Maternal postprandial blood glucose levels and its relation with the pregnancy outcomes

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Abstract
Background: The increasing prevalence of type 2 diabetes in general and in younger people in particular has led to an increasing numbers of pregnancies with the complication of gestational hyperglycaemias. All complications associated with gestational hyperglycaemias are potentially preventable. The aim of this study is to monitor longitudinal changes in blood glucose levels in pregnancy and to co-relate it with various maternal and foetal outcomes.

Material and Methods: The study was conducted in 93 pregnant women. Venous blood was collected and post prandial blood glucose (PPBG) level was estimated by glucose oxidase-peroxidase enzyme method once in every trimester. Pregnancy outcomes including the mode of delivery (spontaneous vaginal delivery or assisted delivery), birth weight of the baby and the neonatal morbidity like asphyxia, hypoglycaemias were noted.

Results: We found 6% of the women in the study group have gestational hyperglycaemias in the first trimester and 27% in the second trimester. The percentages of gestational hyperglycaemias are reduced to 11% in the third trimester. Maternal post prandial blood glucose levels affect the birth weight of the baby and also mode of delivery. Numbers of neonatal complications are higher in subjects with higher blood glucose levels.

Conclusion: We recommend that estimation of maternal PPBG levels should be carried out in all pregnant women at the first antenatal visit and at least once in every trimester. This would help to reduce adverse perinatal outcomes.

Keywords: gestational hyperglycaemias, maternal and foetal complications

1. Introduction
The anatomical, physiological and biochemical adaptations to pregnancy are profound. In response to the rapidly growing foetus and placenta, pregnant women undergo metabolic changes that are numerous and intense. Glucose is the main energy substance for intrauterine growth and is transmitted in a steady stream from mother to fetus. Glucose is produced as a result of maternal metabolism principally from carbohydrate in the diet and from the gluconeogenic amino acids. Changes in the carbohydrate and lipid metabolism are continuous and progressive and may be accentuated in women who develop gestational hyperglycaemias.

Gestational hyperglycaemia is the most common metabolic abnormality occurring during pregnancy. Gestational diabetes mellitus has increased worldwide. Incidence of gestational diabetes mellitus (GDM) has doubled over the last 6–8 years. Gestational diabetes mellitus is defined as glucose intolerance of varying degree and severity with onset or first recognition during pregnancy. Unfortunately gestational hyperglycaemias during pregnancy cause significant increase in foetal and maternal morbidity. It carries long-term implications for the subsequent development of type 2 diabetes in the mother and increased risk for obesity and glucose intolerance in the offspring.

Studies have shown that the whole-body insulin sensitivity is similarly reduced by about two-third of the non-pregnant values in pregnant women with normal-glucose tolerance and women with gestational diabetes mellitus. The insulin sensitivity is restored postpartum in the pregnant women with normal-glucose tolerance and most of the women with gestational diabetes mellitus, but about one-third of the women with gestational diabetes mellitus has a reduced insulin sensitivity an extent that the increased peripheral resistance cannot be overcome; these are the women with diabetes mellitus.

The object of this study was to monitor longitudinal changes in the blood glucose levels in pregnancy and to co-relate maternal post prandial blood glucose levels with the various maternal and foetal outcomes.

2. Material and methods
The study was carried out at civil hospital, Ahmedabad, Gujarat in patient attending OPD of obstetrics and gynaecology department. 93 pregnant women who registered for the antenatal clinic in the first trimester were included in the study. Venous blood was collected for estimation of post prandial blood glucose levels 2 hours after meal (PPBG) in first trimester. Blood glucose estimation was performed by glucose oxidase-peroxidase enzyme method. PPBG was again estimated between 16-24 weeks and between 28-34 weeks. All the women recruited for study were with 20-40 years of age, 10-12 weeks of gestation, and with singleton pregnancy. Women with serious non-obstetric problems like chronic hypertension, Diabetes mellitus type 1, type2, severe Anaemia, with less than 8 gm. /dl haemoglobin or any other serious medical problems were not included in our study. A detailed personal, obstetric and family history was taken. Maternal height and weight were recorded at the first antenatal visit. Pre-gravid weight was obtained by recall. Body mass index was calculated from the height and pregravid weight.
All the subjects were instructed to have their normal dinner the previous night. In the morning they were told to have their regular full meal early any time between 8am to 10 am, and then report one and a half hour later at the hospital so that blood sample will be taken two hours of the meal. Blood glucose estimation was again estimated between 20-24 weeks and between 28-32 weeks. All those who had post prandial blood glucose levels above 130 mg/dl, were given dietary advice and explain for life-style modification. Those showed persistent high reading in spite of dietary advice and life-style modification were put on insulin. Pregnancy outcome including the mode of delivery whether spontaneous vaginal delivery or assisted delivery including forceps assisted or caesarean section was noted. Neonatal morbidity like asphyxia, hypoglycaemia, hyperbilirubinemia, congenital abnormalities and still birth if any were noted.

The subjects were divided into three groups according to the post prandial blood glucose levels recorded between 20-24 weeks of gestation.

Group 1: PP BG levels < 99 mg/dl
Group 2: PP BG levels 99-130 mg/dl
Group 3: PP BG levels > 130 mg/dl

2.1 Statistical analysis:

Statistical analysis was performed using Microsoft excel software, chi-square test had applied, p value of < 0.05 was considered to be statistically significant.

3. Results

Graph 1: Maternal post prandial blood glucose levels in 1st trimester

Out of the total number of 93 women included for the study, 6% were found to have postprandial blood glucose levels more than 130mg/dl, 43% were found to have postprandial blood glucose levels in the range of 99-130mg/dl and the reaming 51% had postprandial blood glucose levels less than 99mg/dl

Graph 2: Maternal post prandial blood glucose levels in 2nd trimester

But subsequently in the 2nd trimester, the group with PP BG level above 130 mg/dl increased to 27%, showing that there is a change in the glucose tolerance during this period. 44% women fell in the group with PP BG of 99-130 mg/dl and 29% of women show PP BG levels of <99mg/dl

Graph 3: Maternal Post prandial blood glucose levels in 3rd trimester

Out of the total number of 93 women included for the study, 6% were found to have postprandial blood glucose levels more than 130mg/dl, 43% were found to have postprandial blood glucose levels in the range of 99-130mg/dl and the reaming 51% had postprandial blood glucose levels less than 99mg/dl
Our results of the third trimester shows 11% women had PP-BG levels >130 mg/dl. Whereas PP-BG of 99-130 mg/dl were 49% and those with PP-BG of <99mg/dl were 40%. Dietary advice and regular follow up may be responsible for the control of PP-BG levels in this trimester.

<table>
<thead>
<tr>
<th>Mode of delivery</th>
<th>Maternal Post Prandial Blood Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;99 mg/dl 99-130 mg/dl &gt;130 mg/dl</td>
</tr>
<tr>
<td>Assisted</td>
<td>18 28 15</td>
</tr>
</tbody>
</table>

P value 0.001. Association is significant at 5% level. Table 1 shows normal indicates normal vaginal delivery and assisted delivery means forceps assisted delivery, vacuum extraction, elective and emergency caesarean section. Incidence of assisted delivery are higher in the group with PP-BG >130 mg/dl.

<table>
<thead>
<tr>
<th>Birth Weight of the baby (kg)</th>
<th>Maternal Post Prandial Blood Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2.5</td>
<td>&lt;99 mg/dl 99-130 mg/dl &gt;130 mg/dl</td>
</tr>
<tr>
<td>≥ 2.5</td>
<td>09 04 04</td>
</tr>
</tbody>
</table>

P value is 0.004. Association is significant at 5% level.

<table>
<thead>
<tr>
<th>Neonatal Complications</th>
<th>Maternal Post Prandial Blood Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>&lt;99 mg/dl 99-130 mg/dl &gt;130 mg/dl</td>
</tr>
<tr>
<td>Absent</td>
<td>2(3.3%) 0(0%) 4(66.6%)</td>
</tr>
</tbody>
</table>

Table 3: Distribution of neonatal complications and maternal post prandial blood glucose

The most common problems of neonates of hyperglycaemic mothers are neonatal hypoglycaemia, neonatal respiratory distress syndrome, neonatal hyperbilirubinemia, congenital abnormality and still birth. According to our finding out of six neonates who suffered with complications four neonates had their maternal PP-BG levels more than 130 mg/dl.

4. Discussion

During early pregnancy, glucose tolerance is normal or slightly improved and peripheral sensitivity to insulin is normal. If gestational hyperglycaemia develops, it normally starts after 20-24 weeks of pregnancy. The most important reason that pregnancy uncovers diabetic tendencies of asymptomatic women is the progressive increase in insulin resistance, which occurs during gestation. The computerised intravenous glucose-tolerance test indicate greater than normal sensitivity to the blood glucose lowering effect of exogenously administered insulin in the first trimester than in the second and third trimesters, and insulin responses to oral glucose are also greater in the first trimester than before pregnancy. Late pregnancy is a state of physiologic insulin resistance compensated by an increase of insulin secretion. Serial studies of insulin action during pregnancy and the increasing insulin requirement in patients of diabetes during gestation, indicates that insulin resistance parallels the increase of fetal-placental unit. Resistance disappears immediately on delivery. The insulin resistance is predominantly located in the muscle tissue, where a reduced activity of certain key enzymes in glucose and lipid metabolism has been demonstrated. The alterations in the hormonal milieu during pregnancy are probably responsible for the reduced insulin sensitivity. Progesterone, oestrogen, prolactin, cortisol may act directly or indirectly to mediate resistance. Plasma levels of placental lactogen increases with gestation and this protein hormone is characterized by growth-hormone-like action that may result in increased lipolysis and increased circulating free fatty acids may facilitate increased tissue resistance.

Gestational hyperglycaemia is not itself an indication for assisted delivery either instrumental or Caesarean section. Because of higher birth weight of the baby and higher chances of preterm birth in the group having gestational hyperglycaemia the chances of assisted deliveries are more in them. High glucose concentration may be a risk factor for the subclinical infection that give rise to chorioamnionitis and preterm birth. Association of glucose intolerance during pregnancy with the rate of complications and the subsequent incidence of diabetes in the mother was continuous throughout the range of glucose concentrations studied. Robertson et al studied pregnancy outcome in women without gestational diabetes mellitus to see whether there was any risk related to maternal glucose level. He concluded that the chances of higher in birth weight increases as maternal blood glucose level increases. Tallarigo et al studied 2 hours postprandial blood glucose levels in 249 pregnant women none of them had previous evidence of diabetes they found that a significant co-relation between the infants birth weight and the mother’s two hour plasma glucose level.

Even limited degrees of maternal hyperglycaemias which are currently considered to be within the normal range may affect the outcome of pregnancy and complications during pregnancy. Maternal hyperglycaemia accounts for only a small fraction of variants with a birth weight of the baby, other factors such as obesity, high concentration of lipids being other contributing factors. The most common problems of neonates of hyperglycaemic mothers are neonatal hypoglycaemia, neonatal respiratory distress syndrome, neonatal hyperbilirubinemia, congenital abnormalities and still birth. Semer et al studied the impact of increasing carbohydrate intolerance on materno-fetal outcome in 3637 women without gestational diabetes mellitus. They concluded that the increasing carbohydrate intolerance in the pregnant women was associated with significantly increased neonatal complication. Berkowitz and colleagues also had reported neonatal respiratory distress syndrome in neonates of mother showing hyperglycaemias. Neonatal hypoglycaemia is one of the most frequent problems in infants of mother showing hyperglycaemias. It is caused by excessive insulin production by the new-borns pancreatic cell, which is enlarged and hyperactive as a result of maternal hyperglycaemias. Neonatal respiratory distress syndrome is another problem in neonates of mothers showing hyperglycaemias, prematurity having significant role. Other problems faced by neonates of hyperglycaemic mother are hyperbilirubinemia because of immaturity of infants liver function. Still births without identifiable causes are a phenomenon found in pregnancies complicated by maternal hyperglycaemias. In utero exposure to maternal hyperglycaemias leads to foetal hyperinsulinaemia, causing an increase in foetal fat cells, which leads to childhood obesity and glucose intolerance is set in motion.
5. Summary & conclusion

The increasing prevalence of type 2 diabetes in general and in younger people in particular has led to an increasing numbers of pregnancies with this complication. We found 6% of gestational hyperglycaemias in the first trimester. The percentage of gestational hyperglycaemia increases to 27% in the second trimester. This is because of the progressive increase in insulin resistance that occurs during gestation, the purpose of which is likely to ensure a sustained postprandial supply of glucose to the growing foetus. With the life style modification, dietary advice and insulin therapy the percentage of gestational hyperglycaemias are reduced to 11% in the second trimester. Higher rate of gestational hyperglycaemias in this study may be because of 75% of the women in the study were belonging to the middle to higher socio-economic class. The smaller sample size may also contribute to the higher incidence of gestational hyperglycaemias.

Maternal postprandial blood glucose affects birth weight of the baby and also affects the mode of delivery. Numbers of neonatal complications is higher in the women with higher maternal postprandial blood glucose levels.

Estimation of postprandial blood glucose levels should be carried out in all pregnant women at the first antenatal visit and at least once in every trimester. This would help to reduce the incidence of assisted deliveries, neonatal morbidity and mortality.

References