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ORIGINAL RESEARCH

A study of glycosylated haemoglobin (HbA1C) levels in non-diabetic patients with hypothyroidism

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Abstract

Background: Hypothyroidism and its related endocrine dysfunctions are commonly associated with alterations in glucose metabolism. In non-diabetic individuals, hypothyroidism may cause a rise in glycated haemoglobin (HbA1c) levels, which could lead to misinterpretations in glycemic control. This study evaluates the relationship between thyroid function and HbA1c levels in non-diabetic patients with hypothyroidism.

Objectives: 1. To evaluate and compare HbA1c levels in non-diabetic hypothyroidism patients and non-diabetic euthyroid controls.

2. To assess correlation between serum TSH and HbA1c levels.

Methods: A cross-sectional study was conducted at the Integral Institute of Medical Science and Research, Lucknow. A total of 80 subjects, including 40 non-diabetic hypothyroid patients and 40 euthyroid controls, were included. Blood samples were collected to evaluate HbA1c, TSH, T3, and T4 levels. Statistical analysis was performed to identify correlations between TSH and HbA1c.

Results: HbA1c levels were significantly higher in the hypothyroid group (5.99 ±0.82%) compared to the euthyroid group (5.15 ±0.53%) ($p < 0.001$). A significant positive correlation was observed between TSH and HbA1c levels ($r = 0.566$, $p < 0.001$).

Conclusion: Elevated HbA1c levels in non-diabetic hypothyroid patients should be interpreted cautiously. The increase in HbA1c may not indicate poor glycemic control but rather a consequence of thyroid dysfunction.

Introduction

Thyroid is a butterfly shaped gland located in the front of neck just above trachea. Thyroid gland produces two hormones, thyroxine or T4 (3,5,3',5 'L- tetraiodothyronine) and triiodothyronine or T3 (3,5,3 'L- triiodothyronine). In addition, the thyroid gland secrets small amounts of biologically inactive 3,3',5 'L-triiodothyronine (reverse T3) and minute quantities of monoiodotyrosine (MIT) and diiodotyrosine (DIT) which are the precursors of T3 and T4[1]. Thyroid dysfunction implies excessive or underproduction of thyroid hormones which is governed by another hormone named as Thyroid stimulating hormone (TSH) that is

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produced by the anterior pituitary and is regulated by thyrotropin releasing hormone (TRH) secreted by the hypothalamus[1].

Thyroid disease is a general term that includes both (i) presence of localized or generalized physical changes in the gland resulting in swelling of the gland (viz. diffuse goiter, multinodular goiter, or single thyroid nodule). These changes may be inflammatory, benign or malignant in nature[2], as well as (ii) physiological or functional changes resulting in increased or decreased plasma concentrations of thyroid hormones (T3, T4 and TSH) and are termed as thyroid dysfunction[2]. Thyroid dysfunction is recognized as the leading endocrinal disorder affecting a significant proportion of population throughout the world. Different studies across the world report its prevalence to be 5-10%[3,4,5]. Clinically, thyroid disorders are amongst the most commonly encountered medical problems. The manifestation of thyroid disorders has a considerable variation in different geographical regions and is primarily dependent on the level of dietary iodine intake[6].

In India, prevalence of thyroid disorders or goiter ranges from 505 per 100,000 per women in Nagaland to 8,696 per 100,000 women in Kerala[7].

Thyroid dysfunction is primarily recognized on the basis of changes in biochemical parameters, especially thyroid hormones. Among these thyroid-stimulating hormone (TSH) is the most important indicator of thyroid dysfunction. “The term subclinical thyroid disease is used to define the state having an abnormal serum thyroid stimulating hormone (TSH) concentration (below or above the statistically defined lower or upper limit of the reference range: 0.45–4.50 mIU/L) in the presence of normal serum thyroid hormones concentrations (T4 thyroxine and T3 triiodothyronine within their reference ranges). Subclinical thyroid disease may progress to overt thyroid disease. Overt thyroid dysfunction is defined by an abnormality of both the TSH and thyroid hormones”[8].

Thyroid hormones play an essential role in regulating energy balance, metabolism of glucose, and lipids. Thyrotropin directly induces adipogenesis and adipokine production, independent of control on energy balance[9,10,11]. Hypothyroidism is associated with obesity, dyslipidemia and increased atherosclerotic vascular disease[12]. A similar cluster consisting of obesity, dyslipidemia, diabetes and hypertension was proposed by Reaven[13] under the name "Metabolic syndrome" in 1988. Thus diabetes, glucose metabolism, lipid metabolism and thyroid hormones seem to have some interrelated relationship.

The thyroid gland is responsible for the 30% of daily energy expenditure at rest. Thyroid hormones regulate many metabolic pathways affecting the process of thermogenesis, lipolysis and BMR. Furthermore, hormones can modulate a number of cellular processes that are essential for resting energy expenditure (REE)[14]. Consequences of obesity include changes in thyroid hormone activity, whereas weight loss leads to their normalization. The increased concentration of thyroid hormones leads to increased REE and results in decrease of the availability of energy, which is accumulated in the form of fat cells. Chronic imbalance between REE, energy supply and its availability can lead to the loss or growth of fat cells[15].

Recent medical literature has documented a relationship between thyroid function and insulin metabolism[16,17,18]. In a step forward, some researchers have attempted to understand the physiological reasons why these inter-relationships take place? Among some mechanisms proposed, one is the oxidative stress cause by vitiation of one of these abnormalities which then triggers the other. For example, thyroid hormones are associated with the oxidative and antioxidative status of the organism. Depression of metabolism due to hypothyroidism has been reported to decrease oxidant production and thus protects tissues against oxidant damage[19,20]. It is assumed that in hypothyroidism patients these mechanisms disturb the metabolic roles of thyroid hormones T3 and T4 in maintaining the balance of glucose homeostasis by playing agonistic and antagonistic roles[21]. Consecutively, a relationship between diabetes and oxidative stress has also been traced[22]. Subsequently, insulin

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resistance in diabetes has been shown to increase mitochondrial reactive oxygen species (ROS) production from free fatty acids and by inactivation of anti-atherosclerosis enzymes by ROS[23]. The impact of diabetes on oxidative stress and lipid levels has also been investigated and established[24,25].

Although, role of hypothyroidism in affecting the insulin metabolism has been highlighted in earlier studies, particularly in diabetic patients however, there are limited studies evaluating effect of thyroid disorder/hypothyroidism on the level of glycemic control in non-diabetic individuals. Hence, the present study was carried out to study the glycated haemoglobin levels of non-diabetic patients with hypothyroidism in order to assess the possible role of thyroid disorder/hypothyroidism in pathogenesis of diabetes

Materials and methods

Study Design

A cross-sectional study was conducted over an 18-month period from September 2022 to March 2024 at the Integral Institute of Medical Science and Research, Lucknow. The study was approved by the Institutional Ethics Committee, and informed consent was obtained from all participants.

Study Population

The study included 40 non-diabetic patients with hypothyroidism and 40 non-diabetic euthyroid controls. The cases were recruited from the outpatient and inpatient departments of the institute.

Inclusion and exclusion criteria were strictly followed to ensure the validity of the results.

Inclusion Criteria:

1. Patients who gave valid written informed consent for the study.
2. Patients who have hypothyroidism, according to ATA guidelines[26].
3. Patients who gave no history of diabetes in the past.
4. Patients who have Normal Thyroid function, according to ATA guidelines[26].

Exclusion Criteria

1. Patients having history of diabetes and those who are diabetic, according to ADA guidelines[27].
2. Patients having hyperthyroidism.
3. Patients having history of recent (< 3months) blood transfusion.
4. Patients having history of any haematological disorder.

Data Collection

Demographic characteristics including age, sex, occupation, and dietary preferences, were recorded. Medical history, including thyroid hormone replacement therapy, blood transfusion, and personal habits, were documented. Anthropometric measurements such as weight, height, and body mass index (BMI) were taken. Blood pressure and systemic examination were performed.

Laboratory Analysis

Fasting blood samples were collected to measure thyroid hormones (T3, T4, TSH), fasting blood sugar (FBS), and HbA1c levels. Blood samples were processed using standardised methods in the Department of Biochemistry.

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Statistical Analysis

Data wereanalysed using SPSS software (version 25.0). Continuous variables were expressed as mean + standard deviation (SD), and categorical variables were presented as percentages. Independent t-tests were used to compare the means of cases and controls. Pearson's correlation was applied to assess the relationship between TSH and HbA1c levels. A p-value < 0.05 was considered statistically significant.

Results

Demographic Characteristics

Out of the 80 participants, 82.5% of the cases and 85% of the controls were female, indicating a female dominance in both groups. The mean age of the hypothyroid patients was 38.88 ±9.60 years, while the mean age of the euthyroid controls was 36.00 ±10.50 years. There were no significant differences in the demographic characteristics of the two groups

Table 1: Comparison of sex profile of cases and controls

SN	Sex	Cases (n=40)		Controls (n=40)		Total (n=80)	
		No.	%	No.	%	No.	%
1	Male	7	17.5	6	15.0	13	16.3
2	Female	33	82.5	34	85.0	67	83.8
$x^2=0.092$; p=0.762							

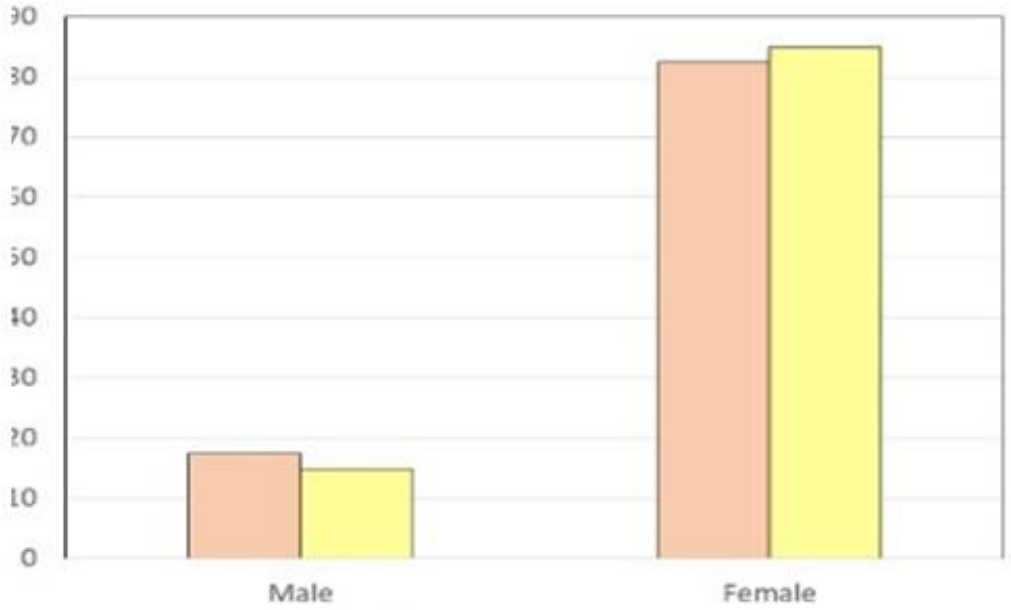

Fig. 1: Comparison of sex profile of cases and controls

Comparison of Hemodynamic and BMI Profile

There was no significant difference in the mean heart rate, systolic blood pressure, diastolic blood pressure, or BMI between the cases and controls ($p > 0.05$). The mean BMI was 25.83 ±2.61 kg/m² in the hypothyroid group and 26.19 ±2.27 kg/m² in the control group, with no significant difference between them

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Table 2: Comparison of Hemodynamic Profile between cases and controls

SN	Parameter	Cases (n=40)		Controls (n=40)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
1	Heart rate (bpm)	78.55	6.51	78.05	10.89	0.249	0.804
2	Systolic blood pressure (mmHg)	119.68	6.54	120.23	5.65	0.402	0.688
3	Diastolic blood pressure (mmHg)	78.40	7.06	76.58	7.97	1.084	0.282

Table 3: Comparison of BMI Profile between cases and controls

SN	BMI	Cases (n=40)		Controls (n=40)		Total (n=80)	
		No.	%	No.	%	No.	%
1	Normal weight (18.5-24.9 kg/m2)	18	45	15	37.5	33	41.3
2	Overweight (25.0-29.9 kg/m2)	22	55	24	60.0	46	57.5
3	Obese (≥30 kg/m2)	0	0	1	2.5	1	1.3
c2=1.360; p=0.507							
Mean BMI±SD (Range) kg/m2		25.83±2.61 (22.3-29.6)		26.19±2.27 (22.0-30.0)		t=0.666; p=0.507	

Thyroid Hormone Levels

The mean TSH levels were significantly higher in the hypothyroid group (15.13 ±19.73 µIU/mL) compared to the control group (2.45 ±1.12 µIU/mL) ($p < 0.001$). However, no significant differences were observed in T3 and T4 levels between the two groups.

Table 4: Comparison of Thyroid Profile between cases and controls

SN	Parameter	Cases (n=40)		Controls (n=40)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
1	T3 (nmol/L)	1.63	1.20	1.26	0.57	1.830	0.071
2	T4 (µg/dL)	8.04	1.55	8.13	1.09	0.329	0.743
3	TSH (µIU/ml)	15.13	19.73	2.45	1.12	4.057	<0.001

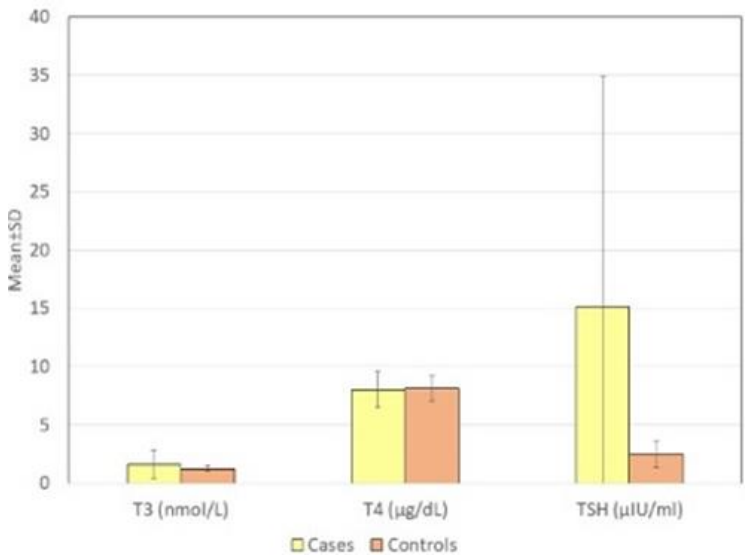

Fig. 2: Comparison of Thyroid Profile between cases and controls

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Glycemic Parameters

There was no significant difference in fasting blood sugar (FBS) and random blood sugar (RBS) levels between the cases and controls. However, HbA1c levels were significantly higher in the hypothyroid group (5.99 ±0.82%) compared to the euthyroid group (5.15 ± 0.53%) ($p < 0.001$).

Table 5: Comparison of Blood sugar and HbA1c levels between cases and controls

SN	Parameter	Cases (n=40)		Controls (n=40)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
1	FBS (mg/dl)	106.45	23.26	101.18	16.50	1.170	0.246
2	RBS (mg/dl)	114.63	8.19	117.70	8.00	1.699	0.093
3	HbA1c (%)	5.99	0.82	5.15	0.53	5.446	<0.001

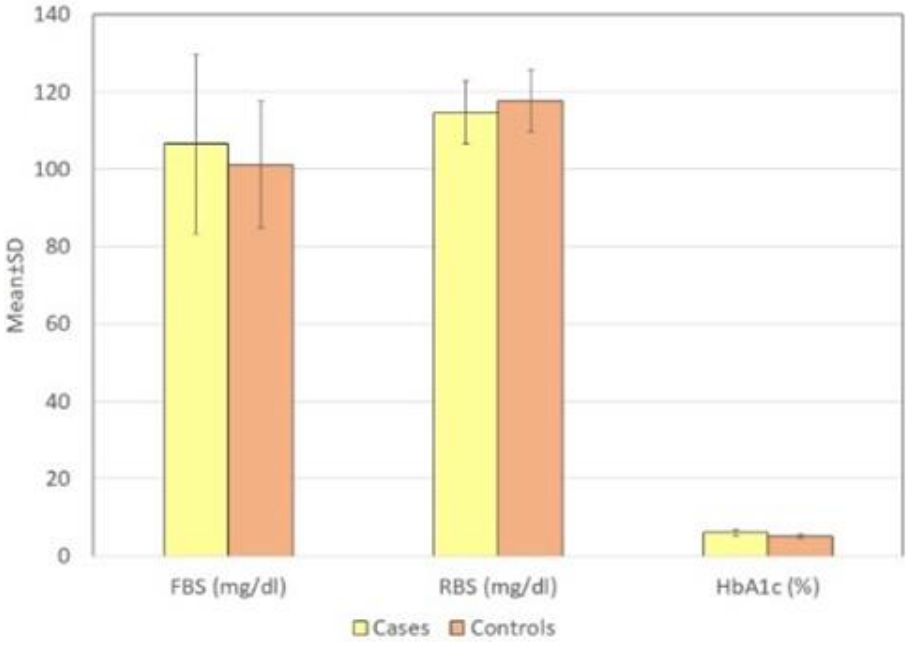

Fig. 3: Comparison of Blood sugar and HbA1c levels between cases and controls

Correlation between TSH and HbA1c

A moderate positive correlation was found between TSH and HbA1c levels ($\rho = 0.566$, $p < 0.001$), indicating that higher TSH levels are associated with increased HbA1c levels. No significant correlation was observed between HbA1c and T3 or T4 levels (Table 5).

Table 6: Correlation of HbA1c levels with Thyroid hormones

Correlation	ρ	'p'	Strength of correlation
T3 vs HbA1c	0.007	0.951	NS
T4 vs HbA1c	0.172	0.127	NS
TSH vs HbA1c	0.566	<0.001	Significant, Moderate positive correlation

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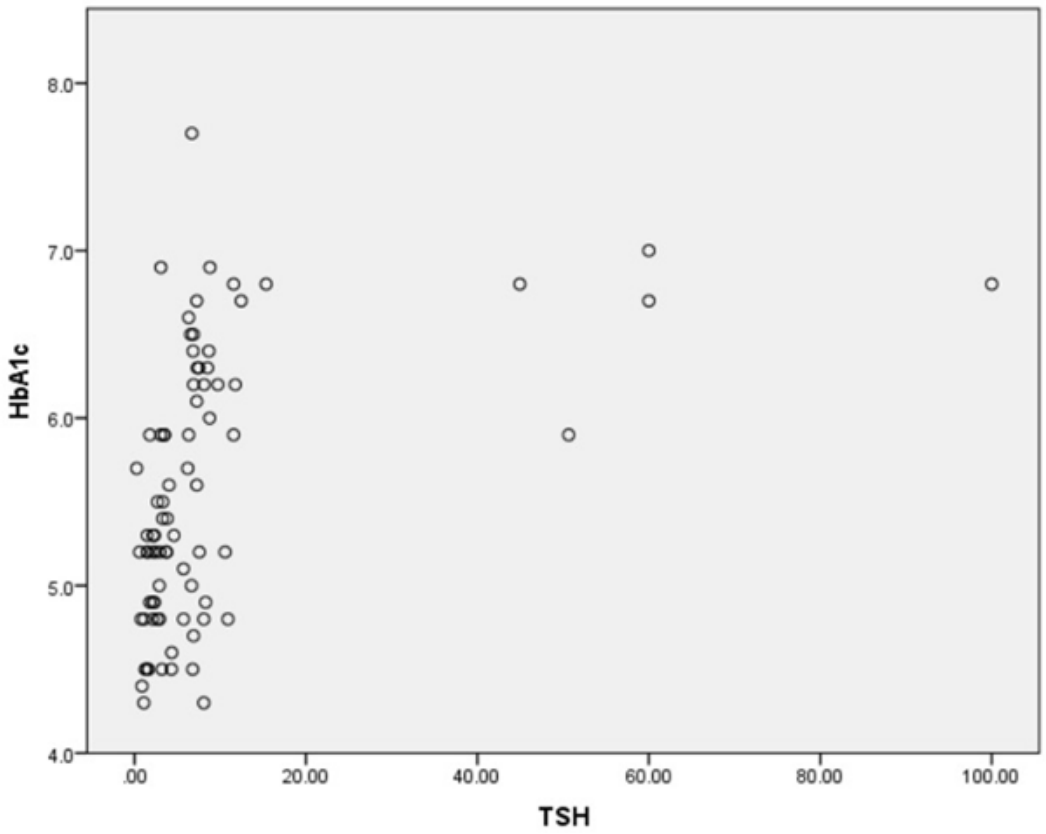

Fig. 4: Correlation between TSH and HbA1c levels

Discussion

The present study found significantly higher HbA1c levels in non-diabetic hypothyroid patients compared to euthyroid controls. This is consistent with previous studies that suggest hypothyroidism may lead to a "false" increase in HbA1c levels due to altered red blood cell turnover and other metabolic changes . The moderate positive correlation between TSH and HbA1c levels further supports the hypothesis that thyroid dysfunction, rather than impaired glucose metabolism, is responsible for the elevated HbA1c in hypothyroid patients.

Our findings emphasise the need for clinicians to interpret HbA1c levels cautiously in patients with thyroid dysfunction, especially in those without a history of diabetes . Misinterpretation of elevated HbA1c levels in hypothyroid patients may lead to unnecessary interventions for diabetes.

The limitations of this study include its cross-sectional design, which limits the ability to establish causality between hypothyroidism and elevated HbA1c levels. A prospective study evaluating the effect of thyroid hormone replacement therapy on HbA1c levels would provide more conclusive evidence.

Conclusion

The present study evaluated an association between HbA1c and hypothyroidism in non-diabetic individuals using a case-control study design. For this purpose, a total of 40 hypothyroid patients (mean age 38.88±13.98 years; 82.5% females) and a total of 40 euthyroid subjects (mean age 36.00±10.50 years; 85% females) were enrolled in the study. Both the patient groups did not have any history of diabetes, thyroid hormone replacement history, any other metabolic disorder or any other relevant medical or family history. Comparison of thyroid hormone profile and glycemic parameters (FBS, RBS and HbA1c) was done. Following were the concluding findings:

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1. Mean HbA1c levels were significantly higher in cases (5.99±0.82%) as compared to that in controls (5.15±0.53%).
2. There was a moderate positive correlation between TSH and HbA1c levels.
3. No statistically significant difference was seen between the two groups for fasting and random blood sugar levels.

The findings of the present study show that hypothyroidism affects the HbA1c levels without affecting the other glycemic parameters. Hence, it should be viewed as a faulty increase and should not be considered as a diagnostic measure for diabetic or pre-diabetic status.

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