International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 24s, 2025
https://theaspd.com/index.php

Biochemical Signatures of Hypothyroidism: Comparative and Correlation Analyses in Overt and Subclinical Subtype

Induja Viswanathan[1], Vickneshwaran Vinayagam[2*], Perumal Muraliswaran[3]
[1]Research Scholar, Department of Biochemistry, Mahatma Gandhi Medical College and Research Institute (Sri Balaji Vidyapeeth- Deemed to be University), Pondicherry, India.
ORCID: 0009-0001-1308-8238
[2]Associate Professor, Department of Biochemistry, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed-to-be-University), Puducherry, India. ORCID: 0000-0002-5374-6880
[3]Professor and Head, Department of Biochemistry, J R Medical College and Hospital, Tamilnadu, India. ORCID: 0000-0001-9200-2617
Corresponding Author: Dr. Vickneshwaran Vinayagam, PhD, Department of Biochemistry, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed-to-be-University), Puducherry, India. ORCID: 0000-0002-5374-6880

ABSTRACT

Background: *Hypothyroidism, characterized by insufficient production of thyroxine (T4) and triiodothyronine (T3), is associated with systemic metabolic and renal alterations. While levothyroxine is standard therapy, persistent metabolic disturbances are frequently observed, and data from the Indian population are limited.*

Objective: *To evaluate metabolic and renal parameters in overt and subclinical hypothyroid patients and examine correlations with thyroid hormones.*

Methods: *In this hospital-based retrospective study (January 2023–December 2024), 532 adults were included: 276 hypothyroid patients and 256 age- and sex-matched controls. Hypothyroid patients were classified as overt hypothyroidism (OH, n = 43) or subclinical hypothyroidism (SCH, n = 233). Assessments included thyroid function (fT3, fT4, TSH), glucose metabolism (FBS, HbA1c), lipid profile (TC, LDL, HDL, TGL, VLDL), and renal function (serum urea, creatinine). Group comparisons and correlation analyses were performed.*

Results: *Hypothyroid patients exhibited higher total cholesterol, triglycerides, fasting glucose, HbA1c, serum urea, and creatinine compared with controls, reflecting a pro-atherogenic, insulin-resistant profile with mild renal impairment. Positive correlations were observed between TSH and lipid/glucose markers. Even SCH patients demonstrated measurable biochemical alterations. Micronutrient status (iodine, selenium, vitamin D) was not assessed, which may influence outcomes.*

Conclusion: *Hypothyroidism in this cohort is associated with dyslipidemia, impaired glucose metabolism, and mild renal dysfunction. Elevated TSH correlates with adverse metabolic markers, highlighting the systemic impact of thyroid dysfunction. Comprehensive metabolic and renal monitoring is recommended to optimize risk stratification and guide management beyond thyroid hormone replacement.*

Keywords: *Hypothyroidism; Subclinical Hypothyroidism; Thyroid Hormones; Dyslipidemia; Insulin Resistance; Glucose Metabolism; Renal Function; Thyroid-Stimulating Hormone; Levothyroxine.*

INTRODUCTION

Hypothyroidism is one of the most common endocrine disorders, characterized by insufficient production and release of thyroxine (T4) and triiodothyronine (T3), resulting in widespread disturbances in cellular metabolism, growth, and homeostasis (1). Globally, it affects 1–2% of the population, with women and older adults being disproportionately impacted (1). In iodine-sufficient countries, autoimmune thyroiditis is the primary cause, whereas iodine deficiency remains a major determinant in developing regions (2). Despite levothyroxine being the standard treatment, many patients continue to report persistent symptoms, suggesting additional mechanisms such as micronutrient imbalance or altered thyroid hormone metabolism (3).

Thyroid hormones play a central role in lipid metabolism, glucose homeostasis, and renal function. Hypothyroidism is commonly associated with dyslipidemia, including elevated total cholesterol, LDL cholesterol, and triglycerides, along with decreased HDL cholesterol (4). It also contributes to insulin resistance and altered glucose metabolism, as well as renal dysfunction manifested by elevated serum urea and creatinine, and decreased glomerular filtration rate. These metabolic alterations increase the long-term risk of cardiovascular disease, diabetes, and chronic kidney disease (5,6).

In India, region-specific data on hypothyroidism remain limited. Most studies are small, single-center, and emphasize thyroid hormone replacement or diagnostic aspects rather than systemic metabolic or renal changes (7,8). Moreover, the contribution of subclinical hypothyroidism to metabolic disturbances is not fully understood (9). Considering the unique genetic, dietary, and environmental background of the Indian population, local data are crucial for informed clinical decision-making (7). This study aims to systematically evaluate metabolic and renal parameters in overt and subclinical hypothyroid patients compared with healthy controls and to assess correlations between thyroid hormones and biochemical markers.

MATERIALS AND METHODS

This hospital-based retrospective study was conducted in the Department of Biochemistry, Mahatma Gandhi Medical College and Research Institute, Puducherry, India, between January 2023 and December 2024. Ethical approval was obtained from the Institutional Human Ethics Committee (MGMCRI/IRC/60/2021/01/IHEC/72), and the study adhered to the principles of the Declaration of Helsinki. Owing to the retrospective use of anonymized hospital records, the requirement for informed consent was waived. A total of 532 participants were included, comprising 276 patients with primary hypothyroidism and 256 age- and sex-matched healthy controls. Hypothyroid patients were further categorized into overt hypothyroidism (OH, n = 43; defined as elevated TSH with reduced fT4) and subclinical hypothyroidism (SCH, n = 233; defined as elevated TSH with normal fT4) as shown in figure 1. Adults aged 20–60 years with complete clinical and biochemical records were included, whereas individuals with secondary or tertiary hypothyroidism, pregnancy, chronic renal failure, cardiovascular disease, diabetes mellitus, or dyslipidemia (in controls) and those with incomplete records were excluded. Demographic data and biochemical parameters were obtained from electronic medical records. Thyroid function was assessed using free T3 (fT3), free T4 (fT4), and thyroid-stimulating hormone (TSH). Glucose metabolism was evaluated using fasting blood sugar (FBS) and glycated hemoglobin (HbA1c), renal function using serum urea and creatinine, and lipid profile using total cholesterol (TC), triglycerides (TGL), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL). Venous blood samples were collected after overnight fasting, and serum was separated by centrifugation at 3,500 rpm for 10 minutes. Biochemical analyses including glucose, urea, creatinine, and lipid profile were performed on a fully automated analyzer (Roche Cobas c311, Germany) using standardized commercial kits. Thyroid hormones were measured by chemiluminescence immunoassay (Roche Cobas e411, Germany), while HbA1c was quantified by ion-exchange high-performance liquid chromatography (Bio-Rad D-10, USA).

Data distribution was assessed using the Shapiro–Wilk and Kolmogorov–Smirnov tests. Normally distributed variables were presented as mean ± standard deviation (SD), and skewed variables as median with interquartile range (IQR). Comparisons between groups were carried out using the independent t-test or one-way ANOVA for normally distributed data, and Mann–Whitney U or Kruskal–Wallis tests for non-parametric data. Categorical variables were analyzed using the Chi-square test. Correlations between biochemical parameters were assessed using Pearson's correlation for normally distributed variables and Spearman's rank correlation for non-parametric variables. A p value < 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS version 19.0 (IBM Corp., Armonk, NY, USA).

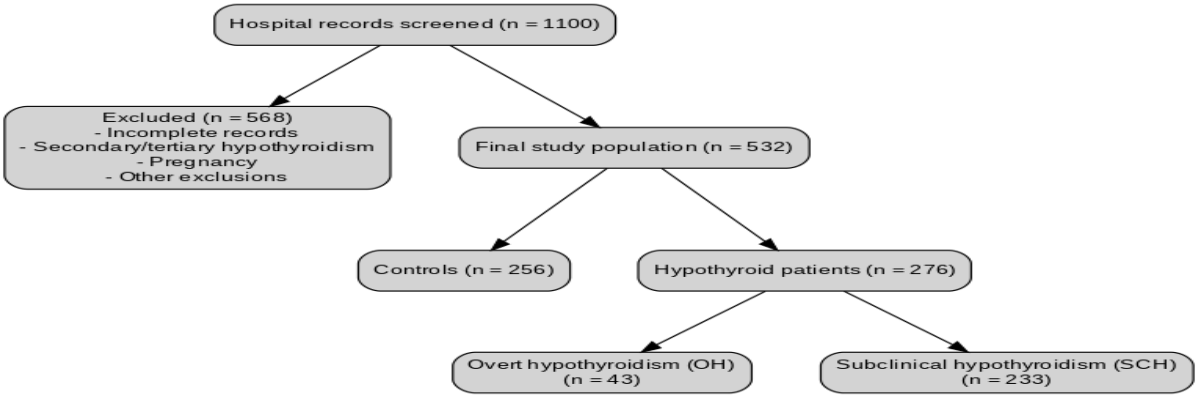

Figure 1. Flowchart of participant selection for the inclusion of study parameters.

Hospital records of 1,100 individuals were initially screened. After applying exclusion criteria, including incomplete or missing records, secondary/tertiary hypothyroidism, pregnancy, and other medical conditions, a total of 532 participants were included in the final analysis. The study population comprised 276 patients with primary hypothyroidism (43 with overt hypothyroidism [OH] and 233 with subclinical hypothyroidism [SCH]) and 256 age- and sex-matched healthy controls.

DISCUSSION

This retrospective study provides insights into the biochemical and metabolic consequences of hypothyroidism. Hypothyroid patients in our cohort exhibited significant elevations in lipid parameters, particularly total cholesterol and triglycerides, indicating a pro-atherogenic lipid profile (4,10,11). These findings align with prior studies demonstrating the effect of thyroid hormone deficiency on lipid metabolism and cardiovascular risk (4,10-12).

Glucose metabolism was also impaired, with higher fasting blood glucose and HbA1c levels observed among hypothyroid patients, reflecting a tendency toward insulin resistance and dysglycemia (13,14). Renal function markers, including serum urea and creatinine, were elevated, consistent with previous reports of reduced renal plasma flow and glomerular filtration rate in hypothyroid individuals (15). Positive correlations between TSH and lipid/glucose markers further highlight the systemic impact of thyroid dysfunction on metabolic homeostasis. Notably, even subclinical hypothyroid patients exhibited measurable biochemical alterations, emphasizing the importance of early detection (12,16).

Collectively, these findings underscore that hypothyroidism affects lipid metabolism, glucose regulation, and renal physiology beyond mere hormone deficiency. Comprehensive metabolic evaluation in hypothyroid patients may aid early identification of comorbidities and help prevent long-term complications, including cardiovascular disease, diabetes, and chronic kidney disease (4,6,16). Routine monitoring of lipid profiles, glycemic markers, and renal parameters may improve risk stratification and guide individualized levothyroxine therapy (6,10,17).

This study has limitations. Being a single-center, regional variations in diet, environment, and genetics may influence observed biochemical patterns. Moreover, the study design prevents assessment of longitudinal effects of thyroid hormone replacement therapy (1,7,18). Micronutrient levels, such as iodine, selenium, and vitamin D, were not assessed, which may influence thyroid function and metabolic outcomes (2,4,19-21)

CONCLUSION

In conclusion, hypothyroid patients in this cohort exhibited dyslipidemia, impaired glucose metabolism, and mild renal dysfunction compared with age- and sex-matched controls. Elevated TSH strongly correlated with adverse metabolic markers, highlighting systemic consequences of thyroid dysfunction. These results support the need for comprehensive metabolic and renal monitoring and suggest that management should extend beyond thyroid hormone replacement alone.

Table: Biochemical and Clinical Parameters of Study Groups

Parameter	Control (n=256)	Hypothyroid (n=276)	Overt Hypothyroid (n=43)	Subclinical Hypothyroid (n=233)
Age (years)	47.9 ± 8.5	48.3 ± 8.4	51.5 ± 5.8*#	47.8 ± 8.7
Male / Female (n)	146 / 110	149 / 127	24 / 19	125 / 108
TC (mg/dL)	152.0 [125–179]	156.8 [79–234]	156.3 [68–244]	156.9 [79–234]
Creatinine (mg/dL)	0.88 [0.50–1.26]	1.51 [–0.74–3.76]*	2.21 [–0.89–5.31]*#	1.38 [–0.61–3.37]*
FT3 (pg/mL)	2.83 ± 0.49	2.51 ± 0.77*	2.07 ± 0.83*#	2.59 ± 0.73
FT4 (ng/dL)	1.24 ± 0.24	1.09 ± 0.31*	0.55 ± 0.19*#	1.19 ± 0.20
Fasting Glucose (mg/dL)	117.7 ± 47.0	121.2 ± 49.9	135.8 ± 60.1*#	118.8 ± 47.8

Parameter	Control (n=256)	Hypothyroid (n=276)	Overt Hypothyroid (n=43)	Subclinical Hypothyroid (n=233)
HbA1c (%)	7.17 [4.75–9.59]	9.23 [3.39–15.07]*	7.61 [5.05–10.17]	9.53 [5.33–13.73]*
HDL (mg/dL)	37.4 ± 11.1	33.9 ± 11.4*	32.2 ± 9.2#	34.2 ± 11.7*
LDL (mg/dL)	94.9 ± 32.2	96.1 ± 48.7	96.8 ± 61.8	96.0 ± 46.0
TGL (mg/dL)	97.2 [58–136]	152.3 [93–211]*	135.5 [56–215]#	155.4 [96–214]*
TSH (μIU/mL)	3.01 [–3.02–9.04]	11.2 [–11.0–33.4]*	33.2 [–14.0–80.4]*#	7.14 [–1.63–15.91]*
Urea (mg/dL)	20.7 [14–27]	36.9 [16–58]*	47.6 [–18–114]*#	34.9 [16–54]*
VLDL (mg/dL)	20.7 ± 11.0	27.6 ± 12.7*	26.0 ± 13.0	27.9 ± 12.7*

Foot note: Hypothyroid patients are subdivided into **Overt Hypothyroidism (OH)**, with elevated TSH and low FT4, and **Subclinical Hypothyroidism (SCH)**, with elevated TSH but normal FT4. Values are presented as **Mean ± SD** for normally distributed variables and **Median [IQR]** for skewed variables (TC, Creatinine, HbA1c, Triglycerides, TSH, and Urea). Abbreviations: TC = Total Cholesterol; TGL = Triglycerides; HDL = High-Density Lipoprotein; LDL = Low-Density Lipoprotein; VLDL = Very Low-Density Lipoprotein; FT3 = Free Triiodothyronine; FT4 = Free Thyroxine; TSH = Thyroid Stimulating Hormone; HbA1c = Glycated Hemoglobin. Statistical comparisons: * indicates significant difference vs. Control ($p < 0.05$), # indicates significant difference vs. Subclinical Hypothyroid ($p < 0.05$). Normally distributed variables were analyzed by **t-test/ANOVA**; skewed variables by **Mann-Whitney U/Kruskal-Wallis test**. Significant increases in TSH, Creatinine, Triglycerides, Urea, and HbA1c highlight metabolic and renal alterations in hypothyroid patients.

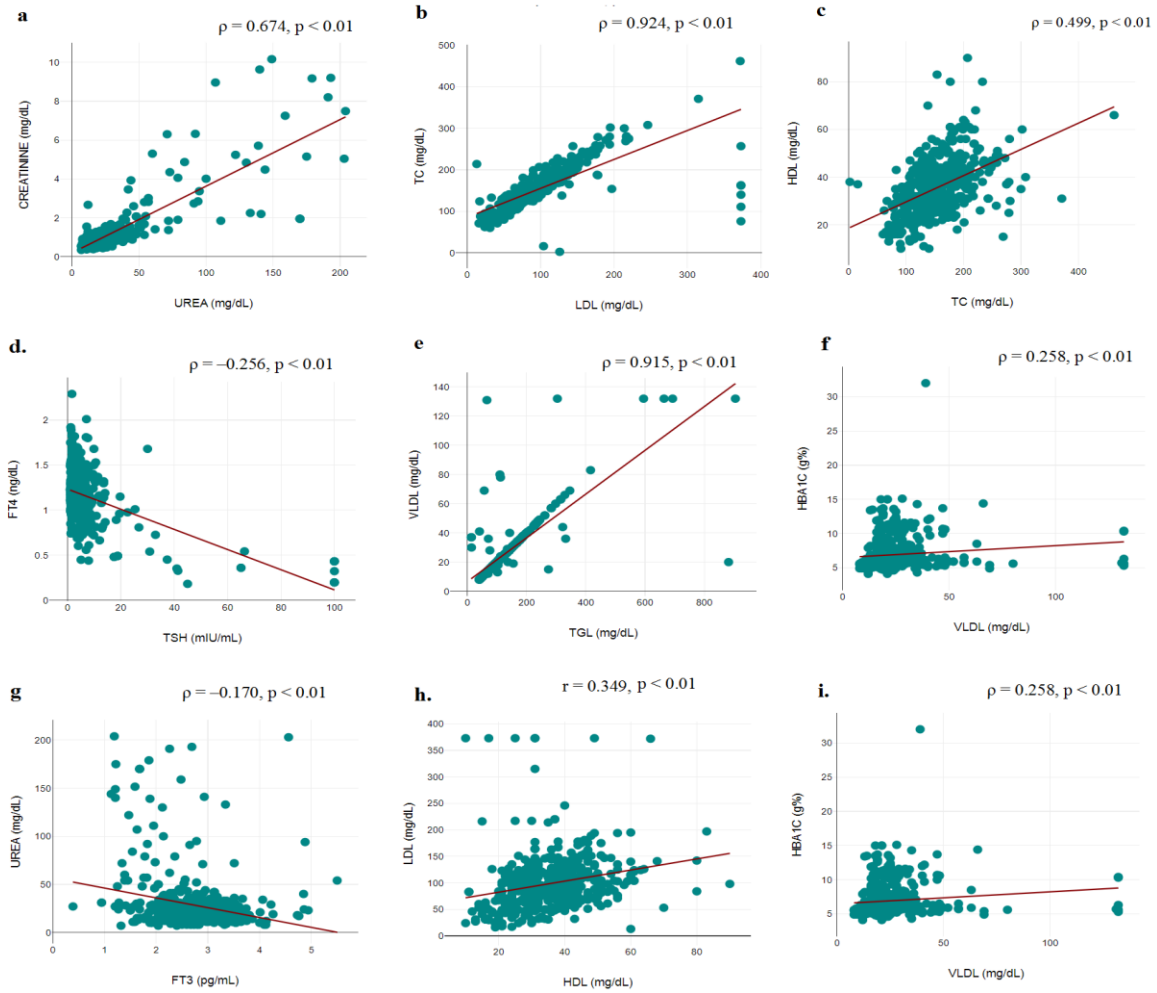

Figure 2. Correlation of biochemical parameters in Hypothyroidism.

Pearson correlation analysis was performed for normally distributed continuous variables, while Spearman's rank correlation was used for non-parametric variables. Significant correlations observed were: creatinine–urea ($\rho = 0.674$, $p < 0.01$), TC–LDL ($\rho = 0.924$, $p < 0.01$), TC–HDL ($\rho = 0.499$, $p < 0.01$), TGL–VLDL ($\rho = 0.915$, $p < 0.01$), fT3–fT4 ($r = 0.385$, $\rho = 0.298$, $p < 0.01$), fT3–TSH ($\rho = -0.257$, $p < 0.01$), fT3–urea ($\rho = -0.170$, $p < 0.01$), fT4–TSH ($\rho = -0.256$, $p < 0.01$), HDL–LDL ($r = 0.349$, $p < 0.01$), HDL–TGL ($\rho = -0.263$, $p < 0.01$), HbA1c–fasting glucose ($r = 0.572$, $p < 0.01$), and VLDL–HbA1c ($\rho = 0.258$, $p < 0.01$). Negative correlations denote inverse associations. Statistical analysis was carried out in IBM SPSS version 19.0 and Image was obtained from datatab.net.

Acknowledgement
The authors acknowledge the host institute, Mahatma Gandhi Medical College and Research Institute, Sri Balaji Vidyapeeth, for providing access to the data.

Conflict of interest:
The authors do not have any conflict of interest

Funding
None.

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

REFERENCES

1. Vanderpump MPJ. The epidemiology of thyroid disease. Br Med Bull. 2011;99(1):39–51.
2. Zimmermann MB. Iodine deficiency. Endocr Rev. 2009;30(4):376–408.
3. McAninch EA, Bianco AC. The history and future of treatment of hypothyroidism. Ann Intern Med. 2016;164(1):50–6.
4. Duntas LH. Thyroid disease and lipids. Thyroid. 2002;12(4):287–93.
5. Maratou E, Hadjidakis DJ, Kollias A, Tsegka K, Peppa M, Alevizaki M, et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. Eur J Endocrinol. 2009;160(5):785–90.
6. Mariani LH, Berns JS. The renal manifestations of thyroid disease. J Am Soc Nephrol. 2012;23(1):22–6.
7. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab. 2011;15(Suppl 2):S78–81.
8. Unnikrishnan AG, Bantwal G, John M, Kalra S, Sahay R, Tewari N, et al. Thyroid disorders in India: Experience from a large center. Indian J Endocrinol Metab. 2011;15(2):198–203.
9. Rodondi N, den Elzen WPJ, Bauer DC, Cappola AR, Razvi S, Walsh JP, et al. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. JAMA. 2010;304(12):1365–74.
10. Duntas LH, Brenta G. The effect of thyroid disorders on lipid levels and metabolism. Med Clin North Am. 2012;96(2):269–81.
11. Subasree S, Shanthi B, Parameaswari PJ. Assessment of lipid profile in subclinical hypothyroidism. J Clin Diagn Res. 2011;5(5):1144–7.
12. Kim HJ, Bae JC, Park SE, Rhee EJ, Park CY, Oh KW, et al. Association of subclinical hypothyroidism and lipid profile according to age. Endocrinol Metab (Seoul). 2015;30(4):470–8
13. Maratou E, Hadjidakis DJ, Kollias A, Tsegka K, Peppa M, Alevizaki M, et al. Studies of insulin resistance in patients with clinical and subclinical hypothyroidism. Eur J Endocrinol. 2009;160(5):785–90
14. Brenta G. Why can insulin resistance be a natural consequence of thyroid dysfunction? J Thyroid Res. 2011;2011:152850
15. Mariani LH, Berns JS. The renal manifestations of thyroid disease. J Am Soc Nephrol. 2012;23(1):22–6.
16. Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev. 2008;29(1):76–131.
17. Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the AACE and the ATA. Endocr Pract. 2012;18(6):988–1028.
18. Taylor PN, Albrecht D, Scholz A, et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nat Rev Endocrinol. 2018;14(5):301–16.
19. World Health Organization. Assessment of iodine deficiency disorders and monitoring their elimination: a guide for programme managers. 3rd ed. Geneva: World Health Organization; 2007. Available from: https://iris.who.int/bitstream/handle/10665/43781/9789241595827_eng.pdf
20. Duntas LH. Selenium and the thyroid: a close-knit connection. Journal of Clinical Endocrinology & Metabolism. 2010;95(6):2363–2372.
21. Wang H, et al. The role of vitamin D in thyroid disease. Journal of Clinical Endocrinology & Metabolism. 2012;97(4):1123–1132.
22.