



RELATIONSHIP OF SUBCLINICAL HYPOTHYROIDISM TO THE INCIDENCE OF GESTATIONAL DIABETES MELLITUS

Obstetrics & Gynaecology

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ABSTRACT

INTRODUCTION: Thyroid hormones play an important role in regulating energy balance, metabolism of glucose and lipids. Many studies have demonstrated that patients with subclinical hypothyroidism have insulin resistance. Some studies have interpreted that subjects with subclinical hypothyroidism have early signs of impairment of glucose metabolism. Because of the similar effects of thyroid hormone and pregnancy on glucose metabolism, women with either abnormally high or low levels of thyroid hormones would be more likely to develop GDM⁶. This study was done to assess the relationship of subclinical hypothyroidism to the incidence of GDM among south Indian pregnant women

METHODOLOGY: This study was done as a prospective observational study at Tirunelveli medical college and hospital for period of 18 months, follow up period was from first antenatal visit till diagnosis of GDM or 36 weeks period of gestation whichever is earlier. A total of 626 patients who satisfied inclusion criteria was included in the study. Patients attending antenatal clinic in the first trimester or second trimester with singleton pregnancy were included in the study. During the first antenatal visit. Serum Free T₄ (FT₄) and Serum Thyroid Stimulating Hormone (TSH) levels were assessed.

RESULTS AND DISCUSSION:

Prevalence of Subclinical hypothyroidism in the study population was found to be 7%. Incidence of GDM was found higher in Subclinical hypothyroid group when compared to the incidence in euthyroid group with a p value 0.016. Patients with subclinical hypothyroidism were found to have increased risk of recurrent abortions with the p value of 0.04. Patients with Subclinical Hypothyroidism were found to have 2-fold the risk, for developing GDM with a p value of 0.016. Universal screening for thyroid disorders must be encouraged to identify such subclinical disease. Treatment of subclinical hypothyroidism should be advocated to maintain a euthyroid state, thereby decreasing the incidence of GDM and other ill effects of Subclinical hypothyroidism.

KEYWORDS

Subclinical hypothyroidism, GDM, pregnancy

INTRODUCTION

The fact that pregnancy is a diabetogenic state has been appreciated for over a century.¹ A possible mechanism for this diabetogenicity was not appreciated until it was first recognized that pregnancy is associated with increased insulin resistance or decreased insulin sensitivity by Burt et al in 1956². The development of gestational diabetes mellitus in late pregnancy is consistent with the hypothesis of decreasing insulin sensitivity with advancing gestation³.

Pregnancies complicated by GDM manifest varying degrees of hyperglycemia, hyperlipidemia and selected alteration in amino acids⁴. Women with GDM and her infant are at an increased risk for maternal and perinatal complications⁵, long term maternal morbidity and morbidity to the offspring. With this understanding of the pathophysiology of GDM and its effect on maternal and fetal wellbeing, it is necessary to identify factors that can contribute to the onset of this disease.

Thyroid hormones play an important role in regulating energy balance, metabolism of glucose and lipids⁶. Maratou et al has demonstrated that patients with subclinical hypothyroidism have insulin resistance⁷. Some studies have interpreted that subjects with subclinical hypothyroidism have early signs of impairment of glucose metabolism. Because of the similar effects of thyroid hormone and pregnancy on glucose metabolism, Tudela et al postulated that women with either abnormally high or low levels of thyroid hormones would be more likely to develop GDM⁸. This study was done to assess the relationship of subclinical hypothyroidism to the incidence of GDM among south Indian pregnant women.

The prevalence rate of GDM in India is between 4.6% and 14% in urban areas, and 1.7% and 13.2% in rural areas. The prevalence of gestational diabetes in Tamil Nadu is around 17.9%⁹. Global prevalence of GDM is estimated to be 7-10%. Global prevalence of hypothyroidism in pregnancy is around 2.5% whereas prevalence of hypothyroidism in pregnancy in India ranges from 4.8% to 11%. Based on above studies our aim is to identify the association between subclinical hypothyroidism and gestational diabetes mellitus among pregnant women, also to detect the incidence of GDM among euthyroid and subclinical hypothyroid pregnant women.

MATERIALS AND METHODS

This study was done as a prospective observational study at Tirunelveli

medical college and hospital for period of 18 months from January 2019 to June 2020 after getting ethical committee approval, follow up period was from first antenatal visit till diagnosis of GDM or 36 weeks period of gestation whichever is earlier. A total of 626 patients who satisfied inclusion criteria was included in the study. Patients attending antenatal clinic in the first trimester or second trimester with singleton pregnancy were included in the study. While those were known case of diabetes mellitus, having first antenatal visit in third trimester, multiple gestation, previous history of GDM, having congenital anomaly were excluded.. Follow up was done in three stages.

During the first antenatal visit. Serum Free T₄ (FT₄) and Serum Thyroid Stimulating Hormone (TSH) levels were assessed for which 3.5 ml of venous sample of blood was collected in a plain vacutainer. Gestational age adjusted reference range for FT₄ and TSH was used to diagnose patients with subclinical hypothyroidism. Oral Glucose Tolerance Test (OGTT) was done.. The diagnosis of gestational diabetes was made according to the IADPSG criteria. Patients who were lost to follow up were excluded from the study (n=63). Analysis was done using SPSS version 22.0. Quantitative variables are expressed as mean and standard deviation and qualitative variables are expressed as proportion. Bi-variate analysis is done using Chi-square test and P-value of less than 0.05 is considered significant.

RESULTS

Total 626 patients were recruited for the study, of those 543 patients were completely evaluated. 18 hypothyroid and 2 hyperthyroid patients were excluded from the study. Among the 543 patients, 38 patients were diagnosed with subclinical hypothyroidism.

The age of the patients in the study was between 18 and 38 years with the mean age distribution of 23.09 years and standard deviation 3.45 years. The total number of patients who have subclinical hypothyroidism was 38 out of the 543 patients included in the study. Our study group was divided into euthyroid and subclinical hypothyroid group. Prevalence of subclinical hypothyroidism in our study group is 7%.

Among the subjects in our study, 37.6% were primigravida and 62.4% were multigravida. About 63.2% of subclinical hypothyroid patients in the study population did not have abortions. Recurrent miscarriage was more common in the subclinical hypothyroid group which was about 5.30% comparing to euthyroid group. Therefore, subclinical

hypothyroidism is found to be a significant risk factor for recurrent abortions. This test was found statistically significant with the p value of <0.04.

BMI was classified according to WHO classification of BMI. Patients with subclinical hypothyroidism was found to have high BMI. 50% of subclinical hypothyroid patients were overweight and 47.40% were obese. Subclinical hypothyroidism was found to be a significant factor for high BMI in the subjects, with a p value of 0.01.

Table 1: Incidence Of Gdm In Euthyroid & Subclinical Hypothyroid Group

	GDM	NO GDM
SUBCLINICAL HYPOTHYROIDISM	12	26
EUTHYROID	82	423

In subclinical hypothyroid group, 12 out of 38 patients developed GDM. Incidence rate of GDM in subclinical hypothyroid group = 315/1000. In euthyroid group, 82 out of 505 patients developed GDM. Incidence rate of GDM in euthyroid group = 162/1000. The incidence of GDM among subclinical hypothyroid was observed higher than euthyroid group. This was found statistically significant with the p value of 0.016.

In both euthyroid and subclinical hypothyroid patients, the majority of the patients were either nulliparous or multiparous. Parity was found to be not a significant factor for the development of GDM in our study in either groups. Presence of family history of diabetes was found to be not a significant factor contributing to the development of GDM. In our study, 91.70% of GDM patients in subclinical hypothyroid group did not have family history of diabetes mellitus. Similarly, in GDM patients in euthyroid group 87.8% of patients did not have family history of diabetes mellitus.

Among both subclinical hypothyroid and euthyroid group more than half of the mothers with GDM were in the age group between 21-25 years. In the subclinical hypothyroid group, we observed that, there were not any subjects above the age group of 30 years.

High BMI was found to be a significant factor in the development of GDM in both euthyroid and subclinical hypothyroid groups with a p value of 0.02.

Table 2: Relative Risk Calculation For Subclinical Hypothyroidism And Gdm

	GDM Present	GDM Absent	Total
Subclinical Hypothyroidism	12	26	38
Euthyroid	82	423	505
Total	94	449	543

The relative risk calculated for Subclinical hypothyroidism was found to be 2.08 (95% CI- 1.16-4.91) and p value of 0.016. Hence it is interpreted that Subclinical hypothyroidism will cause 2-fold increase in the risk of GDM.

DISCUSSION

This study was done to evaluate the relationship of Subclinical hypothyroidism and the incidence of GDM in pregnant women. We conducted a prospective observational study to find out the relationship between Subclinical Hypothyroidism and the incidence of GDM in pregnant women. The study was conducted at the antenatal OPD in Tirunelveli medical college and hospital. Total number of patients included in the study was 626. Among them 543 completed the study with appropriate follow up.

After the initial screening with FT₄ and TSH, 563 patients were found to be Euthyroid, 18 Hypothyroid, 2 Hyperthyroid, 43 subclinical hypothyroid. Patients diagnosed to have Hypothyroid and Hyperthyroid were excluded from the study. Prevalence rate of subclinical hypothyroidism in this population is 7%. The prevalence of GDM in the population was 17.31%.

Age of the recruited subjects was between 18 to 38 years, with the mean age being 23.09 years and a standard deviation of 3.45 years. In a study conducted by Gayatri et al the mean age of study subjects was 25.6 years.

BMI of the subjects recruited in the study ranged between normal to

obese. Mothers with subclinical hypothyroidism were found to have high BMI. Among the 38 mothers with subclinical hypothyroidism 50% were overweight and 47.4% were obese. Subclinical Hypothyroidism was found to be a contributor to the high BMI of the subjects, as it affects the resting energy expenditure. While in the Euthyroid group majority of the patients 72.70% were overweight and only 8.1% was within the normal range of BMI. Comparing this with the National Family Health Survey 2007 data there has been a rise in the prevalence of overweight.

Both among the subclinical hypothyroid group and euthyroid group, patients with GDM were found to have high BMI. About 9 0% of the patients with GDM in the Subclinical hypothyroid group and in euthyroid group were found to have BMI > 25. Similarly, in a study conducted by Rajesh Rajput et al¹⁰, a significant association was found between prevalence of GDM and increasing BMI of participants (P<0.001). Among women having BMI >25.22 % had GDM compared to 4.7% in women with BMI<18.5.

Saldana et al¹¹, also evaluated the association between weight gain at the end of the second semester and the risk of glucose intolerance and gestational diabetes mellitus, finding higher risks than in the previous analyses. Obesity is an important risk factor in the development of GDM as observed in our study. Sheshiah et al¹², also found that GDM was significantly higher in women with higher BMI and higher pregnancy weight.

In our study we found that presence of family history of Diabetes Mellitus was not found to be significantly contributing to the development of GDM. Nearly, 91.70% of patients with GDM patients in the subclinical hypothyroid group did not have any family history of diabetes. Similarly, in the case of patients with GDM in our euthyroid group 87.80% of patients did not have family history of Diabetes Mellitus. This is an unlikely observation we made, as it is a proven fact that family history of diabetes mellitus contributes to GDM. Further studies are needed to find out why this incongruous observation was recorded. It can be hypothesized that this could be because we had majority of rural population in our study, awareness about Diabetes Mellitus was low and the prevalence of Diabetes Mellitus was low in the yesteryears

In this study it was found that increase in parity is not a risk factor for developing GDM. Similarly, in a study conducted by Jang et al.¹³, greater ratio of women with GDM in the group with parity >2 was found, in comparison to primiparas, but after controlling for age, pre-pregnancy BMI, height, family history of diabetes mellitus and weight gain during pregnancy, the results were not statistically significant.

In our study it was found that recurrent miscarriage was more common in the subclinical hypothyroid group which was about 5.30% with the p value of less than 0.04. Similarly, in a study conducted by Zhang et al¹⁴, it was found that subclinical hypothyroidism is a risk factor for miscarriage in women before 20 weeks of pregnancy and early treatment can reduce the risk of early pregnancy loss.

In Subclinical Hypothyroid group GDM was observed in 12 out of 38 patients. In Euthyroid group GDM was observed in 82 out of 505 patients. Incidence rate of GDM was found to be high in Subclinical Hypothyroid group when compared to the Euthyroid group. Incidence rate of GDM in Subclinical hypothyroid group was found to be 0.315 and incidence rate of GDM in Euthyroid group was found to be 0.162.

Calculation of relative risk in of Subclinical Hypothyroidism for development of GDM, revealed a risk of 2.08 with p value of 0.016 (95% CI- 1.16-4.91). Hence in subjects with Subclinical hypothyroidism there is 2-fold rise in the risk of developing Gestational Diabetes Mellitus.

CONCLUSION

Subclinical hypothyroidism was observed to be a significant risk factor for the development of Gestational Diabetes Mellitus. Universal screening for thyroid disorders must be encouraged to identify such subclinical disease. Treatment of subclinical hypothyroidism should be advocated to maintain a euthyroid state, thereby decreasing the incidence or GDM and other ill effects of Subclinical hypothyroidism.

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