

Gestational Diabetes Mellitus in India

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Abstract

Background : Glucose intolerance during pregnancy predisposes the offspring for increased risk of developing glucose intolerance in the future. This vicious cycle is likely to influence and perpetuate the incidence and prevalence of glucose intolerance in any population.

Aim : No data is available about the prevalence of glucose intolerance during pregnancy in our country and hence a study was undertaken on this aspect.

Methods : This study was performed in the antenatal clinic of Government Maternity Hospital, Chennai, India. As a pregnant woman in second or third trimester checks into the antenatal clinic, she was given 50 gm oral glucose load and blood sample was collected after one hour. This test was performed on 1251 pregnant women. They were requested to come after 72 hours for the 75 gm OGTT recommended by WHO. Among the 1251 women, 891 responded. The blood sample was taken in the fasting state and at 2 hours after 75 gm of oral glucose. Diagnosis was based on the WHO criteria for gestational diabetes mellitus (GDM).

Results : The mean age of these pregnant women was 23 ± 4 years. There was a significant increase in the prevalence of GDM in relation to gravida. The effect of BMI did not quite reach statistical significance (χ^2 (df=1) = 3.659, P = 0.055), but a model of linear trend was significant.

Of the 1251 women who underwent the 50 gm oral glucose challenge test, 670 (53.55%) had one hour plasma glucose ≥ 130 mg/dl. Among the 891 pregnant women who had 75 gms OGTT, 168 (18.9%) were diagnosed as GDM, taking both FPG ≥ 126 mg/dl and/or 2 hr PPG ≥ 140 mg/dl as cut-off values. Taking only 2 hr plasma glucose for analysis, 144 (16.2%) had a value ≥ 140 mg/dl.

A similar study was conducted in different parts of the country taking only the 2 hr 75 gm post-glucose value of ≥ 140 mg/dl as diagnostic criteria for GDM. Of the total number of pregnant women (n = 3674) screened, 16.55% of them found to have GDM.

Conclusion : Our study has documented the increased prevalence of GDM in our population necessitating universal screening for glucose intolerance in pregnancy. Using 2 hr plasma glucose ≥ 140 mg/dl as a one step procedure is simple and economical, particularly for the countries ethnically more prone to high prevalence of diabetes. ©

INTRODUCTION

The prevalence of diabetes is increasing globally and India is no exception. The 1997 WHO estimates of the prevalence of diabetes in adults showed an expected total rise of > 120% from 135 million in 1995 to 300 million in 2025. These numbers also include GDM, and should alert physicians

to the need to direct special attention to this population, especially in developing countries.¹ The primary prevention is likely to reverse or halt this trend. For this the need is to focus at the intrauterine environment as the “preventive medicine starts before birth”. Intrauterine exposure to hyperglycemia during the critical period of fetal development programmes the development of pancreas negatively and affects the insulin secretory function.² Hence this study was undertaken to detect the glucose intolerance that occurs during pregnancy as this metabolic disturbance predisposes the offsprings for higher risk of developing glucose intolerance in their later life.³ As of today we have no current national data regarding the occurrence of abnormal glucose tolerance in the pregnant women. The routine screening for

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glucose intolerance during pregnancy is not done in maternity hospitals maintained by the Government, municipality or local bodies that care for the majority of the pregnant women in our country.

MATERIALS AND METHODS

This study was carried out in Raja Sir Ramaswamy Mudhaliar lying hospital attached to the Government Stanley Medical College and Hospital, Chennai, India during the period February to December 2001. To obtain an unbiased data this maternity hospital was chosen for the study as pregnant women from different socioeconomic strata attend this hospital for antenatal check up and confinement.

Consecutive 1251 pregnant women in the second or third trimester attending the antenatal clinic were given a 50 gm oral glucose load and the venous blood was collected after one hour.⁴ Details of family history of diabetes, history of previous pregnancies and the socio-economic status were obtained. Blood pressure was recorded. The body mass index (BMI) of the subjects was calculated and expressed in kg/m². All women were requested to have their regular diet and return after 72 hours for the 75 gm oral glucose tolerance test recommended by WHO.⁵ The blood sample was taken in the fasting state and 2 hr after 75 gm of oral glucose. The plasma glucose was estimated by GOD-POD method by using Bayer's kit. The result of the initial testing (50 gm-1 hr) was considered positive if the plasma glucose \geq 130 mg/dl. This cut-off value was chosen to increase the detection rate.⁴ A woman was considered to have GDM if the FPG \geq 126 mg/dl and/or 2-hr plasma glucose value \geq 140 mg/dl with the 75 gm oral glucose.⁶

Associations were analysed with Mantel-Haenszel technique, providing odds ratios stratified for potential confounders and corresponding χ^2 -based statistics. Confidence limits were estimated by means of the approximated Poisson distribution. P-values <0.05 were considered statistically significant. To standardise the diagnosis of GDM, the WHO has proposed using a 2hr 75gm OGTT, with a threshold plasma glucose concentration of greater than 7.8 mmol/L (140 mg/dl) at 120 minutes similar to that of IGT outside pregnancy.⁵ Moses *et al* adopted WHO criteria in their study, where they used a single 75gm OGTT and diagnosed GDM with 2 hr PPG \geq 140mg/dl.⁷ David Pettit in his editorial titled 'The 75 gm oral glucose tolerance test in pregnancy' favoured WHO recommendation.⁸ More importantly GDM based on 2hr 75 gm OGTT defined by either WHO or ADA Criteria predicts adverse pregnancy outcome.⁹ Hence we chose WHO criteria due to the simplicity and the economical considerations. Further, assuming that the effective treatment is available, WHO criteria of 2 hr PPG \geq 140mg/dl identifying a large number of cases may have a greater potential for prevention.⁹

RESULTS

A total of 1251 pregnant women had the initial 50 gm-1 hr test. Of these, 669 (53.5%) were test-positive. For the subsequent 75 gm-2 hr test 891 (71.2%) women responded.

Among those positive for the 50 gm-1 hr test, 548 (81.9%) responded whereas 343 (58.9%) responded among the women who were negative for the 50 gm-1 hr test (Table 1). The positive association between a positive outcome of the 50 gm-1 hr test and taking part in the subsequent 75 gm-2 hr test was statistically significant (Mantel-Haenszel odds ratio after stratification for age: 3.14, χ^2 (df=1) = 78.067, $P<0.0001$), and there was no evidence of interaction with age (χ^2 (df=4) for heterogeneity = 1.770, $P=0.778$).

Of the 891 women who underwent the 75g OGTT, 24 of them had FPG \geq 126 mg/dl, 133 of them had 2 hr PG \geq 140 mg/dl and 11 had both FPG \geq 126 mg/dl and 2 hr PG \geq 140 mg/dl. Overall, 168 women (18.9%) [95% confidence limits: 16.3%-21.6%] were diagnosed as GDM.

The mean age of these pregnant women was 23 ± 4 years. The prevalence proportion increased with age from 15.7% (confidence limits: 8.6%-25.3%) in the age group 15-19 years to 32.1% (confidence limits: 20.3%-46.0%) for the age groups 30+ years (Fig. 1). With regard to the age effect, a model of linear trend was statistically significant (χ^2 (df=1) = 10.630, $P=0.001$).

Data on BMI was available for 664 (74.5%) and the prevalence proportion of GDM increased with increasing BMI (Fig. 2). This is evident from our study that the prevalence of GDM with BMI \leq 23 and \geq 24 is 19.7% and 24.5% respectively. The effect of BMI did not quite reach statistical significance, but was approaching statistical significance (χ^2 (df=1) = 3.659,

Table 1 : Overview of results of initial 50 gm-1 hr test. In parentheses: Number of women who responded to the subsequent 75 gm-2 hr test

Age group	Result of initial 50 gm-1 hr test		Total
	Positive	Negative	
15-19	49 (40)	78 (43)	127 (83)
20-24	361 (294)	309 (181)	670 (475)
25-29	196 (162)	143 (84)	339 (246)
30-34	32 (26)	22 (15)	54 (41)
35+	12 (9)	8 (6)	20 (15)
Age unknown	19 (17)	22 (14)	41 (31)
Total	669 (548)	582 (343)	1251 (891)

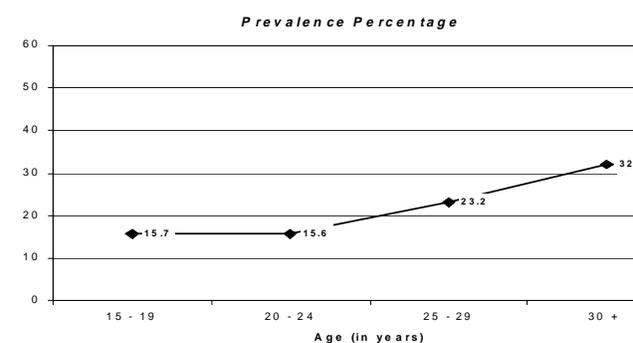


Fig. 1: Prevalence percentage (with 95% confidence intervals) of gestational diabetes by age groups (n=860 after exclusion of 31 subjects because of missing data on age).

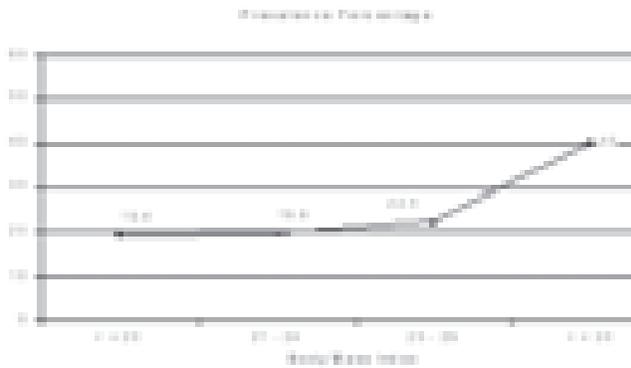


Fig. 2: Prevalence percentage (with 95% confidence intervals) of gestational diabetes by body mass index (n=664 after exclusion of 227 subjects because of missing data on body mass index).

Table 2 : Results of the initial 50 gm-1hr test evaluated against the confirmatory 75 gm-2 hr test. In parentheses: 95% confidence intervals.

	Result of 75 gm-2 hr test		Total	Prevalence proportion
	+ GDM	- GDM		
Positive for 50g-1hr test	134	414	548	0.245 (0.209; 0.283)
Negative for 50g-1hr test	34	309	343	0.099 (0.070; 0.136)
Total	168	723	891	0.189 (0.163; 0.216)
Sensitivity:	0.798 (0.727; 0.854)			
Specificity:	0.427 (0.391; 0.464)			
Predictive value of positive test:	0.245 (0.210; 0.283)			
Predictive value of negative test:	0.901 (0.863; 0.929)			

P = 0.055) by chi square test of linear trend.

The prevalence proportion of GDM increased with gravida, from 18.1% (confidence limits: 14.38% - 22.29%) in the primi gravida to 25.8% (confidence limits: 11.86% - 44.61%) for the gravidas ≥ 4 . (Fig. 3).

DISCUSSION

We believe that the way the study subjects were ascertained provides a representative and unbiased sample of pregnant women, as the bulk of the pregnant women attend hospital of this type for antenatal check-up and confinement in our country.

Among 1251 pregnant women screened with glucose challenge, 891 responded for 2 hr 75 gm OGTT. However, neither positive family history nor parity influenced the reporting for the 75 gm-2 hr test. This phenomenon of no show rate appears to be universal. Magee *et al* reported in their follow up, 91 of the 457 positive screen individuals failed to undergo diagnostic test.¹⁰ Luiz *et al* also observed in their study, that 23% of their screen positive women did not return for OGTT.¹¹ Our prevalence rate was 18.9%. We got this figure as we took into consideration for analysis the FPG value also as this was available besides 2hr PPG. Of the 891 women, 24 had FPG ≥ 126 mg/dl. They might have had pregestational diabetes. We could not confirm this as A_{1c} estimation is not

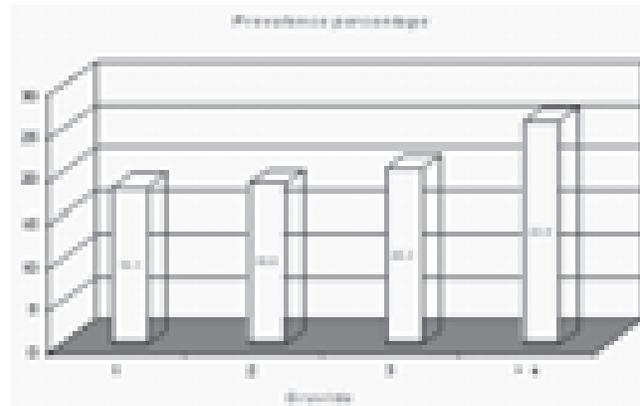


Fig. 3: Prevalence percentage (with 95% confidence intervals) of gestational diabetes by gravida (n= 891).

recommended as routine test for screening and hence we also did not perform the test.¹² If our estimated prevalence proportions among those positive and negative, respectively, for the 50 gm-1hr test were applied to total sample of 1251 women, the revised overall prevalence proportion would be 17.7% (confidence limits: 15.6%-19.9%) against the value of 18.9% found among the 891 women. Another outcome of this study was that the fasting plasma glucose estimation is not necessary for Universal screening as this procedure identified negligible percentage of women with glucose intolerance (2.69%). WHO is also not in favour of estimation of FPG for screening.⁶

An overall prevalence proportion of GDM at 17.7% in this rather young population of pregnant women was considerably high. Subsequent to the observation of the high prevalence of GDM in one centre, a multicentre study was initiated in different parts of the country in 2002 - 2003 taking only the 2 hr 75 gm post glucose value of ≥ 140 mg/dl as diagnostic criteria for GDM. Almost a similar prevalence of 15% was obtained in another govt. maternity hospital affiliated to Madras Medical College in the city of Chennai. This trend of high prevalence of GDM was also found in other parts of the country, 15% in Trivandrum, 21% in Alwaye, 12% in Bangalore, 18.8% in Erode and 17.5% in Ludhiana. The total number of pregnant women screened in these centres was 3674 and an overall GDM prevalence of 16.55% was observed. This study documented a definite increasing trend in the prevalence of GDM compared to that of 2% in 1982¹³ and 7.62% in 1991.¹⁴ This trend is also seen in other countries. For example in Australia at one hospital where the same testing procedure and diagnostic criteria have been used for more than 2 decades, the prevalence has more than doubled.¹⁵

A recent national survey reported the prevalence of IGT in the age group of 20-29 years and 30-39 years as 12.2% and 15.3% respectively.¹⁶ No gender difference was seen in the prevalence of IGT.¹⁶ Further for a given population and ethnicity the risk of diabetes and pregnancy, mirrors that of the underlying frequency of type 2 DM in the general population.¹⁷ We also observed in our study that the prevalence of GDM is closer if not similar to the prevalence

rate of IGT in our population. With this huge population of reproductive age in India, a significant segment of women with abnormal glucose tolerance during pregnancy needs cognizance.

Our attempt and outcome of the screening for glucose intolerance during pregnancy has given an insight for the phenomenal increase in the prevalence of diabetes in India. This view is substantiated by the observation of Dabelea *et al* on Pima Indians. The gestational diabetes mellitus has a far reaching consequence in predisposing the offsprings to glucose intolerance has been documented in Pima Indians. The children born in 1965 to women with gestational diabetes were followed up till 2000. By the time they reached 35 years, more than half of the group had diabetes.³ Hence as a policy to identify GDM and its consequences on the infant a 75 gm OGTT has been recommended to all women in the population during the third trimester of pregnancy.³

In India, both undernutrition and overnutrition exist during pregnancy. There are two reported studies in India which are related to size at birth to future risk of type 2 diabetes. In Mysore, low birth weight did not increase the risk of diabetes but babies who were short and fat (higher body mass index, BMI) at birth were at increased risk.¹⁸ Fall *et al* speculate that the rise in type 2 diabetes in Indian urban populations may have been triggered by mild obesity in mothers, leading to glucose intolerance during pregnancy, macrosomic changes in the fetus and insulin deficiency in adult life.¹⁸ Yet another study by Yajnik *et al* attributes high prevalence of type 2 DM and IGT in Indian people may be linked to poor fetal growth.¹⁹ Same author also suggests that type 2 DM in India may be programmed in fetal life, hence diabetes prevention will have to start in early life (in utero) and continue in later life.²⁰ The importance is that the intrauterine millieur interieur, whether one of nutritional deprivation or one of nutritional plenty, results in changes in pancreatic development and peripheral response to insulin that may lead to adult - onset GDM and type 2 DM.²¹

Our study favours one step procedure recommended by WHO for screening instead of two step procedure using preliminary screening with 50 gm one hr test.⁴ Table 2 shows the results of the evaluation of the outcome of the 50 gm-1 hr test, using the outcome of the 75 gm-2 hr test as standard. The sensitivity of the 50 gm 1 hr test was 79.8% when compared to the low specificity of 42.7%. Combined with a relatively small number of false negative subjects, this yielded reasonable high values of sensitivity (79.8%, confidence limits: 72.7%-85.4%) and predictive value of a negative 50 gm-1 hr test (90.1%, confidence limits: 86.3%-92.9%). However, there was a substantial number of subjects false positive for the 50 gm-1 hr test, resulting in poor values of specificity (42.7%, confidence limits: 39.1%-46.4%) and predictive value of a positive 50 gm-1 hr test (24.5%, confidence limits: 21.0%-28.3%). Since the specificity of using 50 gm-1 hr test is low, instead of performing screening test using 50 gm-1 hr test and then 100 gm / 75 gm OGTT⁴, a one step procedure of performing 75gm OGTT directly is ideal as we need to perform

universal screening for glucose intolerance in pregnancy.

CONCLUSION

In conclusion, our study has documented the increased prevalence of GDM in our population and we venture to give the following observations and recommendations. Universal screening for glucose intolerance during pregnancy is essential as Indian women have high prevalence of diabetes and their relative risk of developing GDM is 11.3 times compared to white women.²² Asian women are ethnically more prone to develop glucose intolerance compared to other ethnic groups.¹⁵ GDM based on 2hr 75gm OGTT defined by WHO predicts adverse pregnancy outcome and warrants treatment.⁹ A 2 hr 75 gm post plasma glucose ≥ 140 mg/dl serves both as screening and diagnostic criteria besides being a simple and economical one step procedure. As the routine screening for glucose intolerance during pregnancy is not done, probably the undiagnosed glucose intolerance that has been occurring in the past has resulted in the increased prevalence of diabetes in India. The timely action taken now in screening all pregnant women for glucose intolerance, achieving euglycemia in them and ensuring adequate nutrition may prevent in all probability, India becoming diabetes capital of the World.

'No single period in human development provides a greater potential than pregnancy for long range pay off via relatively short range period of enlightened metabolic manipulation' - Norbert Fienkel.

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Announcement

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