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Research Article

Relationship of Gestational Diabetes Mellitus with Hypothyroidism in Pregnancy

Das Bishnu Prasad[1], Deka Nabanita[2], Baishya Swagata*[3]
[1]Associate Professor, [2]Assistant Professor, [3]Post Graduate Student, Department of Obstetrics & Gynaecology, Gauhati Medical College & Hospital, Srimanta Sankaradeva University of Health Sciences, Guwahati, Assam.

***Corresponding author**
Dr. Baishya Swagata
Email: baishyaswagata@gmail.com

Abstract: The objective is to study if there is a relationship between gestational diabetes mellitus with hypothyroidism in pregnancy. Between June 2014 and May 2015, serum thyrotropin (TSH) screening was performed on all women who presented for prenatal care. Women identified with elevated thyrotropin level were considered hypothyroid. Out of these 100 women were randomly selected and subjected to oral glucose tolerance test with 75gm oral glucose according to DIPSI guidelines. Along with the hypothyroid cases 100 pregnant women with normal Serum TSH level were also subjected to the oral glucose tolerance test which would act as the control group for the analysis. For this analysis normal thyrotropin values were taken as 0.2 to 3mIU/L as per American Thyroid Association guidelines. The incidence of gestational diabetes mellitus was compared between the study and the control group. Of the 200 women included in the study 100 were euthyroid, 100 were hypothyroid. Gestational diabetes was more in the hypothyroid group (8%) than in the control group (1%).(P=0.0349). The risk of developing gestational diabetes increases with hypothyroidism. This supports a relationship between hypothyroidism and diabetes, diagnosed during pregnancy.
Keywords: GDM(Gestational diabetes mellitus), hypothyroidism, DIPSI(Diabetes In Pregnancy Study Group India), OGTT(Oral Glucose Tolerance Test), TSH(Thyroid Stimulating Hormone), DGGT (Decreased Gestational Glucose Tolerance).

INTRODUCTION

A variety of endocrine disorders complicate pregnancy and vice versa. Diabetes is the most prevalent and thyroid disorders are also very common and can have devastating effects in pregnancy outcome. The clinical manifestations of endocrinopathies result from a complex interplay among genetic, environmental and endogenous factors[2,3].

The impact of pregnancy on maternal thyroid physiology is substantial. Thyrotropin or TSH currently plays a central role in screening and diagnosis of many thyroid disorders. Overt hypothyroidism complicates 2-10pregnancy per 1000[3].

There has been seen increasing prevalance of diabetes in general and in young people in particular,which has led to increase in the number of pregnancy with this complication. Gestational Diabetes Mellitus is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. Maternal hyperglycaemia is associated with adverse perinatal and childhood outcomes. Hence Oral Glucose Tolerance Test holds an important role in modern day screening methods[4].

Overtly abnormal amount of thyroid hormones either excess, as in Graves Thyrotoxicosis or deficient, as in hypothyroidism, have profound effect on insulin secretion. The resulting insulin resistance ,glucose intolerance and dyslipidemia are usually reversible when normal thyroid hormones are restored[5,6]. It is well known that marked insulin resistance progressively increases with gestational age during pregnancy[5]. Thyroid hormone and pregnancy have similar effect in glucose metabolism, so it is reasonable to propose that woman with either raised or decreased thyroid hormone would be more likely to develop gestational diabetes[5].

METHODS AND MATERIALS

In the present study Serum Thyrotropin screening was performed on all women who present for prenatal care in the Obstetrics and Gynaecology Department of Gauhati Medical College and Hospital(GMCH) from June 2014 to May 2015. Women identified with elevated thyrotropin level were considered hypothyroid. Out of them 100 hypothyroid patients were randomly selected after 24weeks of gestation and subjected to oral glucose tolerance test (OGTT) with

75gm oral glucose according to DIPSI guidelines. Along with the hypothyroid cases 100 pregnant women of comparable age and gestational period with normal Thyrotropin (TSH) level were subjected to the oral glucose tolerance test which acted as the control group for the analysis For this analysis normal thyrotropin values were taken as 0.2 to 3mIU/L as per American Thyroid Association guidelines[1]. Clinical data i.e detail history and thorough clinical examination was done and recorded.

Inclusion criteria:

1. Patient with overt hypothyroidism diagnosed before or during pregnancy.
2. Subclinical hypothyroidism diagnosed before or during pregnancy.

Exclusion criteria:

1. Cases with known diabetes mellitus with or without treatment were excluded from the study. Simultaneously 100 healthy pregnant women with normal serum TSH were taken as control group . All the pregnant women taking part in the study gave written consent to be included.

Estimation of Serum TSH was done in the central clinical laboratory (CCL) of GMCH. Diagnosis of GDM was done according to DIPSI guidelines by 2 hour-75gram glucose test.

Statistical Analysis:

Student t-test was used to compare mean values between the 2 groups. Differences between proportions were evaluated by χ^2 test or Fishers exact test.

Criteria For Diagnosis of Gestational Diabetes Mellitus[7]:
With 75 gm OGTT (WHO criteria)

		In Pregnancy	Outside Pregnancy
2 hr	≥ 200 mg/dl	Diabetes	Diabetes
2 hr	≥ 140 mg/dl	GDM	IGT
2 hr	≥ 120 mg/dl	DGGT	—

DGGT decreased gestational glucose tolerance

Thyroid Hormone Level [1,8]

First trimester < 2.5mIU/L;
Second trimester <3mIU/L;
Third trimester <3mIU/L

RESULTS

During this study of 12months, serum thyroid stimulating hormone (TSH) screening was done in all the women who came for antenatal checkup at the antenatal OPD of GMCH. Of all the pregnant women randomly selected for the study, 100 were hypothyroid i.e serum TSH level more than 3m IU/L and 100 were eythyroid (TSH level between 0.2 to 3 m IU/L). Maternal demographics of the study and the control, group are shown in the table.1

Table-1:Maternal demographics of the study

Demographics	Control Group	Study Group
Age(years)	25.38±4.517	24.31±4.194
Parity	-	-
Primi	59	48
Multi	41	52
Duration of pregnancy(weeks)	27.99±3.32	28.38±3.88
BMI(kg/m^2)	25.014±3.362	26.058±4.16

Both the control and the study group were com parable in terms of age, parity, duration of pregnancy and BMI.

The Serum TSH value in the control group ranged from 0.461-3m IU/L. Mean TSH was 1.60 m IU/L ±0.60. The TSH level in the study group ranged from 3.080-25.3 m IU/L ± 4.123.

The difference between the mean TSH in control and the study group is highly significant($p<0.0001$)

Out of the 100 hypothyroid women 56 did not know about the duration of hypothyroidism and were

diagnosed first time at the time of this study. Out of the 44 known cases 33(75%) were on medication.

The OGTT Values in the control in the study group are shown in table 2 and 3 respectively. The mean OGTT Value in the control group was 101.95 mg/dl with SD of ± 18.171. In the control group 1 patient was diagnosed as Gestational diabetes mellitus (GDM).

The mean OGTT in the study group was 110.06 mg/dl SD ± 27.94. 8 patients were diagnosed as GDM in the study group.

Table-2: OGTT Level in the control group at different period of gestation

PERIOD OF GESTATION (weeks)	2HOURS-OGTT (DIPSI) mg/dl	MEAN ± SD mg/dl	NO. OF CASES WITH GDM
24 - <28	64-181	102 ±20.64	1
28 - <32	76-128	99.97±14.55	-
32 - <36	78-134	104±19.16	-
≥36	89-118	107.5±13.02	-

Table-3: OGTT Level in the Study group at different period of gestation

PERIOD OF GESTATION (weeks)	2HOURS-OGTT (DIPSI) mg/dl	MEAN ± SD mg/dl	NO. OF CASES WITH GDM
24 - <28	69-256	111.65±30.65	4
28 - <32	77-138	108.39±17.70	-
32 - <36	71-179	109.55±31.90	3
≥36	79-180	107.28±37.15	1

OGTT-Oral Glucose Tolerance Test
DIPSI-Diabetes In Pregnancy Study group India

The difference in OGTT in the control and the study group was statistically significant (p=0.015). As per DIPSI guidelines 87 patients out of 100 in the control group had normal OGTT values. 12 patients had decreased gestational glucose tolerance test (DGGT) and only 1 patient was diagnosed as GDM.(Table.5) 69 patients out of 100 in the study group had normal OGTT values. 23 patients had decreased gestational glucose tolerance test (DGGT) and 8 patient(8%) was diagnosed as GDM(Table 6).

There were 12 patients (12%) with decreased gestational glucose tolerance test(DGGT) in the control group whereas 23 patients (23%) with DGGT in the study group. However this difference was statistically not quite significant(p=0.0617). There were 8 GDM cases detected in the study group of 100 hypothyroid patients and only 1 GDM detected in the control group of 100 euthyroid pregnant women. This difference was found to be statistically significant.(p=0.0349), by Fishers exact test

Table-5: Number of patients with normal and increased OGTT values in the control group

OGTT Values	NUMBER OF PATIENTS	PERCENTAGE
<120	87	87%
≥120-139	12	12%
≥140	1	1%
TOTAL	100	100%

Table-6: Number of patients with normal and increased OGTT values in the Study group

OGTT Values	NUMBER OF PATIENTS	PERCENTAGE
<120	69	69%
≥120-139	23	23%
≥140	8	8%
TOTAL	100	100

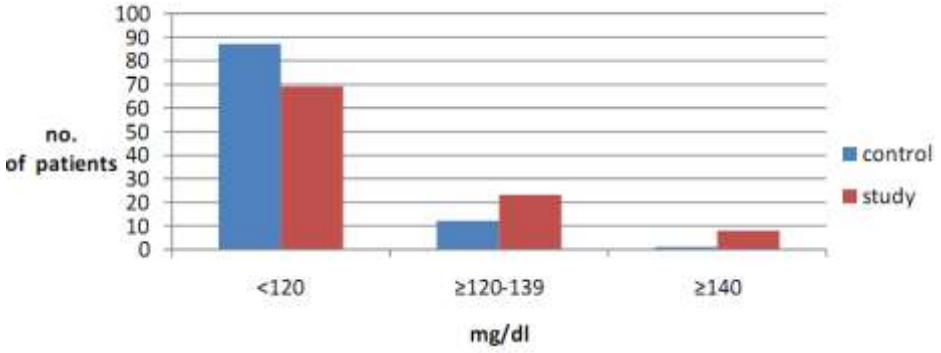

Fig.1: Bar diagram showing OGTT values in control and study group

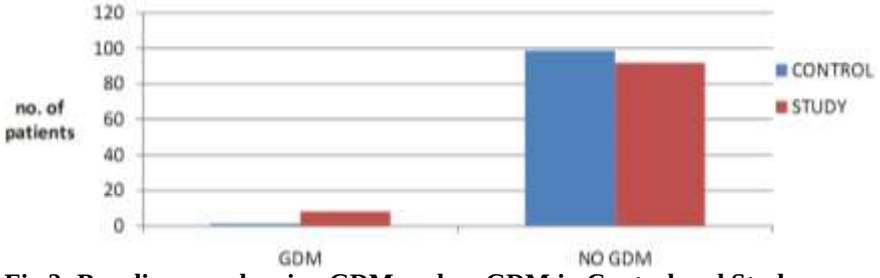

Fig.2: Bar diagram showing GDM and no GDM in Control and Study group

DISCUSSION

As shown in fig.2 there were 8 GDM cases(8%) in the study group as compared to 1 in the control group(1%). P= 0.0349.

These findings are comparable with the reports published earlier by Tudela *et al* [5] ,Olivieri *et al*[6], Velkoska N. *et al* [4] and Karakosta P. *et al* [9].

In Tudela *et al*[5] study, out of the 24,883 women included in the study, 23,771 (95.5%) were euthyroid, 584 (2.3%) had subclinical hyperthyroidism, and 528 (2%) had subclinical hypothyroidism. The likelihood of gestational diabetes increased with thyrotropin level (*P*=0.002). For example, when a pregnant Hispanic woman of average age and weight was used, the predicted percent of gestational diabetes increased from 1.9% to 4.9% as thyrotropin increased from 0.001 to 10 milliunits/L (*P*=0.001).

They concluded that the risk of developing gestational diabetes increases with thyrotropin level. This supports a relationship between subclinical hypothyroidism and diabetes diagnosed during pregnancy. As screening thyrotropin level increased, the likelihood of diabetes complicating pregnancy also increased (*P*=0.002). For example, 2.2% of women identified with subclinical hyperthyroidism had gestational diabetes as compared with 4.2% of euthyroid women and 6.3% of women with subclinical hypothyroidism.

Karakosta *et al* [9] study found that combination of high TSH and thyroid autoimmunity in early pregnancy was associated with a 4-fold increased risk for gestational diabetes [relative risk (RR) 4.3, 95% confidence interval (CI) 2.1– 8.9)].

Olivieri A. *et al*[6] 2000 reported that greater TSH values were found more frequently when glucose tolerance was more severely impaired.(χ^2 trend=3.74, p=0.05).

Velkoska N. *et al* [4] reported in their results that, out of the 83 pregnant women studied, the women who developed GDM showed a mean free thyroxine (f T_4) concentration significantly lower than that observed in the healthy pregnant women and women with diabetes type 1. Among the pregnant women with GDM,10 women or 25% had f T_4 concentrations below the lower cut-off with normal TSH concentration. A statistically significant difference was found in the prevalence of antithyroid antibodies (anti-TPO) between the (30%) women with Type 1 diabetes and(10%) healthy pregnant women ($p<0.05$).In the women positive for anti-TPO ,TSH was significantly higher($p<0.05$). They concluded that significantly higher prevalence of hypothyroxinemia in GDM pregnancies and anti-TPO titres in pregnancies with diabetes type 1, than in healthy pregnant women warrants routine screening for thyroid abnormalities in these groups of pregnant women.

There are previous reports that reinforce a positive relationship between subclinical hypothyroidism and gestational diabetes. The biological plausibility of our findings finds support from studies in nonpregnant adults that describe the metabolic actions of T_4 and insulin. Some of these observations are that both overt and subclinical hypothyroidism cause significantly increased insulin resistance[7]. In fact, this was shown to induce abnormal glucose tolerance test values remarkably similar to those characteristic of normal pregnancy and also as a result of insulin resistance[7]. When taken together, it seems reasonable to speculate that pregnant women with subclinical hypothyroidism have further amplified insulin resistance and thus an increased risk for gestational diabetes.

There are certain studies which refute such likelihood that hypothyroidism is related to increased risk of Gestational diabetes mellitus. Such an association was not found by Cleary Goldman *et al*[10] in a similar study of thyroid analytes in more than 10,000 pregnant women. This may be due to presence of an important factor which is presence of anti thyroid antibody in many of the cohorts. This observation is important in light of findings of [5] 22 who reported that pregnant women with thyroid disease and abnormally high thyroid antibody levels were at inordinately high risk for later developing noninsulin-dependent diabetes mellitus. Also possibly related to the ethnic differences, Hispanic women are at much higher risk for gestational diabetes when compared with white women.

SUMMARY & CONCLUSION

The prevalence of gestational diabetes mellitus found in the study group (8%), when compared with that of, in the control group(1%), was found to be statistically significant.(p=0.0349)

Insulin resistance increases during pregnancy and there is increased chance of impaired glucose tolerance as pregnancy progresses, especially pregnancies complicated with thyroid disorders. And many studies have shown that it is more so in cases of hypothyroidism. It appears from the present study that estimation of oral glucose tolerance test in hypothyroid pregnant women is of great value in detection of gestational diabetes mellitus in significant proportion of cases (8%). As majority of the women are asymptomatic, it may be pertinent to consider thyroid function tests routinely in pregnant women to detect mild and early thyroid dysfunction. And it is also prudent to do oral glucose tolerance in those with abnormal thyroid function in order to detect gestational diabetes at the earliest. However, a long term study covering a wide spectrum of patients with regular follow-up is likely to provide a better knowledge of relationship between gestational diabetes mellitus and hypothyroidism in pregnancy.

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