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## Use of 100 gm. oral glucose tolerance test in postpartum period to diagnose antecedent gestational diabetes mellitus.

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*Gestational diabetes mellitus (GDM) may occur after pregnancy or become overt diabetes mellitus in later life. However, there are many pregnant women who have never been screened for GDM. The purpose of this study was to check the usefulness of the 100-gm oral glucose tolerance test (OGTT) administered within 72 hours postpartum† for diagnosing “antecedent gestational diabetes mellitus”. The study was performed prospectively in Chulalongkorn Hospital between April 1, 1991 and March 31, 1992 on 48 pregnant women who had been diagnosed as having GDM, using the 100-gm OGTT during the study group’s gestational age of 20-40 weeks. Another 125 pregnant women, having the same risk factors for GDM but who were normal when they underwent the 100-gm OGTT, became the study’s control group. The study showed that fasting plasma glucose (FPG) and one-hour plasma glucose (1-hr PG) values during antepartum OGTT were significantly different compared with the correspondy values during postpartum OGTT ( $P < 0.001$ ). These differences were not found in the control group. Using reciever operating characteristic (ROC) analysis, it was found that the threshold values for FPG, 1-hr PG and incremental 1-hr PG from postpartum 100-g OGTT could sustain high specificity (more than 90%) even when they were decreaded to a level which produced the high sensitivity level of more than 60%. The 1-hr PG threshold value of 174 mg%, during postpartum OGTT provides a sensitivity of 87.2% and specificity of 90.4% in diagnosing antecedent GDM.*

**Key words :** *Postpartum, OGTT, Diagnosis, Gestational diabetes millitus.*

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สันทิต บุญยะสง, วงศ์กุลพัทธ์ สนิทวงศ์ ณ อยุธยา. การใช้ 100 กรัม โอรัล กลูโคส ทอลเลอแรนซ์ เทซท ในระยะหลังคลอดเพื่อวินิจฉัยภาวะเบาหวานในระหว่างการตั้งครรภ์. จุฬาลงกรณ์เวชสาร 2536 กันยายน; 37(9) : 561-569

สตรีตั้งครรภ์ที่มีอาการเบาหวานเฉพาะ ระหว่างที่ตั้งครรภ์ (gestational diabetes mellitus หรือ GDM) มีโอกาสที่จะเป็นซ้ำได้ในครรภ์ต่อไป และเป็นเบาหวานในขณะที่ไม่ได้ตั้งครรภ์เมื่ออายุมากขึ้น แต่มีมารดาจำนวนมากที่ไม่ได้รับการตรวจคัดกรองสำหรับ GDM ในระยะก่อนคลอดและมีประวัติหรืออาการแสดงหลังคลอดที่ทำให้คิดว่าอาจจะเป็น GDM การศึกษานี้มีวัตถุประสงค์เพื่อประเมินประโยชน์ของการทดสอบความทนต่อกลูโคส 100 กรัม (100 gram OGTT) ในระยะหลังคลอด 72 ชั่วโมงในการวินิจฉัยภาวะการเป็นเบาหวานขณะตั้งครรภ์ โดยทำการศึกษาแบบไปข้างหน้าที่ภาควิชาสูติศาสตร์ นรีเวชวิทยา โรงพยาบาลจุฬาลงกรณ์ ระหว่างวันที่ 1 เมษายน พ.ศ.2534 ถึงวันที่ 31 มีนาคม พ.ศ.2535 ในสตรีตั้งครรภ์ที่เป็น GDM จำนวน 48 ราย และในสตรีตั้งครรภ์ปกติจำนวน 125 ราย โดยใช้เกณฑ์ในการคัดเลือกเดียวกันและพบว่าค่า น้ำตาลในพลาสมาขณะอดอาหาร และค่าน้ำตาลในพลาสมาหลังได้รับประทานกลูโคส 100 กรัมจากการทดสอบ 1 ชั่วโมง ในระยะก่อนคลอดมีความแตกต่างกับระยะหลังคลอดในกลุ่มที่เป็น GDM อย่างมีนัยสำคัญทางสถิติ ( $P < 0.001$ ) แต่ไม่ต่างกันในกลุ่มที่ไม่เป็น GDM จากการใช้ Receiver operating characteristic (ROC) curve เพื่อวิเคราะห์หาค่า เกณฑ์ในการตัดสินใจ การวินิจฉัยของระดับน้ำตาลในพลาสมาของการทดสอบความทนต่อกลูโคส 100 กรัม พบว่าค่า น้ำตาลในพลาสมาขณะอดอาหาร, ค่า น้ำตาลในพลาสมาหลังได้รับประทานกลูโคส 100 กรัมจากการทดสอบ 1 ชั่วโมง และค่าผลต่างของระดับน้ำตาลในพลาสมาหลังรับประทานกลูโคส 100 กรัมกับค่า น้ำตาลขณะอดอาหาร (incremental 1-hour plasma glucose) ยังคงมีความจำเพาะสูง โดยมีค่าเกณฑ์ในการตัดสินใจการวินิจฉัยของการทดสอบ 100 กรัม OGTT ต่ำสุดที่ยังพอเพียงที่จะมีความไวสูงสุด และค่าของเกณฑ์ในการตัดสินใจวินิจฉัยของค่า น้ำตาลในพลาสมาหลังการทดสอบ 1 ชั่วโมง (1-hour plasma glucose) ที่ 174 มิลลิกรัมเปอร์เซ็นต์ ในระยะหลังคลอดจะให้ความจำเพาะเท่ากับ 90.4 เปอร์เซ็นต์ และความไวเท่ากับ 87.2 เปอร์เซ็นต์ ในการวินิจฉัยภาวะเบาหวานในขณะตั้งครรภ์

Gestational diabetes mellitus (GDM) is defined as abnormal carbohydrate metabolism diagnosed during pregnancy in woman who had been normal before pregnancy. This abnormality will usually disappear when the pregnancy is over. However, these women remain at risk of developing overt DM when they become older. Following a pregnancy complicated by GDM, this risk is 23 percent and 60 percent in the 8 years and 16 years, respectively.<sup>(1,2)</sup>

Maternal hyperglycemia or glucosuria during puerperium and fetal macrosomia, neonatal hypoglycemia, polycythemia and hypocalcemia are not very sensitive indicators of antecedent maternal glucose<sup>(3)</sup> intolerance during pregnancy. A more specific test, which could be performed during puerperium to detect antecedent gestational diabetes mellitus, would be useful when the above-mentioned risk factors are present in gravidas, and when the women have not been screened for GDM during the antepartum period.<sup>(4-7)</sup>

This study was designed to check prospectively the usefulness of the 100 -gram oral glucose tolerance test (OGTT) administered within 72 hours postpartum in order to diagnose -antecedent gestational diabetes mellitus..

## Materials and Methods

This prospective study was performed at Chulalongkorn Hospital between April 1, 1991 and March 31, 1992 on recruited pregnant women, by randomized sampling, who met the following criteria :

### Inclusion criteria

1. Gravidas with no age limits, who attended Chulalongkorn Hospital's Antinatal Clinic. Only pregnancies which ended after 28 weeks of gestation with live or stillborn fetuses weighing more than 1,000 grams, were included.

2. Gravidas with at least one of the following risk factors<sup>(8)</sup>:

- Any degree of glycosuria detected by reagent strips (trace or more than).

- Family history of diabetes mellitus.

- Age over 30 years.

- Body weight more than 20 percent of ideal body weight calculated by the following formula :<sup>(9)</sup>

Ideal body weight (kgs) =  $(0.69 \times \text{height in cms})^2$   
-56.67.

- Multiple pregnancy.

- Previous history of macrosomic fetus (birth weight exceeding 4,000 grams)

- History of stillbirth in previous pregnancy.

### Exclusion criteria

- A metabolic disease (Cushing's syndrome, chronic liver disease, chronic renal failure).

- Known case of overt diabetes mellitus requiring insulin or oral hypoglycemic drugs as treatment.

The participants who fulfilled the inclusion criteria and who had none of the exclusion criteria were selected for the 100-g OGTT during 20 to 40 weeks of gestational age. Those whose 100-g OGTT<sup>(10)</sup> was abnormal would be diagnosed as having GDM and become a member of the study group. Those whose 100-g OGTT was normal would become a member of the control group. In the study of Carpenter M.W.<sup>(7)</sup> the sensitivity of the 100-g OGTT in diagnosing antecedent GDM (gestational diabetes mellitus) was 80 percent. The sample size of our study group was 48 participants and that of the comparative control group 125. All of the participants with GDM (study group) underwent weekly fasting and 2-hour post-breakfast plasma glucose surveillance during the antepartum period.<sup>(11,12)</sup> Insulin therapy was required by 18 of the 48 participants with GDM because of hyperglycemia. In all, normal saline solution was infused during labor. Plasma glucose was measured by the glucose oxidase method.

Within 72 hours of delivery, all participants had a 100-g 3-hour OGTT. All participants fasted more than eight hours and did not have any activity before the test. All were tested between 6 and 9 am.

### Data analysis

1. General data obtained from the study group and the control group were compared by unpaired t-test using the two-tailed p-value of 0.05 or more to determine statistical significance in the differences between the study group and the control group.

2. The differences between antepartum and postpartum data were analyzed by paired t-test using the two-tailed p-value of 0.05 or more to determine whether the differences were statistically significant.

3. Postpartum OGTT values that were evaluated included those samples taken during individual fasting, 1-hour, 2-hour, 3-hour post-glucose ingestion, the sum of incremental 1-hour and 2-hour values ( $[1\text{-hour-fasting}] + [2\text{-hour-fasting}]$  values) as well as the incremental 1-hour values (1-hour-fasting values)

4. The diagnostic utility of each test to detect GDM was evaluated by means of receiver operating characteristic (ROC) curve analysis.<sup>(13)</sup> By this method, the reciprocal relationship of test sensitivity and specificity is displayed through the range of test values, which enables comparisons of functions among competing tests.

### Results

Participants in both the study and control groups were from the same population. There were no differences in their general epidemiological background or indication for performing antepartum 100-g OGTT between the two groups, as show in table 1.

**Table 1.** General data on the participants in the study group and control group (using unpaired t-test).

General features	Study group		Control group		P-value
	Means	SDn-1	Means	SDn-1	
Age (years)	30.71	7.08	30.23	6.23	NS
Height (cm)	153.45	22.55	153.89	6.39	NS
Weight (kg)	63.61	16.52	62.12	12.60	NS
Weight gain (kg)	9.52	4.18	12.27	5.18	NS
Parity (number)	1.15	1.02	1.12	1.22	NS
The gestational age when the OGTT was done (week)	31.27	8.13	31.78	6.02	NS
The postpartum time after delivery when the OGTT was done (day)	2.02	0.81	1.63	0.71	NS
Indication of 100-g OGTT					NS (chi-square)

There were differences in the fasting plasma glucose (FPG) and 1-hour plasma glucose values in the 100-g OGTT during the antepartum and postpartum periods only in the study group, as shown in tables 2 and 3.

**Table 2.** The statistically significant difference between antepartum and postpartum 100-g 3-hour OGTT in the control group.

Plasma glucose values	Study group		
	Means (d)	SD(n-1)	p-value
FPG	13.52	24.05	<0.001
1-hr PG	34.65	44.69	<0.001
2-hr PG	11.38	63.77	NS
3-hr PG	1.31	76.62	NS
Incre. 1-hr PG	21.13	46.63	NS
Incre. 1-hr + 2-hr PG	18.97	91.77	NS

**Table 3.** The statistically significant difference between antepartum and postpartum 100-g 3-hour OGTT in the control group.

Plasma glucose values	Control group values		
	Means (d)	SD(n-1)	p-value
FPG	-1.95	10.81	NS
1-hr PG	-1.78	29.87	NS
2-hr PG	-2.34	33.47	NS
3-hr PG	-0.33	31.42	NS
Incre. 1-hr PG	-0.22	30.81	NS
Incre. 1-hr + 2-hr PG			

Using receiver operating characteristic (ROC) analysis, it was found that the threshold values for FPG, 1-hr PG and incremental 1-hr plasma glucose from the postpartum 100-g OGTT could provide high specificity (more than 90%) even when they were decreased to a level

which achieved the high sensitivity level of more than 60%. The 1-hr PG threshold value of 174 mg% during postpartum OGTT produced a sensitivity level of 87.2% and specificity level of 90.4% in diagnosing antecedent gestational diabetes mellitus, as shown in figures 1 to 6.

### FPG ROC CURVE

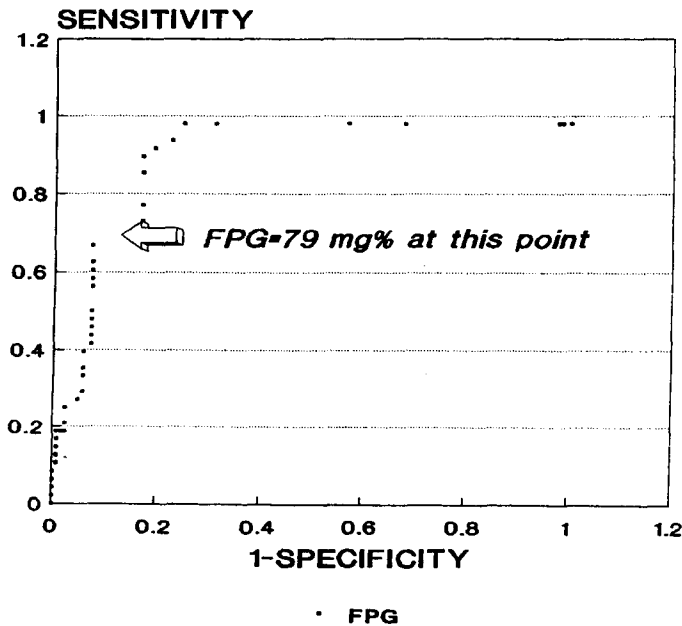


Figure 1.

### 1-HOUR PG ROC CURVE

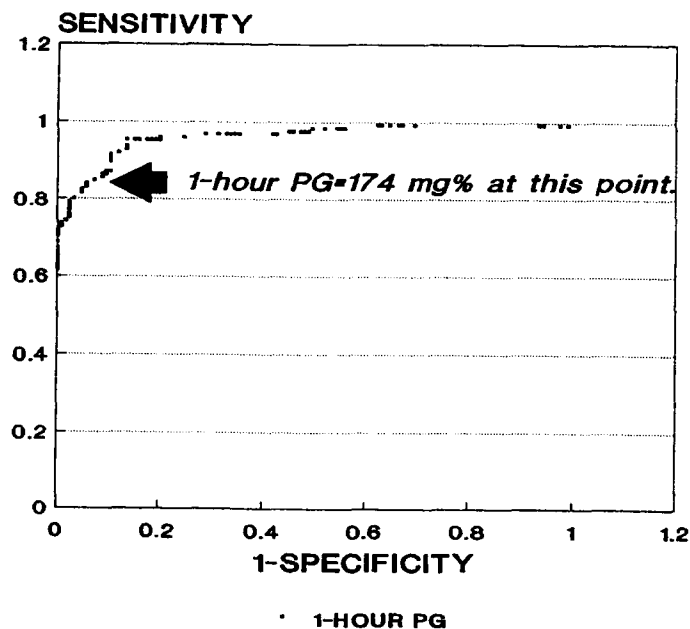


Figure 2.

### 2-HOURS PG THE ROC CURVE

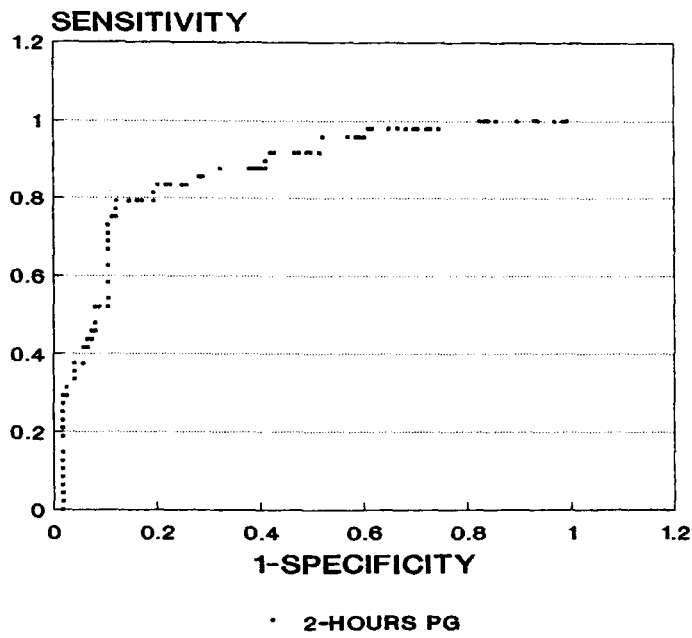


Figure 3.

### 3-HOURS PG THE ROC CURVE

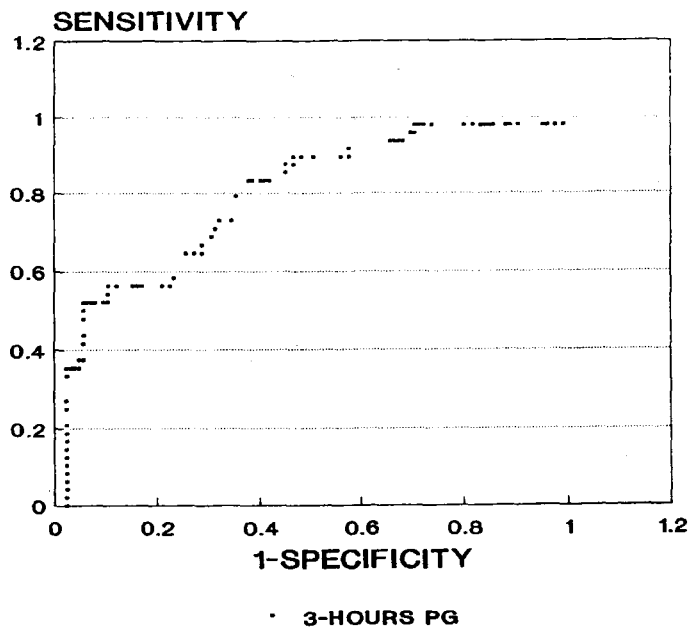


Figure 4.

### INCREMENT 1-HOUR ROC CURVE

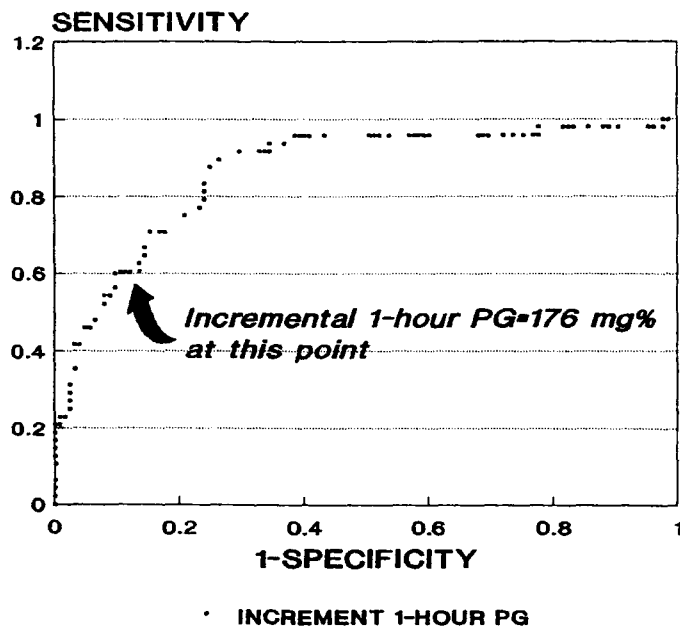


Figure 5.

### 2-HOUR INCREMENT PG ROC CURVE

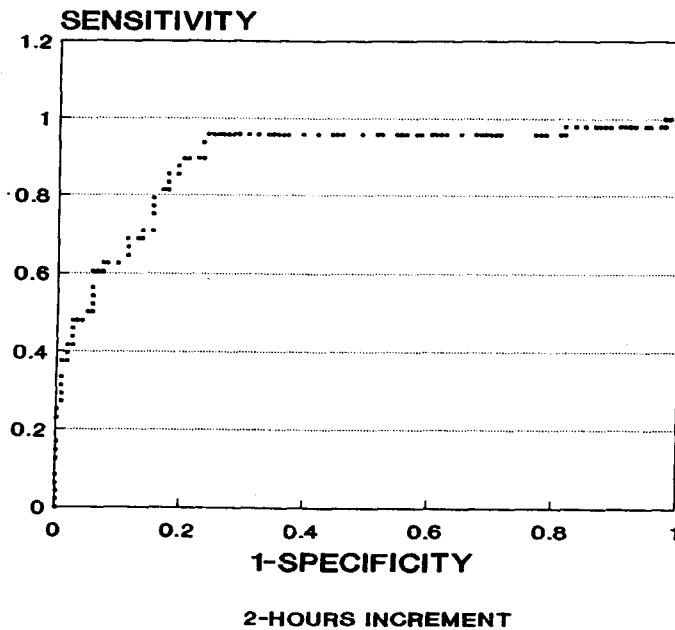


Figure 6.



In the study group, there were 30 cases of GDM class A1 (63%) and all were treated with diet control. There were 18 cases of GDM class A2 (37%) who were

treated with insulin. In the GDM class A1 group, the only statistically significant differences between antepartum and postpartum OGTT were in the 1-hour PG and incremental 1-hour PG values, as shown in tables 4 and 5.

**Table 4.** Information on participants classified as GDM in study group.(2,17)

Class of GDM	No. of Cases	(%)	Treatment	
			Diet control	Insulin
A1	30	(62)	30	0
A2	18	(38)	0	18

**Table 5.** The statistically significant difference between antepartum and postpartum 100-g 3-hour OGTT in participants who were GDM class A1 (using paired t-test).

	GDM A1		
	Means (d)	SD(n-1)	p-value
FPG	3.53	10.314	NS
1-hr	24.10	43.942	0.0055
2-hr	11.83	45.678	NS
3-hr	0.60	45.619	NS
incremental 1-hr PG	20.57	44.343	0.0180
incremental 1-hr+ 2-hr PG	28.87	81.607	NS

## Discussion

Diagnosis of gestational diabetes serves to identify gravid women at risk for perinatal morbidity and mortality.<sup>(14)</sup> Criteria for the insulin treatment in these women depend on degree of abnormality in the antepartum OGTT. O'Sullivan et al<sup>(3)</sup> have demonstrated a detection rate of 53% when historical risk factors alone are used to determine the need for an OGTT. Burt et al<sup>(4)</sup> demonstrated lower insulin and glucose concentrations in response to oral 50 gm. glucose challenge performed 4 day after delivery, compared with those evoked by the same challenge during the third trimester. Reduction in both fasting and 2.5 hours glucose concentrations occur during postpartum 50 gm. glucose challenge, when compared with antenatal values.<sup>(5)</sup> Plasma glucose levels, remained elevated through the fifth postpartum day, in response to the oral glucose challenge test.<sup>(6)</sup>

This study was performed in a population which have the same indications to screen for GDM. Participants were divided into the study group, who have abnormal antepartum 100 gm. OGTT. and comparative group, who have normal antepartum 100 gm. OGTT. Data in table 1 shows basic characteristics which were not statistically different. Their fasting plasma glucose (FPG), 1 hour plasma glucose (PG), 2 hours plasma

glucose(PG), 3 hours plasma glucose (PG), incremental 1 hour plasma glucose and incremental 2 hour plasma glucose values are, however, different both during antepartum and postpartum periods. Because the study group consist of pregnant women with GDM, the abnormal glucose tolerance in the antepartum period, caused by gestational hormones, havely estrogen, progesterone, human placental lactogen, all of which intisferes with insulin function and resulting in poor control of carbohydrate metabolism during antepartum and early postpartum period (first 72 hours).<sup>(15,16)</sup> Persistent effects of pregnancy hormones on carbohydrate metabolism are responsible for the postpartum (within 72 hour) OGTT values being different from those of the comparative group. This result can be used to detect abnormal postpartum carbohydrate tolerance for diagnosing the undetected cases of antecedent GDM.

OGTT values in antepartum and postpartum are not different in the comparative group participants, but are different in the study group. The differences are found only in FGP and 1 hour PG values. It appears that comparative group participants can control their plasma glucose levels both during antepartum and postpartum periods, but the study group participants can not. Gestational hormones interfering with the insulin's

action during antepartum period cause these pregnant women to have abnormal glucose tolerance. After delivery, these hormones are removed with the placenta and glucose tolerance recovers as evident in the decreased values of plasma glucose in 100 gm. OGTT during the postpartum period. However, the values which differ between antepartum and postpartum OGTT in the study group, are only the FPG and 1 hour PG values. This may mean that pregnancy only affects the FPG and 1 hour PG in the 100 gram. OGTT while the other values are not affected. Because of this, we can not use the antepartum criteria for abnormal OGTT to diagnose the antecedent GDM. in the postpartum period. To discover the right threshold of FPG and 1 hour PG in postpartum OGTT for diagnosing antecedent GDM, we use Receiver Operating Characteristic (ROC) curve to analyse threshold values which will give the test sensitivity of 60 percents or more, while maintaining its specificity of 90 percents or more. Analyses reveal that only FPG, 1 hour PG and incremental 1 hour PG can provide such sensitivity and specificity and the best of these three tests is the 1 hour PG at threshold value of 174 mg%, with its sensitivity of 87.2 percents and its specificity of 90.4 percents, in diagnosing the antecedent GDM during first 72 hour postpartum.

However, this study can not identify the overt DM. cases among the study group, because we had not performed OGTT on them before pregnancy. Cases of overt DM in the study group probably make the results different from what they should be.

From data in table 4 and 5, there are 18 cases of GDM class A2 and 30 cases of GDM class A1.<sup>(2,17)</sup> Analyses of data from cases of GDM class A1, which are not cases of overt DM, reveals statistically significant differences between antepartum and postpartum values of 1 hr. PG, incremental 1 hour plasma glucose of 100 gram OGTT. This supports the concept that GDM affects the 1 hour plasma glucose value in the 100 gm. OGTT more than other values. After delivery, insulin effectiveness is restored and plasma glucose levels are under control once again.

## Conclusion

During the 72 hours postpartum period pregnant women who had not been screened for GDM in antepartum period and have risk factors, should have the 100 gm. OGTT. If the one hour plasma glucose value is 174 mg% or more, attempts should be made to diagnose antecedent GDM. during pregnancy and the 100 gm. OGTT should be repeated during the next pregnancy.

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