis & treatment of diabetic patients.* ***Materials & Methods****: The present study was carried out in Department of Biochemistry, GMCH, Nagpur from May 2003 to May 2005, selected from diabetic OPD, GMCH, Nagpur in the age groups of 15 to 80 years. In all 30 controls, 30 type I DM & 30 type II DM patients were selected. The serum thus obtained was used for the estimations of thyroid hormones by ELISA method using Teco Diagnostics Kits.* ***Results:*** *The present study showed highly significant increase in T_3, T_4 & decrease in TSH in Type I DM & Type II DM when compared with controls.* ***Conclusions:*** *Determination of changes in T_3, T_4 & TSH can be considered as valuable diabetogenic factors which result in abnormal glucose metabolism.*

Keywords*: ELISA, Type I DM, Type II DM.*

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Introduction

Diabetes Mellitus (DM) is a chronic disorder characterized by impaired metabolism of glucose and other energy yielding fuels as well as by late development of vascular & neuropathic complications.[1] Hyperglycemia is the common feature of distinct pathogenic mechanism. It is characterized by insulin deficiency or insulin resistance. Lack of Insulin leads to hyperglycemia and metabolic defects. which leads to various complications. It is the leading cause of both mortality and morbidity. DM[2] can be classified[3, 4] as type I & type II DM. Type I DM is also called as IDDM or juvenile onset DM of unknown etiology. Type II DM is also called as NIDDM or adult onset DM resulting from insulin resistance or deficiency or secretory defect. Other specific types include a) genetic defect of β-cell function (e.g. maturity onset diabetes of young- MoDY) b) Genetic defect in insulin action (e.g. Type A insulin resistance & lipoatrophic diabetes) c) Diseases of exocrine pancrease (e.g. trauma, pancreatectomy, neoplasia, cysticfibrosis, hemochromatosis) d) Endocrinopathies (e.g. Acromegaly, Cushing's syndrome, hyperthyroidism, pheochromocytoma, glucagonoma, aldosteronoma, somatostatinoma) e) Infections induced (e.g. congenital rubella, cytomegalovirus) f) Drug/chemical induced (Vacor, pentamidine, Nicotinic acid, Glucorticoids, thyroid hormones, Diazoxide, β blockers, thiazides, phenytoin, α interferon) g) Unknown forms of Immune mediated DM (e.g. Anti insulin receptor Ab, Stiff-man syndrome) h) other genetic diseases (e.g. Down syndrome, Klinefelters syndrome, Turners syndrome, Wolframs syndrome, Freidrichs ataxia, Laurence-moon-Biedl syndrome, Prader willi

syndrome, Porphyrias i) gestational DM j) Obesity (insulin resistance). Substances which can give rise to diabetes are called as diabetogenic substances[5]. They are of two types Exogenous & Endogenous. Exogenous substances are Alloxan, Streptozotocin, viral infection (Mengovirus 2T, Coxsackie B_4 virus, Reovirus type I, Rubella), medications (corticosteroids, phenytoin thiazide diuretics), vacor (Rat Poison), wheat & milk proteins, high nitrosamine content of a smoked mutton & dehydroascorbic acid. Endogenous substances are amino acids (Gly, Ala, Asp, Glu, Trp), hormones (glucagon, glucocorticoids, Ep, NEp, GH, PRL, estrogen, HPL) plasma factors (synalbumin, lipoprotein factor, α_2-β-globulin factor) oxidants, uric acid, Mg^{++}, Ca^{++}, stress (burns & severe trauma).[2] In the present study we have selected T_3, T_4, TSH as the diabetogenic factors. The principal hormones secreted by follicular cells of thyroid[6] are • Thyroxine (T_4) • Tri-iodothyronine (T_3) and reverse T_3. The hormones T_4, T_3 and reverse T_3 are iodinated amino acid tyrosine. The iodine in thyroxine accounts for 80% of the organically bound iodine in thyroid venous blood. Small amounts of reverse T_3, MIT and other compounds are also liberated.

Metabolic role of thyroid hormones[6] :

1) Effect on protein metabolism - plays important role in catabolism of proteins

2) Effects on lipid metabolism i. Increases lipolysis, ii. Increases rate of biosynthesis of cholesterol, a) Increases rate of degradation b) Increases formation of bile acids

3) Calorigenic action - they increase O_2 consumption and O_2 coefficient of almost all metabolically active tissues. They cause increase in heat production and BMR.

4) Vitamins. Administration of large amounts of thyroid hormones increases the requirement of certain members of vitamin B complex and for vitamin C.

5) Effect on carbohydrate metabolism - Increase in blood sugar. Hyperglycemia and glycosuria, - Increases glucose utilization and decrease glucose tolerance, - They are antagonistic to insulin, - Thyroid hormones increase the rate of absorption of glucose from intestine, - Decreased glucose tolerance may be contributed to also by acceleration of degradation of insulin, - DM is aggravated by co-existing thyrotoxicosis or by administration of thyroid hormones, - Increase hepatic glycogenolysis because they enhance the activity of glucose 6 phosphatase, - In addition there is increased sensitivity of catecholamines. They potentiate glycogenolytic effect of epinephrine by increasing β adrenergic receptors on hepatic cell membrane. Stimulate glycolysis as well as oxidative metabolism of glucose via Tri-carboxylic acid cycle (TCA) and also increasing Hexose Monophosphate Shunt (HMPS) pathway. Thyroxine increases the activity of "G-6-PD" enzyme in liver. Thyroid hormones cause a decrease of glycogen store in liver and to a lesser extent in the myocardium and skeletal muscle. At the same time thyroid hormones increase hepatic gluconeogenesis by increasing activity of pyruvate carboxylase and phosphoenol pyruvate carboxykinase (PEP).

Aims and Objectives

Research is continuously going on in the field of DM. One of the most important problems we face today, as regards this challenging disease is that, even much is written & studied about the clinical features & management of patients of DM, exact cause of etiology of various endogenous factors are not studied much. Hence the pathogenesis is less understood. Study of such endogenous factors can help to get exact etiopathogenesis of the disease, which subsequently can help the treatment of patients. The aims & objectives of this study were

1) To estimate the serum levels of thyroid hormones (i.e. T_3, T_4, TSH); in 30 normal, healthy persons who served as controls for this study

2) To estimate the levels of thyroid hormones in sera of 30 Type l and 30 Type 2 DM patients.

3) To assess whether there was any statistically significant difference in the levels of these parameters between controls, Type 1 & Type 2 DM patients.

4) To evaluate if there was any correlation between levels of various parameters and condition of patients in groups of diabetic patient.

5) To assess which of these parameters studied is most suitable parameter for prognosis and treatment of the patients.

Materials and Methods

The present study was carried out in the Department of Biochemistry, G.M.C., Nagpur from May 2003 to May 2005. Cases were selected from amongst the patients attending diabetic O.P.D. of G.M.C. Nagpur, under Department of Medicine. We selected 30 patients diagnosed as having Type I DM and 30 as Type II DM from above mentioned patients population between 15 to 80 yrs. A case of DM was considered to be eligible for inclusion in present study only when the following criteria were being fulfilled, 1) The patient attending diabetic O.P.D. of G.M.C., Nagpur. 2) The patient was willing to enter study. 3) The patient did not have h /o other chronic diseases like HT etc. 4) There was no past h/ o TB to these patients. 5) Only nonsmokers & nonalcoholic patients were included. We selected 30 healthy, normal volunteers with ages ranging from 15 to 80 years, as controls. Ethical clearance was obtained from institutional ethics committee. About 5 ml of fasting[7] venous blood was withdrawn from each control / patient using a disposable syringe & needle and under all aseptic precautions. The blood obtained thus was collected in a sterile bulb and allowed to clot at room temp for at least 20 minutes. After this serum was separated by centrifugation The serum thus obtained was used for the following estimations without further delay. All the water used in following estimations was distilled and deionized and all reagents used were of analytical grade. T_3, T4, and TSH were estimated by kits supplied by ELISA[8] with the help of kits supplied by Teco Diagnostics-A.

Statistical Analysis

Data was analyzed on statistical software Intercostal stata version 7.0. Continuous variables are presented as Mean ± SD (Standard Deviation). Comparison between variables was done by using student-t-test. Analysis of variance (ANOVA) was used to see significant difference between variables. Categorical variables are represented in percentages. Categorical data was analyzed by using Chi-square-test and $p<0.05$ was considered as statistically significant.

Results

Table 1 showed the distribution of male & female patients. It was found that there were 33.33% males and 66.66% females in Type I and Type II DM, whereas, control subjects were also found to be of same percentage e.g. 33.33% males and 66.66% of females. Thyroid function appears to play an important role in DM. Therefore it was thought worthy to evaluate the results of present study in light of thyroid function. Hence T_3, T_4, TSH levels were simultaneous studied in controls, Type I DM patients and type II DM patients. The results of T_3, T_4 and TSH levels were enumerated in table II. T_3 and T_4 levels in type I DM and type II DM were found to be significantly increased as compared to controls whereas TSH levels were found to be decreased significantly in type I and type II DM patients which is suggestive of hyperthyroidism. Thus relationship between thyroid function and DM is definitely established. This shows that there may be thyroid dysfunction in DM.

Table 1 : Distribution of Study Subjects According to Sex

	Controls	%	Type I DM	%	Type II DM	%
Male	10	33.33	10	33.33	10	33.33
Female	20	66.66	20	66.66	20	66.66
Total	30	100	30	100	30	100

Table- 2: T_3, T_4 & TSH levels in controls (c), type I & type II DM patients

Sr. No.	Parameters	Controls (c) Mean ± S.D.	Type I DM Mean ± S.D.	Type II DM Mean ± S.D.	p value
1.	T_3 (ng/ml) (0.6 – 1.86 ng/ml)	0.96 ± 0.30	2.50 ± 0.12	2.18 ± 0.20	c vs type I & type II DM < 0.001
2.	T_4 (μg/dl) (4.8 – 12 μg/dl)	8.879 ± 1.39	14.53 ± 1.20	12.89 ± 2.001	c vs type I & type II DM < 0.001
3.	TSH (μIU/ml) (0.4 to 6 μIU/ml)	5.076 ± 1.90	0.392 ± 0.178	0.401 ± 0.158	c vs type I & type II DM < 0.001

Discussion

During the last few years, there has been an intense research, carried out in the field of DM. As, we all know DM. is a major cause of morbidity and mortality all over the world. This chronic metabolic disorder produces various adverse metabolic derangements in patients. Almost all tissues in the body get affected leading to morbidity and mortality. Although the number of clinical investigations carried and the scientists working on the study of endogenous factors is not small but, because of contradictory results, the present study has been undertaken. Human blood is easy for collection and is a unique biological system for examining the metabolism phenomenon, hence the most ideal choice of a tissue in the human system for study of biochemical alternation in an abnormal metabolic state is without doubt, the circulating blood. It is likely that in DM, there can be changes in biochemical parameters or dysfunction of thyroid hormones which cause few changes to some extent in the immediate environment of blood. Blood tissue system would react to changes and prolong modified environment would find the biochemistry of some hormones and some parameters significantly deviated from the normal. Hence study of thyroid hormones are of interest in Type 1 and Type 2 DM. Abnormal levels and contradictory results in Type 1 and Type 2 DM have arouse the interest of many researchers. Hence in the present investigations we evaluated the levels of thyroid hormones in sera of Type 1 and Type 2 DM patients. In the present study we observed significant increase in T_3, T_4 levels whereas there was parallel significant decrease in TSH. Our findings are in agreement with those of Cooppan R. et al[9] who studied the relationship between hyperthyroidism and diabetes mellitus. They suggested that hyperthyroidism must be considered in any patient whose diabetes is poorly controlled. Our results are similar to the reports of Sidibe E.H. et al[10] who estimated the thyroid hormones in 10 African patients with DM. They found out that thyroid hormone level was elevated in 8 patients. Nijs et al[11] demonstrated increased insulin clearance in patients with IDDM and thyrotoxicosis which was restored to more or less normal after amelioration of thyrotoxic secretion. Bhattacarya A et al[12] carried out study of thyroid hormones in Diabetic ketoacidosis. They have given two case reports where DKA precipitated marked increase in the levels of thyroid hormones and all S/S of thyrotoxicosis, but on T/t both those patients improved. They suggested that in thyrotoxicosis both glucose absorption and production of glucose from glycogen, lactate, glycerol and amino acids was increased. They also suggested that it might be lead to increased peripheral insulin resistance and insulin clearance. Our results in the present study support the concept of Bhattacarya A et al. In contrast to our findings, D. Hansen et al[13] reported increase in prevalence of subclinical hypothyroidism in 3 years follow up of young patients with type II DM. N. Custro et al[14] and Ganz K et al[15] reported increase incidence of mild or subclinical hypothyroidism in patients with IDDM. Hertzel C, Gestein[16] and Guillerno E et al[17] studied correlation between thyroid dysfunction and DM. They also found out that

hypothyroidism was more common type of thyroid dysfunctions in DM. Gasinska T et al[18, 19] found a good correlation between carbohydrate metabolism and hyperthyroid patients. They suggested that disturbed glucose tolerance might be due to increased hepatic glucose production and altered insulin metabolism.

Conclusion

Determination of changes in thyroid hormones in Type I & Type II DM patients can be considered as valuable diagnostic & prognostic parameters in both type I & type II DM patients. Hence, thyroid hormone estimation should be recommended during the treatment of both type I & II DM patients.

Conflict of Interest: *None declared*
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