Evaluation of Thyroid Dysfunction and Autoimmunity in Gestational Diabetes Mellitus

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Abstract

Gestational diabetes mellitus (GDM) is defined as "glucose intolerance first detected in 24–28 weeks of gestation by oral glucose tolerance test (OGTT). In pregnancy, the activity of thyroid hormones is altered and not balanced in some of the pregnant women leading to thyroid dysfunction. GDM and thyroid dysfunctions may cause maternal and fetal complications which includes Preterm birth, macrosomia, cesarean-sections and future risk of type II diabetes mellitus. Aim of our study is to find the association of thyroid hormones status and insulin resistance (IR) in GDM and normal pregnant women. The cross sectional study was conducted between the period of October 2021 to September 2023 at Annapoorana Medical College and hospitals, Salem. Total numbers of samples are 160.OGTT (Oral Glucose Tolerance Test) performed during 24-28 weeks of gestation. Subjects were divided into two groups. Group I: 80 Gestational Diabetes Mellitus women were taken as cases. Group II: 80 normal pregnant women were taken as controls.

We found 13.75 % subclinical hypothyroidism and 6.25% maternal hypothyroxinaemia in 80 GDM women. There was no significance of thyroglobulin antibodies (TG) between cases 73±29.74 and controls 69±18.21. This study suggests that women with GDM should be considered as high risk for hypothyroidism and their TSH levels should be monitored closely during pregnancy. This would help to introduce preventive therapies earlier in GDM and then to prevent maternal fetal complications.

Keywords: Gestational diabetes mellitus (GDM), Hyperglycemia, Insulin resistance (HOMA-IR), Anti TPO, Anti Tg antbodies, Thyroid dysfunction.

Introduction

Gestational diabetes mellitus (GDM) and thyroid dysfunction are most common endocrine disorders in gestation[16]. GDM detected in 24–28 weeks of gestation by oral glucose tolerance test (OGTT) and early detection is necessary to prevent prenatal and maternal complications. The cause of the disease is currently unknown and may be related to genetic factors[18], early pregnancy diet and placental insulin resistance. The pathogenesis of GDM is closely associated with insulin resistance(IR)[2,7,10]. During pregnancy, various physiological hormones like estrogen, thyroid-binding globulin, placental lactogen, human chorionic gonadotropin, cortisol and placental insulin secretion influenced maternal blood glucose levels and thyroid function during pregnancy[15].

In the initial stages of gestation, endocrinal changes occur for an anabolic state establishes in preparation for the energy demands of later pregnancy. In the early pregnancy, the high circulation human chorionic gonadotropin level activates the thyroid-stimulating hormone (TSH) receptor and thus directly stimulates the thyroid to produce more thyroid hormones[1,4,17]. Thyroid hormones may decrease the half-life of insulin and may increase the expression of glucose transporter 2 in liver cell membranes so that they support hepatic glucose output[20]. Furthermore, they accelerate glycogenolysis by activating β adrenergic receptors via cAMP[3].

Hypothyroidism and GDM in pregnancy may contribute to adverse obstetric outcome like increase of placental abruption, first trimester abortions, polyhydramnios, preeclampsia, caesarean sections, preterm deliveries, intrauterine foetal deaths and postpartum haemorrhage[14,15]. Glucose metabolism and thyroid function have common pathways.

Material and Methods

Ethical consideration: The present study was conducted in the Clinical Biochemistry Laboratory after approval (Tracking no. AMCH/IEC/Proc.No.32/2021 dated October 20, 2021) from the Institutional Ethics Committee of Annapoorana Medical College and Hospitals, Salem. Sample collection and processing were done as per the declaration of Helsinki Ethical Guidelines, 2013.

Patient consent statement: Research details were explained to the study subject to their languages and then consent was obtained from the study participants.

Criteria for Diagnosis of GDM: Gestational diabetes mellitus (GDM) is diagnosed during 24–28 weeks of gestation as per American Diabetes Association (ADA) criteria. Oral glucose tolerance test (OGTT) was done with 75 g of anhydrous glucose given to the pregnant women. GDM is identified when any one of the following plasma glucose values exceeded: Fasting Blood Glucose (FBS): ≥92 mg/dl, 1hour: ≥180 mg/dl, 2 hour: ≥153 mg/dl [9]. The study was conducted in women with singleton pregnancy. Total

numbers of samples are 160. Subjects were divided into two groups. Group I*:* 80 Women with Gestational Diabetes Mellitus were taken as cases. Group II: 80 Normal pregnant women were taken as control.

Inclusion criteria

- Pregnant women with gestational diabetes mellitus (GDM).
- Normal pregnant women.
- Age group 20-35 years.

Exclusion criteria

- Patients with previous history of diabetes mellitus (Type I, Type II) before pregnancy.
- Patients with previous history of thyroid disorders.
- Patients on medication that may alter thyroid functions.
- Patients with autoimmune diseases.

Sample collections: Blood samples were collected, serum separated and stored for hormonal analysis.

Estimation of plasma Glucose and Insulin Levels: Fasting Plasma Glucose (FPG) levels were assessed immediately after sample collection in fully auto analyser by glucose oxidase peroxidase (GOD and POD) method. Insulin quantified by ELISA method. HOMO IR was calculated[8,12]:

HOMA-IR = [fasting glucose (mg/dl) × fasting insulin]/405

Thyroid Function Test: Thyroid hormone status evaluation was done based on the guidelines of American Thyroid Association[16]. The levels of anti-thyroid peroxidase antibodies (Anti TPO) were: negative <45 IU/ml; borderline 45-55 IU/ml; positive >55 IU/ml. Positive was considered to increase the prevalence of subclinical hypothyroidism in pregnancy. Anti-thyroglobulin Antibodies (Anti TG): negative < 90 IU /ml; borderline 90-110 IU/ml; Positive >100 IU/ml.[1,5] FT3, FT4, TSH, Anti TG and TPO antibodies were assessed by ELISA method.

Statistical analysis: Data were analysed using SPSS software. The Mann-Whitney U test for parametric test, Chi-square and independent samples t-test were used to identify the differences between the groups. Pearson correlation test was performed for correlation analysis. P value < 0.05 was considered as statistical significance at 95% confidence intervals.

Results

In our study, we analysed total number of 160 study subjects. Group I included 80 GDM and group II included 80 normal pregnant women.

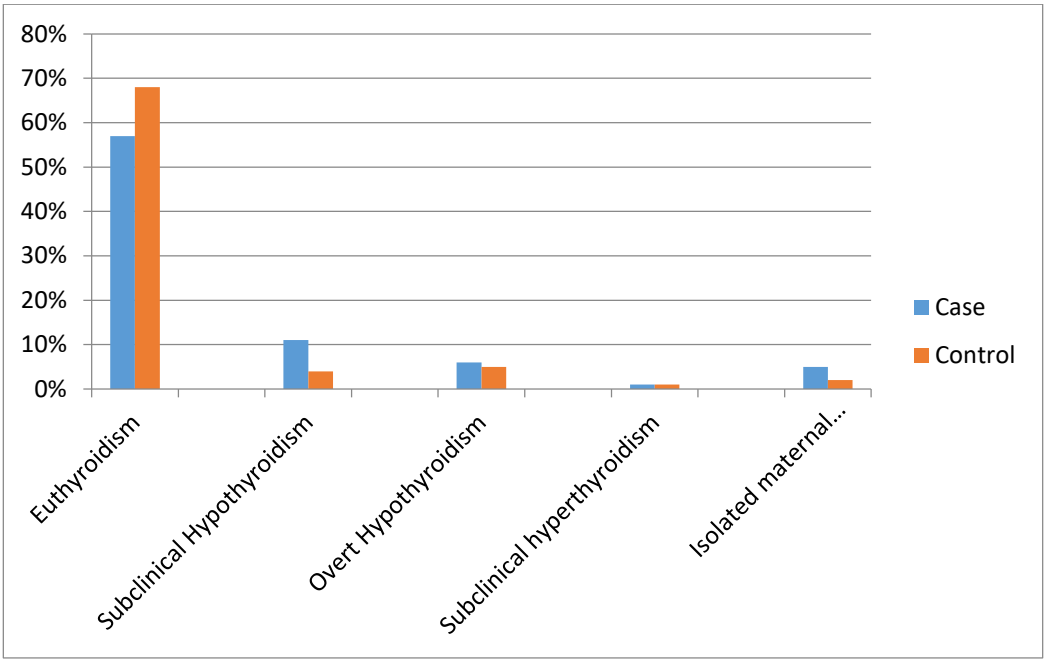
Age was not statistically significant between cases and controls. FPG statistically increased in GDM cases with mean value of 102.2±7.1 compared to normal pregnant women with mean value of 83.7±5.1. Insulin levels were statistically significant increase in GDM 19.71±5.2 when compared to control 10.05±3.9. HOMO IR assessment model of insulin resistance with statistical increased mean value of 5.06±3.96 with control 1.11±0.90. In the thyroid assessment there, was no statistical difference in serum FT3 levels but reduced serum FT4 concentration of 0.90 ±0.2 in GDM than controls 1.5 ± 0.69 which was statistically significant. FT3/FT4 ratio 1.11±0.5 in GDM increased significantly when compared to control 0.53±0.39.

In the analysis of antibodies, GDM statistically significant increased 62.18±59.20. The level of anti TG antibodies increased 73±29.74 in GDM than control 69±18.21 which was not significant. TSH mean value is increased in GDM compared to control but not statistically significant. The above findings were summarised in table 1.

Thyroid Status in GDM and non-GDM: Euthyroid status in our study group was 71.25% in GDM and 85 % in normal pregnant women, so normal thyroid status is present more in controls than cases. Statistically significant increase in the prevalence of subclinical hypothyroidism in GDM is 13.75% than normal pregnant women 5%. This is the most common thyroid dysfunction among pregnancy women with GDM. The prevalence of overt hypothyroidism is not significant (cases 7.5%, controls 6.25%).

Table 1
Laboratory investigations in GDM and non-GDM

Parameters	Group I (Cases	Group II (Control)	P value
Age (years)	25.45±4.41	23.14±3.20	<0.06
FBS (mg/dl)	102.2±7.1	83.7±5.1	<0.001*
Insulin (2-25 mIU/L)	19.71±5.2	10.05±3.9	<0.001*
HOMO IR	5.06±3.96	1.11±0.90	<0.001*
FT3 (1.21-4.1pg/ml)	1.0±0.5	0.8±0.7	0.32
FT4 (0.7-2.1 ng/dl)	0.90 ±0.34	1.5 ± 0.69	<0.001*
FT3/FT4	1.1±0.5	0.53±0.39	<0.001*
TSH (mIU/L)	2.66±1.35	2.18±1.11	0.14
AntiTPO (<45 IU/ml)	62.18± 59.20	19.91±20.28	<0.05*
AntiTG (<90 IU/ml)	73±29.74	69±18.21	0.08



Graph 1: Thyroid Status in GDM and non-GDM

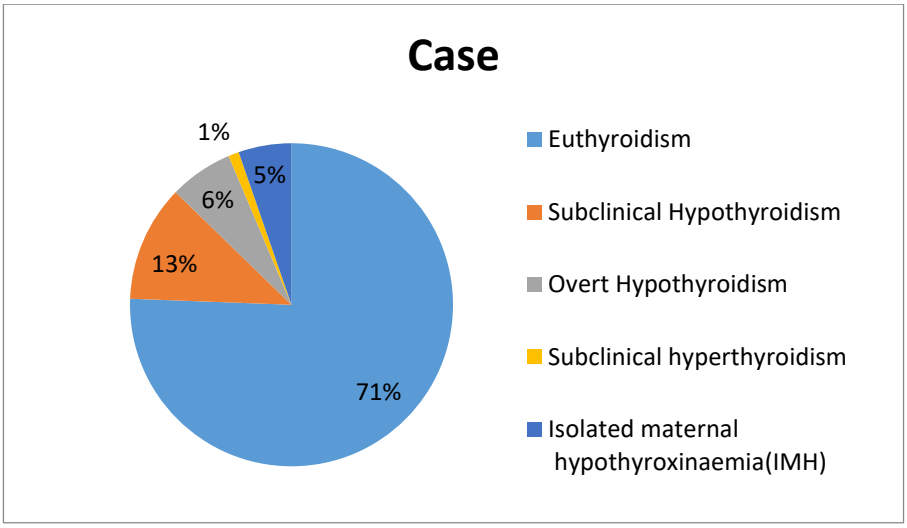


Figure 1: Thyroid Status in GDM

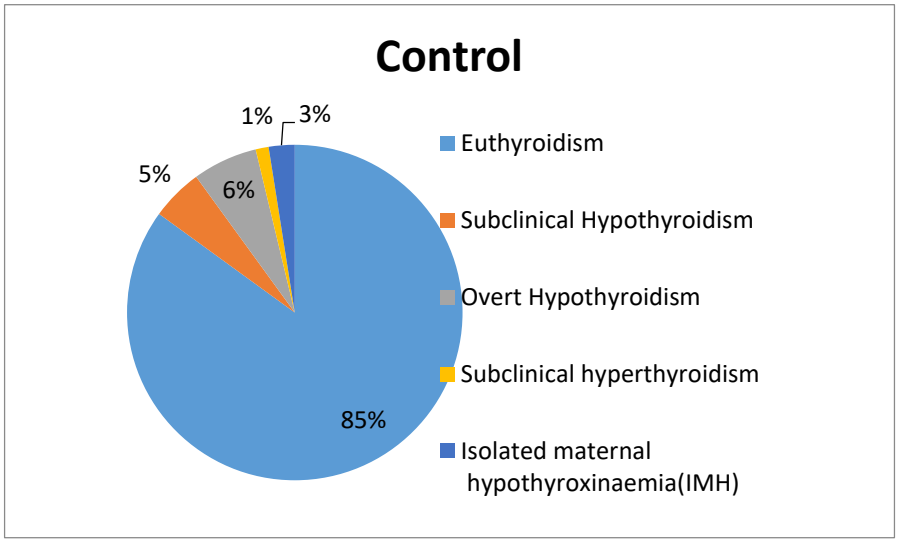


Figure 2: Thyroid Status in non-GDM

Table 2
Thyroid Status in GDM and non-GDM

Thyroid status	Group I (Cases) GDM=80	Group II (Control) Non GDM=80	P value
Euthyroidism	57 (71.25%)	68 (85%)	<0.001*
Subclinical Hypothyroidism	11 (13.75%)	4 (5%)	<0.001*
Overt Hypothyroidism	6 (7.5%)	5 (6.25%)	0.43
Subclinical hyperthyroidism	1 (1.25%)	1(1.25%)	0.31
Isolated maternal hypothyroxinaemia	5 (6.25%)	2(2.5%)	0.001*

Prevalence of Isolated maternal hypothyroxinaemia increased in GDM with 6.25% compared to control 2.5% which is statistically significant. The above findings are summarized in table 2 and graph 1.

Discussion

Thyroid dysfunction status is mentioned in figures 1 and 2. In our study, mean values of FPG increased in GDM were significantly compared to control, similar to the study of Ozisik et al[14]. We also found fasting insulin levels, insulin resistance in GDM, which was statistically significant compared to controls. This higher insulin resistance may cause hyperglycaemia in GDM. Ozışık et al[14] studied no statistically significant TPOAb and TgAb between cases and control. In our study, anti TPO antibodies were positive in 20 (25%) cases and 4(5%) in control. Anti TPO antibodies increased significantly in cases than control. Anti TG antibodies are not significant.

In the analysis of thyroid dysfunction, most of the studies shows increased prevalence of SCH in GDM[5,9]. In our study, the prevalence of subclinical hypothyroidism significantly increased in GDM 11(13.75%) compared to controls 4(5%). In GDM group 57(71.25%), control 68(85%) were euthyroid. The prevalace of euthyroid reduced significantly in GDM. In the study of Nemani et al[13], prevalance of overthypothyroidism 17.3% in GDM and 2.6% in control was found whereas in our study, we found 6(7.5%) in GDM and 5 (6.25%) in control.

The prevalence of isolated maternal hypothyroxinaemia increased in GDM, which is statistically significant. Serum FT4 concentrations reduced significantly in GDM than control which is favour of cause for increasing FT3/FT4 ratio in significantly GDM. There was no statistically significance between FT3 in cases and control. FT3/FT4 ratio was calculated by dividing the serum concentration of FT3 and FT4 and was used to identify deiodinase activity. The FT3/FT4 ratio is constant in normal healthy adults. High or low FT3 / FT4 ratios may affect the peripheral activity of thyroid hormones[11,19].

Weight gain or obesity during pregnancy causes increased leptin levels. Leptin increased deiodinase enzyme activity which is responsible for conversion of FT4 to active FT3. FT3 induces endogenous glucose production leading to hyperglycemia.[6,21] So reduced FT4 levels and increased FT3 levels in blood lead to increasing FT3/FT4 ratio. TSH mean value is increased in GDM but not statistically significant which is similar to the previous studies.[5,13,20]

Outcome of the study: In our study, with 80 GDM and 80 normal pregnant women, we found hyperglycemia, Insulin resistance, increased anti TPO antibodies and hypothyroidism in GDM.

Conclusion

The occurrence of GDM is higher in Asian countries especially in India compared to Western countries. GDM women with thyroid dysfunction should be monitored closely during pregnancy. This would help to introduce preventive therapies earlier in GDM and prevent maternal fetal complications. Hyperglycemia persists immediately beyond pregnancy in some of the women. It is necessary to monitor GDM, this would help to prevent present and future risk of diabetes.

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References

1. Alexander E.K., Pearce E.N. and Brent G.A., Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum, *Thyroid*, **27(3)**, 315–389 **(2017)**

2. Alva P.D., Naresh S., Rai S. and Nalilu S., Correlation between the serum fatty acids and insulin in gestational diabetes, *Biomed Biotechnol Res J*, **8**, 274-8 **(2024)**

3. Das D.K., Bandyopadhyay D., Bandyopadhyay D. and Neogi A., Thyroid hormone regulation of beta adrenogenic receptors and catecholamine sensitive adenylatecyclase in foetal heart, *Aceta Endocrinol Copenh*, **106(4)**, 569-576 **(1984)**

4. Deng et al, Maternal Thyroid-Stimulating Hormone Level and Thyroid Peroxidase Antibody Status in the First and Second Trimester of Pregnancy and Their Relationship with the Risk of Gestational Diabetes Mellitus, *Maternal-Fetal Medicine*, **1(2)**, 81-85 **(2019)**

5. Dhanuja K., Manimegalai S., Prithiba A., Kanthimathi G. and Ancy M.V., Telosma cordata and Zephyranthes candida mediated Green Synthesis of Zinc Oxide Nanoparticles using Plant Extract, *Res. J. Chem. Environ.*, **28(11)**, 99-106 **(2024)**

6. Haddow J.E., Metzger B.E., Lambert-Messerlian G., Eklund E., Coustan D. and Catalano P., Maternal BMI Peripheral deiodinase

activity and plasma glucose: relationships between white women in the HAPO study, *J Clin Endocrinol Metab*, **104(7)**, 2593–2600 **(2019)**

7. Juan J.Y.H.P., Prevention and lifestyle intervention of gestational diabetes mellitus in China, *Int. J. Environ. Res. Public. Health*, **17(24)**, 9517 **(2020)**

8. Kanwar J.B., Manglunia A., Mangaraj S., Swain J., Sahoo A. and Singh J., Clinical and biochemical markers in early pregnancy for prediction of gestational diabetes mellitus, *Indian J Endocr Metab*, **29**,108-15 **(2025)**

9. Karat A., Radhakrishnan C., Thulaseedharan N.K. and Kalam S., Prevalence of thyroid dysfunction and anti–thyroid peroxidase antibody in gestational diabetes mellitus, *J Diabetol*, **12**, 98-103 **(2021)**

10. Kondracki A.J., Valente M.J., Ibrahimou B. and Bursac Z., Risk of large for gestational age births at early, full and late term in relation to pre-pregnancy body mass index: Mediation by gestational diabetes status, *Paediatr Perinat Epidemiol*, **36**, 566-76 **(2022)**

11. Männistö T. et al, Thyroid dysfunction and autoantibodies during pregnancy as predictive factors of pregnancy complications and maternal morbidity in later life, *J Clin Endocrinol Metab*, **95(3)**, 1084–1094 **(2010)**

12. Matthews D.R., Hosker J.P., Rudenski A.S., Naylor B.A., Treacher D.F. and Turner R.C., Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man, *Diabetologia*, **28**, 412-9 **(1985)**

13. Nemani S. and Kurumeti V.K., Prevalence of thyroid dysfunction and autoimmunity among pregnant women with gestational diabetes mellitus in a tertiary care hospital, Visakhapatnam, *Int J Reprod Contracept Obstet Gynecol*, **9**, 4621-6 **(2020)**

14. Ozışık H. et al, Comparison of thyroid function tests in pregnant women with and without gestational diabetes, *Turk J Diab Obes*, **3**, 285-290 **(2021)**

15. Parveen H. et al, Association of hypothyroidism in pregnant women with hyperglycaemia, *Int J Health Sci Res*, **9(9)**, 325-329 **(2019)**

16. Pinto S., Croce L., Carlier L. and Cosson, Thyroid dysfunction during gestation and gestational diabetes mellitus:a complex relationship, *Journal of Endocrinological Investigation*, **46**, 1737–1759 **(2023)**

17. Plows J.F., Stanley J.L., Baker P.N., Reynolds C.M. and Vickers M.H., The pathophysiology of gestational diabetes mellitus, *Int J Mol Sci*, **19(11)**, 3342 **(2018)**

18. Radha V., Kanthimathi S., Anjana R.M. and Mohan V., Genetics of gestational diabetes mellitus, *J Pak Med Assoc*, **66(9 Suppl 1)**, S11-4 **(2016)**

19. Rawal S., Tsai M.Y. and Hinkle S.N., A Longitudinal Study of Thyroid Markers Across Pregnancy and the Risk of Gestational Diabetes, *J Clin Endocrinol Metab*, **103(7)**, 2447–2456 **(2018)**

20. Yang S., Shi F.T., Leung P.C., Huang H.F. and Fan J., Low Thyroid Hormone in Early Pregnancy Is Associated With an Increased Risk of Gestational Diabetes Mellitus, *J Clin Endocrinol Metab*, **101(11)**, 4237-4243 **(2016)**

21. Zimmermann-Belsing T., Brabant G., Holst J.J. and Feldt-Rasmussen U., Circulating leptin and thyroid dysfunction, *Eur J Endocrinol*, **149(4)**, 257–271 **(2003)**.

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