

RISK FACTORS AND BLOOD GLUCOSE LEVEL IN PATIENTS WITH GESTATIONAL DIABETES MELLITUS

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ABSTRACT

Survey of some risk factors and glucose serum concentration in gestational diabetes

Objectives: To determine some risk factors and serum glucose concentrations by 75-g oral glucose tolerance test in gestational diabetes patients. **Subjects and methods:** A cross-sectional descriptive study on 60 gestational diabetes mellitus (GDM) at National Endocrinology Hospital. **Results:** The study results showed: The average of age was 30.32 ± 4.74 years, (mainly 26-30 years old (40%)), pregnancy period was mainly 25-34 weeks (63.3%). The rate of risk factors: overweight/obese prepregnancy was 71.7%; age (> 35 years old) was 26.7%; family history of diabetes was 10%; polycystic ovaries was 6.7%; gestational diabetes history was 3.4%; previous foetal macrosomia > 4000g was 1.7%. The prevalence of increasing in M0 was 36.7%, M1 was 66.7% and M2 was 71.1%. The one of three was 25.0%, the two of three was 45% and all of M0, M1 and M2 was 30.0%. There is a positive relation between maternal weight and fasting glucose (M0). Multivariable analysis showed that there were relationships between height and age of mothers and serum glucose M0 and M1. **Conclusion:** Pregnant women suffered from gestational diabetes, which was mainly at week of 25 - 34 (63.3%). The main risk factor of GDM was overweight/obesity prepregnancy (71.7%). There were relationships between weight, age and height of pregnant women and serum glucose level.

Keywords: *Gestational diabetes mellitus, 75-g oral glucose tolerance test, risk factors and plasma glucose.*

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1. BACKGROUND

Gestational diabetes is the hyperglycemic status that is first discovered in the second and third trimester of pregnancy but it is not a clear diabetes and it increases the risk of adverse pregnancy outcomes. This disease tended to increase together with the development of social economy. Gestational diabetes mellitus is one of the risks for women developing type 2 diabetes after delivery. [3] The regulation of serum glucose level plays a very important role in the development of the fetus [1],[3]. In the period of the first 3 months, severe hyperglycemia can lead to congenital malformation such as open neural tube defects, microcephaly, pericardial effusion. Besides, hyperketonemia can lead to other congenital defects...

In the middle 3 months of pregnancy, maternal hyperglycemia can slow down the development of the fetus, affect the brain development and the intelligence afterwards. Hyperglycemia in the last 3 months will not cause the fetus malformation but can lead to macrosomia, pancreatic islet hyperplasia which increases the rate of delivery accidents, as well as neonatal diabetes... [2],[3]. Therefore, effective management of blood glucose level, early diagnosis of gestational diabetes mellitus play a crucial part in clinical practice and ensuring the safe and healthy gestation period for women. Recent years in Viet Nam, the development of gestational diabetes is rather rapid, to reinforce screening

and diagnosis, we carry out this study with the objective: to determine some risk factors and serum glucose concentrations in gestational diabetes patients.

2. SUBJECTS AND RESEARCH METHODS

1. **Subjects:** 60 pregnant women suffering from gestational diabetes melitus (GDM) being treated at National Hospital in the period from 2017 to 2018.

- Subject selection: Patients who are diagnosed gestational diabetes according to the criteria of vietnamese association of diabetes and endocrinology by 75-gram oral glucose tolerance test. The diagnosis is confirmed when achieving at least one out of the three following criteria: (1) $7 \text{ mmol/l} > Mo \geq 5,1 \text{ mmol/l}$, (2). $M1 \geq 10 \text{ mmol/l}$, (3). $11,1 \text{ mmol/l} > M2 \geq 8,5 \text{ mmol/l}$.

- Exclusion criteria:

+ Had been treated diabetes, type 1 diabetes, type 2 diabetes, diabetes caused by chronic pancreatitis, pancreatic stones, using corticoid, pituitary tumour,...

+ Suffering from severe, miscarriage-threatening gestational toxicosis.

+ Comorbidity: Basedow, Pituitary tumour, SLE, Renal Failure, Heart Failure, Hepatitis, Inflammation, severe anemia...

+ Uncooperative, Do not collect enough research targets.

2. Methods

- Study design: cross-sectional descriptive study

- Choose samples by the method of convenient accumulation.

-Study content and diagnostic criteria:

All study subjects were asked, meticulously conducted clinical examination, carried out subclinical tests and registered research records according to the unified form:

+Inquire medical history, general body examination including respiratory system, cardiovascular system, urinary system, and collecting risk factors for gestational diabetes.

+ Carry out subclinical tests and routine

functional analysis: glucose level, HbA1C, C-peptide, blood lipid level...

- Risk factors for gestational diabetes, according to “national guideline for prevention and control of gestational diabetes” – Department of Maternal and Child Health (Ministry of Health – 2018).

Older than 35

Overweight, Obesity

Family history: Diabetic relatives, especially first-degree relatives.

Macrosomia $> 4000\text{gram}$

History of abnormal glucose tolerance: Previous gestational diabetes, positive glucosuria.

Asean race

Polycystic ovary syndrome.

- Calculate BMI (kg/m^2) = $\text{Body mass}/(\text{height})^2$. Assess BMI according to Asia – Pacific classification.

- Assess lipid disorders according to NCEP ATPIII (2001).

- Diagnose hypertension according to Vietnamese Cardiovascular association (2010).

- Carry out oral glucose tolerance test in pregnant woman (IDF – 2015).

Indication: all pregnant women between 24-28 weeks of gestation were tested by oral glucose tolerance test to diagnose gestational diabetes.

Pregnant women were guided not to eat in at least 8 hours (over night). During the test, prenan women were not allowed to eat, drink and smoke. Draw 5ml to test fasting glucose level (M0). Drink 75g glucose dissolved I 200 – 300 ml water in 5 minutes. Draw 5ml one hour and 2 hours after consumption of the drink. (M1, M2).

Diagnose gestational diabetes according to criteria of vietnamese association of diabetes and endocrinology: achieving at least 1 out of 3 following criteria: (1) $7 \text{ mmol/l} > Mo \geq 5,1 \text{ mmol/l}$, (2). $M1 \geq 10 \text{ mmol/l}$, (3). $11,1 \text{ mmol/l} > M2 \geq 8,5 \text{ mmol/l}$.

3. Data management and data analyses

The data was processed according to Medical statistical algorithms by SPSS 16.0 software.

3. STUDY RESULTS

Table 1. Age characteristics of study population

Age (years)	Frequency (n=60)	Proportion (%)
18–25	10	16,7
26–30	24	40
31–35	16	26,7
36–40	9	15
≥ 41	1	1,7
Mean	30,32 ± 4,74	

Patients aged between 26 – 30 account for the biggest proportion of 40%, the lowest is group from 41 to 45 (1.7%)

Table 2. Distribution of gestational age

Gestational age	Frequency (n=60)	Proportion (%)
12-24	3	5,0
25–34	38	63,3
> 34 tuần	19	31,7

Most of the patients was examined and treated between 24 – 34 weeks gestation.

Table 3. Characteristics of risk factors

Risk factors	Frequency (n=60)	Proportion
Age >35	16	26,7
First-degree relatives with diabetes	6	10,0
Previous baby > 4000g	1	1,7
Previous gestational diabetes	2	3,4
Overweight/Obesity before pregnancy	23 - 24,9	15
	25 - 29,9	21
	≥ 30	7
	Total	43
Polycystic ovary syndrome	4	6,7

Overweight/Obesity before pregnancy takes the highest rank (71.7%), the lowest belongs to macrosomia >4000g (1.7%). In the group of overweight/obesity, most of the patients have the BMI of 25-29kg/m² (35% of total), below 23kg/m² accounts for 28.3% and above 30 k/m² is 11.7%.

Table 4. Proportion of hyperglycemia at different times of glucose tolerance test

Number of hyperglycemic time	Frequency (n=60)	Proportion (%)
1	15	25
2	27	45
3	18	30
Total	60	100

The percentage of patients diagnosed with gestational diabetes by OGTT by 1 time of glucose level above diagnostic threshold is 25%.

Table 5. Proportion of impaired glucose level at different times of glucose tolerance test

Blood glucose		Frequency (n=60)	Proportion (%)
<i>Mo (mmol/L)</i>	$\geq 5,1$	22	36,7
	$< 5,1$	38	63,3
	<i>Mean</i>	4,90 \pm 0,57	
<i>M1 (mmol/L)</i>	$\geq 10,0$	40	66,7
	$< 10,0$	20	33,3
	<i>Mean</i>	10,62 \pm 1,25	
<i>M2 (mmol/L)</i>	$\geq 8,5$ and $< 11,1$	43	71,1
	$< 8,5$	17	28,9
	<i>Mean</i>	9,18 \pm 1,10	

Proportion of gestational diabetes mellitus patients with hyperglycemia at M2 is the highest (71.1%), proportion of M2 hyperglycemia is the lowest (36.7%)

Table 6. Correlation between blood glucose level and some clinical features

Features		M0 (n=60)	M1 (n=60)	M2 (n=60)
Gestational age (week)	r	-0,027	-0,141	-0,100
	p	$>0,05$	$>0,05$	$>0,05$
Fetal weight(kg)	r	-0,135	-0,153	-0,183
	p	$>0,05$	$>0,05$	$>0,05$
Fetal heart rate (bpm)	r	0,047	0,013	0,142
	p	$>0,05$	$>0,05$	$>0,05$
Maternal age (years)	r	-0,167	-0,30	0,176
	p	$>0,05$	$<0,05$	$>0,05$
Present mother's weight (kg)	r	0,342	0,115	-0,102
	p	$<0,01$	$>0,05$	$>0,05$

Blood glucose level at M1 is in a moderately negative correlation with maternal age ($p < 0.05$). Blood glucose level at M0 was in a moderately positive correlation with mother's weight during pregnancy.

Table 7. Multiple regression correlation determines the relationship between fasting blood glucose level and blood glucose 1 hour after glucose tolerance test with the number of kilograms of weight gained during pregnancy, height, maternal age and waist circumference.

Feature	M0 (n=60)			M1 (n=60)		
	β	SE	p	β	SE	p
<i>Weight gained during pregnancy</i>	-0,015	-0,094	$> 0,05$	-0,059	-0,170	$> 0,05$
Height	4,507	2,796	$< 0,01$	8,240	0,309	$< 0,05$
Maternal age	-0,31	-1,697	$< 0,05$	-0,095	-0,355	$< 0,05$
Waist circumference	0,009	0,16	$> 0,05$	-0,002	-0,019	$> 0,05$
Constant	-2,036			1,186		

The fasting blood glucose level and after 1 hour of testing were significantly related to the height and age of the pregnant women: when the height of the mother increased, the blood glucose at Mo and M1 increased; when the maternal age increased, blood glucose of Mo and M1 decreased.

4. DISCUSSIONS

1. Some risk factors of gestational diabetes mellitus

- *Age*: In this study, the mean age of gestational diabetes patients is $30,32 \pm 4,74$ (years). The result of Nguyen The Bach and co-workers among 86 pregnant women with gestational diabetes at Central Obstetrics and Gynecology hospital shows a mean age of $31,7 \pm 5,7$ [7]. Wah Cheung's study among 258 pregnant women with gestational diabetes shows a mean age of 32.5 years [6]. In our study, noticeably, there was 16.7% of the patients aged under 25. This proves that gestational diabetes mellitus is not so rare among the young pregnant women, therefore, we also need to do the screening for pregnant women under 25 years old.

- *BMI before pregnancy*: In this study, the proportion of obesity and overweight patients is 71.7%. 25% of the patients is overweight, and obesity with BMI above 25 (kg/m^2) takes up a large proportion of 46.7%. According to To Thi Minh Nguyet's study, the proportion of Gestational diabetes patient with BMI above 25 was 9.1% [5]. In Vu Bich Nga's study, the proportion of overweight and obesity before pregnancy is 9.9% [2]. It shows that together with the development of the economics and improved living condition, there is a remarkable increase in the rate of obesity and overweight. Therefore, in the future, the proportion of pregnant women with risk of gestational diabetes will increase.

- *History of previous gestational diabetes*: The result of this study shows that the proportion of patients who used to suffer gestational diabetes during their previous pregnancy was 3.4%. The proportion in Vũ Bích Nga's and Tô Thị Minh Nguyệt's was

0.3% and 2.8% respectively. However, in Magenheim's study, this proportion is rather high with 8.5% [8].

- *History of relatives with diabetes mellitus*: In this study, the proportion of patients whose relatives suffered from diabetes mellitus was 10%. Vũ Bích Nga's study shows a proportion of 13.2%. In comparison with Magenheim's study in Hungary which is a developed country, the proportion was higher with 17.4% [8]. This difference may be caused by its better primary health care system so the proportion of diagnosed diabetes mellitus was higher than in Viet Nam.

- *History of Polycystic ovary syndrome*: gestational diabetes and Polycystic ovary syndrome are one of the most common endocrine disorders among women in the age of childbirth. Both disorders are related to insulin resistance and overweight/obesity. In our study, the proportion of gestational diabetes patient with Polycystic ovary syndrome was 6.7%. Mei-Lien - Pan and co-workers studied among 7000 women with a history of polycystic ovary syndrome, with a control group of women without a history of polycystic ovary syndrome and the proportion of gestational diabetes mellitus was 20.46% and 10.54% respectively ($p < 0.05$). This leads to the conclusion that PCOS is an independent and significant risk factor of gestational diabetes. [10]. However, according to S. Mustaniemi's study, increasing risk of gestational diabetes mellitus in women with PCOS is related to the overweight and high maternal age rather than only PCOS, therefore, it should be reconsidered whether to screen gestational diabetes among women with PCOS but none of other risk factors.

2. Discussion on glucose level in patients with gestational diabetes mellitus

The characteristic of glucose metabolism in pregnant women is the decrease in insulin sensitivity, increased blood insulin and low fasting glucose concentration. The decrease in insulin sensitivity tends to increase throughout

pregnant period, to be specific, it falls by 40% in peripheral tissues. As the fetus continuously absorbed glucose and amino acid from the mother's body and because of the increase in circulatory volume, the mother's fasting glucose levels tends to fall down. It is 10 – 20mg/dl (0.55 – 1.1 mmol/l) lower than in those not in pregnancy period. Our study shows that the proportion of increased M0 glucose level is 36.7%. This corresponds with the physiologic characteristics of pregnant women, this raises another matter: if the mother has a normal fasting glucose level, she will think that she is not suffering from gestational diabetes mellitus, and it will lead to a missed diagnose. Therefore, screening pregnant women with risk factors by oral glucose tolerance test is a simple but effective and important method to diagnose implicit gestational diabetes which can only be diagnosed with M1 or M2 glucose level after OGTT.

There is a difference in the changes of the mother's body during her pregnancy between the status of fasting and fullness. In the status of fullness, mother's body develops peripheral insulin-resistance, the total amount of consumed glucose will decrease by 5- - 70% due to the insulin-resistance in this period, setting favourable conditions for fat assimilation during pregnancy to prepare for the times when the mother's body is hungry and can balance the fat breakdown that occurs at the end of pregnancy... In patients with gestational diabetes, the appearance of the disorder of blood glucose regulation, which is mainly the insulin resistance, can take place together with a relative deficiency of insulin secretion. These two are the basic mechanism of the hyperglycemia in patients with gestational diabetes. Our study shows that the proportion of patients with 1-hour-after-OGTT glucose level above 10mmol/l is 66.7%. This reflects the impaired pancreatic functions in these subjects. Meanwhile, the proportion of patients with 2-hour-after-OGTT glucose level between 8.5 and 11.1 mmol/l is the highest (71.1%). The prolonged

increase in glucose level reflects the insulin resistance in these women. This disorder is completely suitable with the pathogenesis of gestational diabetes which is insulin resistance.

We recognize that there is a positive correlation between maternal weight and the fasting blood glucose (FGB) level in this study. BMI and FBG are in a positive correlation. Obesity leads to insulin resistance in fatty tissues and liver, so obesity is considered to be a risk factor of type 2 diabetes. In our study, the number of patients with overweight and obesity BMI takes a large proportion, women also gains a lot of weight during pregnancy, so insulin resistance may have appeared before pregnancy. Insulin resistance weakens the action of insulin in the liver, make it impossible to inhibit the gluconeogenesis to increase glucose level in the status of fasting.

Besides, maternal age is negatively correlated with 1-hour-after-OGTT glucose level (M1). From the second trimester of pregnancy, the increase in HPL, cortisol and prolactin secretion contributes to the decrease in insulin sensitivity in peripheral tissues, skeletal muscles, with the peak of insulin throughout the three trimesters of pregnancy. In addition, the change in the production of inflammation factors (TNF α) and cytokines from fatty tissues contributes to the decrease in insulin sensitivity in peripheral tissues. Therefore, increasing the secretion of insulin and its blood concentration will ensure the nutrition sources for both the mother and the baby. Added to this, as the proportion of overweight/obesity is high, it worsens the insulin-resistant status and the increase in the insulinexcretion of Beta cells. This can help explain the correlation between maternal age and M1 glucose concentration.

The result also shows the correlation between the maternal age, height and the glucose level at M0 and M1. J. Brite and coworkers' study among 135861 pregnant women with 5567 diagnosed with gestational diabetes mellitus showed that the maternal

height was negatively correlated with gestational diabetes, to be specific, the mean height of pregnant women with gestational diabetes mellitus is 1.5cm lower than that of those without gestational diabetes mellitus [9]. However, the mechanism of this correlation remains unclear, and is still affected by heredity and geographic factors, therefore, to clarify this correlation, it is necessary to have analytical research performed on patients from different geographic areas.

CONCLUSIONS

After the study on 60 gestational diabetes patients at National Endocrinology Hospital.

The mean age of patients is $30,32 \pm 4,74$ (years), the dominant group is 26-30 years (40%), main gestational age is 25 – 34 weeks (63.3%). The proportion of risk factors is: 71.7% for overweight/obesity; 26.7% for age older than 35; 10% for first-degree relatives with diabetes, 6.7% for polycystic ovary syndrome, 3.4% for previous gestational diabetes and 1.7% for history of macrosomia greater than 4000g.

Tỷ lệ BN tăng glucose: M0: 36,7%, M1: 66,7%, M2: 71,1%. Tỷ lệ số thời điểm tăng glucose: 1 thời điểm: 25%, 2 thời điểm: 45%, 3 thời điểm: 30%. Có mối tương quan thuận giữa cân nặng với glucose lúc đói (M0). Khi phân tích đa biến thấy chiều cao và tuổi của thai phụ có liên quan với glucose máu M0 và M1.

The proportion of patients with increased glucose level at M0 is 36.7%; at M1 is 66.7%, at M2 is 71.1%. The proportion of patients with increased glucose level at only 1 time is 25%; 2 times is 45%; 3 times is 30%. There is a positive correlation between weight and fasting glucose level. In multivariable analysis, the height and maternal age is related to the M0 and M1 glucose level.

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