

THE THYROID-GLUCOSE NEXUS: INVESTIGATING THE RELATIONSHIP BETWEEN THYROID HORMONAL IMBALANCE AND IMPAIRED GLUCOSE TOLERANCE

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Abstract

Background: Thyroid disease and diabetes mellitus are common endocrine disorders that impact each other's diagnosis and treatment. **Objective:** To investigate the relationship between thyroid dysfunction and impaired glucose tolerance. **Methods:** This cross-sectional observational study involved 72 patients with thyroid dysfunction. Patients underwent oral glucose tolerance tests after a 10-14 hour fast. The test begins with a measurement of fasting blood sugar levels, followed by consumption of a drink containing 75 grams of glucose. Timing starts upon ingestion of the glucose solution, and a blood sample is obtained exactly 2 hours later. The blood glucose concentration is then measured using an enzymatic method to determine the body's ability to regulate glucose levels. **Results:** Hypothyroidism was more prevalent (61%) than hyperthyroidism (39%). The overall prevalence of diabetes was 2.8%, impaired glucose tolerance was 27.8%, and normal glucose tolerance was 69.4%. Hypothyroidism patients had higher impaired glucose tolerance (36.3%) and diabetes (4.6%) rates than hyperthyroidism patients. A statistically significant association was found between thyroid dysfunction and impaired glucose tolerance. **Conclusion:** This study reveals a significant link between thyroid dysfunction and impaired glucose tolerance, particularly in hypothyroidism patients. Early evaluation and management of impaired glucose tolerance in thyroid dysfunction patients can prevent diabetes-related complications. Regular screening and follow-up are recommended for timely detection and management of prediabetes and diabetes in patients with thyroid dysfunction.

Keywords: thyroid dysfunction, impaired glucose tolerance, diabetes mellitus, hypothyroidism, hyperthyroidism.

Introduction

Thyroid disease and diabetes mellitus (DM) are two common endocrine disorders.¹ Thyroid hormones regulate glucose metabolism and pancreatic function, whereas diabetes affects thyroid function tests.¹ Thyroid dysfunction (hyperthyroidism and hypothyroidism) impairs

glucose homeostasis, potentially leading to type 2 diabetes.² In India, over 42 million people suffer from thyroid problems, with prevalence rates of 2.9% for hypothyroidism and 9.4% for subclinical hypothyroidism.^{3,4} Women are more affected than men.³ Despite existing data on thyroid dysfunction in individuals with diabetes, little is known about impaired glucose tolerance in individuals with thyroid dysfunction. This study aims to investigate this knowledge gap and to determine the prevalence of impaired glucose tolerance in individuals with hypothyroidism and hyperthyroidism.

Materials and methods: This cross-sectional observational study was conducted at KR Hospital, Mysore, from October 2022 to September 2023 and involved patients with thyroid dysfunction. A relevant history, clinical examination, and oral glucose tolerance tests were conducted. The oral glucose tolerance test is performed in the morning after a 10-14 hour fast, during which only water is allowed and smoking is prohibited. The test begins with a measurement of fasting blood sugar levels, followed by the consumption of a drink containing 75 grams of glucose. Timing starts upon ingestion of the glucose solution, and a blood sample is obtained exactly 2 hours later. The blood glucose concentration was measured via an enzymatic method. The data were collected via a pretested proforma and analysed via SPSS 22.0 software.

Results

The study included 72 subjects, predominantly females (85%, n=61), with a mean age of 45.20 years. The majority (31.95%) were in the 41-50 years age range. Hypothyroidism was more prevalent (61%, n=44) than hyperthyroidism (39%, n=28). Females accounted for 36 hypothyroid and 25 hyperthyroid cases, whereas males accounted for 8 hypothyroid and 3 hyperthyroid cases. The overall prevalence of diabetes was 2.8% (n=2), impaired glucose tolerance was 27.8% (n=20), and normal glucose tolerance was 69.4% (n=50). Hypothyroidism patients had higher impaired glucose tolerance (36.3%) and diabetes (4.6%) rates than hyperthyroidism patients. A statistically significant association was found between thyroid dysfunction and impaired glucose tolerance (chi-square value: 4.66, $p < 0.05$), indicating a link between thyroid dysfunction and glucose metabolism disorders.

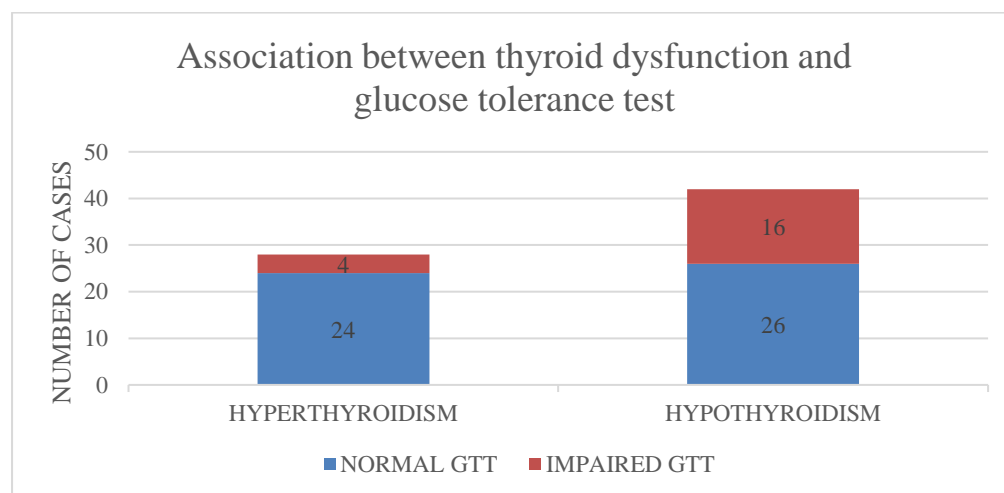


Figure 1: Association between thyroid dysfunction and glucose tolerance test.

Discussion: Thyroid hormones significantly impact glucose metabolism, and thyroid dysfunction is linked to diabetes mellitus.^{5,6} Hypothyroidism decreases glucose absorption, reduces insulin secretion, and increases insulin resistance, whereas hyperthyroidism increases glucose production, insulin demand, and hepatic insulin resistance.^{7,8} Studies have shown a high prevalence of hypothyroidism in type 2 diabetes patients, particularly in South Asian populations.⁹ Thyroid hormone imbalance can contribute to diabetes development and complications by disrupting glucose homeostasis.¹⁰⁻²⁰ Diagnosing thyroid dysfunction in diabetes mellitus patients is challenging because of the impact of DM on thyroid function assessment.¹⁰⁻¹² Diabetes affects T4-to-T3 conversion and TSH release, and can mask or delay the diagnosis of thyroid dysfunction.¹²⁻¹⁶ Type 1 and 2 diabetes can cause "low T3" syndrome, which is characterized by low serum T3 levels.^{17,18} Treating thyroid dysfunction in DM patients requires careful consideration of insulin treatment, thyroid function, and lipid profiles.²¹ Hyperthyroidism alters insulin treatment, whereas hypothyroidism requires adjusted insulin doses and careful L-T4 treatment to avoid iatrogenic hyperthyroidism.²² Hence, patients with diabetes and thyroid dysfunction require adjusted insulin dosages to prevent hypoglycemia or hyperglycemia.

This cross-sectional observational study was conducted at KR Hospital, Mysore, from October 2022 to September 2023 and involved 72 patients with thyroid dysfunction. The mean age was 45.2 years, with 85% females and 15% males. Hypothyroidism was more prevalent (61%) than hyperthyroidism (39%) was. The present study revealed a significant association between thyroid dysfunction and impaired glucose tolerance, with 27.8% impaired and 2.8% diabetic results. Hypothyroidism patients had higher impaired glucose tolerance (36.3%) and diabetes (4.6%) rates than hyperthyroidism patients did.

Research has consistently shown a link between thyroid dysfunction and diabetes risk. Studies have revealed that hypothyroidism increases diabetes risk (Gronich N *et al.*, 2015²³; Roa Dueñas OH *et al.*, 2022²⁴), and other studies have revealed associations between thyroid hormone levels and metabolic disorders: elevated TSH increases lipid and carbohydrate disorders (Korzeniowska K A *et al.*, 2019²⁵); thyroid dysfunction increases type 2 diabetes risk (Chen RH, 2019²⁶); and elevated serum TSH increases the incidence of prediabetes (Chang CH *et al.*, 2017²⁷). Hyperthyroxinemia also contributes to type 2 diabetes (Ittermann T *et al.*, 2017²⁸). Additionally, hypothyroid individuals showed a higher prevalence of impaired glucose tolerance and new-onset diabetes (Ashrafuzzaman SM *et al.*, 2012²⁹). These findings highlight the complex relationship between thyroid function and glucose metabolism. The findings of the present study align with those of previous studies, indicating a link between hypothyroidism and glucose metabolism disorders. A literature review revealed similar studies worldwide, highlighting the importance of screening for glucose intolerance in patients with thyroid dysfunction. Wenhua Du *et al.* (2019) reported the prevalence of thyroid disease in North China, suggesting the use of routine thyroid screening for diabetics and non-diabetics³⁰. Similarly, Chaker L *et al.* (2016) linked low thyroid function to increased type 2 diabetes risk, suggesting that further research on hypothyroidism treatment and screening³¹. Additionally, Kabir *et al.*'s study in Bangladesh (2015) identified South Asian ethnicity and thyroid disease as risk factors for type 2 diabetes, emphasizing the importance of glucose intolerance screening³². The present study also recommends regular screening and follow-up for thyroid dysfunction patients to detect impaired glucose tolerance and manage its complications. Early detection and management can reduce the risk of diabetes mellitus and related complications in patients with thyroid dysfunction.

Conclusion

This study revealed a significant link between thyroid dysfunction and impaired glucose tolerance, affecting 27.8% of patients. Compared with hyperthyroidism, hypothyroidism is associated with a greater prevalence of impaired glucose tolerance. Early evaluation of impaired glucose tolerance in thyroid dysfunction patients enables timely detection and management of prediabetes. This early intervention can prevent diabetes-related microvascular and macrovascular complications through dietary modifications and minimal medication.

References

1. Powers AC, Niswender KD, Evans-Molina C. Endocrinology and metabolism. In: Loscalzo J, Kasper DL, Longo DL, Fauci AS, Hauser SL, Jameson JL, eds. *Harrison's Principles of Internal Medicine*. 21st ed. Vol 2. New York: McGraw Hill LLC; 2022:2926-2945.
2. American Diabetes Association. Classification and diagnosis of diabetes: Standards of Medical Care in Diabetes 2021. *Diabetes Care*. 2021;44(Suppl 1):S15-S33. doi: 10.2337/dc21-S005
3. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. *Indian J Endocr Metab*. 2011;15(Suppl 2):78-81.
4. Ministry of Health and Family Welfare. Status of Goitre or Thyroid Disorders in India. 2022. Release ID: 1796440. <https://pib.gov.in/PressReleasePage.aspx?PRID=1796440>
5. Salvatore D, Davies TF, Schlumberger MJ, Hay ID, Larsen PR. Thyroid physiology and diagnostic evaluation of patients with thyroid disorders. In: Melmed S, Auchus RJ, Goldfine AB, Rosen CJ, Kopp PA, eds. *Williams Textbook of Endocrinology*. Elsevier Health Sciences; 2024:333-488.
6. Ganong WF, Barrett KE. The thyroid gland. In: Ganong WF, Barrett KE. *Ganong's Review of Medical Physiology*. 26th ed. New York: McGraw-Hill Education; 2016:337-350.
7. Johnson JL. Diabetes control in thyroid disease. *Diabetes Spectr*. 2006;19(3):148-153. doi: 10.2337/diaspect.19.3.148
8. Wondmkun YT. Obesity, Insulin Resistance, and Type 2 Diabetes: Associations and Therapeutic Implications. *Diabetes Metab Syndr Obes*. 2020;13:3611-3616. doi: 10.2147/DMSO.S275898
9. Subekti I, Pramono LA, Dewiasty E, Harbuwono DS. Thyroid dysfunction in type 2 diabetes mellitus patients. *Acta Med Indonesiana*. 2018;49(4):314.
10. Schroder-van der Elst JP, van der Heide D. Effects of streptozocin-induced diabetes and food restriction on quantities and source of T4 and T3 in rat tissues. *Diabetes*. 1992;41(2):147-152.
11. Moura EG, Pazos CC, Rosenthal D. Insulin deficiency impairs thyroid peroxidase activity. A study in experimental diabetes mellitus. In: Medeiros-Neto G, Gaitan E, eds. *Frontiers in Endocrinology*. Boston, MA: Springer; 1986:627-630.
12. Chopra IJ, Wiersinga W, Frank H. Alterations in hepatic monodeiodination of iodothyronines in the diabetic rat. *Life Sci*. 1981;28(15-16):1765-1776.
13. Ortiz-Caro J, Obregón MJ, Pascual A, Jolin T. Decreased T4 to T3 conversion in tissues of streptozotocin-diabetic rats. *Acta Endocrinol (Copenh)*. 1984;106(1):86-91.
14. Islam S, Yesmine S, Khan SA, Alam NH, Islam S. A comparative study of thyroid hormone levels in diabetic and nondiabetic patients. *Southeast Asian J Trop Med Public Health*. 2008;39(5):913-916.

15. Bazrafshan HR, Ramezani MA, Salehi A, Shirafkan AA, Mohammadian S, Farajollahi M, Raiszadeh F, Azizi F. Thyroid dysfunction and its relation with diabetes mellitus (NIDDM). *J Gorgan Uni Med Sci.* 2000;2(1):5-11.
16. Dimitriadis G, Hatzigelaki E, Mitrou P, Lambadiari V, Maratou E, Raptis AE, Gerich JE, Raptis SA. Effect of hyperthyroidism on clearance and secretion of glucagon in man. *Exp Clin Endocrinol Diabetes.* 2011;119(4):214-217. doi: 10.1055/s-0029-1246194
17. Kunishige M, Sekimoto E, Komatsu M, Bando Y, Uehara H, Izumi K. Thyrotoxicosis masked by diabetic ketoacidosis: a fatal complication. *Diabetes Care.* 2001;24(1):171. doi: 10.2337/diacare.24.1.171
18. Naeije R, Golstein J, Clumeck N, Meinhold H, Wenzel KW, Vanhaelst L. A low T3 syndrome in diabetic ketoacidosis. *Clin Endocrinol (Oxf).* 1978;8(6):467-472.
19. Suzuki Y, Nanno M, Gemma R, Tanaka I, Taminato T, Yoshimi T. The mechanism of thyroid hormone abnormalities in patients with diabetes mellitus [in Japanese]. *Nippon Naibunpi Gakkai Zasshi.* 1994;70(4):465-470.
20. Vigersky RA, Filmore-Nassar A, Glass AR. Thyrotropin suppression by metformin. *J Clin Endocrinol Metab.* 2006;91(1):225-227. doi: 10.1210/jc.2005-0653
21. Biondi B, Kahaly GJ, Robertson RP. Thyroid dysfunction and diabetes mellitus: two closely associated disorders. *Endocr Rev.* 2019;40(3):789-824. doi: 10.1210/endrev/bnz005
22. Chubb SA, Davis WA, Davis TM. Interactions among thyroid function, insulin sensitivity, and serum lipid concentrations: the Fremantle Diabetes Study. *J Clin Endocrinol Metab.* 2005;90(9):5317-5320. doi: 10.1210/jc.2005-0631
23. Gronich N, Deftereos SN, Lavi I, Persidis AS, Abernethy DR, Rennert G. Hypothyroidism is a risk factor for new-onset diabetes mellitus: a cohort study. *Diabetes Care.* 2015;38(9):1657-1664. doi: 10.2337/dc14-2736
24. Roa Dueñas OH, Van der Burgh AC, Ittermann T, Ligthart S, Ikram MA, Peeters R, *et al.* Thyroid Function and the Risk of Prediabetes and Type 2 Diabetes. *J Clin Endocrinol Metab.* 2022;107(6):dgac014. doi: 10.1210/clinem/dgac014
25. Korzeniowska KA, Brzeziński M, Szarejko K, Radziwiłł M, Anyszek T, Czupryniak L, *et al.* The association of thyroid-stimulating hormone (TSH) and free thyroxine (fT4) concentration levels with carbohydrate and lipid metabolism in obese and overweight teenagers. *Endokrynol Pol.* 2019;70(2):172-178.
26. Chen RH, Chen HY, Man KM, Chen SJ, Chen W, Liu PL, *et al.* Thyroid diseases increased the risk of type 2 diabetes mellitus. *Medicine (Baltimore).* 2019 May;98(20):e15631. doi: 10.1097/MD.00000000000015631
27. Chang CH, Yeh YC, Shih SR, Lin JW, Chuang LM, Caffrey JL, *et al.* Association between thyroid dysfunction and dysglycaemia: a prospective cohort study. *Diabet Med.* 2017 Jul;34(11):1584-1590. doi: 10.1111/dme.13423
28. Ittermann T, Schipf S, Dörr M, Thuesen BH, Jørgensen T, Völzke H, *et al.* Hyperthyroxinemia is positively associated with prevalent and incident type 2 diabetes mellitus in two population-based samples from Northeast Germany and Denmark. *Nutr Metab Cardiovasc Dis.* 2018 Feb;28(2):173-179.
29. Ashrafuzzaman SM, Taib AN, Rahman R, Latif ZA. Prevalence of diabetes among hypothyroid subjects. *Mymensingh Med J.* 2012 Jan;21(1):129-132.
30. Du W, Wang F, Zhao M, Zhang H, Zhang X, Zhao J, Gao L. Prevalence of thyroid disorders and associated risk factors with various glycemic status in North China. *Biotechnol Biotechnol Equip.* 2019;33(1):1244-1250. doi: 10.1080/13102818.2019.1656106

31. Chaker L, Ligthart S, Korevaar TIM, *et al.* Thyroid function and risk of type 2 diabetes: a population-based prospective cohort study. BMC Med. 2016;14:150. doi: 10.1186/s12916-016-0693-4
32. Kabir MA, Kamrul-Hasan ABM, Faruque MO, Hoque F, Selim S, Hasanat MA, *et al.* Frequency and predictors of hyperglycemia in patients with various thyroid disorders attending a tertiary hospital of Bangladesh. Sri Lanka J Diabetes Endocrinol Metab. 2019 Apr;9(1):18.