

Need for testing glucose tolerance in the early weeks of pregnancy

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ABSTRACT

Aims: This observational study aims to determine the frequency of occurrence of glucose intolerance in the early weeks of pregnancy. **Materials and Methods:** New World Health Organization 2013 guidelines recommends "A Single Step Procedure" (SSP) as an option for diagnosing gestational diabetes mellitus (GDM). Pregnant women attending 131 prenatal clinics across India for the first time underwent SSP consisting of administration of 75 g oral glucose irrespective of the last meal timing and to diagnose GDM with 2 h plasma glucose (PG) value ≥ 7.8 mmol/L (7.8 mmol/L). **Results:** In a cohort of $n = 11,785$, the number of pregnant women who underwent the test in first, second, and third trimesters were 4300, 4632, and 2853, respectively. Documented blood glucose values were available for 9282 pregnant women and in them, diagnosis of GDM was made in 740 (8%). Among them, 233 (31.5%), 320 (43.2%), and 187 (25.3%) were in the first, second and third trimesters, respectively. Positive family history of diabetes (43%) and history of fetal loss in previous pregnancy (27%) was more common in women diagnosed with GDM in the first trimester compared to GDM diagnosed in the second or third trimester. **Conclusion:** Manifestation of GDM in the early weeks of gestation is quite common.

Key words: Gestational diabetes mellitus, plasma glucose, single step procedure

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.^[1] Hyperglycemia in pregnancy is associated with serious complications for both mother and offspring. It has been shown that the negative consequences on the fetus and the mother increase linearly with increasing maternal blood glucose.^[2] Women with a history of GDM are also at increased risk of future diabetes, predominantly type 2

diabetes, as are their children.^[3] GDM may play a crucial role in the increasing prevalence of diabetes and obesity.^[4] Therefore, all pregnant women should be screened for GDM, even if they have no symptoms, according to new recommendations.^[5] In India, with approximately 27 million pregnancies annually, for this recommendation to be widely implemented, the diagnostic procedure has to be simple and feasible at the grass root level, acceptable to those undertaking the test as well as those giving the test, economical and backed with reasonable evidence. New World Health Organization 2013 while recommending International Association of Diabetes Pregnancy Study Group criteria also recommends "A Single Step Procedure" (SSP) as an

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option to diagnose GDM.^[6] Diabetes in Pregnancy Study Group in India (DIPSI) follows the SSP to diagnose GDM. This diagnostic test can be performed in the fasting or nonfasting state irrespective of the last meal timing. GDM is diagnosed if 2 h plasma glucose (PG) ≥ 7.8 mmol/L after ingestion of 75 g oral glucose. This has been endorsed by the Maternal Health Division of the Ministry of Health and Family Welfare Government of India^[7,8] and recently in the National Guidelines for the Diagnosis and Management of Gestational Diabetes Mellitus released in December 2014.^[7] The DIPSI approach has been also endorsed by the Federation of Obstetrics and Gynaecological Society of India (FOGSI) and the Association of Physicians of India.^[9,10] National Institute of Clinical Excellence 2015 also recommends the glycemic cut-off level of 2 h PG >7.8 mmol/L to diagnose GDM with 75 g oral glucose.^[11]

While the standard practice is to test women for GDM between 24 and 28 weeks of gestation there is evidence to suggest that many women manifest hyperglycemia early in pregnancy as a consequence of previously unknown diabetes or higher levels of insulin resistance and reduced capacity to increase insulin secretion resulting in earlier decompensation manifesting as early onset GDM.^[12] The relevance of early screening has not been well established in the national and intermediate scenario. Hence, this study was initiated to assess the need and utility of testing for GDM in the early weeks of pregnancy.

MATERIALS AND METHODS

As part of a large training initiative of FOGSI and DIPSI to increase awareness of the need to test for GDM, 13 obstetricians participating in the program from different parts of India working both in private and public institutions, volunteered to participate in an observational study. This multi-center, observational study was undertaken from August 2013 to December 2013, after protocol approval from the Institutional Ethics Committee (Dr. V. Seshiahand, Dr. Balaji's Diabetes Research Institute). A cohort of $n = 11,785$ pregnant women attending the prenatal services of the participating centers were enrolled into the study irrespective of the trimester at presentation after obtaining their informed consent. They were registered, and a thorough clinical examination was undertaken. Details regarding age, height, weight, age at first pregnancy, gravida, previous obstetric history including history of GDM in previous pregnancies, previous history of delivery of large babies, fetal loss or other adverse pregnancy outcomes, previous history of diabetes, history of diabetes in the family, socioeconomic status, and past history of infertility were elicited and recorded. Pregnant

women with diabetes and those refusing to undertake blood glucose measurements were excluded. The body mass index (BMI) was calculated using the height and prepregnancy weight when known. Pre pregnancy weight was not known in over a third of the cases, similarly because of the mixed nature of population studied, including those with low education and poor socioeconomic background many aspects of the historical information including accurate age, family history of diabetes and history of previous pregnancy outcome was not available in many cases. During their first visit, irrespective of the gestational age, they were offered the 75 g SSP test. Venous PG was tested at 2 h at the local laboratory by glucose oxidase/peroxidase method.^[13,14] Descriptive statistics were done for continuous and discrete variables and summary tables were depicted for grouped data.

RESULTS

In this study, a cohort of $n = 11,785$ pregnant women were enrolled. The number of pregnant women who underwent the test in the first, second, and third trimesters were 4300, 4632, and 2853, respectively. Documented blood glucose values were available for 9282 pregnant women and in them a diagnosis of GDM was made in 740 (8%). Among them 233 (31.5%), 320 (43.2%), and 187 (25.3%) were in the first, second, and third trimesters, respectively [Table 1].

Mean (standard deviation) age of women with GDM in all three trimesters was similar both in those below and above 25 years of age [Table 1]. The risk of GDM increased with increasing age. In the first trimester prevalence of GDM doubled from 4.8% in the 17–19 years age group to 9.6% in the 35–40 years age group. A similar trend was noted in women diagnosed with GDM in the second trimester, with prevalence increasing from 3.5% in the 17–19 years

Table 1: Demographic findings of GDM women

	First trimester N=233	Second trimester N=320	Third trimester N=187
Age <25 years (n=207)	62 (27.1%)	93 (29.9%)	52 (29.2%)
Mean age (SD)	21.6 (1.95)	21.8 (1.78)	22.3 (1.55)
Age >25 years (n=511)	167 (72.9%)	218 (70.1%)	126 (70.8%)
Mean age (SD) (n=718)	29.7 (3.59)	28.9 (3.36)	29.2 (3.59)
BMI <25 kg/m ² (n=212)	72 (44.2%)	101 (41.9%)	39 (32.8%)
Mean (SD)	21.5 (2.26)	21.3 (1.93)	21.8 (1.76)
BMI ≥ 25 kg/m ² (n=311)	91 (55.8%)	140 (58.1%)	80 (67.2%)
Mean (SD)	29.3 (5.28)	30.9 (12.75)	30.0 (15.61)
History of GDM in previous pregnancy (n=63)	21 (9.4%)	29 (9.6%)	13 (7.6%)
Positive family history of diabetes (n=247)	94 (42.9%)	98 (32.2%)	55 (31.3%)
History of Foetal Loss in previous pregnancy (n=137)	62 (27.3%)	48 (15.7%)	27 (15.3%)

age group to 6.8% in the 35–40 years age group. A quarter of women diagnosed with GDM (25.8%) in the first trimester were <25 years of age and close to a third (30%) diagnosed in the second trimester were also <25 years of age. About 9% of multi gravid women with GDM gave a history of GDM in previous pregnancy. Positive family history of diabetes (43%) and history of fetal loss in previous pregnancy (27%) was more common in women diagnosed with GDM in the first trimesters compared to GDM diagnosed in second or third trimester. Among GDM women with BMI >25 kg/m², 56%, 58%, and 67% were diagnosed in the first, second, and third trimesters, respectively [Table 1].

DISCUSSION

GDM is a significant and growing health problem worldwide, especially in certain vulnerable populations because of genetic, social, and environmental factors.^[5] The short-term and long-term maternal and fetal consequences of GDM, including a predisposition to obesity, metabolic syndrome, cardiovascular disease, and diabetes later in life are well established. Early identification and intervention including diligent postpartum follow-up and continuing healthy lifestyle recommended during pregnancy is expected to have positive health impact both on women with GDM and their offspring. An elegant study by Bartha *et al.*, showed that women in the later screening group were likely to have hydramnios (12.7 vs. 2.1%; $P < 0.0001$) and preterm deliveries (11.8 vs. 5.5%; $P = 0.03$). All cases of preterm premature rupture of membranes and fetal anomalies took place in the later screening group ($P = 0.03$, $P = 0.007$, respectively). Early glucose tolerance screening could avoid some diabetes-related complications in women with gestational diabetes.^[15]

The standard recommendation for GDM screening is to test women between 24 and 28 weeks of gestation. There are reports that claim between 40% and 66% of gestational diabetes can be detected in early pregnancy.^[16-18] Recently, early testing for glucose tolerance including in the first trimester, of all pregnant women irrespective of risk factors has been advocated.^[12,18-20] In India, this would require testing 27 million pregnant women annually three times during pregnancy. Given the magnitude of the challenge, it is important that the recommendations are based on evidence collected in a cross-section of India. No large scale epidemiological data is available in India to support a recommendation for early testing for GDM. In this cross-sectional observational study carried out in 131 centers across India we have shown that almost a third of all GDM cases (233/740) were diagnosed during testing in the first trimester. Further twice as many of

these women gave a history of fetal loss in their previous pregnancies compared to women diagnosed in the second or third trimester (27% vs. 15%). It may be conjectured that these women may have had early hyperglycemia (either GDM or type 2 diabetes) which remained undetected, resulting in fetal loss and indicating the need to test for glucose intolerance in the pre-pregnancy and as well as in the early pregnancy stage. IADPSG also recommends Galsore commends testing for GDM in the early weeks of pregnancy so that overt diabetes is not missed.^[11] A1C was not done as in this study, a huge population was included, and the cost of performing this test is not only prohibitive but also due to lack of facility in different study centers. Yet another reason is that in Asian population glycosylated hemoglobin concentration has much lower sensitivity.^[21]

Finding in this study confirms the higher risk of gestational diabetes with increasing age and BMI similar to the observation published in the earlier studies.^[22,23] However, it is noteworthy that a sizeable number of women with GDM had BMI <25 kg/m² and age <25 years. The family history of diabetes mellitus, as well as previous history of GDM, is associated with increased risk of a diagnosis of GDM.^[22,23] In our study, family history of diabetes was particularly more common in women with first trimester diagnosis but the previous history of GDM was noted in only 9% cases; this is to be expected when screening for GDM is an exception rather than a rule. It should be noted that a majority of women detected with GDM in this study did not have family history of diabetes, history of diabetes in previous pregnancy or history of fetal loss supporting the concept of universal screening. Thus, universal screening appears to be the better approach than screening based on risk factors.^[6] Increased occurrence of GDM in the first trimester is not only an Indian phenomenon but also that of other population.^[15]

CONCLUSION

In this Pan-India study, one-third of pregnant women were diagnosed to have GDM in the first trimester itself. Over a quarter of them had a history of fetal loss in the previous pregnancies. Early glucose intolerance testing and implementing the treatment could avoid complications such as hydramnios, fetal anomalies, and preterm birth. This study reveals the necessity of screening all pregnant women for glucose intolerance in the early weeks of pregnancy.

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Conflicts of interest

There are no conflicts of interest.

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