

A1C in Gestational Diabetes Mellitus in Asian Indian Women

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Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of varying degrees of severity with onset or first recognition during pregnancy. The current recommendation is to perform screening test between 24 and 26 weeks of gestation, although there are reports claiming that between 40 and 66% of women with GDM could be detected during early pregnancy (1,2). The policy of screening in the third trimester has resulted in a significant number of pregnant women delivering big babies, despite good glycemic control (3), whereas an early screening for glucose intolerance and care has resulted in the reduction of some of the hyperglycemia-related complications (4). Pregnant women diagnosed as having glucose intolerance in the first trimester are likely to have unrecognized type 2 diabetes before pregnancy (pre-GDM) or pregnancy-induced glucose intolerance during pregnancy (GDM) (5,6). These two clinical situations need to be delineated, as pre-GDM women are likely to have more morbidity and require immediate attention. Hence, we undertook this study to find out whether estimation of A1C levels, along with oral glucose tolerance tests (OGTTs), would help us to distinguish between these two groups, as A1C is directly related to the average concentration of blood glucose in the previous weeks. We also wanted to assess the A1C level during normal pregnancy in our population.

RESEARCH DESIGN AND METHODS

We screened 507 consecutive pregnant women for diabetes and pregnancy who were attending our referral center, irrespective of trimesters, with a 75-g OGTT. Women with a history of type 2 diabetes and GDM were excluded from this study. Blood samples were drawn at fasting and at 1 and 2 h for estimating plasma glucose. The plasma glucose was estimated by GOD-POD method using a Hitachi autoanalyzer 902. In the fasting sample, in addition to plasma glucose, A1C and hemoglobin were measured. A1C was estimated by high-performance liquid chromatography (Bio-Rad). Diagnosis of GDM was based on the World Health Organization criteria of a 2-h plasma glucose level ≥ 140 mg/dl. Details regarding family history, previous obstetric history, treatment for any concomitant diseases, and food habits were obtained. All of the patients underwent routine physical examination.

RESULTS— Among the 507 women screened, 255 (50.3%) were in the first trimester of pregnancy. In this group, 86 (33.7%) had GDM (16.96% of the total women screened), and their mean age, BMI, and gestational weeks at screening during the first trimester were 30.63 ± 4.62 years, 25.56 ± 4.00 kg/m², and 9.0 ± 3.03 weeks, respectively. In women with normal glucose tolerance, the mean age, BMI, and gestational weeks at screening during the first trimester were 28.01 ± 4.72 years, 24.48 ± 4.41 kg/m², and 9.45 ± 3.44 weeks, respectively.

There was no statistically significant difference among age, BMI, and gestational weeks of the women in the normal glucose tolerant and GDM groups ($P > 0.05$). The mean A1C level of the women with normal glucose tolerance was $5.36 \pm 0.36\%$, and that of the GDM women detected in the first trimester was $5.96 \pm 0.63\%$.

The mean A1C level of the 155 (30.6%) GDM women, irrespective of trimesters, was found to be 6%. Applying this cutoff level of 6%, we divided the women diagnosed as having GDM or normal glucose tolerance in the first trimester into four groups (Fig. 1). Group 1: There were 33 (12.94%) women with a 2-h plasma glucose level ≥ 140 mg/dl and A1C $\geq 6\%$. Group 2: A total of 53 (20.6%) women had a 2-h plasma glucose level ≥ 140 mg/dl and A1C $< 6\%$. Group 3: In this group, there were 10 (3.9%) women with a 2-h plasma glucose level < 140 mg/dl and A1C $\geq 6\%$. Group 4: This group included 159 (61.9%) women with a 2-h plasma glucose level < 140 mg/dl and A1C $< 6\%$.

CONCLUSIONS— The screening for glucose intolerance is usually performed at ~ 24 – 28 weeks of gestation. However, a statistically significant number of GDM mothers deliver big babies despite good glycemic control in the third trimester (3). This is due to the influence of maternal hyperglycemia on fetal growth in the early weeks of gestation (7,8). The priming of β -cell mass in early gestation may account for the persistent fetal hyperinsulinemia throughout pregnancy and the risk of accelerated growth, even when the mother enjoys good metabolic control in later pregnancy (9).

In our study, the mean A1C of the women with normal glucose tolerance was 5.3%. Radder and Van Roosmalen (10) documented that A1C levels varied between 5 and 6% in healthy pregnant women. We were able to establish from our study the mean A1C level in women with GDM at diagnosis during different trimesters as 6% (6.04 ± 0.81). We analyzed our finding, taking into consideration the OGTT and A1C values, to categorize the women in whom glucose intolerance was diagnosed in early preg-

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Received for publication 15 November 2006 and accepted in revised form 25 March 2007.

Published ahead of print at <http://care.diabetesjournals.org> on 6 April 2007. DOI: 10.2337/dc06-2329.

Abbreviations: GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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Group 1 (N = 33, 12.94%)	Group 2 (N = 53, 20.6%)	Group 3 (N = 10 3.9%)	Group 4 (N = 159, 61.9%)
2 hr PG \geq 140mg/dl and A1c \geq 6%	2 hr PG \geq 140mg/dl and A1c < 6%	2 hr PG < 140mg/dl and A1c \geq 6%	<p style="text-align: center;">2hr PG <140mg/dl and A1c also < 6%</p> <p style="text-align: center;">159 (61.9%)</p> <div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> <p>A1c < 6% but > 5.3% 78 (49%)</p> <div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> <p>2hr PG \geq120 and < 140 23 (29.5%)</p> </div> <div style="text-align: center;"> <p>2hr PG < 120 55 (70.5%)</p> </div> </div> </div> <div style="text-align: center;"> <p>A1c < 5.3 81 (50.9%)</p> </div> </div>

Figure 1—Correlation between 2-h plasma glucose (2hr PG) and A1C.

nancy as pre-GDM, GDM, or normal glucose tolerant.

In group 1, women diagnosed with GDM in the first trimester also had A1C \geq 6%. In them, glucose intolerance was detected in the early weeks of pregnancy, and they were likely to be pre-GDM or have type 2 diabetes before conception but were detected during pregnancy. The women in group 2 were diagnosed to have GDM by OGTT, but their A1C level was <6%. In them, the abnormal glucose tolerance would have manifested in the early weeks of pregnancy, but the duration of exposure to hyperglycemia was not long enough to effect the changes in the A1C level. Thus, these women were considered to have pregnancy-induced glucose intolerance (GDM). Women in group 3 had normal OGTTs but A1C \geq 6%. Historically, they had pregnancy-induced disturbances in alimentation, which occurs in some women in the early weeks of pregnancy. This would probably have resulted in a normal OGTT. They are an ominous group and are more likely to be pre-GDM and need repeat OGTTs in subsequent trimesters. On follow-up, we found that all women in group 3, who had normal glucose tolerance, developed GDM in the subsequent trimester. In group 4, there were 159 (61.9%) women who had a 2-h plasma glucose level <140 mg/dl and A1C also <6%. Among them, 78 had an A1C <6% but \geq 5.3%. Of the 78 women with a 2-h plasma glucose level <140 mg/dl and A1C <6% but >5.3%,

16 (20.5%) developed GDM in the subsequent visits. When we analyzed the 2-h plasma glucose levels in this subgroup of women, 23 (29.5%) of them had values scattered between 120 and 140 mg/dl (Fig. 1). This subgroup needs special attention as in the opinion of de Sereday et al. (11): a 2-h, 75-g OGTT value using a cutoff point of 119 mg/dl would maximize both its sensitivity and specificity in predicting macrosomia. Sermer et al. (12) stated that increased carbohydrate intolerance in women without overt GDM was associated with a graded increase in the incidence of macrosomia. We also observed in our population that the occurrence of macrosomia was continuum as the 2-h plasma glucose increased from 120 mg/dl (3). In our study, A1C values between 5.3 and 6.0% was confirmatory to the splay of abnormal glucose intolerance values between 120 and 140 mg/dl.

Women with an early diagnosis of GDM, in the first half of pregnancy, represent a high-risk subgroup within the GDM population and have an increased incidence of obstetric complications, recurrent GDM in subsequent pregnancies, and future development of type 2 diabetes (5). Hence, women with GDM in early pregnancy could benefit from earlier metabolic control.

In our study population, during normal pregnancy, the A1C level was 5.3%. In women with GDM, the A1C level was 6%. These values would help to distinguish between pre-GDM, GDM, and

normal glucose tolerance during pregnancy. Pregnant women with normal OGTTs but A1C >6% and women with A1C values between 5.3 and 6% require utmost attention.

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