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"A Comparative Study of Serum Insulin Levels and Insulin Resistance in Patients Suffering with Hypothyroidism and Healthy Controls"

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Abstract

Background Glucose homeostasis is influenced by thyroid hormones and this homeostasis is disturbed in hypothyroidism which further results in insulin resistance.

Aim and Objectives Present study was conducted to evaluate the levels of fasting blood glucose, fasting insulin levels and insulin resistance in diagnosed female hypothyroid patients and normal controls.

Materials and Methods

The current study was a hospital based observational cross sectional study which was conducted in the department of Biochemistry in collaboration with department of Medicine, Faculty of Medicine and Health Sciences, SGT University, Gurugram, Haryana. Study was conducted on total 160 subjects. Among these 80 hypothyroid females were taken as cases and 80 age matched healthy individuals as controls. Fasting blood samples were collected from all subjects included in the study and evaluated for fasting plasma glucose, fasting Insulin and thyroid profile (FT3, FT4 and TSH). Fasting Insulin and thyroid profile were estimated by chemiluminescence immunoassay (CLIA) on MAGLUMI 1000 fully autoanalyser. Fasting blood glucose was estimated by glucose oxidase-peroxidase (GOD-POD) method on Erba 360 fully autoanalyser. Insulin resistance was estimated Insulin resistance was calculated by homeostatic model index (HOMA IR=fasting insulin (µIU/ml) x fasting glucose (mg/dl) /405). Results were subjected to statistical evaluation and presented as mean ± SD. P value (≤ 0.05) was considered as statistically significant.

Results:

It was observed that the mean age ± SD of cases was 34.01 ± 8.28 years and for controls it was 32.59 ± 7.76 years with no significant difference. The mean serum TSH, fasting glucose, fasting insulin and insulin resistance were significantly increased ($p<0.001$) in hypothyroid patients compared to controls. In contrast the mean serum FT3 and FT4 were significantly ($p<0.001$) in patients compared to controls. It was also observed that there was a

significant positive correlation (r = 0.846) between serum TSH levels and Insulin resistance in hypothyroid patients.

Conclusion: The results demonstrated that hypothyroidism was associated with increased insulin levels and insulin resistance.

Keywords: Hypothyroidism, Thyroid stimulating hormone (TSH), Insulin resistance

Introduction

Approximately 42 million people in India suffer with thyroid diseases. The prevalence of overt hypothyroidism and sub-clinical hypothyroidism is 3.9 % and 9.4 % respectively.[1] The risk of hypothyroidism in females (15.8%) is approximately three times more in comparison to the males (5.01%).[1] Clinical symptoms of hypothyroidism are non specific and may be subtle, especially in older persons.[2]

Thyroid gland synthesizes and secretes thyroid hormones that have influence on basal metabolic activities. It controls development, growth, metabolism and maintenance of the internal environment of the body. Functional abnormalities of thyroid gland can be categorized as hypothyroidism and hyperthyroidism. Hypothyroidism is an endocrine disorder, arises due to the failure of thyroid gland to secret adequate amount of thyroid hormones to meet the metabolic demands of the body or insufficient stimulation by the pituitary gland or hypothalamus.[3]

Regulation of blood glucose level is supported by thyroid hormones. Thyroid hormones behave as both insulin agonist and antagonist. Thyroid hormones and insulin show collaborative role in maintenance of glucose homeostasis. Thyroid hormones play very important part in the metabolism of carbohydrates by stimulating the different processes such as gluconeogenesis, glycogenolysis and by upregulating the expression of glucose transporter (GLUT-4) and phosphoglycerate kinase. Thyroid hormones act collectively to insulin by assisting glucose uptake and its utilisation in peripheral tissues. [4-7]

To maintain glucose homeostasis in the body, pancreatic β cells increase insulin secretion, leading to chronic hyperinsulinemia. The equilibrium is disturbed in hypothyroidism and alter the glucose metabolism, which further results in insulin resistance.[8] Insulin resistance is the major patho-physiological phenomenon that is responsible for other metabolic disorders.[9]

Insulin Resistance, can be concluded as reduced hepatic and peripheral tissues response for the existing insulin hormone in comparison to the normal healthy individual.[10-11]The reduced sensitivity to insulin can be determined by the diminished insulin dependent absorption of glucose by cells and tissues.[12]

Several studies were conducted to establish a connection between hypothyroidism and effects of insulin on glucose homeostasis.[13-16] In few studies no significant difference in insulin levels and HOMA IR was observed comparing hypothyroids with the normal individuals.[15]

Hence this study was performed to determine the serum insulin level and insulin resistance in female hypothyroid patients and to find out the correlation between insulin resistance and thyroid stimulating hormone.

Materials and Methods

The present study was a hospital based observational cross sectional study which was conducted in the department of Biochemistry in collaboration with department of Medicine, Faculty of Medicine and Health Sciences, SGT University, Gurugram, Haryana. Study was conducted on total 160 subjects. Among these 80 hypothyroid females were taken as cases and 80 age matched healthy individuals as controls. Fasting blood samples were collected from all subjects included in the study and evaluated for fasting blood glucose, fasting Insulin and thyroid profile (FT3, FT4 and TSH).

Inclusion criteria: Female patients of the age between 20-50 years attending Medicine OPD of SGT Hospital and diagnosed with hypothyroidism based on clinical examination and Laboratory findings were included in the study.(TSH >5mIU/L and/or decreased levels of FT3 and FT4).[16]

Exclusion criteria: Alcoholics and/ or chronic smoker, patients taking vitamin D supplements, pregnant and lactating women were excluded from the study.

The study was carried out after permission of Institution's ethics committee and informed consent was obtained from all the participants. Under strict aseptic conditions and 12 hours of fasting, 7 ml of venous blood sample was collected into properly labeled plain polystyrene tubes for insulin and thyroid hormone estimation and sodium fluoride tubes for blood glucose estimation. Fasting blood glucose was estimated by glucose oxidase- peroxidase (GOD-POD) method on Erba 360 fully autoanalyser within 2 hours of collection. Serum for thyroid hormones (TSH, FT3, and FT4) and insulin estimation were collected in vials and stored at -20°C till the analysis. The analysis was done in batches. Frozen samples were thawed to room temperature before analysis.

Thyroid profile was estimated by chemiluminescence immunoassay (CLIA) on MAGLUMI 1000 fully autoanalyzer. The reference range for serum FT3, FT4 and TSH in an apparently healthy individual were (2.0 - 4.2 pg/ml), (0.79 – 2.44 ng/dl) and 0.465 – 4.68 µU/ml respectively.

The serum insulin was estimated by sandwich immunoassay using direct chemiluminiscence technology which uses constant amount of two antibodies, on fully automated Maglumi 1000. The reference range for apparently healthy individual was 4.03 – 23.46 µU/ml.

Insulin resistance (IR) was calculated from Homeostatic model assessment (HOMA- IR), method for assessing β-cell function and peripheral insulin resistance from fasting insulin and glucose concentrations.[17] HOMA-IR = Insulin (µU/ml) × Glucose (mmol/L)/22.5)[18] or fasting insulin (µIU/ml) x fasting glucose (mg/dl) /405).

Statistical Analysis

The data was collected, tabulated and calculated on MS excel work sheet and analysis was carried out using SPSS (Statistical Software version 20). Mean and Standard Deviation of continuous variables were calculated. Data were analyzed using independent student't' test for their level of significance. Correlation between serum TSH and insulin resistance was evaluated using Pearson's coefficient of correlation. In results, p value <0.05 was considered statistically significant.

Observations and Results

Biochemical parameters including serum FT3, FT4, TSH, fasting blood sugar and insulin levels in hypothyroid female patients and healthy controls were compared in the present study. Results obtained were presented as mean ± SD and for the level of significance.

Table 1 shows the demographic details and anthropometric parameters of the study subjects. The mean age ± SD of patients was 34.01 ± 8.28 years and for the controls it was 32.59 ± 7.76 years. There was no significant difference with respect to age distribution in cases and controls (p=0.263, Table 1).

Table 1. Mean and SD of anthropometric parameters in patients suffering with hypothyroidism and in controls.

Parameters	**Patients** **Mean ± SD**	**Control** **Mean ± SD**	**P value**	**Statistical Significance**
Age (years)	34.01 ± 8.28	32.59 ± 7.76	0.263	Not Significant
Weight (Kgs)	61.61 ± 5.87	54.1 ± 4.79	<0.001	Significant
BMI (kg/m^2)	26.02 ± 2.21	21.54 ± 1.6	<0.001	Significant

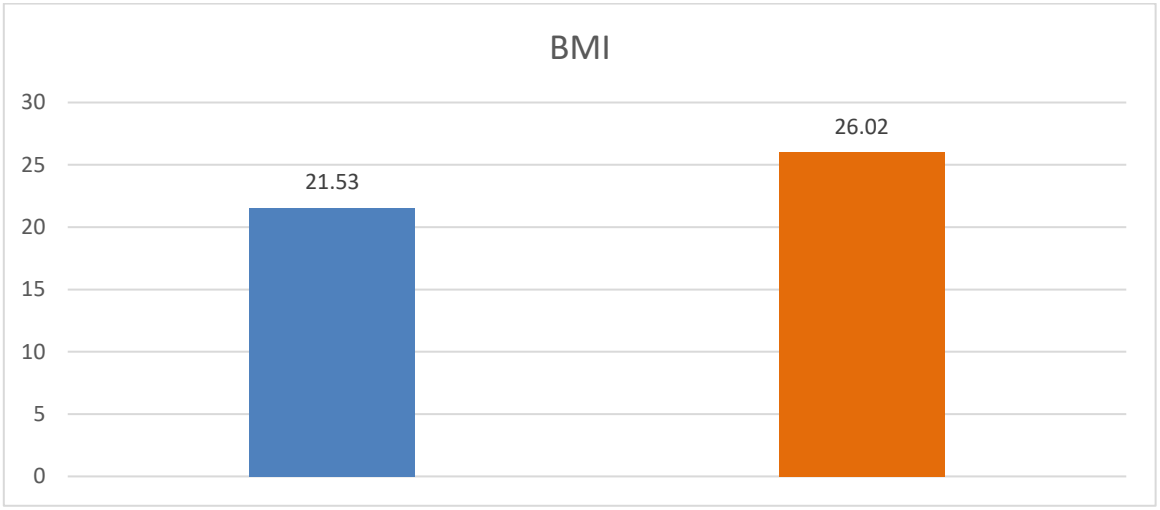

Figure 1. Graph representing Body mass index (BMI) of patients with hypothyroidism and control

Table 2 shows the comparison of the mean levels of FT3, FT4, Thyroid stimulating hormone (TSH), fasting insulin and insulin resistance between the cases and controls. The level of serum thyroid stimulating hormone was found to be significantly higher in hypothyroid patients in comparison to healthy females. It was observed that the mean TSH of hypothyroid patients and controls was 15.75 ± 13.96 µIU/ml and 3.02 ± 0.78 µIU/ml respectively. The comparison of serum TSH levels between two groups were statistically significant with P value (<0.001). In contrast the levels of serum FT3 and FT4 were significantly decreased in patients in comparison to controls.

The level of fasting plasma glucose and fasting insulin were found to be significantly higher in hypothyroid patients in comparison to healthy females. The mean fasting insulin level was (10.25 µIU/ml) in patients and it was (7.1 µIU/ml) in controls. Insulin resistance was calculated and was found to be significantly increased in patients 2.46 ± 1.17 than controls 1.4 ± 1.17 with the p value (<0.001).

Table 2. Comparison of biochemical parameters between patients with hypothyroidism and controls.

Parameters	**Cases** **Mean ± SD**	**Controls** **Mean ± SD**	**P value**
FT3 (pg/ml)	2.43 ± 0.55	2.78 ± 0.52	<0.001
FT4 (ng/dl)	1.14 ± 0.13	1.35 ± 0.2	<0.001
TSH (µIU/ml)	15.75 ± 13.96	3.02 ± 0.78	<0.001
FBS (mg/dl)	94.14 ± 13.03	78.7 ± 11.74	<0.001
Fasting Insulin(µIU/ml)	10.26 ± 3.58	7.11 ± 1.26	<0.001
Insulin resistance	2.46 ± 1.17	1.4 ± 1.17	<0.001

P value (≤ 0.05) is considered statistically significant

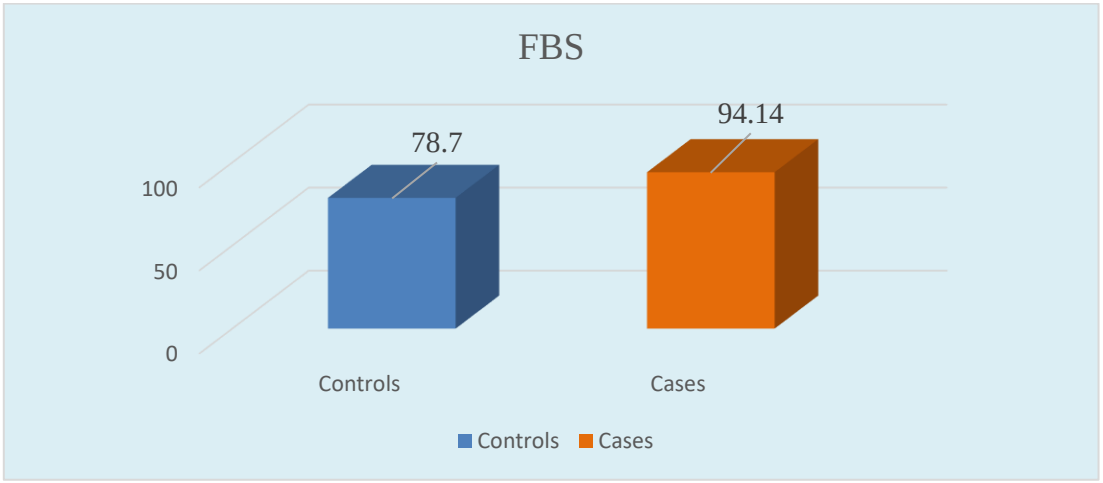

Figure 2. Graph representing fasting blood glucose in patients and controls.

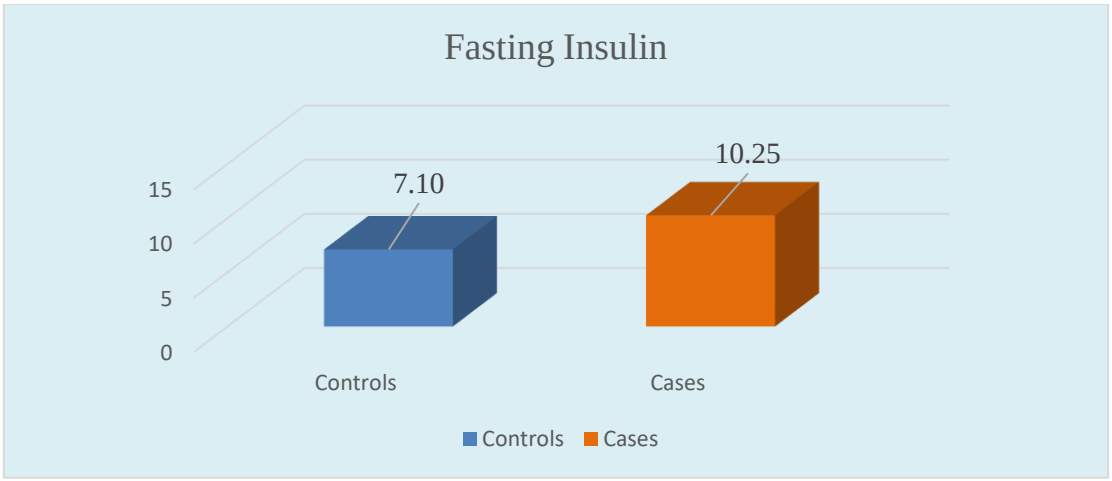

Figure 3. Graph representing fasting Insulin in patients and controls.

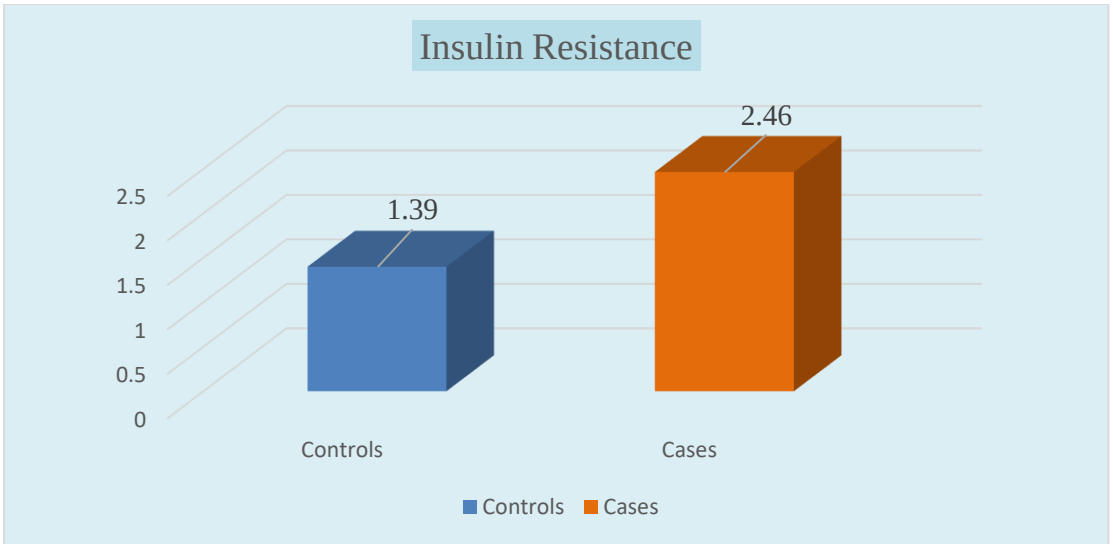

Figure 4. Graph representing comparison of insulin resistance in patients and controls.

Correlation Analysis

Significant correlation was found between serum thyroid stimulating hormone and insulin resistance. Insulin resistance showed positive correlation with serum TSH and it was found statistically significant (r = 0.846, p <0.001).

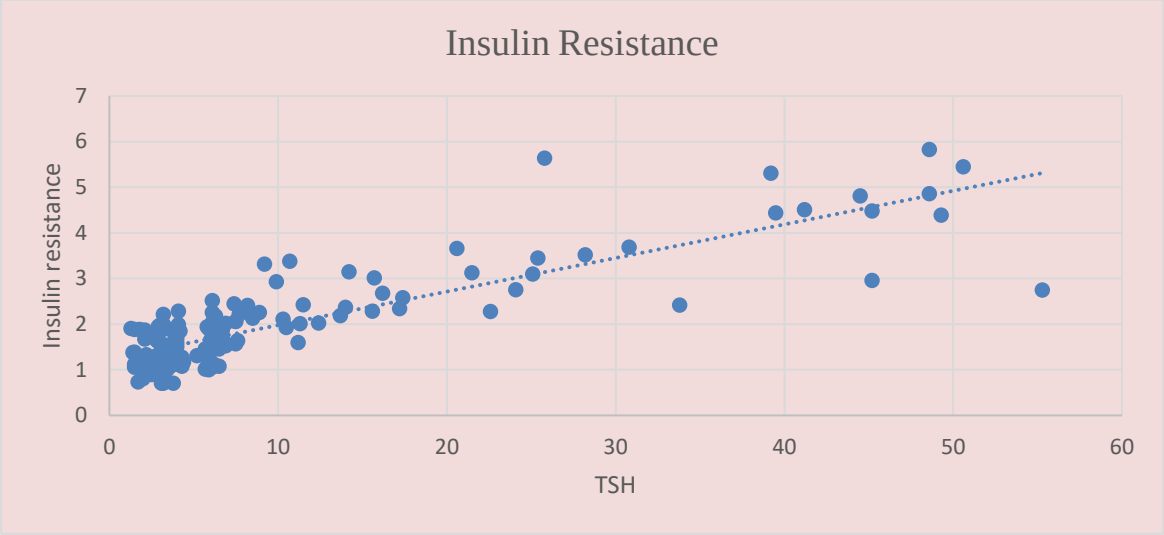

Figure 5.Scatter plot graph showing Pearson's correlation between Insulin resistance and serum thyroid stimulating hormone

Discussion

The present study intended to determine whether there was a link between hypothyroidism and insulin resistance. Our study suggested a strong association of insulin resistance with thyroid dysfunction. Hypothyroidism may lead to adverse effects on glucose metabolism and further leads to alteration in several other biochemical parameters that may be a cause of other abnormalities. Hypothyroidism results in impairment in glucose absorption from the gastrointestinal tract, delay in peripheral glucose assimilation and gluconeogenesis.[19] Insulin resistance is thought to be associated with decreased glucose disposal, a result of decreased skeletal muscle and adipose tissue sensitivity to insulin.[20-21]

Hypothyroidism is associated with insulin resistance and glucose intolerance and treatment of hypothyroidism returns to euthyroid state is associated with improved insulin sensitivity.[22-23]

Thyroid dysfunction is responsible for alteration in glucose metabolism and it further increases the risk for cardiovascular disorders.

Lekakis et al suggested that insulin resistance in hypothyroidism is due to impairment in flow mediated endothelial vasodilatation.[24] In a research study conducted on patients with sub clinical hypothyroidism, significantly high levels of insulin were found, where as HOMA-IR was statistically insignificant.[15]

Vyakaranam S et al in their study, measured the serum insulin levels and insulin resistance (HOMA IR) in subclinical hypothyroidism. They reported insulin levels and HOMA-IR were significantly higher in patients when compared with euthyroids. A positive correlation was observed for TSH with insulin and HOMA IR. Also, thyroid hormones (FT3 & FT4) had negative correlation with insulin and HOMA- IR -which indicates, lower thyroid hormones in plasma lowers the sensitivity of tissues to insulin.[25]

Sayed et al in his study found significantly higher insulin levels in SCH when compared with controls, where as HOMA-IR was not statistically significant.[26] In our study insulin resistance was found to be significantly increased in patients 2.46 ± 1.17 than controls 1.4 ± 1.17 with the p value (<0.001). Similar results were observed by Shaik et al**,** they conducted a study on patients diagnosed with subclinical hypothyroidism and compared it

with euthyroids. They observed that HOMA IR was increased in patients as it was 3.10 ± 1.05 in patients and 1.78 ± 0.63 in controls. The increase was statistically significant ($p<0.001$).[27]

Conclusion

According to our findings the majority of hypothyroid patients shown increased insulin resistance. Further, there was a significant relationship between insulin resistance and TSH. Thyroid dysfunction is responsible for alteration in glucose metabolism and it further increases the risk for cardiovascular disorders. We may conclude that insulin resistance is associated to hypothyroidism and their measurement could be beneficial in the monitoring of the patients. Estimation of these parameters may provide useful information in the prognosis of the disease.

Source of Funding

None

Conflict of Interest

The authors declare no conflict of interest

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