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The Impact of Gestational Diabetes Mellitus on Motor Development in 12-Month-Old Children Referred to Qazvin University of Medical Sciences, Iran

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Abstract

Background

The development of the brain during fetal period affects the functioning of the nervous system the whole of the lifetime. Numerous maternal disorders during pregnancy can affect fetal neural development, one of which is gestational diabetes. Gestational diabetes mellitus (GDM) can have a long-term negative impact on the fetal neural development. The aim of this study was to investigate the effect of gestational diabetes on motor development of 12-month-old children.

Materials and Methods: In this prospective cohort study, 439 pregnant mothers referred to Qazvin University of Medical Sciences, Qazvin, Iran, who met the inclusion criteria were sampled at 24-28 weeks of gestation. Then these women were followed-up until child birth and after birth until 12 months afterwards. The process of motor development of their children at the age of 12 months was studied using the Age and Stage Questionnaire.

Results: The results of this study showed that among the women who participated in the study, 87 mothers had gestational diabetes. Of the 12-month-old children of the mothers who participated in this study, from 24 children with motor developmental delays, 11 children belonged to GDM mothers (87 women), whereas the rest (11), were born from the non-diabetic women (352 women). The relative Risk of motor developmental delay in children born to mothers with gestational diabetes was 1.49 (95%, CI = 0.98-1.87).

Conclusion

The present study showed that gestational diabetes can be a powerful risk factor for child motor developmental delay (both fine and gross motor skills).

Key Words: Child, Gestational Diabetes Mellitus, Gross Motor Skills, Motor Developmental.

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1- INTRODUCTION

In recent years, the rate of diabetes mellitus in developed countries has increased dramatically, and in parallel with this increase, studies on the impact of this disease on people's health have been prioritized (1). One of the important areas for research is to investigate the impact of this disease on pregnancy and health of women and their children. Pregnancy is a diabetogenic condition (2), that factors such as being overweight before pregnancy, especially in combination with rapid weight gain during pregnancy, can provide the basis for the onset of gestational diabetes mellitus (GDM) (3). GDM is a known risk factor for the mother and fetus health (1). GDM appears to be associated with neonatal micronutrient status, anthropometric status at birth, and neural development of the infant (4). The development of the brain during embryonic and early life plays a decisive role in the lifelong functioning of the brain in various cognitive, motor, linguistic and behavioral domains. The third trimester of pregnancy is the most important time for neurodevelopment, synapsogenesis, and arborization of embryonic dendrites (5-7).

Therefore, changes in the intrauterine environment at different stages of fetal life can have long-lasting effects on brain function and development (8, 9). Gestational diabetes is one example of such changes (9). In recent years, several studies have shown that children born to mothers with gestational diabetes are at risk of delayed speech, motor development, neurodevelopment, and cognitive impairment at different stages of childhood (10-13). Child motility may play an important predictor of neurodevelopmental problems in adulthood, and because previous studies have suggested contradictory results in this regard (11,12,14,15), the aim of this study was to investigate the impact of gestational diabetes mellitus on motor development in 12-month-old children referred to Qazvin University of Medical Sciences, Iran.

2- MATERIALS AND METHODS

2-1. Study design and population

This was a prospective cohort study. This study was conducted in Qazvin, Iran between June 2018 and April 2019. Participants were 439 pregnant women who met the inclusion criteria as gestational age 24 to 28 weeks, aged 18 to 35 years, 18<BMI<25, single pregnancy, the number of pregnancies less than 4, uncomplicated pregnancy, with no presented chronic history, never smokers and alcohol, term labor. Gestational diabetes was diagnosed using a "one-step" 2-h 75-g oral glucose tolerance test (OGTT) at 24–28 weeks' gestation. Diagnosis of GDM was based on the American Diabetes Association guidelines (1): women whose plasma glucose level met one of the following criteria were considered as having GDM: fasting plasma glucose level (FPG) ≥ 92 mg/dL, 1 h OGTT≥180 mg/dL, and 2 h OGTT≥153 mg/dL (1). Exclusion criteria included: infants and neonates with congenital malformations, birth weight less than 2500 grams, child with any disease affecting the development of the child.

2-2. Sample size calculation

The sample size was calculated based on the articles (10-12), and type one error (α) of 0.05 and type two errors (β) of 0.20 with the power of 80%, the calculated sample size with considering10% dropouts was 439 persons. A purposive sampling was conducted on the basis of the household population of health centers affiliated to Qazvin University of Medical Sciences and in this study sampling was conducted purposeful and accessible.

2-3. Method

In the present study, the primary outcome was motor development in 12-month-old children of mother with GDM. The secondary outcomes were the fine and gross development in 12-month-old children in mother with GDM. Anthropometric measurements were conducted by a trained midwife at baseline and at the end of the study. Weight and height were measured using a Seca 713 scale without shoes and in light clothing to the nearest 0.1 kg and 0.1 cm, respectively. The scale was calibrated after weighting 10 times. BMI was calculated as the ratio of the current body weight to height squared (kg/m2). Demographic and midwifery characteristics (such as mother's and father's age, mother's and father's education, mode of child birth) were collected by researcher-made questionnaire.

Midwifery questionnaire included pre-pregnancy BMI, level of education, mode of delivery, parity, smoking and alcohol consumption during pregnancy, history of chronic illnesses and adverse pregnancy outcomes in present or previous pregnancies, which were asked through interviewing with pregnant mothers. Variables such as maternal age, socioeconomic status (including mother's education level, father's education level, mother's job, father's job, monthly income adequacy, housing status), being exposed to cigarette smoke, and maternal weight gain during pregnancy, gestational age and birth weight were controlled by statistical tests. The motor development of the children born of these women at the age of 12 months was assessed by the Ages and Stages Questionnaire (ASQ). All mothers were asked to complete the questionnaire at home and to submit it to the midwife within a two-week period (15). Contact number was given to all mothers to communicate if necessary with the midwife. After obtaining the questionnaires, the scores of each domain were calculated and summed. Also, children's medical history including weight, height, head circumference and APGAR at birth, gestational age at birth, and infant feeding (breast milk, infant formula or combination) were also extracted from children's medical records. The reliability of ASQ, determined by Cranach's alpha ranged from 0.86 and the inter-rater reliability was 0.93. The validity determined by factor analysis was satisfactory.

2-4. Ethics statements

This study was approved by the Ethics Committee of the Shahid Beheshti University of Medical Sciences (IR.SBMU.PHARMACY.REC.1398.092). Qazvin University of Medical Sciences**,** Iran gave permission for sampling**.** All participants provided written and informed consent.

2-5. Statistical analysis

All statistical analyses were performed using statistical package for social sciences (version 21; SPSS Inc., Chicago, IL, USA). All statistical tests were two-sided and a significant association was confirmed at P-value < 0.05, and the confidence coefficient was 95%. We used two independent samples-t test for quantitative variables, chi-square test for qualitative variables and Mann-Whitney test for ranking variables. Normality of variables was checked by a histogram chart and one-sample Kolmogorov-Smirnov test. To control the effect of confounder variables (mother's age, father's age, mother's education, father's education, mode of child birth) on the study results, these variables were matched in both groups. All conflicted variables were matched in both groups. Also, we used multivariate logistic regression model for determining the relative risk of motor developmental delay in children born to gestational diabetic mothers.

3- RESULT

In this study, 439 pregnant women with the research characteristics referring to health centers related to Qazvin University of Medical Sciences were followed since 24-28 weeks of pregnancy up to 12 month-old children. Among all participants, 87 (19.8%) mothers were diagnosed with gestational diabetes. The mean of mother's age with gestational diabetes was 25.7±2.5 years and the mean of healthy mother's age was 25.3±2.4 years. The majority of mothers in both groups were first time mother (87% in mothers with gestational diabetes mellitus and 91% in healthy mothers). Two groups (mothers with gestational diabetes and healthy mothers) did not have a statistically significant difference in terms of age, gestational age and gravidity. The midwifery and demographic characteristics of mothers participating in this study are listed in **Table.1**. There was no statistically significant difference between the two groups in terms of neonatal sex, socioeconomic status (p> 0.05).

Table-1: Distribution of mothers based on midwifery and demographic characteristics in both groups (mothers with gestational diabetes mellitus and healthy mothers).

Characteristics	GDM	Healthy mother	P-value
Mother's age (year)	25.7±2.5	25.3±2.4	0.23
Neonatal Sex (girl)	44(50/57%)	186(52.84%)	0.11
Mode of Delivery (normal vaginal delivery)	48(55.17)	201(57.1%)	0.55
Mother's Education (diploma)	71(81.60%)	294(83.52%)	0.74
Mother's job	80(91.95%)	329(93.46%)	0.17
Father's Education (diploma)	76(87.35%)	301(85.5%)	0.69
Father's job (self-employment)	58(66.66%)	230(65.34%)	0.36

GDM: Gestational diabetes mellitus.

Characteristics of medical history of children including weight, height, head circumference and Apgar at birth, gestational age at birth, and infant feeding (breastfeeding, bottle feeding or combination) in two groups of mothers (with gestational diabetes and healthy mothers)separately has been shown in **Table.2** and these characteristics of children in both groups were not significantly different (p> 0.05).

Table-2: Distribution of 12-month-old children based on baseline characteristics divided into both groups (mothers with gestational diabetes mellitus and healthy mothers).

Characteristics	GDM	Healthy mother	P-value
Birth weight (gr)	3465±1753	3127±1581	0.45
Birth height (cm)	50±2.5	50±2.1	0.11
Birth head circumstance (cm)	33±1.1	33±1.4	0.55
APGAR min 1(score9)	81(93.1%)	330(93.75%)	0.74
APGAR min 5 (score10)	87(100%)	352(100%)	0.17
Mode of feeding (breastfeeding)	70(80.45%)	280(79.54%)	0.23
Birth gestational age (weeks)	38±5	39±1	0.64

GDM: Gestational diabetes mellitus.

According to **Figure.1**, among the total number of 12-month-old children of the mothers participating in this study, 24 (5.46%) children had motor developmental delays, of which 11 (12.6%) children were classified as being born to the mothers with gestational diabetes mellitus and 13 (3.69%) children were classified as being born to healthy mothers. Multivariate logistic regression model showed that the relative risk of motor developmental delay in children were born of mothers with gestational diabetes was about 1.5 times more than children who were born of healthy mothers (RR = 1.49, 95% CI = 0.98- 1.87), (**Table.3**). Of these children with motor developmental delay, 14 children (58.33%) had developmental delays in fine motor skills and 10 children (41.67%) had developmental delays in gross motor skills. Among the 14 children with developmental delays in fine motor skills, 8 children (9.1%) were born of mothers with gestational diabetes mellitus and 6 children (1.70%) were born of the healthy mothers. Multivariate logistic regression model showed that the relative risk of developing fine motor skills delay in infants born of mothers with gestational diabetes is about 1.6 times more than children who were born of healthy mothers (RR=1.59, 95%CI= 0.88-1.92), (**Table.3**). Of the 10 children with gross motor skills developmental delays, 6 (5.7%) children were born of the mothers with gestational diabetes mellitus and 4 (13.1%) children were born of healthy mothers. Multivariate logistic regression model showed that the relative risk of developing gross motor skills delay in infants who were born of mothers with gestational diabetes is about 1.4 times more than children who were born of healthy mothers (RR=1.37, 95% CI= 0.81-1.73) (**Table.3**).

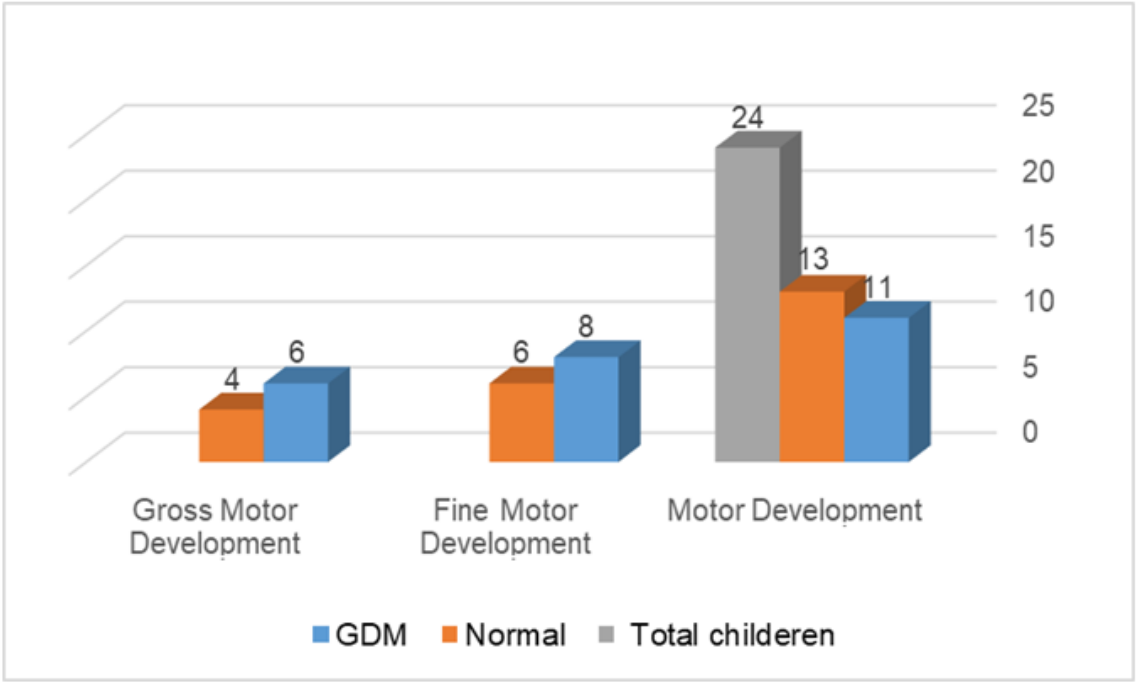

Fig.1: Distribution of 12-month-old children based on motor developmental delay and developmental delays in fine and gross motor skills domain in both groups (mothers with gestational diabetes mellitus and healthy mothers).

Table-3: Multi varieties logistic regression (95% CI) for developing motor development delay based on mother with GDM.

Developmental Delay	Relative Risk	95% CI	P-value
Motor Developmental Delay	1.49	0.98-1.87	0.03
Fine Motor Developmental Delay	1.59	0.88-1.92	0.02
Gross Motor Developmental Delay	1.37	0.81-1.73	0.02

CI: Confidence interval, GDM: Gestational diabetes mellitus.

4- DISCUSSION

The objective of this study was to investigate the impact of gestational diabetes mellitus on child motor development. The present study showed that gestational diabetes can be a potentially powerful risk factor for childhood motor developmental disorders (both fine and gross motor skills). Although there has been a lot of research in this area, there is still no specific model that illustrates how maternal gestational diabetes affects motor development in children (17). High blood sugar can make unfavorable conditions inside the cavity of the uterus and this increases the likelihood of disturbance in brain development (12). Maternal gestational diabetes can be associated with low general intelligence, speech disorders, attention deficit disorder, irritability and behavioral problems in children (18). Robles et al. (2015) found that gestational diabetes mellitus was not significantly associated with delayed motor development in children, but these children were significantly affected by intra- and postnatal events (17). In the present study, there were no postnatal risk factors in the sampled children and factors such as prematurity, low birth weight and low Apgar at birth were considered as high risk pregnancies and children with these characteristics were not included in the present study. Among the variables of maternal age, maternal body mass index, maternal socioeconomic status, neonate sex, birth weight and maternal gestational diabetes in the logistic regression model, only gestational diabetes was associated with delayed motor development in 12-month-old children. Gestational diabetes mellitus is one of the adverse consequences of pregnancy that in severe and uncontrolled cases can damage the fetus's brain cells and there is still no indicator or cut off point that indicates developmental delays or child's brain dysfunction may be due to this condition, so it is necessary to get a complete history (18). In addition, maternal gestational diabetes can increase the likelihood of the infant being admitted to intensive care units, infant complicated breathing, and breathing with mechanical ventilation and oxygen therapy (19). Dionne et al. (20) examined the motor and linguistic development of children born of diabetic mothers and healthy mothers from the age of 18 months to 7 years. They found that infants who were born of diabetic mothers had significantly lower linguistic and motor developmental (in fine and gross motor skills) scores than infants who were born of healthy mothers at several time points, such as at 18 months of age. In our study, after using the logistic regression model, we found that 12-month-old children who were born of mothers with gestational diabetes were more likely to have motor developmental delays. This result is in line with the results of the previous study. Numerous studies have shown that following accumulation of ketone bodies due to inadequate and poor control of blood glucose, the level of blood β-O-hydroxy butyrate (β-OHB) is

increased and that leads to acidosis and damage to fetal nerve cells (15). Damm et al. (2016) found that increased maternal blood glucose during pregnancy can adversely affect children's psychomotor development and whatever the increase in the level of blood glucose and β-OHB, children are more likely to have a disorder in their psychomotor development. That way the verbal development score of children who were born of diabetic mothers was 101.1 versus 108.10 in children who were born of healthy mothers and the motor developmental score of children that were born of diabetic mothers was 97.3 versus 100.5 in children that were born of healthy mothers (21).

Numerous studies have investigated the psychomotor performance of children born of diabetic and healthy mothers (18-21). The results of these studies showed that children who were born of diabetic mothers have greater degrees of attention deficit, low cognitive scores, and delayed motor development in both fine and gross motor skills. The results showed that there was a negative relationship between psychomotor development and β-OHB levels. The controversy about this situation still remains and studies have not yet reached a consensus (15). From the strengths of this study, control of many confounder variables influencing child development such as gestational age, high maternal age, complicating pregnancy (1), maternal mental disorder (22), socioeconomic status, mother's and father's job and education (23). Also, all of the children's assessment in this study were full term and did not have any developmental malformations or congenital diseases. According to the findings, further studies are necessary to understand other risk factors influencing children's motor developmental delays. We also recognize some limitations. Firstly, the number of cases was relatively small and the study was only conducted in one city. Therefore, the findings do not necessarily apply to all children. Further studies at a national level should be assessed. Secondary, the answers provided by mothers on the questionnaire may be incomplete or inaccurate due to recall bias. This may have influenced our results.

5- CONCLUSION

In this study, there was a significant impact of maternal gestational diabetes mellitus on motor delay in 12-month-old children in both the fine and gross motor skills. Since the development of the child, especially child motor development is an important indicator that can influence all stages of a child's life. Results present notable implications for the clinical practice such as the necessity of screening for gestational diabetes for all pregnant mothers and appropriate treatment to control the blood glucose of diabetic mothers, to inform the mothers about the effect of gestational diabetes and maternal high blood glucose on the motor development of the children. It is suggested that pregnant mothers to take part in programs , in order to increasing pregnant mother's physical activity and modify their life style and diet in order to control maternal blood glucose.

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7- CONFLICT OF INTEREST: None.

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