Journal of Manmohan Memorial Institute of Health Sciences Vol 11 | Issue 1 | 2026

ORIGINAL ARTICLE

Subclinical Hypothyroidism as an Independent Risk Factor for Type 2 Diabetes Mellitus: A Cross-Sectional Study

Anit Lamichhane[1] ✉, Susmita Humagain[1], Anil Khadka[1,2], Rabina Maharjan[1], Sudip Khanal[3], Aashish Acharya[3], Sujan Gautam[4], Mahendra Prasad Bhatta[5]

[1]*Department of Lab Medicine, Manmohan Memorial Institute of Health Sciences, Kathmandu, Nepal*
[2]*Nepal Cancer Hospital and Research Center Ltd, Lalitpur, Nepal*
[3]*Department of Public Health, Manmohan Memorial Institute of Health Sciences, Kathmandu, Nepal*
[4]*Department of Public Health, Nepalese Army Institute of Health Sciences, Kathmandu, Nepal*
[5]*Department of Lab Medicine, Nepalese Army Institute of Health Sciences, Kathmandu, Nepal*

✉ **Anit Lamichhane,**
Department of Lab Medicine, Manmohan Memorial Institute of Health Sciences, Soalteemode, Kathmandu, Nepal
Email: anit.mmu@gmail.com

Received: April 10, 2026
Accepted: June 2, 2026
Published: June 5, 2026

https://doi.org/10.3126/jmmihs.v11i1.92677

How to Cite

Lamichhane A, Humagain S, Khadka A, Maharjan R, Khanal S *et al.* Subclinical Hypothyroidism as an Independent Risk Factor for Type 2 Diabetes Mellitus: A Cross-Sectional Study. J. Manmohan Memorial Inst. Health Sci. 2026;11(1):70–73. https://doi.org/10.3126/jmmihs.v11i1.92677

ABSTRACT

Introduction: Type 2 Diabetes Mellitus (T2DM) is a progressive metabolic disorder characterized by insulin resistance and impaired insulin secretion. Subclinical hypothyroidism (SCH), defined by elevated thyroid-stimulating hormone (TSH) with normal circulating thyroid hormones, has been increasingly linked to metabolic dysregulation that may contribute to T2DM risk. This study aimed to assess biochemical alterations and evaluate the association between SCH and T2DM risk.

Method: A cross-sectional study was conducted at Manmohan Memorial Teaching Hospital, Kathmandu, involving 399 participants, comprising 272 euthyroid individuals and 127 individuals with SCH. Fasting Blood Glucose (FBS), lipid profile, and thyroid function parameters using standardized automated analyzer and chemiluminescence immunoassay methods. Statistical analysis was performed using SPSS 26, including independent t-tests, correlation analysis, and multinominal logistic regression, with statistical significance set at $p < 0.05$.

Result: Females showed a higher prevalence of SCH compared to males. Compared with euthyroid individuals, SCH subjects had significantly higher VLDL levels ($p=0.018$), lower FT3 and FT4 levels ($p=0.001$ and $p<0.001$), and markedly elevated TSH levels ($p<0.001$). Other lipid and glucose parameters showed no significant differences. In SCH cases, TSH showed a significant positive correlation with fasting blood sugar($r=0.199$; $p<0.001$). Multinomial logistic regression revealed that triglycerides, FT4, and TSH were significant predictors of glycemic status. Importantly, SCH was independently associated with higher odds of diabetes compared to euthyroid individuals (AOR = 3.98, 95% CI: 2.23–7.09, p = <0.001).

Conclusion: SCH is associated with altered thyroid function, dyslipidemia, and increased risk of T2DM. Early detection and monitoring of thyroid dysfunction may help in identifying individuals at higher risk of metabolic complications and diabetes development.

Key words: **Sub Clinical Hypothyroidism; Type 2 Diabetes Risk; Dyslipidemia**

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a major metabolic disorder characterized by insulin resistance and impaired insulin secretion, leading to persistent hyperglycemia[1]. The prevalence of T2DM is increasing globally due to sedentary lifestyle, obesity, unhealthy diet, and genetic predisposition [2]. Subclinical Hypothyroidism(SCH) is a condition in which serum thyroid-stimulating hormone (TSH) levels are elevated while thyroid hormone levels remain within the normal range[3].

In subclinical hypothyroidism, insulin resistance, dysregulated lipid metabolism, chronic low-grade inflammation, and reduced peripheral glucose utilization are commonly observed[4]. Elevated TSH levels may reduce insulin sensitivity, leading to impaired glucose uptake by cells[4]. Subclinical hypothyroidism is also associated with weight gain, dyslipidemia, and reduced basal metabolic rate, all of which contribute to an increased risk of developing T2DM. Furthermore, thyroid hormone imbalance may negatively affect pancreatic β-cell function and insulin secretion, resulting in disturbances in glucose metabolism[5,6]. Therefore, assessing the risk of Type 2 Diabetes Mellitus among individuals with subclinical hypothyroidism is essential for early identification, prevention, and management of metabolic complications.

METHODS

Study design and Participants: A cross-sectional study was conducted at Manmohan Memorial Teaching Hospital, Kathmandu, Nepal, among patients attending the Endocrinology Outpatient Department (OPD). A total of 399 participants were included in the study. Among them, 272 were euthyroid and 127 had subclinical hypothyroidism. Participants were classified according to their thyroid status for comparison between the two groups euthyroid and Subclinical Hypothyroidism. This study was conducted between september 2023 and June 2024.

Inclusion and Exclusion criteria: Patients diagnosed with thyroid disorders attending the endocrinology department at MMTH were included in the study. Patients with a history of diabetes mellitus and those receiving hypoglycemic medications were excluded from the study.

Informed Consent: Written informed consent was obtained from all participants after thoroughly explaining the procedures to them in the Nepali language. Participants were guaranteed anonymity and confidentiality.

Experimental Protocol: A self-administered questionnaire was used to collect the data. Five-milliliter fasting samples (8 to 12 hours of fasting) and postprandial (2 hours after

a meal) blood samples were collected via venipuncture. The collected sample was separated into different sample collection tubes. A yellow vial (BD Vacutainer® SST™ Tubes) was used for serum separation, a fluoride vial (BD Vacutainer® SST™ Tubes) was used for glucose estimation. The biochemistry parameters, such as fasting blood sugar, Cholesterol (TC), Triglyceride (TG), High density lipoprotein (HDL), Low Density Lipoprotein (LDL), were analyzed by using a fully automated chemistry analyzer (VITROS® 350 Chemistry System, USA). Thyroid hormones (FT3, FT4 and TSH) were estimated by Chemiluminescence Immunoassay (CLIA-MAGLUMI X3, China). Internal quality control was performed according to the manufacturer's instructions using commercially available RANDOX control materials to ensure the accuracy and precision of all biochemical and immunoassay analyses. In this study, the levels of FBS, TC, TG, HDL, LDL, and VLDL were expressed in mg/dL, whereas free T3, and Free T4, expressed in pg/ml and TSH was expressed in µlU/ml.

Ethical approval: Ethical consideration was obtained from NEHCO-IRC (Ref no: NEHCO-IRC/080/009) in October 2023.

Statistical analysis: Data were collected using a structured questionnaire and entered into a Microsoft Excel 2019 database. The data were subsequently imported into IBM SPSS 26 Statistics for analysis. Descriptive statistics were computed, including means and standard deviations for continuous variables. Differences in mean values between groups were assessed using the independent-samples t-test. Associations between continuous variables were examined using Pearson's correlation analysis. Multinomial logistic regression analysis was performed to identify factors associated with categorical outcome variables. Statistical significance was considered at a p-value < 0.05.

RESULT

Among 399 participants included in the study, 272 participants were with Euthyroid and 127 participants were cases with Sub Clinical Hypothyroidism. Among Euthyroid group 147(54.0%) were females and 125(46.0%) were males whereas, among SCH cases 80(63.2%) were female and 47(36.8%) were male. This data demonstrates a higher overall prevalence of SCH in females as shown in Figure 1.

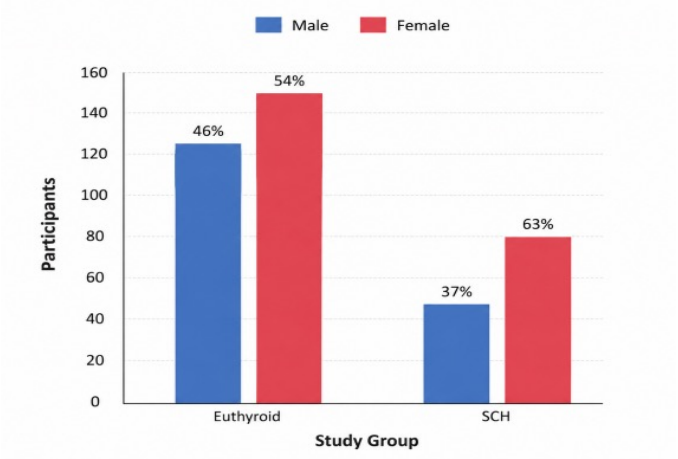

Figure 1: Distribution of participants in the study

Comparison between euthyroid and subclinical hypothyroid (SCH) groups showed, Total cholesterol, Triglycerides, HDL, LDL, and TC:HDL ratio were higher in the SCH group; however, these differences were not statistically significant (p>0.05). FBS and VLDL levels were significantly elevated in the SCH group compared to the euthyroid group. Thyroid hormone parameters demonstrated significant differences between the two groups, with lower FT3 and FT4 levels observed in SCH subjects (p=0.001 and p<0.001, respectively). TSH levels were markedly increased in the SCH group (15.49±11.81 µIU/ml) compared to the euthyroid group (2.52±1.30 µIU/ml), showing a highly significant difference (p<0.001). Overall, SCH was associated with significant alterations in thyroid profile, VLDL levels and FBS levels as shown in Table 1.

Table 1: Comparison of different biochemical variables between euthyroid and Subclinical hypothyroidism cases.

Variable	Euthyroid Mean±SD	SCH Mean±SD	p value
FBS (mg/dl)	110.40±49.72	130.13±41.49	<0.001*
TC (mg/dl)	173.28±45.18	169.27±50.01	0.193
TG (mg/dl)	140.54±83.53	155.61±110.24	0.356
HDL (mg/dl)	43.12±11.768	44.20±14.29	0.172
LDL (mg/dl)	101.69±38.83	96.89±39.07	0.926
VLDL (mg/dl)	28.03±16.87	32.45±26.99	0.018*
TC: HDL	4.64±4.49	4.94±5.45	0.211
FT3 (pg/ml)	3.43±0.36	3.29±0.51	0.001*
FT4 (pg/ml)	13.33±1.76	12.46±2.97	<0.001*
TSH (µlU/ml)	2.52±1.30	15.49±11.81	<0.001*

*Independent samples t-test; *Statistically Significant*

Among SCH cases, a positive correlation was found between FT3 and LDL ratio at a significant level (p<0.05) and TSH was found positively correlated with FBS at a significant (p<0.05) level as shown in Table no 2.

Table 2: Correlation between Thyroid profile and Biochemical variables among SCH cases

Variable		FBS	TC	TG	HDL	LDL	VLDL	TC: HDL
FT3 (pg/ml)	r	-0.091	0.081	-0.001	-0.063	0.136**	-0.008	0.094
	p	0.069	0.105	0.984	0.209	0.007	0.872	0.060
FT4 (pg/ml)	r	0.077	-0.002	-0.080	0.001	-0.035	-0.029	-0.012
	p	0.127	0.965	0.112	0.979	0.488	0.568	0.813
TSH (µlU/ml)	r	0.199	-0.035	0.010	-0.024	-0.046	0.061	0.044
	p	<0.001*	0.480	0.850	0.637	0.361	0.225	0.378

*Pearson Correlation; *Statistically Significant*

Multinomial logistic regression analysis was applied to predict glycemic status. VLDL, LDL, TC:HDL ratio and outliers were excluded from the multinomial logistics regression analysis due to multicollinearity and data cleaning; resulting in a final analyzed sample of 343 participants out of 399. The regression model showed that TG, FT4, and TSH were significant predictors of glycemic status. Higher TG levels were associated with increased odds of both prediabetes and diabetes. Elevated FT4 was significantly associated with diabetes (AOR = 1.207, 95% CI: 1.06–1.37, p = 0.004).

Similarly, higher TSH levels significantly increased the odds of both prediabetes and diabetes. Importantly, individuals with subclinical hypothyroidism (SCH) had significantly higher odds of diabetes compared to euthyroid individuals (AOR = 3.975, 95% CI: 2.23–7.09, p < 0.001), This indicated that SCH was associated with 3.98 fold higher odds of diabetes compared to euthyroid individuals, confirming SCH as an independent risk factor for diabetes as shown in table 3.

Table 3: Multinomial Logistic Regression Analysis of Factors Associated with Prediabetes and Diabetes

Variable	Prediabetes vs Non-Diabetics AOR (95% CI)	p-value	Diabetes vs Non-Diabetics AOR (95% CI)	p-value
TC (mg/dl)	0.995 (0.987–1.003)	0.203	0.995 (0.988–1.003)	0.208
TG (mg/dl)	1.004 (0.999–1.009)	0.102	1.007 (1.003–1.011)	<0.001*
HDL (mg/dl)	1.007 (0.981–1.034)	0.596	1.004 (0.981–1.027)	0.743
FT3 (pg/ml)	1.141 (0.641–2.030)	0.654	0.975 (0.596–1.595)	0.920
FT4 (pg/ml)	0.983 (0.864–1.120)	0.801	1.207 (1.061–1.374)	0.004*
BMI (kg/m^2)	1.035 (0.973–1.102)	0.275	1.024 (0.968–1.084)	0.409
SCH vs Euthyroid	2.387 (1.230–4.631)	0.010*	3.975 (2.228–7.094)	<0.001*

AOR = Adjusted Odds Ratio, CI = Confidence Interval, Outcome reference: Non-diabetics, Thyroid reference: Euthyroid; Nagelkerke R^2=0.224

DISCUSSION

Subclinical hypothyroidism (SCH) is characterized by elevated TSH levels with normal FT3 and FT4 concentration[2]. Insulin resistance is a key factor in the development of type 2 diabetes mellitus (T2DM) and is closely associated with thyroid dysfunction, where elevated TSH and reduced FT4 levels are linked to a higher risk of diabetes and progression from prediabetes to diabetes[5].

In this study FBS, TC, TG, HDL, LDL, and TC:HDL ratio were higher in SCH compared to euthyroid individuals; however, these differences were not statistically significant. Similar findings were reported in different studies[7-8]. Thyroid hormones are closely involved in glucose and lipid metabolism, and even mild thyroid dysfunction may impair insulin sensitivity and glucose utilization[9]. The absence of significant differences in most lipid parameters may be due to population variability or the early stage of thyroid dysfunction.

Among the lipid parameters, VLDL levels were significantly elevated in SCH subjects compared to euthyroid individuals, similar finding reported in different publications[10-11]. Elevated VLDL is commonly linked with insulin resistance and abnormal lipid metabolism. Reduced thyroid hormone activity may impair hepatic lipid clearance and lipoprotein metabolism, resulting in increased triglyceride-rich lipoproteins which is reported by Duntas LH *et al.* and Huang JK *et al.*[12-13]. Therefore, elevated VLDL levels in SCH individuals may increase the risk of cardiovascular disease and metabolic syndrome, both of which are strongly associated with T2DM.

In thyroid function test FT3 and FT4 levels were significantly decreased, while TSH levels were significantly elevated in the SCH group compared to euthyroid individuals. TSH showed a significant positive correlation with fasting blood sugar levels and similar finding was reported in different publications[14-15]. Elevated TSH may contribute to insulin resistance and impaired glucose metabolism, thereby increasing the risk of T2DM. Further multinominal regression analysis showed that TSH was significantly associated between SCH and dysglycemia. Individuals with SCH had 2.39 times higher odds of prediabetes and 3.98 times higher odds of diabetes compared with euthyroid individuals, suggesting that SCH may contribute to the progression of impaired glucose metabolism. In addition, higher TG levels were independently associated with diabetes, indicating the important role of dyslipidemia in the development of insulin resistance and hyperglycemia. Increased FT4 levels were also significantly associated with diabetes risk, suggesting that alternations in thyroid hormone activity may influence glucose homeostasis and contributes to the pathogenesis of diabetes. Together, these findings support the potential role of thyroid dysfunction and lipid abnormalities as important factors in the development of prediabetes and diabetes.

CONCLUSION

Subclinicial Hypothyroidism is associated with increased odds of both prediabetes and diabetes, suggesting that SCH may be an important risk factor for dysglycemia. Early screening and monitoring of thyroid function may help identify high-risk individuals and prevent future metabolic complications.

REFERENCES

1. Accili D, Deng Z, Liu Q. Insulin resistance in type 2 diabetes mellitus. Nature Reviews Endocrinology. 2025 Jul;21(7):413-26.
2. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nature reviews endocrinology. 2018 Feb;14(2):88-98.
3. Biondi B, Cappola AR, Cooper DS. Subclinical hypothyroidism: a review. Jama. 2019 Jul 9;322(2):153-60.
4. Sarker PK, Sultana N, Islam H, Bashir MS, Ali MS. Thyroid dysfunction and metabolic dysregulation: a cross-sectional study of hormonal and glycemic parameters.

Mol Mech Res. 2025;3(2):10227.
5. Biondi B. Subclinical hypothyroidism in patients with obesity and metabolic syndrome: a narrative review. Nutrients. 2023 Dec 27;16(1):87.
6. Chen C, Xie Z, Shen Y, Xia SF. The roles of thyroid and thyroid hormone in pancreas: physiology and pathology. International journal of endocrinology. 2018;2018(1):2861034.
7. Reddy H. A Study of Serum Lipid Profile and High Sensitive C-Reactive Protein in Subclinical Hypothyroidism and Its Correlation with Cardiovascular Profile (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)), 2018.
8. Luo Y, Wu F, Huang Z, Gong Y, Zheng Y. Assessment of the relationship between subclinical hypothyroidism and blood lipid profile: reliable or not?. Lipids in Health and Disease. 2022 Dec 13;21(1):137.
9. Gierach M, Gierach J, Junik R. Insulin resistance and thyroid disorders. Endokrynologia Polska. 2014;65(1):70-6.
10. Zhang Y, Lu P, Zhang L, Xiao X. Association between lipids profile and thyroid parameters in euthyroid diabetic subjects: a cross-sectional study. BMC endocrine disorders. 2015 Mar 27;15(1):12.
11. Kumar DV, Mathur DS, Tuteja DR. Effects of thyroid dysfunction on lipid profile. Int J Med Biomed Stud. 2019;3(6):76-84.
12. Duntas LH, Brenta G. A renewed focus on the association between thyroid hormones and lipid metabolism. Frontiers in endocrinology. 2018 Sep 3;9:511.
13. Huang JK, Lee HC. Emerging evidence of pathological roles of very-low-density lipoprotein (VLDL). International journal of molecular sciences. 2022 Apr 13;23(8):4300.
14. Hussein S, Alblooshi N, Kandakurti P, Osman H, Mostafa A, Abdelfatah M, Alsubhi A, Algarni A, Ali E, Dawod O, Abdalhabib E. Serum TSH, FT3, FT4, and fasting blood glucose levels to investigate the association between thyroid dysfunction and type 2 diabetes mellitus. Georgian medical news. 2025 May 1(362):209-13.
15. Liu D, Jiang F, Shan Z, Wang B, Wang J, Lai Y, Chen Y, Li M, Liu H, Li C, Xue H. A cross-sectional survey of relationship between serum TSH level and blood pressure. Journal of human hypertension. 2010 Feb;24(2):134-8.

ACKNOWLEDGEMENT

We sincerely acknowledge and thank all the participants for their valuable cooperation and involvement in this study. We are also deeply grateful to the laboratory staff and our colleagues for their continuous support and assistance throughout the research process. Special appreciation is extended to Manmohan Memorial Teaching Hospital for providing the necessary facilities and resources that contributed to the successful completion of this study.

AUTHOR CONTRIBUTIONS

Anit Lamichhane designed the study and supervised the research process. Susmita Humagain, Rabina Maharjan, and Anil Khadka performed data collection and data processing. Sudip Khanal, Aashish Acharya, Sujan Gautam and Mahendra Prasad Bhatt contributed in data analysis, interpretation, review and manuscript drafting.

CONFLICT OF INTEREST

The authors declare no competing interests

FUNDING

None