

# THE ANALYZATION OF TIME-BLOOD GLUCOSE CURVE DURING ORAL GLUCOSE TOLERANCE TEST IN PREGNANT WOMEN

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Received Date: January 12, 2018 Accept Date: April 1, 2018 Published Date: June 20, 2018

**Abstract:** Aims: To analyse the shape of time-blood glucose curve during oral glucose (OGTT) tolerance test in pregnant women, and providing reference for future tracing scheme of blood glucose monitoring postpartum for women with a history of gestational diabetes mellitus (GDM). Methods: From January 2012 to September 2015, Pregnant women who have regular antenatal examination in the first affiliated hospital of JINAN university were selected as subjects (N=12390 cases). The OGTT was carried out during 24 to 28 weeks and the results were analysed retrospectively. Results: (1) The detection rate of GDM and PGDM were 21.63% and 1.24% respectively. (2) The majority of subjects in the GDM group was those with impaired glucose tolerance (IGT) (66.92%), followed by normal glucose tolerance (NGT) (31.02%). (3) In the GDM-IGT subgroup, the percentage of subject with type B curve was the largest (74.2%). In the GDM-NGT subgroup, the percentage of subject with type III curve was the largest (93.2%). (4) The majority of subjects in the NGDM group was those with impaired glucose tolerance (IGT) (11.18%). In the GDM-IGT subgroup, the percentage of subject with type B curve was the largest (66.82%). Conclusions: In summary, for women with a history of GDM, not all the people (about 25.82%) have high risk of development of type 2 diabetes. However, in women without a history of GDM, about 66.82% of the population still needs to be vigilant in order to prevent type 2 diabetes in the future. **Keywords** Pregnancy; High blood glucose; Oral glucose tolerance test; Curve shape; Insulin metabolism

## 1. INTRODUCTION

High blood glucose is one of the most common problems among pregnant women, and the morbidity of gestational diabetes mellitus (GDM) is increasing by years [1]. Oral glucose tolerance test (OGTT) is the golden screening and diagnostic standard for this disease, and it could predict the risk of future type 2 diabetes (T2DM) postpartum because of the each time point OGTT curve which contains evolutive information of the disease[2]. According to the shape of OGTT curve, researcher evaluated the metabolism condition and found that people with monophasic OGTT had higher insulin resistance and decreased beta-cell function

compared to those with diphasic OGTT [3-5]. Abdul *et al.* found that the insulin sensitivity and beta-cell function of subjects with normal glucose tolerance (NGT) were well if the plasma glucose soon returns to fasting plasma glucose (FPG) during OGTT, and the risk of developing T2DM was low[6]. The area under the curve (AUC) of OGTT curve reflects the geometric mean value of plasma glucose at 3 points, and it could reflect the change trend and time accumulation effect of plasma glucose, even more reflects the characteristics of glucose metabolism[7]. Even though most women with GDM can recover naturally postpartum, it is still an early warning of diabetes, metabolic syndrome and cardiovascular disease in later life [8]. Epidemiologic studies shown that

women with a history of GDM have increased risk of diabetes [9-11]. In 2017, the guideline of GDM from the American College of Obstetricians and Gynecologists recommend: (1) women with GDM should take OGTT again (4 to 12 weeks after delivery) to determine whether there was diabetes, reduced glucose tolerance or impaired fasting glucose. (2) Screening for diabetes every 1-3 years postpartum. If pregnancy again, the frequency of examination should be increased accordingly. But the guideline didn't recommend to assess pregnant women during pregnancy and predict the risk of T2DM in later life. To sum up, the risk of future T2DM is closely related to plasma glucose curve during OGTT, and comparing to other indexes, the shape of OGTT curve is more easilier used to predict the future risk of T2DM and metabolic status. However, is there any difference in the management and monitoring scheme postpartum for GDM women with different OGTT curve shape and AUC? Until now, there is no study about how to draft the management and monitoring scheme postpartum according to the different OGTT curve during pregnancy. So our study aim to analyze the shape and the AUC of OGTT curve during pregnancy, and providing reference for future tracing scheme of blood glucose monitoring postpartum for women with a history of GDM.

## 2. METHODS

From January 2012 to September 2015, Pregnant women who have regular antenatal examination in the first affiliated hospital of JINAN university were selected as subjects (N=12390 cases). The OGTT (75 grams suger) was carried out during 24 to 28 weeks and the plasma glucose were measured at 0, 60 and 120 min. According to the guidelines from The World Health Organization (2013), Based on the results of fasting plasma glucose (FPG) and 2-h post-load plasma glucose during OGTT, the subjects were divided into different group:

PGDM and GDM[12]

According to the results of OGTT, the subjects were divided into three groups:

1. Pre-gestational diabetes mellitus (PGDM): (1) FPG  $\geq 7.0$ mmol/L; and/or (2)

2-h PG  $\geq 11.1$ mmol/L during OGTT; or (3) random plasma glucose  $\geq 11.1$ mmol/L and accompanying diabetic symptom.

2. Gestational diabetes mellitus (GDM): one or more of the following standards is achieved during OGTT: (1) 5.1mmol/L < FPG < 6.1 mmol/L; (2) 1-h PG  $\geq 10$ mmol/L; (3) 8.5 mmol/L < 2-h PG < 11.0mmol/L

3. Normal Gestational diabetes mellitus (NGDM): the plasma glucose is normal before and during pregnancy.

### Impaired fasting plasma glucose (IFPG) and Impaired glucose tolerance (IGT)

Taking FPG  $\geq 6$ mmol/L and 2-h PG  $\geq 7.8$ mmol/L as nodes, subjects in the GDM group and NGDM group were divided into different subgroups:

(1) normal glucose tolerance (NGT); (2) impaired fasting glucose (IFG); (3) impaired glucose tolerance (IGT); (4) combined glucose intolerance (CGI).

GDM-NGT group: FPG < 5.1mmol/L, 1-h PG > 10mmol/L and 2-h PG < 7.8mmol/L, 5.1 mmol/L < FPG < 6.1 mmol/L and 2-h PG < 7.8mmol/L;

GDM-IFG group: FPG  $\geq 6.1$ mmol/L and 2-h PG < 7.8mmol/L;

GDM-IGT group: FPG < 5.1mmol/L, 1-h PG > 10mmol/L and

7.8 mmol/L < 2-h PG < 8.5mmol/L ; FPG < 5.1mmol/L and 8.5mmol/L < 2-h PG < 11.1mmol/L ; 5.1 mmol/L < FPG < 6.1 mmol/L and 2-h PG  $\geq 7.8$ mmol/L;

NGDM-NGT group: FPG < 5.1mmol/L, 1-h PG < 10mmol/L and 2-h PG < 7.8mmol/L;

NGDM-IGT group: FPG < 5.1mmol/L, 1-h PG < 10mmol/L and 7.8  $\leq$  2-h PG < 8.5mmol/L.

### The shape of OGTT curve

1. According to the time when plasma glucose concentration dropped to FPG (60 or 120 min) during OGTT, subjects in the NGT subgroup and IFG subgroup were divided into three types:

Type I: FPG  $\geq$  1-h PG;

Type II : FPG < 1-h PG and FPG  $\geq$  2-h PG;

Type III: FPG < 1-h PG and FPG < 2-h PG

2. According to the relationship between 1-h PG and 2-h PG, subjects in the IGT subgroup and CGI subgroup were divided into two types:

Type A: 1-h PG < 2-h PG (Biphase OGTT)

Type B : 1-h PG $\geq$ 2-h PG (monophase OGTT)

Statistical methods

#### Calculations of the area under the curve (AUC)

AUCs of OGTT curve from different glycometabolic status (NGT, IFG, IGT and CGI) were calculated by the trapezoid rule respectively, so did the curve of type I-III and type A/B. Trapezoid area = (upper bottom + bottom bottom) X high/2, AUC=FPG/2+1-h PG+2-h PG

Statistical analyses were performed with the SPSS statistical software package (19.0). Datas are presented as mean  $\pm$  S.E.M. The means were compared with T test and one-way ANOVA. Categorical variables were tested with Chi square test. Statistical significance was set at  $P < 0.05$ .

### 3. RESULTS

Table 1 The Baseline characteristics of NGDM、GDM and PGDM groups

	NGDM	GDM	PGDM	P
Age(years)	28.46 $\pm$ 4.12	30.08 $\pm$ 4.52	30.85 $\pm$ 5.34	<0.05
Number	9493	2663	153	
Constituent ratio	77.12%	21.63%	1.24%	
AUC	12.74 $\pm$ 1.73	16.31 $\pm$ 2.65	21.20 $\pm$ 4.49	<0.001

According to diagnostic criteria, subjects (n=12309) in our study were divided into three groups:(1) GDM group (n=2663); (2)NGDM group(n=9493); (3)PGDM group(n=153). The detection rate of GDM and PGDM were 21.63% and 1.24% respectively. In pregnant women with hyperglycemia, the proportion of PGDM was 5.43%.

Table 2 The Baseline characteristics of four subgroups in GDM group

	GDM-NGT	GDM-IFG	GDM-IGT	GDM-CGI	P
Age(years)	28.99 $\pm$ 4.53	29.42 $\pm$ 3.56	30.56 $\pm$ 4.44	31.61 $\pm$ 3.86	<0.0001
Number	826	19	1782	36	
Constituent ratio	31.02%	0.71%	66.92%	1.35%	
AUC	15.21 $\pm$ 3.75	13.55 $\pm$ 2.85	16.80 $\pm$ 1.67	19.06 $\pm$ 2.34	<0.0001

In GDM group, the proportion of different glycometabolism state was IGT(66.92%)> NGT(31.02%)>CGI(1.35%)>IFG(0.71%), and the age and area under curve (AUC) increased sequentially, and the difference was statistically significant. ( $P<0.0001$ ) .

Table 3 The comparison of three type cruve in GDM-NGT subgroup (n=826)

	I	II	III	P
GDM-NGT	19(2.3%)	37(4.5%)	770(93.2%)	
AUC	9.89 $\pm$ 0.96	13.21 $\pm$ 1.88	15.44 $\pm$ 3.74	<0.0001

In NGT subgroup, the number of people with type III curve was the largest (n=770), and its corresponding AUC was also the largest (difference has statistical significance). ( $P<0.0001$ )

Table 4 The comparison of two types of curves in GDM-IGT subgroup (n=1782)

	A	B	P
GDM-IGT	460(25.8%)	1322(74.2%)	
AUC	15.13 $\pm$ 1.55	17.38 $\pm$ 1.28	<0.0001

Comparing to Type A curve, the percentage of type B curve was 74.2% in IGT subgroup, and the AUC of type B was larger than type A,( difference has statistical significance) ( $P<0.0001$ ) .

Table 5 The comparison of two subgroups in NGDM group

	NGDM-NGT	NGDM-IGT	P
Age(years)	28.30 $\pm$ 4.09	29.76 $\pm$ 4.12	<0.0001
Number	8432	1061	
Constituent ratio	88.82%	11.18%	
AUC	12.50 $\pm$ 1.64	14.66 $\pm$ 1.16	<0.0001

In NGDM group, the percentage of NGT was greater than IGT (88.82% VS 11.18%). The age

and AUC of NGT were both higher and the difference was statistically significant. (P<0.0001)

Table 6 The comparison of two types of curves in NGDM-IGT subgroup

	A	B	P
NGDM-IGT	352(33.18%)	709(66.82%)	
AUC	13.40±0.95	15.82±0.62	<0.0001

In IGT subgroup, the percentage and AUC of type B curve were both larger than type A curve, and the difference was statistically significant (P<0.0001) .

#### 4. DISCUSSION

*The general conditions of PGDM, GDM and NGDM groups based on OGTT during pregnancy*

The results in our study shown that: (1) the percentage of PGDM and GDM were 1.24% and 21.63% respectively (as shown in table 1); (2) the percentage of GDM-NGT and GDM-IGT were 31.02% and 66.92% respectively; (3) In NGDM group, the percentage of women with IGT was 11.18%. So is it the same management scheme for women with and without a history of GDM postpartum?

##### 1. The management scheme for women with a history of GDM

*Abdulghani et al.*[13] analysed the clinical datas of subjects who received an OGTT at baseline and after 7-8 years of follow-up, and found that: (1) comparing to subjects whose 2-h PG was still above the FPG (type III), subjects whose 1-h PG was below the FPG (type I) had high insulin sensitivity and good pancreatic secretion function, and the risk of T2DM will be lower in the future, which means subjects belong to type III had metabolic abnormality and imparied islet function. In our study, we calculated the AUC of type III and found its AUC was the largest (table 3). The larger the AUC of OGTT curve, the higher the risk of developing T2DM in the future. So in the clinical work, for GDM-NGT women with the characteristics of type III curve, clinician should monitoring the plasma glucose 4-12 weeks after delivery and every 1-3 years postpartum, giving them diet and exercise intervention as early as possible to reduce their future risk of T2DM. Meanwhile, *Abdulghani et al.*[13] also found that in IGT subgroup, comparing to subjects whose 1-h PG was higher than 2-h PG ( type B), subjects whose 2-h PG was higher than 1-h PG (type A) had high insulin sensitivity and good  $\beta$  cells function, and the risk of T2DM will be lower in the future. In patients with IGT (7.8mmol/L< 2-h PG <11.1mmol/L), those with the characteristics

of type A curve had better outcomes in the future. In our study, the percentage of GDM-IGT subjects with type A curve was 25.8% (n=460) and type B cruve was 74.2% (n=1332). The AUC of type B was larger than type A. So we speculate that in women with a history of GDM, 25.8% of women had a lower risk of developing T2DM in the future, and the plasma glucose monitoring after delivery could be reduced appropriately. However, for women with type B curve (about 74.2%), clinician should monitoring the plasma glucose 4-12 weeks after delivery, giving them diet and exercise intervention as early as possible to reduce their future risk of T2DM.

##### 2. The management scheme for women without a history of GDM

The results of our study showed that NGDM pregnant women could be divided into NGT and IGT subgroup, and the number of people in NGT subgroup was higher. Comparing to NGT subject, the age of IGT subject was older and the AUC of the OGTT curve was larger (differences are statistically significant). In the NGDM-NGT subgroup, the percentage of type III curve was 95.17% and its AUC was the largest. We should strengthen the plasma glucose monitoring and management for them postpartum, giving them diet and exercise intervention as early as possible to reduce their future risk of T2DM. In the NGDM-IGT subgroup, about 66.82% of subjects had the characteristic of type B curve. Because people with type B curve had insulin resistance and decreased beta-cell function, and they had a 2-fold increase in the future risk of T2DM compared to people with type A curve, clinician should strengthen the plasma glucose monitoring and management for them postpartum to reduce their future risk of T2DM.

In summary, for women with a history of GDM, if 2-h PG  $\geq$  7.8mmol/L and 1-h PG <2-h PG (type A), about 25.82% of people (n=460) may not be necessary to

monitor blood glucose once every 1-3 years postpartum (which was recommended by guidelines), the time for blood glucose monitoring could be prolonged. For women without a history of GDM, if 2-h PG  $\geq$  7.8mmol/L and 2-h PG < 1-h PG (type B), about 66.82% of people (n=709) should continue be monitored blood glucose after delivery and be alerted to the occurrence of type 2 diabetes

*Inadequacies:* This study did not follow up postpartum blood glucose in every pregnant woman. In our later work, we will trace all the subjects' plasma glucose to verify the correctness of our research results.

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