Egyptian Journal of Medical Research

Print ISSN: 2682-4396 / Online ISSN: 2682-440X

Original article

Correlation between Insulin Resistance and Thyroid Dysfunction

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Article Info

Article history:

Received 27 October 2024

Accepted 27 November 2024

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Keywords

Thyroid

Insulin Resistance

HOMA

IR.

Abstract:

Background: Thyroid hormones T3 and T4 maintain a fine balance of glucose homeostasis by acting as insulin agonistic and antagonistic. **Objective**: In this study we aim to asses insulin resistance in patients who have thyroid disorders. **Methods:** the current inquiry was a case-control study with 60 participants. The subjects were split into three equal groups: 20 individuals with a hypothyroidism, 20 individuals with hyperthyroidism and 20 euthyroid individuals. Gathering medical history and measure body mass index. In addition, check the thyroid gland locally. Testing for HOMA-IR, TSH, Free T3, and Free T4 .**Results:** There was a statistically significant moderate negative linear correlation between free T4 and HOMA-IR (r=-0.491, p=0.028) only in hypothyroid patients' group. There was a statistically significant moderate negative linear correlation

between free T3 and HOMA-IR (r=-0.505, p<0.001) in all studied population, however this significant correlation lost in studying each group separately (p-values >0.05). There was a statistically significant moderate positive linear correlation between TSH and HOMA-IR (r=0.644, p<0.001) in all studied population, however this significant correlation lost in studying each group separately (p-values >0.05). **Conclusion:** There is a significant association between thyroid dysfunction and HOMA-IR.

1. Introduction:

Insulin resistance is identified as the impaired biologic response of target tissues to insulin stimulation. Insulin resistance impairs glucose disposal, resulting in a compensatory increase in beta-cell insulin production.**[1]**

The gold standard for measurement of insulin resistance is the hyperinsulinemic-euglycemic glucose clamp technique. This research technique has limited clinical applicability; however, several clinically useful surrogate measures of insulin resistance include HOMA-IR, HOMA2, QUICKI, serum triglyceride, and triglyceride/HDL ratio. In addition, several measures assess insulin resistance based on serum glucose or insulin response to a glucose challenge **[2]**

Hypothyroidism and hyperthyroidism are the two main categories of thyroid disorders, which are further divided into overt and subclinical variants. The prevalence of thyroid disorder is mainly influenced by sex and age. Alteration in thyroid function is especially seen in women than men and in older adults compared to the younger age group. The prevalence rate of overt hyperthyroidism is 1.4% in women aged 60 and above. In men above 60 years of age, the incidence of hyperthyroidism is 0.13%. **[3]**

Thyroid hormones T3 and T4 maintain a fine balance of glucose homeostasis by acting as insulin agonistic and antagonistic. Hypothyroidism can break this equilibrium and alter glucose metabolism, which can lead to insulin resistance. Insulin resistance is the central pathophysiological phenomenon underlying the metabolic syndrome, which is

a major cardiovascular risk factor. Previous studies have established overt hypothyroidism as a risk factor for insulin resistance, In hyperthyroidism, impaired glucose tolerance may be the result of mainly hepatic insulin resistance [**4]**

In this study we aim to assess insulin resistance in patients who have thyroid disorders.

2. Material and Methods:

2.1. Patients: This case-control study was conducted on 60 subjects , three equal groups:20 individuals with hypothyroidism , 20 individuals with hyperthyroidism and 20 euthyroid individuals. The patients were recruited from Diabetes and Endocrinology Outpatient Clinic at Beni-Suef University Hospitals in upper Egypt during the period from Nov 2023 to April 2024. This study was approved by the local research ethical committee in Beni-Suef university Hospital (Approval No:FMBSUREC/03102023/Ahmed). The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (Faculty of Medicine, Beni-Suef University) and with the Helsinki Declaration of 1975, as revised in 1983. All participants provided informed consent to participate in this study.

The study include patients known to have hypo and hyperthyroidism and exclude Diabetic and Pre diabetic patients. All patients will be subjected to the following: History taking ,Physical Examination including Body Mass Index and Local Examination of Thyroid gland and Investigations :TSH , Free T3& Free T4, Lipid profile ,Fasting blood sugar (FBS) ,HbA1c , Fasting insulin level , HOMA IR :fasting insulin (micro/L) x fasting glucose (nmol/L)/22.5 [**5]**.

2.2 Statistical Analysis:

Data collected and coded to facilitate data manipulation and double entered into Microsoft Access and data analysis performed using the Statistical Package of Social Science (SPSS) software version 22 in windows 7 (SPSS Inc., Chicago, IL, USA).Simple descriptive analysis in the form of numbers and percentages of qualitative data, and arithmetic means as central tendency measurement, standard deviations as a measure of dispersion of quantitative parametric data. The significance of the results was assessed in the form of P-value that was differentiated into: Non-significant when P-value > 0.05, Significant when P-value ≤ 0.05 and highly significant when P-value ≤ 0.001

3. Results:

The study included 60 participants : 20 Hypothyroid patients, 20 Hyperthyroid Patients and 20 Euthyroid.

Table (1): Age and gender distribution of the studied subjects; (N= 60):

		Studied Groups			p-value*
		Hypothyroid N= 20	Hyperthyroid N= 20	Euthyroid N= 20	
Age; (years)	Mean ±SD	30.10 ±6.78	27.65 ±6.33	31.45 ±5.85	0.166
	Minimum - maximum	19.00 - 40.00	18.00 - 40.00	19.00 - 40.00	
Sex; N (%)	Male	2 (10.0%)	1 (5.0%)	2 (10.0%)	0.804
	Female	18 (90.0%)	19 (95.0%)	18 (90.0%)	

Table (2):A comparison of BMI between the three studied groups; (N= 60):

Demonstrates a comparison of BMI between the three studied groups. BMI is statistically significantly highest among Hypothyroid patients' group, followed by Euthyroid patients' group, while it was lowest among Hyperthyroid patients' group, (see figure-1).

		Studied Groups			p-value*
		Hypothyroid N= 20	Hyperthyroid N= 20	Euthyroid N= 20	
BMI; (kg/m^2)	Mean ±SD	27.78 ±2.67	20.04 ±1.88	22.10 ±1.90	<0.001*
	Minimum - maximum	23.00 - 33.00	17.00 - 24.00	18.80 - 24.50	<0.001[a]* <0.001[b]* 0.004[c]*

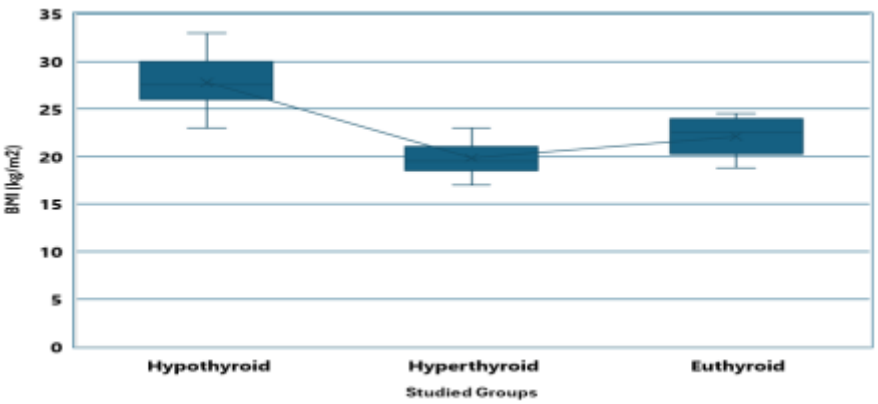


Figure (1)

Table (3) demonstrates a comparison of thyroid function tests between the three studied groups.

		Studied Groups			p-value*
		Hypothyroid N= 20	Hyperthyroid N= 20	Euthyroid N= 20	
Free T4 (ng/dl)	Mean ±SD	0.39 ±0.19	5.20 ±3.08	1.34 ±0.24	<0.001*
	Minimum – maximum	0.10 - 0.70	1.90 - 12.20	0.90 - 1.80	<0.001[a]* 0.098[b] <0.000[c]
Free T3 (pg/ml)	Mean ±SD	1.59 ±0.60	4.99 ±0.84	3.37 ±0.59	<0.001*
	Minimum – maximum	0.11 - 2.30	3.80 - 6.80	2.40 - 4.20	<0.001[a]* <0.001[b]* <0.001[c]*
TSH (Uiu/ml)	Mean ±SD	17.17 ±8.06	0.08 ±0.05	2.58 ±1.10	<0.001*
	Minimum – maximum	8.00 - 38.00	0.01 - 0.18	0.80 - 4.10	<0.001[a]* <0.001[b]* 0.106[c]

Table (4&5) demonstrates a comparison of Cholesterol and Triglyceride between the three studied groups. Cholesterol is statistically significantly highest among Hypothyroid patients' group as compared with hyper- and euthyroid patients' group, on the other hand there was non-statistically significant difference between hyper- and euthyroid patients' group.

Table (4): A comparison of Cholesterol between the three studied groups; (N= 60):

		Studied Groups			p-value*
		Hypothyroid N= 20	Hyperthyroid N= 20	Euthyroid N= 20	
Cholesterol; (mg/dl)	Mean ±SD	240.20 ±79.79	139.55 ±28.41	147.15 ±27.13	<0.001*
	Minimum – maximum	146.00 - 466.00	90.00 - 192.00	96.00 - 185.00	<0.001[a]*
	Normal up to 200 mg/dl	9 (45.0%)	20 (100.0%)	20 (100.0%)	<0.001[b]*
	Elevated	11 (55.0%)	0 (0.0%)	0 (0.0%)	0.864[c]

Table (5): A comparison of Triglyceride between the three studied groups; (N= 60):

		Studied Groups			p-value*
		Hypothyroid N= 20	Hyperthyroid N= 20	Euthyroid N= 20	
Triglyceride; (mg/dl)	Mean ±SD	197.20 ±61.58	119.75 ±20.35	121.90 ±21.44	<0.001*
	Minimum - maximum	120.00 - 314.00	88.00 - 150.00	88.00 - 149.00	<0.001[a]*
	Normal up to 150 mg/dl	8 (40.0%)	20 (100.0%)	20 (100.0%)	<0.001[b]*
	Elevated	12 (60.0%)	0 (0.0%)	0 (0.0%)	0.642[c]

Table (6) demonstrates a comparison of HOMA-IR between the three studied groups. Triglyceride is statistically significantly highest among Hypothyroid patients' group as compared with hyper- and euthyroid patients' group, on the other hand there was non-statistically significant difference between hyper- and euthyroid patients' group, (see figure-2).

Table (6): A comparison of HOMA-IR between the three studied groups; (N= 60):

		Studied Groups			p-value*
		Hypothyroid N= 20	Hyperthyroid N= 20	Euthyroid N= 20	
HOMA-IR	Mean ±SD	2.23 ±1.01	1.17 ±0.44	0.99 ±0.43	<0.001*
	Minimum - maximum	0.70 - 4.30	0.60 - 1.90	0.40 - 1.90	<0.001[a]*
	Normal up to 1.95	8 (40.0%)	20 (100.0%)	20 (100.0%)	<0.001[b]*
	Elevated	12 (60.0%)	0 (0.0%)	0 (0.0%)	0.409[c]

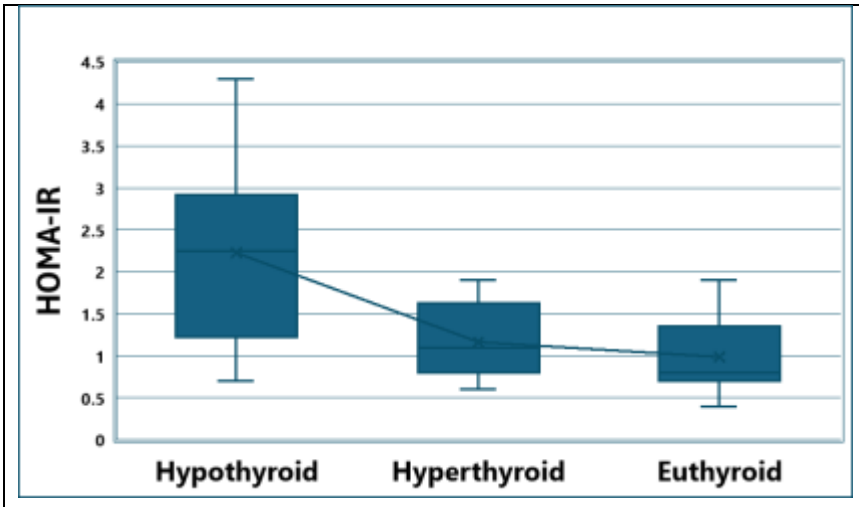
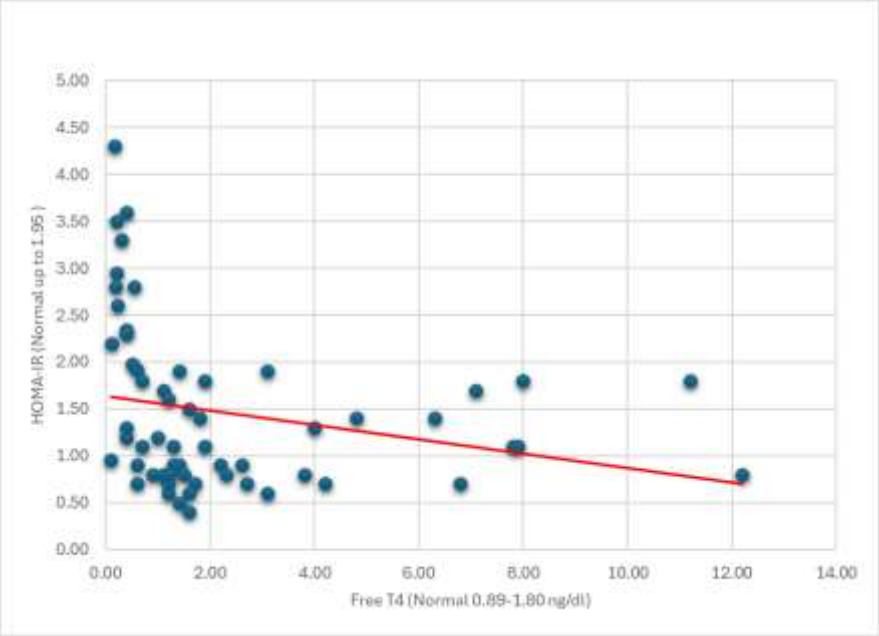
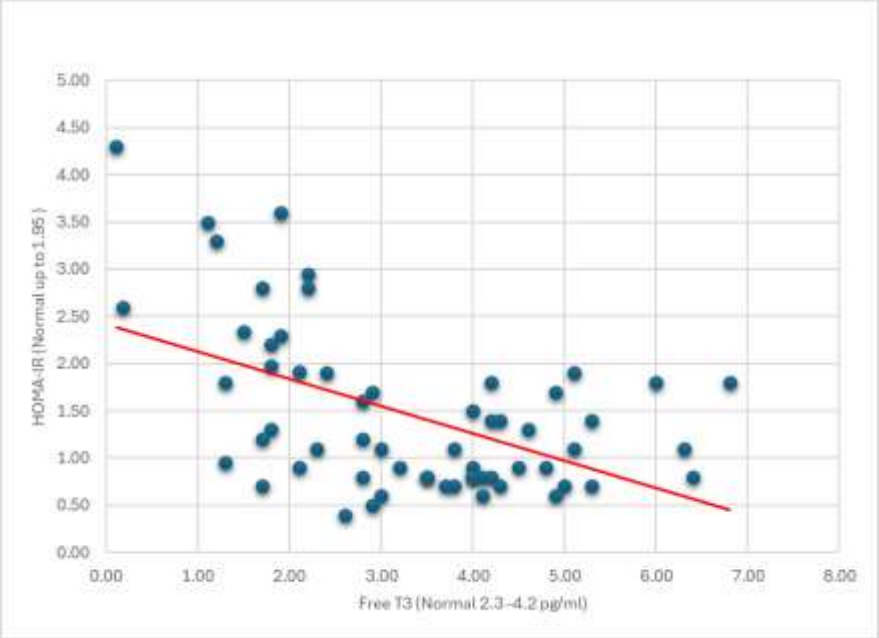


Figure (2): A comparison of HOMA-IR between the three studied group.

Table (7): Correlation between thyroid function tests and HOMAIR in all studied groups and in each group separately; (N= 60): There was a statistically significant moderate negative linear correlation between free T4 and HOMA-IR (r=-0.491, p=0.028) only in hypothyroid patients' group. There was a statistically significant moderate negative linear correlation between free T3 and HOMA-IR (r=-0.505, p<0.001) in all studied population, however this significant correlation lost in studying each group separately (p-values >0.05). There was a statistically significant moderate positive linear correlation between TSH and HOMA-IR (r=0.644, p<0.001) in all studied population, however this significant correlation lost in studying each group separately (p-values >0.05) (see figure-3).

		Hypothyroid	Hyperthyroid	EUTHYROID	All Studied Population
		HOMA-IR			
Free T4	r	-.491-*	0.210	-0.051	-0.241
	p-value	0.028	0.374	0.831	0.064
	N	20	20	20	60
Free T3	r	-0.433	0.244	-0.207	-.515-**
	p-value	0.056	0.301	0.382	0.000
	N	20	20	20	60
TSH	r	0.312	-0.206	0.357	.644**
	p-value	0.181	0.398	0.122	0.000
	N	20	20	20	60


HOMA-IR (Normal up to 1.95)
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
Free T4 (Normal 0.89-1.80 ng/dl)


HOMA-IR (Normal up to 1.95)
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0.00
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
Free T3 (Normal 2.3-4.2 pg/ml)

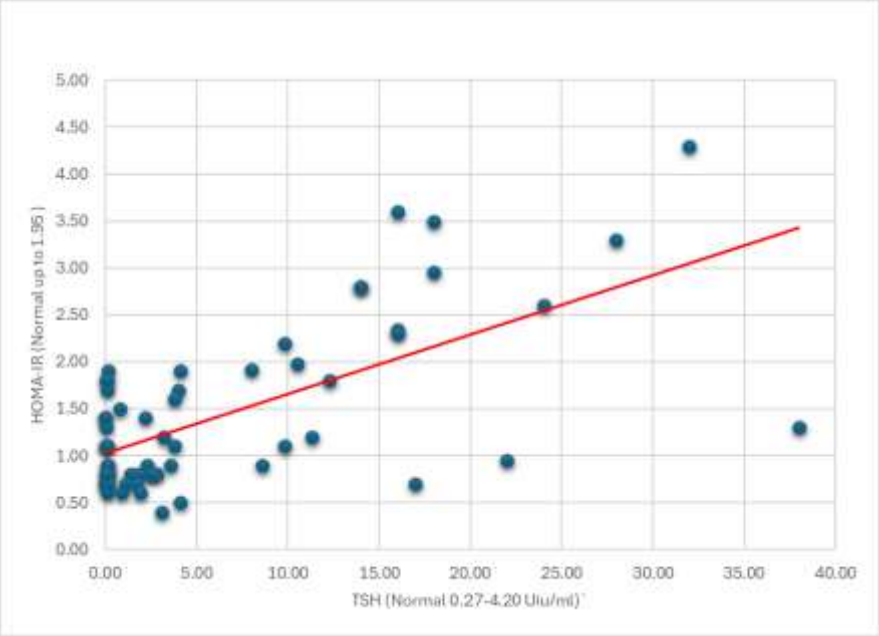


Figure (3): Correlation between thyroid function tests and HOMA-IR in all studied groups.

4. Discussion:

The role of Thyroid Hormones in controlling blood sugar levels is well-documented. Thyroid Hormones influences glucose metabolism in several organs such as the pancreas, adipose tissue, skeletal muscles, liver, gastrointestinal tract, and central nervous system, and it has also been linked to pancreatic β-cell production **[6].**

The onset of T2DM is facilitated by insulin resistance. Insulin resistance is associated with thyroid function in both those with diabetes mellitus and those whose glucose tolerance is normal. Although they do so in different ways, hyperthyroidism and hypothyroidism may both affect insulin resistance**.[7]**

The purpose of this case-control study was to assess insulin resistance in thyroid disease patients; the sample size was 60 people. The subjects were split into three equal groups: Twenty hypothyroid patients ,twenty Hyperthyroid patients and Twenty people whose thyroid functions normally.

According to our study, HOMA-IR levels are significantly greater in the hypothyroidism group than in the hyperthyroid and euthyroid groups. On the other hand, the hyperthyroid and euthyroid patient groups did not vary significantly from one another.

We performed this analysis for all groups that were studied and for each group separately to determine the relationship between thyroid function tests and HOMAIR. There was a statistically significant moderate negative linear correlation between free T4 and HOMA-IR (r=-0.491, p=0.028).The whole study sample showed a moderately negative linear correlation (r=-0.505, p<0.001) between free T3 and HOMA-IR. This connection was statistically significant. Nevertheless, when examining each group separately (p-values >0.05), this significant correlation was not seen.

Within the examined population, a moderately positive linear correlation between TSH and HOMA-IR was observed, with a statistical significance of 0.644 and a p-value less than 0.001. Nevertheless, when examining each group separately (p-values >0.05), this significant correlation was not seen.

Researchers Maratou et al. found that those with hypothyroidism or subclinical hypothyroidism had higher HOMA indexes, faster fasting plasma insulin levels, and postprandial plasma insulin levels than people with normal thyroid function.**[8]**.

A robust and significant correlation was found between hypothyroidism-related TSH levels and HOMA-IR in research by Singh et al. Changes in glucose and lipid metabolism brought on by a malfunctioning thyroid increase the likelihood of cardiovascular disease. **[9]**.

Researchers Sridevi et al. and Garduño-Garcia et al. found that fasting insulin levels were correlated with HOMA-IR and blood thyroid hormone levels, but not with TSH levels. Insulin levels were significantly higher in the control group than in the group of Kuwaiti women with subclinical hypothyroidism, according to research by Al Sayed et al. Despite this, the HOMA-IR scores of the two groups were not significantly different. **[10]**, **[11]**,**[12]**.

Researchers Lambadiari et al. found that HOMA-IR was positively correlated with fT4 and fT3 levels in people with type 2 diabetes mellitus. Thyroid hormones may be involved in the pathogenic processes that lead to the development of type 2 diabetes mellitus, as the researchers found a clear correlation between insulin resistance and high thyroid hormone levels. **[13]**

Several other studies have looked at insulin resistance and thyroid function in people with normal thyroid function, but they haven't come to any firm conclusions. According to Kwon H., a recent Korean study indicated a favorable correlation between free T3 and HOMA-IR.On the other hand, a different research works by Garduño-Garcia,

it was shown by et al. that free T4 and HOMA-IR are inversely related. .**[11] [14].**

We found a strong and statistically significant positive linear connection (r=743, p<0.001) between the blood level of cholesterol and HOMA-IR in both the hypothyroid patient group and the whole population we studied.
In both the group of hypothyroid individuals and the overall population, a somewhat positive linear relationship between Triglyceride and HOMA-IR was seen (r=0.488, p<0.001).

Our study found that those with hypothyroidism had far higher cholesterol levels than those with hyperthyroidism or normal thyroid function. Hyperthyroidism patients and those with normal thyroid function did not vary significantly in terms of cholesterol levels.

Medical researchers have recently focused on the link between insulin resistance and lipid metabolism. Insulin resistance and changes in lipid profiles seem to have a complicated and poorly understood interaction in metabolic syndrome patients. **[15]**.

Hypothyroidism is associated with a much greater BMI than euthyroidism, while hyperthyroidism is associated with the lowest BMI, according to our study's results.

Research involving the selection of a baseline group of obese individuals and evaluation of their thyroid hormone levels has historically shown the relationship between hypothyroidism and obesity. According to many studies, the incidence of hypothyroidism is greater in obese individuals than in the general population **[16]**. These results have led some writers to suggest that even mild thyroid malfunction may increase the risk of overweight and obesity by causing significant shifts in body weight. Nevertheless, Reihner T. investigated thyroid function in relation to obesity. For "Molecular and Cellular Endocrinology," the acronym "Mol Cell Endocrinol" is used fail to definitively prove a cause-and-effect relationship **[17]**.

Hyperthyroidism leads to a decrease in body fat and lean mass because of an increased basal energy expenditure, which in turn induces weight loss.

5. Conclusion:

To conclude, there is a significant association between thyroid dysfunction and HOMA-IR. Individuals diagnosed with hypothyroidism should prioritize frequent blood tests, specifically incorporating HA1C and fasting plasma glucose tests, to detect high blood sugar levels, which are often associated with insulin resistance.

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