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Association between Pre-, Intra-, and Postpartum Risk Factors with Developmental Delay in Infants: A Case-Control Study

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ABSTRACT

Background: Developmental delay (DD) is an important problem in children, and recognizing the factors affecting it is very critical in diagnosing and improving development. The aim of this study was to investigate the relationship between pre-, intra-, and postpartum risk factors with DD in infants.

Methods: In this case-control study, 110 infants with DD and 110 healthy infants from health centers in Rafsanjan were studied. At 12 months, the developmental status of infants was assessed using the ages and stages questionnaire (ASQ) at the age of 12 months. Information on risk factors was collected in a researcher-made checklist.

Results: The mean age of mothers during pregnancy was 28.83 ± 5.27 years in the case group and 29.21 ± 4.86 years in the control group (P = 0.57). Frequency of diploma or less education (P <0.001), rural residence (P<0.001), preterm infants (P = 0.045), and pathological jaundice (P = 0.027) were significantly higher in the case group. There was an association between DD with maternal education level (OR = 2.745, 95% CI: 1.587-4.747), number of pregnancies (OR = 1.494, 95% CI: 1.156-1.930), and history of pathological neonatal jaundice (OR = 3.963, 95% CI: 1.074-14.662).

Conclusion: According to the results of the study, Low maternal education, more pregnancies, and a history of pathological neonatal jaundice were factors affecting DD. It is recommended that more attention be paid to risk factors to prevent future adverse events.

Keywords: Ages and stages questionnaire, Developmental delay, Infant, Maternal education, More pregnancies, Neonatal jaundice

Introduction

Developmental delay (DD) is failure to reach the expected milestones for the child's age or a difference of at least 1.5 standard deviations (SD) from the milestones set for the child's age in at least one of the areas of gross motor skills, fine motor skills, speech, personal-social skills, as well as daily and cognitive activities that can be permanent or transient. These children do not show the developmental characteristics that are expected of them according to their age (1,

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Copyright© 2025 Jalali F et al. Published by Mashhad University of Medical Sciences. This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/). NonCommercial uses of the work are permitted, provided the original work is properly cited. 2). If there is a significant delay in two or more areas in a child under the age of five, it is known as general DD (3). These disorders affect a child's physical, learning, and functional conditions. DD includes a variety of sensory, motor, seizure, attention deficit hyperactivity disorder, autism spectrum disorders, mental retardation, and learning disabilities (4). Estimates show that 10-15% of preschool children have at least one DD (3). In 2017, it was estimated that 200 million children under the age of 5 in low- and middle-income countries were at risk of not fulfilling their developmental potential (5). In the United States, 15-20% of children had at least one DD (6). The prevalence of these disorders in Iran has been reported to be 18.7% to 19.8% (7).

The main cause of DD remains unknown since the child's development is affected by hereditary, biological, psychosocial, and environmental factors.⁷ The roots of many behavioral, cognitive, and physical disorders in adults can be traced back to the fetus and early childhood (8, 9). Known risk factors affecting the development of children in general include social factors determinate of health (poverty, inaccessibility to education. environmental stressors. poor sanitation and water); physical caregiver's and child's health (mother's illness and nutrition, malnutrition, low birth weight, infections); and mother's psychosocial health (mother's depression, substances use, and intimate partner violence [IPV]) (10, 11).

Diagnosis and treatment of disorders, control of underlying factors, and early support of children are among the determining factors in children's development. There are significant benefits in early diagnosis and intervention in children with DD (1, 12). Given the speed of growth and development in the first two years of life. the importance of examining the developmental dimensions of infants and taking timely action during this period becomes more apparent (13). The prerequisite for early treatment is early diagnosis of disorders with accurate tools and tests (14). Unfortunately, only a small number of children who benefit from early intervention are diagnosed early (15), and almost half of these children are not diagnosed before school age and, therefore, are not treated (16). A study in Iran on 11,000 children aged 4-60 months showed that 3.69-4.31% of seemingly healthy children had undiagnosed DD in various areas, which is associated with adverse social, educational, health, and behavioral consequences (17). In another study, 49.2% of children, including 65.5% of boys and 34.5% of girls, had delayed diagnosis of speech and language DD (18).

According to infant and child care programs in Iran, most infants, after birth, periodically go to health centers for vaccination and measurement of growth parameters, height, weight, and head circumference (19). A visit by a pediatrician alone is not enough to diagnose these disorders since 30-50% of psychomotor developmental disorders are not diagnosed by this method (20). Therefore. screening, regular visits to the doctor and checkups, as well as the study of risk factors associated with DD, can improve the correct and early diagnosis (6) Children with physical or environmental problems need special attention in order to develop properly. These children are more prone to DD than other children, causing different types and degrees of motor, mental, speech, auditory, and visual disabilities in them. Children are the most valuable asset of any society, and due to the major problems of having a child with DD, early diagnosis and timely referral are very important. Children with developmental disabilities and their families benefit the most from this health measure. Identifying risk factors and early diagnosis is very valuable for the prevention and treatment of these children.⁴ Therefore, the present study aimed to investigate the relationship between pre-, intra-, and postpartum risk factors with DD.

Methods

Study Design

The present case-control study was performed on two groups of 110 infants with DD (case group) and healthy infants (control group) from April to September 2021. Sampling from the centers carrying out the development screening plan in Rafsanjan citv (8) comprehensive urban health service centers) by convenience sampling method.

Measures

According to the national guidelines, all infants at the age of 12 months in these centers are screened with the Ages and Stages Questionnaire (ASQ) in terms of developmental status.²¹ If there are signs of abnormal development, they will be referred to urban health center No. 5 for further investigation. The validity and reliability of the ASQ were assessed in the study by Sajedi et al. Cronbach's alpha coefficient for the questionnaire was 0.79, and the construct validity of the questionnaires was confirmed by factor analysis.²² ASQ assesses the developmental status of children aged 4-60 months in 19 age groups (4-6-8-10-12-14-16-18-20-22-24-27-30-33-36-42-48-54, and 60 months of age) in five developmental areas (gross motor skills, fine motor skills, speech, personal-social skills, and problem-solving) and compares them with the predetermined cut-off point. A total of 30 questions (six questions for each developmental domain) were designed for each age group, and the highest score was 10 for each question and 60 for each developmental domain (22, 23). The questionnaire questions were designed in such a way that all parents with at least primary education could complete it. The options for each question were yes (10 points), sometimes (5 points), and not yet (zero score). The answer 'ves' indicated the child can do it now. 'sometimes' indicated that the child has just started to do it, and the answer 'not yet' indicated that the child is not vet able to do it. Scores for each area were collected separately. After scoring the questionnaire and comparing the scores obtained with the predetermined cut-off point in the test instructions, the child's developmental status was assessed. Infants who scored less than the cut-off point -2 SD in each of the five domains were referred to health center No. 5. In case of scores between -1 to -2 SD, the child was followed for two weeks, and the test was repeated, and if the score in that area was still less than -1 SD, the child was referred to the health center (22). The case group was selected based on the ASQ questionnaire, consisting of 12-month-old infants with DD. The control group was also selected from healthy infants who were matched with the case group in terms of age and sex (individual matching). To facilitate this matching process, subsequent to diagnosing the infant with a growth disorder, individuals of similar age and gender were chosen as the control group from among other infants participating in the health center's screening test. The inclusion criteria consisted of completing the ASQ at 12 months of age in the Integrated Health System (SIB) and the informed consent of the parents to participate in the study. The exclusion criteria included the existence of organic and structural defects of the central nervous system, genetic and metabolic diseases, and any congenital anomalies.

Sample Size

The sample size was calculated using the following sample size formula, using the study by Dabrowska et al (24). All risk factors were placed

separately in the formula, and the largest sample size was calculated at 110 people in each group according to the estimated frequency of abortion in the case group $P_1 = 18\%$ and the estimated frequency of abortion in the control group $P_2 = 7.7\%$, $\alpha = 0.05$, and $\beta = 0.20$.

$$n = 2 \frac{(z_1 - \alpha/2 + z_1 - \beta)^2 \overline{\rho q}}{(\rho_1 - \rho_2)^2}$$

The demographic and clinical data was collected by completing a researcher-made checklist from the mothers' health records and Integrated Health System. The checklist included two sections, including mother and child demographic information (place of residence, Maternal education level, household head's occupation, maternal age during pregnancy, and child's gender) and pre-, intra-, and postpartum risk factors. Prenatal risk factors include infection during pregnancy, chronic maternal diseases (diabetes, hypertension, hypothyroidism, kidney disease, and liver disease), Gestational diabetes, number of pregnancies, addiction, and history of abortion. Intrapartum risk factors are gestational age and type of delivery. Postpartum risk factors include birth weight (<2500g/≥2500g), history of jaundice, Pregnancy pathological outcome (term/preterm), and type of feeding in the first six months of life.

Statistical Analysis

The data were analyzed using SPSS.22 software and SAS.9.2 software. Kolmogorov-Smirnov test was used to evaluate the normality of the data, and independent t-test, chi-square, Fisher's exact test, and multivariate logistic regression were used to examine the factors associated with DD. The relationship between independent predictors and DD was expressed in the final model with odds ratio (OR) and 95% confidence interval (CI). Model differentiation was measured using C statistic, which is equal to the area under the receiver operating characteristic (ROC) curve. The model was rated using the Hosmer-Lemeshow (HL) proportionality statistic; higher P-values indicated that the model is more consistent with the observed data. If the P-value in the univariate analysis was less than or equal to 0.10, the variables were included in the multivariate model. The significance level in the tests was considered 0.05.

Ethical Approval

The ethical number is IR.RUMS.REC.1399.216

which was approved by the Ethics Committee of the Rafsanjan University of Medical Sciences, Rafsanjan, Iran. All the methods included in this study are in accordance with the declaration of Helsinki.

Results

The results of the present study showed that the mean age of mothers during pregnancy was 28.83 ± 5.27 years in the case group and $29.21 \pm$ 4.86 years in the control group (P = 0.57). In the case group, most mothers had high school diploma or less and in the control group, most of them had academic degrees (P <0.001). In terms of the household head's occupation, the frequency of self-employment was higher in the case group, and official employment was higher in the control group (P = 0.012). Moreover, the city residence was more frequent in the control group (P <0.001). The mean number of pregnancies in the case group was significantly higher (P = 0.001) (Table 1).

Table 2 shows the frequency distribution of variables related to infants in two groups of infants with DD and healthy infants. The

frequency distribution of age and sex was not significantly different between the two groups (matched in terms of age and sex) (P = 0.084 and P = 1.000, respectively). The frequency of preterm infants and pathological jaundice in the case group was significantly higher (P = 0.027 and P = 0.045, respectively).

Table 3 shows the results of the ASQ scores based on developmental domains compared to the related cut-off points. In the case group, a respective percentage of infants requiring followup and referral were observed: 18.2% and 49.1% for gross motor skills, 11.8% and 22.7% for fine motor skills, 12.7% and 21.8% for communication, 12.7% and 16.4% for problem-solving, and 15.5% and 9.1% for personal-social skills. In the control group, 1.8% required follow-up for gross motor skills, and 0.9% needed attention in the problemsolving domain. Additionally, the table results indicate that, within the case group, the greatest number of typically developing infants was noted in the personal-social skills and problem-solving domains.

The results of the factors affecting the DD of infants using a multivariable stepwise logistic

Table 1	. Demographic and	clinical information	of mothers in the	case and contro	ol groups
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Variable	Case	Control	- D value	
	(n=110)	(n=110)	i -value	
maternal age during pregnancy (mean ± SD)	28.83 ± 5.27	29.21 ± 4.86	0.577^{*}	
Maternal education level (number (%))				
Diploma or less	73 (66.4)	46 (41.8)	< 0.001**	
Academic	37 (33.6)	64 (58.2)		
(number (%)) Household head's occupation				
Unemployed	4 (3.6)	1 (0.9)	0.012***	
Self-employed	81 (73.6)	66 (60.0)	0.012	
Official employee	25 (22.7)	43 (39.1)		
Place of residence (number (%))				
City	79 (71.8)	110 (100)	< 0.001***	
Village	31 (28.2)	0		
Type of delivery (number (%))				
Normal vaginal	53 (48.2)	53 (48.2)	1.000**	
Cesarean section	57 (51.8)	57 (51.8)		
Number of pregnancies (mean ± SD)	2.35 ± 1.28	1.85 ± 0.99	0.001^{*}	
History of abortion (number (%))	32 (29.1)	17 (15.5)	0.015**	
Infection (number (%))	10 (9.1)	5 (4.5)	0.181^{**}	
Addiction (number (%))	1 (0.9)	0	0.999***	
Gestational diabetes (number (%))	6 (5.5)	8 (7.3)	0.581**	
Diabetes (number (%))	1 (0.9)	1 (0.9)	1.000***	
Hypertension (number (%))	6 (5.5)	0	0.029**	
Hypothyroidism (number (%))	18 (16.4)	13 (11.8)	0.333**	
Kidney disease (number (%))	1 (0.9)	0	0.999***	
Liver disease (number (%))	1 (0.9)	1 (0.9)	1.000***	
Chronic maternal diseases (number (%))	25 (22.7)	15 (13.6)	0.080***	
* Independent t test and significance level is 0.0E				

* Independent t-test and significance level is 0.05. ** Chi-square test and significance level is 0.05.

** Chi-square test and significance level is 0.05.

*** Fisher's exact test and significance level is 0.05.

Table 2.	Demographic a	nd clinical inform	nation of infants i	n the case and	control groups
	D onnogi apino c	na omnour mornor	idenoir or mindrico i	in the cabe and	control groupo

	Grou	ıp	P-value	
Variable	Case	Control		
	(n=110)	(n=110)		
gender				
Boy	65 (59.1)	65 (59.1)	1.000*	
Girl	45 (40.9)	45 (40.9)		
Birth weight				
<2500 g	16 (14.5)	8 (7.3)	0.084^{*}	
≥2500g	94 (85.5)	102 (92.7)		
Pregnancy outcome				
Preterm infant	10 (9.1)	3 (2.7)	0.045*	
Term infant	100 (90.9)	107 (97.3)		
History of pathological jaundice	11 (10.0)	3 (2.7)	0.027*	
Feeding type				
Breast milk	72 (65.5)	81 (73.6)	0.214*	
powdered milk	30 (27.3) 26 (23.6)		0.214	
Breast milk + powdered milk	8 (7.3)	3 (2.7)		

* Chi-square test and significance level is 0.05.

regression model are shown in Table 4. In this analysis, variables with P-value ≤ 0.01 in univariate analysis were included in the regression model. The variables included maternal education level, household head's occupation, place of residence, number of pregnancies, history of abortion, chronic maternal disease, gestational age, birth weight, and history of pathological jaundice. The results showed that maternal education (P = 0.003 and OR = 2.74), number of pregnancies (P = 0.002 and OR = 1.49), and pathological jaundice (P = 0.03 and OR = 3.96) were associated with DD. Accordingly, the odds ratio of children with developmental disorders in mothers with lower education, higher number of pregnancies, and infants with pathological jaundice was higher.

|--|

Group	
Control	P-value
0) (n=110)	
7) 108 (98.2))
2) 2 (1.8)	< 0.001
1) 0	
5) 110 (100)	
8) 0	< 0.001*
7) 0	
.,)	
.5) 110 (100)	0.001*
7) 0	< 0.001*
8) 0	
.9) 109 (99.1))
.7) 1 (0.9)	< 0.001
4) 0	
.5) 110 (100)	
.5) 0	< 0.001*
1) 0	
	Group \circ Control \circ (n=110) .7) 108 (98.2) .2) 2 (1.8) .1) 0 .5) 110 (100) .8) 0 .7) 0 .5) 110 (100) .7) 0 .5) 110 (100) .7) 0 .5) 109 (99.1) .7) 1 (0.9) .4) 0 .5) 110 (100) .5) 0 .5) 0 .5) 0

* Fisher's exact test and significance level is 0.05.

Table 4. Factors associated with DD

Variable	Unadjusted			Adjusted		
variable	OR	95% CI for OR	P-value	OR	95% CI for OR	P-value
Maternal education level ≤ Diploma vs. academic	2.745	1.587 - 4.747	0.0003	2.447	1.378 - 4.345	0.0003
number of pregnancies	1.494	1.156 - 1.930	0.0022	1.398	1.072 - 1.823	0.0144
Jaundice	3.963	1.074 - 14.622	0.0387	4.820	1.250 - 18.579	0.0143

OR: Odds Ratio, CI: Confidence Interval, DD: developmental delay

For Adjusted Model:

Hosmer-Lemeshow goodness-of-fit test; P= 0.7573

Area under the ROC (Receiver Operating Characteristic) curve; C= 0.6924

Variables were entered into the multivariable stepwise logistic regression model if the p-value was found to be less than or equal to 0.10 in univariate analysis. These variables included "Mother education, household head's occupation, Residence, Gravid, Abortion, Chronic disease, BW, GA and Jaundice".

Discussion

DD is one of the most common problems in children that can have adverse consequences, such as learning and behavioral problems and dysfunction in future life (21). The results of the present study showed that low maternal education level, number of pregnancies, and history of neonatal jaundice were effective factors in DD in infants. The household head's occupation, place of residence, number of pregnancies, history of abortion, and pregnancy outcome were not associated with developmental delays in infants.

The results of this study showed that the odds ratio of infants with DD was higher in mothers with lower education. In this regard, the results of the study by Sharma et al. showed that low maternal education is associated with DD in infants (25). In the study by Wrigglesworth et al., high level of parental education was suggested as a preventive factor in DD in infants (26). The results of the study by Demirci et al. showed that there is a significant relationship between DD in infants and maternal age, parental education, and family socioeconomic status (12). The Salah El Din et al. also reported that low maternal education is one of the factors associated with lower mean developmental score in infants and as a result higher DD (27). It can indicate low awareness of mothers about the factors affecting the development of children. Awareness and concern of caregivers and parents about the development and DD of the child are among the factors affecting the developmental process of children. Parents have a significant role in the initial diagnosis of DD (26). In studies conducted in developed countries, in the United States, 58% and in Australia, 52% of parents paid attention to various domains of their children's development and expressed concern (28, 29). However, in a study conducted in Iran, about 9% of parents expressed concern and paid attention to the developmental symptoms of their children and the most important related factors were low education level of parents and place residence (30). Therefore, it seems that a high level of awareness and education of parents is associated with more attention to the signs and symptoms of growth and development of children. It can prevent the occurrence and progression of DD in children as a preventive factor (30).

Another finding of this study was that the odds ratio of infants with DD was higher in mothers who had more pregnancies. Sharma et al. stated that a greater number of children reduces the risk of DD in communication and speech (25). Sajedi et al. reported that having less than five children is not associated with an increased risk of DD in children, but sixth and more pregnancies, as highrisk pregnancies, require more care (19). The results of the study by Soleimani et al. indicated that there is no relationship between the number of children in the family and DD in the child (31). Different results of studies on the relationship between the number of pregnancies and children with DD can be related to differences in culture and parenting style in different societies. In India, for example, the older children of the family play an important role in bringing up other children25, but in societies such as Iran, parents and the school play a more important role. Therefore, having fewer children in the family improves the quality of education and bringing up children, and parents can spend more time and money on educating their children. Children can fulfill their developmental potential through safe and sustainable housing, adequate and nutritious food, and access to medical care, secure relationships with adult caregivers, responsive parenting, and high-quality learning opportunities at home, and school. In multiple children's families, children face high instability in their lives (32).

The study results indicated that the odds ratio of infants with DD was higher in infants with pathological jaundice. The study by Sajedi et al. on the factors affecting DD showed that neonatal jaundice is one of the factors affecting these disorders (19). A similar finding was reported in the study by Dabrowska et al (24). Maimburg et al. also reported that there is a positive association between neonatal jaundice with autism and DD (33). The importance of neonatal jaundice is mostly related to the dangerous side effects of increasing bilirubin in the brain, which leads to mild to severe irreversible brain damage, hearing loss in premature infants, and even infant death (34). The results of studies have shown that neonatal jaundice affects different domains of development (35, 36).

Based on the findings of our study, the highest frequency of DD was related to gross motor skills. Studies conducted on infants with DD have provided different reports in the domains where they had the most problems. In the study by Karimi et al., the highest frequency of disorders was in the domains of gross and fine motor skills (37). In the study of Zhang et al., the highest frequency of DD was related to the domain of fine motor skills (38), and in the study by Wrigglesworth et al., the highest frequency of DD was related to the domain of communication (26). These differences can be due to the differences in the age group of the children under study and also the variety in the screening tools used in these studies (39, 40).

Limitations

It is recommended to study other risk factors for developmental delays in infants, including family history, genetic diseases, history of developmental problems in other children or firstdegree relatives, duration of labor, neonatal seizures, medications used during pregnancy, twinning or multiple births, and other factors in infants such as nutrition status after 6 months and child's education. Studies with larger sample sizes can also be designed to investigate this relationship. The ASQ heavily relies on the child's cooperation, responsiveness, and the information furnished by parents or caregivers. This reliance can influence the accuracy and validity of the assessment conducted using ASQ. Indeed, due to its design, the ASQ might not detect certain developmental issues or furnish the necessary information required for comprehensive assessment. One of the most important limitations of the case-control study is the potential for recall bias, which was also one of the limitations of this study.

Conclusion

Our results indicated that low maternal

education, more pregnancies, and a history of pathological neonatal jaundice were factors affecting DD in infants. Focusing on preventive strategies regarding DD in the pre-, peri-, and postnatal risk factors identified in this study can be useful.

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Conflicts of interest

The authors declare no competing interests.

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