

Determinants of variations of blood glucose levels in normal pregnancy

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Abstract

Evaluation of the longitudinal change in carbohydrate metabolism in pregnant women with normal glucose tolerance should improve our understanding of carbohydrate metabolism in these women. The primary purpose of this study is to describe the changes in carbohydrate metabolism during pregnancy in apparently normal women. This study is designed to determine the pattern of fasting blood glucose and oral glucose response in healthy pregnant women, in whom blood glucose was measured in the fasting state and after oral glucose load in the 1st, 2nd and 3rd trimesters, at term and 12 weeks after delivery in the same subjects. Each patient gave her informed written consent. None of them had a history of impaired glucose tolerance. None had any other disease or were taking any medications (such as corticosteroids, anti-convulsants or warfarin sodium) that might affect glucose metabolism. Women who had multiple gestations or pregestational diabetes were excluded from the study. Subjects were also excluded if a first degree relative had type 2 diabetes mellitus or received treatment for hyperglycemia. Women who had fasting blood glucose levels exceeding 105 mg/dl in 1st trimester were excluded from the study because pregestational diabetes could not be ruled out; and women with elevated screening levels (at least 135 mg/dl) were instructed to have the 3 hour oral GTT. Each patient subsequently delivered a healthy child at term without difficulty. In the present study the mean fasting blood glucose and the mean GCT levels are found to be increasing with an increase in BMI. Even in the non-pregnant state the mean fasting blood glucose and the mean GCT levels are found to be increasing with an increase in BMI and the effect of BMI seems to be greater in the fasting state compared to GCT results.

Keywords: Determinants, blood glucose levels, normal pregnancy

Introduction

In evaluating the underlying pathophysiology of gestational diabetes mellitus, investigators have sought to identify metabolic abnormalities common to the development of NIDDM. Various reports have shown evidence for either decreased insulin sensitivity or decreased insulin response as potential mechanisms for the development of GDM. In contrast, basal endogenous glucose production rates have not been shown to differ between control and gestational diabetic women [1, 2].

Based on the studies carried out during a period of 16 months after gestational diabetes mellitus, Catalano *et al.* have hypothesized that decreased peripheral insulin sensitivity is the primary metabolic abnormality associated with the development of gestational diabetes mellitus superimposed on the many alterations in carbohydrate metabolism that normally occur during human gestation. Catalano *et al.* have found that in lean women in whom gestational diabetes mellitus developed there was a decrease in insulin sensitivity primarily before conception and in early gestation [3].

It is now suggested that all pregnant women should be screened for carbohydrate intolerance not later than 28 to 30 weeks' gestation, because the clinical history has been demonstrated to be an insensitive screening factor in the detection of gestational diabetic patients. To diagnose diabetes mellitus in pregnant women who do not have overt symptoms or a clearly abnormal blood glucose level, the only tool available is the oral glucose tolerance test (OGTT). Criteria for the abnormal oral glucose tolerance test have been proposed by some investigators, using either a 50-g oral glucose load or the 100 g standard load, during the second or third trimester of pregnancy. Glucose determinations were done either on whole blood or serum [4, 5].

Fasting glucose measurement is used in the diagnosis of diabetes in pregnancy and to monitor the patients' glycaemic control during the course of pregnancy. It is also found to be useful in screening for gestational diabetes

A lot of research has been invested in an effort to find the best screening test. The most popular screening test recommended by the Third and Fourth International Workshop Conference on Gestational Diabetes and the American Diabetes Association is the 1-hour plasma glucose level after a 50-g oral glucose challenge test (GCT), performed at 24-28 weeks gestation [6].

A recent survey confirmed that 98.5% of practitioners in obstetrics and gynecology used the 50-g glucose challenge test as a screening test for gestational diabetes mellitus. The suggested strategy is that all pregnant women should undergo the screening. If the screening test result is over a threshold value, the patient is then given the diagnostic 100-g oral glucose tolerance test (OGTT). A plasma glucose value between 130 and 140 mg/dl is commonly used as a threshold for performing a diagnostic oral glucose tolerance test (OGTT).

Evaluation of the longitudinal change in carbohydrate metabolism in pregnant women with normal glucose tolerance should improve our understanding of carbohydrate metabolism in these women.

The primary purpose of this study is to describe the changes in carbohydrate metabolism during pregnancy in apparently normal women. This study is designed to determine the pattern of fasting blood glucose and oral glucose response in healthy pregnant women, in whom blood glucose was measured in the fasting state and after oral glucose load in the 1st, 2nd and 3rd trimesters, at term and 12 weeks after delivery in the same subjects.

Methodology

Thirty one normal pregnant women were selected for this study. The study was approved by the ethical committee of the Medical College.

Selection of subjects

Women attending the Obstetrics & Gynecology outpatient department of the Govt. Medical College, were interviewed and from many volunteers 31 were selected as being in good general health, of average build, free from any family history of diabetes, and were sure of their last menstrual dates. Each patient gave her informed written consent. None of them had a history of impaired glucose tolerance. None had any other disease or were taking any medications (such as corticosteroids, anti-convulsants or warfarin sodium) that might affect

glucose metabolism. Women who had multiple gestations or pregestational diabetes were excluded from the study. Subjects were also excluded if a first degree relative had type I diabetes mellitus or received treatment for hyperglycemia. Women who had fasting blood glucose levels exceeding 105 mg/dl in 1st trimester were excluded from the study because pregestational diabetes could not be ruled out; and women with elevated screening levels (at least 135 mg/dl) were instructed to have the 3 hour oral GTT. Each patient subsequently delivered a healthy child at term without difficulty.

On the first visit the aim of the study was explained to the patients, and their cooperation was requested. The tests were performed under similar circumstances during 1st trimester, 2nd trimester, 3rd trimester and at term and 10 to 12 weeks after delivery. The last test during pregnancy was at 38 weeks rather than at 40 weeks gestation to avoid patients being lost to the series due to early onset of labor. The post-delivery tests provided non-pregnant control data.

Test procedure

To ensure homogenous testing conditions, the patients were asked to attend the unit between 8:00 and 9:00 am after overnight fasting. After sitting quietly in a chair, 50 g. of glucose in about 200 ml of water was given orally over one to two minutes. The patients remained in the chair for the whole test. Capillary blood samples were taken by finger-prick method under aseptic conditions. Prior to the glucose drink and at 60 minutes from the time the drink was started blood samples were taken. A small drop of blood is applied to the test strip and it is inserted into the glucometer. The meter showed the amount of blood glucose on its digital display.

Results

Table 1: Subjects and test characteristics

Characteristics		
Age	25.3 ± 4.1 yrs	(19-38 yrs)
Weight at beginning	52.9 ± 8.9 kg	(35-72 kg)
Parity	1.5	(1-3)
BMI	21.63 ± 3.0 kg/m ²	(15.56-28.84 kg/m ²)

The mean maternal age was 25 ± 4 yrs (range 19-38) and the mean BMI (body mass index) was 21.63 ± 3 kg/m². Of the 31 subjects selected 18 (58%) were primigravida. Parity range between 1-3 and the mean weight at the beginning of pregnancy was 52.9 ± 9 kg.

Table 2: Age distribution of the subjects

Age Group	Age (Years)	Percentage (O/o)
I	< 20	9.7
II	20 - 25	35.5
III	26 - 30	35.5
IV	31 - 35	16.1
v	> 35	3.2

Majority of patients belonged to the age group 20-30 yrs.

Distribution of BMI (body mass index) among the subjects is given in table 3.

Table 3: Distribution of BMI among subjects

BMI Groups	BMI (kg/m ²)	Percentage 010
I	>18.5	12.9
II	18.5-24.9	77.4
III	25-30	9.7

Effect of Age on blood glucose

In the present study it is observed that as age increases the fasting blood glucose is found to be increasing. The mean fasting blood glucose values of patients in group 5 (>35 yrs) were higher in all the trimesters compared to the mean fasting levels of subjects in group 1 (<20 yrs).

The effect of age on mean fasting glucose levels in the non-pregnant state shows a gradual increase in fasting levels, but the mean fasting level of group 5 is lower which may be due to small sample size.

The present study could not find any association between maternal age and glucose challenge test results.

These results may not be applicable to larger groups because the sample size was small in each group. Therefore no statistical conclusions have been made in the present study regarding the effect of age on blood glucose level. Pregnancy in subjects over the age of 35yrs and under the age of 20yrs is not common in our population.

Effect of BMI on blood glucose

In the present study the mean fasting blood glucose and the mean GCT levels are found to be increasing with an increase in BMI. Even in the non-pregnant state the mean fasting blood glucose and the mean GCT levels are found to be increasing with an increase in BMI and the effect of BMI seems to be greater in the fasting state compared to GCT results.

This result may not be applicable to larger groups because the sample size was small in each group and therefore no statistical conclusions have been made in the present study. In our population obese pregnant subjects with a BMI over 30 are rare.

Discussion

Regarding changes in the fasting plasma glucose concentration through the rest of pregnancy most studies show a modest further decline in plasma glucose between the first and second trimester, whereas a few others detect no change. Between the second and third trimesters, no decrease or even an increase is observed in some studies, whereas others show a further decrease.

One of the important confounders in studying fasting plasma glucose levels is the length of the overnight fast. It has been shown by Metzger & co-workers that a fast longer than 12 hours in pregnancy can cause a marked further decline in plasma glucose. It is possible that the decline in glucose in the later trimesters in some of the earlier studies were due to a longer period of fasting or even poor maternal nutrition.

Regarding influences of other factors on the plasma glucose concentrations, the present study shows that age and BMI might be influencing the plasma glucose level. As age increases the mean fasting glucose is found to be increasing in each trimester. But the present study could not find any association between age and GCT results.

This study also found that as BMI increases there is an increase in mean fasting glucose levels and GCT values in each trimester. The mean fasting glucose and GCT values in the non-pregnant controls were also found to be increasing as BMI increases. It is seen that the

effect of BMI is more on the fasting levels. These observations are similar to that made by Mills & colleagues who have shown that severely obese pregnant women (BMI > 30.0 kg/m²) experience an increase in blood glucose possibly relating to insulin resistance [2].

Gestational diabetes mellitus has long been regarded as a precursor of overt diabetes, particularly type 2 diabetes. The reasoning is that pregnancy is a time of decreased insulin sensitivity or, to put it another way, increased insulin resistance. Women with a propensity toward development of diabetes would be likely to have this occur transiently during pregnancy. To confuse matters, gestational diabetes mellitus is not a single entity but appears to affect a heterogeneous group of individuals, some of whom are obese and some of whom are lean, some of whom have strong family or ethnic risk of type 2 diabetes and some of whom may be on their way to development of type 1 diabetes [7].

Gestational diabetes must be searched for with screening tests and objective biochemical criteria for carbohydrate intolerance, because the clinical history of the patient is neither a specific nor a sensitive method of detecting women at risk. Oral glucose tolerance test appears to be the best tool for detecting class A diabetes and hyperglycemia. Tallarizo *et al.* suggests that even the limited degrees of maternal hyperglycemia considered to be within the normal range may adversely affect the outcome of pregnancy [8].

Conclusion

- The present study shows that age and BMI might be influencing the plasma glucose level. As age increases the mean fasting glucose is found to be increasing in each trimester
- This study also found that as BMI increases there is an increase in mean fasting glucose levels and GCT values in each trimester.

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