Correlation study between body mass index, body fat, glycemic indices and lipid profile with insulin resistence and secretion in healthy euthyroid individuals

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Abstract

Introduction: Insulin resistance and secretion are highly dependent on variable influencing factors, in the developmental process of Diabetes mellitus. Growing incidence of diabetes prompt us to study the various contributing factors in the development of Diabetes mellitus in healthy individuals.

Objective: To study the relationship associated between anthropometric measurements, plasma lipids, glycemic indices, thyroid stimulating hormone with Insulin resistance and secretion in healthy individuals.

Materials and Methods: A cross-sectional study was conducted in normal healthy individuals, from general population.(n=142).Body mass index, body fat, were measured, Glycemic indices, fasting glucose, post prondial glucose, Glycated hemoglobin, fasting insulin levels, Thyroid stimulating hormone, fasting lipid profile were analysed.

Result: Insulin resistance (HOMA IR) is positively correlated with Glycemic indices (FBS, PPBG, HbA1C) $P<0.05$, Body mass index $P<0.05$, Body fat $P<0.05$, and Cholesterol/HDL ratio. Serum Thyroid Stimulating Hormone (TSH) $P<0.05$ is negatively associated with Insulin Secretion. Glycemic Indices, Triacylglycerol, cholesterol, LDL are negatively correlated with Insulin Secretion.

Conclusions: Glycemic indices, body mass index, body fat and lipid profile are intrinsically related to Insulin resistance and Insulin secretion. Increased TSH is associated with decreased insulin secretion leading to increase blood glucose levels, which indicates that thyroid hormone is important for pro insulin expression and translation, providing the evidence that, effects of thyroid hormones on carbohydrate metabolism also include the control of proinsulin gene expression, the possible role of thyroid hormones on insulin secretion.

Keywords: FBS: Fasting blood sugar, **HbA1C:** Glycated Haemoglobin, **HOMA IR:** Homeostatic Model Assessment –Insulin Resistance, **HOMA-B:** Homeostatic Model Assessment- Beta cell secretion, **TSH:** Thyroid Stimulating Hormone, **PPBG** – Post Prondial Blood Glucose.

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Introduction

Diabetes Mellitus and thyroid dysfunction are the two most common endocrine disorders prevalent world wide and in India. According to International Diabetes Federation,[1] around 415 million people suffer with DM in 2015 and the number expected to increase by 642 million by 2040. Among that India having 69.1 million diabetes mellitus patients, estimated to have second largest number of DM cases in the world after china. The prevalence of diabetes in India ranges from 5–17%, with higher levels found in the southern part of the country and in urban areas.[2-7] Similarly it has been estimated from various studies that about 42 million people in India suffer from thyroid diseases.[8]

Thyroid hormones play an important role in the metabolism of carbohydrates, lipids and proteins.[9] Thyroid hormones stimulate hepatic gluconeogenesis and glycogenolysis and upregulate the expression of genes of glucose transporters (GLUT-4) and phosphoglycerate kinase, involved in glucose transport and glycolysis respectively, thus acting synergistically with insulin and facilitates glucose uptake and utilisation in peripheral tissues. Studies found, high prevalence of thyroid disease in patients with diabetes mellitus indicating a possible interrelationship between thyroid status and insulin resistance.[10-14]

Homeostatic model assessment (HOMA) is a method for assessing β-cell function and insulin resistance (IR) from basal (fasting) glucose and insulin.[15] In the light of the existing reports, we decided to evaluate the correlation between IR and thyroid state in normal healthy euthyroidsand to assess β-cell function and IR by HOMA-IR.

Materials and Methods

Across-sectional study done in 142 healthy controls,between the age group of 20 to 50 years. Divided into two age groups younger group between 20 – 35 yearsand older group between 36 to 50 years (Table:1). All the subjects selected were non diabetic and euthyroid, were enrolled after informed consent was obtained, and thorough physical and medical examination was done to rule out any acute or chronic systemic illness. Oral glucose tolerance tests and HbA1c tests were performed to rule out diabetes. Body mass index and body fat were calculated based on the anthropometric measurements.

Table: 1

Group	Age in years	Number
Younger group	20 - 35	75
Older group	36 - 50	67
Total		142

The study was performed in department of Biochemistry. Shadan Institute of Medical Sciences, Teaching hospital and Research Centre, Hyderabad.

Collection of blood sample

Under aseptic conditions, Fasting blood sample (6 ml) were drawn from antecubital veins of all the subjects. 2 ml of blood sample was collected in EDTA vacutainers for HbA1C, 3 ml of blood sample was transferred into plain vacutainer was allowed to clot for 30 minutes and then centrifuged at 2000 rpm for 15 minutes for clear separation of serum.1ml fasting and 1ml post prandial blood samples are collected in fluoride vacutainers for glucose estimation. Serum was taken for the analysis of Thyroid stimulating hormone, Insulin, Triglycerides, total Cholesterol, HDL-cholesterol and LDL cholestrerol.

Insulin and Thyroid stimulating hormone were measured by Chemiluminisence Immune Assay (CLIA) method, HbA1C by HPLC method, glucose by glucose oxidase and peroxides (GOD-POD) method and Triglycerides, total Cholesterol, HDL-cholesterol and LDL cholestrerol were analysed by Enzymatic colorimetric assay method. HOMA IR and HOMA B were calculated from fasting sugar and fasting insulin levels. HOMA IR=fasting insulin (μIU/ml) multiplied by fasting glucose (mmol/L) divided by 22.5 and HOMA B=20 multiplied by fasting insulin (μIU/ml)-3.5 divided by fasting glucose (mmol/L) (15).

Statistical analysis

All values of analysed parameters were expressed as mean ± SD. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS/PC; SPSS-9, Chicago, USA). Pearson's correlation was applied to correlate between the parameters. A p value of <0.05 was considered statistically significant.

Results

On pearson correlation of the parameters within the health control group we found Insulin resistance (HOMA IR) is positively correlated ($p<0.05$)with Body mass index, body fat, Glycemic indices (Fasting blood sugar, Post Prondial blood sugar and Glycated hemoglobin and Total cholesterol.

Insulin secretion (HOMA B) is negatively correlated ($p<0.05$) with Thyroid stimulating hormone, Glycemic indices(Fasting blood sugar,Post Prondial blood sugar and Glycated hemoglobin.) and triglyceride, cholesterol and LDL cholesterol.

On Comparison between age groups 20-35years (n=75) and 36-50 years (n=67), TSH, FBS and PPBG is significantly increased and HOMA B is decreased in higher age group compared to younger age group. Indicating a significant relationship between increased thyroid stimulating hormone and decreased insulin secretion and increased glycemic indices.

Table 1: Descriptives

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
BMI	142	22.817	2.8986	.2432	22.336	23.298	16.0	27.7
BODY FAT	142	23.42	5.5	.467	22.515	24.324	15.46	35.18
FBS	142	83.42	8.485	.712	82.01	84.83	70	100

PPBG	142	124.35	17.724	1.487	121.41	127.29	94	157
HbA1C	142	5.710	.6228	.0523	5.607	5.813	4.5	6.9
TSH	142	2.286	1.3852	.1162	2.056	2.516	.4	6.0
TAG	142	83.37	26.290	2.206	79.00	87.73	37	148
Cholesterol	142	140.04	27.898	2.341	135.41	144.67	90	225
HDL	142	42.32	7.147	.600	41.14	43.51	28	56
LDL	142	79.02	24.118	2.024	75.02	83.02	27	151
VLDL	142	16.679	5.2836	.4434	15.802	17.555	7.4	30.0
Ratio: cholestero/ HDL	142	3.320	.6690	.0561	3.209	3.431	2.0	5.0
LDL : HDL	142	1.862	.5707	.0479	1.768	1.957	.5	3.2
Homa IR	142	1.7831	.63294	.05312	1.6781	1.8881	.63	3.00
HomaB	142	176.90	76.209	6.395	164.26	189.54	81	520

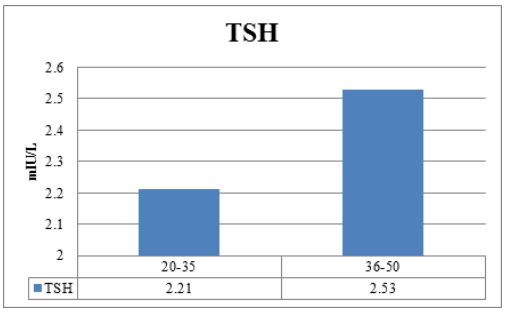

Fig. 1: TSH

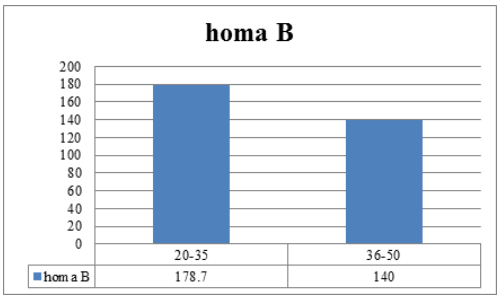

Fig. 2: homa B

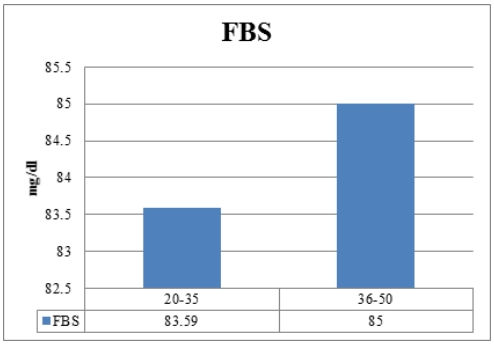

Fig. 3: FBS

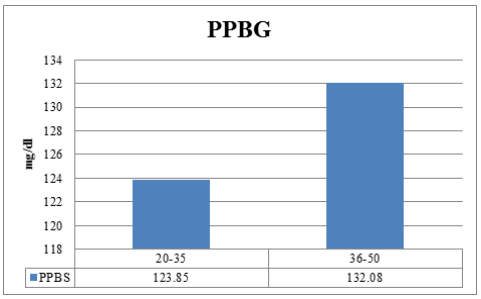

Fig. 4: PPBG

On comparison with younger age group (20-35years) TSH is elevated ($p<0.001$) in older age group(36-50years), associated with significant decrease($p<0.001$) in Insulin secretion (HOMA B) and significant increase($p<0.001$) in Fasting and postprondial blood glucose levels.

Discussion

The present study shows that thyroid hormones have significant role on insulin secretion in normal healthy euthyroid individuals. In comparison to other contrasting studies, where in one study T3 levels were found to enhance proinsulin mRNA levels during beta cell differentiation in pancreas from human duct cell line(hPANC-1), and in another study opposite effects were found where T3 and T4 levels leading to decrease in proinsulin gene expression inRIN-m54 cells and pancreatic beta cells of rat.[16-18] In our study we found with in physiological range TSH is negatively correlated with insulin secretion. Indicating the possible role of thyroid function in Insulin secretion.

On comparison of different age groups, we found older age group (36-50years) have reduced insulin secretion and increase TSH levels compared to the younger age group (20-35years). Where both age and TSH have profound impact on the insulin secretion. Inturn old age group is

associated with increase in fasting and postprandial blood glucose levels with in physiological reference ranges, but no significant difference is found in glycated haemoglobin levels.

Thyroid hormone plays an important role in cholesterol synthesis, uptake, lipoprotein metabolism and lipolysis by inducing the expression of different enzymes.[19-21] In the present study we correlated TSH and Lipid profile with in normal healthy individuals, results found that TSH is negatively correlated with High density lipoprotein indicating the direct relation between thyroid hormones and HDL metabolism. Thyroid hormones influence high density lipoprotein metabolism by increasing cholesteryl ester transfer protein (CETP) activity, which exchanges cholesteryl esters from HDL2 to the very low density lipoproteins (VLDL) and TGs to the opposite direction. Studies in subclinical hypothyroidism have shown that TSH is positively correlated with all the lipid parameters, indicating the risk of atherosclerosis and myocardial infarction in subclinical hypothyroidism.[20] Decreased thyroid function results in reduction of cell surface receptor for LDL and decrease in there activity leading the decrease in LDL and IDL catabolism and subsequent increase in Total cholesterol and LDL concentration, Decreased thyroid function also leads to decrease activity of hepatic lipase associated with increased levels of VLDL and high TG concentration.

The effects of variation in body mass index (BMI; kg/m2) and body fat on insulin resistance and secretion were determined in a group of nonobese non-diabetics healthy individuals. Our results show that BMI and body fat have positive associations with insulin resistance estimated by HOMA-IR a tool to estimate insulin sensitivity, which is closely correlated with the insulin resistance index as assessed by the euglycemic clamp. But no significant correlation was found with Insulin secretion HOMA-B.

Studies have shown that many endocrine, inflammatory, neural, and cell-intrinsic pathways functional in various metabolic tissues- fat, liver and muscle, were dysregulated in obesity, underlies the pathophysiology of insulin resistance.[22] Endocrine factors like fatty acids, elevated in obese individuals impairs insulin signalling by increasing the inhibitory serine phosphorylation of insulin receptor substrate leading to insulin resistance. Similarly increased levels of inflammatory markers like interlukin-6 and tumour necrosis factor alpha in obesity implicated in the pathogenesis of type 2 diabetes mellitus.Accumulation of lipids also leads generation of Reactive oxygen species leading to the activation of serine/ threonine kinases which inhibit insulin signalling. When one pathway is disturbed, its Most of the metabolic pathways are interconnected, when one pathway is disturbed it leads to changes in other systems that exacerbate the problem.[22] Our study shows that BMI and Body fat are positively associated with insulin resistance, indicating the possible role of endocrine, neuro and inflammatory markers in the pathophysiology of insulin Resistance.

Similar to other studies, In the present study in normal healthy individuals, we found Glycemic indices: Fasting, post prandial blood sugars and glycated haemoglobin are positively correlated with insulin resistanceand negatively correlated with insulin secretion.Insulin resistance is defined as a state of decreased ability of insulin to stimulate the uptake and metabolism of glucose in target cells at physiological concentration. Leading to hyperglycemia and development of type 2 diabetes mellitus. As discussed the various factors leading to insulin resistance, including lipid profile, BMI, body fat, endocrine, inflammatory and neuro pathways, we observed in our study insulin resistance positively correlated with glycemic indices, as insulin resistance increases beta cells compensate by increasing insulin secretion, resulting in compensatory hyperinsulinemia and maintenance of normal glucose tolerance. As we found in our study Increase in insulin resistance is leading to increase in glycemic indices, compensated by increased insulin secretion.

Conclusion

1. Body mass index, Body fat and lipid profile do have a direct correlation with insulin resistance and secretion, even in normal healthy individuals. It's important to regularly monitor these parameters by normal healthy individuals to prevent the onset of early Diabetes mellitus.
2. With Increase in age we found there is increase in TSH leading to decrease insulin secretion, with in physiological ranges. This observation is highly relevant in population with high prevalence of Thyroid disorders, and prompt us to question, individuals with hypothyroidism should be assessed for their glycemic indices.

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