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Comparative Study of Risk of Development of Diabetes Mellitus in Hypothyroid & Euthyroid Subjects

KEYWORDS

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ABSTRACT *Background : There may be a link between diabetes and thyroid diseases, the American Diabetes Association (ADA) has proposed that people with diabetes be checked for thyroid disorders In the light of the above facts, this work intends to see the possible link of Impaired glucose tolerance with hypothyroid subjects. Objective : To study the oral glucose tolerance test in hypothyroid patients. Methodology :A total of 101 cases – 22 males and 79 females within the age of 21 to 54 years, were included in this study.The blood samples collected from the subjects were analysed for the estimation Serum T3 , T4 ,& fasting & post prandial glucose estimation for OGTT. Data was analysed using appropriate statistical analysisResults:FBS & PPBS levels in hypothyroids show a statistically significant increase (p value 0.003) when compared to Euthyroids. Overall in all hypothyroid cases (n=51) the prevalence of IGT is 49% (n =25) (odds ratio 3.84, P value <0.001)& in all euthyroid controls (n= 50) the prevalence of IGT is 20% (n= 10).Conclusion:Impaired glucose tolerance is found to be more prevalent in hypothyroids. IGT imply that Hypothyroidism are more prone to develop Type 2 DM. Hence, Hypothyroids should be monitored regularly for glucose levels*

Introduction :

The International Diabetes Federation estimates that near 285 million people have known type 2 diabetes: their number will probably double within 20 years[1]. Furthermore, worldwide, the number of persons with prediabetes, defined as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)[2], is estimated to be 314 million and is expected to be 418 million in 2025[3]. This scenario, amplified by the fact that several subjects do not know they have, has a predictable consequence: as the prevalence and progression to type 2 diabetes continues to increase and the afflicted population's age rises, the associated complications of diabetes inevitably will emerge as a major public health care issue[3]. The risk associated with progression to diabetes and cardiovascular complications increases along a continuum, occurs at much lower glucose levels than those required to diagnose diabetes. Consequently, relying exclusively on diabetic glucose level may delay treatment[4], as we need to maximize our efforts in diabetes prevention, detection and early disease management. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "diabetes capital of the world". Most recent studies have projected that by 2030, India will have 79- 87 million adults with diabetes.[6-9]

The influence of endocrine and non-endocrine organs other than pancreas on diabetes mellitus is documented. Thyroid diseases are, among the commonest endocrine disorders worldwide. Thyroid abnormalities may coexist and interact with diabetes mellitus.Worldwide about 42 million people have thyroid dysfunction on various categories in the post iodization phase. In India , thyroid disorders are most common among all endocrine disorders and hypothyroidism being more common than hyperthyroid state and carcinoma thyroid[1]. The incidence of overt hypothyroidism is about 4.1 cases per 1000 women / year and 0.6 cases per 1000 men. The prevalence has been reported to be 1-2% in women and 0.1% in men. Primary hypothyroidism accounts for 99.5% and central and secondary causes account for the remaining 0.5%[10].

The hypo-and hyper-functioning thyroid gland influences carbohydrate metabolism at the levels of pancreatic islets and glucose utilizing target tissues. Excess or deficiency of either insulin or thyroid hormones can result in functional abnormalities of one another, as both of them are closely involved in cellular metabolism. Possibly, thence, diabetes and thyroid disorders have a propensity to appear together in patients. Patients with T2D commonly display the symptoms of hypothyroidism, and symptoms of hyperthyroidism have been documented in patients with type 2 diabetes.[11]

An overall prevalence of 13.4% of thyroid diseases[12] in diabetics with the highest prevalence in type 2 female diabetics (31.4%) and lowest prevalence in type 2 male diabetics (6.9%) has been identified. Recently, a prevalence of 12.3% was reported among Greek diabetic patients and 16% of Saudi patients with type 2 diabetes were found to have thyroid dysfunction. In Jordan, a study reported that thyroid dysfunction was present in 12.5% of type 2 diabetic patients.[7]

Since there may be a link between diabetes and thyroid diseases, the American Diabetes Association (ADA) has proposed that people with diabetes be checked for thyroid disorders [13]Long back, thyroid function was assessed only by clinical examination , Basal metabolic rate (BMR) calculation and total cholesterol estimation. It was the time , when patients with high serum cholesterol concentration were regarded as evidence for 'pre myxoedema' in the absence of symptoms of hypothyroidism, rather than measurement of serum T_4 and TSH. Mild and subclinical hypothyroidisms which were identified only as a biochemical entity gained its importance only in 1990's. Hormone measurement has now assumed a position of pivotal role in practice of scientific medicine.

The OGTT is a provocation test to examine the efficiency of the body to metabolise glucose.[14]The OGTT provides information on latent diabetes states. The OGTT distinguishes metabolically healthy individuals from people with impaired glucose tolerance and those with diabetes. The OGTT is more sensitive than FPG for the diagnosis of diabetes. Nevertheless the final diagnosis of diabetes should not be based on a single 2 h post-load glucose

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>11,1mmol/L (>2,00 g/L) but should be confirmed in subsequent days (FPG and/or casual glucose estimation). The OGTT is more sensitive for the diagnosis of diabetes than fasting plasma glucose. The OGTT is not used for the monitoring of day to day blood glucose control, which is done by HbA1c-, and repeated glucose measurement. The OGTT is used mainly for diagnosis of IGT and in epidemiological population studies, but is not recommended or necessary for routine diagnostic use.[15]In the light of the above facts, this work intends to see the possible link of Impaired glucose tolerance with hypothyroid subjects.So the objectives of the study was to study the oral glucose tolerance test in hypothyroid patients .

Methodology :

The subjects for the present study are selected from the cases referred to department of Biochemistry for valuation of thyroid status and other biochemical parameters from the patients attending various outpatientdepartments . A total of 101 cases – 22 males and 79 females within the age of 21 to 54 years, were included in this study. Internal controls from the study groups (age & gender matched) were contributed by euthyroid subjects from the general population.Hypothyroid patients of age group 20- 50 years were included in the study. Patients with DM ,Pregnant patient ,Post thyroidectomy patients patient with Acute /chronic infections& on any other treatment were excluded from the study. For all cases clinical history was taken, general examination of these patients including weight, height, waist and hip circumference, heart rate, Bp measurement was done and recorded in a structured protocol format.

The fasting blood sample of total 5ml was collected in serum vacationer under aseptic condition. The blood samples collected as above were analysed for the estimation Serum T3, T4 ,TSH by Enzyme Immunoassay method . For OGTT, fasting & post prandial glucose estimation by Glucose Oxidase Peroxidasemethod . Data was analysed using appropriate statistical analysis.

The value for TSH e range from 0.01- 41 µIU/ml. TSH offers the sensitivity of 0.078 µIU/ml. Low normal range-0.39 µIU/ml .High normal range -6.16 µIU/ml

As many studies have given various reference range and classification especially for hypothyroid case, we have adopted the following guideline values given below- Subclinical Hypothyroid Group [TSH> 5µIU/ml ; normal fT_4 and fT_3 Group I - Mild Hypothyroid [TSH 5.0- 10 µIU/ml] . Group II - Moderate Hypothyroid [TSH 10 – 20 µiu/Ml] Group III - Severe Hypothyroid [TSH > 20.0µIU/ml] Control Group with TSH 0.39 – 5.0 µIU/ml] .

Statistical analysis was done using appropriate statistical tests & p value was calculated.

Results :

Table 1: Comparison of FBS levels with Hypothyroid & Euthyroid subjects.

CATEGORY	No.of sample	FBS (mg/dl) MIN MAX	FBS (mg/dl) MEAN ±SD	t-Value	P value
Hypothyroids	51	59 108	85.9 ±9.9	57.45	0.025*
Euthyroids	50	68 106	80.74 ±6.9	44.42	

Table 2: Comparison of PPBS levels with Hypothyroid & Euthyroid subjects

CAT-EGORY	No.of sam-ple	PPBS (mg/dl) MIN MAX	PPBS (mg/dl) MEAN ± SD	t-Value	P value
Hypothy-roids	51	83 188	141.8 ± 23.2	59.47	0.003**
Euthyroids	50	80 186	126.1 ± 17.1	42.36	

FBS & PPBS levels in hypothyroids show a statistically significant increase (p value 0.003) when compared to Euthyroids.

TABLE 3: Comparison of OGTT withHypothyriod& Euthyroid group

GROUPS [TSH in µ IU/ml] (n)	TSH [µ IU/ml] Mean ±SD (Range)	FBS [in mg/ dl] Mean ±SD (Range)	PPBS [in mg/dl] Mean ±SD (Range)	IGT [FBS<126mg/ dl PPBS <140mg/ dl upto 199 mg/dl] n (%)	Odds ratio	P value
Cases (51)	18.18 ±12.03 (5.23 to 66.9)	85.9 ± 9.9 (59 – 108)	141.8 ± 23.2 (83 – 194)	25(49%)	3.84	<0.001*
Controls [0.39- 5.0] (50)	2.23 ± 0.62 (0.4 to 4.6)	80.74 ± 6.9 (68-106)	126.1 ± 17.1 (80 – 186)	10 (20%)		

(* - significant)

Overall in all hypothyroid cases (n=51) the prevalence of IGT is 49% (n =25) (odds ratio 3.84, P value <0.001)& in all euthyroid controls (n= 50) the prevalence of IGT is 20% (n= 10)

Discussion :

In our study, fasting blood glucose levels in all hypothyroid cases (n=51) and euthyroids (n = 50) are in normal reference range (less than 110 mg/dl).

Among all hypothyroid cases (n=51) , 26 had PPBS levels in normal range (less than 140 mg/dl). 25 (49%) had PPBS in Impaired Glucose Tolerance range (≥140 mg/dl to <200 mg/dl) Amongeuthyroids (n=50), 40 were in normal range and 10 (20%) in Impaired Glucose Tolerance range based on PPBS values. Prevalence of IGT is observed to be high in hypothyroids than in euthyroids (49% in hypothyroids , 20% in euthyroids) With increasing severity of hypothyroidism there is an increase in prevalence of IGT. Based on PPBS levels 35% of Mild hypothyroids(7/20), 57% of Moderate hypothyroids (8/14), and 67% of severe hypothyroids (8/12) has Impaired Glucose Tolerance.

In Subclinical hypothyroids there is an increased prevalence of IGT (0%) which is more than Mild hypothyroids (35%). Hypothyroids with IGT are found to be in an younger age group (mean age of 36.9 yrs) when compared to euthyroids with IGT (mean age 39.2 yrs). In hypothyroid cases, with advancing age an increased prevalence of IGT is observed. In euthyroids this age related increase in prev-

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alence of IGT is not observed.[16,17]

Conclusion :Impaired glucose tolerance is found to be more prevalent in hypothyroids. They are also found to have IGT imply that Hypothyroids are more prone to develop Type 2 DM. Hence, Hypothyroids should be monitored regularly for glucose levels.

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