INTER-RELATIONSHIP OF GLYCEMIC CONTROL AND THYROID STATUS IN TYPE – 2 DIABETES MELLITUS

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Abstract

Introduction: The inter-relationship between diabetes mellitus & thyroid disorders involves biochemical, genetic, hormonal and pathophysiological mechanisms under the influence of endocrine and non-endocrine organs other than the pancreas. Several studies document the prevalence of thyroid dysfunction among type-2 diabetes mellitus patients to be varying from 2.2 to 17 %. However, fewer studies have estimated much higher prevalence of thyroid dysfunction (31 % and 46.5%) in Type – 2 diabetes mellitus.

Materials and Methods: This cross-sectional pilot study involved 81 confirmed cases ofType – 2 diabetes mellitus (on treatment) aged between 18-70 years of either sex(male-24, female-57). Blood samples were analyzed for FBS, PPBS, RBS and thyroid profile (Total T3, total T4 & TSH) tests. The results obtained were expressed asMean ± SD.

Results: The prevalence of thyroid dysfunction was 37% [Hypothyroidism - 30% & Hyperthyroidism - 7%].Based on glycemia control & thyroid status, following subcategories of cases were observed: Euglycemic Euthyroid (42%) > Hyperglycemic euthyroid (21%) > Euglycemic hypothyroidism / Euglycemic subclinical hypothyroidism (11%) > Hyperglycemic subclinical hypothyroidism (5%) > Euglycemic subclinical hyperthyroidism (4%) > Hyperglycemic hypo/hyperthyroidism (2%).

Conclusion: Determining thyroid status may be useful for better management of type – 2 DM and its prognosis.

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1. INTRODUCTION

Diabetes mellitus (DM), characterized by hyperglycemia due to insulin resistance or insulin secreting defect by pancreatic β-cells or both (multifactorial) is found to be associated with thyroid disorders. Thyroid dysfunction in diabetes mellitus manifests either as hypothyroidism (clinical or subclinical) or hyperthyroidism (clinical or subclinical) and is reflected in the circulating levels of Thyroid hormones, namely tri-iodothyronine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) which might have an impact on blood glucose homeostasis. [1, 2]

The inter-relationship between diabetes mellitus & thyroid disorders involves various complex biochemical, genetic, hormonal and pathophysiological mechanisms under the influence of endocrine and non-endocrine organs other than the pancreas.Several studies document the prevalence of thyroid dysfunction among diabetes patients to be varying from 2.2 to 17 %. However, fewer studies have estimated much higher prevalence of thyroid dysfunction (31 % and 46.5%) in diabetes. [3]

The problem of thyroid dysfunction in diabetes mellitus is an unexplored entity in South India which may explain the morbidity& mortality in diabetic patients. This pilot study aims to determine the prevalence & patterns of thyroid dysfunction in patients with diabetes mellitus.

2. MATERIALS AND METHODS:

This cross-sectional pilot study involved 81 cases ofType-2 diabetes mellitus aged between 18-70 years of either Sex(male-24, female-57). Inclusion criteria included patients diagnosed as Type-2 diabetes mellitus (mean duration of 3-5 years) based on previous fasting plasma glucose levels > 126 mg/dl , postprandial blood glucose > 200 mg/dland who were receiving oral hypoglycaemic agents & or insulin with diabetic diet and physical exercise. In addition, they had no previous history of thyroid dysfunction. A self-administered questionnaire was used to determine age, sex, smoking status, family status, family history, treatment status etc. In addition, a review of Hospital records of the diabetic cases was carried out regarding their past lipid profile results, the adequacy of their glycaemic controls, the presence of complications and medication history. Obese (BMI _ 30 kg/m2) subjects, dyslipidemia, smokers, chronic renal failure, chronic liver disease, known atherosclerotic cardiovascular disease or malignancies, patients taking lipid lowering drugs, antioxidant vitamin supplements, acetylsalicylic acid, antihistamines etc were excluded from the study.

Fasting & 2 hrs-post-prandial blood samples were collected by venepuncture from the cases. The serum was separated by centrifugation at 10,000 rpm for 15 minutes at room temperature. Serum samples were stored at -20°C until tested. For glucose estimation 1 ml of blood was placed in a tube containing fluoride. The plasma was separated and analyzed within a few hours of collection. Plasma glucose was measured by standard enzymatic methods using fully automated Biochemistry analyzer.Frozen sera was thawed and assayed for TSH, T3 and T4 in three runs, each on a different day by chemiluminescence method.

The normal reference range of thyroid hormones in our lab is as follows:T3 = 1.2-2.8 nmol/l,T4= 60-160 nmol/land TSH= 0.17-4.04 mU/l. An elevated TSH & low T4 was interpreted as clinical hypothyroidism. An elevated TSH & normal T4 was interpreted assubclinical hypothyroidism. Low TSH & a high T4 was interpreted as clinicalhyperthyroidism. Low TSH & a normal T4 was interpreted as subclinical hyperthyroidism. The glycaemic control was assessed by their fasting (FBS) and 2 hour post prandial glucose (PPBS) levels. The Glycaemic Control was graded as "euglycemic" if FBS < 110 mg/dl) and PPBS is < 140 mg/dl), and

"hyperglycemic" if either FBS is >126 mg/dl or PPBS is >200 mg/dl. [4, 5]

The results obtained from the above investigation were analysed and expressed asMean ± SD.Statistical analysis was done using SPSS version 16 software.

3. RESULTS

Out of 81 study subjects, the thyroid status observed as evident from TABLE 1 was as follows: Euthyroid (N=51,63%), thyroid dysfunction was 37% out of which Hypothyroidism (N=24, 30%) [Clinical hypothyroidism (N=11, 14%) & Subclinical hypothyroidism (N=13,16%)] & Hyperthyroidism (N=6,7%) [Clinical hyperthyroidism (N=2, 2%) & Subclinical hyperthyroidism (N=4, 5%)] were prevalent.

TABLE 1: Thyroid Function Status in Type-2 Diabetic Cases.

	MALES		FEMALES		TOTAL	
	N	%	N	%	N	%
Eauthyroid	18	75	33	58	51	63
Clinical Hypothyroidism	3	12.5	8	14	11	14
Subclinical hypothyroidism	3	12.5	10	18	13	16
Clinical Hypothyroidism	0	0	2	4	2	2
Subclinical hypothyroidism	0	0	4	7	4	5
TOTAL CASES	24		57		81	

Based on glycemic control & thyroid status, following subcategories of cases were observed (TABLE 2 & TABLE 3): Euglycemic Euthyroid (42%) > Hyperglycemic euthyroid (21%) > Euglycemic hypothyroidism/Euglycemic subclinical hypothyroidism (9%) > Hyperglycemic subclinical hypothyroidism / Euglycemic subclinical hyperthyroidism (4%) > Hyperglycemic hypo/hyperthyroidism (2%).

TABLE 2: Subcategories Based on Glycemic Control and Thyroid Dysfunction

	MALES		FEMALES		TOTAL	
	N	*%*	N	*%*	N	*%*
Euglycemic hypothyroidism	2	*8*	7	*12*	9	*11*
Hyperglycemic hypothyroidism	1	*4*	1	*2*	2	*2*
Euglycemic subclinical hypothyroidism	1	*4*	8	*14*	9	*11*
Hyperglycemic subclinical hypothyroidism	2	*8*	2	*4*	4	*5*
Hyperglycemic hyperthyroidism	0	*0*	2	*4*	2	*2*
Euglycemic subclinical hyperthyroidism	0	*0*	4	*7*	4	*5*
Hyperglycemic euthyroid	7	*29*	10	*18*	17	*21*
Euglycemic euthyroid	11	*46*	23	*40*	34	*42*
TOTAL CASES	**24**		**57**		**81**	

TABLE 3: Mean Biochemical Values in The Cases

	Mean age (yrs)	Mean RBS (mg/dl)	Mean FBS (mg/dl)	Mean PPBS (mg/dl)	Mean T3 (nmol/l)	Mean T4 (nmol/l)	Mean TSH (mU/l)
Euglycemic hypothyroidism	53	112.89	86.78	114	0.94	71.06	17.71
Hyperglycemic hypothyroidism	38.5	177	138	208	0.79	75.3	3.13
Euglycemic subclinical hypothyroidism	58.89	102.44	84.89	105.33	1.92	105.38	6.87
Hyperglycemic subclinical hypothyroidism	40.25	188.75	130.00	189.75	1.67	126.87	16.47
Hyperglycemic hyperthyroidism	44.5	233	219.5	286	1.36	154.84	0.14
Euglycemic subclinical hyperthyroidism	50.50	108.25	341.00	112.25	1.73	114.95	0.11
Hyperglycemic euthyroid	53.06	202.76	146.44	225.11	1.51	106.85	2.50
Eugllycemic euthyroid	42.91	105.59	85.28	118.47	1.55	96.64	2.14

Overall, most common thyroid dysfunction was subclinical hypothyroidism followed by clinical hypothyroidism. [Females (32%) > Males (25%)].Hyperthyroidism was less common.

4. DISCUSSION

The complex interrelationship between diabetes mellitus & thyroid disorders depends primarily on the influence of insulin and thyroid hormones on the metabolism of carbohydrates, proteins, and lipids. Disturbance in blood glucose homeostasis and consistent efforts of the physiological system to rectify the imbalance in carbohydrate metabolism place an overexertion on the endocrine system. Thyroid dysfunction is commonly found in most forms of DM which is associated with advanced age in type 2 diabetes and autoimmune diseases in type 1diabetes. [6]

5'- Adenosine monophosphate activated protein kinase (AMPK) is a central target for modulation of insulin sensitivity and feedback of thyroid hormones associated with appetite and energy expenditure. The hyperglycaemia seen in Type-2 diabetics is known to have negative effects on thyroid function precisely blunting the pituitary TSH response to stimulation by hypothalamic TRH. This may be due to possible alteration of post translational glycosylation of TRH thus affecting the biological activity. It also affects the conversion of T4 to T3 in the peripheral tissue. Marked hyperglycemia causes reversible reduction of the activity and hepatic concentration of T4-5-deiodinase, low serum concentration of T3, elevated levels of reverse T3 and low, normal, or high level of T4. [7,8]

Prevalence of thyroid dysfunction as per our study was 37%.In our study, subclinical hypothyroidism & clinical hypothyroidism were most common & these findings are in accordance with previous studies. Autoimmunity has been

implicated to be the major cause of thyroid-dysfunction associated diabetes mellitus. Although hypothyroidism (Hashimoto's thyroiditis) or thyroid over activity (Graves' disease) has been found to be associated with diabetes mellitus, hypothyroidism is the most common thyroid dysfunction which has greater risk of dyslipidemia and cardiovascular disease. The variations in the observed prevalences in these studies can be attributed to age, sex, racial & methodological differences between the populations studied. Factors such as sedentary lifestyle, dietary modifications, ethnicity, hypertension and obesity have led to a dramatic increase in the incidence of diabetes mellitus.[9, 10, 11]

Insulin, which plays an essential role in cellular uptake of glucose from plasma (including those of the skeletal muscle), is absolutely deficient in type 1 diabetics and relatively deficient in type 2 diabetics.On the contrary, elevated levels of free circulating thyroid hormones (hyperthyroidism) produce hyperglycaemia by causing polyphagia, enhancing glucose absorption from the gastro-intestinal tract, accelerating insulin degradation and stimulating glycogenolysis. Reduced levels of the hormones (hypothyroidism) may cause hypoglycaemia. [12, 13]In this study, we found that there was no association between the glycemic control & thyroid function status. Also, no significant association was found between medications used and thyroid function status. The limitation here is that many other (confounding) variables, notably treatment compliance which influence glycemic control cannot be monitored.

5. CONCLUSION

This pilot study shows thyroid dysfunction in Type-2 diabetes mellitus. Early detection ofabnormal thyroid hormone level in subclinical thyroid patients with type-2 diabetes mellitus may be useful for better management and prevention ofcomplications

6. REFERENCES

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