ORIGINAL ARTICLE

Retrospective Analysis on Biochemical and Metabolic Profile of Hypothyroid Patients: Correlative Evaluation of Cardiometabolic and Renal Alterations

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Abstract

Background: Hypothyroidism is a common endocrine disorder affecting multiple metabolic pathways. Although its association with dyslipidemia, glucose abnormalities, and renal dysfunction is known, region-specific data from India remain limited. To compare thyroid, metabolic, and renal profiles between hypothyroid patients on levothyroxine and healthy controls, and assess the prevalence of associated metabolic abnormalities.

Methods: A retrospective study was conducted at a tertiary care center in Puducherry from January 2023 to December 2024, including 285 hypothyroid patients on levothyroxine and 38 age- and sex-matched controls. Clinical data and biochemical parameters—thyroid profile (thyroid-stimulating hormone TSH, FT3, FT4), glucose metabolism (fasting blood sugar [FBS], HbA1c), renal function (urea, creatinine), and lipid profile (TC, LDL, HDL, triglycerides, very low-density lipoprotein [VLDL])—were analyzed using independent t-tests. Significance was set at $p<0.05$.

Results: Hypothyroid patients had significantly higher FBS, HbA1c, triglycerides, VLDL, urea, and creatinine (p<0.001), and lower HDL (p<0.001) compared to controls. Total cholesterol was slightly elevated (p=0.028†). No significant differences were observed in FT3, FT4, or LDL. Clinically, 26.3% had overt hypothyroidism; 73.7% subclinical. Comorbidities included diabetes (29.5%), prediabetes (42.8%), dyslipidemia (68.1%), and renal dysfunction (18.9%).

Conclusion: Despite levothyroxine therapy, hypothyroid patients showed significant metabolic and renal alterations. Routine screening for glycemic, lipid, and renal abnormalities is warranted to prevent long-term complications. Further prospective studies are recommended to explore causality and guide management in the Indian context.

Keywords: Hypothyroidism; Levothyroxine; Dyslipidemia; Cardiometabolic risk; Renal dysfunction; Glycemic abnormalities**.**

Introduction

Hypothyroidism is a common endocrine disorder resulting from inadequate synthesis and secretion of thyroxine (T4) and triiodothyronine (T3), leading to widespread effects on metabolism, growth, and cellular function (1). It affects about 1% to 2% of the global population, with a higher prevalence in women and older adults (2,3). Autoimmune thyroiditis is the predominant cause in iodine-sufficient regions, whereas iodine deficiency remains a major contributor in developing countries (4,5). Despite effective levothyroxine therapy, many patients continue to report symptoms, suggesting contributions from additional factors such as micronutrient deficiencies (6). Thyroid hormones are central regulators of lipid metabolism, glucose homeostasis, and renal function. Hypothyroidism is associated with dyslipidemia, including elevated total cholesterol, LDL-C, and triglycerides with reduced HDL-C (7,8), impaired insulin sensitivity and glucose metabolism (9,10), and reduced glomerular filtration rate with elevated serum creatinine and urea (11). These disturbances contribute to an increased risk of cardiovascular disease, diabetes, and renal dysfunction (12,13). Although hypothyroidism has been extensively studied worldwide, there is a paucity of region-specific comparative data from India. Most available studies are cross-sectional, single-center, and limited by small sample sizes, focusing primarily on thyroid hormone replacement and diagnosis rather than broader systemic effects or micronutrient status (14–17). The role of subclinical hypothyroidism in metabolic derangements also remains underexplored (18,19). Given India's unique genetic, dietary, and environmental background, region-specific evidence is essential to guide clinical management (20–

23). This study addresses these gaps by systematically comparing metabolic and renal parameters between hypothyroid patients and healthy controls, and examining their correlation with thyroid hormone levels (24).

Materials and Methods

Ethics statement

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Institutional Human Ethics Committee of the host institute (MGMCRI/IRC/60/2021/01/IHEC/72). All patient records were anonymized to maintain confidentiality, and the requirement for informed consent was waived owing to the retrospective design.

Study design and setting

This was a retrospective observational study conducted at the Department of Biochemistry, Mahatma Gandhi Medical College and Research Institute, Puducherry, India, between January 2023 and December 2024. The study was designed to evaluate biochemical and metabolic parameters in patients with hypothyroidism compared with age- and sex-matched healthy controls.

Study Participants

Hospital records of 1,100 subjects were screened, and 323 subjects met the eligibility criteria and were included in the analysis. The study population comprised 285 patients diagnosed with primary hypothyroidism and 38 controls without a present or past history of thyroid disease. Adults aged 20 to 60 years with complete clinical and biochemical records were included. Exclusion criteria were secondary or tertiary hypothyroidism, pregnancy, and incomplete or missing medical records.

Variables and data sources

Data were extracted from hospital electronic medical records, including demographic details, clinical characteristics, and biochemical parameters. The primary variables of interest were Thyroid function tests such as free T3 (fT3), free T4 (fT4), thyroid-stimulating hormone (TSH), Glucose metabolism markers such as fasting blood sugar (FBS), glycated hemoglobin (HbA1c), Renal function indicators such as serum urea, creatinine, and Lipid profile parameters such as total cholesterol (TC), triglycerides (TGL), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL)

Laboratory assessment of biochemical investigations

All biochemical measurements were performed on fasting venous blood samples (2 mL). Serum was separated by centrifugation at 3,500 rpm for 10 minutes and analyzed immediately. Serum glucose, urea, creatinine, and lipid profile were measured using commercially available kits on a fully automated clinical chemistry analyzer (Roche Cobas c311, Germany). Thyroid hormones (fT3, fT4, TSH) were assessed using

chemiluminescence immunoassay (Roche Cobas e411, Germany). HbA1c was measured by ion-exchange high-performance liquid chromatography on the D-10 system (Bio-Rad, USA).

Statistical analysis

Continuous variables were expressed as mean±standard deviation (SD) or median with interquartile range (IQR), depending on the distribution, which was tested using the Shapiro–Wilk and Kolmogorov–Smirnov tests. Group comparisons between hypothyroid patients and controls were performed using independent *t*-test or Mann–Whitney U test, as appropriate. Associations between biochemical markers were analyzed using Pearson's. All statistical analyses were performed using IMB SPSS ver. 19.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 323 participants were included in the analysis, comprising 285 hypothyroid patients receiving levothyroxine therapy and 38 euthyroid controls. There was no significant difference between groups with respect to age (hypothyroid: 48.38 ± 8.44 years; controls: 47.18 ± 11.75 years; $p = 0.763$) or sex distribution ($p = 0.100$). Among hypothyroid patients, 75 (26.3%) had overt hypothyroidism and 210 (73.7%) had subclinical hypothyroidism. Metabolic and renal comorbidities were common: 29.5% were diabetic, 42.8% were pre-diabetic, 68.1% had dyslipidemia, and 18.9% showed evidence of renal dysfunction. The mean daily levothyroxine dose was 85 ± 23 µg. Hypothyroid patients demonstrated significant metabolic and renal alterations compared with controls. Serum creatinine, fasting blood sugar (FBS), glycated hemoglobin (HbA1c), triglycerides (TGL), thyroid-stimulating hormone (TSH), urea, and very-low-density lipoprotein (VLDL) were all significantly higher in hypothyroid patients (all $p < 0.001$). High-density lipoprotein (HDL) levels were significantly lower in the hypothyroid group ($p < 0.001$). Total cholesterol (TC) was marginally higher in hypothyroid patients; statistical significance was achieved only when equal variances were not assumed ($p = 0.028$). No significant differences were observed for free triiodothyronine (FT3), free thyroxine (FT4), or low-density lipoprotein cholesterol (LDL). These findings indicate persistent dysregulation of glycemic control, lipid metabolism, and renal parameters in hypothyroid patients despite levothyroxine therapy. (Table 1) Pearson correlation analysis revealed several moderate to strong associations among study variables. Lipid parameters were strongly intercorrelated, with a very strong positive correlation between TC and LDL ($r = 0.919$, $p < 0.001$) and a moderate positive correlation between TC and HDL ($r = 0.454$, $p < 0.001$). Triglycerides correlated positively with VLDL ($r = 0.423$,

$p < 0.001$). Thyroid function markers demonstrated expected physiological relationships: FT3 correlated positively with FT4 ($r = 0.370$, $p < 0.001$) and inversely with TSH ($r = –0.316$, $p < 0.001$), while FT4 also showed a strong inverse association with TSH ($r = –0.454$, $p < 0.001$). Glycemic indices were strongly associated, with FBS showing a strong positive correlation with HbA1c ($r = 0.669$, $p < 0.001$). Renal markers were closely related, with a strong positive correlation between creatinine and urea ($r = 0.821$, $p < 0.001$). Age demonstrated modest positive correlations with FBS, HbA1c, urea, and TSH. Sex was weakly but significantly associated with HDL and VLDL. These relationships are visually summarized in the correlation heat map (Figure 1), where red indicates positive correlations and blue indicates inverse correlations, with color intensity reflecting strength of association. (Table 2, Figure 1) Receiver operating characteristic (ROC) curve analysis was conducted to evaluate the ability of selected biochemical parameters to discriminate between hypothyroid patients and controls. HbA1c demonstrated good diagnostic accuracy (AUC = 0.828), followed by triglycerides (AUC = 0.803). FBS showed fair discrimination (AUC = 0.759). TSH exhibited perfect discrimination with an AUC of 1.000, confirming its central diagnostic role in hypothyroidism. It is noted that FBS, HbA1c, and TGL showed ties between positive and negative groups, which may slightly influence AUC estimates. (Table 3, Figure 2) Multivariate linear regression analysis identified several independent predictors of biochemical outcomes among hypothyroid patients. Age was positively associated with HbA1c ($\beta = 0.233$, 95% CI: 0.034–0.432) and urea ($\beta = 0.206$, 95% CI: 0.152–0.260). Thyroid function showed distinct associations: TSH was inversely related to FT4 ($\beta = –0.454$) and FT3 ($\beta = –0.175$), and positively associated with HbA1c ($\beta = 0.163$). FBS was independently predicted by creatinine ($\beta = 0.203$) and HbA1c ($\beta = 0.637$). Conversely, HbA1c was positively associated with FBS, age, and TSH, but inversely associated with creatinine. Urea and creatinine showed strong reciprocal associations, highlighting tight renal interdependence. Lipid parameters exhibited robust interrelationships. Total cholesterol was strongly predicted by LDL ($\beta = 0.858$) and also showed positive associations with FT3, HDL, TGL, and VLDL. Triglycerides were inversely associated with HDL and LDL, and positively associated with total cholesterol. LDL demonstrated inverse associations with FT3 and HDL, and a strong positive association with total cholesterol. These multivariate findings are illustrated in the forest plot (Figure 3), where standardized beta coefficients and 95% confidence intervals are shown. Predictors to the right of the reference line indicate positive

associations, while those to the left indicate inverse relationships. (Table 4, Figure 3).

Table 1. Demographic, clinical and biochemical characteristics of hypothyroid patients and controls

Parameter	Hypothyroid (n=285)	Control (n=38)
Age (yr)	48.38±8.44	47.18±11.75
Sex (M/F)	153/132 (53.7%/46.3%)	18/16 (52.9%/47.1%)
Overt Hypothyroidism (n,%)	75 (26.3%)	–
Subclinical hypothyroidism (n,%)	210 (73.7%)	–
Diabetic (n,%)	84 (29.5%)	–
Pre-diabetic (n,%)	122 (42.8%)	–
Dyslipidemia (n,%)	194 (68.1%)	-
Renal Dysfunction (n,%)	54 (18.9%)	-
Levothyroxine Dose (µg/day)	85±23	–
TSH (µIU/mL)	11.05±17.87	2.26±0.69*
FT3 (pg/mL)	2.53±0.79	2.52±0.52
FT4 (ng/dL)	1.10±0.34	1.19±0.25
FBS (mg/dL)	121.44±50.06	87.07±14.00*
HbA1c (%)	6.95±2.20	5.33±0.35*
Total Cholesterol (mg/dL)	158.50±55.89	146.03±27.74*
LDL (mg/dL)	95.48±49.81	88.29±28.85
HDL (mg/dL)	34.28±11.33	43.68±7.22*
Triglycerides (mg/dL)	152.28±110.89	77.45±31.02*
VLDL (mg/dL)	26.98±12.95	16.00±5.78*
Creatinine (mg/dL)	1.50±1.64	0.78±0.22*
Urea (mg/dL)	36.57±38.51	19.68±6.20*

Data are expressed as mean±standard deviation (SD) for continuous variables and number (percentage) for categorical variables. Comparisons between hypothyroid patients (n=285) and control subjects (n=38) were conducted using independent samples t-test for continuous variables

and Chi-square test for categorical variables. Statistical significance was defined as $p<0.05$. The difference in total cholesterol was significant only when equal variances were not assumed ($p=0.028$). Biochemical parameters assessed include thyroid-stimulating hormone (TSH, μIU/mL), free triiodothyronine (FT3, pg/mL), free thyroxine (FT4, ng/dL), fasting blood sugar (FBS, mg/dL), glycated hemoglobin (HbA1c, %), total cholesterol (mg/dL), low-density lipoprotein cholesterol (LDL, mg/dL), and high-density lipoprotein cholesterol (HDL, mg/dL).

Table 2. Moderate to strong Pearson correlations between study variables

Variable 1	Variable 2	r
TC	HDL	.454
TC	LDL	.919
Creatinine	FT3	–.240
Creatinine	Urea	.821
FT3	FT4	.370
FT3	TSH	–.316
FT4	TSH	–.454
FBS	HbA1c	.669
FBS	TGL	.284
HbA1c	TSH	.241
HDL	LDL	.335
HDL	TGL	–.198
HDL	VLDL	–.256
TGL	VLDL	.423

Only moderate ($|r| \geq 0.3$) and strong ($|r| \geq 0.5$) correlations are highlighted. Weak but clinically relevant associations (e.g., creatinine with FT3, HbA1c with TSH) are included for context. TC, total cholesterol; FBS, fasting blood sugar; HbA1c, Glycated hemoglobin; TGL, Triglycerides; VLDL, Very low-density lipoprotein.

Table 3. Predictive performance of biochemical parameters for the outcome (AUC analysis)

Test Variable	AUC
FBS	0.759
HbA1c	0.828
TGL	0.803

AUC, area under the receiver operating characteristic curve, FBS, Fasting Blood Sugar; TGL; Triglycerides

Table 4. Multivariate linear regression for significant predictors of biochemical outcomes in hypothyroid patients (multivariate regression)

Outcome	Predictor	Standardized beta (β)	SE (approx)	95% CI (lower – upper)	Direction of association
Age	HbA1c	0.233	0.366	0.034 – 0.432	Direct
	Urea	0.206	0.027	0.152 – 0.260	Direct
TSH	FT4	-0.454	0.050	-0.554 – -0.354	Inverse
	FT3	-0.175	0.064	-0.301 – -0.049	Inverse
	HbA1c	0.163	0.074	0.018 – 0.308	Direct
FBS	Creatinine	0.203	2.579	0.051 – 0.355	Direct
	HbA1c	0.637	1.178	0.595 – 0.679	Direct
HbA1c	FBS	0.615	0.025	0.566 – 0.664	Direct
	Age	0.130	0.011	0.108 – 0.152	Direct
	TSH	0.123	0.006	0.111 – 0.135	Direct
	Creatinine	-0.227	0.111	-0.445 – -0.009	Inverse
Urea	Creatinine	0.799	0.951	0.576 – 0.976	Direct
Creatinine	Urea	0.776	0.102	0.576 – 0.976	Direct
	FBS	0.126	0.051	0.026 – 0.226	Direct
	HbA1c	-0.145	0.051	-0.245 – -0.045	Inverse
Total cholesterol (TC)	FT3	0.029	0.013	0.003 – 0.055	Direct
	HDL	0.204	0.011	0.182 – 0.226	Direct
	LDL	0.858	0.012	0.834 – 0.882	Direct
	TGL	0.239	0.012	0.215 – 0.263	Direct
	VLDL	0.071	0.012	0.047 – 0.095	Direct
Triglycerides (TGL)	HDL	-0.563	0.043	-0.652 – -0.474	Inverse
	LDL	-2.291	0.119	-2.524 – -2.058	Inverse
	TC	2.642	0.126	2.394 – 2.890	Direct
LDL	FT3	-0.039	0.940	-0.093 – -0.015	Inverse
	HDL	-0.209	0.064	-0.335 – -0.083	Inverse
	VLDL	-0.068	0.055	-0.178 – -0.022	Inverse
	TC	1.113	0.014	1.085 – 1.141	Direct
	TGL	-0.268	0.006	-0.280 – -0.256	Inverse

All values represent results from multivariate linear regression analyses. Outcome refers to the dependent variable in each model. Predictor refers to independent variables included in the model. Standardized Beta (β) indicates the strength and direction of the association between predictor and outcome. SE is the approximate standard error of the standardized beta. 95% CI (Lower – Upper) represents the 95% confidence interval for the standardized beta coefficient. Direction of Association**:** "Direct" indicates a positive association; "Inverse" indicates a negative association. All analyses adjusted for potential confounding variables as listed in the regression models. Significance levels are not explicitly shown here but were considered in model selection ($p<0.05$).

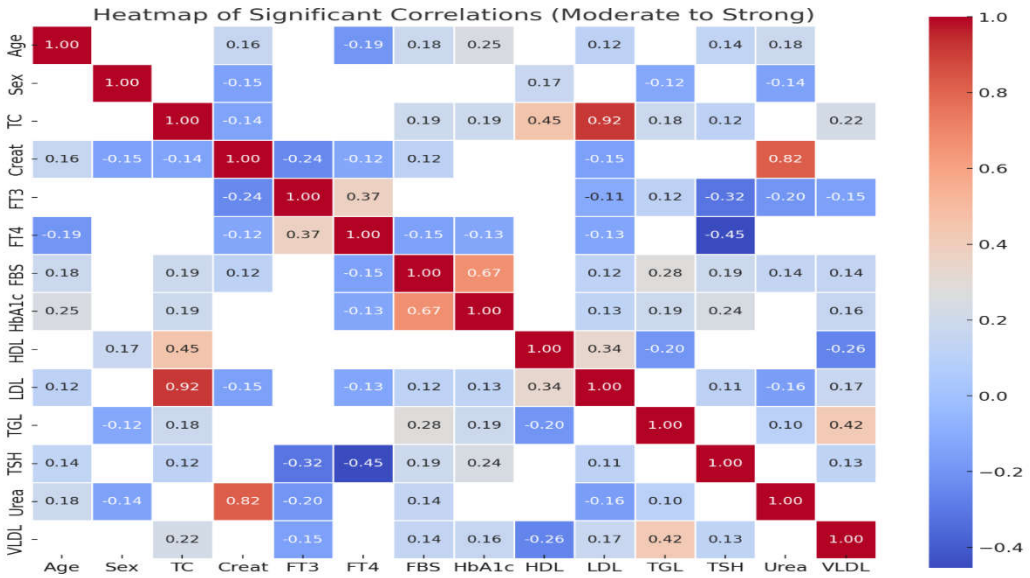

Figure 1. Heat Map of Pearson's Correlation Between Demographic and Biochemical Parameters. *Pearson's correlation coefficients (r) are shown. $p < 0.05$ (*), $p < 0.01$ (**).* N varies due to missing data. Abbreviations: TC = Total Cholesterol, Creat = Creatinine, FT3 = Free Triiodothyronine, FT4 = Free Thyroxine, FBS = Fasting Blood Sugar, HbA1c = Glycated Hemoglobin, HDL = High-Density Lipoprotein, LDL = Low-Density Lipoprotein, TGL = Triglycerides, TSH = Thyroid Stimulating Hormone, VLDL = Very-Low-Density Lipoprotein.

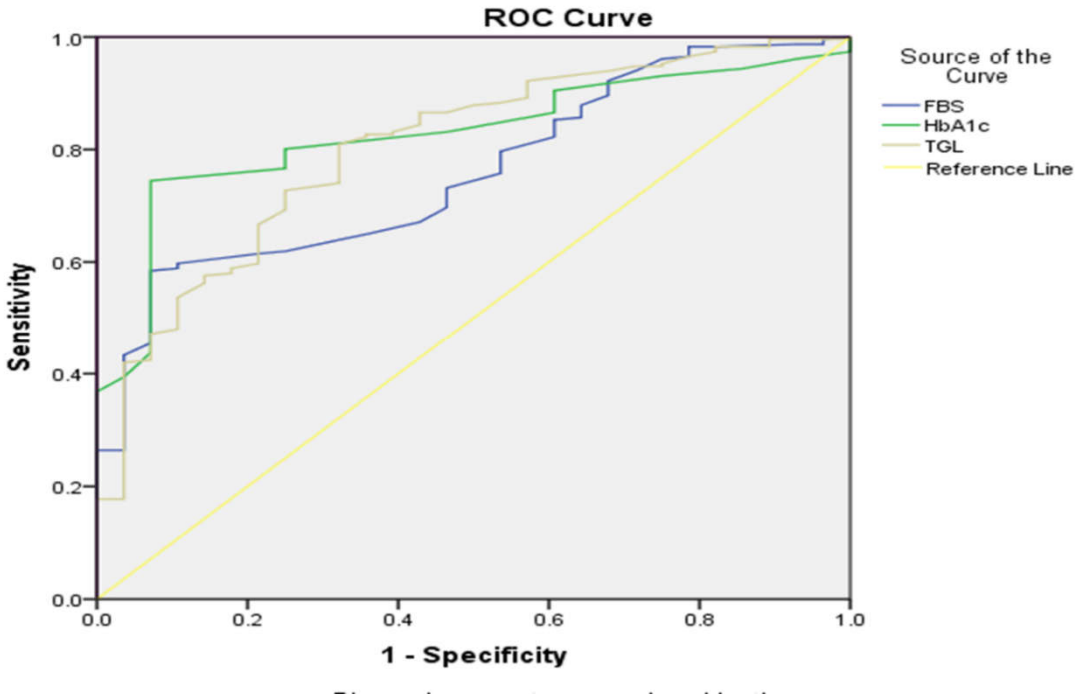

Figure 2. Receiver Operating Characteristic (ROC) Curves for FBS, HbA1c, TGL, and TSH in Predicting the Outcome. ROC curves illustrate the diagnostic performance of each parameter. AUC values indicate predictive accuracy: FBS = 0.759, HbA1c = 0.828, TGL = 0.803, TSH = 1.000. FBS, and HbA1c show ties between positive and negative groups, which may slightly bias estimates.

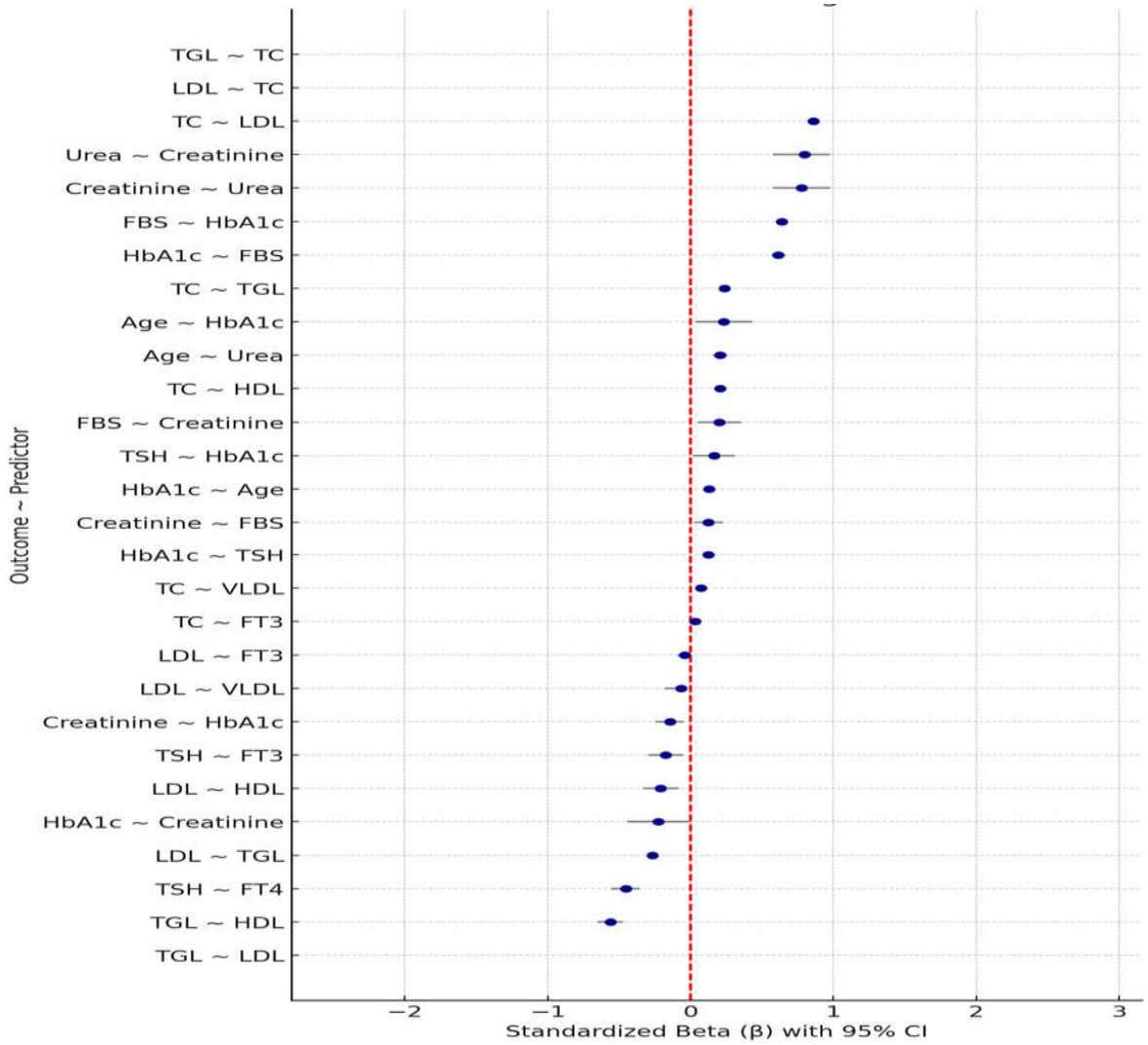

Figure 3. Forest plot for predictors of Biochemical outcomes in Hypothyroid patients. Total Cholesterol (TC). **Blue bars** indicate significant predictors: FT3, HDL, LDL, TGL, and VLDL. Each point represents the standardized beta (β) coefficient with 95% confidence interval. Values to the right of the red dashed line indicate a direct (positive) association,

and values to the left indicate an inverse (negative) association.

All analyses adjusted for potential confounders; only significant predictors ($p < 0.05$) are shown.

Discussion:

The present retrospective analysis provides important insights into the systemic metabolic and biochemical alterations associated with hypothyroidism. Our findings revealed significant elevations in lipid profile parameters, particularly total cholesterol, and triglycerides, in hypothyroid patients compared to healthy controls, consistent with a proatherogenic lipid pattern reported in prior studies (25). These alterations highlight the contribution of thyroid dysfunction to cardiovascular risk (12). In addition, markers of glucose metabolism, including fasting blood glucose and HbA1c, were markedly elevated in hypothyroid patients, indicating an increased risk of impaired glucose tolerance and insulin resistance, in line with earlier reports linking hypothyroidism to metabolic syndrome (26).

Renal function markers, such as serum urea and creatinine, were also significantly altered in hypothyroid patients. This supports evidence that thyroid hormone deficiency can impair renal plasma flow and glomerular filtration rate, with potential reversibility following adequate thyroid hormone replacement therapy (27). Importantly, strong positive correlations were observed between serum TSH levels and key metabolic parameters, including total cholesterol and fasting blood glucose, reinforcing the role of thyroid dysfunction as a systemic contributor to metabolic homeostasis (28). This aligns with findings from meta-analyses demonstrating that even subclinical hypothyroidism is associated with increased cardiometabolic risk (29).

Collectively, these findings emphasize that hypothyroidism extends beyond thyroid hormone imbalance to affect lipid metabolism, glucose homeostasis, and renal physiology. Comprehensive metabolic assessment, therefore, becomes essential in hypothyroid patients to enable early detection of comorbidities and prevent long-term complications such as cardiovascular disease, diabetes, and chronic kidney disease. Routine monitoring of lipid profiles, glycemic markers, and renal parameters should be integrated into hypothyroidism management strategies. Clinically, this could aid in improved risk stratification, individualized levothyroxine dosing, and targeted interventions to mitigate cardiometabolic burden (30). This study includes uneven selection of control and hypothyroid study subject which could be limitation to the study. Being a single-center study conducted in a tertiary care setting, the findings may not be generalizable across different populations, especially considering regional variations in dietary, environmental, and demographic factors influencing hypothyroidism. Moreover, the lack of longitudinal follow-up limits the ability to assess progression of metabolic disturbances or the long-term impact of thyroid hormone replacement therapy. Future prospective, multicenter studies with extended follow-up are warranted to validate these findings and to better delineate the dynamic relationship between thyroid dysfunction and systemic comorbidities. In conclusion, hypothyroid patients in this retrospective cohort exhibited significant dyslipidemia, impaired glucose metabolism, and mild renal dysfunction compared to healthy controls, with strong correlations observed between elevated TSH and adverse metabolic parameters. These results underscore the importance of integrating metabolic and renal monitoring into the routine management of hypothyroidism to reduce long-term cardiometabolic risks. While the retrospective, single-center nature of this study limits generalizability, the findings are consistent with existing evidence and highlight the systemic impact of thyroid dysfunction.

Tailored management strategies that account for regional variations and patient profiles are essential. Prospective, multicentre studies with longitudinal follow-up are needed to establish causal relationships and evaluate the long-term benefits of optimized thyroid hormone replacement on systemic health outcomes.

Conclusion:

Hypothyroid patients on levothyroxine therapy exhibited significant dysglycemia, dyslipidemia, and renal dysfunction compared with healthy controls. These findings indicate that metabolic and renal abnormalities may persist despite treatment, highlighting the need for routine cardiometabolic and renal monitoring in the management of hypothyroidism.

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Conflict of interest:

The authors do not have any conflict of interest

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Authors contribution:

Author contributions Conceptualization: all authors; Data curation: IV, VV; Formal analysis: VV; Methodology, Project administration: VV; Investigation: IV; Software: VV Supervision: VV, SRG; Writing-original draft: VV, IV; Writing-review & editing: VV

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