Comparison of Insulin Sensitivity in Subclinical and Overt Hypothyroidism

Anusha Kini¹, Anupama Hegde²*, Jaseem T³, Satish Rao⁴, Neelam M Pawar⁵

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ABSTRACT
Objective: To assess the association of thyroid hormone levels with insulin sensitivity in patients with subclinical (SCH) and overt hypothyroidism (OH).

Materials and methods: The present cross-sectional case-control study observed the association of thyroid hormone levels with insulin sensitivity in patients with SCH and OH as compared to their age-matched controls with euthyroidism (ET). Thyroid profile status, fasting blood sugar and triglyceride level, and basic anthropometric measurements were noted. Fasting insulin level (FIL) was analyzed using serum. Body mass index (BMI) and quantitative insulin sensitivity check index (QUICKI) were calculated.

Results: Insulin levels were found to be significantly increased ($p=0.038$) in patients with SCH as well as those with OH when compared with age-matched ET controls. Insulin sensitivity index (ISI) was comparable among the subjects of the three groups.

Conclusion: Subclinical hypothyroidism (SCH) and OH had high insulin levels but without statistically significant association between thyroid-stimulating hormone (TSH) levels and QUICKI.

INTRODUCTION
Insulin resistance (IR) and dyslipidemia are key to the pathological health complications associated with thyroid disorders.¹⁻⁶ It is established that clinical hypothyroidism is considered an insulin-resistant state,⁷⁻⁸ but the exact mechanism connecting hypothyroidism to IR and dyslipidemia is a matter of research.⁹

Thyroid hormonal dysregulation influences glucose metabolism by furthering the progress of IR or blunting insulin sensitivity. In hyperthyroidism, IR affecting the liver results in impaired glucose tolerance, whereas influencing the peripheral tissues prevails in hypothyroidism.⁶,¹⁰,¹¹

Finding a correlation of thyroid profile parameters with insulin sensitivity in patients with SCH and overt hypothyroidism (OH) was the aim of this study (Fig. 1). Fasting insulin level (FIL) and quantitative insulin sensitivity check index (QUICKI) were used as surrogate indices for assessing insulin sensitivity.

MATERIALS AND METHODS
Study Design
This observational cross-sectional case-control study was conducted at the Center of Basic Sciences, Biochemistry and Department of Medicine, KMC Hospitals, Mangaluru, Karnataka, India, over 4 months duration. Institutional ethical clearance was obtained. Fasting glucose, lipid profile, and thyroid function levels of patients aged between 20 and 60 years who came for routine biochemical tests were noted. Leftover fasting serum samples collected for the routine biochemical tests were preserved suitably and used for insulin assay only after obtaining informed consent. QUICKI was calculated from fasting plasma glucose (FPG) and insulin.

Relevant demographic patient data and history details were recorded. Waist circumference (WC), weight, and height were noted. On the basis of thyroid profile values and inclusion criteria, subjects were assigned to euthyroid, SCH, and OH groups.

This study involved 105 study subjects with the following thyroid status: euthyroid ($n=35$), SCH ($n=35$), and OH ($n=27$).

Patients on lipid-lowering drugs/antihypertensives/being treated for endocrinopathies/diabetes mellitus/past thyroid disorder, on treatment altering thyroid function were excluded, including pregnant/lactating women.

Sample Collection and Analysis
Fasting glucose, triglyceride, and thyroid function tests [thyroid-stimulating hormone

Fig. 1: Correlation of TSH with ISI

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(TSH), thyroxine (T4), and triiodothyronine (T3) levels analyzed for routine biochemical tests on Roche COBAS 6000 by hexokinase, enzymatic colorimetric, and electrochemiluminescence immunoassay methods, respectively, were noted from electronic laboratory reports. Serum samples were stored at −20°C in a refrigerator, and fasting serum insulin was estimated by enzyme-linked immunosorbent assay (DRG kit, solid phase).

Anthropometric Measurements

Height, weight, and WC were measured. Body mass index (BMI) was calculated using the formula—weight in kilograms/height in meters².

Insulin sensitivity was calculated using QUICKI method with the following formula:

\[
\text{QUICKI} = \frac{1}{\log I_0(\muU/ml) + \log G_0(\text{mg/dL})}
\]

Where \(I_0\) is fasting insulin, and \(G_0\) is fasting glucose.

A QUICKI of >0.4 is treated as normal, and a decline in values indicates a decline in insulin sensitivity or the presence of IR.

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 17.0 software. Normally, distributed data are presented as mean ± standard deviation (SD). Differences between the means were analyzed by one-way analysis of variance. Tukey’s test analyzes differences in baseline characteristics between the study groups and the control group. \(p < 0.05\) was considered statistically significant.

RESULTS

Both T3 and T4 were significantly decreased \((p ≤ 0.05)\) in OH. TSH was significantly higher \((p < 0.005)\) in OH and SCH groups. A statistically significant increase was observed in insulin values of OH (Tables 1 and 2).

Bivariate correlation across different categories of thyroid status [euthyroidism (ET), SCH, OH] was done between thyroid hormones (T3, T4, and TSH) and with insulin sensitivity and triglycerides (TG). In the OH group, T3 was significantly negatively correlated with TG \((r = -0.386, p = 0.047)\). In ET, TSH showed a significant negative correlation with TG \((r = -0.383, p = 0.023)\).

DISCUSSION

In the present study, we used FIIL and QUICKI as indices of insulin sensitivity. Statistically significant increases in insulin levels were seen in patients with SCH and OH compared to euthyroid individuals. However, there was no statistically significant association between thyroid hormone levels and both these indices. Insulin sensitivity index (ISI) was found to be similar across all the groups, indicating ET subjects to be bordering on IR, too. Pispasert et al. advocated caution in using indices based on glucose and insulin levels as measures of peripheral insulin sensitivity when comparing mixed-gender and mixed-race populations.

In contrast, the study by Maratou et al. demonstrated a significant positive correlation between the Masti index and both free T3 and free T4 levels \((r = 0.41, p = 0.04)\), suggesting IR in both SCH and OH groups when compared to the control group. The study by Al Sayed et al. could not deduce a statistically significant association of thyroid hormones with homeostatic model assessment (HOMA) IR in SCH. Gayoum et al. found a significant positive correlation between TSH and TG \((r = 0.47, p = 0.002)\) and HOMA-IR \((p = 0.001, r = 0.51)\).

In the present study, TSH correlated to TG to a certain extent. Though there were subjects with varying TSH values, there was no significant correlation between TSH and HOMA-IR in the present study.

CONCLUSION

Though high insulin levels were observed in patients with SCH and OH, there was no statistically significant association between TSH levels and QUICKI. This could be attributed to the fact that the ISI of euthyroid subjects was decreased, too. Stringent categorization of subjects based on metabolic syndrome criteria and comparison with thyroid hormones may provide insight into the correlation.

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