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Risk Factors of Developmental Delay in Children Under 5 Years Old in Tabriz: A Case-control Study

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ABSTRACT

Introduction: Developmental Delay (DD) refers to a child's inability to attain developmental milestones compared to healthy peers. Although evidence shows that DD has irreparable impacts on children's lives, several aspects continue to remain unknown.

Objective: This study aimed to investigate the risk factors of DD in children under 5 years old in Tabriz, Iran.

Materials and Methods: This case-control study was conducted in 2022 on 150 mothers of children with DD (case group) and 150 mothers of healthy children under five years without DD (control group). The case group was selected via convenience sampling from the Comprehensive Developmental Center in Tabriz. The DD was diagnosed using the Ages and Stages Questionnaires (ASQ). The control group was selected via cluster sampling from the health centers in Tabriz. The data collection tool was a questionnaire measuring sociodemographic/clinical/obstetric/child-related characteristics. In bivariate analysis, independent t-test, chi-square test, and chi-square test for trend (linear-by-linear association) were used. The variables with significant differences were entered into a multivariate logistic regression model (enter method) to find the predictors.

Results: The mean age of mothers was 33.4±6.2 years in the case group and 30.3±5.1 years in the control group. Male children comprised 65.3% of the case group and 52% of the control group. According to the multivariate regression model, mother's secondary school education or lower (OR=0.81, 95% CI; 1.25%, 6.28%, P=0.012), history of child hospitalization (OR=3.02, 95% CI; 1.69%, 5.40%, P=0.001), emergency cesarean-section (OR=2.47, 95% CI; 1.10%, 5.53%, P=0.028), maternal infection during pregnancy (OR=5.0, 95% CI; 1.48%, 16.85%, P=0.009), and Intrauterine Growth Restriction (IUGR) (OR=3.7, 95% CI; 1.1%, 12.6%, P=0.038) were significantly associated with increased risk of DD; whereas, breastfeeding (OR=0.49, 95% CI; 0.27%, 0.87%, P=0.016) and male gender (OR=0.53, 95% CI; 0.32%, 0.89%, P=0.016) were significantly associated with decreased risk of DD.

Conclusion: Given the risk factors of DD in children under five in Tabriz, targeted developmental screening and early intervention for high-risk children are recommended. Promoting maternal education, prenatal care, and breastfeeding, alongside improved neonatal monitoring, can help mitigate DD risks.

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Highlights

- The development of children is affected by various factors.
- Male gender and breastfeeding can predict the decreased risk of DD in children under five years.
- Emergency cesarean section, mother's low education, history of child hospitalization, and maternal infection can predict the increased risk of DD in children under five years.

Plain Language Summary

The development of children is affected by socioeconomic, biological, maternal, environmental, nutritional, and genetic factors. This study aimed to investigate the factors predicting Developmental Delay (DD) in children under 5 years old in Tabriz City. Two groups of mothers of children with and without DD participated. It was found that the key predictors were the child's male gender, emergency cesarean delivery, low maternal education, history of child hospitalization, maternal infections during pregnancy, intrauterine growth restriction (IUGR), and breastfeeding. These results highlight the importance of maternal health and early-life factors in child development.

Introduction

Developmental Delay (DD) in children refers to a condition in which a child under five years fails to achieve expected developmental milestones compared to peers in one or more domains, including motor, language, cognitive, social, or emotional skills [1]. The DD can cause persistent difficulties in learning, communication, and daily functioning, resulting in long-term educational and social challenges and imposing emotional and financial burdens on families [2-5]. The global prevalence of DD is high, especially in low- and middle-income countries, with a pooled prevalence of 18.83% [3]. In Iran, the reported prevalence ranges from 4.3% to 26%, depending on age and assessment methods [4]. Early detection and intervention during the first years of life are critical to reduce DD [2].

Child development is influenced by various biological, socioeconomic, maternal, and environmental factors [6]. In the prenatal period, the risk factors include genetic disorders, maternal infections (such as rubella, cytomegalovirus, and toxoplasma), and exposure to drugs or toxins [7]. In the perinatal and postnatal periods, the risk factors include preeclampsia, Intrauterine Growth Restriction (IUGR), asphyxia, hypoglycemia, meningitis, and trauma [8, 9]. Family and environmental factors such as low parental education, poverty, large family size, and lack of stimulating home environments further increase the risk of DD [10, 11]. Biological factors including preterm birth and low birth weight are strongly linked with motor, cognitive, and behavioral problems [12-16]. Maternal characteristics also play a major role. Children born to teenage mothers or to mothers with depression, stress, or chronic conditions such as diabetes or thyroid disorders have poorer developmental outcomes [17-24]. Moreover, maternal mental health and proper prenatal care significantly influence children's neurocognitive growth and social adjustment [17-19].

Despite extensive research, several aspects of DD remain unclear [2]. Considering the high prevalence and serious long-term consequences of DD, identifying modifiable risk factors is essential for its prevention and early intervention. Therefore, the present study aimed to investigate predictors of DD among children under five years old in Tabriz, Iran.

Materials and Methods

This case-control study was conducted from January to August 2022. The case group included mothers of children diagnosed with DD by a pediatrician in the Comprehensive Development Center in Tabriz, Iran. They were selected via convenience sampling. The control group included mothers of children under five years without DD, referred to health centers in Tabriz. They were selected via cluster sampling and the simple random sampling method using the Random Website [25]. First, a quarter (20 centers) of the 80 health centers in Tabriz were randomly selected. From each center, participants were randomly selected using a computer program and based on the determined sample

size. The appropriate sample size for each selected center was calculated as a fraction of the total sample size, according to the demographics of the center. The researcher contacted the parents by phone to briefly explain the study objectives and methodology to them and invite them. Considering that most study variables were related to children's characteristics (15 items) and that 10 samples were accounted for per item [26], the sample size was estimated at 150 per group. The inclusion criterion was having a child under five years. Children with congenital abnormalities or intellectual disability were excluded. The outcome was DD and exposures included socio-demographic variables. Matching was conducted based on the children's ages in both groups. Each case was matched with one control, resulting in a 1:1 ratio. Figure 1 shows the sampling process.

The data collection instrument was a researcher-made questionnaire surveying sociodemographic/ clinical/ obstetric characteristics of the mothers and the characteristics of their children. The questionnaire was reviewed and confirmed based on the opinions of a panel of experts, including pediatricians and developmental specialists. Socio-demographic characteristics included parents' age and educational level, family's monthly income, mother's occupation, type of marriage, and parents' history of tobacco and hookah use. Clinical/obstetric characteristics included gravida, pregnancy method, type of delivery, history of chronic diseases before pregnancy, history of disorders during pregnancy (pre-eclampsia or high blood pressure, gestational diabetes, anemia, thyroid disease, depression, and receiving medication for them), and maternal use of iron, folic acid, and other drugs. Child-related characteristics included gender and age of the child, gestational age at birth, IUGR in the child, wanted/unwanted child, use of iron, multivitamin or A+D drops by the child, breastfeeding the child, reading books to the child, child sleep time, child play time, blaming or punishment of the child, and history of prolonged icterus, metabolic diseases, and hospitalization.

The Ages and Stages Questionnaires - Third Edition (ASQ-3) was also used in this study [27] to diagnose the DD in children. This instrument contains 19 items to screen for DD in children aged 4-60 months. It has five domains (communication, problem-solving, personal-social skills, fine motor, and gross motor), each with six items. Parents can answer the questions with "yes, (10 points)", "sometimes, (5 points)", or "not yet (0 points)". The total score for each domain ranges from 0 to 60. Higher scores indicate better performance in that domain. The scores for each domain are summed up to obtain the questionnaire's total score, which is then plotted against the cutoff point to determine whether the child is on schedule, needs monitoring, or requires further assessment. A score above the cutoff point indicates that the child's development in that domain is on schedule. A score equal to or below the cutoff point suggests possible risk of DD and the need for further evaluation or intervention. The overall developmental status is therefore coded as a binary variable: 1=DD and 0=normal development [27]. The adaptation and standardization of the Persian version were conducted in Iran by Vameghi et al., who demonstrated the test's ability to detect DD at >96% [28].

After providing comprehensive information about the study objectives, benefits, results, and confidentiality of the information during a face-to-face visit with the participants, their informed consent was obtained. The questionnaires were then completed through interviews with mothers, ensuring complete responses from all participants. The collected data were analyzed in SPSS software, version 24. The dependent variable was developmental status (1=case with DD, 0=control without DD), and the independent variables were so-

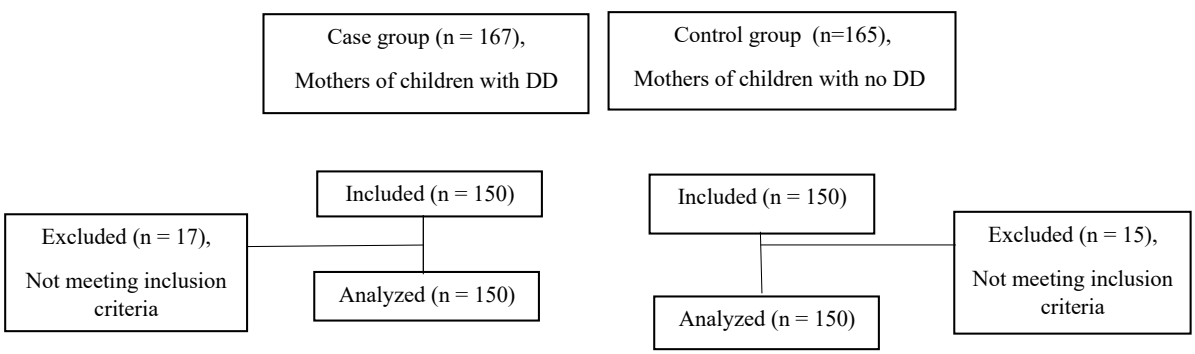

Figure 1. Flow diagram of the sampling and allocation processes

cio-demographic, clinical, obstetric, and child characteristics. To determine the relationship of these characteristics with DD, an independent t-test, chi-square test, and Chi-square for trend (linear-by-linear association) were used in bivariate analysis. Multivariable logistic regression using the enter method in a single-step analysis was performed to identify independent predictors of DD.

Results

In total, 300 mothers with children aged under five years in two equal case and control groups were assessed. The mean age of mothers was 33.4±6.2 years in the case group and 30.3±5.1 years in the control group. Male children comprised 65.3% of the case group and 52% of the control group. Most mothers in both groups were housewives (86.7% in the case group and 76.0% in the control group), and the majority had an academic education (49.3% in the case group and 61.3% in the control group). Table 1 shows the socio-demographic, clinical, obstetric, and child characteristics of case and control groups and the results of the independent t-test, chi-square, and chi-square for trend (linear-by-linear association).

According to the multivariate logistic regression, secondary school education or lower (OR=0.81, 95% CI; 1.25%, 6.28%, P=0.012), history of child hospitalization (OR=3.02, 95% CI; 1.69%, 5.4%, P=0.001), delivery by emergency cesarean section (OR=2.47, 95% CI; 1.10%, 5.53%, P=0.028), history of infection during pregnancy (OR=5.0, 95% CI; 1.48%, 16.85%, P=0.009), and IUGR in the child (OR=3.7, 95% CI; 1.1%, 12.6%, P=0.038) were significantly associated with the increased risk of DD, whereas, breastfeeding the child (OR=0.49, 95% CI; 0.27%, 0.87%, P=0.016) and male gender of the child (OR=0.53, 95% CI; 0.32%, 0.89%, P=0.016) were significantly associated with the decreased risk of DD (Table 2).

Discussion

This case-control study investigated predictors of DD in children under five years in Tabriz, Iran. According to the results, male gender, emergency cesarean delivery, IUGR, mother's educational level (secondary school or lower), child's history of hospitalization, maternal infection during pregnancy, and breastfeeding were significant predictors of DD.

Children born via emergency cesarean delivery were about three times at higher risk of DD compared to those with vaginal delivery. Consistent with these results, the studies in Turkey [29] and Poland [30] found a significant association between cesarean delivery and DD. Proposed mechanisms include altered stress responses and changes in the gut microbiome affecting brain development [31-33]. A study in Australia indicated reduced cognitive outcomes among children with cesarean birth [34]. Emergency conditions before delivery increase the risk of brain injury and DD [35]. The risk of DD in boys was half the risk in girls, consistent with the results of a study in Norway [36], but against the results of studies from Taiwan, which reported higher DD rates among boys [37, 38]. These discrepancies suggest that gender differences in development may vary across populations, and further studies are warranted.

Our findings showed that the risk of DD in children born to mothers with a secondary school education or lower was about three times higher than that of mothers with a university education, which may be because mothers with a low educational level pay less attention to the developmental status of children and are less sensitive to this matter, causing negligence in the development progress of their children. Results from other studies have also confirmed a direct relationship between parents' low education and DD in children [39, 40]. Given that educational attainment among women directly affects their independence, educated mothers are more likely to make independent decisions about their children's health [41]. Maternal infection during pregnancy was found to lead to a fivefold increase in the risk of DD. Previous studies have also linked prenatal infections, particularly in the third trimester, with later cognitive impairments, reduced IQ, and problem-solving difficulties [42-44]. Intrauterine inflammation is also associated with long-term neurodevelopmental disorders such as cerebral palsy [45, 46], possibly due to cytokine-mediated effects on the fetal nervous system [43]. The child's hospitalization history was another significant predictor. An Iranian study on 231 children showed similar results [47]. A cross-sectional study found that 26% of hospitalized children showed DD in at least one domain [48]. Since factors such as hypoxia, thyroid hormones, and environmental conditions (e.g. temperature, sound) can affect infant development—especially in neonatal intensive care units, where these factors may be hard to control—monitoring and managing them in neonatal wards is crucial.

Table 1. The parental and child characteristics of the study groups

Variables		Mean±SD		P
		Case Group (n=150)	Control Group (n=150)	
Mother's age (y)		33.4±6.18	30.3±5.1	0.951*
Father's age (y)		39.0±6.3	37.3±5.1	0.493*
Child's age (y)		3.2±1.3	3.2±1.3	1.000*
Gender of the child	Boy	98(65.3)	78(52)	0.019**
	Girl	52(34.7)	72(48)	
Gestational age at birth (week)	<32	12(8.1)	3(2)	0.001***
	32-37	59(39.3)	34(22.6)	
	≥38	79(52.6)	113(75.4)	
Child's sleep time	Before 10 PM	74(49.3)	75(50)	0.589***
	10-11 PM	37(24.7)	34(22.7)	
	After 12 PM	39(26)	41(27.3)	
Blaming the child	Daily	13(8)	13(8.7)	0.161***
	Sometimes	56(37.3)	67(44.7)	
	Seldom	51(34)	53(35.3)	
	Never	30(20.7)	17(11.3)	
Punishment	Daily	12(8)	11(7.3)	0.362***
	Seldom	26(17.3)	36(24)	
	Never	112(74.7)	103(68.7)	
Child's duration of playing games/ watching TV (minutes)	Never	36(24)	37(24.7)	0.399***
	<60	17(11.3)	15(10)	
	60-120	54(36)	65(43.3)	
	>120	43(28.7)	33(22)	
Gravida	1	68(45.3)	69(46)	0.768***
	2	56(37.3)	51(34)	
	3	26(17.3)	30(20)	
Mother's education	Secondary school or lower	27(18)	13(8.7)	0.018***
	High school or diploma	49(32.7)	45(30)	
	Academic	74(49.3)	92(61.3)	

Variables		Mean±SD		P
		Case Group (n=150)	Control Group (n=150)	
Father's education	Secondary school or lower	30(20)	19(12.7)	0.001***
	High school or diploma	48(32)	28(18.7)	
	Academic	72(48)	103(68.7)	
Mother's occupation	Housewife	130(86.7)	114(76)	0.018**
	Employed	20(13.3)	36(24)	
Type of marriage	Relative	33(22)	24(16)	0.185**
	Non-relative	117(78)	126(84)	
Adequacy of family income	Completely adequate	34(27.7)	28(18.7)	0.766***
	Relatively adequate	22(14.7)	19(12.7)	
	Inadequate	94(62.7)	103(68.7)	
Mother's tobacco use	Yes	2(1.3)	0(0)	0.498**
	No	148(98.7)	150(100)	
Father's tobacco use	Yes	42(28)	28(18.7)	0.056**
	No	108(72)	122(81.3)	
Mother's hookah use	Yes	1(0.7)	5(3.3)	0.214**
	No	149(99.3)	145(96.7)	
Father's hookah use	Yes	12(8)	9(6)	0.497**
	No	138(92)	141(94)	
Wanted or unwanted child	Wanted child	122(81.3)	130(86.7)	0.208**
	Unwanted child	28(18.7)	20(13.3)	
History of child hospitalization	Yes	57(38)	25(16.7)	0.001**
	No	93(62)	125(83)	
Breastfeeding the child	Yes	101(67.3)	120(80)	0.013**
	No	49(32.7)	30(20)	
Frequency of iron drop use by the child	Regular use	143(95.3)	140(93.3)	0.454**
	Irregular use	7(4.7)	10(6.7)	
Frequency of multivitamins or A+D drops use	Regular use	144(96)	141(94)	0.427**
	Irregular use	6(4)	9(6)	

Variables		Mean±SD		P
		Case Group (n=150)	Control Group (n=150)	
Prolonged icterus	Yes	24(16)	13(8.7)	0.053**
	No	126(84)	137(91.3)	
Metabolic disease	Yes	7(4.7)	2(1.2)	0.173**
	No	143(95.3)	148(98.7)	
Child caregiver	Parents	141(94)	137(91.3)	0.673***
	Mother	5(2.3)	7(4.7)	
	Father	4(2.7)	6(4)	
IUGR in the child	Yes	14(9.3)	4(2.7)	0.015**
	No	136(90.7)	146(97.3)	
Pregnancy method	Normal	144(96)	146(97.3)	0.266***
	In vitro fertilization	3(2)	0(0)	
	Ovulation-stimulating drugs	2(1.3)	3(2.3)	
	Intrauterine insemination of sperm	1(0.7)	0(0)	
	Other methods	0(0)	1(0.7)	
Type of delivery	Emergency cesarean section	48(32)	24(16)	0.004***
	Elective cesarean section	80(53.3)	95(63.3)	
	Vaginal	22(14.7)	31(20.7)	
History of a chronic disease before pregnancy	Yes	124(82.7)	127(84.7)	0.629**
	No	26(17.3)	23(15.3)	
Preeclampsia and high blood pressure during pregnancy	Yes	14(9.3)	15(10)	0.845**
	No	136(90.7)	135(90)	
Gestational diabetes	Yes	10(6.7)	14(9.3)	0.395**
	No	140(93.3)	136(90.7)	
Infection during pregnancy	Yes	15(10)	4(2.7)	0.009**
	No	135(90)	146(97.3)	
Anemia during pregnancy	Yes	15(10)	17(11.3)	0.708**
	No	135(90)	133(88.7)	
Thyroid disease during pregnancy	Yes	6(4)	10(6.7)	0.304**
	No	144(96)	140(93.3)	

Variables		Mean±SD		P
		Case Group (n=150)	Control Group (n=150)	
Depression during pregnancy	Yes	87(58)	64(42.9)	0.724**
	No	63(42)	86(57.1)	
Receiving antidepressants	Yes	72(48)	61(40.6)	0.180**
	No	78(52)	89(59.4)	
Other mental illnesses	Yes	4(2.7)	4(2.7)	0.639**
	No	146(97.3)	146(97.3)	
Maternal use of folic acid	Yes	149(99.3)	146(97.3)	0.162**
	No	1(0.7)	4(2.7)	
Frequency of folic acid use by the mother	Regular	136(90.6)	138(92)	0.278**
	Irregular	14(9.3)	12(8)	
Maternal use of iron	Yes	146(97.3)	141(94)	0.156**
	No	4(2.7)	9(6)	
Frequency of iron use by the mother	Regular	134(89)	135(95.1)	0.059**
	Irregular	16(11)	15(142)	
Maternal use of other drugs	Yes	36(24)	39(26)	0.689**
	No	114(76)	111(74)	

*Independent t-test, **Chi-square, ***Chi-square for trend (linear-by-linear association).

It was found that IUGR in the child could increase the risk of DD by more than 3.5 times, consistent with prior evidence linking IUGR to cognitive, sensory, and motor deficits [49]. Structural brain changes, limited social skills, and lower anthropometric measures may contribute to these developmental differences [50]. Lack of breastfeeding was also significantly associated with the risk of DD, consistent with the results of previous studies [30, 51, 52]. Breastfed children often have higher IQ scores [53, 54], likely due to long-chain polyunsaturated fatty acids supporting neural development, or enhanced emotional bonding between mother and child [55]. Promoting breastfeeding, therefore, may improve cognitive and developmental outcomes in the child.

Attention to the identified risk factors and designing preventive and interventional programs based on these factors can reduce DD incidence. Preventive care for pregnant women and early screening of children at high risk of DD are essential for better developmental outcomes. One of the strengths of this study is the involvement of a specialist in children's growth and development for diagnosing DD, and matching the age of children in the two groups. However, there were some limitations, including the existence of potential biases such as social desirability bias and recall bias. Overall, based on the identified risk factors of DD in children under five years in Tabriz (emergency cesarean delivery, low maternal education, maternal infection, child hospitalization, IUGR, and lack of breastfeeding), targeted screening and early interventions are recommended. Healthcare providers should integrate these risk factors into routine child assessments and emphasize maternal education and breastfeeding promotion. Further longitudinal studies are recommended to clarify causal relationships and explore biological mechanisms, especially regarding gender and cesarean delivery.

Table 2. Regression coefficients for predictors of DD in children under 5 years old

Variables		B	Adjusted OR	95% CI (Lower, Upper)	Standard Error	P*
Mother's education	Secondary school or lower	1.17	2.81	1.25, 6.28	0.46	0.012
	High school or diploma	0.84	1.41	0.80, 2.46	0.44	0.233
	Academic (Ref.)					
History of child hospitalization	Yes	1.07	3.02	1.69, 5.40	0.32	0.001
	No (Ref.)					
Breastfeeding the child	Yes	-0.66	0.49	0.27, 0.87	0.31	0.016
	No (Ref.)					
Type of delivery	Emergency cesarean section	0.67	2.47	1.10, 5.53	0.43	0.028
	Elective cesarean section	0.44	1.30	0.64, 2.6	0.35	0.457
	Vaginal (Ref.)					
Infection during pregnancy	Yes	1.63	5.0	1.48, 16.85	0.62	0.009
	No (Ref.)					
Child gender	Boy	-0.68	0.53	0.32, 0.89	0.27	0.016
	Girl (Ref.)					
Child IUGR	Yes	1.30	3.7	1.1, 12.6	0.63	0.038
	No (Ref.)					
Gestational age at birth	<32 weeks	0.42	1.5	0.32, 7.1	0.78	0.597
	32-37 weeks	-0.14	0.87	0.18, 4.1	0.79	0.857
	≥38 weeks (Ref.)			1		

OR=Odds ratio.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Research Ethics Committee of Tabriz University of Medical Sciences, Tabriz, Iran (Code: IR.TBZMED.REC.1400.679). Written informed consent to participate in the study was obtained from all the participants before enrolment.

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Authors' contributions

Conceptualization, study design, review, editing, and final approval: All authors; Writing the initial draft: Somayeh Abdolalipour; Statistical analysis: Mojgan Mirghafourvand.

Conflict of interest

The authors declared no conflict of interest.

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