GLYCOSYLATED HAEMOGLOBIN IN GESTATIONAL DIABETES MELLITUS
IN ASIAN INDIAN WOMEN

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Abreviations:

Gestational Diabetes Mellitus (GDM), Diabetes (DM), Oral Glucose Tolerance Test (OGTT),
Glucose Oxidase Peroxidase (GOD - POD), Glycosylated Hemoglobin (A1c), High Pressure
Liquid Chromatography (HPLC), World Health Organisation (WHO), Body Mass Index (BMI),
Normal Glucose Tolerance (NGT)
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 24-26 weeks of gestation, though there are reports claiming that, between 40% and 66% of women with GDM could be detected early during 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 to have glucose intolerance in the first trimester are likely to have unrecognized type 2DM before pregnancy(preGDM) or pregnancy induced glucose intolerance during pregnancy(GDM)[5,6]. These two clinical situations need to be delineated, as preGDM 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 OGTT would help us to distinguish between these two groups, as A1c is directly related to 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 consecutive 507 pregnant women attending our referral centre for diabetes and pregnancy, irrespective of trimesters with 75gm OGTT. Women with history of type 2DM and GDM were excluded from this study. Blood samples were drawn at fasting, 1hour and 2hour for estimating plasma glucose. The plasma glucose was estimated by GOD-POD method using Hitachi autoanalyser 902. In the fasting sample, in addition to plasma glucose, A1c and hemoglobin were measured. A1c was estimated by HPLC(Biorad). Diagnosis of GDM was based on the WHO criteria of 2hrPG ≥ 140mg/dl. Details regarding family history, previous obstetric history, treatment for any concomitant diseases and food habits were obtained. All of them 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, 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. In women with NGT the mean age, BMI and gestational weeks at screening during the first trimester were 28.01±4.72 years, 24.48±4.41, and 9.45±3.44 weeks. There was no statistically significant difference between the age, BMI and gestational weeks of the women in NGT and GDM group ( p > 0.05). The mean A1c level of the NGT women was 5.36±0.36 and that of the GDM women detected in the first trimester was 5.96±0.63.

The mean A1c level of the 155(30.6%) GDM women irrespective of trimesters were found to be 6%. Applying this cut off level of 6%, we divided the women diagnosed to have GDM or NGT in the first trimester into 4 groups (Fig – 1). Group 1: There were 33(12.94%) women with a 2hr PG ≥ 140mg/dl & A1c ≥ 6%. Group 2:A total of 53(20.6%) women had a 2hr PG mg/dl ≥ 140 & A1c < 6%. Group 3: In this group there were 10(3.9%) women with 2hr PG < 140 mg/dl & A1c ≥ 6%. Group 4 had 159(61.9%) women with 2 hr PG < 140mg/dl and A1c < 6%.

DISCUSSION: The screening for glucose intolerance is usually performed around 24-28 weeks of gestation. But 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 in the early weeks of gestation on fetal growth [7,8]. The priming of beta cell mass in early gestation may account for the persistent fetal hyperinsulinaemia 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 NGT women was 5.3%. Radder JK et al documented that A1c level varied between 5% and 6% in healthy pregnant women [10]. We were able to establish from our study the mean A1c level in 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 pregnancy as pre GDM, GDM and NGT.

In group1, women diagnosed to have GDM in the first trimester also had A1c ≥6%. In them though glucose intolerance was detected in the early weeks of pregnancy, they were likely to be preGDM or type 2DM prior to conception, but however detected during pregnancy. The women in group2 were diagnosed to have GDM by OGTT but their A1c<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 group3 had normal OGTT, but A1c≥6%. Historically they had pregnancy induced disturbances in alimentation that occurs in some women in the early weeks of pregnancy. Probably this would have resulted in normal OGTT. They are ominous group and are more likely to be preGDM and need repeat OGTT in subsequent trimesters. On follow up we found that all women in group3, who had NGT developed GDM in the subsequent trimester. In group4, there were 159(61.9%) who had 2hrPG<140mg/dl and A1c also<6%. Among them 78 had an A1c <6% but ≥5.3%. Out of the 78 women with 2hr PG < 140 and A1c < 6% but > 5.3%, 16(20.5%) developed GDM in the subsequent visits. When we analyzed the 2hr PG in this sub group of women, 23(29.5%) of them had values scattered between 120 and 140mg/dl(Fig 1). This sub group needs special attention as in the opinion of Martha de Sereday et al, a 2hr, 75g OGTT value using a cut off point of 119mg/dl had a greater diagnostic effectiveness in pregnancy and a high risk for GDM[11]. Sermer et al stated that increased carbohydrate intolerance in women without overt gestational diabetes was associated with a graded increase in the incidence of macrosomia [12]. We also observed in our population that the occurrence of macrosomia was continuum as the 2hr plasma glucose increased from 120mg/dl[13]. In our study, A1c value between 5.3% and 6.0% was confirmatory to the splay of abnormal glucose intolerance values between 120 and 140mg/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 type2DM[5]. Hence, women with gestational diabetes 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 PreGDM, GDM and NGT during pregnancy. Pregnant women with normal OGTT but
A1c>6% and women with A1c values between 5.3% and 6% require utmost attention.
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Fig – 1: Correlation between 2hr plasma glucose and A1c

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<thead>
<tr>
<th>Group 1 (N = 33, 12.94%)</th>
<th>Group 2 (N = 53, 20.6%)</th>
<th>Group 3 (N = 10, 3.9%)</th>
<th>Group 4 (N = 159, 61.9%)</th>
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<td>2 hr PG ≥ 140mg/dl and A1c ≥ 6%</td>
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<td>2hr PG &lt;140mg/dl and A1c also &lt; 6% 159 (61.9%)</td>
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<tr>
<td>A1c &lt; 6% but &gt; 5.3% 78 (49%)</td>
<td>A1c &lt; 5.3 81 (50.9%)</td>
<td>2hr PG ≥ 120 and &lt; 140 23 (29.5%)</td>
<td>2hr PG &lt; 120 55 (70.5%)</td>
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