Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/h5rjzh22

THYROID STATUS IN GESTATIONAL DIABETES MELLITUS- A CASE CONTROL STUDY.

Gulshan Prakash[1], Sumit Dokwal[2], Ujyala Singh[3], Soniya Dahiya[4*], Spoorthi S[3], Reetu[3], Rakesh Kumar[3], Bhavika Khemani[3], Sabiya Parveen[3]

[1]Assistant Professor, Dept. of Biochemistry, Pt. B D Sharma PGIMS Rohtak
[2]Professor, Dept. of Biochemistry, Pt. B D Sharma PGIMS Rohtak
[3]PG students, Dept. of Biochemistry, Pt. B D Sharma PGIMS Rohtak
[4]Associate Professor, Dept. of Obstetrics and Gynaecology, Pt. B D Sharma PGIMS Rohtak

Corresponding Author: Dr. Sonia Dahiya
[*]Associate Professor, Dept. of Obstetrics and Gynaecology, Pt. B D Sharma PGIMS Rohtak. Ph. +91 8708493205, Email id: dr.soniyadahiya2000@gmail.com

ABSTRACT

Introduction: Gestational diabetes mellitus (GDM) is a significant pregnancy complication associated with maternal and fetal risks. Thyroid dysfunction, particularly altered thyroid hormone levels, has been implicated in various pregnancy-related disorders, including GDM.

Materials and Methods: This case-control study aimed to investigate the relationship between thyroid function markers—thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4)—and GDM in pregnant women. A total of 120 pregnant women (60 with GDM and 60 controls) were enrolled in the study, and demographic, biochemical, and clinical data were collected. Blood samples were analyzed for fasting blood sugar (FBS) levels and thyroid function markers (TSH, FT3, FT4).

Results: The results showed a significant difference in FBS levels between GDM and control groups, confirming the presence of hyperglycemia in GDM patients. However, no significant differences were observed in TSH, FT3, and FT4 levels between the two groups. While some studies have suggested an association between thyroid dysfunction and GDM, our findings indicate that thyroid hormone levels did not significantly vary between women with GDM and those without.

Conclusion: These results suggest that thyroid dysfunction may not directly contribute to GDM risk in the studied population. However, the potential role of thyroid autoimmunity and subclinical thyroid dysfunction warrants further investigation. Larger, longitudinal studies are needed to better understand the complex relationship between thyroid function and GDM.

Keywords: Gestational diabetes mellitus, thyroid-stimulating hormone, free triiodothyronine, free thyroxine, thyroid dysfunction, pregnancy.

INTRODUCTION

Gestational diabetes mellitus (GDM), can be characterized as glucose intolerance identified for the first time during pregnancy, constitutes a major public health issue recently flooding the obstetric OPD and in certain cases the labour rooms with complications to the maternal and fetal part both. The clinical spectrum of gestational diabetes mellitus (GDM) varies from asymptomatic

hyperglycemia to severe hyperglycemia, which may pose life-threatening risks to both the mother and foetus (American Diabetes Association, 2022).[1] The pathogenesis of gestational diabetes mellitus (GDM) principally has a condition of insulin resistance that develops during pregnancy. The pancreatic β-cells fails to adequately enhance insulin production resulting in glucose intolerance. Both genetic and environmental factors contribute to the risk of gestational diabetes mellitus (GDM). Genetic predisposition is demonstrated by familial aggregation and the discovery of susceptibility genes.[2] Non-genetic risk factors encompass advanced maternal age, obesity, a sedentary lifestyle, and dietary practices.[3]

Gestational diabetes mellitus (GDM) impacts 5–7% of pregnancies in high-income nations worldwide.[4] In India, its prevalence is estimated to be 1.3%.[5] Concerning statistics indicate that the incidence of gestational diabetes mellitus (GDM) has increased over the last ten years, presumably because to increasing obesity rates and evolving lifestyles.[6] Gestational diabetes mellitus (GDM) pose significant health issues to both the mother and fetus, including as macrosomia, pre-eclampsia, stillbirth, newborn hypoglycemia, and an elevated risk of maternal type 2 diabetes and cardiovascular disease in the future.[7]

Thyroid dysfunction, a prevalent endocrine disease during pregnancy, is closely associated with maternal and foetal outcomes. Subclinical hypothyroidism (SCH), characterised by increased thyroid-stimulating hormone (TSH) levels alongside normal free thyroxine (FT4) concentrations, affects roughly 3% of pregnancies.[8-9] In contrast, overt hypothyroidism (OH), marked by elevated TSH and diminished fT4 levels, is less prevalent but poses considerable hazards, including spontaneous miscarriage, gestational hypertension, and impaired foetal brain development.[10] Thyroid autoimmunity amplifies these risks, increasing the probability of pregnancy associated illnesses, including pre-eclampsia and preterm birth.[11]

Physiological changes generated by pregnancy significantly impact glucose metabolism and thyroid hormone activity. Increased levels of β-human chorionic gonadotropin (β-hCG) enhance thyroid hormone synthesis, resulting in a rise in iodine demands by as much as 50%.[12] Iodine deficiency adversely affects thyroid hormone synthesis, potentially leading to pregnancy problems. Thyroid dysfunction may aggravate insulin resistance by hindering glucose absorption in muscle and adipose tissue, thus associating hypothyroidism with gestational diabetes mellitus (GDM).[13] Furthermore, abnormal placentation linked to thyroid dysfunction may interfere with placental hormone release, hence increasing susceptibility to insulin resistance.[14]

Numerous studies have investigated the association between thyroid dysfunction and gestational diabetes mellitus, although the results remain ambiguous. In light of these discrepancies, additional research is necessary to elucidate the function of thyroid hormones in the pathophysiology of gestational diabetes mellitus (GDM). This study seeks to examine the correlation between thyroid hormone levels and gestational diabetes mellitus (GDM) in pregnant women, enhancing the comprehension of the connection between these endocrine illnesses.

MATERIALS AND METHODS

This case-control study was conducted at the Department of Obstetrics and Gynaecology, in collaboration with the Department of Biochemistry, PGIMS, Rohtak, Haryana. Sample size was calculated by using a statistical formula, which was found to be minimum of 60 cases of GDM and equal number of control subjects.

Pregnant women diagnosed with gestational diabetes mellitus (GDM) attending the outpatient department (OPD) were enrolled as cases, while controls were selected from pregnant women without GDM who met the inclusion criteria. Scientific and Ethical clearance was obtained from the Institutional Scientific and Ethics committees, and written informed consent was taken from all participants. Inclusion criteria comprised pregnant women with GDM, gestational age of 20 weeks or above, age below 35 years, and low-risk pregnancies with vertex or non-vertex presentations. Exclusion criteria included abnormal placental presentations, obstetric complications such as pre-eclampsia or multiple gestations, other medical complications, and non-consenting individuals. Detailed demographic, anthropometric, and biochemical data were collected, alongside

comprehensive clinical histories and examinations by the Obstetrician and based on the biochemical tests and OGTT/GCT the patients were included in the study. Venous blood samples (4 mL) were collected aseptically in red-capped vacuum tubes. After clotting, samples were centrifuged at 2000 rpm for 10 minutes to separate serum. One aliquot of serum was analyzed on the same day for routine biochemical investigations, while another was preserved at -20°C for batch analysis of special investigations, including Free T3, Free T4, and Thyroid-Stimulating Hormone (TSH).
For routine biochemical investigations, serum samples were analyzed using an autoanalyzer with standard methods. The routine parameter like KFT, LFT etc were assessed. Special investigations, including free T3 (pg/mL), free T4 (ng/mL), and TSH (µIU/mL), were performed using Chemiluminescence immunoassay techniques.

Statistical Analysis:
The statistical analysis of the collected data was carried out using Statistical Package for Social Sciences (SPSS) version 20.0 for Windows. Laboratory test results were summarized as mean ± standard deviation. Comparisons between the study groups were conducted using the Student's t-test, and the frequencies of abnormal results were analyzed using the chi-square (χ^2) test. A 95% confidence interval (CI) was considered, and the data were compiled and analyzed using appropriate statistical methods.

RESULTS

Table 1 Showing demographic and biochemical results in the two groups.

Mean value	Cases (n=60)	Controls (n=60)	P-value
Age(years)	28.15±4.56	26.16±4.14	0.01*
FBS(mg/dL)	155.11±36.66	95.16±19.08	<0.001**
S. TSH(µIU/mL)	2.83±1.73	3.23±2.23	0.28
S. FT4(ng/mL)	0.97±0.19	0.94±0.17	0.54
S. FT3(pg/mL)	2.85±0.49	2.94±0.58	0.37

The demographic and biochemical characteristics of the study participants, including cases (n=60) and controls (n=60), were compared to evaluate differences between the two groups. The mean age of the participants in the case group was 28.15 ±4.56 years, which was significantly higher than that of the control group, whose mean age was 26.16 ±4.14 years (p=0.01). This indicates that age may be a potential risk factor for gestational diabetes mellitus (GDM).
Fasting blood sugar (FBS) levels were markedly elevated in the case group, with a mean value of 155.11 ±36.66 mg/dL, compared to 95.16 ±19.08 mg/dL in the control group. The difference in FBS levels between the groups was highly significant (p<0.001), which reflects the hyperglycemic state associated with GDM. This result aligns with the known pathophysiological characteristics of GDM, where glucose intolerance leads to elevated fasting blood sugar levels.
Thyroid hormone levels, including serum thyroid-stimulating hormone (TSH), free thyroxine (FT4), and free triiodothyronine (FT3), were also analyzed. The mean TSH levels in the case group were slightly lower (2.83 ±1.73 µIU/mL) compared to the control group (3.23 ±2.23 µIU/mL); however, this difference was not statistically significant (p=0.28). Similarly, the mean FT4 levels were 0.97 ± 0.19 ng/mL in cases and 0.94 ±0.17 ng/mL in controls, with no significant difference observed between the groups (p=0.54). FT3 levels were also comparable between cases (2.85 ±0.49 pg/mL) and controls (2.94 ±0.58 pg/mL), showing no statistically significant difference (p=0.37).

The absence of significant differences in thyroid hormone levels (TSH, FT4, and FT3) between the case and control groups suggests that thyroid dysfunction may not be directly associated with GDM in the study population. However, the observed trends underscore the need for further investigations into the potential role of thyroid hormones in GDM, particularly in larger and more diverse populations. Overall, while significant differences were observed in age and FBS levels, thyroid hormone levels did not show statistically significant variation between the groups, indicating that the association between thyroid function and GDM requires further exploration.

DISCUSSION

This study examined the correlation between thyroid function indicators, specifically thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4), in pregnant women diagnosed with gestational diabetes mellitus (GDM). The results revealed no statistically significant variations in TSH, FT3, or FT4 levels between women with gestational diabetes mellitus and healthy controls. These findings advance the current discourse regarding the influence of thyroid dysfunction in the aetiology of gestational diabetes mellitus (GDM).

The function of the thyroid gland in glucose metabolism

Thyroid hormones, particularly thyroxine (T4) and triiodothyronine (T3), are crucial modulators of glucose metabolism. These hormones augment insulin sensitivity in peripheral tissues, including muscle and adipose tissue, by increasing insulin receptor expression, thus facilitating glucose uptake.[13] Triiodothyronine, T3 directly increases gluconeogenesis and glycogenolysis in the liver, hence enhancing hepatic glucose synthesis.[14] In hypothyroid conditions, diminished thyroid hormone levels hinder glucose uptake and exacerbate insulin resistance, while hyperthyroidism may enhance insulin sensitivity but can result in glucose intolerance.[15] Moreover, thyroid hormones affect glucose utilisation by promoting glycolysis in skeletal muscle, hence facilitating efficient glucose metabolism. During pregnancy, abnormal thyroid function can aggravate diseases such as gestational diabetes mellitus (GDM), where disrupted thyroid hormone regulation may lead to glucose intolerance.[16] Consequently, thyroid hormones are essential for regulating glucose homeostasis, with abnormalities possibly leading to metabolic diseases such as diabetes.

Numerous research have investigated the relationship between thyroid function and gestational diabetes mellitus (GDM), producing inconsistent findings.[17-19] Our results correspond with research indicating no substantial change in thyroid hormone levels between women with gestational diabetes mellitus and control subjects. Thyroid hormones are essential regulators of glucose metabolism, affecting insulin sensitivity and glucose absorption in peripheral tissues. Nonetheless, this study indicates that the absence of significant variations in FT3 and FT4 levels implies that thyroid hormone-related influences on glucose homeostasis may not have been substantially impaired in the study cohort.

Conversely, studies have indicated that modified TSH levels, even within the normal spectrum, may affect the risk of GDM. Korevaar et al. established that elevated normal TSH levels correlated with compromised glucose metabolism and heightened insulin resistance in pregnant women.[20] A cohort research by Dosiou et al. shown that subclinical hypothyroidism, characterised by raised TSH levels, was linked to a heightened risk of gestational diabetes mellitus (GDM).[13] These findings underscore the significance of acknowledging minor thyroid dysfunctions that may elude detection by standard biochemical measures.

The second trimester seems to be a crucial phase for the interaction between thyroid function and the risk of gestational diabetes mellitus (GDM). Chen et al. conducted a study indicating that increased TSH levels during the second trimester, especially when accompanied with thyroid peroxidase antibodies (TPOAb), correlated with a heightened risk of developing gestational diabetes mellitus (GDM).[21] Despite the exclusion of TPOAb measures in our investigation, the lack of substantial changes in TSH levels among groups may indicate that thyroid autoimmunity, rather than isolated thyroid hormone variations, could be a more pertinent role in the pathogenesis of GDM.

Furthermore, research has examined the influence of FT3 and FT4 on glucose metabolism throughout pregnancy. Research conducted by Maraka et al. indicated that diminished FT4 levels correlated with negative pregnancy outcomes, including gestational diabetes mellitus (GDM).[14] In this study, FT3 and FT4 levels remained within normal limits in both groups, suggesting that thyroid hormone synthesis and control were predominantly maintained in the studied population.

Pregnancy causes substantial alterations in thyroid physiology, influenced by increased human chorionic gonadotropin (hCG) levels and augmented iodine demands.[22] These adaptations may obscure mild thyroid dysfunctions. For example, hCG exerts a thyrotropic action, inhibiting TSH levels, especially during the first trimester.[23] This physiological suppression may elucidate why TSH levels exhibited no significant changes between groups in this investigation.

The findings of this study should be understood within the framework of its limitations, notably the lack of data on thyroid autoantibodies and the very small sample size. Extensive, longitudinal studies are necessary to clarify the involvement of thyroid dysfunction in the pathogenesis of gestational diabetes mellitus (GDM). Future study should examine the potential interactions between thyroid function and other metabolic and inflammatory markers in gestational diabetes mellitus (GDM).

Conclusion: This study concluded that there were no significant differences in TSH, FT3, or FT4 levels between women with GDM and controls, indicating that thyroid dysfunction may not independently influence GDM risk. The possible influence of thyroid autoimmunity and subclinical thyroid irregularities necessitates additional research to comprehensively assess their effects on pregnancy outcomes.

REFERENCES

1. American Diabetes Association. (2022). Standards of Medical Care in Diabetes—2022. Diabetes Care, 45(Suppl 1): S1-S264.
2. Shaat, N., & Groop, L. (2007). Genetics of gestational diabetes mellitus. Current Medicinal Chemistry, 14(5), 569-583.
3. Miao, Z., et al. (2020). Maternal age and obesity: Impact on pregnancy outcomes. Frontiers in Endocrinology, 11, 109.
4. Egan, A. M., et al. (2021). Epidemiology of gestational diabetes mellitus. Best Practice & Research Clinical Obstetrics & Gynaecology, 74, 3-12.
5. Mohan, V., et al. (2020). Prevalence of gestational diabetes mellitus in urban and rural areas of India. Indian Journal of Endocrinology and Metabolism, 24(1), 4-10.
6. Zhu, Y., et al. (2019). Global trends in diabetes prevalence and its impact on pregnancy outcomes. The Lancet Diabetes & Endocrinology, 7(5), 392-398.
7. Preda A, Iliescu DG, Comănescu A, Zorilă GL, Vladu IM, Forțofoiu MC, Țenea-Cojan TS, Preda SD, Diaconu ID, Moța E, Gheorghe IO, Moța M. Gestational Diabetes and Preterm Birth: What Do We Know? Our Experience and Mini-Review of the Literature. J Clin Med. 2023 Jul 9;12(14):4572.
8. Fard BB, Houshyar J, Zareizadeh J et al. Comparison of vitamin D level in pregnant women with and without gestational diabetes. Rev Latinoam Hipertens. 2020; 15: 33–35.
9. Gozutok V, Ozyurek E, Kafadar D et al. Association of altered thyroid hormone levels with insulin resistance and vitamin D levels in pregnancy. Ann Med Res 2020; 27: 1492.
10. Solha STG, Mattar R, Teixeira PFDS, Chiamolera MI, Maganha CA, Zaconeta ACM, Souza RT. Screening, diagnosis and management of hypothyroidism in pregnancy. Rev Bras Ginecol Obstet. 2022 Oct;44(10):999-1010.
11. Lee SY, Pearce EN. Assessment and treatment of thyroid disorders in pregnancy and the postpartum period. Nat Rev Endocrinol. 2022 Mar;18(3):158-171
12. Daniel Glinoer, The Regulation of Thyroid Function in Pregnancy: Pathways of Endocrine Adaptation from Physiology to Pathology, Endocrine Reviews.1997; 18; 404–433.

13. Dosiou, C., et al. . Thyroid and pregnancy: Implications for gestational diabetes mellitus. Thyroid, 2012;22(5), 410-420.
14. Maraka, S., & O'Keeffe, D. T. (2021). Thyroid dysfunction and pregnancy outcomes. BMJ, 374, n1443.
15. Eom YS, Wilson JR, Bernet VJ. Links between Thyroid Disorders and Glucose Homeostasis. Diabetes Metab J. 2022 Mar;46(2):239-256.
16. Pinto S, Croce L, Carlier L, Cosson E, Rotondi M. Thyroid dysfunction during gestation and gestational diabetes mellitus: a complex relationship. J Endocrinol Invest. 2023 Sep;46(9):1737-1759.
17. Casey BM, Dashe JS, Wells CE, et al. Subclinical hypothyroidism and pregnancy outcomes. Obstetrics & Gynecology. 2005;105(2):239-245.
18. Catalano PM, Ehrenberg HM. The short- and long-term implications of maternal obesity on the mother and her offspring. BJOG: An International Journal of Obstetrics & Gynaecology. 2006;113(10):1126-1133.
19. Pearce EN, Lazarus JH, Moreno-Reyes R, et al. Thyroid function and pregnancy: what is normal? Clinical Chemistry. 2010;56(1):18-28.
20. Korevaar TI, Schalekamp-Timmermans S, de Rijke YB, et al. Hypothyroxinemia and TSH in relation to cognitive functioning in early childhood: a prospective population-based cohort study. Lancet Diabetes Endocrinol. 2016;4(1):35-43.
21. Chen LM, Du WJ, Dai J, et al. Effects of subclinical hypothyroidism on maternal and perinatal outcomes during pregnancy: a single-center cohort study of a Chinese population. PLOS ONE. 2014;9(10):e109364.
22. Glinoer D. The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. Endocrine Reviews. 1997;18(3):404-433.
23. Feki M, Omar S, Menif O, et al. Thyroid disorders in pregnancy: frequency and maternal-fetal implications. Journal of Gynecology Obstetrics and Human Reproduction. 2008;36(1):1-8.