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ORIGINAL RESEARCH ARTICLE

Correlation between Clinical Parameters and Pharmacological Effects on HbA1c, Thyroid Function, and Quality of Life in T2DM Patients with Hypothyroidism

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Abstract

Background and Objectives: Diabetes mellitus (DM) and thyroid disorders (TD) are the most common endocrine disorders seen in the general population. These two disorders are mutually associated and influence each other. This study examines the link between clinical variables and drug efficacy on glycated hemoglobin (HbA1c) and thyroid hormone (TH) levels in patients with type 2 diabetes mellitus (T2DM) and hypothyroidism.

Methods: A total of 154 participants were included in this research study: 54 controls and 100 patients diagnosed with type 2 diabetes mellitus (T2DM) and hypothyroidism and all of whom were receiving medication for both conditions. Blood samples were collected under standardized conditions, and analyses were conducted using high-precision laboratory techniques.

Results: In this study, the prevalence of coexistence of T2DM and hypothyroidism was higher in females, 91 (91%). Patients tended to be older, and a significant proportion of the patient group had sleep disorders. There were substantial differences in body mass index (BMI), HbA1c, and serum glucose levels across the groups ($P < 0.0001$). Thyroid markers, including thyroid-stimulating hormone (TSH), free Triiodothyronine (FT3), and FT3/Free thyroxine (FT4) ratio were shown to be strongly correlated to HbA1c levels. Furthermore, analysis of antidiabetic medications indicated a strong correlation between HbA1c levels and particular treatment combinations.

Conclusion: There is a significant interaction between DM and hypothyroidism. Unexpectedly low levels of TSH were observed in patients who were non-adherent to levothyroxine treatment. This phenomenon is believed to be related to the effects of metformin on thyroid hormones, as has been previously investigated.

Keywords

Diabetes mellitus, Hyperglycemia, Thyroid dysfunction, Hypothyroidism, Hormones

Introduction

Both T2DM and TD are chronic disorders that require lifetime care and have a long-term impact on cardiovascular health (Kalra, et al. 2019) [1]. DM is a chronic condition caused by the body's failure to metabolize and regulate blood glucose, owing to the over-secretion of insulin from the pancreas or the inability of insulin to regulate blood glucose levels (Mohammed, et al. 2024) [2]. In diabetes, chronic hyperglycemia is associated with damage, malfunction, and failure of different tissues and organs (Bashir, et al. 2024) [3]. The global incidence of DM is quickly growing due to urbanization, an ageing population, and related lifestyle changes (Archana, et al. 2025) [4]. In 2019, an estimated 1.5 million deaths directly related to diabetes which making it the ninth leading cause of mortality, according to the WHO's fact sheets on diabetes (A. Singh, et al. 2022) [5].

The thyroid is affected by 10-18% of diabetic patients compared to just 6% of non-diabetics (Hadgu, et al. 2024) [6]. Hyperthyroidism and hypothyroidism are more common in diabetic patients with poor glycemic control (Sakyi, et al. 2023; Kadiyala, et al. 2010) [7,8]. There is a bidirectional relationship between diabetes and hypothyroidism in T2DM, with a high frequency

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of subclinical hypothyroidism and a low incidence of subclinical hyperthyroidism (Biondi, et al. 2019) [9]. However, the mechanisms linking type 2 diabetes to TD remain unclear (Grigoriadis, et al. 2023) [10]. When lifestyle changes fail to reduce HbA1c below 6.5% within 2-3 months, pharmacological therapy is recommended to treat T2DM (Chaudhury, et al. 2017) [11]. Hemoglobin A1c must be maintained less than 7.0% to decrease complications in the microvascular system, according to the American Diabetes Association (Varghese, 2017) [12]. Thiazolidinedione, biguanides, sulfonylureas, sodium-glucose co-transporter 2 inhibitors (SGLT2 inhibitors), meglitinide, α-glucosidase inhibitors, and dipeptidyl peptidase 4 inhibitors (DPP-4 inhibitors) are considered Oral antidiabetic drugs11, and it is thought that biguanides are both safe and effective for treating T2DM, making them the most usable oral antidiabetic drug (Grigoriadis, et al. 2023; Wang, et al. 2016) [10,13]. The available research indicates that metformin therapy is associated with better clinical outcomes when compared to other oral antidiabetic medications such as insulin, especially in patients with heart failure (Kułaczkowska, et al. 2021) [14].

A complex relationship between T2DM and hypothyroidism exists and is also not fully understood. While some researchers have explored hypothyroidism in T2DM patients, but there is still limited research data and information on clinical parameters and medications of this population. Therefore, this study aims to investigate clinical factors contributing to HbA1c variability, including BMI and thyroid hormones, in patients with T2DM and hypothyroidism. Furthermore, to assess the effectiveness of antidiabetic drugs (Metformin, Sulfonylureas, DPP-4 inhibitors, and SGLT2 inhibitors) in improving glycemic control in this population and examine their correlation with biochemical parameters like BMI, serum glucose, TSH, FT3 and FT4.

Materials and Methods

Study design

This study is a Case-Control study conducted for 5 months at Zakho Chronic Diseases Center, Zakho General Hospital, and Nawroz Private Hospital. The study involved 154 adults aged between 28 and 73 years, comprising 100 patients and 54 controls. Blood samples and relevant data were collected from both groups, focusing on various variables, including demographics, comorbid conditions, the duration of diabetes and hypothyroidism, and the types and dosages of medications prescribed for T2DM and hypothyroidism.

Collection of samples

Blood samples were collected from each participant using EDTA tubes to measure HbA1c levels. Gel tubes were employed for serum separation to assess the thyroid hormone profile, including TSH, FT3, and FT4, as well as fasting serum glucose levels. Participants' fasting status was confirmed prior to blood collection. Data collection took place from June 1st to December 20th. To ensure consistency among groups, control participants underwent the same procedures. All samples were processed in a single central laboratory following established protocols to guarantee uniformity. The Cobas 6000 c501 autoanalyzer system (Roche Diagnostics, HITACHI) was utilized to measure fasting serum glucose, while the Cobas 6000 c601 autoanalyzer system (also from Roche Diagnostics, HITACHI) was used to analyze the levels of FT4, FT3, and TSH in each sample. The Cobas c311 autoanalyzer system (also from Roche Diagnostics, HITACHI) was used for measuring HbA1c levels.

Inclusion and exclusion criteria

Patients diagnosed with coexisting T2DM and hypothyroidism were included in this study, regardless of age or gender. They were receiving appropriate pharmacological therapies. Exclusion criteria for the study included pregnancy, breastfeeding, prediabetes, isolated thyroid dysfunction, type 1 diabetes mellitus (T1DM), severe cognitive or psychiatric disorders, major comorbidities (such as cardiovascular disease, chronic kidney disease, and liver disease), as well as recent thyroid surgery or radioactive iodine therapy.

The control group consisted of healthy individuals who had no chronic illnesses, were biochemically verified to be free of DM and hypothyroidism, and were not taking any medications. An HbA1c level of less than 5.7% was considered normal, and thyroid hormone levels were required to fall within the standard reference ranges: FT3 between 3.1 and 8.6 pmol/L, FT4 between 11.9 and 21.6 pmol/L, and TSH between 0.25 and 4.3 μIU/mL. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared and categorized according to WHO recommendations as follows: normal (18.5-24.9), overweight (25.0-29.9), and obese (greater than 30.0).

Statistical analysis

Quantitative data were presented as means ± standard deviation (SD), percentages, and frequencies when applicable. The normality of the data was assessed using the Kolmogorov-Smirnov test and histograms. Spearman's correlation coefficient was calculated to determine the correlation between clinical parameters, and scatter plots were used to illustrate the direction of the correlation (positive or negative).

For categorical data, the chi-squared test was employed to assess associations. To compare differences between two groups, an independent samples t-test was utilized, while one-way analysis of variance (ANOVA) was used to identify any statistically significant differences among the means of multiple independent groups. A two-tailed p-value of less than 0.05 was considered statistically significant.

Multiple linear regression analysis was conducted to predict the effects of various parameters on HbA1c and TSH levels. To investigate the relationship between HbA1c levels and the likelihood of being prescribed one of six classes of antidiabetic medications, multinomial logistic regression analysis was conducted. Variables in the multiple logistic regression model were selected based on their statistical significance in the univariate analysis ($p < 0.05$) and clinical relevance determined by prior literature. All statistical calculations were carried out using Microsoft Excel 2019 and SPSS (Statistical Package for the Social Sciences).

Results

Table 1 presents the demographic and biochemical characteristics of the group of diabetic patients with hypothyroidism (n = 100) and the control group (n = 54). Compared to the control group, the patients DM and hypothyroidism were older, with an average age 55 ± 11.05 years. Additionally, there was a higher proportion of females in the patient group, with 91 (91%) out of 100. The Body Mass Index (BMI) was also significantly higher in the patient group, averaging (32.9 ± 5.8), compared to the control group, which had an average BMI (28.9 ± 4.6), with a p-value of less than 0.0001.

The duration of DM among patients varied significantly, ranging from 1 year to 28 years, with a mean duration (9.3 ± 7.4). In contrast, the duration of hypothyroidism ranged from 1 year to 15 years, with a mean duration (4.1 ± 4.7). In terms of occupation, the majority of patients (91%, n = 91) were non-workers. No significant differences were found in marital status ($p = 0.290$). Regarding sleep quality and sleep disorders, a significant difference was noted between the patient group and the control group ($p < 0.0001$ for both). The patient group exhibited poor sleep quality, with 58 patients (58%) reporting difficulty sleeping, compared to only 10 individuals (19.2%) in the control group. When comparing vaccination status between patients and controls, the proportion of vaccinated individuals with post-COVID status was similar in both groups, with no significant differences observed ($p > 0.05$).

As predicted, patients exhibited significantly higher levels of HbA1c and glucose compared to the control group (8.1 ± 1.7 Vs. 5.4 ± 0.2 and 159 ∓ 65mg/dL Vs.

Table 1: Baseline and biochemical characteristics of subjects participating in the study.

Category	Controls N = 54	Patients N = 100	P-value	Chi-square value
Age (Years)	46.5 ∓ 6.8	55 ∓ 11.05	< 0.0001*	N/A
HbA1c mg/Dl	5.4 ± 0.2	8.1 ∓ 1.7	< 0.0001	N/A
Serum Glucose mg/dL	98.5 ∓ 17.1	159 ∓ 65	< 0.0001*	N/A
BMI (kg/m²)	28.9 ∓ 4.6	32.9 ∓ 5.8	< 0.0001*	N/A
Duration of DM (Years)	-	9.3 ± 7.4	-	N/A
Duration of TD (Years)	-	4.1 ± 4.7	-	N/A
TSH µIU/mL	2.5 ± 2.3	5.4 ± 6.8	< 0.0001	N/A
FT3 µIU/mL	6.3 ± 0.6	5.6 ± 0.7	< 0.0001	N/A
FT4 µIU/Ml	15.5 ± 2.1	15.7 ± 2.7	0.378	N/A
FT3/FT4 ratio	0.41 ± 0.56	0.366 ± 0.08	0.001	N/A
Gender			0.021*	7.684
Female	38 (70.4%)	91 (91%)		
Male	16 (29.6%)	9 (9%)		
Occupation			< 0.0001	21.493
Worker	27 (50%)	9 (9%)		
Non-worker	27 (50%)	91 (91%)		
Marital status			0.315	1.009
Single	1 (1.9%)	0 (0%)		
Married	53 (98.1%)	100 (100%)		
Sleep quality:			< 0.0001	22.85
Bad	10 (19.2%)	65 (65%)		
Good	24 (44.2%)	22 (22%)		
Perfect	20 (36.6%)	13 (13%)		
Sleep disorders			< 0.0001	27.9
Yes	10 (43%)	58 (58%)		
No	44 (57%)	42 (42%)		
Post-covid:			0.982	0.0005
Yes	30 (55.6%)	59 (59%)		
No	24 (44.4%)	41 (41%)		
Pre-vaccinated:			0.865	0.029
Yes	31 (57.4%)	53 (53%)		
No	23 (42.6%)	47 (47%)		

Independent samples T-test and Chi-square test comparing cases and controls. *Significant at $p < 0.05$.

98.5 ∓ 17.1, respectively). In the analysis of thyroid function profiles, significant differences were also observed between patients and controls in terms of TSH, FT3, and the FT3/FT4 ratio (5.4 ± 6.8 Vs. 2.5 ± 2.3), (5.6 ± 0.7 Vs. 6.3 ± 0.6), and (0.366 ± 0.08 Vs. 0.41 ± 0.56), respectively.

The prevalence of symptoms related to T2DM and hypothyroidism

In our study, we surveyed diabetic patients who also had hypothyroidism and evaluated the prevalence of symptoms linked to both conditions. The results showed that a significant percentage of patients reported common diabetes symptoms, such as increased thirst, frequent urination, fatigue, weight fluctuations, and sensitivity to temperature (see Table 2). Furthermore, symptoms typically associated with hypothyroidism, including hair loss, depression, and stress, were also observed in a notable proportion of patients (see Table 2).

Correlation between clinical parameters

In our analysis using Spearman correlation, we examined the relationships between HbA1c, TSH, and various clinical parameters. We found that HbA1c was positively correlated with age ($r = 0.452$, $p < 0.0001$) and displayed a similar trend with glucose ($r = 0.579$, $p < 0.0001$), duration of DM ($r = 0.450$, $p = 0.003$), BMI ($r = 0.3$, $p = 0.002$), TSH ($r = 0.295$, $p = 0.002$), and the FT3/FT4 ratio ($r = 0.297$, $p = 0.002$). Conversely, HbA1c was negatively correlated with sleeping hours ($r = -0.197$, $p = 0.038$) and FT3 ($r = -0.374$, $p < 0.0001$) (see Table 3 and Figure 1).

Regarding TSH, we observed a significant positive correlation between TSH and BMI ($r = 0.280$, $p = 0.005$). Additionally, TSH exhibited an inverse correlation with FT3 ($r = -0.374$, $p < 0.0001$) and FT4 ($r = -0.263$, $p < 0.006$). TSH did not show significant correlations with other variables (see Table 3).

The association of HbA1c and TSH with other clinical parameters

A multiple linear regression analysis was conducted to assess the effects of clinical parameters on HbA1c levels. The regression model indicated that both the duration of DM and serum glucose levels are significant positive predictors of HbA1c ($p = 0.049$ and $p = 0.0003$, respectively). This suggests that a longer duration of

Table 2: Comparison of the prevalence of symptoms associated with diabetes and hypothyroidism.

Symptoms	N = 100	
	N (%) Yes	N (%) No
Frequent urination	64 (64%)	36 (36%)
Increased thirst	75 (83.33%)	16 (16%)
Fatigue	92 (92%)	8 (8%)
Weight gain	83 (83%)	17 (17%)
Temperature sensitivity	83 (83%)	17 (17%)
Hair loses	79 (79%)	21 (21%)
Mood changes (Depression)	87 (87%)	13 (13%)
Stress	79 (79%)	21 (21%)

Table 3: Shows the correlation coefficients (r) and their corresponding p-values for various clinical parameters and biomarkers in the studied population.

HbA1c	**Correlation Coefficient**	**P-value**
Age	0.452*	< 0.0001
Serum Glucose	0.579*	< 0.0001
Duration of DM	0.450*	0.003
Duration of DTD	0.107	0.485
BMI	0.3*	0.002
Sleeping Hours	-0.197*	0.038
TSH	0.295**	0.002
FT3	-0.416*	< 0.0001
FT4	-0.062	0.528
FT3/FT4 ratio	0.297*	0.002
TSH	**Correlation Coefficient**	**P-value**
Serum glucose	0.086	0.38
Duration of DTD	0.063	0.659
Duration of DM	-0.082	0.565
BMI	0.280*	0.005*
Sleeping hours	-0.136	0.161
FT3	-0.374*	< 0.0001*
FT4	-0.263*	0.006
FT3/FT4 ratio	0.027	0.781

Spearman correlation analysis, *p-value < 0.05.

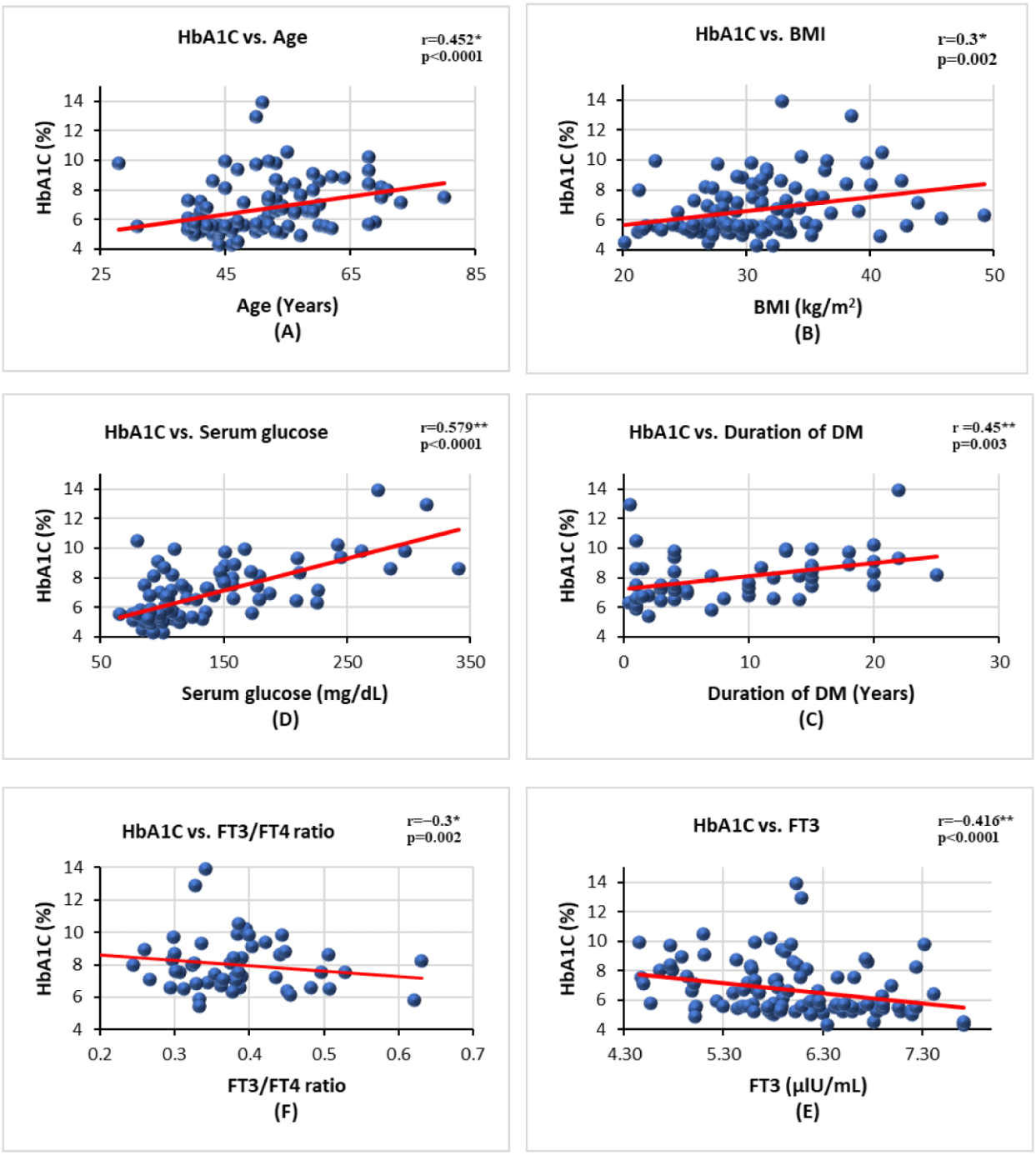

Figure 1: Scatter plots illustrating the direction of linear correlation between HbA1c and various parameters, along with the corresponding (r) values and p-values.

DM and higher serum glucose levels are associated with increased HbA1c levels. The model explained 49.3% of the variance in HbA1c ($R^2 = 0.493$), indicating a moderate fit between the independent variables and HbA1c. However, other variables included in the model did not emerge as significant predictors of HbA1c (see Table 4).

Regarding the predictors of TSH, the clinical parameters did not yield significant values. This suggests that these parameters do not effectively predict TSH concentrations. However, FT3 emerged as a highly significant negative predictor for TSH (B = -3.192, p = 0.003) (see Table 4), which aligns with the physiological principle of negative feedback.

Prescribed antidiabetic and thyroid dysfunction medications

Prescribed antidiabetic medications included metformin (Biguanides), DPP-4 inhibitors, sulphonylureas, and SGLT2 inhibitors (Table 5). All the patients were receiving metformin (Biguanides), making it the most widely used drug, both alone and in combination with other medications. Significant differences were observed between the mean HbA1c and TSH levels across the various diabetes medication classes, when compared to the control group ($p < 0.0001$ and $p = 0.019$, respectively). Patients receiving biguanides alone had the lowest mean Hba1c levels,

Table 4: Multiple regression analysis of key predictors of HbA1c and TSH in the study population.

Dependent Variable	Predictor Variables	B	S. E	95% CI		t-value	p-Value
				Lower	Upper		
HbA1c	Age	-0.018	0.026	-0.684 to 0.498		-0.684	0.498
	Duration of DM	0.098	0.048	2.039 to 0.049		2.039	0.049*
	Duration of TD	-0.023	0.064	-0.364 to 0.718		-0.364	0.718
	BMI	-0.019	0.045	-0.421 to 0.677		-0.421	0.677
	Glucose	0.014	0.004	3.213 to 0.003		3.213	0.003*
	TSH	0.047	0.049	0.969 to 0.339		0.969	0.339
	FT3	0.611	0.846	0.722 to 0.475		0.722	0.475
	FT4	-0.126	0.296	-0.427 to 0.672		-0.427	0.672
	FT3/FT4 ratio	-10.067	12.555	-0.802 to 0.428		1.499	0.143
TSH	Age	1.499	0.143	-0.06 to 0.399		1.499	0.143
	Duration of DM	-1.263	0.215	-0.724 to 0.169		-1.263	0.215
	Duration of TD	0.510	0.613	-0.434 to 0.725		0.510	0.613
	BMI	0.534	0.597	-0.299 to 0.512		0.534	0.597
	Glucose	0.417	0.679	-0.036 to 0.054		0.417	0.679
	HbA1c	0.594	0.556	-1.091 to 1.994		0.594	0.556
	FT3	-1.981	0.055	-6.462 to 0.078		-1.981	0.055
	FT4	-3.521	0.001	-2.07 to -0.556		-3.521	0.001

*p-value < 0.05

Table 5: Prescribed diabetes medications.

Type of Therapy	Mean HbA1c %	Mean TSH (µIU/mL)	N = 100 N (%)
Biguanides	7.1	10.1	20 (20%)
Biguanides + DPP-4 inhibitor	8.6	4.2	13 (13 %)
Biguanides + Sulfonylureas + DPP-4 inhibitor	8.8	3.7	17 (17%)
Biguanides + Sulfonylureas + SGLT2 inhibitor	8.2	5.5	13 (13 %)
Biguanides + SGLT2 inhibitor + DPP-4 inhibitor	9.3	9.5	15 (15%)
Biguanides + Sulfonylureas + DPP-4 inhibitor + SGLT2 inhibitor	8.2	3.3	22 (22%)

Values are expressed as mean or number, frequency (%).

Table 6: Analysis of associations between antidiabetic drug combinations and HbA1c levels in the study population by multinomial logistic regression analysis.

Category	p-value	OR	95% C.I. for OR	
			Lower	Upper
Biguanides + DPP-4 inhibitor / HbA1c	0.04*	2.605	1.026	6.613
Biguanides + Sulfonylureas + DPP-4 inhibitor / HbA1c	0.051	2.769	0.995	7.708
Biguanides + Sulfonylureas + SGLT2 inhibitor / HbA1c	0.154	2.139	0.752	6.085
Biguanides + SGLT2 inhibitor + DPP-4 inhibitor / HbA1c	0.028*	3.268	1.134	9.414
Biguanides + Sulfonylureas + DPP-4 inhibitor + SGLT2 inhibitor / HbA1c	0.094	2.172	0.876	5.385

Multinomial logistic regression analysis; OR: Odds Ratio; C.I: Confidence interval; * = p < 0.05

while those receiving a combination of biguanides, an SGLT2 inhibitor, and a DPP-4 inhibitor exhibited the highest HbA1c levels in comparison with other classes and the control group (see Table 5 and Figure 2). Among the participants, 78 patients (78%) were adherent to levothyroxine sodium (LT4) at specific dosages determined by their thyroid function profiles, while 22 patients (22%) were non-adherent to LT4. Additionally, significant differences were found in the mean HbA1c and TSH levels between the adherent and non-adherent LT4 patients compared to the controls ($p < 0.0001$) (see Figure 2 and Figure 3).

Logistics regression analysis

In the multinomial logistic regression analysis, we examined the relationship between HbA1c levels and the likelihood of being prescribed various combinations of antidiabetic drugs, using single-oral therapy Biguanides (Metformin) as the reference category (see Table 6). The results indicated that higher HbA1c levels were significantly associated with an increased likelihood of being prescribed the combination of Biguanides and DPP-4 inhibitors (OR = 2.605, p = 0.04), as well as the combination of Biguanides, SGLT2 inhibitors, and DPP-4 inhibitors (OR = 3.268, p = 0.028). However, HbA1c levels were not significantly associated with the likelihood of being prescribed the other combinations, compared to Biguanides alone. These findings suggest that individuals with higher HbA1c levels are more likely to be prescribed the combinations of Biguanides and DPP-4 inhibitors or Biguanides, SGLT2 inhibitors, and DPP-4 inhibitors rather than just Biguanides. However, HbA1c

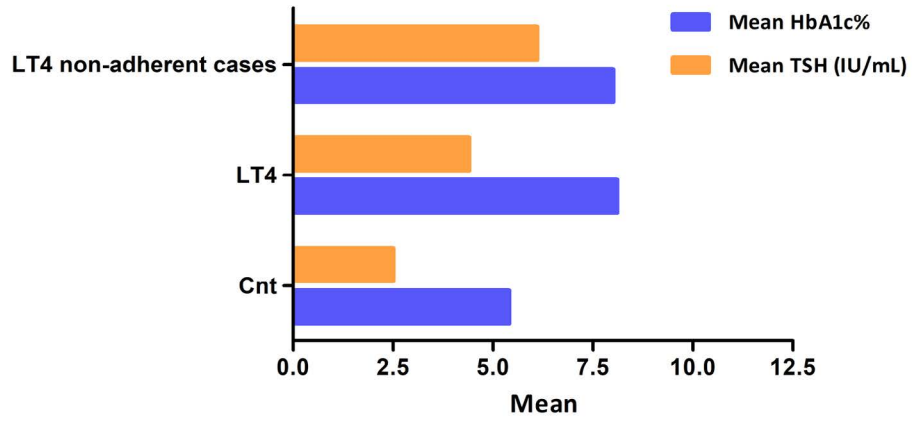

Figure 2: Bar chart, showing the differences in HbA1c and TSH levels in LT4 adherent and non-adherent patients compared to the control group.

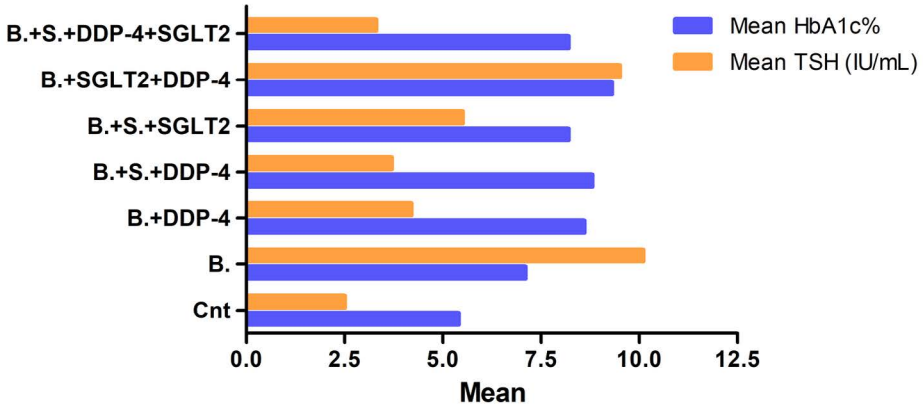

Figure 3: Bar chart, showing the differences in HbA1c and TSH levels in each drug class compared to the control group.

Note: Cnt: Controls; B: Biguanides; SU: Sulfonylureas; DPP-4: Dipeptidyl peptidase 4 inhibitors; and SGLT2: Sodium-glucose co-transporter 2 inhibitors

levels do not significantly influence the prescription of other combinations over the single-oral therapy with Biguanides.

Logistics regression analysis

In the multinomial logistic regression analysis, we examined the relationship between HbA1c levels and the likelihood of being prescribed various combinations of antidiabetic drugs, using single-oral therapy Biguanides (Metformin) as the reference category (see Table 6). The results indicated that higher HbA1c levels were significantly associated with an increased likelihood of being prescribed the combination of Biguanides and DPP-4 inhibitors (OR = 2.605, p = 0.04), as well as the combination of Biguanides, SGLT2 inhibitors, and DPP-4 inhibitors (OR = 3.268, p = 0.028). However, HbA1c levels were not significantly associated with the likelihood of being prescribed the other combinations, compared to Biguanides alone. These findings suggest that individuals with higher HbA1c levels are more likely to be prescribed the combinations of Biguanides and DPP-4 inhibitors or Biguanides, SGLT2 inhibitors, and DPP-4 inhibitors rather than just Biguanides. However, HbA1c levels do not significantly influence the prescription of other combinations over the single-oral therapy with Biguanides.

Discussion

In this study, clinical characteristics and metabolic associations of diabetic patients with hypothyroidism are examined. Coexistence of DM and hypothyroidism was more prevalent in females than males, which aligns with previous studies that indicate that thyroid disorders are more prevalent in women due to hormonal and autoimmune causes. There is a significant association between gender and coexistence of both conditions (p = 0.021), suggesting that female diabetic patients might need to monitor their thyroid function more frequently (Shaphe, et al. 2023) [15]. While the results reported by Vamshidhar & Rani, in 2020 [16] indicate a greater prevalence of thyroid dysfunction in males in their study population. They performed a cross-sectional study and

found that of 50 diabetic patients, 8(16%) had thyroid dysfunction, of which 5(10 %) were males and 3(6%) were females (Vamshidhar & Rani, 2020) [16].

Patients had significantly higher BMI levels, which aligns with the effect of hypothyroidism on weight gain due to a decreased metabolic rate. Additionally, the strong link between BMI and thyroid dysfunction highlights the metabolic issues in these patients. Similarly, these results are consistent with the study by Boye and colleagues, who found that among all people with T2D, higher BMI was associated with higher HbA1c levels (Boye, et al. 2021) [17]. Our findings emphasize the importance of both measurements in evaluating glycemic control and may influence clinical monitoring and treatment strategies.

The results from this study indicate no significant correlation between TSH levels and hours of sleep per night; on the other hand, there was a significant association between coexistence of both conditions and quality of sleep. The observed differences in sleep quality and sleep disorders between the groups highlight the complex interplay between thyroid hormones, glucose metabolism, and sleep regulation. The mechanism behind this interplay is complex and involves multiple physiological pathways, including neuroendocrine, metabolic, and autonomic systems (Jia, et al. 2024) [18]. Studies have illustrated that in hypothyroidism, low thyroid hormone levels increase fatigue and excessive daytime sleepiness (Violante-Ortiz, et al. 2025) [19]. Furthermore, insulin resistance and metabolic dysregulation in hypothyroid patients lead to intermittent hypoxia, which disrupts sleep patterns (Punjabi, 2008) [20].

In biochemical analyses, diabetics differed significantly from controls in key metabolic markers, including HbA1c and serum glucose. HbA1c and thyroid function markers (TSH, FT3, and FT3/FT4 ratio) showed a significant correlation, suggesting there might be a bidirectional relationship between glycemic control and thyroid dysfunction and implying that greater glycemic management is linked to decreased FT3 levels (Banerjee, et al. 2024) [21]. T2DM has been linked to aberrant thyroid hormone levels, according to a meta-analysis. It demonstrated an inverse association with free triiodothyronine and FT4 and a positive relationship with TSH (Ogbonna, et al. 2019) [22].

TSH levels in patients were not significantly correlated with clinical parameters such as age, sleeping hours, or diabetes duration of both conditions in further correlation analysis. This suggests that TSH levels in diabetic patients are more influenced by thyroid hormone imbalances than traditional metabolic risk factors. This data was confirmed by Rong and his colleagues (Rong, et al. 2021) [23]. The significant negative correlation between TSH and thyroid supports the hypothalamic-pituitary-thyroid axis's physiological feedback mechanism (Li, et al. 2022) [24].

Serum glucose levels and the duration of DM were found to be significant predictors of HbA1c by multiple regression analysis, although age and BMI were not. This implies that rather than long-term anthropometric measurements, the duration of the disease and acute glucose levels have a more direct impact on glycemic management in diabetes patients with thyroid dysfunction (Bonora, et al. 2001) [25]. Conversely, TSH levels were largely impacted by FT4 levels, but not by blood glucose or HbA1c, supporting the idea that glycemic management has little bearing on thyroid hormone regulation (Iwakura, et al. 2023) [26].

Additional information on the treatment of these individuals was obtained through medication analysis. The most widely prescribed antidiabetic treatment was metformin, which was frequently used either by itself or in conjunction with other medications. Higher HbA1c values were seen in individuals on stronger drug treatments, such as Biguanides combined with SGLT2 inhibitors and DPP-4 inhibitors, suggesting that these patients may have had more severe or poorly managed diabetes (Singh, et al. 2021) [27]. A study found that higher initial HbA1c was a significant predictor of the addition of drugs such as sodium-glucose cotransporter-2 inhibitors (SGLT-2i), sulfonylureas, and dipeptidyl peptidase-4 inhibitors (DPP-4i) to metformin treatment. This implies that combination medicines are more likely to be administered to individuals who had worse baseline glycemic control (Tan, et al. 2023) [28].

Additionally, the usage of LT4 was evaluated; levothyroxine was the main treatment for patients. It's interesting to note that mean TSH levels varied significantly amongst LT4 adherent and non-adherent LT4 groups compared to controls, indicating differing levels of responsiveness to treatment (Antonelli, et al. 2021) [29]. Also, unexpected low levels of TSH were observed in LT4 non-adherent patients, which attributed to the effects of metformin on thyroid function improvement as previously investigated. Similar findings have been reported in previous studies, indicating that metformin consistently lowers TSH levels in individuals with T2DM who have overt or subclinical hypothyroidism, whether treated or untreated, while FT4 levels remain unaffected. In contrast, TSH levels remain stable in euthyroid patients with T2DM after using metformin (Lupoli, et al. 2014) [30].

Despite the insights gained from this investigation, certain limitations must be addressed. Our study compared T2DM patients with hypothyroidism to healthy controls, which may not fully capture the impact of hypothyroidism. Future research should focus on diabetic patients both with and without hypothyroidism. Although we tried to adjust for age and

gender using regression analysis, the groups were not matched at baseline, which could affect the observed associations. This limitation arises primarily from the practical challenge of finding age- and gender-matched individuals who are completely free of chronic illnesses. In our setting, it is particularly difficult to identify genuinely healthy elderly individuals, especially females without any metabolic or cardiovascular comorbidities, which can lead to significant delays in recruitment. Furthermore, BMI was significantly higher in the patient group, and both groups remained within the overweight or obese categories. Nevertheless, this difference may still contribute to metabolic dysregulation and was taken into account during the regression adjustment.

Conclusion

This work emphasizes the complex connection between T2DM and hypothyroidism, which has important metabolic and therapeutic significance. Regular thyroid function tests may be helpful in this population, as hypothyroidism is quite prevalent among diabetes patients, especially in women. Furthermore, the strong correlations between HbA1c and thyroid indicators highlight the necessity of treating these disorders holistically. To better understand the causal links between T2DM and hypothyroidism and investigate the best therapeutic options for enhancing patient outcomes, future research should concentrate on longitudinal studies.

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Declarations

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Author contribution

Both authors contributed to the study conception and design. Rondic Naif participated in the gathering and analysis of the data, interpreted the results, and wrote the article. Chinar M. Mohammed developed the concept, coordinated the research, and approved the final draft of the manuscript.

Conflicts of interest

There are no competing interests declared by the authors.

Data availability

Upon reasonable request, all relevant data that support the findings can be provided by the corresponding author.

Ethics approval

The study was approved by the Research and Ethics Committee of Zakho University College of Science, Kurdistan Region of Iraq, the approval number (OCT2024/UOZ18 dated September 1, 2024). Further, the study carefully implemented the ethical guidelines outlined in the Declaration of Helsinki of the World Medical Association. Each participant supplied written informed consent prior to inclusion.

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