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Association of Insulin Resistance with Pulmonary Function in Hypothyroid Patients

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Abstract

Background: Hypothyroidism is associated with various metabolic disturbances, including insulin resistance and altered pulmonary function. This study aimed to assess the association between insulin resistance and pulmonary function in patients with newly diagnosed hypothyroidism.

Methods: A total of 100 participants were enrolled, including 50 patients with newly diagnosed hypothyroidism and 50 age- and sex-matched healthy controls. Metabolic parameters, including BMI, fasting glucose, insulin levels, and HOMA-IR, were measured. Pulmonary function tests (FEV_1, FVC, and FEV_1/FVC ratio) were performed to evaluate lung function.

Results: The hypothyroid group showed significantly higher BMI, TSH levels, and HOMA-IR values compared to controls ($p < 0.001$), indicating increased insulin resistance. Pulmonary function tests revealed significantly reduced FEV_1 and FVC in the hypothyroid group, while the FEV_1/FVC ratio remained unchanged, suggesting a restrictive ventilatory defect. A positive association was observed between increased insulin resistance and reduced lung function parameters.

Conclusion: Patients with hypothyroidism exhibit significant insulin resistance and impaired pulmonary function. The findings suggest a potential link between metabolic dysfunction and restrictive lung abnormalities in hypothyroid patients, highlighting the importance of early metabolic and respiratory assessment in this population.

KEYWORDS: Hypothyroid, Insulin Resistance, Pulmonary Function, BMI.

INTRODUCTION

"Hypothyroidism is an endocrine disorder characterized by insufficient production of thyroid hormones, resulting in a generalized slowing of metabolic functions. Subclinical hypothyroidism represents an early, often asymptomatic stage of this condition, marked by elevated serum thyroid-stimulating hormone (TSH) levels while circulating thyroid hormone levels (such as thyroxine) remain within the normal range." (1) Hypothyroidism is a common endocrine disorder characterized by deficient production of thyroid hormones, which are critical regulators of metabolism, growth, and tissue differentiation. The global prevalence of hypothyroidism is estimated to be around 4–5%, with higher rates observed in iodine-deficient regions and among females and older adults (2). In India, studies have reported a prevalence ranging from 10% to 11%, with subclinical hypothyroidism being particularly common (3). "Thyroid hormones are essential regulators of carbohydrate and lipid metabolism. They help maintain blood glucose levels by counteracting insulin's effects and stimulating processes such as gluconeogenesis and glycogenolysis. In hyperthyroidism, the body enters a hypermetabolic state, marked by increased resting energy expenditure, weight loss, enhanced lipolysis, elevated gluconeogenesis, and reduced cholesterol levels. In contrast, hypothyroidism leads to a hypometabolic state, characterized by decreased energy expenditure, weight gain, diminished lipolysis and gluconeogenesis, and elevated cholesterol levels. Both conditions can contribute to disturbances in glucose metabolism, potentially resulting in hyperglycemia."(4)

Insulin resistance (IR) is a pathophysiological condition in which the body's cells become less responsive to insulin, leading to compensatory hyperinsulinemia and altered glucose metabolism. IR is a central feature of metabolic syndrome and a known risk factor for type 2 diabetes mellitus and cardiovascular disease (5). Emerging evidence suggests a bidirectional relationship between thyroid function and insulin sensitivity. Hypothyroid states—especially when untreated or poorly controlled—are often associated with increased insulin resistance, possibly due to altered lipid metabolism, reduced glucose uptake, and weight gain (6,7).

In recent years, attention has turned to the potential impact of metabolic disorders on pulmonary function. Several studies have demonstrated that insulin resistance may contribute to impaired lung function, possibly through mechanisms involving systemic inflammation, oxidative stress, and Microvascular dysfunction (8,9). Additionally, hypothyroidism itself can affect the respiratory system, leading to reduced ventilatory drive, respiratory muscle weakness, and altered gas exchange (10,11). However, the combined effect of hypothyroidism and insulin resistance on pulmonary function remains underexplored.

Given the overlapping metabolic disturbances in hypothyroidism and insulin resistance, it is plausible that IR may exacerbate pulmonary dysfunction in hypothyroid patients. Understanding this association could have clinical implications for early screening and targeted interventions. Therefore, this study aims to assess the association between insulin resistance and pulmonary function parameters among patients with primary hypothyroidism.

MATERIALS AND METHODS

The study received approval from the Institutional Ethics Committee of Government Medical College, Ongole, under protocol number IEC/GMC-OGL/263/2025. It was conducted in the Department of Tuberculosis and Chest Diseases at Government General Hospital, Ongole. All participants provided written informed consent.

Study Population

A total of 100 adult patients aged 18–60 years with newly diagnosed or untreated primary hypothyroidism were enrolled. Diagnosis was based on elevated serum TSH (>5 μIU/mL) with low or normal free T_4 levels, as per American Thyroid Association guidelines "A total of fifty newly diagnosed primary hypothyroid patients and fifty euthyroid individuals, aged between 18 and 60 years, were selected based on their thyroid-stimulating hormone (TSH) levels. The normal TSH reference range was defined as 0.18–4 μIU/mL. After obtaining informed consent, participants underwent a detailed medical history assessment and were screened using a structured pro forma. Individuals with a known history of diabetes mellitus, tuberculosis, polycystic ovarian syndrome, liver or kidney disorders, cardiac conditions, or those taking oral contraceptives or medications affecting thyroid function, lipid profiles, or glucose metabolism were excluded. Pregnant and postmenopausal women were also not included in the study. Blood samples were collected after an 8–12 hour fasting period. The biochemical parameters measured included plasma glucose, serum insulin, serum T3, serum T4, and serum TSH. Insulin resistance was evaluated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR), which is calculated based on fasting glucose and insulin levels to estimate β-cell function and insulin sensitivity."**(12)**

HOMA-IR was calculated using the formula:

$$\text{HOMA-IR} = \frac{\textbf{Fasting Insulin(μU/mL)} \times \textbf{Fasting Glucose(mg/dL)}}{\textbf{405}}$$

Pulmonary function measurements

Dynamic pulmonary function tests were conducted using a computerized spirometer (Spirowin Version 2.0 of Genesis Medical systems pvt. Ltd) which gives ERS- 93 predicted values at BTPS conditions. The parameters

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measured included Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1), the FEV_1/FVC ratio (FEV_1%), Forced Expiratory Flow at 25–75% of the pulmonary volume (FEF_{25-75}%), and Peak Expiratory Flow Rate (PEFR). All measurements were performed with participants in a standing position and with a nose clip applied to ensure accurate readings. Testing was conducted at noon, prior to lunch, to account for the diurnal variation in expiratory flow rates, which are typically highest at that time. Each participant performed three satisfactory spirometric maneuvers, with a minimum rest period of five minutes between trials, in accordance with standard testing protocols. All anthropometric and pulmonary function measurements were completed in a single session on the same day for each subject.

Statistical Analysis

Data were analyzed using **SPSS software version 25**. Continuous variables were expressed as **mean ± standard deviation** and compared using **independent t-tests**. Categorical variables were compared using the **Chi-square test**. Correlation between HOMA-IR and pulmonary function parameters was assessed using **Pearson's correlation coefficient**. A **p-value < 0.05** was considered statistically significant.

RESULTS

The study included 100 participants, equally divided into two groups: 50 patients with newly diagnosed hypothyroidism and 50 age- and sex-matched healthy controls. The mean age was comparable between the two groups (33.7 ± 5.6 vs. 35.0 ± 5.4 years, p = 0.24). A female predominance was noted in both groups (70%). Significant differences were observed in several metabolic parameters. The hypothyroid group had a higher mean BMI (28.1 ± 3.1 kg/m² vs. 23.9 ± 2.7 kg/m², p < 0.001**)** and TSH levels (11.8 ± 4.0 µIU/mL vs. 2.4 ± 0.8 µIU/mL, **p < 0.001**) compared to controls. Markers of insulin resistance were also elevated in the hypothyroid group, with significantly higher fasting glucose, fasting insulin, and HOMA-IR values (4.08 ± 1.22 vs. 1.95 ± 0.44, **p < 0.001**), indicating the presence of insulin resistance. Table no 3 shows that Both **FEV_1** and **FVC** were significantly reduced in the hypothyroid group, suggesting impaired lung function. However, the FEV_1/FVC ratio did not differ significantly between groups, indicating a restrictive ventilatory defect rather than an obstructive pattern. The hypothyroid group **has** significantly higher HOMA-IR values, indicating increased insulin resistance compared to controls.(Graph-1)

Table no- 1 Baseline Characteristics of Study Participants

s.no	Parameter	Hypothyroid Group (n=50)	Control Group (n=50)	p-value
1	Age (years)	33.7 ± 5.6	35.0 ± 5.4	0.24
2	Female (%)	68%	70%	0.82
3	BMI (kg/m²)	28.1 ± 3.1	23.9 ± 2.7	<0.001

Table no: 2 Mean serum values of various parameters of insulin resistance in hypothyroid and euthyroid group

s.no	Parameter	Hypothyroid Group (n=50)	Control Group (n=50)	p-value
1	TSH (µIU/mL)	28.1 ± 3.	23.9 ± 2.7	<0.001
2	Fasting Glucose (mg/dL)	| 105 ± 12	90 ± 10	<0.001
3	Fasting Insulin (µU/mL)	15.1 ± 4.1	9.0 ± 2.1	<0.001
4	HOMA-IR	4.08 ± 1.22	1.95 ± 0.44	<0.001

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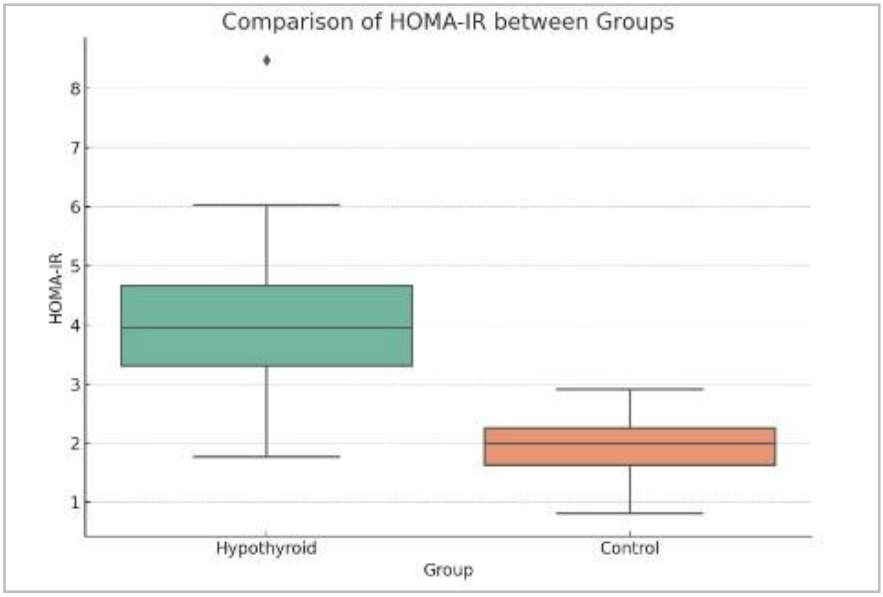
Table no -3 Pulmonary Function Test (PFT) Parameters

s.no	Parameter	Hypothyroid Group (n=50)	Control Group (n=50)	p-value
1	**FEV_1**	81.9 ± 7.6	91.2 ± 5.6	<0.001
2	**FVC**	84.2 ± 4.6	93.1 ± 4.6	<0.001
3	**FEV_1/FVC Ratio (%)**	97.5 ± 10.4	98.2 ± 8.5	0.61



Graph no -1 comparison of HOMA- IR between groups

DISCUSSION

The present study evaluated the association between insulin resistance (IR) and pulmonary function in patients with newly diagnosed hypothyroidism. The results demonstrate that hypothyroid individuals exhibit significantly impaired pulmonary function and higher insulin resistance, suggesting a possible link between thyroid dysfunction, metabolic status, and respiratory performance.

Pulmonary Function Impairment in Hypothyroidism

Hypothyroidism has long been associated with altered respiratory physiology, though it is often under-recognized in clinical practice. In our study, both FEV_1 and FVC were significantly reduced in the hypothyroid group compared to healthy controls, while the FEV_1/FVC ratio remained within normal range, indicating a restrictive ventilatory defect. These findings are in line with prior studies, such as those by Laroche et al. (14), who observed similar reductions in lung volumes among hypothyroid individuals. The underlying mechanisms may involve: Reduced respiratory muscle strength due to myopathy commonly seen in hypothyroidism. Decreased pulmonary compliance resulting from mucopolysaccharide deposition in the alveolar interstitium. Blunted ventilatory drive, which reduces tidal volume and overall lung ventilation (13,14). These physiologic alterations may predispose patients to respiratory complaints such as dyspnea and reduced exercise tolerance, even in the absence of overt pulmonary disease.

Insulin Resistance in Hypothyroidism

Our findings also confirm that hypothyroid patients demonstrate marked insulin resistance, as shown by significantly elevated HOMA-IR values compared to healthy individuals. This is consistent with the literature, including studies by Maratou et al. (15) and Duntas (16), which document that hypothyroidism adversely affects glucose homeostasis through: Decreased glucose disposal rates in peripheral tissues, Reduced insulin-

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mediated suppression of hepatic gluconeogenesis, Alterations in lipid metabolism and adipokine levels (e.g., leptin, adiponectin). Chronic thyroid hormone deficiency alters gene expression and mitochondrial activity in skeletal muscle and liver, leading to systemic metabolic inflexibility and the development of insulin resistance (15).

The IR–Lung Function Connection

One of the most critical and novel observations in our study is the inverse correlation between insulin resistance (HOMA-IR) and pulmonary function indices (FEV_1, FVC), particularly in the hypothyroid group. These findings suggest that insulin resistance may play a contributory role in the decline of respiratory function.

Several mechanisms have been proposed in previous research to explain this connection:

Systemic inflammation-associated with insulin resistance may result in low-grade inflammation within lung tissues, impairing their elasticity and gas exchange (17). Oxidative stress and endothelial dysfunction may compromise pulmonary microcirculation. Impaired muscle glucose uptake in insulin-resistant states may reduce respiratory muscle endurance and strength. Lazarus et al. (17) first demonstrated that insulin resistance in non-diabetic individuals was independently associated with lower lung function. Forno et al. (18) extended these findings to adolescents, suggesting this relationship exists across age groups and disease states. Our findings add further support to the hypothesis that metabolic dysregulation can directly influence pulmonary physiology, even in early disease stages like newly diagnosed hypothyroidism.

Clinical and Public Health Implications

The recognition of insulin resistance as a modifiable metabolic factor that may impact lung function in hypothyroid patients has several implications:

Early screening for insulin resistance in hypothyroid patients may help identify those at higher risk of developing respiratory symptoms or dysfunction. Integrating lifestyle interventions (diet, exercise, and weight loss) alongside levothyroxine therapy may improve both metabolic and pulmonary outcomes. Further investigation into the synergistic effects of thyroid hormone replacement and insulin sensitizers (e.g., metformin) on respiratory function may offer new therapeutic strategies. Additionally, the restrictive pattern seen on spirometry in hypothyroid patients may be reversible with appropriate thyroid hormone replacement, as shown in prior studies. Thus, pulmonary function testing may also serve as a non-invasive tool for monitoring disease progression or treatment response in hypothyroid individuals.

CONCLUSION

In conclusion, this study highlights a clear association between insulin resistance and reduced pulmonary function in newly diagnosed hypothyroid patients. The findings emphasize the importance of evaluating metabolic status in the respiratory assessment of hypothyroid individuals. Future longitudinal studies with larger sample sizes are warranted to explore the reversibility and causal direction of this relationship.

REFERENCES

1. Sekhar R, Srinivas CH, Das MC. Lipid profile in “newly diagnosed” and “on treatment” hypothyroid. J Clin Diagn Res 2011;5:998-1000.
2. Vanderpump MPJ. The epidemiology of thyroid disease. *Br Med Bull*. 2011;99:39–51.
3. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. *Indian J Endocrinol Metab*. 2013;17(4):647–652.
4. Baskin HJ, Duick DS, Guttler RB, Kaplan MM, Segal RL, Hamilton CR, *et al*. American association of clinicalendocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. Endocr Pract 2002;8:457-69.

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5. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab 2011;15:S78-81.
6. Mullur R, Liu YY, Brent GA. Thyroid hormone regulation of metabolism. Physiol Rev 2014;94:355-82.
7. Reaven GM. Insulin resistance: the link between obesity and cardiovascular disease. *Med Clin North Am*. 2011;95(5):875–892.
8. Maratou E, Hadjidakis DJ, Peppa M, et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. *Eur J Endocrinol*. 2009;160(5):785–790.
9. Duntas LH, Orgiazzi J, Brabant G. The interface between thyroid and diabetes mellitus. *Clin Endocrinol (Oxf)*. 2011;75(1):1–9.
10. Forno E, Han YY, Muzumdar RH, Celedón JC. Insulin resistance, metabolic syndrome, and lung function in US adolescents with and without asthma. *J Allergy Clin Immunol*. 2015;136(2):304–311.
11. Lawlor DA, Ebrahim S, Smith GD. Association between insulin resistance and lung function in older women: cross sectional findings from the British Women's Heart and Health Study. *Thorax*. 2004;59(1):90–93.
12. Yokoyama H, Emoto M, Fujiwara S, Motoyama K, Morioka T, Komatsu M, *et al*. Quantitative insulin sensitivitycheck index and reciprocal index a of homeostasis model assessment in normal range weight and moderately obeseType 2 diabetic patients. Diabetes Care 2003;26:2426-32.
13. Mancini, D. M., & Henson, D. (1986). Altered respiratory muscle function in hypothyroidism. *The American Journal of Medicine*, 80(3), 377–383.
14. Laroche, C., et al. (1988). Respiratory muscle function and ventilatory drive in hypothyroidism. *Thorax*, 43(6), 488–492.
15. Maratou, E., et al. (2009). Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. *European Journal of Endocrinology*, 160(5), 785–790.
16. Duntas, L. H. (2002). Thyroid disease and lipids. *Thyroid*, 12(4), 287–293
17. Lazarus, R., et al. (2003). Association of insulin resistance with lung function in nondiabetic individuals. *American Journal of Respiratory and Critical Care Medicine*, 168(4), 394–399.
18. Forno, E., et al. (2014). Insulin resistance and lung function in US adolescents with and without asthma. *The Journal of Allergy and Clinical Immunology*, 134(2), 304–311.
19. Sood, A., et al. (2008). Association between insulin resistance and chronic obstructive pulmonary disease in never-smokers. *Thorax*, 63(4), 335–341.
20. Al Mutair, A. N., et al. (2019). Pulmonary function in patients with hypothyroidism. *Cureus*, 11(4), e4501.

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