

# Correlation between high-risk pregnancy and developmental delay in children aged 4–60 months

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**Background:** The future development of children is considered more than ever now due to the advances in medical knowledge and thus the increase in survival rates of high-risk infants.

This study investigated the correlation between high-risk pregnancy and developmental delay in children aged 4–60 months.

**Methods:** This descriptive study was conducted on 401 mothers and their children (4–60 months) who visited health service centers affiliated to Isfahan University of Medical Sciences, Iran, in 2011. Sampling was carried out in several stages, and the Ages and Stage Questionnaire was completed by the participants. Data were analyzed with SPSS 18 software and independent *t*-test; Mann-Whitney and logistic-regression tests were used.

**Results:** The average age of children in the low-risk pregnancy group was  $22 \pm 16$  months, and that in the high-risk pregnancy group was  $18.9 \pm 14.8$  months. The majority of children were female (53.1%). The prevalence of high-risk pregnancies was 80.5%, and the prevalence of developmental delay was 18.7%. Multiple pregnancies, low birth weight, habitual abortions, maternal medical disorders in pregnancy, and gestational diabetes had significant correlations with developmental delay in children ( $P < 0.04$ ). In the logistic model, male gender, low birth weight, family marriage, and maternal medical disorders during pregnancy showed significant correlations with developmental delay in children ( $P < 0.05$ ). Additionally, abnormal body mass index (BMI) and social and economic status showed probability values close to the significance level ( $P = 0.05$ ), whereas other high-risk pregnancy variables had no correlation with developmental delay in children. A correlation between high-risk pregnancy and developmental delay ( $P = 0.002$ ) and fine motor delay was observed ( $P = 0.02$ ), but no correlation was observed between high-risk pregnancy and other developmental domains.

**Conclusion:** This study showed that some high-risk pregnancy variables had a significant correlation with developmental delay. Moreover, a significant correlation was observed between high-risk pregnancy and fine motor developmental delay.

Keywords: *high-risk pregnancy; development delay; Ages and Stages Questionnaire*

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Pregnancy is considered high-risk if the mother, fetus, or infant is more exposed to death, disability or sickness (1). The most important factors for these risks are maternal malnutrition, pregnancy at  $< 18$  years or  $> 35$  years, short interval between pregnancies, more than five pregnancies, preeclampsia, placental abruption, immaturity and intrauterine growth restriction, mother's underlying diseases, addiction, and

being deprived of primary care during pregnancy (2). Based on the mother's history, 10–20% of pregnancies are considered high-risk, and, in general, 50% of perinatal mortality and morbidity are among those pregnancies that are considered high-risk (3).

Improvements in medical science have succeeded in increasing the survival of vulnerable infants and have raised the issue of future development of these

children (4). Developmental delay is a term that generally refers to children who do not show the expected developmental properties according to their age (5). The main causes of developmental disabilities remain unknown. Infants who are in danger of developmental delay have a history of one or more risk factors in the period before, during, or after birth. In these high-risk infants, gross motor developmental delay is 30% more than in a 'normal' population. Most infant deaths and developmental disorders are related to immaturity, low birth weight, maternal complications during pregnancy, and congenital malformations (chromosomal and metabolic) (6). According to Piek et al., only gestational age affects fine motor skills at school age (7). Newborn disabilities increase with decreasing gestational age, but this factor has no influence on child development, and there is no difference between preterm children (34–37 weeks) and term children ( $\geq 39$  weeks) from a developmental aspect (8). In another study, variables such as maternal age at delivery, kind of delivery, Apgar score, consanguineous marriage of parents, and gender were irrelevant to developmental delay (9). In the study of Ryan-Krause et al., low maternal age at birth was considered an important factor affecting child development (10). Hediger et al. reported that low levels of parental education, age of the mother, high gravidity, low birth weight, and preterm labor are significantly associated with delayed motor and social development (11). In one study, first-minute Apgar scores  $< 7$ , maternal age, emergency or elective cesarean, postpartum hemorrhage, and threatened abortion were significant factors for cognitive and communicative-social development, whereas factors such as preeclampsia and premature rupture of the membrane had no significant relationship (12). In a study conducted in the city of Karaj in Iran, diabetes and hypertension during pregnancy, vaginal bleeding and spotting, and a history of previous abortion were factors affecting motor development of children (9). In a study by Squires et al., the use of assisted reproductive methods was associated with developmental problems in children (13). Thus, different studies have not reached a consensus on this issue.

Due to the numerous problems involved with having a child afflicted by developmental delay, early diagnosis and timely referral are very important and can benefit children with developmental disabilities and their families (14). Thus, monitoring child development and screening to detect such problems at each child visit is very important. The developmental evaluation should include five motor development areas (gross and fine motor skills), cognitive and emotional development, communication (perception and speech) development, problem-solving development, and socio-personal development (3).

Because only 30% of children with developmental problems are detected by primary healthcare providers

during routine examinations, detection of high-risk pregnancies is necessary to focus more on developmental care services during infancy and childhood in this group of children (6) and children diagnosed with developmental threatening factors in fetal life should be followed immediately after birth. The objective of this study is to investigate the correlation between high-risk pregnancy and developmental delay in children aged 4–60 months.

## Materials and methods

This study was cross-sectional in which the correlation between high-risk pregnancy and developmental delay in children from 4 to 60 months old in health centers affiliated with the Isfahan University of Medical Sciences, Iran, in 2011 was evaluated.

Inclusion criteria included Iranian mothers who had 4–60-month-old children, at least elementary education, recorded prenatal care in their dossier, and additionally, the child that was not hospitalized after birth for non-obstetric reasons. Exclusion criteria included gravidity of five or higher, birth interval of less than 3 years, smoking or alcohol consumption during their pregnancy, prolonged pregnancy ( $> 42$  full weeks), children living with a single parent, and obvious congenital anomalies.

High-risk pregnancy was defined as having at least one of the following variables:

General factors include maternal body mass index (BMI)  $\geq 26$  or  $< 20$  and maternal age  $< 20$  years or  $\geq 35$  years. Pregnancy and childbirth factors include chronic diseases (anemia, diabetes, high blood pressure, and thyroid, autoimmune, cardiovascular, renal, and neurological diseases), diseases during pregnancy (eclampsia and preeclampsia, gestational diabetes mellitus), bleeding during pregnancy, multiple pregnancies, preterm labor, low birth weight, history of infertility, pregnancy by assisted reproductive technology, or emergency cesarean section.

All information provided by the mother was recorded in their health dossier.

Sampling was carried out in a multistage format. First, the list of all health centers affiliated with the Isfahan University of Medical Sciences and Health Services was obtained from the Department of Health of Isfahan. After dividing the city into nine areas – North, Northwest, Northeast, South, Southwest, Southeast, Central, East and West-healthcare centers were selected as clusters based on the population of children younger than age 5 years that covered by each center. Sampling days from each center were selected randomly using an Excel program, and each center was coded on a map. The minimum required sample size was estimated to be 356 by using the following formula:

$$n \geq \frac{z_{1-\alpha/2}^2(1 - P)}{\varepsilon^2 P}$$

where

$$\begin{aligned}\alpha = 0.05 &\Rightarrow z_{1-\alpha/2} = 1.96, \\ P &= 0.75, \\ \varepsilon &= 0.06.\end{aligned}$$

Data gathering tools included an informational form containing demographic, economic, social, medical, and reproductive history (the recent pregnancy and previous ones). Other information was collected from pregnancy medical reports based on the designed checklist.

The developmental status of children was measured in five areas using the Ages and Stages Questionnaire. This questionnaire has been used in many studies (15–18). A researcher using interview, observation, and examination techniques completed it. This test consisted of 19 questionnaires at ages 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 27, 30, 33, 36, 42, 48, 54, and 60 months. There were 30 questions for each age group that consisted of six questions for each of the five areas of communication such as gross motor skills, fine motor skills, problem-solving skills, and personal–social skills. Three options were available for each of the 30 questions: ‘yes’ for when the baby was fully able to perform the activity in the question, ‘not yet’ for the activities in question that have never been done, and ‘sometimes’ for the ability to perform the activity in some cases. The answer ‘yes’ was awarded 10 points, the answer ‘sometimes’ was awarded 5 points, and the answer ‘no’ with zero points. After completing the questionnaires, the scores were compared with predetermined cut-off points based on standardization. Adaptation and standardization in Iran was finished in 2009 under the observation of University of Welfare and Rehabilitation Sciences, Ministry of Health and Medical Education, UNICEF, the Education of Exceptional Children Organization, Office of Population, and the Family Health and Institute of Exceptional Children, with a validity of 0.84 and a reliability of 0.94. The ability of this test for determining developmental disorders is >96% (19). If a child fails to obtain the cut-off score in each of the five areas, he/she has a problem in that area and should be followed up by a specialist to determine whether he/she is healthy or has a disorder.

The content validity method was used to validate the informational form. First, questions were set, and they were corrected by asking the opinions of 10 members of the faculty and professors of obstetrics and gynecology at Shahid Beheshti University of Medical Sciences. The questionnaire was also given to 10 mothers to complete in order to check its functionality. The reliability of the form was measured by the re-testing method with the same 10 mothers after 1 week. A significant correlation was observed in answers to quantitative questions (Pearson’s correlation coefficient was 98%) and answers

to qualitative variables questions (McNemar test and Kappa coefficient of  $P = 1$ ).

The reliability of this checklist was measured using the simultaneous measurement method (the correlation coefficient was 94% from 10 checklists).

The Ages and Stages Questionnaire has validity of 0.83–0.88, reliability of 0.90–0.94, sensitivity of 38–91%, and specificity of 79.3–91% (7, 10, 20, 21).

However, after researchers identified children with developmental delays, they were referred to medical centers to repeat the Ages and Stages Questionnaire to make sure that the diagnosis was correct.

After introducing and explaining the research objectives to the parents and obtaining verbal consent from them, sampling began. The subjects were free to accept or reject participation in the study, and they could withdraw from the study at their own discretion. After completing the study, results were given to heads of research centers of this study.

Data were analyzed with SPSS version 18 (Chicago, IL, USA). The following statistical methods were used: the independent *t*-test for maternal age variables, head circumference at birth, and the child’s age and socioeconomic status; the chi-square test for BMI, multiple pregnancies, chronic diseases, infertility, pregnancy with assisted reproductive techniques, vaginal bleeding during pregnancy, and type of delivery; the Mann–Whitney test for premature infant variables; odds ratios for two-way qualitative variables; and the logistic regression test for the correlation between high-risk pregnancy variables and developmental delay in children.

## Results

The average age of low-risk pregnancy mothers was  $31.26 \pm 1.3$  years, and that of high-risk pregnancy mothers was  $27.56 \pm 4.7$  years. The majority of them were housewives (87.8%) with a high-school level education (45.9%). The average age of the children was  $22 \pm 16$  months in the low-risk pregnancy group, and  $18.9 \pm 1.48$  months in the high-risk pregnancy group. The majority of children were female in high-risk pregnancy (52.3%) and in low-risk pregnancy (62.5%) group.

The prevalence of high-risk pregnancy was 80.5% in the city of Isfahan, and the most common causes of high-risk pregnancy were abnormal BMI (16.7% underweight, 15% overweight, and 7.7% obese), emergency cesarean delivery (7.37%), medical diseases during pregnancy (7.21%), consanguineous marriage of parents (7.18%), and vaginal bleeding during pregnancy (7.15%).

The prevalence of childhood developmental delay was 18.7%. The highest prevalence of developmental delay was in the area of fine motor skills (7.2%), and the lowest was in the area of socio-personal skills (1.7%).

There was a significant correlation between high-risk pregnancy and developmental delay (Table 1).

The variables of multiple pregnancy, low birth weight, gestational diabetes, habitual abortion, disorders during pregnancy and child's age showed a significant correlation with developmental delay (Table 2), and variables of abnormal maternal BMI and socioeconomic status demonstrated cross-border probability (Table 3). Other high-risk pregnancy variables showed no significant correlation with developmental delay.

Male gender, low birth weight, consanguineous marriage of parents, and disorders during pregnancy were also significantly correlated with developmental delay (Table 2).

### Discussion

In this study, there was a significant correlation between high-risk pregnancy and developmental delay in children. During these pregnancies, the probability of complications such as abortion, fetal death, preterm labor, intrauterine growth restriction, fetal or neonatal diseases, congenital malformations, trauma and asphyxia during labor, complications resulting from hospitalization in neonatal intensive care units, and mental retardation is higher than in other pregnancies.

In the year 2004, Sajedy and Alizadeh found that prenatal risk factors have no significant association with developmental delay, but these children were more affected by risk factors during and after birth (6). In separate evaluations, some high-risk pregnancy variables were significantly correlated with developmental delay. Additionally, average developmental domain scores regarding pregnancy status showed that the average score of each of the five developmental domains in children from low-risk pregnancies was higher; hence, there was only a significant correlation between high-risk pregnancy and developmental delay in the area of fine motor skills.

Among the high-risk pregnancy variables, multiple pregnancy, low birth weight, habitual abortion, diabetes, and medical disorders during pregnancy were significantly correlated with developmental delay in children. Multiple pregnancies are associated with complications such as prematurity and low birth weight, which can indirectly be a factor in developmental delay. In these pregnancies, other complications such as fetal distress and asphyxia are frequently seen, and these can affect

child development (6). Generally, infant mortality rate, infant cerebral palsy, and hydrocephalus have a reverse relationship with low birth weight (3). In contrast, those factors that reduce intrauterine growth of a fetus also cause problems during infancy, and those problems lead to developmental disorders in children.

In addition, the effect of gestational diabetes on fetal development is unknown, but studies show that gestational diabetes has little effect on cognitive development of a child in the future. Habitual abortion increases the detection of genetic abnormalities, presence of lupus anticoagulants, anti-cardiolipin antibodies, or an unfavorable physical environment in the uterus. Hence, the probability of impaired brain development as a result of fetal damage during pregnancy increases (22).

Disorders during pregnancy place a pregnancy at risk, and not only can they affect brain development of the fetus, but they also put the neonate in a high-risk group and, consequently, admission into a neonatal unit, where breathing with a mechanical ventilator and oxygen therapy is inevitable. Thus, these medical disorders can affect fetal and childhood development (6).

Conversely, in the logistic model, male gender, low birth weight, consanguineous marriage of parents, and medical disorders during pregnancy were also significantly correlated with developmental delay in children.

In this study, male gender was significantly correlated with developmental delay in children. Hediger et al. found that developmental delay in social and motor areas is significantly higher in boys than in girls (11). Kerstjens et al. believed that developmental delay is 1.5–4.7 times more frequent in boys than in girls (21). In contrast, in the study of Piek et al., gender was not effective on children's development (7). Lin et al. reported that developmental delay occurs two times more often in boys than in girls (14). Also, Chakrabarti and Fombonne found that the prevalence of pervasive developmental disorders is significantly higher in boys than that in girls (23). Unlike other results, Soleymani et al. reported that gender is not significantly correlated with developmental delay (9). Additionally, Sajedy and Alizadeh considered gender has no effect on developmental delay (6). It may be that gender is not significantly correlated with developmental delay, but the correlation in other areas such as socio-

**Table 1.** Correlation of high-risk pregnancy and developmental delay (and 5 domains of development)

Domains	High-risk pregnancy (%)	Low-risk pregnancy (%)	P
Communication delay	6.5	1.3	0.09
Gross motor delay	4.6	1.3	0.1
Fine motor delay	8.7	1.3	0.02 (OR = 7.3)
Problem-solving delay	6.2	2.6	0.2
Personal-social delay	2.2	0	0.3
Developmental delay	21.7	6.4	0.002 (OR = 4.04)

**Table 2.** Risk factors associated with developmental delay in children aged 4–60 months

Risk factors	Developmental delay group		P	Odds ratio (OR)
	Frequency	%		
Medical disorders in pregnancy	24	27.6	0.01	1.96
Gestational diabetes	7	38.9	0.03	2.95
Habitual abortion	4	50	0.04	4.4
Multiple pregnancy	5	50	0.02	4.6
Consanguineous marriage	19	25.3	0.049	1.84
Male gender	42	22.3	0.04	1.7
Low birth weight	14	43.8	>0.001	4.6

economic and communication may be higher. Therefore, this study also showed a significant probability.

As a result, congenital metabolic disorders, which are transferred mainly as an autosomal recessive gene, are associated with developmental delay in children. This factor, consanguineous marriage of parents, which causes these sorts of diseases, is easily preventable (6).

In low birth weight neonates, due to contexts and factors leading to intrauterine growth retardation, this can cause many problems during infancy such as low blood sugar, asphyxia, polycythemia, hypothermia, and dysmorphology. Additionally, it is possible that due to low birth weight and its underlying complications, admission to neonatal intensive care units is more frequent and leads to developmental disorders in children.

Kerstijens et al. found that underweight and premature children (<32 weeks) were significantly different from the control group regarding all developmental areas, and that

**Table 3.** Correlation of high-risk pregnancy variables with developmental delay in children aged 4–60 months.

Variable	Developmental delay	Normal development	P
Maternal BMI (kg/m <sup>2</sup> )			
Underweight (BMI <19/8)	16 (23.9)	51 (76.1)	0.051
Normal (BMI =19/8–26)	38 (15.6)	205 (84.4)	
Overweight (BMI=26–29)	14 (23.3)	46 (76.7)	
Obese (BMI >29)	7 (22.6)	24 (77.4)	
Socioeconomic status	–0.2 (1.1)	0.04 (0.97)	0.053

low birth weight and prematurity increase the chance of developmental delay (21). Hediger et al. also considered that low birth weight is relevant to developmental delay in social and motor areas (11). However, Glasson and Petterson reported that children with impaired cognitive development had similar birth weights in comparison with a control group (12).

Soleimanyhezad et al. found that low birth weight is associated with motor developmental delay (4, 9). Additionally, Sajedi and Alizadeh confirmed this result in their study (6). Furthermore, Piek et al. found the same result (7). Moreover, Golombok et al. reported that low birth weight does not affect the emotional and behavioral development of a child, but these children have a weaker performance in language developmental skills (24). In contrast, Piek et al. believed that low birth weight has a significant relationship only with fine motor skills at school age ( $r=0.4$  and  $P=0.022$ ) (7). Glasson and Petterson also reported that anthropometric indices (head, weight, and head circumference at birth) are not significantly associated with autism (12). Hediger et al. reported that low birth weight is the most important prenatal predictor of development in girls, whereas both low birth weight and gestational age are associated with social and physical developmental delay in boys (11).

Furthermore, we found that a child's age was significantly correlated with developmental delay, and the incidence of developmental delay was higher in older age groups ( $P>0.001$ ). The age at which the developmental problem is detected depends on three factors: (1) the intensity and complexity of the child's problem; (2) the socioeconomic status of the family; and (3) the quality of personal healthcare (including doctors and healthcare providers) (14). Older children can perform major developmental activities such as sitting, walking, and speaking. This explains why parents are more concerned about a delay in such activities and take action to find the cause, whereas developmental delay is noticed less by parents of younger children.

Therefore, it is necessary to pay more attention to the development of children of high-risk pregnancy. Also, this study showed that children with developmental delays are detected at older ages. Despite the 'integrated child health care' program, problems with children's development still exist. Therefore, it is necessary to pay attention to educating midwives, medics, and healthcare students about these problems.

## Conclusions

To increase the survival rate of neonates and effectiveness of early intervention, the aforementioned risk factors could be considered valuable clues. Routine neurodevelopmental screening of neonates and infants for early detection of neurodevelopmental delay is highly recommended. If economic limitations prevent mass screening

of neonates, at least high-risk infants should be routinely evaluated.

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