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# Effects of abnormal 75 g oral glucose tolerance test at different time points on neonatal complications and neurobehavioral development in the pregnant women with gestational diabetes mellitus (a STROBE-compliant article)

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**Abstract**

With the improvement of living standard, gestational diabetes mellitus (GDM) incidence is increasing every year. We observed the effects of abnormal 75 g oral glucose tolerance test (OGTT) at different time points on neonatal complications and neurobehavioral development in GDM.

A total of 144 newborns whose mothers were diagnosed with GDM and received prenatal examination and childbirth in our hospital from October 2015 to April 2016, were observed in this study. Pregnant women underwent 75 g OGTT and the blood glucose level was recorded on an empty stomach, as well as postprandial 1 and 2 hours, respectively. Based on the frequency of 75 g OGTT-abnormal time points, the pregnant women were divided into group 1 (OGTT abnormality at 1 time point), group 2 (OGTT abnormality at 2 time points), and group 3 (OGTT abnormality at 3 time points). Neonatal behavioral neurological assessment (NBNA) was performed on the 3 groups, respectively.

In the total score of NBNA, there was a significant difference among the 3 groups ($F = 17.120$, $P = .000$), and there were significant differences between the 3 groups (all $P < .05$). The incidence of neonatal hypoglycemia was significantly lower in groups 1 and 2 than in group 3, and the incidence of macrosomia was significantly lower in groups 1 than in groups 2 and 3 (all $P < .05$). In the 144 newborns, NBNA scoring was significantly lower in the newborns with hypoglycemia than in the newborns with normal blood glucose level, and in macrosomia than in the newborns with normal body weight (all $P < .01$).

With the increase of OGTT-abnormal time points in the pregnant women with GDM, the incidences of neonatal hypoglycemia and macrosomia rise and neonatal NBNA score decreases. Therefore, reasonable measures should be adopted as early as possible to prevent poor prognosis in the pregnant women with GDM.

**Abbreviations:** GDM = gestational diabetes mellitus, NBNA = neonatal behavioral neurological assessment, OGTT = oral glucose tolerance test.

**Keywords:** gestational diabetes mellitus, neurobehavioral development, newborns, oral glucose tolerance test

## 1. Introduction

Gestational diabetes mellitus (GDM), a kind of common high-risk pregnancy, is characterized by abnormal glucose metabolism during pregnancy. In China, with the improvement of living standard, GDM incidence is increasing every year. GDM may affect neonatal nervous system, and lead to irreversible nervous lesion in severe cases.[1,2] Zhang et al[3] have reported that the frequency of OGTT-abnormal time points is associated with pregnant outcomes; and with the increase of OGTT-abnormal time points, the risk of adverse pregnancy outcomes rises. The effects of OGTT-abnormal time point frequency in pregnant women on neonatal neurobehavioral development have not been reported. The neonatal behavioral neurological assessment (NBNA) was made by Chinese Bao et al[4] based on Brazelton behavioral assessment scale for neonates and Amiel-Tison neurologic assessment. The NBNA has been proved to be a practical, economical, effective and non-invasive method for screening neonatal early brain injury by a multi-center cooperative group from 12 Chinese cities.[5] The aim of this study was to investigate the effects of 75 g OGTT-abnormal time point frequency in pregnant women on neonatal complications and neurobehavioral development.

## 2. Subjects and methods

All study methods were approved by Institutional Review Board and Ethics Committee of North China University of Science and

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Technology Affiliated Hospital. All the subjects enrolled into the study gave written informed consent.

## 3. Subjects

A total of 144 newborns whose mothers were diagnosed with GDM and received routine prenatal examination and childbirth in our hospital from October 2015 to April 2016, were observed in this study. The average gestational weeks were (39.2 ± 1.0) in these pregnant women. The inclusion criteria were the pregnant women aged between 20 and 35 years having single full term-live birth; the pregnant women without other pregnant complications and history of drug use during pregnancy; and the pregnant women without the histories of fetal distress and asphyxia.

## 4. Methods

### 4.1. GDM diagnosis and grouping

According to GDM-diagnostic guidelines[6] made by American Diabetes Association in 2011, pregnant women underwent 75 g OGTT between 24 and 28 gestational weeks, and then the blood glucose level was recorded on an empty stomach, as well as postprandial 1 and 2 hours, respectively. It was diagnosed as GDM when the blood glucose level at any time point was higher than the blood glucose threshold (5.1 mmol/L on an empty stomach, 10.0 mmol/L at postprandial 1 hour, and 8.5 mmol/L at postprandial 2 hours). Based on the frequency of 75 g OGTT-abnormal time points, the pregnant women were divided into group 1 (OGTT abnormality at 1 time point), group 2 (OGTT abnormality at 2 time points), and group 3 (OGTT abnormality at 3 time points).

### 4.2. NBNA

Newborns received Chinese NBNA[4,5] performed by the same qualified medical staff within postnatal 3 to 5 days. NBNA includes 5 aspects containing behavioral capacity, passive muscle tension, active muscle tension, primitive reflex and general status, as well as 20 items. Each item is graded as 0, 1, and 2 scores with a total of 40 scores. The score is positively associated with neurologic function, and the NBNA <35 scores was regarded to be abnormal.

### 4.3. Diagnosis of neonatal hypoglycemia

Blood was taken from neonatal heelstick within 30 minutes after birth for determination of blood glucose level and the blood glucose level <2.2 mmol/L (40 mg/dL) was diagnosed as neonatal hypoglycemia.[7]

### 4.4. Diagnosis of macrosomia

The neonatal birth weight ≥4000 g was diagnosed as macrosomia.[8]

### 4.5. Main outcome measures

Neonatal NBNA and the incidence of neonatal complications were compared between the 3 groups. NBNA was compared between the normal newborns and the newborns with complications.

### 4.6. Statistical analysis

Statistical treatment was performed using SPSS17.0 software (SPSS, Inc., Chicago, IL). Measurement data were expressed as $x \pm s$, and underwent $t$ test and analysis of variance. Numeration data were analyzed using chi-square test or Fisher test. Statistical significance was established at $P < .05$.

## 5. Results

### 5.1. Comparison of neonatal NBNA between the 3 groups

In the total score of neonatal NBNA, there were significant differences between the 3 groups (all $P < .05$). In behavioral capacity and passive muscle tension, neonatal NBNA score was significantly lower in group 3 than in groups 1 and 2, and in group 2 than in group 1 (all $P < .05$). In active muscle tension, neonatal NBNA score was significantly lower in groups 2 and 3 than in group 1 (all $P < .05$). In primitive reflex and general status, neonatal NBNA score did not show statistical differences between the 3 groups (all $P > .05$) (Table 1).

### 5.2. Comparison of neonatal complications between the 3 groups

The incidence of neonatal hypoglycemia was 5.2% in group 1, 6.2% in group 2, and 23.0% in group 3, respectively, with a statistical difference among the 3 groups ($X^2 = 9.214$, $P = .01$). The incidence of neonatal hypoglycemia was significantly higher in group 3 than in groups 1 ($X^2 = 6.718$, $P = .01$) and 2 ($X^2 = 6.769$, $P = .009$), but there was no statistical difference between group 1 and group 2 in the incidence of neonatal hypoglycemia ($X^2 = 0.047$, $P = .828$). The incidence of macrosomia was 5.2% in group 1, 18.7% in group 2, and 33.3% in group 3, respectively, with a statistical difference among the 3 groups ($X^2 = 12.814$, $P = .002$). The incidence of macrosomia was significantly lower in group 1 than in groups 2 ($X^2 = 4.628$, $P = .03$) and 3 ($X^2 = 9.170$, $P = .002$), but there was no statistical difference between group 2

**Table 1**

**Comparison of neonatal NBNA between the 3 groups (score, $\bar{x} \pm s$).**

| Groups | n | BC | PMT | AMT | PR | GS | Total NBNA |
|---|---|---|---|---|---|---|---|
| Group 1 | 57 | 10.56 ± 0.59*,# | 7.12 ± 0.46*,# | 7.00 ± 0.50*,# | 5.76 ± 0.45 | 5.75 ± 0.43 | 36.16 ± 1.08*,# |
| Group 2 | 48 | 10.44 ± 0.54* | 7.04 ± 0.50* | 6.67 ± 0.59 | 5.86 ± 0.40 | 5.77 ± 0.42 | 35.60 ± 1.19* |
| Group 3 | 39 | 10.15 ± 0.54 | 6.77 ± 0.42 | 6.59 ± 0.49 | 5.65 ± 0.59 | 5.69 ± 0.46 | 34.85 ± 0.90 |
| *F* values | | 6.123 | 6.872 | 8.414 | 0.373 | 0.282 | 17.120 |
| *P* values | | **.003** | **.001** | **.000** | .373 | .755 | **.000** |

AMT = active muscle tension, BC = behavioral capacity, GS = general status, NBNA = neonatal behavioral neurological assessment; PMT = passive muscle tension, PR = primitive reflex.

* Indicates $P < .05$ as compared with group 3.

# Indicates $P < .05$ as compared with group 2.

**Table 2**

**Comparison of neonatal complications between the 3 groups (n [%]).**

| Groups | n | Hypoglycemia | Macrosomia |
|---|---|---|---|
| Group 1 | 57 | 3 (5.2)* | 3 (5.2)*,# |
| Group 2 | 48 | 3 (6.2)* | 9 (18.7) |
| Group 3 | 39 | 9 (23.0) | 13 (33.3) |
| $X^2$ values | | 9.214 | 12.814 |
| *P* values | | .010 | .002 |

*Indicates $P<0.05$ as compared with group 3.
#Indicates $P<0.05$ as compared with group 2.

and group 3 in the incidence of macrosomia ($X^2=3.073$, $P=.08$) (Table 2).

### 5.3. Comparison of NBNA between the newborns with complications (hypoglycemia or macrosomia) and the newborns with normal blood glucose level or normal birth weight

In the total score of NBNA, there were a significant difference between the newborns with hypoglycemia ($34.73\pm0.96$) and the newborns with normal blood glucose level ($35.71\pm1.14$) ($P<.01$). In behavioral capacity and passive muscle tension, NBNA score was significantly lower in the newborns with hypoglycemia than in the newborns with normal blood glucose level (all $P<.05$). In active muscle tension, primitive reflex and general status, NBNA score did not show statistical differences between the newborns with hypoglycemia and the newborns with normal blood glucose level (all $P>.05$) (Table 3). In the total score of NBNA, there were a significant difference between the macrosomia ($35.00\pm1.08$) and the newborns with normal birth weight ($36.74\pm1.13$) ($P<.01$). In behavioral capacity, NBNA score was significantly lower in the macrosomia than in the newborns with normal birth weight ($P<.05$). In passive muscle tension, active muscle tension, primitive reflex, and general status, NBNA score did not show statistical differences between the macrosomia and the newborns with normal birth weight (all $P>.05$) (Table 4).

## 6. Discussion

With the improvement of living standard, GDM incidence is increasing due to high fat diet, lack of exercise, and postponement of pregnant women's age. GDM not only increases the risks of type 2 diabetes mellitus and cardiovascular diseases for pregnant women themselves, but also affects fetal and neonatal development, allowing the chance of fetal congenital malformation to be 7 to 10 times higher than that in normal pregnant women. At the same time, GDM can increase the incidences of neonatal hypoglycemia and macrosomia, and may even cause damage to neonatal brain and other important organs. Recently, more and more attention has been paid to the adverse effects of GDM on the development of the neonatal nervous system.[9] NBNA, a simple and comprehensive method for neurological examination, has high sensitivity and specificity in the diagnosis of neurobehavioral abnormalities, and is widely used in the evaluation of neonatal brain development and brain injury in China.[10]

Our results indicated that in behavioral capacity and passive muscle tension, neonatal NBNA score was significantly lower in group 3 than in groups 1 and 2, and in group 2 than in group 1, demonstrating that the frequency of OGTT-abnormal time points is more in pregnant women, neonatal behavioral capacity and passive muscle tension is poorer. This may be related to the following 2 causes. Firstly, the most of pregnant women with GDM have placental vascular lesions, which make the placental vessel wall thicker and the vessel lumens narrower, readily leading to fetal intrauterine ischemia and anoxia.[11,12] Ischemia and hypoxia in fetal brain tissue will affect cerebrum, cerebellum, and brainstem function. Xie and Gou[8] have reported that the gray levels in thalamic basal nucleus as well as white matter of frontal lobe and occipital lobe, and the baseline oxygen saturation in brain tissue are lower in the newborns from the women with GDM, especially in the women with poor blood glucose control than in the newborns from women without GDM; and the newborns from women with GDM exhibit different degrees of nervous system abnormalities mainly including motor development retardation and muscular tension abnormality. Secondly, the newborns have stayed in GDM maternal hyperglycemia for a long time, so they still have postnatal hyperinsulinemia which easily leads to postnatal hypoglycemia. Repeated hypoglycemia may result in abnormal development of fetal nervous system such as cognitive disorder, visual impairment, occipital lobe epilepsy, and cerebral palsy. The abnormality of passive muscle tension may occur at the earliest.

Our results indicated that the incidence of neonatal hypoglycemia was significantly higher in group 3 than in groups 1 and 2, the incidence of macrosomia was significantly lower in group 1 than in groups 2 and 3; and NBNA scoring was significantly lower in the newborns with hypoglycemia than in the newborns with normal blood glucose level, and in macrosomia than in the newborns with normal body weight. Our results suggest that neonatal low NBNA score in the pregnant women with GDM is associated with high incidences of neonatal hypoglycemia and macrosomia, which is consistent with previous reports.[13,14]

Our results suggest that the frequency of OGTT-abnormal time points is more in pregnant women, the incidence of neonatal hypoglycemia or macrosomia is higher and neonatal NBNA score is lower; so stratified management should be performed on the pregnant women with GDM. GDM, a high-risk pregnancy, has been paid more and more attention, and we have

**Table 3**

**Comparison of NBNA between the newborns with hypoglycemia and the newborns with normal blood glucose level (score, $\bar{x}\pm s$).**

| Groups | n | BC | PMT | AMT | PR | GS | Total NBNA |
|---|---|---|---|---|---|---|---|
| Normal glucose | 129 | 10.43±0. 57 | 7.02±0.49 | 6.78±0.55 | 5.76±0.42 | 5.68±0.46 | 35.71±1.14 |
| Hypoglycemia | 15 | 10.07±0. 59 | 6.73±0.45 | 6.67±0.48 | 5.67±0.48 | 5.47±0.51 | 34.73±0.96 |
| *t* values | | 2.351 | 2.176 | 0.772 | 0.784 | 1.672 | 3.196 |
| *P* values | | .020 | .031 | .441 | .435 | .097 | .002 |

AMT = active muscle tension, BC = behavioral capacity, GS = general status, NBNA = neonatal behavioral neurological assessment, PMT = passive muscle tension, PR = primitive reflex.

**Table 4**

**Comparison of NBNA between the newborns with macrosomia and the newborns with normal birth weight (score, $\bar{x} \pm s$).**

| Groups | n | BC | PMT | AMT | PR | GS | Total NBNA |
|---|---|---|---|---|---|---|---|
| Normal weight | 119 | 10.45 ± 0.56 | 7.03 ± 0.49 | 6.80 ± 0.56 | 5.76 ± 0.42 | 5.68 ± 0.46 | 36.74 ± 1.13 |
| Macrosomia | 25 | 10.16 ± 0. 62 | 6.84 ± 0.47 | 6.64 ± 0.49 | 5.68 ± 0.47 | 5.46 ± 0.50 | 35.00 ± 1.06 |
| *t* values | | 2.261 | 1.713 | 1.309 | 0.885 | 1.155 | 2.978 |
| *P* values | | .025 | .089 | .193 | .377 | .097 | .003 |

AMT = active muscle tension, BC = behavioral capacity, GS = general status, NBNA = neonatal behavioral neurological assessment, PMT = passive muscle tension, PR = primitive reflex.

accumulated a lot of management experience for GDM. We should pay more attention to the pregnant women with abnormal OGTT at all the 3 time points, and they should receive integrated management provided by a healthcare team containing obstetric department, pediatrics, and nutrition department. Firstly, set up medical records for the high-risk pregnant women and let pregnant women fully understand GDM harm, improving the compliance of pregnant women. Secondly, one-to-one guidance for nutrition and exercise is performed, diet and exercise program are made based on required calorie intake, the body weights of pregnant women are regularly monitored and OGTT is re-detected during late-gestation if necessary. Thirdly, the blood sugar level should be under real-time control. If the diet treatment fails to control blood sugar satisfactorily, insulin should be used as early as possible to effectively control blood sugar, reducing the occurrence of macrosomia. Fourthly, the conditions of pregnant women and fetal intrauterine situation are regularly assessed. Delivery plan is made timely and the timing of pregnancy termination is determined. During childbirth, the maternal blood glucose level and fetal intrauterine situation are monitored. Neonatal hypoglycemia should be actively prevented and treated after birth.

The limitation of this study was that the neonatal outcomes were not stratified according to glycaemic control in pregnancy and intra-partum, which will be further investigated in our future studies. In addition, we only performed NBNA in newborns within postnatal 3 to 5 days. However, it has been reported that Continuous NBNA scoring can discover some problems in infant growth and development, and help to carry out effective intervention measures.[14,15]

In summary, the frequency of OGTT-abnormal time points is more in pregnant women, the incidence of neonatal hypoglycemia or macrosomia is higher and neonatal NBNA scoring is lower. Therefore, stratified management should be performed on the pregnant women with GDM, especially on the pregnant women with abnormal OGTT at all the 3 time points.

## Author contributions

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**Methodology:** Jie Wen.
**Writing – original draft:** Jian-li Zhou.
**Writing – review and editing:** Jun Xing.

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