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Original Research Article

Deciphering the prolactin-thyroid-lipid nexus in type 2 diabetes and hypothyroidism: insights into metabolic interactions and dysregulation

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ABSTRACT

Background: Prolactin, thyroid hormones, and lipid metabolism play critical roles in maintaining metabolic homeostasis. Their dysregulation in type 2 diabetes and hypothyroidism may contribute to disease progression and complications. This study investigates the associations between prolactin, thyroid function, lipid metabolism, and glycemic parameters in individuals with type 2 diabetes and hypothyroidism.
Methods: A cross-sectional study was conducted on patients diagnosed with type 2 diabetes and hypothyroidism. Serum levels of fasting blood glucose (FBS), postprandial blood sugar (PPBS), glycated hemoglobin (HbA1c), thyroid hormones [free T3 (FT3), free T4 (FT4), and thyroid stimulating hormone (TSH)], lipid parameters, and prolactin were measured. Correlation analyses were performed to determine associations between prolactin, thyroid function, lipid profile, and glycemic markers.
Results: Significant alterations were observed in metabolic parameters among diabetic and hypothyroid patients. Prolactin levels showed a significant negative correlation with HbA1c ($r=-0.42$, $p<0.05$) and triglycerides (TG) ($r=-0.38$, $p<0.05$), suggesting a potential role in metabolic regulation. A positive correlation was found between prolactin and thyroid hormones FT3 ($r=0.44$, $p<0.05$) and FT4 ($r=0.39$, $p<0.05$), highlighting the interplay between the pituitary-thyroid axis and metabolism.
Conclusions: The findings emphasize the need for routine screening of thyroid function in diabetic patients and lipid profile monitoring in individuals with thyroid dysfunction to prevent metabolic complications. Prolactin may serve as a potential biomarker for metabolic dysregulation, warranting further investigation into its diagnostic and prognostic significance.

Keywords: Prolactin, Thyroid hormones, Lipid metabolism, Type 2 diabetes, Hypothyroidism, Glycemic control, Metabolic dysregulation

INTRODUCTION

Type 2 diabetes mellitus (T2DM) and hypothyroidism frequently coexist, contributing to significant metabolic disturbances, including dyslipidemia, insulin resistance, and increased cardiovascular risk. While both conditions independently disrupt lipid metabolism and glucose homeostasis, their combined effects, particularly in relation to prolactin (PRL) dysregulation, remain underexplored. Prolactin, traditionally recognized for its role in lactation, has been increasingly implicated in metabolic regulation, lipid homeostasis, and pancreatic β-cell function.[1] Notably, hypothyroidism is a well-established cause of hyperprolactinemia due to the

upregulation of thyrotropin-releasing hormone (TRH), which stimulates both TSH and PRL secretion. Elevated prolactin levels have been associated with increased insulin resistance, altered lipid profiles, and a higher risk of cardiovascular disease.[2] Given the inherent metabolic disruptions in T2DM, understanding the prolactin-thyroid-lipid axis in patients with concurrent T2DM and hypothyroidism is essential for identifying novel biomarkers and refining therapeutic strategies.[3]

Dyslipidemia is a hallmark of both hypothyroidism and T2DM, characterized by elevated low-density lipoprotein cholesterol (LDL-C) and TG, along with reduced high-density lipoprotein cholesterol (HDL-C). Thyroid hormones, particularly triiodothyronine (T3), play a critical role in hepatic lipid clearance and peripheral lipid metabolism. In hypothyroid patients, decreased lipoprotein lipase (LPL) activity and reduced hepatic LDL receptor expression contribute to hyperlipidemia and heightened cardiovascular risk.[4] Additionally, hypothyroidism-induced dyslipidemia further exacerbates insulin resistance, complicating glycemic control in T2DM patients.[5]

Prolactin has emerged as a potential metabolic regulator influencing lipid and glucose homeostasis. Hyperprolactinemia in hypothyroid patients, driven by excessive TRH stimulation, is associated with insulin resistance, increased visceral fat accumulation, and pro-inflammatory cytokine release, which collectively contribute to metabolic dysfunction.[6] Furthermore, PRL receptors are widely expressed in adipose tissue, the liver, and pancreatic β-cells, highlighting PRL's role in lipid storage, insulin secretion, and energy balance.[7] While physiological prolactin levels may exert insulin-sensitizing effects, excessive secretion has been linked to lipotoxicity, β-cell dysfunction, and chronic inflammation, all of which exacerbate diabetic dyslipidemia.[8]

This study aims to explore the interplay between prolactin levels, thyroid dysfunction, and lipid abnormalities in patients with T2DM and hypothyroidism. By investigating the prolactin-thyroid-lipid interplay, this study seeks to bridge the existing knowledge gap, providing novel insights into metabolic derangements in patients with concurrent hypothyroidism and diabetes. A deeper understanding of these relationships may pave the way for targeted interventions, leading to improved metabolic health and reduced cardiovascular risks in affected populations. Given the rising prevalence of both T2DM and thyroid disorders, identifying novel biomarkers, such as prolactin levels and lipid alterations, may enhance diagnostic accuracy and therapeutic precision for diabetes and thyroid dysfunction-related dyslipidemia.[9,10] Additionally, the findings of this study could contribute to the development of more personalized treatment approaches, integrating endocrinological and metabolic perspectives to mitigate the adverse effects of these intertwined disorders.

METHODS

Study design and participants

This prospective observational study aimed to assess thyroid function in individuals with diabetes. Participants were recruited from the outpatient department (OPD) and inpatient wards of ESIC model hospital, Rajajinagar, Bangalore-10, between 2014 and 2015. The study enrolled 200 adult males, categorized into four groups: healthy, age-matched, normoglycemic, and euthyroid controls (n=50); patients with subclinical hypothyroidism without T2DM (n=50); patients with T2DM without hypothyroidism (n=50); and patients diagnosed with both conditions (n=50). Clinical history was documented, and a comprehensive clinical examination was conducted to assess metabolic and endocrine status.[11]

Female participants were excluded due to significant physiological variations in prolactin levels. Additionally, individuals with conditions affecting prolactin regulation, secondary hypothyroidism, severe diabetic complications (e.g., myocardial infarction, cerebrovascular accidents), or those on medications influencing hormonal and lipid profiles were also excluded to minimize confounding variables.[12] The study received institutional ethics committee approval and adhered to the Helsinki declaration. Informed consent was obtained from all participants, ensuring compliance with international research ethics.[13] Informed consent was obtained from all participants, ensuring compliance with international research ethics.[14]

Sample collection

After a 12-hour overnight fast, 5 ml of venous blood was collected aseptically into a plain Vacutainer for serum separation, and an additional 2 ml was drawn into an EDTA-containing Vacutainer for glycosylated hemoglobin (HbA1c) analysis. Samples were centrifuged at 2500 RCF for 15 minutes to separate serum and plasma for biochemical analysis. FBG was measured using the glucose oxidase-peroxidase enzymatic method, while HbA1c levels were determined via high-performance liquid chromatography (HPLC).[15] Thyroid function tests (TFT), including TSH, FT3, and FT4, were analyzed using standardized chemiluminescent immunoassays, ensuring accuracy and reproducibility through strict quality control measures.[16]

Biochemical assays

Blood glucose profile

The blood glucose profile is an essential tool for assessing glucose metabolism and diagnosing diabetes. It includes FBG, postprandial blood glucose (PPBG), and HbA1c, each reflecting different aspects of glycemic control. FBG represents basal glucose homeostasis, while PPBG evaluates the body's response to a glucose load. HbA1c,

measured via ion-exchange HPLC, provides an average blood glucose estimate over the past 8-12 weeks and serves as a key marker for long-term glycemic control.[17] The hexokinase method, widely used in autoanalyzers such as the COBAS INTEGRA-400 PLUS, enzymatically phosphorylates glucose, leading to glucose-6-phosphate oxidation and NADPH formation, which is quantified spectrophotometrically at 340 nm.[18] Regular blood glucose and HbA1c monitoring is essential for diagnosing, managing, and preventing diabetes-related complications.

Lipid profile

Lipid profiling is a critical assessment of lipid metabolism, essential for evaluating cardiovascular risk and metabolic disorders. The test includes total cholesterol (TC), HDL-C, LDL-C, and TGs. TC is measured via the cholesterol oxidase-phenol aminoantipyrine (CHOD-PAP) method, where cholesterol esters undergo hydrolysis, oxidation, and red quinoneimine dye formation, which is quantified at 520 nm.[19] HDL-C is estimated after precipitating chylomicrons, very-low-density lipoprotein (VLDL), and LDL, leaving only HDL in the supernatant for enzymatic analysis.[20] TGs are hydrolyzed into glycerol and fatty acids, with glycerol undergoing a series of enzymatic reactions to produce a red quinoneimine dye measured at 512 nm.[21] LDL-C is calculated using the Friedewald formula:

LDL-C= TC-HDL-C-(TGs/5)\text{LDL-C}=\text{TC}-\text{HDL-C}-(\text{TGs}/5)LDL-C=TC-HDL-C-(TGs/5)

Provided TGs are ≤400 mg/dl.[22] These parameters are crucial for diagnosing dyslipidemia, monitoring treatment, and predicting cardiovascular disease risk.

TFT

TFT, including free T3, free T4, and TSH, were analyzed using the access-2 autoanalyzer (Beckman coulter) based on immunoenzymatic assay protocols. Free T3 and Free T4 were measured using a competitive binding enzyme immunoassay, with detection ranges of 1.4-4.2 pg/ml and 0.8-2.0 ng/dl, respectively, where luminescence intensity was inversely proportional to hormone concentration.[23] TSH was quantified using 2-site sandwich immunoassay, with a detection range of 0.4-4.0 µIU/ml, where luminescence intensity was directly proportional to TSH levels.[24] Assays calibrated using Bio-Rad immunoassay plus controls (Levels 1-3), ensuring analytical accuracy with a coefficient of variation below 5%.[25]

Prolactin estimation

Prolactin levels were measured using the Access 2 Autoanalyzer (Beckman Coulter) via a one-step immunoenzymatic assay. This test employs paramagnetic particles coated with monoclonal anti-prolactin antibodies and a goat anti-prolactin alkaline phosphatase conjugate, forming a sandwich immunoassay, where luminescence intensity is proportional to prolactin concentration.[26] Calibration was performed using access prolactin calibrators (0-200 ng/ml) and validated through Bio-Rad immunoassay plus controls (Levels 1-3).[27] Quality control protocols ensured reproducibility within reference ranges: males (2.64-13.13 µg/l) and females (<50 years: 3.34-26.72 µg/l; >50 years: 2.74-19.64 µg/l).[28]

Statistical analysis

Statistical analysis was performed using GraphPad Prism (version 6 for Windows), with results expressed as mean±SD. One-way analysis of variance (ANOVA) was applied to compare means across groups, using the F-statistic to assess variance differences. Post-hoc Tukey's multiple comparison test was conducted for pairwise comparisons.[29] The Pearson correlation coefficient was used to evaluate relationships between numerical variables, with values ranging from-1 (perfect inverse correlation) to +1 (perfect direct correlation), and values near zero indicating weak or no correlation.[30] Statistical significance was set at p≤0.05 for all analyses.

RESULTS

This study investigated the intricate relationship between prolactin, thyroid function, and lipid metabolism in individuals with type 2 diabetes and hypothyroidism. A total of 200 male subjects were categorized into four groups: control (n=50), diabetes without hypothyroidism (n=50), hypothyroidism without diabetes (n=50), and coexisting diabetes-hypothyroidism (n=50). Key biochemical markers, including fasting and postprandial glucose, HbA1c, lipid profiles, thyroid hormones, and prolactin, were analyzed. The mean age of participants was comparable across groups, with no statistically significant differences (ANOVA, p=0.71; Tukey's post-hoc test) (Figure 1).

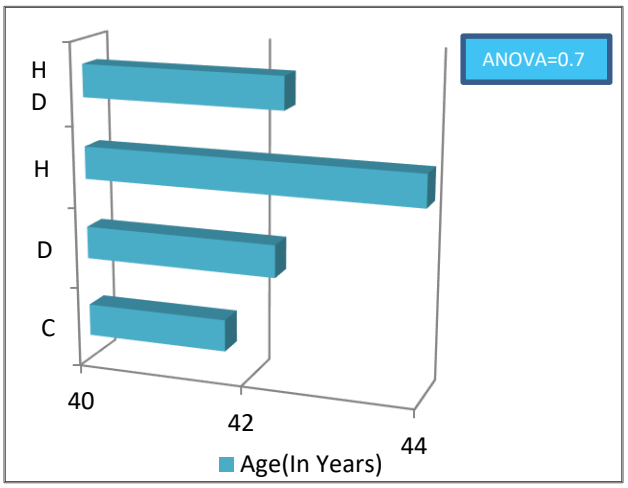

Figure 1: Comparison of age within 4 study groups.
C=Control group, D=Diabetic group, FBS=Fasting blood sugar, H=Hypothyroid group, HD=Hypothyroid diabetic group; n=50 males in each group.

Glycemic parameters and metabolic dysregulation

FBS and PPBS were markedly elevated in the diabetic (161.1±73.87 mg/dl) and hypothyroid diabetic (135.9±16.45 mg/dl) groups compared to controls (84.07±12.82 mg/dl) and the hypothyroid group (89.27±19.29 mg/dl). Similarly, PPBS was highest in the diabetic (346.9±80.10 mg/dl) and hypothyroid diabetic (329.9±68.16 mg/dl) groups, with significant differences from the control (123.5±16.89 mg/dl) and hypothyroid (129.6±21.16 mg/dl) group. HbA1c levels followed the same trend, with significantly elevated values in the diabetic (7.53±1.91%) and hypothyroid diabetic (6.92±1.08%) groups compared to the control (5.16±0.8%) and hypothyroid (5.58±0.97%) groups. Tukey's post-hoc analysis confirmed these differences, highlighting that the control and hypothyroid groups had significantly lower FBS, PPBS, and HbA1c levels than the diabetic and hypothyroid diabetic groups. Additionally, the diabetic group exhibited slightly higher values compared to the hypothyroid diabetic group across all three parameters. These findings are summarized in Table 1.

Lipid dysregulation in the context of diabetes and hypothyroidism

Lipid profile assessment revealed significant disturbances in diabetic and hypothyroid diabetic groups. TC was significantly elevated in the diabetic (319.3±65.04 mg/dl) and hypothyroid diabetic (304.7±57.87 mg/dl) groups, in contrast to controls (189.4±36.82 mg/dl) and hypothyroid individuals (237.7±61.61 mg/dl). LDL levels followed a similar pattern, with higher values in diabetic (250.6±68.89 mg/dl) and hypothyroid diabetic (235.9±57.43 mg/dl) groups, compared to the control (144.2±42 mg/dl) and hypothyroid (172.4±57 mg/dl) groups. HDL levels showed no significant variation among groups. TG were highest in the hypothyroid diabetic (165.5±43.47 mg/dl) and diabetic (161.2±29.2 mg/dl) groups, significantly exceeding those in the control (110.5±31.4 mg/dl). Tukey's post-hoc analysis confirmed the statistical significance of these variations and. findings are summarized in Table 2.

Thyroid hormone dysregulation and its metabolic implications

Thyroid function tests revealed significantly elevated TSH levels in the hypothyroid (27.00±13.81 µIU/ml) and hypothyroid diabetic (35.27±18.55 µIU/ml) groups compared to controls (3.37±31.4 µIU/ml) and diabetics (5.43±2.25 µIU/ml). Concurrently, FT3 levels were significantly lower in the hypothyroid (1.82±0.44 pg/ml) and hypothyroid diabetic (2.24±0.76 pg/ml) groups compared to the control (2.95±0.54 pg/ml) and diabetic (2.85±0.97 pg/ml) groups. FT4 levels followed a similar trend, being reduced in the hypothyroid (0.80±0.49 ng/dl) and hypothyroid diabetic (0.87±0.55 ng/dl) groups, with significant differences from the control (1.55±0.35 ng/dl) and diabetic (1.23±0.54 ng/dl) groups. These differences were statistically significant and are concluded in Table 3.

Prolactin variations and their association with metabolic disorders

Prolactin levels exhibited significant intergroup differences. The control group had the highest prolactin levels (9.5±3.2 ng/ml), which were significantly greater than those observed in diabetic (4.2±2.7 ng/ml), hypothyroid (6.4±2.7 ng/ml), and hypothyroid diabetic (5.0±3.1 ng/ml) groups (Figure 2). Tukey's multiple comparison test confirmed that prolactin levels were significantly lower in the diabetic group compared to the hypothyroid group, suggesting an interplay between prolactin secretion, thyroid function, and metabolic dysregulation.

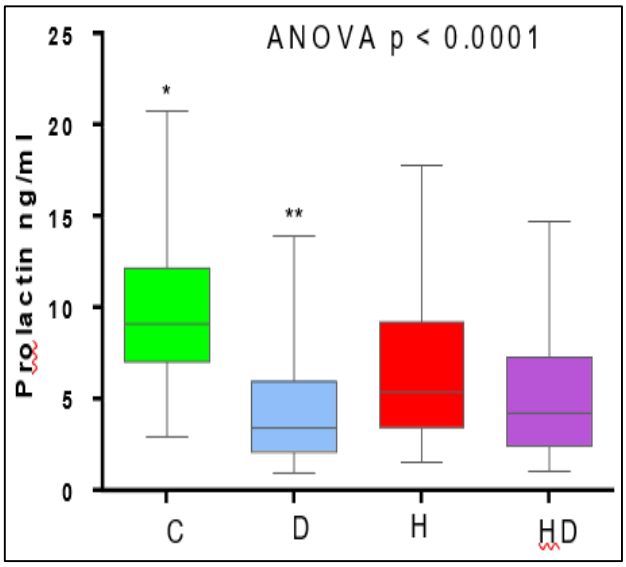

Figure 2: Comparison of prolactin within the four study groups.

C=Control group, D=Diabetic group, H=Hypothyroid group, HD=Hypothyroid diabetic group, TG=Triglycerides; *significantly different from all the other three groups, **Significantly different from Hypothyroid group; n=50 males in each group.

Prolactin-thyroid-lipid interactions in metabolic disorders

The correlation analysis presented in Tables 4-6 provides crucial insights into the complex interplay between prolactin, thyroid function, lipid metabolism, and glycemic parameters in individuals with T2DM, hypothyroidism, and their coexistence. Table 1 highlights that prolactin exhibits a significant negative correlation with HbA1c (r=-0.35, p=0.05) and TG (r=-0.38, p=0.03) in diabetic patients, suggesting a potential role of prolactin in glucose and lipid homeostasis. Interestingly, FT3 and FT4 are positively correlated with prolactin in hypothyroid diabetics (r=0.37, p=0.04 and r=0.38, p=0.04, respectively), indicating a possible link between prolactin

and thyroid hormone regulation in metabolic disorders. Table 2 further reveals that TG significantly correlate with fasting blood sugar (FBS) in diabetic individuals (r=0.39, p=0.03) and TSH in hypothyroids (r=0.39, p=0.03), emphasizing the interdependence of lipid and thyroid dysfunction in metabolic disorders. Moreover, TG strongly correlate with TC (r=0.81, p<0.0001) and LDL-C (r=0.81, p<0.0001) in controls, while LDL-C also shows a significant association with TG in diabetics (r=0.36, p=0.04). Finally, Table 3 supports these findings, as TC exhibits robust associations with TG and LDL-C, underscoring lipid dysregulation as a hallmark of metabolic imbalance in these conditions. Collectively, these results reinforce the prolactin-thyroid-lipid nexus in T2DM and hypothyroidism, shedding light on the metabolic dysregulation and interlinked pathophysiological mechanisms underlying these disorders.

Table 1: Comparison of FBS, PPBS, and HbA1c levels among study groups.

Parameters	Control (C)	Diabetic (D)	Hypothyroid (H)	Hypothyroid diabetic (HD)	Statistical significance (Tukey's test)
FBS (mg/dl)	84.07±12.82	161.1±73.87	89.27±19.29	135.9±16.45	D, HD >C, H (p<0.05)
PPBS (mg/dl)	123.5±16.89	346.9±80.10	129.6±21.16	329.9±68.16	D, HD >C, H (p<0.05)
HbA1c (%)	5.16±0.8	7.53±1.91	5.58±0.97	6.92±1.08	D, HD >C, H (p<0.05)

Note: Values are presented as mean±SD. n=50 males in each group. Statistical significance (p<0.05) indicates that the Diabetic (D) and hypothyroid diabetic (HD) groups had significantly higher values compared to the control (C) and hypothyroid (H) groups.

Table 2: Comparison of lipid profile among study groups.

Parameters	Control (C)	Diabetic (D)	Hypothyroid (H)	Hypothyroid diabetic (HD)	Statistical significance (Tukey's test)
TC (mg/dl)	189.4±36.82	319.3±65.04	237.7±61.61	304.7±57.87	C<D, H, HD (p<0.05); H<D, HD (p<0.05)
LDL-C (mg/dl)	144.2±42.00	250.6±68.89	172.4±57.00	235.9±57.43	C, H<D, HD (p<0.05)
HDL-C (mg/dl)	36.40±11.4	36.68±10.0	37.66±11.8	36.14±8.7	No significant difference (p>0.05)
Triglycerides (mg/dl)	110.5±31.4	161.2±29.2	139.0±32.6	165.5±43.47	C <D, H, HD (p<0.05); D>H (p<0.05); H<HD (p<0.05)

Note: Values are presented as mean±SD. n=50 males in each group. Statistical significance (p<0.05) indicates significant differences between groups as described in the Tukey's post-hoc test.

Table 3: Thyroid function parameters in study groups.

Parameters	Control (C)	Diabetic (D)	Hypothyroid (H)	Hypothyroid diabetic (HD)	Statistical significance
TSH (µIU/ml)	3.37±1.40	5.43±2.25	27.00±13.81	35.27±18.55	C, D<H, HD; H<HD
FT3 (pg/ml)	2.95±0.54	2.85±0.97	1.82±0.44	2.24±0.76	C, D>H, HD; H<HD
FT4 (ng/dl)	1.55±0.35	1.23±0.54	0.80±0.49	0.87±0.55	C, D>H, HD; H<HD

Table 4: Correlation of prolactin with other parameters of all groups.

Variables	Control		Diabetics		Hypothyroids		Hypothyroid diabetics	
	R	P	R	P	R	P	R	P
FBS (mg/dl)	-0.28	0.12	-0.31	0.09	0.05	0.78	-0.02	0.91
PPBS (mg/dl)	-0.18	0.32	-0.24	0.91	0.28	0.12	0.12	0.52
HbA1c (%)	-0.05	0.78	-0.35	0.05*	0.01	0.95	-0.01	0.97
TC (mg/dl)	0.21	0.26	0.22	0.23	0.03	0.85	0.22	0.23
TG (mg/dl)	-0.08	0.66	-0.38	0.03*	0.19	0.29	0.10	0.59
LDL-C (mg/dl)	-0.19	0.31	0.24	0.18	0.03	0.85	0.21	0.26
HDL-C (mg/dl)	0.29	0.18	0.01	0.95	-0.05	0.76	-0.02	0.89
TSH (µIU/ml)	-0.25	0.19	0.09	0.62	0.08	0.66	0.08	0.67
FT3 (pg/ml)	0.03	0.88	0.19	0.30	0.26	0.15	0.37	0.04*
FT4 (ng/dl)	-0.31	0.09	0.01	0.97	0.27	0.14	0.38	0.04*

FBS=Fasting blood sugar, FT3=Free triiodothyronine, FT4=Free thyroxine, HbA1c=Haemoglobin A1c, HDL-C=High density lipoprotein cholesterol, LDL-C=Low density lipoprotein cholesterol, PPBS=Post prandial blood sugar, TC=Total cholesterol, Test.=Testosterone, TG=Triglycerides, TSH= Thyroid stimulating hormone; *p<0.05, ** p<0.01; n=50.

Table 5: Correlation of triglycerides with other parameters of all groups.

Variables	Control		Diabetics		Hypothyroids		Hypothyroid diabetics	
	R	P	R	P	R	P	R	P
FBS (mg/dl)	0.18	0.33	0.39	0.03*	-0.15	0.22	-0.27	0.62
PPBS (mg/dl)	0.10	0.58	0.30	0.10	0.22	0.23	-0.31	0.78
HbA1c (%)	0.26	0.16	-0.02	0.92	-0.12	0.52	-0.42	0.69
TC (mg/dl)	0.62	0.0002**	-0.27	0.14	0.81	<0.0001***	-0.18	0.30
LDL-C (mg/dl)	0.81	<0.0001***	0.36	0.04*	0.77	<0.0001***	-0.36	0.99
HDL-C (mg/dl)	0.02	0.91	0.14	0.43	0.07	0.72	-0.35	0.93
TSH (µIU/ml)	-0.02	0.92	-0.05	0.80	0.39	0.03*	-0.34	0.92
FT3 (pg/ml)	-0.81	0.33	-0.15	0.40	0.03	0.84	-0.17	0.29
FT4 (ng/dl)	0.50	0.004**	0.20	0.27	-0.35	0.06	-0.11	0.17
Prol. (ng/ml)	-0.08	0.66	-0.38	0.03*	0.18	0.29	-0.26	0.59
Test. (ng/ml)	-0.14	0.46	0.02	0.92	0.19	0.30	-0.51	0.32

FBS=Fasting blood sugar, FT3=Free triiodothyronine, FT4=Free thyroxine, HbA1c=Haemoglobin A1c, HDL-C=High density lipoprotein cholesterol, LDL-C=Low density lipoprotein cholesterol, PPBS=Post prandial blood sugar, Prol.=Prolactin, TC=Total cholesterol Test.=Testosterone, TSH=Thyroid stimulating hormone; *p<0.05, **p<0.01, ***p <0.0001; n=50.

Table 6: Correlation of TC with other parameters of all groups.

Variables	Control		Diabetics		Hypothyroid		Hypothyroid diabetics	
	R	P	R	P	R	P	R	P
FBS (mg/dl)	0.19	0.53	0.20	0.28	-0.03	0.85	-0.01	0.97
PPBS (mg/dl)	-0.08	0.65	0.23	0.23	0.12	0.51	0.18	0.35
HbA1c (%)	0.41	0.02*	0.05	0.79	-0.01	0.96	-0.19	0.30
TG (mg/dl)	0.63	0.0002**	-0.27	0.14	0.81	<0.0001***	0.18	0.30
LDL-C (mg/dl)	0.70	0.0004**	0.98	<0.0001***	0.97	<0.0001***	0.96	<0.0001***
HDL-C (mg/dl)	0.17	0.39	-0.16	0.38	0.21	0.26	0.12	0.53
TSH (µIU/ml)	-0.24	0.91	-0.04	0.82	0.26	0.16	-0.13	0.49
FT3 (pg/ml)	-0.20	0.28	0.14	0.45	0.08	0.64	0.19	0.31
FT4 (ng/ dl)	0.10	0.57	0.47	0.14	-0.39	0.03*	0.35	0.85
Prol. (ng/ml)	0.21	0.26	0.22	0.23	0.03	0.85	0.22	0.23
Test. (ng/ml)	0.23	0.22	0.02	0.90	0.20	0.28	0.16	0.37

FBS=Fasting blood sugar, FT3=Free triiodothyronine, FT4=Free thyroxine, HbA1c=Haemoglobin A1c, HDL-C=High density lipoprotein cholesterol, LDL-C=Low density lipoprotein cholesterol, PPBS=Post prandial blood sugar, Prol.= Prolactin, Test.=Testosterone, TG=Triglycerides, TSH=Thyroid stimulating hormone; *p<0.05, **p<0.01, ***p<0.0001; n=50,

DISCUSSION

The findings of this study highlight the intricate interplay between prolactin, thyroid function, lipid metabolism, and glycemic regulation in individuals with type 2 diabetes and hypothyroidism. The significant elevation of FBS, PPBS, and HbA1c levels in diabetic and hypothyroid-diabetic groups underscores the heightened risk of glycemic dysregulation in these conditions. Prior studies have reported that thyroid dysfunction, particularly hypothyroidism, is associated with impaired insulin sensitivity and glucose metabolism, which may exacerbate hyperglycemia in diabetic individuals.[31] The observed lipid abnormalities, including elevated TC, LDL, and TG in diabetic and hypothyroid-diabetic patients, further corroborate the well-established link between hypothyroidism and dyslipidemia.[32,33] Increased LDL levels in these groups may be attributed to decreased LDL receptor expression, reduced hepatic clearance, and altered bile acid metabolism, as suggested in previous research.[34]

Furthermore, the significant reduction in prolactin levels in diabetic individuals, compared to the control and hypothyroid groups, suggests a potential modulatory role of prolactin in metabolic homeostasis. Prolactin has been implicated in pancreatic β-cell function, glucose regulation, and lipid metabolism, with lower levels correlating with impaired glucose tolerance and dyslipidemia.[35,36]

The observed negative correlation between prolactin and HbA1c (r=-0.35, p=0.05) and the TG (r=-0.38, p=0.03) suggests a potential protective role of prolactin in metabolic regulation, which aligns with earlier findings linking prolactin to insulin secretion and the lipid metabolism. Moreover, the positive correlation between prolactin and thyroid hormones (FT3 as well as FT4) in the hypothyroid diabetic individuals (r=0.37, p=0.04 and r=0.38, p value of=0.04, respectively) indicates a bidirectional relationship between thyroid function and

prolactin secretion, which has been previously noted in the studies examining pituitary-thyroid axis interactions.[37]

From a clinical perspective, these findings have significant implications for the management of metabolic disorders. Given the established link between thyroid dysfunction and diabetes, routine screening for thyroid hormone levels in diabetic patients and vice versa may help in early diagnosis and targeted intervention.

Treatment strategies should focus on optimizing thyroid hormone replacement in hypothyroid-diabetic individuals to improve glycemic control and lipid metabolism. Levothyroxine therapy has been shown to reduce LDL cholesterol and improve insulin sensitivity, thereby mitigating the cardiovascular risk associated with these metabolic disorders.[38] The lipid-lowering therapies such as statins may be beneficial in managing the dyslipidemia observed in diabetic and hypothyroid-diabetic patients, though caution must be exercised due to potential drug interactions with thyroid hormone replacement therapy.[39]

In terms of biomarker evaluation, prolactin may serve as a potential diagnostic and prognostic marker for metabolic dysregulation in diabetes and hypothyroidism. Given its association with glucose and lipid metabolism, future studies should explore the utility of prolactin as a biomarker for predicting metabolic complications in these patients. Additionally, the strong correlations observed between TGs, LDL-C, and TC emphasize the need for comprehensive lipid profiling in metabolic disorder management. Emerging biomarkers such as adiponectin, fibroblast growth factor 21 (FGF21), and thyroid hormone metabolites may further enhance the stratification and therapeutic targeting of patients with diabetes and thyroid dysfunction.[40]

Present study underscores the necessity for an integrated approach in managing patients with coexisting metabolic disorders. Prolactin-thyroid-lipid interactions should be considered in routine clinical evaluations to optimize therapeutic outcomes and reduce cardiovascular risks in diabetic and hypothyroid individuals.[41] Further research is warranted to elucidate the mechanistic pathways underlying these interactions and to identify novel therapeutic targets for improving metabolic health in these patient populations.

This study provides valuable insights, but certain limitations should be considered. The cross-sectional design limits causal interpretation, yet it establishes important metabolic correlations that can guide future longitudinal and interventional research. The sample size, though moderate, highlights significant trends that warrant further exploration in larger populations. While some confounding factors were not fully controlled, the findings contribute to a deeper understanding of the prolactin-thyroid-lipid nexus, encouraging further clinical investigations.

CONCLUSION

The intricate interplay between prolactin, thyroid hormones, lipid metabolism, and glycemic control in individuals with type 2 diabetes and hypothyroidism. The observed alterations in FBS, PPBS, HbA1c, lipid parameters, and prolactin levels emphasize the metabolic burden associated with these conditions. Notably, the significant negative correlation between prolactin and both HbA1c and TGs suggests a potential regulatory role of prolactin in metabolic homeostasis. Additionally, the positive correlation between prolactin and thyroid hormones (FT3 and FT4) in hypothyroid-diabetic patients reinforces the interdependence of the pituitary-thyroid axis in metabolic regulation. From a clinical perspective, these findings underscore the importance of routine screening for thyroid function in diabetic patients and vice versa to ensure early diagnosis and optimal management. The strong associations between lipid abnormalities and thyroid dysfunction further highlight the necessity of lipid profile monitoring in these patients to mitigate cardiovascular risks. Furthermore, the potential of prolactin as a biomarker for metabolic dysregulation warrants further investigation to explore its diagnostic and prognostic value. A targeted approach that considers prolactin-thyroid-lipid interactions in the clinical evaluation of patients with diabetes and hypothyroidism may contribute to better disease management and therapeutic outcomes. Future studies should focus on elucidating the molecular mechanisms underlying these interactions and assessing the impact of targeted interventions on metabolic health.

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