Iran J Pediatr. 2018 October; 28(5):e14393. doi: 10.5812/ijp.14393.

Published online 2018 August 18. **Research Article**

Study of Developmental Delay and Its Related Factors in Low Birth Weight Infants

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Received 2017 May 31; **Revised** 2018 February 25; **Accepted** 2018 May 15.

Abstract

Background: Advances in medical science and success in increasing the survival rate of vulnerable infants have raised the future evolution issues of these children. Developmental and behavioral disorders are the most common problem in children after discharge from NICU. A lot of factors are involved in the occurrence of developmental disorders.
Objectives: According to the importance of the subject and lack of accurate regional information, this study aimed to investigate the developmental disorders and related factors in low weight infants.
Methods: This retrospective cohort study was performed on 76, 4 - 12 month-old infants with a history of hospitalization in NICU of Shiraz Hazrat Zeinab Hospital with an average weight of 1800 grams. These infants were evaluated developmentally by ASQ (Age and stage questionnaire). The data was analyzed by statistical tests.
Results: Using ASQ, 17% of children were detected as having developmental disorders. The percentages of developmental disorders for fine and gross motor domains, problem solving ability, communication and personal-social behaviors were 14.5%, 23.7%, 19.7%, 17.6% and 14.5%, respectively. The correlation coefficient statistical test did not show any significant relationship between developmental disorder with mechanical ventilation, duration of hospitalization, surfactant and betamethasone injection, and final diagnosis of diseases ($r < 1$).
Conclusions: Although improvement in respiratory therapy, monitoring system, non-invasive procedures and developmental care have decreased neonatal mortality rate and prematurity complications, but we cannot find any relationship between related risk factors and neurological outcomes. Developmental delay of low birth weight infants must be detected and rehabilitation started soon after discharge from NICU.

Keywords: Low Birth Weight, Developmental Disorders, Neonatal Intensive Care Unit (NICU)

1. Background

Today, human resources in the society are considered as one of the important pillars of community improvement in various areas and paying attention to children as future generation will be one of the most basic strategies to achieve this important goal. In this regard, it is important to address the issue of children's development, especially their neurodevelopmental issues (1). Proper neurodevelopment in early life is an important factor in creating conditions that lead individuals to have a healthier life in different dimensions including physical, emotional, cognitive and social dimensions (2). Any damage on or disorder in the central nervous system during the first critical period of life can introduce irreversible effects on neurodevelopment in children. Neurodevelopmental indices are defined and standardized for children from two months up to the age of five years. These developmental indices include motor (gross or fine), speech/language, cognitive, social, and daily activities. Developmental indices may be delayed from birth (developmental delay) or they may become descending after a fairly normal course that means developmental regression. Also sometimes the indices may be eliminated suddenly, temporarily or permanently due to some events or severe diseases (3).

A wide range of risk factors have been proven to create a developmental delay. Prenatal factors include family marriage, high maternal age during pregnancy, multiple pregnancies, chronic illness (such as diabetes, hyper-

tension), infection during pregnancy, drug use or toxin, and contact with teratogenic agents during pregnancy. Antenatal factors include oligo or polyhydramnios, preterm birth, asphyxia, and prolonged labor. Postnatal factors are hypoxia, hyperoxia, prematurity, anemia, infection, hypoglycemia, severe jaundice, intraventricular hemorrhage, etc. These risk factors have been recognized as etiology of developmental disorders in children, but in many cases the main cause of developmental disability usually remains unknown and a clear defined factor cannot be mentioned (4, 5).

Developmental and behavioral problems are the most common problem in pediatric medicine after infections and trauma. The prevalence of this problem is not in the same range in the world, and even in the advanced countries a high rate is dedicated to this problem. This rate is reported at a rate of 30% in at risk populations. In the United States, approximately 12.84% to 15.04% of children have some degree of developmental or behavioral disability (6). In Iran, this rate has been reported from 18.7% to 22.5% in different cities (7). Because only 30% of children with behavioral and developmental problems are identified by current primary health workers, American Academy of Pediatrics advice the developmental screening for all healthy children (without any developmental delay). Since screening for all children is difficult, screening of high risk children seems more reasonable. One of the risk factors of developmental problems is the history of admission to the Neonatal Intensive Care Unit (NICU). Except for a few cases of inherited syndromes with a specific brain disorder and a known prognosis, other illnesses that lead to the admission of a child to the NICU have an uncertain effect on his neurodevelopment. Therefore, screening and early detection of developmental delay in children, especially in high risk children, is necessary and seems to be the most reasonable solution (8, 9).

2. Objectives

The present study, based on the above-mentioned factors, was conducted to evaluate the developmental disorders and related factors in low birth weight infants (LBW) admitted to NICU by ASQ questionnaire.

3. Methods

In this retrospective cohort study, 76 infants aged 4 - 12 months admitted to the Shiraz Hazrat-e-Zeynab Hospital after birth during 2013 - 2014 were evaluated. The proportion of low birth weight premature babies with breathing problems was 11% and by considering $\alpha = 0.05$ and $d = 0.04$, a sample size of 109 infants was estimated, but only 76 infants could be followed.

Inclusion criteria included: (1) birth weight less than 2500 grams, (2) have been under care in NICU due to respiratory distress, (3) infants' families were available, (4) immediate family members were literate, (5) the family agreed with collaboration in the study.

Infants with specific illness (congenital anomalies, infections, inherited metabolic disorders and chromosomal abnormalities) were excluded.

After obtaining the necessary permissions, 109 children were selected according to inclusion criteria but of whom only 76 families agreed to precipitate in the study. The necessary information including history, duration of hospitalization, duration of mechanical ventilation, use of surfactant, history of prenatal corticosteroid injection, high risk delivery and hospitalization complications was extracted from hospital records. After a complete physical examination, the parents were asked to complete ASQ and a complementary form which were reviewed, approved and completed by the physician.

The ASQs are a series of 19 questionnaires designed to be completed by parents when their infant/child is 4 to 60 months of age. Each questionnaire contains 30 items equally divided across the areas of communication, fine motor, gross motor, personal-social, and problem solving skills (10). Parents answer each question considering 10 points for (yes), 5 points for (sometimes) and 0 points for the answer (not yet). Then the scores for each of development areas are compared by determining the "cut-off point" for the same developmental area in the "cut-off points" of the ASQ of related age group. A problem in one area is considered as a mild developmental disorder while problem in two areas is valued as moderate developmental disorder. These problems in three or more areas are considered as severe developmental disorder.

Test-retest reliability, at a two-week interval, was found to be 94%. Interobserver reliability was also 94%. Sensitivity ranged from 51% for 4-month ASQ to 90% for 36-month ASQ, with a 75% overall sensitivity rate. Specificity ranged from 81% for 16-month ASQ, to 92% for 36-month ASQ, with an overall specificity rate of 86% (11). The validity (0.84) and reliability (0.94) of this questionnaire has also been confirmed in Iran (12).

The data were analyzed by the SPSS software, version 18. Descriptive statistics, including tables, graphs and distribution and, in some cases if necessary to examine the significance of relationships, statistical t-Test, ANOVA and Chi-square were used. P value less than 0.05 was considered significant.

4. Results

Of the 76 studied infants 58% were boys and 42% were girls. 7% had a birth weight less than 1 k g, 36% weighed 1.5 - 2 kg, and 28% more than 2 kg. Only 8% were born after 35 weeks of gestation and the rest less than 35 weeks. 36% of the infants were living in the city, 41% in the province and 18% in villages (Table 1).

Overall in developmental indices, in the area of communication, 70.4% of infants had a normal development, 17.6% of examined infants had severe developmental problems and 12% of them had moderate problem (needed training). The gross motor movement in 66.9 had a natural development, 23.7% had a severe developmental problem and 9.4% had a moderate developmental problem. The fine motor movements in 73.7% had a natural development, 14.5% had a severe developmental problem and 11.8% had a moderate developmental problem. In problem solving ability, 72.4% had a natural development, 19.7% had a severe developmental problem and 7.9% had a moderate developmental problem. In the development of personal-social behaviors, 75.9% of infants had a natural development, 14.5% had severe developmental problems and 9.4% had moderate problem (needed training) (Table 2).

Pearson correlation test showed no significant correlation between developmental disorder of children (4 - 12 months) and duration of mechanical ventilation (P = 0.2). The correlation coefficient between developmental impairment of children and hospitalization time was -0.108. This figure represents the amount of inverse linear relationship between developmental disorder of children and duration of hospital stay. The correlation was not significant (P = 0.52).

There was a reverse linear relationship between developmental disorder in children with history of admission and use of surfactant (r = -0.77). That is, the lower the average developmental scores in these children, the higher the use of surfactants. The correlation was not significant (P = 0.65).

There was an inverse linear relationship between children with developmental disorders and history of injection of betamethasone (r = 0.17). The correlation was not significant (P = 0.32) (Table 3).

Statistical Independent T-test showed no significant difference between the mean high risk labor of children with developmental disorders and healthy children (without any developmental delay) (P = 0.88). However, because the difference in the mean risk of delivery in healthy children and children with a disorder equals 0.001, it can be concluded that the amount of developmental disorder is slightly higher in cases of high risk labor. Also, the results indicated that the mean value of performing advanced resuscitation surgery in children with developmental disorder and healthy children was not significantly different (P = 0.662). However, the difference between the two groups was equal to 0.08, which indicates that the rate of developmental disorder in the neonates who need advanced resuscitation surgery is slightly higher.

The findings showed that there was no significant difference in the number of transitional infants (P = 0.64) with complications of hospitalization (P = 0.77) and rural residents (P = 0.135) in healthy children and children with developmental disorder (Table 4).

Pearson correlation test showed no significant difference between the developmental disorder of children and early diagnosis of diseases (r = -0.0118) which represents the inverse linear correlation between the mean developmental range and the presence of various diseases in the initial diagnosis of these infants. Correlation coefficient (r = -0.28) also showed a reverse correlation between developmental disorder of children with final diagnosis of diseases while this correlation was not significant (P = 0.22) (Table 3).

5. Discussion

The results showed that the highest percentage of developmental delay was in the gross motor and the lowest in the fine motor and personal-social behaviors. This is consistent with the study of Fallah et al. (13) and Karimi et al. (14), but different with that of Dorre and Fatahi Bayat (15) which showed the highest percentage of developmental delay in communication domain and the lowest in individual-social behaviors. The reason of these different results can be sought in using different samples and methods.

We found no significant relationship between developmental disorder of children and duration of mechanical ventilation, complications of hospitalization or hospitalization duration. HuiTsai et al reported that developing a brain-protective respiratory support strategy in response to real-time cerebral hemodynamics and oxygenation changes has the potential to improve neurodevelopmental outcomes in low birth weight infants (16) which could not be confirmed with respect to the results of our study. Among the reasons for this lack of significant relationship, may be mentioned the applying of a better respiratory and supportive care in the recent years.

Developmental disorder in infants showed a linear and reversed relationship with the use of surfactant and prenatal betamethasone injection. The lower the average developmental scores in these children, the higher the use of surfactant and betamethasone injection was. The correlation was not significant. The possible reason for may be

Table 1. The Frequency and Percentage of Infants Based on Demographic Variables

Category	No. (%)	Category	No. (%)
Birth weight (Kg)		**Gender**	
< 1	5 (6.6)	Boy	32 (42.1)
1 - 1.5	23 (30.3)	Girl	44 (57.9)
1.5 - 2	27 (35.5)	**Advanced cardiopulmonary resuscitation**	
> 2	21 (27.6)	Developmental delay	
Birth age (weeks)		Not essential	12 (31.6)
27	2 (2.6)	Essential without CPR team	2 (66.7)
28	4 (5.3)	CPR is done	5 (45.5)
29	5 (6.6)	Healthy	
30	13 (17.1)	Not essential	26 (68.4)
31	12 (15.8)	Essential without CPR team	1 (33.3)
32	7 (9.2)	CPR is done	6 (54.5)
33	15 (19.7)	**Interhospital transmission**	
34	11 (14.5)	Developmental delay	
35	6 (7.9)	Shiraz	5 (62.5)
Residence		Others town	2 (20)
City	27 (35.5)	Healthy	
County	31 (40.8)	Shiraz	3 (37.5)
Rural	14 (18.4)	Others town	5 (80)
High risk pregnancy		**Mechanical ventilation**	
Developmental delay		Developmental delay	
Yes	29 (51.8)	Used	11 (40.7)
No	1 (50)	Not used	26 (53.3)
Healthy		Healthy	
Yes	27 (48.2)	Used	16 (59.3)
No	1 (50)	Not used	21 (44.7)
High risk delivery		**Surfactant use**	
Developmental delay		Developmental delay	
Yes	18 (56.3)	Yes	16 (44.4)
No	2 (40)	No	21 (55.3)
Healthy		Healthy	
Yes	14 (43.8)	Yes	20 (55.5)
No	3 (60)	No	17 (44.7)
Bethamethasone injection (prophylaxis)		**Hospital complications**	
Developmental delay		Developmental delay	
Yes	33 (55)	Yes	5 (38.5)
No	2 (33.3)	No	32 (51.6)
Healthy		Healthy	
Yes	27 (45)	Yes	8 (61.5)
No	4 (66.7)	No	30 (48.4)

that with standardization of our NICU usage of surfactant and betamethasone has been improved and its efficacy increased.

The correlation between developmental disorders of children with the amount of high risk labor was the same for both the developmental disorder children and healthy subjects. However, because the difference in the mean of the risk of labor in healthy children and children with disorder is 0.001, it can be concluded that the developmental disorder in the case of high-risk labor was slightly

Table 2. The Frequency and Percentage of Developmental Disorders of Low Weight Birth Infants Admitted to NICU

Developmental Domains	Severe Developmental Disorder, No. (%)	Moderate Developmental Disorder, No. (%)	Without Developmental Disorder, No. (%)	Total, No. (%)
Communication	14 (17.6)	9 (12)	53 (70.4)	76 (100)
Gross motor movements	18 (23.7)	7 (9.4)	51 (66.9)	76 (100)
Fine motor movements	12 (14.5)	10 (11.8)	54 (73.7)	76 (100)
Problem solving ability	16 (19.7)	7 (7.9)	53 (72.4)	76 (100)
Individual-social behaviors	12 (14.5)	8 (9.4)	56 (75.9)	76 (100)

Table 3. The Relationship Between Developmental Disorders and Its Effective Factors

Effective Factors	r	P	Total
Duration of mechanical ventilation	-0.21	0.2	37
Duration of hospitalization	-0.108	0.52	37
Surfactant use	-0.077	0.65	37
Betamethasone injection	-0.17	0.32	35
Early detection	-0.118	0.42	37
Final diagnosis	-0.128	0.22	37

higher. The reasons for the same correlation in the two groups may be better management of high-risk mothers, improved follow-up programs and the prenatal care. These findings are consistent with the results of Kerstjens et al. (17) who found that multiple births, small gestational-age, low birth weight, preexisting maternal obesity, male sex and medical disorders during pregnancy had a significant correlation with the developmental delay of children (17). It was also consistent with another study in which the variables of male gender, low birth weight, familial marriage, pregnancy disorders, mother's body mass index as well as economic and social status showed a significant correlation with the developmental delay in children but no significant correlation between high-risk pregnancy and other developmental domains (16-18).

Among other results of this study there was no statistically significant difference between the rate of advanced resuscitation in children with developmental disorder and healthy children (P = 0.62). However, because the difference in the two groups was 0.08, it seems that the amount of developmental disorder in infants who needed advanced resuscitation was slightly higher.

The present study showed a relationship between children's developmental disorder and ontime diagnosis of the disease. Ontime diagnosis of developmental disorder is associated with lower average developmental scores in these children. This correlation was not significant. Shahshahani et al indicate that the performance of children whose hearing impairment was diagnosed from birth to the age of one year was significantly better in the tasks of receptive and expressive language than children whose hearing impairment was diagnosed between the ages of 13 and 36 months (18). Among the possible reasons of the non-significant results of our study is lack of developmental care in the NICU program at the time of the study and a small sample size. It is expected hat with meaningful and timely providing of developmental care that is currently underway in NICU, significant findings can be obtained.

Reduction of the cases during the research is considered as a limitation in this study. The main reason for this reduction in number of samples was that most of the subjects were from the surrounding cities and their timely presence in sessions was not possible, a number of samples were not accessible and a limited number of infants died. Also this study was done in Shiraz province and the results cannot be generalized. Therefore, further studies in other geographical areas and with greater sample size will be advisable.

Since the results of other Iranian studies also indicate the various prevalence of developmental disorders in children (19-22), it is an urging appeal on health authorities to adopt appropriate strategies for prevention of prematurity, control of risk factors, emphasize the early detection of disorders at lower ages and provide early intervention services.

5.1. Conclusions

Although improvements in respiratory care, monitoring system, non-invasive methods and developmental care have been shown to decrease the incidence of prematurity and reduce mortality rate of premature infants; in this study, no relationship was observed between developmental status of 4 - 12 months old infants and their problems in the intensive care unit. In order to achieve better developmental results, one must identify developmental disorders as soon as possible and start rehabilitation of low birth weight infants soon after discharging from the intensive care unit. Early diagnosis of these disorders can help organizations such as Welfare Organization for the timely rehabilitation of children which leads to reduced costs of

Table 4. Mean Difference of Related Factors in Healthy Babies and Babies with Developmental Disorders

Related Factors	T	Df	P	Mean Difference	Std Error	Confidence Interval	
						Lower Limit	Upper Limit
High risk delivery	0.14	73	0.88	0.001	0.117	-0.021	0.0251
Advanced CPR	1.89	73	0.062	0.083	0.044	-0.0043	0.171
Transmission babies	0.47	73	0.64	-0.0117	0.024	-0.061	0.038
Hospital complications	-0.29	73	0.77	-0.0045	0.015	-0.035	0.026
Infants living in deprived areas	0.14	73	0.88	0.001	0.117	-0.021	0.0251

treatment. Moreover, it contributes significantly to modify the diagnostic and therapeutic processes in NICUs.

Acknowledgments

We thank Dr. Nasrin Shokrpour for editorial assistance and all personnel of Shiraz Hazrat-e-Zeynab Hospital and participants in this project.

Footnote

Funding/Support: This article is based on research project number 6970 in Shiraz University of Medical Sciences. Hereby, we would like to show our gratitude to Assistant Professor of Research in Shiraz University of Medical Sciences for financial support.

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