Original Article

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Developmental Disorders in Preterm Neonates during the First Two Years of Life Using the Ages and Stages Questionnaire

H. Baskabadi (MD)[1], F. Bagheri (MSc)*[2], Z. Askari Hosseini (MSc)[3]

1.Department of Pediatrics, Mashhad University of Medical Sciences, Mashhad, I.R.Iran

2.Department of Nursing, Islamic Azad University, Mashhad, I.R.Iran

3.Evidence-Based Research Center, Faculty of Nursing & Midwifery, Mashhad, I.R.Iran

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ABSTRACT

BACKGROUND AND OBJECTIVE: With the advancement of medical care procedures, survival rate of preterm neonates has increased remarkably. In Iran, few studies have assessed the extent and severity of developmental disorders in these infants. This study aimed to evaluate developmental disorders in premature neonates.

METHODS: This cohort study was conducted on 270 premature infants born in Ghaem Hospital in Mashhad, Iran with mean birth weight of 1460±40 grams. Data on pregnancy, parturition and complications during hospitalization were recorded. Moreover, preterm neonates were evaluated in terms of developmental delay at 6, 12, 18 and 24 months of age based on the Ages and Stages questionnaire (ASQ).

FINDINGS: In this study, symptoms of developmental delay were observed in 152 neonates (56%) at six months, 115 neonates (42.7%) at 12 months, 101 infants (37.5%) at 18 months, and 49 neonates (18%) at 24 months. In addition, abnormal development was detected in different areas, including communication (n=21, 7.8%), major movements (n=53, 19.6%), minor movements (n=74, 27.5%), social interactions (n=89, 33%), and problem solving (n=153, 57%). After a two-year follow-up, 27 infants (60%) had asphyxia, 29 (28%) had respiratory distress syndrome, and 20 infants (15%) had developmental disorders.

CONCLUSION: According to the results of this study, about one-sixth of preterm neonates had developmental delay at two years of age. The highest rate of developmental disorders was observed in the area of problem solving, which should be taken into account in neonatal rehabilitation services. On the other hand, appropriate monitoring of neonatal asphyxia and jaundice is likely to reduce the risk of other complications during infancy.

KEY WORDS: *Growth and development, Premature infant.*

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***Corresponding author: F.Bagheri (MSc)**

Address: Department of Nursing, Shahinfar Faculty of Medicine, Islamic Azad University, Mashhad, I.R.Iran

Tel: +98 51 32280280

E-mail: bagherifatemeh59@yahoo.com

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Introduction

Recent advancement in the field of perinatology has significantly increased the survival rate of high-risk infants, especially premature neonates. Although use of methods such as intrauterine insemination and in-vitro fertilization has increased the fertility rate of sterile mothers, it has heightened the risk of premature birth. According to recent statistics, 12% of deliveries have been reported as premature in the U.S. (1, 2). Unfortunately, reduction in the mortality rate of preterm neonates has not diminished the complications associated with low birth weight.

On the contrary, statistics are suggestive of increased rates of cerebral palsy and severe disabilities among premature neonates, which impose socio-economic and emotional burdens on families, society and health care systems (3).

With the remarkable decline in neonatal mortality rate, special attention has been drawn to the enhancement of quality of life in high-risk newborns in order to guarantee their well-being in the future (4). This population is at a higher risk of cognitive disorders and poor educational outcomes (5).

Many of these complications could affect the lifelong health and developmental process of preterm infants. In comparison with term neonates, premature infants may show symptoms of developmental delay at older ages. In one study, Schonhaut et al. evaluated 1,667 neonates aged 8-18 months and reported no significant correlation between gestational age and developmental delay based on the Ages and Stages questionnaire (ASQ). Moreover, their findings were indicative of a higher rate of developmental delay in premature infants (6).

Early diagnosis of developmental delay is of paramount importance in high-risk neonates (7). These infants require at least five years of close follow-up (8, 9). Standard developmental factors are defined for each month of growth in the areas of major and minor movements, communication and language, and cognitive and behavioral patterns (10, 11).

Only 30% of infants with behavioral and developmental problems are diagnosed by primary health care providers; therefore, the American Academy of Pediatrics has strongly recommended developmental screening for healthy infants (12). Since screening of all neonates is a heavy task, monitoring of high-risk neonates seems to be a more viable option. Among the criteria for high-risk infants referring for therapy are history of admission at the neonatal intensive care unit (NICU) and prolonged hospitalization (13).

Screening apparatuses used for the identification and follow-up of developmental disorders in high-risk infants are being manufactured increasingly. These tools enable medical experts to distinguish between infants with minor issues from others in order to refer them to specialized centers for comprehensive examinations. Screening tools should be easy to use for non-expert individuals as well, including parents (14).

Several international studies have analyzed the evaluation of preterm infants in different aspects. In recent years, this issue has drawn the attention of many researchers in Iran; however, only a few studies have been conducted in this regard. With the improvement of prenatal and neonatal care and development of specialized health centers in recent decades, the survival rate of premature infants has increased remarkably in our country.

Therefore, it is recommended that quality of life of preterm neonates be promoted through the reduction of complications associated with premature birth. Since preterm neonates with chronic disorders require special evaluations, this prospective study aimed to determine the developmental status of preterm infants during the first two years of life.

Method

This cohort study was conducted on 270 premature infants with history of NICU admission in Ghaem Hospital in Mashhad, Iran during two years. All infants with gestational age less than 37 weeks of gestation, born in Ghaem Hospital from 21december 2008 until the required sample size, were enrolled. Sample size of the study was determined based on the formula proposed by Brien et al., and rate of disabilities in preterm neonates was estimated at 11% (14). With variables of α=0.05 and d=0.04, the sample size was calculated at 235 preterm infants. Considering the specific characteristics of longitudinal studies and possibility of sample loss, we increased the sample size to 320 neonates at the beginning of the research.

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However, only 270 infants could be followed-up for two years.

After obtaining official permit from the university and informed consent from all the parents of preterm neonates, required data of the infants with history of NICU admission were extracted from their medical files. According to the World Health Organization (WHO), neonates who are born before 37 weeks of gestation (first day of the last menstrual cycle) are defined as premature infants. Premature birth is associated with several complications, such as low birth weight and intrauterine growth restriction (15). Exclusion criteria of this study were neonates with inborn anomalies, infections, congenital metabolic disorders and chromosomal abnormalities. In this study, gestational age was determined based on the Ballard scale, last menstrual period or sonography results during the first trimester of pregnancy. Afterwards, data on pregnancy, parturition, need for admission and complications during hospitalization were recorded for all the mothers.

Moreover, neonatal examinations were performed thoroughly, and in case of pathological issues, the infant would be registered for follow-up. Follow-up of the neonates was carried out at 6-24 months of corrected gestational age.

To do so, the parents were asked to refer their newborns to the pediatric clinic of Ghaem Hospital for regular assessments if they were willing to participate in the study. After the initial examinations, instructions regarding the ASQ were provided for the parents, and they completed the questionnaires. Questionnaires were reviewed by a physician, and appropriate measures were taken if there were developmental disorders in children. ASQ consists of 19 sets of questions applying to 19 different age groups. Each section contains 30 items about the developmental pattern of infants.

In each section, questions are classified into five categories, as follows: 1) communication; 2) major movements; 3) minor movements; 4) social interactions and 5) problem solving (16). In this study, ASQ was graded as follows: “Yes” (score: 10), “Sometimes” (score: 5), and “Not yet” (score: zero). In the next stage, scores achieved in each developmental domain were compared with the cut-off point of ASQ in different age groups of the patients (16). Low scores in only one domain were indicative of mild developmental disorder, while low scores in two domains denoted moderate developmental disorder, and low scores in three domains indicated severe developmental problems in the neonates.

Validity of ASQ has been confirmed in several studies (17,18). In the present study, we excluded eight neonates at six months, 12 neonates at 12 months, 16 neonates at 18 months, and 14 neonates at 24 months of age due to lack of access to their parents. Data analysis was performed in SPSS using descriptive statistics (mean, standard deviation and frequency). In addition, we drew tables and charts, and distribution of the collected data was also determined. Other statistical measures were Chi-square and Mann-Whitney U tests, and P value of less than 0.05 was considered significant.

Results

Out of 270 studied infants, 125 (46.3%) were male and 145 (53.7%) were female. According to our findings, normal developmental was observed in domains of communication (92.2%), major movements (81.4%), minor movements (73.5%), problem solving (43%), and social interactions (67%). In this study, no significant correlation was observed between different domains of developmental patterns and factors such as gender, length of hospital stay, birth weight and duration of mechanical ventilation.

On the other hand, 151 preterm infants (56%) at six months, 115 infants (42.6%) at 12 months, 101 infants (37.5%) at 18 months, and 49 infants (18%) at 24 months manifested symptoms of developmental delay (table 1).

By the end of the second year of life, 221 neonates had normal development, 10 infants had mild developmental delay, 29 infants had moderate developmental delay, and 10 infants had severe developmental delay (table 1).

Among the studied neonates,106 cases had respiratory distress syndrome (RDS), 138 infants had jaundice requiring phototherapy, and 46 infants had asphyxia at birth. The main causes of hospitalization among the neonates in this study were RDS, prematurity, jaundice, asphyxia, hypothermia, hypoglycemia, meningitis, dehydration, and heart

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conditions. In addition, 52 infants required mechanical ventilation, and 45 infants received surfactant therapy. Out of 10 infants with positive blood cultures, six cases had *Klebsiella pneumoniae*, and four infants had coagulase-negative *staphylococci*. Moreover, eight neonates (80%) had positive cultures for developmental delay. In neonates with developmental delay, birth weight, gestational age and five-minute Apgar scores were lower compared to other infants (table 2).

Table 1. Developmental status of premature infants at different ages

Disorders / Age(Months)	Normal Development N(%)	Mild N(%)	Moderate N(%)	Severe N(%)
Six	119(44)	84(31)	51(19)	16(6)
12	155(57.4)	56(20.6)	43(16)	16(6)
18	169(62.5)	75(27.5)	20(7.5)	6(2.5)
24	221(82.1)	10(3.6)	29(10.7)	10(3.6)

Table 2. Comparison of Neonatal Characteristics with Developmental Delay and Normal Development

Group Variable	Normal (Mean±SD)	Delay (Mean±SD)	P-value
Birth weight (g)	1616.66±405.74	1321.42±429.02	0.034
One-minute apgar score	6.85±1.71	6.62±1.81	0.308
Five-minute apgar score	7.6±1.06	7.01±1.23	0.046
Gestational age (weeks)	32.12±2.63	30.33±2.82	0.032
Bilirubin level (mg/dl)	10.57±5.56	9.57±4.50	0.122
Hematocrit (%)	46.53±7.2	46.69±7.3	0.881
Sodium levels (mmol/L)	09.8±34.140	48.12±46.143	0.160
Potassium levels (mmol/L)	5.22±1.23	5.7±10.26	0.745
White blood cells	10.78±6.62	10.65±5.40	0.938

Developmental disorders were also observed in neonates with asphyxia (n=27, 60%), RDS (n=29, 28%), and jaundice (n=20, 15%) during the two-year follow-up (fig 1).

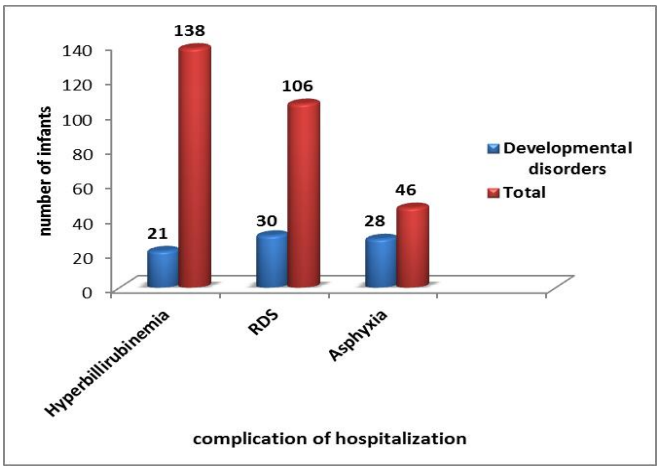

Figure 1. Relationship between Complications of Hospitalization and Prognosis of Neonates (two years after birth)

Discussion

In the present study, 10 infants had symptoms of developmental delay in almost all the measured domains two years after birth. Moreover, about half of the studied infants showed a degree of developmental delay at six months of age.

Evidence suggests that developmental disorders could be treated gradually with the normal growth of preterm neonates, and rehabilitation measures will be able to recover two-third of these disorders within two years after birth. In one study by Dorre et al., 6% of all the premature infants (n=114) had symptoms of developmental delay in all the related areas of ASQ (10).

This difference with the results of the present study could be due to the variable gestational age of neonates at birth. Furthermore, we evaluated premature neonates, and our sample size was twice larger compared to the study by Dorre et al. According to the current study, 221 neonates (82.1%) had normal developmental pattern, whereas 3.6%, 11% and 3.7% had mild, moderate, and severe developmental delay at the second year of life, respectively. Therefore, it could be concluded that the majority of preterm infants suffered from mild or moderate developmental delay, while severe developmental delay was observed in only 4% of the cases.

In the present study, developmental disorders were detected in areas of communication (n=21, 7.8%), major movements (n=53, 19.6%), minor movements

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(n=74, 27.5%), social interactions (n=89, 33%) and problem solving (n=153, 57%). In the study by Dorre et al, developmental disorders were mainly observed in the communication area (2.20%), while the lowest scores belonged to social interactions (16.7%).

In the current study, developmental disorders had the highest score in the area of problem solving, while the lowest score belonged to the domain of communication. Therefore, it is suggested that rehabilitation measures be performed in accordance with the severity of the symptoms and type of disabilities in neonates with developmental delay. In another research, Aziminejad reported that 2.8-27.8% of infants showed symptoms of developmental disorders in different areas, and the highest rate of developmental delay was observed in the domain of communication.

On the other hand, no significant correlation was found between the cause of hospitalization and rate of developmental disorders (10). In the study by Fallah et al., the highest rate of developmental disorders was observed in the areas of major movements and social interactions in neonates aged six and 12 months (19). This finding is in line with the results of the present study denoting the higher prevalence of developmental disorders among the neonates of this particular age group. In the present study, preterm neonates with lower birth weight and gestational age were at a higher risk of developmental disorders.

As such, infants with lower birth weight by 300 grams and gestational age by two weeks were more frequently affected by developmental disorders. According to the findings of Datar et al., very low birth weight infants are likely to suffer from severe mental and motor development within the first two years of life (20).

In the study by Kerstjens et al., the most common disorders in premature infants were in the areas of minor movements, communication and social interactions. Based on the results of the aforementioned studies, it could be concluded that low birth weight in preterm infants leads to developmental delay in different domains (21).

Therefore, it is recommended that infants with low birth weight be closely monitored during hospitalization. Variable results of the present research with other studies regarding the prevalence of developmental disorders among premature infants could be due to the differences in methods of evaluation, gestational age and rehabilitation measures. According to the literature, developmental delay is likely to occur in neonates who receive mechanical ventilation.

Mechanical ventilation denotes the severity of underlying diseases and poor prognosis of infants in the future. In one research conducted in Mexico, Fernandez et al. evaluated 134 infants aged two years with history of NICU admission, mean gestational age of 32 weeks, and mean birth weight of 1,677 grams. Furthermore, mean length of hospital stay was 51 days, and 75% of the neonates received mechanical ventilation.

Among these infants, 8.2% were reported to have symptoms of severe developmental defects. According to the other results of the study, significant correlations were found between the rate of developmental disorders and mechanical ventilation, length of NICU admission and gestational age.

Moreover, 80% of the infants with positive blood cultures were reported to have symptoms of developmental delay (22). In another study by Ferrerira et al., 44.3% of the neonates were reported to have sepsis, 40.7% of whom had abnormal neurological and motor development (23). In this regard, Hentges et al. evaluated 411 preterm infants with mean age of 29 weeks, 94 of whom were reported to have sepsis. Furthermore, motor development delay was observed in preterm neonates with gram-positive infections (24).

In conclusion, findings of the current study indicated that developmental delay among premature infants had the highest rate in the areas of problem solving, social interactions and minor movements, which gradually improved with the age of infants. In addition, it was observed that most developmental disorders were mild to moderate, and about 4% of the infants with severe developmental delay had lower birth weight, gestational age and five-minute Apgar scores compared to other neonates.

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