GESTATIONAL DIABETES MELLITUS- TESTING IN THIRD TRIMESTER- NEW DATA AND FRESH THINKING

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ABSTRACT

BACKGROUND

Gestational Diabetes Mellitus (GDM) is a common complication of pregnancy that is associated with adverse pregnancy outcomes. Studies have shown that GDM responds to early and effective intervention, which improves maternal and neonatal outcomes and reduces long-term risk of Type 2 Diabetes Mellitus (T2DM) in mother and child. The guidelines of the Diabetes in Pregnancy Group in India (DIPSI) currently recommend GDM testing twice during pregnancy, i.e. at the first antenatal visit and at 24 - 28 weeks' gestation; however, GDM has been shown to develop in the third trimester.

MATERIALS AND METHODS

Pregnant women receiving antenatal care at Divakars Speciality Hospital, Bengaluru, India, took part in the study. The participants were recruited on their first antenatal visit, and informed consent was obtained. GDM testing was carried out at 12 weeks and 22 - 24 weeks' gestation, in keeping with the DIPSI guidelines. GDM testing was also carried out at 32 weeks' gestation based on clinical findings and scan reports. GDM prevalence rates at each time point were obtained, and Pearson chi-square tests were used to determine whether a GDM diagnosis was associated with age, parity and BMI.

RESULTS

The mean age of the participants was 29.06 ± 4.28 yrs., and their average BMI was 25.67 ± 4.52 kg/m^2. The prevalence of GDM during the first trimester, second trimester and third trimester were 8.60%, 11.1% (universal testing) and 8.1% (selective testing) respectively. For each of the study points, i.e. 12 weeks' gestation (T_1), 22 - 24 weeks' gestation (T_2) and 32 weeks' gestation (T_3), significant differences were not found between the ages (P (T_1) = 0.247; P (T_2) = 0.953; and P (T_3) = 0.252), BMIs (P (T_1) = 0.917; P(T_2) = 0.098; and P (T_3) = 0.670), and parities (P (T_1) = 0.172; P (T_2) = 0.321; and P (T_3) = 0.321) of women who were diagnosed with GDM and those who tested negative for GDM.

CONCLUSION

Our study shows that additional testing of pregnant women in the third trimester would identify cases of late onset GDM that would have otherwise gone undetected; making a case for considering universal testing once in every trimester.

KEYWORDS

Gestational Diabetes Mellitus, Third Trimester, India, Prevalence, Guidelines.

HOW TO CITE THIS ARTICLE: Divakar H, Dutta S, Singh R, et al. Gestational diabetes mellitus- testing in third trimester- new data and fresh thinking. J. Evid. Based Med. Healthc. 2017; 4(44), 2668-2672. DOI: 10.18410/jebmh/2017/530

BACKGROUND

Gestational Diabetes Mellitus (GDM) is defined as a "carbohydrate intolerance with recognition or onset during pregnancy."[1] A common pregnancy complication, GDM is responsible for 85.1% of all glucose intolerance reported among pregnant women.[1] Furthermore, its prevalence is closely linked with those of obesity and Type 2 Diabetes Mellitus (T2DM).[1,2]

GDM is associated with adverse short-term and long-term maternal and perinatal outcomes.[3,4] In addition, if left unmanaged it increases long-term risk of T2DM in both mothers and their offspring.[5-7] Timely GDM treatment is effective in improving pregnancy and infant outcomes.[8,9] Moreover, it presents an opportunity to reduce the growing global burden of T2DM.

Studies have shown that women of Indian ethnicity are at an increased risk of developing GDM[10-12] and it has been reported that more than four million women in India have GDM.[1] Given its effects on maternal and neonatal health,

Financial or Other, Competing Interest: None.
Submission 05-05-2017, Peer Review 12-05-2017,
Acceptance 25-05-2017, Published 30-05-2017.
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DOI: 10.18410/jebmh/2017/530

GDM should be effectively diagnosed and managed; however, there is currently a lack of a global consensus regarding screening procedure, frequency of GDM testing, approach and plasma glucose cut-offs.[13-15]

The International Federation of Gynaecology and Obstetrics (FIGO)[16] has redefined the term as Hyperglycaemia in Pregnancy (HIP). The FIGO guidelines recommended for low resource countries like India is in keeping with the guidelines of Government of India (GOI), the Diabetes in Pregnancy Group in India (DIPSI) and of the National Professional Body, Federation of Obstetrics and Gynaecological Societies of India (FOGSI). GDM/HIP testing is offered to all pregnant women (universal testing) at booking and at 24 - 28 weeks' gestation using the one-step 75-g OGTT procedure whether in a fasting or non-fasting state.[17,18,19]

Although, GDM testing is recommended twice during pregnancy, studies have shown that GDM can develop after 28 weeks' gestation in high-risk women increasing the incidence of adverse perinatal and maternal outcomes.[20,21] Women of Indian ethnicity are high risk for GDM, owing to their ethnicity as well as the high incidence of T2DM in India. However, studies on the prevalence of GDM among pregnant women in India throughout pregnancy, especially during late pregnancy are limited.

The purpose of this study therefore was to determine the prevalence of GDM during the first, second and third trimesters among pregnant women in India. By determining the number of women who developed GDM during each trimester, this study will determine whether current guidelines regarding the frequency of GDM testing during pregnancy are sufficient.

MATERIALS AND METHODS

Study Participants-

Pregnant women who received antenatal care at Divakars Speciality Hospital Bengaluru, India were recruited on their first antenatal visit irrespective of whether their pregnancies were single or multi foetus. The details of the study were explained to each mother in English and their native language, and informed consent was obtained thereafter through a signature. The study protocol was approved by the Institutional Ethics Committee of Divakars Specialty Hospital. Demographic information such as age, height, parity and weight were obtained from clinical history and examination at the first antenatal visit.

The study participants were followed from booking at early or mid-pregnancy until delivery. The participants' pregnancies were dated through gestational age calculated by the date of the last menstrual period and also by ultrasound biometry.

GDM Testing

GDM testing was carried out according to the DIPSI guidelines. In essence, participants ingested 75-g glucose that had been dissolved in 300 mL water. After 2 h, the participants' venous blood glucose levels were measured with an autoanalyser. GDM was diagnosed if the blood glucose levels were > 7.8 mmol/L or > 140 mg/dL. The test was carried out regardless of whether the study participants were in a fasting or non-fasting state.

GDM testing was carried out at the following study points: during the first trimester and the second trimester, i.e. 12 weeks and 22 to 24 weeks, in keeping with the standard recommendations of DIPSI, the Federation of Obstetric and Gynaecological Societies of India (FOGSI) and the Government of India. The test was repeated in the third trimester at 32 weeks' gestation, only if indicated by clinical findings or scan reports. Only those women whose tests were valid and normal at a previous study point were tested again at the subsequent study point. The participants' obstetricians were aware of the study and had access to the GDM diagnosis. Those women who tested positive for GDM were placed on a treatment regimen and were not subjected to additional GDM tests for the remainder of the study.

Statistical Analysis

For descriptive statistics the number of subjects, mean, Standard Deviation (SD), minimum and maximum values were calculated for continuous variables and the case number and percentage were computed for categorical values. For group comparison, Pearson chi-square was used with $P < 0.05$ considered as significant. Body Mass Index (BMI) was calculated using the weight in kilograms divided by the square of the height in meters (kg/m2). Analyses were conducted with IBM SPSS Statistics version 22.

RESULTS

This study was carried out from October 2015 to November 2016. A total of 375 pregnant women were enrolled in the study. Their demographic information including age and BMI indices are shown in Table 1. The average age of the participants was 29.06 ± 4.28 yrs., and their average BMI was 25.67 ± 4.52 kg/m2. Most of the participants were in the 19 - 30 age group (63.5%) and had a BMI that fell between 25.0 - 29.9 (37.9%).

Three hundred and seventy-four women were enrolled in the study; however, two dropped out, data was not available for five women and 53 were excluded because they made a late booking, i.e. they had their first antenatal visit after 14 weeks' gestation. Of the remaining 314 women, 287 had normal blood plasma glucose values and 27 were diagnosed as having GDM. Thus, the incidence of GDM during the first trimester was 8.76% (Table 3). Age and BMI data were not available for six women with normal blood plasma glucose values; therefore, the women were removed from further analyses. Statistically significant differences were not found between women who were diagnosed with GDM and those who had normal blood plasma glucose values regarding age ($P = 0.247$), parity ($P = 0.917$) and BMI ($P = 0.172$) (Table 2).

The 281 pregnant women who had normal blood plasma glucose values after the first test were eligible to be tested at the subsequent time point. However, three women dropped out of the study and data was not available for seven women. Of the remaining 277 women, 245 had

normal blood plasma values and 32 had developed GDM. Thus, the incidence of GDM during the second trimester was 11.43% (Table 3). Age and BMI data were not available for five women with normal blood plasma glucose values and one woman with GDM; these women were removed from further analyses. A Pearson Chi-square test showed that significant differences did not exist between the ages (P = 0.953), BMIs (P = 0.098), and parities (P = 0.321) of women who were diagnosed with GDM and those who tested negative for GDM (Table 4).

The 240 pregnant women who did not test positive for GDM after the second test were eligible to be tested at the subsequent time point. However, four women dropped out of the study. Of the remaining 236 women only 147 women were tested, based on clinical suspicion of maternal weight gain, a large baby and polyhydramnios (selective testing). Of these 147 women, 125 had normal blood plasma glucose values and 12 were diagnosed as having GDM. This gives us the incidence of late onset GDM in the group with clinical suspicion of GDM was 8.95% (Table 3). We do not have the data on 104 women who were not tested, because third trimester GDM testing is not a mandatory recommendation in India. BMI data were not available for three women with normal blood plasma glucose values; therefore, the women were removed from further analyses. Significant differences were not found between the ages (P = 0.252), BMIs (P = 0.670), and parities (P = 0.321) of women who were diagnosed with GDM and those that had normal blood plasma glucose values (Table 5).

Baseline Characteristic	Participants n = 364
Age	
Age (Y)	29.06 (±4.28)
19 – 30	231 (63.5%)
31 – 35	110 (30.2%)
36 – 42	23 (6.3%)
BMI	
BMI (kg/m^2)	25.67 (± 4.52)
< 18.5	10 (2.7%)
18.5 – 24.9	153 (42.0%)
25.0 – 29.9	138 (37.9%)
≥ 30.0	63 (17.3%)

Table 1. Baseline Characteristics of Women Enrolled in the Study

Demographic Characteristics	Normal (n = 281)[#]	GDM1 (n = 27)	P (T_1)
Age			
Age (Y)	29.01 (±4.32)	30.93 (±4.09)	0.247
19 – 30	178 (63.3%)	13 (48.1%)	
31 – 35	82 (29.2%)	12 (44.4%)	
36 – 42	21 (7.5%)	2 (7.4%)	
BMI			
BMI (kg/m^2)	25.58 (±4.56)	26.22 (±5.06)	0.172
< 18.5	6 (2.1%)	2 (7.4%)	
18.5 – 24.9	123 (43.8%)	9 (33.3%)	
25.0 – 29.9	108 (38.4%)	9 (33.3%)	
≥ 30.0	44 (15.7%)	7 (25.9%)	
Parity			
First Pregnancy	199 (71.3%)	19 (70.4%)	0.917
Multipara	80 (28.7%)	8 (29.6%)	

Table 2. Demographic Variables of Women Tested for GDM during the First Trimester

[#]Two hundred and eighty-seven women had normal blood plasma glucose values; however, since age and BMI data were not available for 6 women, only data from 281 women were used to determine whether differences in age, parity and BMI were present.

	T_1	T_2	T_3
Variable	n (%)	n (%)	n (%)
Negative for GDM	281 (91.23)	240 (88.57)	122 (91.05)
Positive for GDM	27 (8.76)	31 (11.43)	12 (8.95)
Total	**308 (100)**	**271 (100)**	**134 (100)**

Table 3. Prevalence of GDM in First (T_1), Second (T_2) and Third Trimesters (T_3)

Demographic Characteristics	Normal (n = 240)[#]	GDM2 (n = 31)[‡]	P (T_2)
Age			
Age (Y)	28.97 (± 4.82)	29.55 (± 4.11)	0.953
19 – 30	150 (62.5%)	20 (64.5%)	
31 – 35	71 (29.6%)	9 (29.0%)	
36 – 42	19 (7.9%)	2 (6.5%)	
BMI			
BMI (kg/m^2)	25.26 (± 4.25)	28.61 (± 5.88)	0.098
< 18.5	6 (2.5%)	0 (0.0%)	
18.5 – 24.9	108 (45.0%)	8 (25.8%)	
25.0 – 29.9	93 (38.8%)	2 (41.9%)	
≥ 30.0	33 (13.8%)	10 (32.3%)	
Parity			
First Pregnancy	165 (69.6%)	25 (78.1%)	0.321
Multipara	72 (30.4%)	7 (21.9%)	

Table 4. Demographic Characteristics of Women Tested for GDM during the Second Trimester (GDM2) of Pregnancy

[#]Two hundred and forty-five women had normal blood plasma glucose values; however, the age and BMI data of five women were not recorded. Therefore, BMI, parity and age data of only 240 women were analysed further.[‡] Thirty-two women were diagnosed as having GDM; however, the age and BMI data of one woman was not recorded. Therefore, BMI, parity and age data of only 31 women were analysed further.

Demographic Characteristics	Normal (n = 122)[#]	GDM3 (n = 12)	P (T_3)
Age			
Age (Y)	28.49 (±4.37)	29.42 (±4.68)	0.252
19 – 30	76 (62.3%)	7 (58.3%)	
31 – 35	40 (32.8%)	3 (25.0%)	
36 – 42	6 (4.9%)	2 (16.7%)	
BMI			
BMI (kg/m^2)	25.38 (± 4.12)	26.50 (± 4.85)	0.670
< 18.5	1 (0.8%)	0 (0.0%)	
18.5 – 24.9	57 (46.7%)	6 (50.0%)	
25.0 – 29.9	47 (38.5%)	3 (25.0%)	
≥ 30.0	17 (13.9%)	3 (25.0%)	
Parity			
First Pregnancy	199 (71.3%)	19 (70.4%)	0.321
Multipara	80 (28.7%)	8 (29.6%)	

Table 5. Demographic Characteristics of Women Tested for GDM during the Third Trimester (GDM3) of Pregnancy

#One hundred and twenty-five women had normal blood plasma glucose values; however, the age and BMI data of three women were not recorded. Therefore, BMI, parity and age data values of only 122 women were analysed further.

DISCUSSION

The prevalence of GDM in India has been shown to vary by region, social-economic status and dietary habits; however, the values reported in the literature indicate that in general GDM prevalence in India varies between 3.8% and 21%.[22-26] In the present study, the prevalence of GDM in the first and second trimesters were found to be 8.76% and 11.43% respectively, falling within the range of values reported in the literature. The upward trend in GDM prevalence observed in this study may be attributed to the increased detectability of GDM during the late second to early trimester: Studies have shown that insulin resistance in pregnant women who have GDM increases with and becomes more detectable with gestational age up to the early third trimester.[27]

The DIPSI guidelines recommend GDM testing twice during pregnancy, i.e. at the first antenatal visit and 24 – 28 weeks' gestation.[19] Perhaps, owing to this recommendation, few studies have investigated the prevalence of GDM among pregnant women in India in the third trimester. Studies from Chile[21] and France[20] in pregnant women at a high risk of developing GDM reported GDM prevalence of 35% and 18% among women in the third trimester. In this study, the prevalence of GDM in the third trimester was found to be 8.95%; however, it should be noted that data of 104 pregnant women who had tested negative for GDM at 22 - 24 weeks' gestation were not available, as GDM testing in the third trimester is not routinely conducted. Therefore, it is plausible that the prevalence of GDM during the third trimester might be higher than that reported in this study.

Our findings indicate that GDM can develop in the third trimester, and if testing is recommended during the third trimester more women with GDM can be identified. This would limit the number of GDM cases that go undiagnosed and reduce instances of the adverse short-term and long-term outcomes associated with untreated GDM.[3,4] Furthermore, since GDM increases lifetime risk of developing T2DM in mother and offspring,[5-7] testing pregnant women in India for GDM during the third trimester, considering the high incidence of T2DM in India[28] provides an opportunity to definitively test and track women who are at risk of developing T2DM throughout their lives, therefore preventing the development of T2DM and its long-term complications.

Several studies have shown an association between GDM and risk factors such as parity, age and BMI. A study conducted in women attending an antenatal clinic in Haryana, India, found that GDM was associated with increasing age, higher BMI, family history of diabetes or hypertension and a past history of GDM.[29] Studies conducted in other parts of India have reported similar findings.[31-34] In the present study, however, we did not find significant differences between the ages, parities and BMIs of women who tested positive for GDM and those who tested negative for GDM. This result further underscores the importance of universal, rather than selective screening of women for GDM, even in the third trimester.

Our study was not without limitations. First, we did not determine whether glucose intolerance during the first trimester was due to GDM or pre-existing, undiagnosed T2DM; thus, it is possible that GDM prevalence during the first trimester might actually be lower than that reported in this study. Second, the study had a small sample size and was not powered to detect differences in age, parity and BMI. As a result, any differences between these three variables might have been obscured. Third, if universal testing were done in third trimester, we may have reported lesser prevalence of late onset disease.

CONCLUSION

This study indicates that GDM manifests in all trimesters. Furthermore, it is not associated with age, BMI or parity. The current DIPSI guidelines recommend GDM screening twice during pregnancy; however, our study shows that additional selective testing of pregnant women in the third trimester would identify cases of GDM that would have otherwise gone undetected. This raises a thought for universal testing once in every trimester. This would only bolster current efforts targeted at reducing adverse maternal and neonatal outcomes associated with GDM as well as incidences of T2DM in the community.

ACKNOWLEDGEMENT

We gratefully acknowledge Prof. Isaac Manyonda for his constant support; the Staff of Divakars Speciality Hospital, Bengaluru, for their co-operation; Janos Fakete for statistical analysis; Lorriane M for the help in scientific writing.

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