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Original Article

Biochemistry Section

Thyroid Function In Type 2 Diabetes Mellitus and in Diabetic Nephropathy

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ABSTRACT

Introduction: Diabetic patients have higher prevalence of thyroid disorders than the general population which may have an influence on diabetic management. The present study compared the levels of thyroid hormones, serum creatinine, glycated haemoglobin and urine microalbumin between type 2 diabetics without any complications, type 2 diabetics with nephropathy and age and sex matched normal controls.

Result: The mean serum T3 level in type 2 diabetics without any complications was 91.27 ± 14.56 ng/dl , in type 2 diabetics with nephropathy was 88.5320 ± 30.87 ng/dl and in controls was 134.98 ± 28.55 ng/dl. The mean serum T4 level in type 2 diabetics without any complications was 7.73 ± 1.42 µg/dl, in type 2 diabetics with nephropathy was 7.25 ± 2.72 µg/dl and in controls was 8.61 ± 1.73 µg/dl. The mean serum TSH level in type 2 diabetics without any complications was 3.99 ± 1.87 µIU/ml, in type 2 diabetics with nephropathy was 4.27 ± 1.62 µIU/ml and in controls was 2.07 ± 1.09 µIU/ml. Correlations between T3, T4, TSH with serum creatinine, glycated haemoglobin were not statistically significant in type 2 diabetes without any complications and diabetic nephropathy. We found a statistically significant correlation between T3 and urine microalbumin in patients with diabetic nephropathy.

Conclusion: Failure to recognize the presence of abnormal thyroid hormone levels may be a primary cause of poor management of diabetes mellitus type 2. Therefore there is a need for the routine assay of thyroid hormones in type 2 diabetics and diabetic nephropathy in order to improve the quality of life and reduce the morbidity.

Key words: Thyroid function, Diabetes Mellitus type 2

INTRODUCTION

Diabetes mellitus is an important health problem affecting major populations worldwide. It is characterized by absolute or relative deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycaemia and disturbances of carbohydrate, lipid, and protein metabolism [1]. Diabetic patients have higher prevalence of thyroid disorder when compared with the normal population, with hypothyroidism being the most common disorder [2]. Prevalence of thyroid dysfunction varied from 2.2%–17% in diabetics. Diabetic women are more frequently affected than men and hypothyroidism is more common than thyrotoxicosis [3].

Thyroid hormones are insulin antagonists, both insulin and thyroid hormones are involved in cellular metabolism. Excess or deficit of any one can result in functional derangement of the other [4]. Sub–clinical hypothyroidism is an independent risk factor for development of diabetic nephropathy [5]. Serum TSH and tissue insulin sensitivity have important effects on serum lipid parameters in type 2 diabetic patients. At low insulin sensitivity, relatively minor changes in TSH levels are associated with marked changes in lipid risk factors and thus cardiovascular risk [6]. Unrecognized thyroid dysfunction may impair metabolic controls in patients with diabetes and in addition may amplify existing cardiovascular risk. Recognition and treatment of thyroid dysfunction in diabetic patients will benefit glycaemic control, attenuate cardiovascular risk, and improve general well being [7].

Diabetic nephropathy, a major microvascular complication of type 2 diabetes mellitus,is an important cause of chronic kidney disease. It results from interactions between haemodynamic and metabolic factors [8].

The aim of the present study was to compare and correlate the thyroid hormones levels (T3 and T4), TSH, serum creatinine, glycated haemoglobin, urine microalbumin in type 2 diabetics with and without complications and age and sex matched controls.

MATERIAL AND METHODS

This study was conducted on 75 individuals in the age group of 40-70 years during the year 2010-2012. The study group consists of 25 individuals who were diagnosed as type 2 diabetics without any complications (newly diagnosed or known diabetics on treatment), 25 individuals with type 2 diabetes with diabetic nephropathy and 25 ages and sex matched healthy individuals (control). Individuals with previous history of thyroid disease, co-existing hepatobiliary disease, pregnancy, on systemic drug therapy such as thyroxine, antithyroid drugs, glucocorticoids and oral contraceptives are not included in the study group to avoid its influence on various parameters analyzed in this study.

After obtaining the informed consent, by the aseptic precautions 7 ml of blood was collected from anticubital vein after 8-12 hours of fasting. Blood was collected in EDTA vacutainer (2ml) and plain vacutainer (5ml). Urine sample (5ml) was also collected in a clean, dry and sterile container. Blood collected in plain vacutainer was processed to obtain serum. Serum T3 [9], Serum T4 [10], Serum TSH [11] were measured by chemiluminescence method in immulite 1000 autoanalyzer. Serum creatinine [12] was measured by modified Jaffe's method in semi–autoanalyzer using commercially available kit. Blood collected in EDTA tube was used for estimation of glycated haemoglobin [13] measured by ion-exchange resin method using commercially available kit.

Urine collected was used for estimation of urine microalbumin [14] measured by turbidimetric immunoassay using Turbilyte-MA Tulip Diagnostics kit in semiautoanalyzer.

RESULT

Serum T3, T4, TSH levels were compared between three groups using ANOVA. Serum T3 levels were found to be decreased in type 2 diabetics without any complications and type 2 diabetics with nephropathy which was statistically significant. Serum T4

levels were found to be decreased in type 2 diabetics without complications and type 2 diabetics with nephropathy, but this decrease was not statistically significant. Serum TSH levels were found to be increased in type 2 diabetics without any complications and type 2 diabetics with nephropathy, when compared to controls, which was statistically significant [Table/Fig-1].

Serum creatinine, glycated haemoglobin levels and urine microalbumin were compared between the three study groups using ANOVA and observed statistically highly significant increase in serum creatinine, HbA1c levels and urine microalbumin levels between three study groups [Table/Fig-2].

When data was analyzed by pearson correlation, we observed a negative correlation between serum T3 and T4 with glycated haemoglobin, serum creatinine, urine microalbumin, in type 2 diabetics without any complications which was not statistically significant. There was a positive correlation between serum TSH with glycated haemoglobin, serum creatinine, urine microalbumin, without any statistical significance [Table/Fig-3].

In type 2 diabetics with nephropathy when data was analyzed by pearson correlation it had shown a negative correlation between serum T3 and T4 with glycated haemoglobin and serum creatinine that was not statistically significant. Serum T3 and urine microalbumin is negatively correlated and it is statistically significant. Serum T4 and urine microalbumin was negatively correlated but not statistically significant. Serum TSH in type 2 diabetics with nephropathy had shown a positive correlation with glycated haemoglobin, serum creatinine, urine microalbumin, which was statistically not significant [Table/Fig-4].

	Controls	Type 2 diabetics without complications	Type 2 diabetics with nephropathy	p value
T3 (ng/dl) Mean ± SD	134.98 ± 28.55	88.53 ± 30.87	91.27 ± 14.56	< 0.001
T4 (µg/dl) Mean ± SD	8.61 ± 1.73	7.73 ± 1.42	7.73 ± 1.42	0.06
TSH (µIU/ml) Mean ± SD	2.07 ± 1.09	4.27 ± 1.62	3.99 ± 1.87	< 0.001

[Table/Fig-1]: Comparison of serumT3, (ng/dl),T4 (µg/dl) and serum TSH (µIU/ml)between the study groups
p = <0.05 Significant

	Controls	Type 2 diabetics without complications	Type 2 diabetics with nephropathy	p value
Serum Creatinine Mean± SD	0.81 ± 0.11	1.08 ± 0.34	6.70 ± 1.75	< 0.001
HbA1c Mean ± SD	5.45 ± 0.50	6.92 ± 1.40	8.93 ± 2.35	< 0.001
Urine Microalbumin Mean ± SD	14.12 ± 3.79	17.24 ± 4.56	166.12 ± 34.45	< 0.001

[Table/Fig-2]: Serum creatinine, glycated haemoglobin (HbA1c) and urine microalbumin in diabetics without complications, with nephropathy and control groups
p= <0.05 significant

Parameters correlated	r value	p value
T_3 with • Glycated Hemolobin • Serum Creatinine • Urine microalbumin	 r = - 0.37 r = - 0.48 r = - 0.19	 p = 0.069 p = 0.819 p = 0.819
T_4 with • Glycated Hemolobin • Serum Creatinine • Urine microalbumin	 r = - 0.01 r = - 0.49 r = - 0.04	 p = 0.978 p = 0.816 p = 0.836
TSH with • Glycated Hemolobin • Serum Creatinine • Urine microalbumin	 r = 0.04 r = 0.22 r = 0.11	 p = 0.853 p = 0.296 p = 0.587

[Table/Fig-3]: Correlation between T3, T4, TSH, serum creatinine, glycated haemoglobin and urine microalbumin in diabetics without complication
p= <0.05 significant

Parameters correlated	r value	p value
T_3 with • Glycated Hemolobin • Serum Creatinine • Urine microalbumin	 r = - 0.28 r = - 0.12 r = - 0.43	 p = 0.181 p = 0.573 p = 0.032
T_4 with • Glycated Hemolobin • Serum Creatinine • Urine microalbumin	 r = - 0.29 r = - 0.25 r = - 0.13	 p = 0.159 p = 0.231 p = 0.528
TSH with • Glycated Hemolobin • Serum Creatinine • Urine microalbumin	 r = 0.18 r = 0.16 r = 0.31	 p = 0.384 p = 0.435 p = 0.135

[Table/Fig-4]: Correlation between T3, T4, TSH, serum creatinine, glycated haemoglobin and urine microalbumin in diabetics with nephropathy
p= <0.05 significant

DISCUSSION

The present study was undertaken to evaluate the levels of serum T3, T4 and TSH, serum creatinine, glycated haemoglobin and urine microalbumin in type 2 diabetics without any complications and type 2 diabetics with nephropathy.

The study showed that the serum T3 and serum T4 levels were decreased, and serum TSH levels were increased in type 2 diabetics without any complications and type 2 diabetics with nephropathy when compared to controls. We have observed that there is no substantial change in the levels of serum T3, T4 and TSH among diabetics without complications and diabetics with nephropathy.

A study by Singh G et al., showed that patients with type 2 diabetes had abnormal thyroid hormone levels. The level of T3, T4, FT3 and FT4 were significantly lower while the levels of TSH were significantly higher in type 2 diabetics as compared to non-diabetics. Significantly higher levels of serum creatinine, glycated haemoglobin was observed in diabetics as compared to non-diabetics subjects [4] which agrees with the findings of our study.

A study by Swamy RM et al., showed that the serum T4 level was low and TSH was high in type 2 diabetics when compared with controls and this difference was statistically significant. T3 was also low in type 2 diabetics when compared with controls but this difference was not statistically significant [15] which correlates with our findings. A study by Chubb SA et al., had shown that the prevalence of subclinical hypothyroidism among type 2 diabetics is 8.6% [16].

A study by Islam S et al., showed that the levels of FT3 was significantly lower in type 2 diabetics when compared with the controls. FT4 and TSH did not show any statistically significant difference between type 2 diabetics and controls. The mean serum ratio of FT3/FT4 was significantly lower in type 2 diabetics than in the control group [17]. Presence of hypothyroidism among diabetics when compared to controls has also been documented by Saha et al., [18].

Udiong CEJ et al., in Nigeria showed TSH levels in diabetics were significantly lower than the non–diabetics. The levels of T4 in diabetics were higher than the non–diabetics, T3 levels did not differ significantly between diabetics and controls [19]. On contrary we found decrease in the levels of T3 and T4 and increase in serum TSH levels in diabetics when compared to controls.

In diabetes mellitus there is influence of endocrine and non-endocrine organs other than pancreas. There are alterations in the hypothalamus-pituitary-thyroid axis. Hypothalamic and plasma

TRH, pituitary and plasma TSH, as well as TSH secretion rates are reduced, and the TSH response to TRH is decreased. Despite normal peripheral TSH metabolism.T3 and T4 production and iodide uptake by the thyroid are diminished. There are important structural changes in the thyroid gland and pituitary that are accompanied by marked alterations in their secretary activities. T4 deiodination to T3 in peripheral tissues is decreased. Iodothyronines are insulin antagonist with high levels being diabetogenic, while absence of the hormone inhibits the development of diabetes. These situations may prevail in diabetics and would be aggravated in poorly controlled diabetics. Stress, which is associated with diabetes, may also cause changes in the hypothalamus anterior-pituitary axis in diabetics [19, 20].

Serum creatinine, glycated haemoglobin, urine microalbumin, were increased in type 2 diabetics without any complications and type 2 diabetics with nephropathy when compared with controls. The correlation of Serum T3, Serum T4 and Serum TSH with serum creatinine, glycated haemoglobin, was not statistically significant in type 2 diabetics without any complications and type 2 diabetics with nephropathy. Correlation between T3 and Urine microalbumin in study group with diabetic nephropathy was statistically significant.

Chronic Kidney Disease (CKD) influences hypothalamo – pituitary - thyroid axis. Secretion of hypophyseal Thyroid Stimulating Hormone (TSH) is disturbed and the TSH response to the hypothalamic Thyrotropin Releasing Hormone (TRH) is reduced. CKD affects the thyroid function by lowering levels of circulating thyroid hormones, interfering with hormones binding to protein carriers, disrupting metabolism and elimination of thyroid hormones [21].

We have observed that the abnormal thyroid hormone levels among type 2 diabetics without any complications and type 2 diabetics with nephropathy. The study on a larger population will help to give further information about the relationship between the glycated haemoglobin, urine microalbumin and Serum creatinine and thyroid function. Failure to recognize the presence of abnormal thyroid function may be a primary cause of poor managemen of diabetes mellitus. Therefore there is a need for the routine assay of thyroid hormones in type 2 diabetics and diabetic nephropathy in order to improve the quality of life and reduce the morbidity.

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