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A Cross-Sectional Study to Compare the Insulin Resistance in Hypothyroid and Euthyroid Subjects Using HOMA IR Values

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ABSTRACT:

Background: Hypothyroidism and insulin resistance are significant contributors to metabolic dysfunction and cardiovascular risk. Understanding the interplay between these conditions is crucial for optimising patient care and outcomes. This study aimed to analyse the association between insulin resistance and lipid profiles affecting blood T3, T4, and TSH levels in patients with hypothyroidism.
Methods: This study involved the screening and enrolment of 25 patients diagnosed with hypothyroidism and 25 euthyroid patients from the Outpatient Department (OPD) of a tertiary care hospital. This study compared metabolic parameters, including Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) values, thyroid-stimulating hormone (TSH) levels, and insulin levels between hypothyroid and euthyroid individuals.
Results: The hypothyroid group exhibited significantly higher HOMA-IR values (mean 3.68 vs. 2.53), TSH levels (mean 10.57 vs. 3.25), and insulin levels (mean 12.65 vs. 9.18) compared to the euthyroid group, indicating greater insulin resistance in hypothyroid individuals. A HOMA-IR cut-off value of 2.65 demonstrated excellent diagnostic accuracy for identifying insulin resistance, with an Area under the Curve (AUC) of 0.795, sensitivity of 68%, and specificity of 76%.
Conclusion: The identified HOMA-IR cutoff value serves as a valuable clinical tool for assessing insulin resistance in patients with hypothyroidism and for guiding tailored management strategies.

Keywords: Hypothyroidism, Insulin resistance, HOMA-IR, Thyroid-stimulating hormone, metabolic health

1. Introduction

Hypothyroidism is an endocrine condition caused by an insufficient supply of thyroid hormones that slows down metabolic processes.[1] Hypothyroidism is a clinical illness characterised by low thyroid hormone release from the thyroid gland. Subclinical hypothyroidism is diagnosed when thyroid hormone levels are within the normal reference range (0.45-4.5 mIU/L), but thyroid stimulating hormone (TSH) is increased, whereas overt thyroid illness is diagnosed when serum thyroid hormone levels (free T4, with or without T3) are abnormal. Subclinical hypothyroidism was defined as slightly elevated TSH (4.5-10 mIU/L) or substantially high TSH (≥10 mIU/L), with normal fT4 values in both groups.[2]
Insulin resistance occurs when the body develops insulin tolerance, which renders the hormone ineffective. Insulin resistance is regarded as a significant and independent contributor to cardiovascular disease, a leading cause of morbidity and death globally.[2] Triiodothyronine (T3) and thyroxine (T4) are hormones secreted by the thyroid gland that can affect almost all cells in the body as well as basal metabolism. The release of thyroid hormones (TH) is regulated by the thyroid-stimulating hormone (TSH) of the pituitary gland, and it influences glucose metabolism by influencing many pathways in organs such as the pancreas, adipose tissue, and liver. Diabetes and thyroid diseases have been proven to impact one another, and the link between these two ailments has been demonstrated.[3]
Volzke et al. discovered that individuals with TSH levels between 2.5 and 4 mU/L were more likely to develop cardiovascular illness.[5] Recent investigations have indicated that elevated blood TSH levels are related to cardiovascular illnesses, psychological diseases, and the development of overt thyroid dysfunction.[6] Clinical and subclinical hypothyroidism have been identified as risk factors for MetS.[7] Several studies have examined the association between thyroid hormone levels and IR. In general, thyroid dysfunction is assumed to be associated with IR; however, the results have been inconsistent.[8-10] Peppa et al. observed that endocrine diseases (polycystic ovarian syndrome (PCOS), adrenal disorders, and thyroid function abnormalities) are related to glucose and insulin metabolism difficulties.[11]
Insulin resistance in hypothyroidism can be caused by a variety of factors, including changes in the insulin signalling system, oxidative stress, and reduced blood flow to organs.[4] This study aimed to analyse the association between insulin resistance and lipid profiles affecting blood T3, T4, and TSH levels in patients with hypothyroidism.

2. Materials and Methods

This study involved the screening and enrolment of 25 patients diagnosed with hypothyroidism and 25 euthyroid patients from the Outpatient Department (OPD) of a tertiary care hospital.

Inclusion Criteria
The inclusion criteria comprised patients aged 18–45 years with hypothyroidism confirmed by elevated TSH levels and either reduced T3 and T4 levels or normal T3 and T4 levels. These patients either attended the Medicine OPD or were admitted to the medicine ward.

Exclusion Criteria
Exclusion criteria included type 2 diabetes mellitus, polycystic ovarian disease, tuberculosis, and medications such as statins that affect lipid levels.
Ethical approval was obtained from the institutional ethics committee before the study commenced. Venous blood samples (5 ml) were aseptically collected from each participant after obtaining their written consent. Fasting blood samples were collected and transported to the laboratory in ice containers.

The samples were used to analyse various parameters, including fasting plasma glucose, T3, T4, TSH, insulin, and lipid profile (triglycerides, total cholesterol, HDL-cholesterol, LDL-cholesterol, and VLDL-cholesterol). Additionally, the Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) was calculated for each group and correlated with the respective TSH values.

Statistical analysis:

3. Results

The patient demographic evaluation reported a mean age in the hypothyroid group was 32.40 ± 7.46 years, while the euthyroid group had a mean age of 31.24 ± 7.63 years; however, this difference was not statistically significant (p = 0.589). HOMA-IR was significantly higher in the hypothyroid group (3.68 ± 1.37) than in the euthyroid group (2.53 ± 0.50), with a p-value <0.0001. Similarly, the levels of TSH were significantly elevated in the hypothyroid group (10.57 ± 3.02) than in the euthyroid group (3.25 ± 0.77), with a p-value <0.0001.

Insulin levels followed a similar pattern, being higher in the hypothyroid group (12.65 ± 3.18) than in the euthyroid group (9.18 ± 1.26), with a p-value <0.0001. However, there was no statistically significant difference in fasting glucose levels between the two groups (p = 0.260) (Table 1).

Table 1: Patient characteristics in both group

	Group		**P value**
	Hypothyroid	Euthyroid	
Age	32.4 ± 7.46	31.24 ± 7.63	0.589
Homa IR	3.68 ± 1.37	2.53 ± 0.5	<0.0001
TSH	10.57 ± 3.02	3.25 ± 0.77	<0.0001
Insulin	12.65 ± 3.18	9.18 ± 1.26	<0.0001
Glucose	116.16 ± 15.55	111.76 ± 11.43	0.26

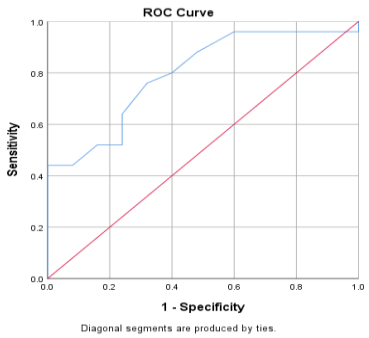

Figure 1: ROC curve of HOMA-IR with group comparison

Among the euthyroid individuals, 17 patients exhibited a HOMA-IR value of less than 2.65, while 8 patients had a value exceeding 2.65. In contrast, within the hypothyroid cohort, six patients had a HOMA-IR value below 2.65, whereas 19 patients had a value higher than 2.65 (Table 2).

Table 2: Comparison of HOMA-IR values in both group

Homa IR	Group	
	Euthyroid	Hypothyroid
<2.65	17	6
>2.65	8	19

The identified HOMA-IR cut-off value of 2.65 has an AUC of 0.795, showing good discrimination. It had a highly significant p-value < 0.0001, with a sensitivity of 68%, specificity of 76%, PPV of 74%, and NPV of 70% (Table 3).

Table 3: Sensitivity and Specificity Analysis of HOMA-IR Values

Cut-off value	2.65
AUC	0.795
P value	<0.0001
Sensitivity	68%
Specificity	76%
PPV	74%
NPV	70%

4. Discussion

IR is a hallmark of obesity, diabetes, and metabolic syndrome and is associated with cardiovascular disease.[11] As a result, IR testing is critical in various clinical conditions in which insulin sensitivity is reduced. HEC is the gold standard approach for determining insulin sensitivity[12] but it is intrusive, time-consuming, costly, and can only be used for research purposes. As a result, several surrogate markers have been created and enhanced to easily assess IR.[13]

Previous investigations have indicated an enhanced HOMA-IR index and a decreased Matsuda index in hypothyroidism and hyperthyroidism.[14-17] Other investigations have investigated the relationship between thyroid function and IR in euthyroid patients; however, the results were inconclusive.[18] In a recent Korean study, free T3 was positively connected with HOMA-IR26, although another study found an inverse correlation between free T4 and HOMA-IR.[19] The variation in IR levels observed in thyroid disorders could stem from the diverse effects of thyroid hormones on different organs. Thyroid hormones can interfere with insulin action by boosting hepatic glucose production and enhancing glucose transport and glycolysis in the peripheral tissues. This dual effect, involving both the hindrance and facilitation of glucose metabolism, suggests a complex interplay between thyroid hormones and insulin in regulating metabolic processes.[20]

This study aimed to compare the metabolic parameters between individuals with hypothyroidism and those with normal thyroid function (euthyroidism). Patient demographics showed no significant age difference between the hypothyroid (32.40 years) and euthyroid (31.24 years) groups. However, the metabolic analyses revealed substantial differences. The hypothyroid group exhibited significantly higher Homeostasis Model Assessment for Insulin

Resistance (HOMA-IR) values (3.68) than the euthyroid group (2.53), indicating greater insulin resistance. Similarly, thyroid-stimulating hormone (TSH) and insulin levels were markedly elevated in the hypothyroid group. Our study findings align with the study conducted by Vyakaranam et al., where insulin and HOMA-IR levels were significantly higher in patients with subclinical hypothyroidism than in euthyroid subjects.[21] In addition, the mean TSH levels were moderately correlated with insulin and HOMA-IR levels. Singh et al. also reported a positive association between TSH levels and HOMA-IR in hypothyroid patients.[22]

Further analysis using a HOMA-IR cut-off value of 2.65 demonstrated robust diagnostic accuracy in identifying insulin resistance, with an Area Under the Curve (AUC) of 0.795, significant p-value (<0.0001), and notable sensitivity (68%) and specificity (76%). The Receiver Operating Characteristic (ROC) curve visually highlighted the clear differentiation between the two groups based on HOMA-IR values, reinforcing the clinical utility of this cut-off in assessing insulin resistance in varying thyroid statuses. A study from Taiwan revealed that individuals with subclinical hypothyroidism have a higher risk of mortality. After adjusting for various factors such as age, sex, BMI, diabetes mellitus (DM), hypertension, dyslipidaemia, smoking, alcohol consumption, physical activity, income, and education level, the risk of all-cause death increased by 1.68 times in those with subclinical hypothyroidism compared to that in euthyroid individuals. Additionally, patients with subclinical hypothyroidism also experienced elevated risks of cardiovascular events and all-cause mortality compared to their euthyroid counterparts.[23] In addition, the study conducted by Aksoy et al., also reported no association of IR with BMI in patients with high-normal (2.5–4.2 µIU/mL) and subclinical (4.2-10 µIU/mL) TSH levels.[24]

5. Conclusion

Our findings underscore the significant impact of hypothyroidism on insulin sensitivity, as evidenced by elevated HOMA-IR values and insulin levels in hypothyroid individuals compared with euthyroid subjects. The identified HOMA-IR cut-off value of 2.65 demonstrates excellent diagnostic accuracy in detecting insulin resistance, highlighting its clinical relevance as a screening tool in patients with hypothyroidism. Future research should delve into the longitudinal effects and therapeutic interventions to optimise the outcomes for these patient populations.

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