Plasma Glucose and Plasma Insulin Values During the 75g Glucose Tolerance Test (75g GTT) in Pregnancy

TEIJI HAMADA, KIYOTAKA YOSHIMATSU, TOSHIYUKI OOSHIMA, NORIO KUBO,
MASAHIRO TETSUO, TAKAMOTO MATSUNAGA AND TOSHI KATO

*Department of Obstetrics and Gynecology, Kurume University School of Medicine,
Kurume, 830 Japan*

Received for publication September 18, 1985

Summary: The 75g GTT was performed on 722 pregnant women to clarify the glucose tolerance during pregnancy. The results were as follows: (1) Plasma glucose values after 75g GTT were the same in category A (with potential diabetes or glycosuria) before and after 28 weeks of pregnancy, but for women in categories B (without potential diabetes and glycosuria) and C (excluding the neonatal complications in category B), the plasma glucose values were higher during or after 28 weeks of pregnancy than before the 28th week. (2) The plasma glucose after glucose loading was higher in category A than in category B or C, but there was no difference between category B and C. (3) The plasma insulin values in category B were the same before and after 28 weeks of pregnancy; but for women in categories A and C, the values were significantly higher after 28 weeks of pregnancy. (4) The incidence of a low insulinogenic index was 12.1% in category A, which was significantly higher than the indexes for categories B and C. These results may be useful to establish the normal limit of glucose values after 75g glucose loading during pregnancy.

Key words: carbohydrate metabolism—pregnancy—75g glucose tolerance test—plasma glucose value—plasma insulin value

Introduction

The recovery of glucose concentrations after glucose loading during pregnancy is delayed compared to that in non-pregnant females, and the delay increases with the length of the pregnancy. In pregnant women with diabetes, this not only can aggravate metabolic regulation, but also is the cause of gestational diabetes. The change in glucose tolerance during pregnancy is also important for establishing the diagnostic criteria for gestational diabetes.

The 75g glucose tolerance test was performed on many pregnant women, and

attempts were made to establish the upper limit during pregnancy.

Subjects and Methods

The 75g glucose tolerance test (75g GTT) was performed on 722 pregnant women visiting the Obstetric and Gynecology Department of Kurume University Hospital. At the start of the test, the subjects were classified as those before and those in or after the 28th week of pregnancy. They were further classified as having or not having episodes of maternal or fetal complications as shown in Table 1.

General precautions for the glucose tolerance test were followed for the 75g GTT. The blood was taken from the brachial vein, and the plasma glucose was analyzed by the glucose oxidase method with an autoanalyzer. Simultaneously, the plasma insulin (immunoreactive insulin, IRI) was measured by radioimmunoassay using the double antibody method. The values were statistically analyzed by the student's t-test.

Results

1. Mean plasma glucose for pregnant women

The venous plasma glucose values during the 75g GTT were examined for pregnant women in each group. Table 2 and Fig. 1. show the results. The fasting values for the group before 28 weeks of pregnancy (22 ± 4 weeks of pregnancy) and those for the group at 28 or more weeks (32 ± 3 weeks of pregnancy) were the same

TABLE 1
Clinical features of subjects enrolled in the study

Category A :	1) with an episode of potential diabetes suspect*
	2) occurrence of glycosuria during present pregnancy
Category B :	1) no episodes of potential diabetes suspect
	2) absence of glycosuria during present pregnancy
Category C :	1) no episodes of potential diabetes suspect
	2) absence of glycosuria during present pregnancy
	3) without maternal complications of polyhydroamnious and severe hypertension during present pregnancy
	4) without perinatal mortality and morbidities** during present pregnancy

* episode of potential diabetes suspect:

past history of heavy-for-date baby, history of stillbirth and neonatal death of unknown causes, family history of diabetes mellitus, and obesity greater than 20 % of ideal body weight.

** perinatal morbidity:

heavy-for-date baby, respiratory distress syndrome, asphyxia, hypoglycemia, hyperbilirubinemia, polycythemia, and congenital anomalies.

TABLE 2
Mean plasma glucose values after 75g GTT in pregnant women from each category

Categories	No of cases	Gestation week GTT performed	Plasma glucose values (M $\pm$ SD mg/dl)				
			Fasting	(time after glucose load.)			
				30 min	60 min	120min	180min
category A	40	28 weeks>	89 $\pm$ 8	137 $\pm$ 27	133 $\pm$ 36	115 $\pm$ 22	100 $\pm$ 22
	198	28 weeks $\leq$	87 $\pm$ 8	136 $\pm$ 21	140 $\pm$ 32	115 $\pm$ 22	104 $\pm$ 24
category B	43	28 weeks>	83 $\pm$ 7	116 $\pm$ 25	112 $\pm$ 28	100 $\pm$ 23	95 $\pm$ 20
	441	28 weeks $\leq$	84 $\pm$ 7	129 $\pm$ 18	127 $\pm$ 27	109 $\pm$ 20	99 $\pm$ 26
category C	28	28 weeks>	82 $\pm$ 7	115 $\pm$ 24	111 $\pm$ 24	100 $\pm$ 24	96 $\pm$ 19
	332	28 weeks $\leq$	84 $\pm$ 7	128 $\pm$ 18	126 $\pm$ 28	108 $\pm$ 18	102 $\pm$ 28
unselected	83	28 weeks>	86 $\pm$ 8	126 $\pm$ 28	122 $\pm$ 33	107 $\pm$ 24	97 $\pm$ 19
	639	28 weeks $\leq$	85 $\pm$ 8	131 $\pm$ 19	131 $\pm$ 29	111 $\pm$ 20	102 $\pm$ 25

Fig. 1. Mean plasma glucose values after 75g GTT in pregnant women from each category

Fig. 2. Mean plasma insulin values after 75g GTT in pregnant women from each category

TABLE 3

Mean plasma insulin (immunoreactive insulin, IRI) values after 75g GTT in pregnant women from each category

Categories	No of cases	Gestation week GTT performed	Plasma insulin values ($M \pm SD$ $\mu U/ml$)				
			Fasting	(time after glucose load.)			
				30 min	60 min	120min	180min
category A	33	28 weeks >	8 ± 6	65 ± 32	60 ± 37	52 ± 27	40 ± 26
	187	28 weeks $\leq$	9 ± 7	54 ± 30	62 ± 34	48 ± 30	38 ± 28
category B	39	28 weeks >	5 ± 3	38 ± 22	37 ± 21	30 ± 22	24 ± 20
	427	28 weeks $\leq$	7 ± 7	57 ± 33	58 ± 35	43 ± 31	36 ± 34
category C	25	28 weeks >	5 ± 3	35 ± 19	35 ± 17	28 ± 21	20 ± 20
	324	28 weeks $\leq$	7 ± 7	55 ± 32	57 ± 35	42 ± 30	44 ± 36
unselected	72	28 weeks >	7 ± 5	50 ± 30	47 ± 32	40 ± 27	28 ± 24
	614	28 weeks $\leq$	8 ± 7	56 ± 32	60 ± 35	45 ± 31	38 ± 29

TABLE 4

Insulinogenic index ($\Delta IRI/\Delta PG$) thirty minutes after glucose loading in pregnant women from each category

Categories	No of cases	Gestation week GTT performed	Average rate ($M \pm S D$)	Incidence of low index (index below 0.4)	
				N	%
category A	33	28 weeks >	1.3 ± 0.8	3	9.1
	182	28 weeks $\leq$	1.1 ± 0.9	22	12.1
category B	35	28 weeks >	0.9 ± 0.6	3	8.6
	418	28 weeks $\leq$	1.2 ± 0.9	25	6.0
category C	23	28 weeks >	0.9 ± 0.6	3	13.0
	316	28 weeks $\leq$	1.2 ± 1.0	24	7.6
unselected	67	28 weeks >	1.2 ± 0.7	6	9.0
	600	28 weeks $\leq$	1.2 ± 0.9	47	7.8

for all categories. Values were obtained 30 minutes, and 1, 2 and 3 hours after loading. The values after 30 minutes and 1 hour for categories B and C were higher in the women who were pregnant for 28 weeks or more than in the women who were pregnant for less than 28 weeks.

The plasma glucose values after 28 weeks of pregnancy, which included most of the subjects, were examined according to category. The fasting plasma glucose values were similar for all categories. The plasma glucose after glucose loading was higher in category A than in category B and C, but there was no difference between categories B and C.

2. The plasma insulin (immunoreactive insulin, IRI) values for pregnant women in each category

The plasma insulin values obtained during the 75g GTT was examined for each category of pregnant women. Table 3 and Fig. 2. show the results. The fasting plasma insulin obtained in the group which had the 75g GTT before the 28th week of pregnancy and those which had it after the 28th were not different for any category. The values after glucose loading for category A did not vary with the period of pregnancy, but the values for cate-

gories B and C after the 28th week of pregnancy were clearly higher than those before the 28th week.

The plasma insulin was determined for each category in the group given the 75g GTT after the 28th week of pregnancy. The fasting values and the values after glucose load did not significantly differ between categories. The mean value of the insulinogenic index at 30 minutes ($\Delta IRI/\Delta PG$, 30 min.), which indicates the insulin secretory response for the glucose load, did not significantly differ between categories. However, the incidence of cases with an insulinogenic index of less than 0.4, which indicates a poor insulin response, was 6.0 and 7.6 % for categories B and C, respectively, which were not significant different, the percentage was 12.1 for category A, which was significantly higher than percentages for categories B and C.

Discussion

The changes in blood glucose during pregnancy have been described before, but the data have not always been consistent. The recent reports are, however, consistent in that the fasting glucose gradually

decreases with the duration of pregnancy (Lind, 1980). This may occur because the mother during the fasting state utilizes lipids as energy to provide the fetus and placenta with glucose. This results in a state of accelerated starvation similar to the hypoglycemia occurring during starvation. On the other hand, after the mother eats, the glucose tolerance tends to be reduced because the insulin responsiveness is lowered (Kühl, 1975). As a results of this observation, glucose metabolism during pregnancy is considered to differ from that during non-pregnancy, and considerable attention must be paid to this difference during the treatment and diagnosis of diabetes during pregnancy.

Glucose intolerance during pregnancy will also occur in women with gestational diabetes. Therefore, glucose tolerance during pregnancy must also be examined to establish the diagnostic criteria for gestational diabetes.

In 1980, the WHO recommended a classification system and diagnostic criteria for diabetes mellitus (WHO Expertcommittee, 1980). This recommendation approved diagnostic criteria for gestational diabetes that were based on the diagnostic criteria prepared by the National Diabetes Data Group (NDDG, 1979) after the report of O'Sullivan and Mahan (1964). The criteria of O'Sullivan have been used most frequently in Europe and the United States. The mean blood glucose value plus 2 standard deviations was used as the cut off point for 752 unselected pregnant women. This method has been commonly used. Schwartz and Brenner (1982) suggested the name, impaired gestational glucose tolerance (IGGT), rather than gestational diabetes, however they used the mean GTT value of the pregnant women + 2SD as the cut off point. The mean glucose value of pregnant women was examined in this study, because it is indispensable for the determination of gestational diabetes. The results obtained for the 75g

glucose load are particularly important because few such studies have been performed.

There are several factors that affect the pregnant woman's glucose value rather than the period of pregnancy. Women who give birth to heavy-for-date babies, who have had a stillbirth or experienced a neonatal death in the past for unknown causes, who have a family history of diabetes, or who are obese are likely to have an abnormal glucose metabolism.

According to a report by Guttorm (1975), a decrease in glucose tolerance is found in 0.3 % of pregnant women who have a non-potential diabetes without glycosuria, in 3-4 % of pregnant women who have a non-potential diabetes with glycosuria and potential diabetes without glycosuria, and in 10.5 % of pregnant women who have a potential diabetes with glycosuria. The frequency of potential diabetes with glycosuria was 33 times the frequency of non-potential diabetes without glycosuria. Our subjects were classified into these categories and their mean plasma glucose values were examined after the 28th week of pregnancy, when the effect of pregnancy on glucose tolerance becomes clear. The difference in the fasting glucose values of the pregnant women from different categories was only 3 mg/dl, and was not statistically significant. The mean plasma glucose value after the glucose load for the subjects with potential diabetes or glycosuria (category A) was higher than that for the subjects with neither potential diabetes nor glycosuria (category B), a finding that indicates a difference in glucose tolerance. To determine the normal mean plasma glucose value during pregnancy, it is necessary to determine the value on subjects who had no obstetric abnormalities that might lead to abnormal glucose metabolism. The values for such a group, category C, were not very different from the values for category B. The mean plasma glucose value in normal

pregnancy $\pm 2SD$, the diagnostic criteria for gestational diabetes, was determined for categories B and C; but there was no difference between the two categories. The largest difference was 5 mg/dl, observed 2 hours after a glucose load.

Plasma insulin (immunoreactive insulin, IRI) was measured simultaneously with the 75 g GTT. In pregnant women, the fasting value (the basic insulin value) is considered to increase gradually with the length of pregnancy (Kühl, 1975); but in the present results, no clear difference was detected between the group less than and the group more than 28 weeks pregnant. On the other hand, the insulin secretion after glucose loading in categories B and C was greater after the 28th week of pregnancy than before, confirming the concept that the insulin reaction after glucose loading increases with the progress of pregnancy (Kühl, 1975; Spellacy and Goetz, 1963).

The insulin response against a glucose load is best reflected in the insulinogenic index, 30 minutes after glucose loading. The mean insulinogenic indexes for the categories did not differ. However, the incidence of women with insulinogenic indexes of 0.4 or less, considered to be a low response, was more frequent in category A than in category B and C. This shows that category A contains many more cases of lowered insulin secretion than category B or C.

From the above, it appears that measurement of glucose tolerance and the re-

lated blood insulin reaction during pregnancy using the 75 g GTT is useful in the detection of gestational diabetes.

References

- GUTTORM, E. (1975). Practical screening for diabetes mellitus in pregnant women. In *Carbohydrate metabolism in pregnancy and the new-born* ed. Sutherland, H.W. and Stowers, J.M., p. 142-152. London: Churchill Livingstone.
- KUHL, C. (1975). Glucose metabolism during and after pregnancy in normal and gestational diabetic women. *Acta Endocrinol.* **79**, 709-719.
- LIND, T. (1980). Carbohydrate metabolism. In *Clinical physiology in obstetrics* ed. Hytten, F. and Chamberlain, G., p. 234-256. London: Blackwell Scientific Pub.
- National Diabetes Data Group (1979). Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes*, **28**, 1039-1057.
- O'SULLIVAN, J.B. and MAHAN, C.M. (1964). Criteria for the oral glucose tolerance test in pregnancy. *Diabetes*, **13**, 278-285.
- SCHWARTZ, M.L. and BRENNER, W.E. (1982). The need for adequate and consistent diagnostic classifications for diabetes mellitus diagnosed during pregnancy. *Am. J. Obstet. Gynecol.* **143**, 119-124.
- SPELLACY, W.N. and GOETZ, F.C. (1963). Plasma insulin in normal late pregnancy. *New Engl. J. Med.* **268**, 988-994.
- WHO Expert Committee on Diabetes Mellitus, second report (1980). WHO Technical Report Series, No. 646.