Indian Journal of Basic & Applied Medical Research; September 2012: Vol.-1, Issue-4, P. 251-258

"THE EVALUATION OF SELENIUM AND THYROID HORMONES AMONG THE POPULATION WITH DIABETES MELLITUS."

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Background: The **aim** of this study is to evaluate the association between selenium and thyroid hormones among diabetes. Both diabetes and thyroid disorders involves dysfunction of the endocrine system.

Materials & Methods: both type I & II diabetes mellitus patients attending the Diabetic OP of Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research, Melmaruvathur, Tamilnadu. Study was conducted on 46 diabetes(30 NIDDM & 16 IDDM) along with 30 age sex matched healthy control in age group between 45-75years. The investigations carried out were FBS, HbA_{1c}, Thyroid Profile and Selenium.

Results:- In both Type I & II diabetes There were increased FBS, Hb A_{1c} levels , decreased serum selenium &T3 was observed. The higher prevalence of thyroid dysfunction in both type I & II diabetes than in the general population. In type I DM the T3 syndrome is more severe than Type II DM.

Conclusion: - Rigorous Selenium & thyroid profile monitoring & control needs to be followed as it is known for health benefits, so as to prevent Diabetic complications & cardiovascular disease, thereby increasing the quality of life among diabetics.

Keywords: Selenium; Diabetes Mellitus; Thyroid Profile; Cardiovascular disease.

Introduction:

Cardiovascular manifestations are a frequent finding in Diabetes, hyperthyroidism and hypothyroidism. There is clear evidence for direct effects of Thyroid hormones on the myocardium in addition to indirect ones.(1) A typical pattern of altered thyroid hormone metabolism characterized by low T3 circulating levels has been described in patients with Diabetes mellitus. (2) T3 exerts its effects mainly at the cellular level through activation of mRNA coding for specific proteins via binding to specific nuclear receptors.

(3) T3 increases cellular amino acid and sugar uptake in the presence of a protein-synthesis inhibitor. (4) It has been postulated that the low T3 state may produce a hypothyroid-like syndrome that contributes to the worsening or exacerbation of the intrinsic cardiac disease. (5-6).

Selenium is an important component of the antioxidant enzyme, glutathione peroxidase (GSH-Px) that protects cells from the adverse effects of free radicals and lipid peroxides. A deficiency of selenium lowers the tissue activity of GSH-Px which in turn may have unfavorable

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effects on lipoprotein and arachidonic acid metabolism [7,8]. These metabolic changes associated with compromised selenium status may lead to damage of the vascular endothelium and increased platelet adhesion which increase the risk of Diabetes mellitus [9]. Studies in rats show a beneficial effect of selenium supplementation on lipid abnormalities in plasma, aorta, and adipose tissue [10]. Since selenium mediates a number of insulin- like actions both in vivo and in vitro, this may be a potential mechanism for these actions [11]. These data suggest that selenium may be beneficial in insulin resistance and potentially can modify the risk of cardiovascular disease (CVD). One important reason for the paucity of data from epidemiological studies on selenium status and the risk of diabetes, CVD & Hypothyroidism is the difficulty in estimating dietary selenium. The level of selenium in different foods varies widely depending on the soil content in the geographic area where the food is grown [12].

Several syndromes, such as "euthyroid sick syndrome" and "low T3 syndrome," have been classified within the medical literature. The common feature of these disorders is a low level of circulating T3, with generally normal to slightly elevated blood T4 levels and either normal or slightly suppressed TSH levels.

This pattern of altered thyroid hormone levels is generally agreed to be a result of impairment in extra-thyroidal peripheral metabolism. Hepatic and renal pathology, as well as catabolic states such as those induced subsequent to severe injury, illness, or trauma result in consistent shifts in the thyroid hormone profile, secondary to their impact on peripheral enzyme pathways.

Lifestyle factors, such as stress, caloric restriction, and exercise, influence peripheral metabolism of thyroid hormones. Exposure to toxic metals, chemical poisons, and several drugs can also influence the peripheral fate of thyroid hormones. While the role of vitamins, minerals, and botanical extracts in thyroid hormone metabolism requires further elucidation, current evidence supports a role for selenium in the hepatic 5'-deiodination enzyme.(13 -15)

Three deiodinase families are recognized and are termed isoforms type I, II, and III These three families differ in terms of their tissue distribution, reaction kinetics, efficiency of substrate utilization, and sensitivity to inhibitors.[19]

In this concern we undertake the present study to evaluate effect of Selenium status on circulation thyroid hormones among diabetic population.

Materials and Methods:

The present study is carried out on both type I & II diabetes mellitus patients attending the Diabetic OP of Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research, Melmaruvathur, Tamilnadu. Study was conducted on 46 diabetes(30 NIDDM & 16 IDDM) along with 30 age sex matched healthy control with no known history of any disease. All the patients were examined clinically and all information pertaining to age, sex, past history was recorded in special patient consent proforma. 5ml of blood drawn into fluoride container for estimation of blood glucose and another 5ml of heparinized blood was collected for estimation serum TFT profile after an overnight fast. Blood samples were centrifuged at 2000 rpm for 15mins. Separated plasma was stored at -50 ^{0}C until analysis.

Determination of Selenium

Serum samples were diluted with an equal volume deionized water to estimate serum selenium. Spectrophotometer was used to estimate the level of these elements in the diluted sera. Level of sera Selenium was calculated after application of

absorbance on suitable calibration curve for this element from standard solutions.

STATISTICAL METHODS

Student t test of independent samples has been used to find the significance of difference between the cases and controls for various parameters. The significance level of 5% is taken as critical value to find the difference between the mean values of cases and controls. Correlation of different parameters was done by using Pearson correlation

DISCUSSION:

The prevalence of Low T3 syndrome is 82% in patients with type I diabetes and 77% in patients with type 2 diabetes. The low T3 syndrome is significantly present in women than men, even though their plasma glucose and HbA_{1C} are lower than men. This may need further large prospective study.

Diabetic patients have a higher prevalence of thyroid disorders compared with the normal population. Because patients with one organ-specific autoimmune disease are at risk of developing other autoimmune disorders, and thyroid disorders are more common in females, it is not surprising that up to 30% of female type 1 diabetic patient have thyroid disease.

More than 80% of the biologically active hormone triiodothyronine (T3) derives from peripheral conversion of prohormone thyroxine (T4) secreted by the thyroid gland. The principal pathophysiological mechanism underlying low circulating T3 is the reduced enzyme activity of 5' monodeiodinase which is a selenium dependent enzyme is responsible for converting T4 into T3 in peripheral tissues. This low-T3 syndrome has commonly been interpreted by the medical community as a euthyroid sick syndrome, an adaptive compensatory and thus beneficial response that decreases energy consumption in diseased states (16).

In euthyroid individuals with diabetes mellitus, the serum T3 levels, basal TSH levels and TSH response to thyrotropin releasing hormone (TRH) may all be strongly influenced by the glycemic status (2). In the present study all the diabetic subjects were said to be euthyroid. 77% Type II DM and 82% Type I DM is showed low T3 levels, low serum selenium and the levels of serum T3, selenium are negatively correlated with glycemic status. This study is agreement with Kabadi et al(29). The low T3 syndrome is more significantly seen in women than men with diabetes (Table 3).

Diabetes is a disorder characterized by an overabundance of glucose (sugar) in the blood due to insufficient insulin production by the pancreas (type 1 diabetes) or the inability of the body to utilize insulin to transport glucose into the cells (type 2 diabetes).

The effect of insulin on the deiodinases has also been studied. Insulin upregulates hepatic T3 production, as has been described in 'low T3 syndromes'. In insulin deprivation (as in diabetes and fasting), T3 production is low due to low hepatic D1 deiodinase activity and mRNA (25), leading to low serum T3 levels.(6)

Present data on glycemic status shows that all cases are poor glycemic controls. T3 levels are significantly lowered in both the cases when compared with controls. Poorly controlled diabetes, both Type 1 and Type 2, may induce a "Low T3 state" characterized by low serum total and free T3 levels, increase in reverse T3 (rT3) but near normal serum T4 and TSH concentrations (17).

In our study strong negative correlation exists between Plasma Glucose and T 3 in poor Glycemic status among Type I DM ($r = -0.74$, $Glc \geq 459$). In contrast, type II DM patients were showing similar pattern when they were been in long term poor Glycemic status ($r = -0.24$, $HbA_{1C} \geq 7.6$). Present study we found that low T3 syndrome is severe in Type I DM who is very poor diabetic control compared with Type II DM.

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In the study of Kabadi et al(25), fasting plasma glucose greater than 200 mg/dl, serum rT3 raised to (96 ± 5 to 128 ± 5 ng/dl) and T3 is declined (26.3 ± 10.4 ± 1.4 ng/dl) on improvement of hyperglycemia (fasting plasma glucose less than 140 mg/dl) after intensive therapy for 6 to 8 weeks. Glycosylated hemoglobin levels declined as well (14.6 ± 0.9% to 9.3 ± 0.7%). These data indicate thyroid hormone metabolism may be altered in diabetes mellitus with a fall in serum T3 and a reciprocal rise in rT3 concentrations may serve as indicators of metabolic control in diabetes mellitus. (14).

In the study of Tahirović H et al(30), confirm that euthyroid sick syndrome does exist in type I diabetic children and adolescents with poor metabolic control and ketoacidosis. The inverse relationship found between T3 and HbA1c percentage (low T3 and high HbA1c) points to the poor diabetic control. (25)

An association between diabetes and thyroid disease has long been recognized, although the reported prevalence of thyroid dysfunction in diabetic populations varies widely between studies (1, 18 &20).

The decrease in serum selenium levels in diabetes patients is in agreement with the studies of other researchers indicating the important role of selenium in controlling the thyroid gland functions (23 &24)

Statistically significant correlations were found among indexes of selenium status and indexes of thyroid hormone metabolism and function. Concomitant deficiencies of both key elements for thyroid hormone metabolism are especially dangerous and Se from the point of thyroid hormone regulative functions (22)

In other studies, using animals, selenium deficiency in rats inhibited the production of T3 from T4. It is concluded that, since both T3 production and catabolism are inhibited by selenium deficiency, there is little change in hepatic T3 stores (26). Selenium deficiency in rats is characterized by elevated serum T4 and decreased serum T3 concentrations, and low liver iodothyronine 5' deiodinase I and brain iodothyronine 5'- deiodinase II activities (27). The iodothyronine deiodinases, which are responsible for the conversion of thyroxine (T4) to its active form, triiodothyronine (T3), are selenoenzymes (21). However, another data reported that in hypothyroid patients, a poor Se status was associated with a diminished 5-ódeiodinase, leading to increase T4 levels and decreased T3/T4 ratios (28).

The present study clearly shows the existence of a strong association between the reduction of biologically active T3 and poor Glycemic control in both Type I & II diabetes cases. In type I DM the T3 syndrome is more severe than Type II DM; due to their glycemic control is dependent on insulin intake. The similar pattern observed in Type II when they were been in long term poor glycemic control. when selenium is depleted, there is less Se to form the deiodinase enzymes which convert T4 to T3, resulting in low T3 and hypothyroidism. In addition, there is less selenium to form glutathione peroxidase, one of the body's prime antioxidants. This results in greater levels of reactive oxygen species and hydrogen peroxide, which lead to increased damage to the endothelial cells which may worse the diabetic complications. Rigorous Selenium & thyroid profile monitoring & control needs to be followed as it is known for health benefits, so as to prevent Diabetic complications & cardiovascular disease, thereby increasing the quality of life among diabetics.

RESULTS:

Table 1 : Number of Case & Control Distribution

	Controls	Patients	
		Type I DM	Type II DM
Total Number	30	16	30
No. of Males	15	8	15
No. of Females	15	8	15
Mean Age	47.64	48.62	49.03

Table 2: Biochemical parameters in all the three groups

	Controls	Type I DM	Type II DM
BMI	23.13±1.53	26.38± 2.40	26.17±2.32
Plasma Glucose	102.27±10.76	459.06 ±221.99	307.85±161.96
Hb A_{1c}	5.55±0.68	8.36± 1.30	7.60 ± 0.99
T3	1.17±0.35	0.53± 0.30	0.82 ± 0.65
T4	8.54±1.61	12.04 ± 3.88	11.50 ± 4.21
TSH	2.17±0.76	1.45 ±0.97	2.09 ± 0.81
Serum Selenium Micro Moles / Lit	1.29±0.10	1.180±.097	1.23±0.077

Table 3 : Biochemical parameter variation in between male and female

	CONTROL		Type I DM		Type II DM	
	Males	Females	Males	Females	Males	Females
BMI	23.86	21.86	25.91	26.84	26.43	25.90
Plasma Glucose	102.68	101.55	476.50	441.63	336.88	278.82
Hb A_{1c}	5.54	5.56	8.11	8.63	7.90	7.30
T3	1.14	1.22	0.54	0.52	0.87	0.77
T4	8.45	8.70	10.61	13.45	12.20	10.80
TSH	1.98	2.48	1.51	1.39	2.05	2.13
Serum Selenium Micro Moles / Lit	1.29	1.29	1.19	1.17	1.25	1.21

Table 4 Biochemical parameter variation in between Type I & Type II DM

	HbA1c	T3	T4	TSH	Serum Selenium	
Controls Vs Type I DM	8.686	8.512	1.604	2.972	4.508	**T test**
	P<0.001**	P<0.001**	P>0.1	P>0.1	P<0.001**	**P value**
Controls Vs Type II DM	12.056	3.144	.4095	0.548	4.694	**T test**
	P<0.001**	P<0.001**	P>0.1	P>0.1	P<0.001**	**P value**

**** highly significant**

Table 5 Coefficient of correlation(r) between plasma Glucose, HbA_{1C}, Selenium and T3 among the different groups

r-value	Glucose vs T3	HbA1c vs T3	Serum Selenium Micro Moles / Lit Vs T3
Control s	-0.101	-0.220	-0.021
Type I DM	0.747**	0.088	0.226
Type II DM	-0.244	-0.254	0.166

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Date of manuscript submission: 23 January 2012
Date of initial approval: 5 February 2012
Date of Peer review approval: 2 August 2012
Date of final draft preparation: 25 August 2012
Date of Publication: 5 September 2012
Conflict of Interest: Nil, Source of Support: Nil.