Impact of Pregnancy on C-peptide Levels of Type-II Diabetic Women

SEEMEN GHAFOOR1, AZRA SALEEM2, SHAHEENA3, ABDUL WAHAB SHAIKH4

ABSTRACT

Objectives: The present study proposes to observe the changes in serum C-peptide levels, HbA1c and fasting blood sugar (FBS) levels in pregnant and non-pregnant diabetes mellitus type II (D.M) patients and compare these changes.

Method: Thirty pregnant women with D.M type II were selected for the study. The subjects were evaluated for pregnancy status and presence of D.M and then FBS, HbA1c and serum C-peptide levels were assessed.

Results: Results showed significantly decreased (P< 0.001) levels of FBS and HbA1c in pregnant group as compared to non-pregnant group where as serum c-peptide levels were significantly increased (P<0.001) in pregnant group when compared to non-pregnant diabetic group.

Conclusion: It is concluded that FBS and HbA1c levels were lowered in pregnant diabetics as compared with non-pregnant diabetics. This lowering is accompanied with increased levels of circulating C-peptide of insulin, suggesting a state of hyperinsulinemia.

Key words: C-peptide, HbA1c, Type II Diabetes Mellitus, Pregnancy

INTRODUCTION

Pregnancy is potentially diabetogenic consequently in healthy women the insulin response to glucose stimulation is augmented. The changes appear to ensure the optimal availability of nutrients for both the fetus and mother. The physiological adjustment of glucose homeostasis is closely associated with a progressive increase of fasting levels of circulating insulin as well as augmented response to glucose or a mixed meal. Rising levels of progesterone, estrogens, cortisol and human placental lactogen are held responsible for this marked increase in insulin resistance which is mediated at part receptor levels. This physiologic insulin resistance requires an increase of maternal insulin to maintain glucose homeostasis. In normal pregnancy the fasting glucose is lower than, in the non-pregnant state as a consequence of increased fetal utilization and post prandially normal glucose level is maintained at the cost of hyperinsulinemia. Pregnancy is normally characterized by progressive insulin resistance and pancreatic beta cell function I unable to compensate for insulin. Insulin resistance and hyperinsulinemia are frequently seen in overt D.M and impaired glucose tolerance. The insulin resistance of normal pregnancy may also contribute to intensify the condition in women who were already suffering from D.M. Clinical recognition and control of D.M is important because therapy, including diet and insulin and antepartum fetal surveillance can reduce the well described perinatal morbidity and mortality and maternal complications associated with these conditions.

C-peptide of insulin is a small polypeptide cleared in an equimolar ratio from pro-insulin when the body convert it to insulin. The currently available information establishes that C-peptide is not as biologically inert as previously believed. Instead, it now emerges as an active peptide hormone with potentially important physiological effects. We should consider the possibility that C-peptide is a separate entity with biochemical and physiological characteristics that are different from those of insulin. It is cleared more slowly than insulin and its circulating levels are therefore a more stable indicator of β-cell secretion than insulin itself. Serum C-peptide measurement can assist clinical management of diabetes.

Hyperglycemia as seen in DM is one of the most common medical complication during pregnancy, leads to greater percentage of maternal and fetal complication, specifically fetal malformation. Recent studies have confirmed the link between maternal hyperglycemia and adverse perinatal outcomes of which large for gestational age newborns are among the most important ones.
We know that glycosylated haemoglobin (HbA1c) levels reflect long term glucose control. A single measurement of HbA1c levels provides us an index of the average blood glucose levels over the preceding 6-8 weeks. Indeed it is a good adjunct in the management of D.M. Normally HbA1c is 4% of total Hb in non-diabetic individuals and can reach up to 15% or more in diabetics. A close monitoring of HbA1c could be used to detect the pregnant diabetes at special risk. High HbA1c values estimated in early pregnancy can indicate malformation. Poor metabolic control of maternal diabetes during the second trimester is associated with a clearly increased risk of perinatal mortality. Bad control during third trimester indicates morbidity in neonatal period.

Our study aimed to determine the changes in maternal FBS, HbA1c and C-peptide levels in the third trimester as compared to non pregnant status, in order to get a closer look at metabolic environment available for the fetus of diabetic mothers.

SUBJECTS AND METHODS

This study was undertaken in the department of Biochemistry, Basic Medical Sciences Institute Jinnah Postgraduate Medical Centre Karachi. A total of 60 women were screened for this study. The subjects were chosen from Gynae and Obs. Wards 8 and 9 JPMC and ward 7 Diabetic Clinic JPMC. Subjects included thirty pregnant diabetic women of gestational age 26-30 weeks and thirty, age matched, non pregnant diabetic women. The total number of women was divided into two groups.

Group A: 30 non-pregnant diabetic women.
Group B: 30 pregnant women with diabetes mellitus.

Group A included women with diagnosed cases of type 2 D.M of child bearing age. Group B consisted of diabetic women in their last trimester of pregnancy with single fetus. Twin pregnancies and first and second trimester pregnancies were not included. Patients suffering from type 1 D.M were not included in the study.

The subjects were asked to come in the morning after an overnight fast of at least 8-10 hrs. About 6 ml of blood was drawn from the antecubital vein after all aseptic measurer. For HbA1c estimation, 1ml of blood was saved in covered glass bottles with 1mg EDTA powder. Rest of the blood was allowed to clot in the syringe. After 30 minutes serum was centrifuged and used for estimation of glucose and C-peptide levels. Serum glucose was determined by enzymatic colorimetric (GOD-PAP) method using kit, Cat No. iod.1001191 supplied by Spinreact, SA, Spain. HbA1c was estimated by fast ion exchange resin separation method, using the kit supplied by Human-Germany Cat no.10658, C-peptide of insulin in the serum was determined by enzyme linked immunosorbent (ELISA) Kit, Cat No. Dsl-10-7000 supplied by diagnostic Systems Laboratories, Texas, USA. Results were analysed on SPSS version 10 with significance at <0.05.

RESULTS

A total of 60 subjects were studied. 30 diabetic females of child bearing age but not pregnant at the time of study were selected for group A and 30 diabetic females who were diabetic for at least 1 year and had started treatment for DM before pregnancy, were included in group B. Table 1 shows the distribution of subjects into groups A and B according to their diabetic and pregnancy status. Table 2 shows the comparison of clinical and physiological characteristics of subjects. There was no significantly difference in age, weight, height and body mass index of both groups. Group B had an average of gestational age 31.± 0.74 weeks. Fasting serum glucose was highly significantly low (p<0.001) and HbA1c was also found significantly low (p<0.001) in group B subjects with pregnancy when compared to group A of diabetes without pregnancy. Serum C-peptide levels were found to be significantly high (p<0.001) in the diabetes with pregnancy group when compared to non-pregnant group A (Table 3). Same results are shown in Fig I in the bar diagram fashion.

Table 1: Distribution of diabetic subjects according to pregnancy status

<table>
<thead>
<tr>
<th>Group</th>
<th>Distribution of subjects</th>
<th>Diabetic Status</th>
<th>Pregnancy Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>30</td>
<td>Diabetic</td>
<td>Non-pregnant</td>
</tr>
<tr>
<td>Group B</td>
<td>30</td>
<td>Diabetic</td>
<td>Pregnant</td>
</tr>
</tbody>
</table>

All Values are expressed as mean±S.E.M. The number of observation are given in parenthesis.

Table 2: Comparison of clinical and physiological characteristics of subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30.33±1.18</td>
<td>29.86±1.29</td>
</tr>
<tr>
<td>Gestational age</td>
<td>-</td>
<td>31.4±0.74</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>58.39±1.59</td>
<td>61.23±1.54</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.56±0.008</td>
<td>1.58±0.002</td>
</tr>
<tr>
<td>BMI</td>
<td>23.68±0.66</td>
<td>24.4±0.76</td>
</tr>
</tbody>
</table>

Group A= Diabetics non-pregnant, Group B= Diabetics Pregnant

Table 3: Comparisons of fasting Serum Glucose, HbA1c and C-peptide of insulin levels among group A and B. All the values are expressed as Mean±S.E.M

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS (mg/dl)</td>
<td>187.53±11.42</td>
<td>96.2***±4.40</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>10.15±0.54</td>
<td>7.60***±0.42</td>
</tr>
<tr>
<td>C-Peptide (ng/dl)</td>
<td>6.08±0.42</td>
<td>11.4***±0.90</td>
</tr>
</tbody>
</table>

***P<0.001 as compared to group A.
DISCUSSION

Diabetes mellitus is known to be associated with alteration in carbohydrates metabolism leading to glucose intolerance. Similarly pregnancy produces hormonal changes that like wise affects carbohydrates metabolism. Therefore it might be expected that any defects would be exaggerated when the two conditions co-exist. Prenatal morbidity and mortality is still higher in DM group, inspite of good vigilance which may be due to disturbance in glycemic control. The parameters studied in this study are studied by many scientists the world over during recent years.

It was confirmed decades ago that the fasting plasma glucose value is lowered during pregnancy. In our study the results were in agreement of the above statement. Group B which consisted of diabetic pregnancy had highly significantly low (P<0.001). Fasting glucose levels than group A patients, the actual values being group B (96.42±4.40) and group A (187.53±20.11). These results confirm the fasting glucose levels in pregnancy even in diabetics when compared to non-pregnant diabetics. This lowering of fasting serum glucose during pregnancy was due to utilization of glucose by conceptus.

Measurement of HbA1c provides a retrospective index of glycemic control over the 4 to 8 weeks before its determination; hence it is useful in assessing the quality of diabetic control during early pregnancy. In a study carried out by T. Lind and GA Cheyne it was found that HbA1c Levels Drops Significantly (P<0.01) than non pregnant values by 20-22 weeks of gestation and remain so thereafter. They states that HbA1c remains significantly low in third trimester in normal pregnancy than non-pregnant status, which is our period of study. In a study conducted by MD Kilby in UK it was found that HbA1c was significantly greater in Type 1 DM mothers than non-diabetic mothers being 9.6% and 6.8% respectively. Result of our study showed mean levels of HbA1c is 10.15±0.54 and 7.60±0.42 in groups A and B respectively. These results when compared, it was seen that HbA1c levels of group B are significantly low (P<0.001) than group A. This decrease could be partly due to better vigilance during pregnancy.

Normal pregnancy is associated with insulin resistance and it is noted that higher levels of insulin are necessary to achieve euglycemia. The rise in insulin requirement is also seen in diabetic patients during pregnancy. C-peptide cleaved from proinsulin is cleared more slowly than insulin and its circulating levels are therefore more stable indicator of β-cell secretion than insulin. A study done in Istanbul, Turkey by Zeynap Ersanati et al showed higher C-peptide values in gestational DM patients when compared to normoglycemic pregnant women by a difference of P<0.06. Francesco Fallucca presented his views an insulin resistance and hyperinsulinemia by reporting higher levels of C-peptide in poorly controlled diabetic mothers than better controlled diabetic mothers, Result of our study are in agreement with the above statements. Diabetic pregnancy group B revealed significantly higher values (P<0.001) when compared to non-pregnant diabetics group B. These results suggest that β-cells are functioning their levels best to coup with increased demands set by pregnancy along with glucose intolerance but pancreas is in able to fulfill the demand leading to hyperglycemia.

CONCLUSION

Normal pregnancy does not develop glucose intolerance and this euglycemia is achieved by hyperinsulinemia as confirmed by higher levels of C-peptide of insulin. Our study shows that in diabetic pregnancy hyperglycemia ensues even after over
functioning of β-cells of islets of Langerhan. In developing countries where basic health facilities are inadequate, female health care is often neglected. Attention must be paid to this issue because thorough knowledge of pregnant diabetics is required in order to improve neonatal mortality and morbidity.

REFERENCES

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