Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies

Journal home page: www.jamdsr.com doi: 10.21276/jamdsr ICV 2018= 82.06

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Original Research

Association of gestational diabetes mellitus and thyroid status during pregnancy: A cross-sectional study in a tertiary health care center

Dr. Sri Charan K N[1], Dr Pandurangaiah R[2], Dr. Meghana H C[3], Dr Madhusudan H C[4], Dr Shruthi K M[5], Dr Prashant Hubballi[6]

[1]MBBS, MD, Associate professor, Department of General Medicine, A J Institute of Medical Sciences and Research Centre, Kuntikana Mangalore, Karnataka;
[2]MBBS DNB (OBG), Assistant Professor, Dept of Obstetrics and Gynaecology, Kannur Medical College, Anjarkandy, Kannur, Kerala;
[3]BDS, MDS, Assistant professor Department of oral medicine and radiology, A J Institute of dental sciences, Mangalore, Karnataka 575004;
[4]Consultant Nephrologist, Mangala Hospital, Sampige road, Hassan 573115, Karnataka;
[5]Consultant Radiologist, Mangala hospital, Sampige road, Hassan 573115, Karnataka;
[6]Assistant Professor, Dept of General Medicine, A J Institute of Medical Sciences & Research Center, Mangaluru, Karnataka.

ABSTRACT:

Introduction: Insulin and thyroid are two of the most encountered hormones during pregnancy. Hence in the present study we aim to evaluate if any association is seen between gestational diabetes mellitus (GDM) and thyroid status (TS) throughout pregnancy in a tertiary health care center. **Material and Methodology**: We conducted a cross-sectional study, on randomly chosen 628 patients attending the tertiary health care center. After taking a detailed history, oral glucose tolerance test was done for all the participants. If eligible, then thyroid-stimulating hormone (TSH) and free thyroxine (F.T4) tests were done. *t*-test and Chi-square test were used to compare variables between various classes as necessary. **Results**: The mean gestational age in GDM and non-GDM groups was 20.5 ± 9.1 years and 17.5 ± 9.2 years, which were significantly different (p<.001). There was a substantial (p<.001) high incidence of thyroid disorder (TD) in the non-GDM community. Mean F.T4 of the GDM group was lower in all three trimesters. The mean TSH of the GDM group was more deficient in the early stage of pregnancy but higher in the later stage (3rd trimester). Euthyroid cases were significantly higher (83.8%; p<.001) while subclinical hypothyroidism (9.5%; p<.001) and transient hyperthyroidism (2.4%; p<.001) cases were significantly lower in GDM group. **Conclusion**: Even though GDM and TD are the most prevalent endocrine disorders during pregnancy, neither TS during pregnancy nor any risk factors for TD have been associated with the development of GDM.

Key words: Gestational Diabetes mellitus (GDM), Thyroid status, Pregnancy.

Received: 11-10- 2019 Revised: 29-10-2019 Accepted: 23-11-2019

Corresponding author: Dr Pandurangaiah R, MBBS DNB (OBG), Assistant Professor, Department of Obstetrics and Gynaecology, Kannur Medical College, Anjarkandy, Kannur, Kerala.

This article may be cited as: N Sri CK, R Pandurangaiah, C Meghana H, C Madhusudan H, M Shruthi K, Hubballi P. Association of gestational diabetes mellitus and thyroid status during pregnancy: A cross-sectional study in a tertiary health care center. J Adv Med Dent Scie Res 2019;7(12): 268-271.

INTRODUCTION

Pregnancy is a state where every woman undergoes various degrees of hormonal changes to facilitate physiological changes. Insulin and thyroid are two of the most encountered hormones during pregnancy. As a result, gestational diabetes mellitus (GDM) and thyroid disorders (TDs) are the most common endocrine disorders diagnosed during pregnancy [1,2]. Despite that, there are different schools of thought regarding the relationship between GDM and thyroid status (TS) during pregnancy [3–9]. As there are very little data on the relationship between GDM and TS during pregnancy in our country, this study tried to explore any possible association between DM and TS through this study.

MATERIAL AND METHODS

Study design and participants

This cross-sectional study was conducted at a tertiary health care center. Randomly selected 628 patients, who visited the antenatal clinic were taken as cases for this study. Known cases of diabetes mellitus (DM) and TD, patients taking any drugs which may alter the glucose level and TS, critically ill patients were not eligible for selection. Detailed history taking and physical examination of all selected cases were done, emphasizing on the presence of family history of TD and the presence of goiter.

Out of 628 patients, 377 were diagnosed as GDM patients and the rest were found normal. All subjects were divided into two groups – the GDM group and the non-GDM group based on that.

Plasma glucose was estimated by IMMULITE 1000 immunoassay analyzer (Siemens, Berlin, Germany). Selected subjects were investigated for thyroid-stimulating hormone (TSH) and free thyroxine (FT4). Thyroid peroxidase antibody (TPOAb) was advised if the subject's TSH was 2.5 lIU/mL. TSH receptor antibody (TRAb) was estimated if there was a diagnostic dilemma about the types of hyperthyroidism – transient hyperthyroidism of pregnancy (THP) vs. Graves' disease (GD). Subjects with gestational weeks beyond 18, who presented with features of overt hyperthyroidism both clinically and according to laboratory reports, were not advised for TRAb as THP may persist up to 18 weeks of pregnancy [11].

Thyroid status was classified according to the American Thyroid Association (ATA) guideline – euthyroid, hypothyroxinemia, subclinical hypothyroid (SCH), hypothyroidism (Hypo.Th) THP, subclinical hyperthyroidism (SCHy.Th), and hyperthyroidism (GD and toxic multi- nodular goiter). Considering ATA and hospital laboratory reference value,

Clinical and laboratory evaluation

All the subjects went for oral glucose tolerance test (OGTT) with 75 g glucose. Those who were already in 2nd and 3rd trimester were advised to go for OGTT immediately, but the rest, who were in 1st trimester, were recommended for OGTT if they had any risk factors for GDM, and others were advised to go for OGTT after 20 weeks of pregnancy [10]. GDM was diagnosed according to the international association of diabetes and pregnancy study group (IADPSG) criteria if any of the following plasma glucose values were met or exceeded [10].

pregnant woman with TSH 0.35–3.99 lIU/mL was diagnosed as euthyroid, TSH in the range of 4–9.9 lIU/mL was SCH and HypoTh was diagnosed if TSH was 10 lIU/mL. If TSH was <0.35 lIU/mL; FT4, FT3, and TRAb were elevated then the diagnosis was GD. But in case of negative TRAb but elevated b-human chorionic gonadotropin (HCG) level, then the diagnosis was THP. THP is common around 8–14 weeks of gestation [11]. When TSH was < 0.35 lIU/mL with negative TRAb and low/normal b-hCG, then the possibility of other causes of hyperthyroidism were explored. SCHy.Th was diagnosed if TSH was < 0.35 lIU/mL but FT4, FT3 were normal. Isolated hypothyroxinemia is defined as a normal maternal TSH concentration in conjunction with FT4 levels in the lower 2.5th percentile of the reference range [11]. TSH, FT4, FT3, TPOAb, TRAb, and b-HCG were analyzed by using chemiluminescent sequential immunometric assay with IMMULITE 1000 immunoassay analyzer.

Statistical analysis

Statistical analysis was done using SPSS 23 software (SPSS Inc., Chicago, IL). *t*-test and Chi-square test were used for comparing the variables between different groups as appropriate. *p* Value <.05 was considered to be significant.

RESULTS

It was found that the incidence of TD in the non-GDM group (32.27%) were significantly (p<.001) higher than the GDM group (16.44%). The patients from non-GDM group went for TSH test significantly (p<.001) earlier than the GDM group (17.50 vs. 20.47 weeks). The proportion of positive family history of TD, presence of goiter, and presence of TPOAb were 7.95%, 7.69%, and 3.71% in GDM group, respectively. In the non-GDM group, these proportions were 9.16%, 9.76%, and 5.97%, respectively (Table 1).

Compared to non-GDM group, the mean TSH level of the GDM group were lower in the earlier stage of pregnancy (2.45 vs. 2.83, and 2.20 vs. 2.58, respectively, in 1st and 2nd trimester) but higher in the later stage of pregnancy (2.83 vs. 2.73 in 3rd trimester), though the differences were insignificant. Mean F.T4 of the GDM group was lower in all three trimesters than the non-GDM group (1.05 vs. 1.23, 0.96 vs. 1.03, and 0.97 vs. 0.98, respectively) (Table 2).

While evaluating the TS during pregnancy, we found that euthyroid cases were significantly higher (83.81% vs. 66.93%; p<.001) in GDM group along with SCH (9.54% vs. 21.11%; p<.001) and THP (2.38% vs. 7.96%; p<.001) cases were higher in non-GDM group. But cases of hypothyroidism, hyperthyroidism, hypothyroxinemia, and subclinical hyperthyroidism had no significant differences between GDM and non-GDM groups (Table 3).

Table 1. Comparison of clinical characteristics between gestational diabetes mellitus and non-gestational diabetes mellitus groups

Variables	Gestational diabetes mellitus	Non-gestational diabetes mellitus	*p* Value
Gestational age at the time of measuring TSH level (weeks)	20.47 -L 9.11	17.50 I- 9.17	<.001’
Positive family history of TD (96)	7.95	9.16	.594
Presence of goiter (%)	7.69	8.76	.630
Presence of TPOAb (6)	3.71	5.97	.244
Incidence of TD (%)	16.44	32.27	<.001’

TSH: thyroid-stimulating hormone; TD: thyroid disorders; TPOAb: thyroid peroxidase antibody.
All values are in percentage (%) except for gestational age at the time of measuring TSH level, which is in mean ± standard deviation. ’Significant difference between the two groups.

Table 2. Trimester specific thyroid-stimulating hormone values of gestational diabetes mellitus and non-gestational diabetes mellitus groups

Time	Variables	Gestational diabetes mellitus	Non-gestational diabetes mellitus	*p* Value
1st trimester	TSH	2.45 ± 4.01	2.83 ± 3.09	.464
	F.T4	1.05 ± 0.29	1.23 ± 0.46	.071
2nd trimester	TSH	2.20 ± 1.57	2.58 ± 2.20	.085
	F.T4	0.96 ± 0.22	1.03 ± 0.39	.234
3rd trimester	TSH	2.83 ± 4.65	2.52 ± 2.03	.666
	F.T4	0.97 ± 0.35	0.98 ± 0.21	.858

TSH: thyroid-stimulating hormone; F.T4: free thyroxine. TSH levels are measured in µ IU/mL unit and F.T4 levels are measured in ng/dL; all values are in mean ± standard deviation.

Table 3. Thyroid status of gestational diabetes mellitus and non-gestational diabetes mellitus groups in pregnancy

Variables	Gestational diabetes mellitus	Non-gestational diabetes mellitus	*p* Value
Euthyroid	83.81	66.93	.001
Subclinical hypothyroid	9.54	21.11	.001’
Transient hyperthyroidism of pregnancy	2.38	7.96	.001’
Hypothyroidism	1.59	1.59	.998
Hyperthyroidism	0.79	0.79	.999
Hypothyroxinemia	0.53	0.39	.814
Subclinical hypenhyroidism	1.32	1.19	.886

All values are in percentage (s6). ’Significant difference between the two groups

DISCUSSION

Thyroid function assessment is important during gestation, in particular for women at risk of TD, i.e. women with prior history of TD, history of unexplained abortion, autoimmune dis- orders, and family history of TD, according to the ATA [11]. ATA also suggests that women with TD risk factors should check thyroid function before planning for pregnancy and as soon as the pregnancy is confirmed. Yang et al. reported that low thyroid hormone in early prenancy is associated with an increased risk of developing GDM, therefore suggested earlier evaluation of thyroid hormone status during pregnancy [6]. This study showed that the average levels of serum F.T4 of the GDM group were lower than the non- GDM group in all three trimesters, though statistically insignificant. Average levels of TSH were also insignificantly lower in the GDM group during 1st and 2nd trimester. Regarding insignificant differences in thyroid function tests, our study was in agreement with the previously conducted studies [3,4]. But in this study, we have found that the

non-GDM group underwent for thyroid function test earlier than the GDM group. Despite the report of Shahbazian et al. regarding the absence of any significant difference of TS between two groups but we have found a significantly high incidence of euthyroidism in the GDM group along with SCH as well as THP in the non-GDM group [7].

Overall, the incidence of TDs was significantly higher in the non-GDM group. Toulis et al. suggested that the increased incidence of SCH in GDM patients which our finding differed as we found a significantly higher incidence of SCH in the non-GDM group [12]. Gong et al. reported an association between Hypo.Th and incidence of GDM, whereas this study did not find anything significant [8]. The incidence rate of Hypo.Th, hyperthyroidism, hypothyroxinemia, and SCHy.Th were mostly similar in both groups. However, Yang et al. and Velkoska Nakova et al. reported a higher incidence of hypothyroxinemia in GDM patients [6,13]. There are different reports regarding thyroid autoimmunity and the development of GDM. Hornnes et al. reported that patients with thyroid autoimmunity are prone to develop glucose intolerance during pregnancy, while other reports had different opinions [5,14,15].

CONCLUSION

In this study, we neither found any association of thyroid autoimmunity with the development of GDM, nor any role of the presence of goiter and positive family history of TD in glucose intolerance during pregnancy.

REFERENCES

1. Negro R, Mestman JH. Thyroid disease in pregnancy. Best Pract Res Clin Endocrinol Metab. 2011;25(6):927–943.
2. Yuen L, Saeedi P, Riaz M, et al. Projections of the prevalence of hyperglycaemia in pregnancy in 2019 and beyond: results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2019;157:107841.
3. Agarwal M, Dhatt G, Punnose J, et al. Thyroid function abnormalities and antithyroid antibody prevalence in pregnant women at high risk for gestational diabetes mellitus. Gynecol Endocrinol. 2006;22(5): 261–266.
4. Vitacolonna E, Lapolla A, Di Nenno B, et al. Gestational diabetes and thyroid autoimmunity. Int J Endocrinol. 2012;2012:867415–867416.
5. Montaner P, Juan L, Campos R, et al. Is thyroid autoimmunity associated with gestational diabetes mellitus? Metabolism. 2008;57(4): 522–525.
6. Yang S, Shi FT, Leung PCK, et al. Low thyroid hormone in early pregnancy is associated with an increased risk of gestational diabetes mellitus. J Clin Endocrinol Metab. 2016;101(11):4237–4243.
7. Shahbazian H, Shahbazian N, Baniani MR, et al. Evaluation of thyroid dysfunction in pregnant women with gestational and pre-gesta- tional diabetes. Pak J Med Sci. 2012;29(2):638–641.
8. Gong L, Liu H, Liu L. Relationship between hypothyroidism and the incidence of gestational diabetes: a meta-analysis. Taiwan J Obstet Gynecol. 2016;55(2):171–175.
9. Vafaeimanesh J, Asgarani F, Bagherzadeh M, et al. Thyroid function in pregnant women with gestational diabetes: is screening necessary? Thyroid Res Pract. 2015;12(1):3.
10. Power D. Standards of medical care in diabetes. Diabetes Care. 2006; 29(2):476; author reply 476–7.
11. Alexander EK, Pearce EN, Brent GA, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. Thyroid. 2017; 27(3):315–389.
12. Toulis K, Stagnaro-Green A, Negro R. Maternal subclinical hypothyroidism and gestational diabetes mellitus: a meta-analysis. Endocr Pract. 2014;20(7):703–714.
13. Velkoska Nakova V, Krstevska B, Dimitrovski C, et al. Prevalence of thyroid dysfunction and autoimmunity in pregnant women with gestational diabetes and diabetes type 1. Prilozi. 2010;31(2):51–59.
14. Soytac Inancli S, Yayci E. Evaluation of thyroid autoimmunity in gestational diabetes mellitus. J Diabetes Metab. 2016;7(6):2014–2016.
15. Hornnes P, Rasmussen N, Hegedu s L, et al. Glucose tolerance and incidence of pancreatic islet cell antibodies in pregnancy in women with thyroid autoantibodies. Horm Metab Res. 1991;23(3):122–125.