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Original Research Article

Correlation of Thyroid Hormone Levels with Insulin Resistance in Newly Diagnosed Hypothyroidism

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Abstract

Background: Obsessive–compulsive symptoms (OCS) and obsessive–compulsive disorder (OCD) are Background: Hypothyroidism is associated with several metabolic abnormalities, including insulin resistance (IR), which increases the risk of type 2 diabetes mellitus and cardiovascular disease. This study evaluated the correlation between thyroid hormone levels and insulin resistance in patients with newly diagnosed hypothyroidism.

Methods: A hospital-based cross-sectional study was conducted among 90 newly diagnosed hypothyroid patients. Demographic and clinical data were recorded, and fasting blood samples were analysed for thyroid-stimulating hormone (TSH), free triiodothyronine (free T3), free thyroxine (free T4), fasting blood glucose, and fasting serum insulin. Insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Correlation analysis and multiple linear regression were performed to identify predictors of insulin resistance. Results: The mean age of the participants was 41.8 ± 12.6 years, and 68.9% were females. The mean HOMA-IR was 3.98 ± 1.72, with 73.3% of patients demonstrating insulin resistance. Serum TSH showed a significant positive correlation with HOMA-IR ($r = 0.621$, $p < 0.001$), whereas free T3 ($r = -0.441$, $p < 0.001$) and free T4 ($r = -0.514$, $p < 0.001$) showed significant negative correlations. Multiple linear regression identified TSH and BMI as independent positive predictors, while free T3 and free T4 were independent negative predictors of HOMA-IR.

Conclusion: Insulin resistance is highly prevalent in newly diagnosed hypothyroidism and is significantly associated with the severity of thyroid dysfunction. Early assessment of insulin resistance may help identify patients at increased metabolic risk and facilitate timely therapeutic intervention.

Keywords: Hypothyroidism; Insulin resistance; HOMA-IR; Thyroid-stimulating hormone; Free triiodothyronine; Free thyroxine; Thyroid hormone

Introduction

Thyroid hormones are essential regulators of growth, development, thermogenesis, and metabolic homeostasis. They play a crucial role in carbohydrate, lipid, and protein metabolism, thereby maintaining energy balance and normal cellular function.[1] Hypothyroidism, characterized by reduced synthesis and secretion of triiodothyronine (T3) and thyroxine (T4) with a compensatory rise in thyroid-stimulating hormone (TSH), is one of the most common endocrine disorders worldwide. It is associated with widespread metabolic disturbances that adversely affect glucose metabolism, lipid profile, body composition, and cardiovascular health.[1,2]Insulin resistance (IR) is a metabolic condition in which peripheral tissues exhibit reduced responsiveness to insulin, resulting in impaired

glucose uptake and compensatory hyperinsulinaemia. Increasing evidence indicates that thyroid dysfunction contributes to insulin resistance through multiple mechanisms, including reduced basal metabolic rate, impaired glucose transporter activity in skeletal muscle and adipose tissue, altered hepatic glucose metabolism, and dysregulated lipid metabolism.[1,2] Furthermore, hypothyroidism is commonly associated with dyslipidaemia and increased adiposity, both of which further reduce insulin sensitivity and increase the risk of type 2 diabetes mellitus and cardiovascular disease.[2]Adipose tissue is now recognized as an active endocrine organ that secretes numerous biologically active molecules known as adipokines, including leptin, adiponectin, resistin, chemerin, visfatin, and omentin. These adipokines regulate appetite, inflammation, insulin sensitivity, glucose homeostasis, and lipid metabolism, thereby serving as important mediators linking obesity, insulin resistance, and endocrine disorders.[3–5] Alterations in adipokine secretion may therefore contribute to the metabolic abnormalities observed in thyroid dysfunction.Several studies have demonstrated that thyroid hormones influence adipokine production and secretion. Altered circulating concentrations of leptin, adiponectin, and resistin have been reported in patients with hypothyroidism, suggesting a close interaction between thyroid status and adipose tissue endocrine function.[6–10] More recently, newer adipokines such as chemerin, visfatin, and omentin have attracted attention because of their roles in insulin signalling, inflammation, and metabolic regulation. Clinical studies have shown altered circulating levels of chemerin and visfatin in thyroid dysfunction, supporting the concept that thyroid hormones regulate adipose tissue function beyond the classical adipokines.[11–13]Although previous studies have reported significant alterations in adipokine profiles and insulin sensitivity in hypothyroidism, the relationship between thyroid hormone levels and insulin resistance remains incompletely understood, with inconsistent findings across studies.[6–13] Patients with newly diagnosed hypothyroidism provide an ideal population for evaluating this association because they have not yet received thyroid hormone replacement therapy, eliminating the confounding metabolic effects of treatment.

Therefore, the present study was undertaken to evaluate the correlation between serum thyroid hormone levels (TSH, free T3, and free T4) and insulin resistance in patients with newly diagnosed hypothyroidism.

Methodology:

Materials and Methods

This hospital-based observational cross-sectional study was conducted in the Department of General Medicine.

Study Population

The study included 90 consecutive patients with newly diagnosed hypothyroidism who fulfilled the eligibility criteria and attended the outpatient or inpatient services of the Department of General Medicine during the study period.

Eligibility Criteria

Inclusion Criteria

- Patients fulfilling all of the following criteria were included:
- Age ≥18 years.
- Newly diagnosed primary hypothyroidism confirmed by biochemical investigations.
- Patients who had not received thyroid hormone replacement therapy.
- Patients willing to provide written informed consent.

Exclusion Criteria

- Patients with any of the following conditions were excluded:
- Previously diagnosed hypothyroidism receiving levothyroxine therapy.
- Diabetes mellitus or use of antidiabetic medications.
- Pregnancy or lactation.
- Hyperthyroidism or secondary hypothyroidism.
- Chronic kidney disease, chronic liver disease, malignancy, or severe systemic illness.
- Acute infection or inflammatory disorders.
- Patients receiving corticosteroids, lipid-lowering agents, or medications known to affect glucose metabolism or thyroid function.
- Patients unwilling to participate.

Study Procedure

After obtaining informed consent, a detailed clinical history was recorded using a predesigned case record form. Information regarding demographic characteristics, presenting complaints, duration of symptoms, medical history, family history, and medication history was documented. A comprehensive general physical examination and systemic examination were performed for all participants.

Anthropometric measurements, including height, weight, and body mass index (BMI), were recorded using standard techniques. Blood pressure was measured in the sitting position after an adequate period of rest.

Laboratory Investigations

Following an overnight fast of 8–12 hours, approximately 5–7 mL of venous blood was collected from each participant under aseptic precautions.

The following laboratory investigations were performed:

- Serum thyroid-stimulating hormone (TSH)
- Free triiodothyronine (fT3)
- Free thyroxine (fT4)
- Fasting blood glucose (FBG)
- Fasting serum insulin

Serum TSH, free T3, and free T4 concentrations were estimated using a chemiluminescent immunoassay (CLIA) on an automated immunoassay analyser according to the manufacturer's instructions. Fasting plasma glucose was measured by the glucose oxidase-peroxidase method, while fasting serum insulin was estimated using a chemiluminescent immunoassay.

Assessment of Insulin Resistance

Insulin resistance was assessed using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) according to the following formula:

HOMA-IR = [Fasting Plasma Glucose (mg/dL) × Fasting Serum Insulin (μIU/mL)] ÷ 405

Higher HOMA-IR values indicated greater insulin resistance.

Outcome Measures

Primary Outcome

Correlation between serum TSH, free T3, and free T4 levels and insulin resistance (HOMA-IR).

Secondary Outcomes

- Association of thyroid hormone levels with fasting blood glucose and fasting serum insulin.
- Relationship between demographic and anthropometric variables and insulin resistance.
- Comparison of insulin resistance across different categories of hypothyroidism, where applicable.

Data Management

All demographic, clinical, anthropometric, and laboratory data were entered into a structured data collection proforma and subsequently transferred to a Microsoft Excel spreadsheet. Data were checked for completeness and accuracy before statistical analysis.

Statistical Analysis

The collected data were analysed using Statistical Package for the Social Sciences (SPSS) software version 26.0 (IBM Corp., Armonk, NY, USA).Continuous variables were tested for normality using the Shapiro–Wilk test. Normally distributed data were expressed as mean ± standard deviation (SD), whereas non-normally distributed variables were presented as median with interquartile range (IQR). Categorical variables were expressed as frequencies and percentages.

Comparisons between groups were performed using the Independent Student's t-test for normally distributed continuous variables and the Mann–Whitney U test for non-parametric variables. Categorical variables were analysed using the Chi-square test or Fisher's exact test, wherever appropriate.

The correlation between thyroid hormone parameters (TSH, free T3, and free T4) and insulin resistance (HOMA-IR) was assessed using Pearson's correlation coefficient for normally distributed variables or Spearman's rank correlation coefficient for non-normally distributed variables.

A p-value <0.05 was considered statistically significant.

Results:

A total of 90 patients with newly diagnosed hypothyroidism were included in the study. The baseline demographic and clinical characteristics of the study participants are presented in Table 1. The mean age of the participants was 41.8 ± 12.6 years, with the majority (34.4%) belonging to the 31–45 years age group. Females predominated the study population, accounting for 68.9% of the participants. The mean body mass index (BMI) was 26.1 ± 4.3 kg/m², while the mean systolic and diastolic blood pressures were 124.7 ± 11.4 mmHg and 79.2 ± 7.6 mmHg, respectively (Table 1).

The thyroid function parameters and metabolic profile of the study population are summarised in Table 2 and illustrated in Figure 1. The mean serum TSH level was 18.4 ± 8.7 μIU/mL, whereas the mean free T3 and free T4 levels were 2.18 ± 0.54 pg/mL and 0.71 ± 0.22 ng/dL, respectively. The mean fasting blood glucose was 97.6 ± 13.8 mg/dL, mean fasting serum insulin was 16.5 ± 6.9 μIU/mL, and the mean HOMA-IR value was 3.98 ± 1.72 (Table 2, Figure 1).

Based on HOMA-IR values, 66 patients (73.3%) were found to have insulin resistance (HOMA-IR >2.5), whereas 24 patients (26.7%) had normal insulin sensitivity. The distribution of patients according to insulin resistance status is shown in Table 3 and Figure 2.

Correlation analysis demonstrated a significant positive association between serum TSH levels and HOMA-IR ($r = 0.621$, $p < 0.001$). Conversely, both free T3 ($r = –0.441$, $p < 0.001$) and free T4 ($r = –0.514$, $p < 0.001$) showed significant negative correlations with HOMA-IR, indicating that lower thyroid hormone concentrations were associated with greater insulin resistance (Table 4).

Comparison of patients according to insulin resistance status demonstrated that individuals with insulin resistance had significantly higher BMI, serum TSH, fasting blood glucose, and fasting serum insulin levels than those without insulin resistance. In contrast, free T3 and free T4 concentrations were significantly lower among patients with insulin resistance. Although patients with insulin resistance were slightly older, the difference in age between the two groups was not statistically significant (Table 5).

Multiple linear regression analysis identified serum TSH and BMI as independent positive predictors of HOMA-IR, whereas free T3 and free T4 were identified as significant negative predictors after adjustment for other study variables. Age and female gender were not independently associated with HOMA-IR. The regression model is presented in Table 6, while the standardized regression coefficients are illustrated in Figure 3.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (n = 90)

Variable	Value
Age (years), mean ± SD	41.8 ± 12.6
Age group (18–30 years), n (%)	22 (24.4)
Age group (31–45 years), n (%)	31 (34.4)
Age group (46–60 years), n (%)	25 (27.8)
Age group (>60 years), n (%)	12 (13.3)
Male, n (%)	28 (31.1)
Female, n (%)	62 (68.9)
Weight (kg), mean ± SD	67.5 ± 11.2
Height (cm), mean ± SD	160.8 ± 8.6
BMI (kg/m²), mean ± SD	26.1 ± 4.3
Systolic BP (mmHg), mean ± SD	124.7 ± 11.4
Diastolic BP (mmHg), mean ± SD	79.2 ± 7.6

Table 2. Thyroid Function Parameters and Metabolic Profile (n = 90)

Parameter	Mean ± SD
TSH (µIU/mL)	18.4 ± 8.7
Free T3 (pg/mL)	2.18 ± 0.54
Free T4 (ng/dL)	0.71 ± 0.22
Fasting Blood Glucose (mg/dL)	97.6 ± 13.8
Fasting Serum Insulin (µIU/mL)	16.5 ± 6.9
HOMA-IR	3.98 ± 1.72

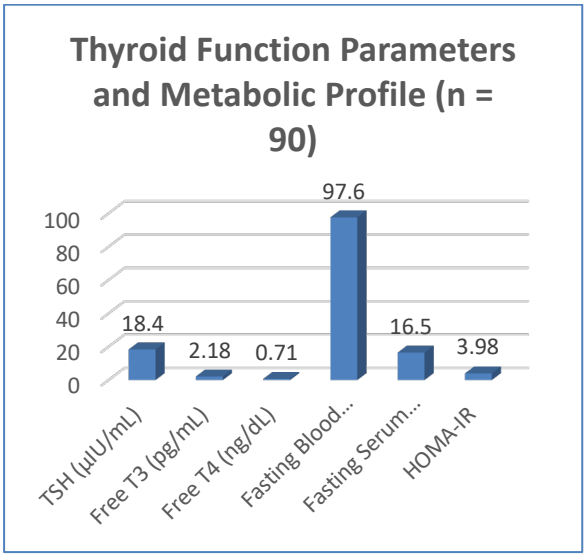

Figure 1 Thyroid Function Parameters and Metabolic Profile (n = 90)

Table 3. Distribution of Patients According to Insulin Resistance (HOMA-IR)

HOMA-IR Category	Number (%)
≤2.5 (Normal insulin sensitivity)	24 (26.7)
>2.5 (Insulin resistance)	66 (73.3)
Total	**90 (100)**

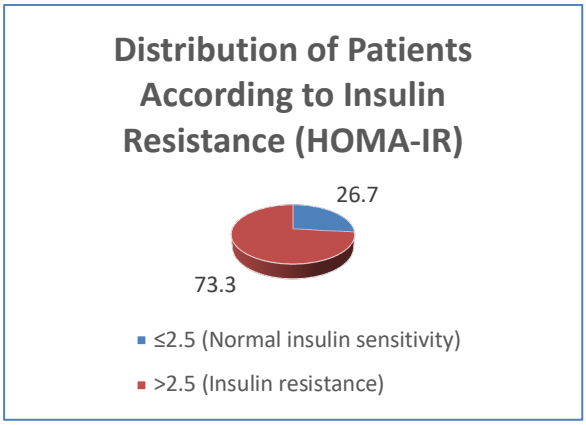

Figure 2 Distribution of Patients According to Insulin Resistance (HOMA-IR)

Table 4. Correlation Between Thyroid Hormone Levels and Insulin Resistance (HOMA-IR)

Variable	Correlation coefficient (r)	p-value
TSH	0.621	<0.001
Free T3	−0.441	<0.001
Free T4	−0.514	<0.001

Table 5. Comparison of Clinical and Biochemical Parameters According to Presence of Insulin Resistance

Variable	HOMA-IR ≤2.5 (n=24)	HOMA-IR >2.5 (n=66)	p-value
Age (years)	39.2 ± 11.4	42.8 ± 12.9	0.21
BMI (kg/m²)	23.9 ± 3.5	26.9 ± 4.2	0.002
TSH (µIU/mL)	12.8 ± 5.4	20.5 ± 8.6	<0.001
Free T3 (pg/mL)	2.46 ± 0.49	2.08 ± 0.51	0.001
Free T4 (ng/dL)	0.84 ± 0.18	0.66 ± 0.20	<0.001

Fasting Glucose (mg/dL)	92.5 ± 10.2	99.5 ± 14.1	0.03
Fasting Insulin (µIU/mL)	10.7 ± 2.6	18.6 ± 6.4	<0.001

Table 6. Multiple Linear Regression Analysis Showing Predictors of HOMA-IR

Variable	β Coefficient	Standard Error	p-value
Age	0.06	0.02	0.15
Female gender	0.09	0.24	0.33
BMI	0.29	0.05	0.003
TSH	0.48	0.02	<0.001
Free T3	−0.22	0.11	0.021
Free T4	−0.31	0.19	0.006

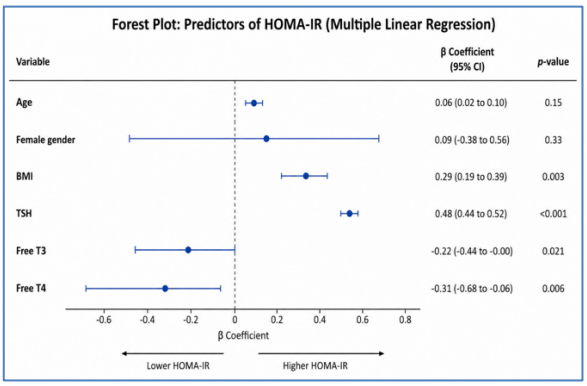

Figure 3 Multiple Linear Regression Analysis Showing Predictors of HOMA-IR

Discussion

The present study evaluated the relationship between thyroid hormone levels and insulin resistance in 90 patients with newly diagnosed hypothyroidism. Insulin resistance was highly prevalent, with 73.3% of patients demonstrating a HOMA-IR value >2.5. Serum TSH showed a significant positive correlation with HOMA-IR ($r=0.621$, $p<0.001$), whereas free T3 ($r=-0.441$, $p<0.001$) and free T4 ($r=-0.514$, $p<0.001$) were significantly negatively correlated. Multiple linear regression analysis further identified TSH, BMI, free T3, and free T4 as independent predictors of insulin resistance.The demographic profile revealed a mean age of 41.8 ± 12.6 years, with most participants aged 31–45 years (34.4%), and females accounting for 68.9% of the study population. This female predominance is consistent with the known epidemiology of hypothyroidism and agrees with findings from an Indian tertiary-care study reporting similar demographic characteristics. Serum TSH (18.4 ± 8.7 µIU/mL), free T3 (2.18 ± 0.54 pg/mL), and free T4 (0.71 ± 0.22 ng/dL) confirmed overt hypothyroidism, while the mean HOMA-IR of 3.98 ± 1.72 reflected a substantial burden of insulin resistance. Comparable findings were reported by Sengupta et al.[14], who observed significantly higher HOMA-IR values among hypothyroid patients than euthyroid controls.

A major finding was that nearly three-fourths of patients had insulin resistance, supporting previous reports that impaired insulin sensitivity is common in untreated hypothyroidism. Earlier Indian studies similarly demonstrated significantly higher HOMA-IR values in overt hypothyroidism than in euthyroid individuals, indicating that thyroid hormone deficiency adversely affects glucose metabolism and insulin action.[14,15]

The present study demonstrated a significant positive correlation between TSH and HOMA-IR, consistent with Sengupta et al.[14], who reported an even stronger association ($r=0.945$, $p<0.001$). Likewise, Singh et al.[15] observed that increasing TSH levels were associated with worsening insulin resistance in both overt and subclinical hypothyroidism. Conversely, free T3 and free T4 showed significant negative correlations with

HOMA-IR, supporting evidence that reduced thyroid hormone levels impair glucose uptake, insulin-mediated glucose disposal, and overall metabolic function.

Patients with HOMA-IR >2.5 had significantly higher BMI, TSH, fasting insulin, and lower free T3 and free T4 levels than those without insulin resistance, indicating that greater thyroid dysfunction is accompanied by more severe metabolic abnormalities. BMI independently predicted HOMA-IR (β=0.29, p=0.003), highlighting the additive role of obesity in promoting insulin resistance through adipokine imbalance, chronic inflammation, and impaired insulin signalling. Similar observations have been reported in recent studies evaluating metabolic dysfunction in hypothyroidism.[15]

Among all variables analysed, serum TSH emerged as the strongest independent predictor of insulin resistance (β=0.48, p<0.001), followed by BMI, free T3, and free T4, whereas age and sex were not independently associated with HOMA-IR. These findings are biologically plausible, as hypothyroidism reduces peripheral glucose uptake, GLUT-4 translocation, mitochondrial oxidative metabolism, and insulin receptor signalling while increasing visceral adiposity and inflammation.

The clinical implications are important. Since 73.3% of newly diagnosed hypothyroid patients exhibited insulin resistance, routine assessment of fasting insulin or HOMA-IR may facilitate early identification of individuals at risk of metabolic syndrome, type 2 diabetes mellitus, and cardiovascular disease. Furthermore, prospective studies have demonstrated that levothyroxine therapy significantly reduces TSH, fasting insulin, BMI, and HOMA-IR after restoration of euthyroidism, indicating that these metabolic abnormalities are largely reversible.

Conclusion

The present study demonstrated a high prevalence of insulin resistance among patients with newly diagnosed hypothyroidism, with nearly three-quarters exhibiting elevated HOMA-IR values. Serum TSH showed a significant positive correlation, whereas free T3 and free T4 demonstrated significant negative correlations with insulin resistance. TSH and BMI emerged as independent predictors of HOMA-IR, highlighting the influence of thyroid dysfunction on glucose metabolism. These findings underscore the importance of early assessment of insulin resistance in newly diagnosed hypothyroid patients to facilitate timely intervention and reduce the future risk of metabolic and cardiovascular complications.

Limitations

The present study was conducted at a single tertiary care centre with a relatively small sample size, which may limit the generalisability of the findings. Owing to its cross-sectional design, a causal relationship between thyroid hormone levels and insulin resistance could not be established. Additionally, the study did not evaluate adipokines, inflammatory markers, or long-term changes following thyroid hormone replacement therapy, which could have provided further insight into the underlying mechanisms.

Ethical approval

Ethical approval for this study was obtained from the Institutional Ethics Committee prior to the commencement of the study. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and applicable institutional guidelines.

Informed Consent

Written informed consent was obtained from all participants prior to their enrolment in the study.

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Conflict of Interest Declaration

The authors declare no conflict of interest.

Data Availability Statement

All data generated or analysed during this study are available from the corresponding author upon reasonable request.

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