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Developmental Statue of Preterm Infants Up to Two Years of Age and Related Risk Factors using the Ages and Stages Questionnaire

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Abstract

Background: Preterm infants often face challenges in achieving developmental milestones compared to their full-term peers. This study aimed to investigate developmental abnormalities in preterm infants up to two years of age, identify related risk factors using the Ages and Stages Questionnaire (ASQ).

Methods: This descriptive cross-sectional study evaluated the developmental status of premature infants aged ≤ 2 years who attended the developmental clinic at Namazee Hospital, Shiraz, Iran, during the year 2020. Developmental assessments were performed by reviewing medical charts and utilizing ASQ. Developmental items of communication, gross movements, fine movements, problem solving and social interactions at the ages of 4 months, 12 months, 18 months, and 24 months were evaluated.

Results: Out of 77 studied infants, 28 (36.4%) were girls and 49 (63.6%) were boys with the mean gestational age of 32.78 ± 2.74 weeks. Developmental disorders had the highest impairment in gross movement at 12 months (77%) and the lowest impairment in communication at 4 months (39%). There was a significant correlation between social interactions and mode of delivery (p= 0.008), problem solving with parental consanguinity (p= 0.013), NICU admission with communication (p= 0.04), and birth weight with fine movement (p= 0.02) as well as folic acid consumption with gross movement (p= 0.03). Following, pairwise comparisons revealed a significant difference in communication scores between 4 months and 48 months of age (p= 0.033).

Conclusion: Monitoring the developmental progress of preterm infants using tools like the ASQ is vital for identifying those who may require additional support.

Key Words: ASQ, Communication Skills, Developmental Delay, Motor Skills, Premature.

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1- INTRODUCTION

Child development is indeed a multifaceted journey that unfolds from birth to adulthood, with the early years marked by rapid and significant growth (1, 2). Key developmental domains are gross motor, fine motor, language, cognition, and social-emotional behavior. The first year of life is the time for holding his head, grasping, crawling, sitting, standing, and walking. This is also the time when learn to smile and babble on language. As they grow, they show interest in others and their surroundings and learn to follow simple commands. Once they reach 12 months, they can point to the desired object and understand the meaning of numbers. Development from one to two years includes learning more words, combining them, scribbling, running, and playing with another infant (3-5).

Child development can be significantly affected by various factors, including maternal diseases, low birth weight, neonatal illness, prematurity, and environmental factors. Research studies highlight the significant challenges faced by preterm infants; the integrity of white matter, which is crucial for effective brain communication, tends to be poorer in infants born at lower gestational age leading to potential cognitive and motor delays (6, 7). Larroque et al. indicate that only 61% of infants born at 24 to 32 weeks of gestational age had no impairment by age 5 (8). Sajedi et al. conducted a study involving 396 infants aged 1 month to 3 years and identified that the most significant risk factors for developmental delay are prematurity and low birth weight (9). Mitha et al. specifically examined the long- term neurodevelopmental outcomes of children born at various gestational ages, with a focus on those born between 32 and 33 weeks. The study suggests that children born moderately (32- 33 weeks) or late preterm (34-36 weeks) are at a higher risk of experiencing adverse neurodevelopmental outcomes compared to those born at full term (10).

The Ages and Stages Questionnaire (ASQ) is a standardized screening tool which evaluates developmental milestones across various domains, including communication (language), gross motor, fine motor, problem-solving (cognitive), and personal-adaptive skills. ASQ is a relatively inexpensive and quick to administer scale which nicely encourages parental involvement (11, 12).

Identifying developmental delays through tools like ASQ can lead to timely interventions, enhancing a child's potential for growth and learning. Understanding these developmental milestones helps parents and caregivers support children effectively through their formative years.

The present study aimed to investigate the incidence of developmental abnormalities in preterm infants up to two years of age, and identify related risk factors using ASQ among preterm infants in Fars province, Southwestern Iran.

2- MATERIALS AND METHODS

2-1. Design and setting

This descriptive cross-sectional study aimed to evaluate the developmental status of premature children ≤ 2 years of age who attended the developmental clinic at Namazee Hospital, affiliated with Shiraz University of Medical Sciences, Shiraz, Iran. This clinic is the first and largest teaching treatment center in Southwestern Iran, specializing in pediatric development. The study was conducted in the year 2020, employing a full enumeration method (census) to review medical charts. If more information was needed, a specific time was arranged to talk with the parents.

2-2. Samples

To review the medical records of premature and full- term infants from the hospital archive, totally 1084 files were

evaluated. The diagnosis of prematurity was based on gestational age < 37 weeks.

2-2-1. Inclusion and Exclusion Criteria

Inclusion criteria for premature infants were age from 4 months and 24 months and complete medical records. Infants with age > 24 months or < 2 months, neuromuscular disease, congenital metabolic disorders, and severe congenital anomalies as well as incomplete records were excluded. In total, the eligible premature infants were 77 in the final sample.

2-3.Procedure

Medical charts with Persian questionnaires were reviewed by a physician, and appropriate measures were taken if developmental disorders were identified during the review process.

This study considered 4 months, 12 months, 18 months and 24 months, which monitor the child's developmental progress across five key domains. After the initial scoring, ASQ forms were reviewed by a physician during each visit. The physician checked the forms to correct any discrepancies or misunderstanding in the parents' interpretation of questions.

2-4. Instrument

The implemented scale was ASQ- 3 which is a parent reported developmental screening instrument divided into five key developmental domains of communication, gross movements, fine movements, personality- social interactions, and problem solving, each of which is assessed through specific questions (11, 12). The ASQ uses a three- point scale for each question, which allows parents to indicate the child's ability in each developmental area: "Yes" (score: 10 points), "Sometimes" (score: 5 points), and "Not yet" (score: 0 points). After scoring all items within each developmental domain, the total scores are calculated. Each of the five developmental domains has a total score ranging from 0 to 60 points. This score is then interpreted based on how far it deviates from age- specific- cut –off points that have been predetermined based on normative data. Scores of 50- 60 points are equivalent to more than -1 SD, indicating that the child's developmental performance is within the typical for their age group. Scores of 30- 40 points are equivalent to between -1 SD and -2 SD which suggest that the child is slightly delayed in development but the delay is not severe. Scores of 0, 10, or 20 points are equivalent to less than -2 SD, showing a significant developmental delay compared to age- related norms. Children who score in this range may require further assessment and early interventions.

Based on the scores and their SD equivalents, the developmental abilities of the child are divided into three groups; group 1 with scores falling above -1SD (i.e., scores between 50 and 60 points) and this group represents children who are developing on track with their age-appropriate milestones, Group 2 with scores falling between -1 SD and -2 SD (i.e., scores between 30 and 40 points) and children in this group are at risk for developmental delays but may only need monitoring or mild intervention to catch up, group 3 with scores falling below -2 SD (i.e., scores between 0,10, or 20 points) and this group represents children with significant developmental delays, who will likely need more intensive interventions and possibly referral to specialists for further evaluation.

2-5. Data analysis

Data analyses were conducted using SPSS version 6 statistical software. The following methods were employed; descriptive statistics for frequency and percentage of qualitative observations and comparative analysis for comparing responses across the four stages of measurement. Friedman's test was utilized along with its associated post hoc test. A P

value of less than 0.05 was considered statistically significant for all tests.

3- RESULTS

Out of 77 studied infants, 28 (36.4%) were girls and 49 (63.6%) were boys. The mean gestational age of premature newborns was 32.78 ± 2.74 weeks with a range of 26 to 36 weeks. The mean of neonates' birth weight was 2447± 1296 grams. Demographic data of the 77 studied premature newborns are summarized in Table 1.

Table-1: Demographic data of the 77 studied premature newborns

Characteristic		Number	Percentile
Sex	girls	28	36.4
	boys	49	63.6
Mode of delivery	Vaginal	23	25.8
	Cesarean section	66	74.2
Multiple pregnancy	Single	65	84.4
	Two	11	14.3
	> two	1	1.3
Maternal disease	Before pregnancy	15	19.5
	During pregnancy	7	7.9
	No	55	72.6
parental consanguinity	Yes	45	50.6
	No	44	49.4
Maternal education	Elementary	11	14.3
	Diploma	40	51.9
	College	26	3.8
Developmental disease in family	Yes	22	24.7
	No	67	75.3
Folic acid treatment	Complete	50	64.9
	Incomplete	24	31.2
	Not	3	3.9
Gestational age, weeks	< 27	3	3.4
	27-33	28	31.5
	31-32	12	13.5
	33-34	20	22.4
	35-36	26	29.2
Birth weight, gram	<1000	7	9.1
	1000 - 1499	15	19.5
	1500-1999	25	32.5
	2000-2499	17	22.1
	>2500	13	16.9
NICU admission	Yes	63	81.8
	No	14	18.2
Jaundice need phototherapy	Yes	44	57.1
	No	33	42.9

Developmental items of communication, gross movements, fine movements, problem solving, and social interactions at the ages of 4 months, 12 months, 18 months and 24 months in premature newborns are shown in Table 2-5.

According to our findings in the first visit, normal development was observed in domains of communication (61%), gross movements (29.9%), fine movements (41.6%), problem solving (41.6%), and social interactions (51.9%) (Table 2).

There was no significant correlation between different domains of developmental patterns and factors such as gender, multiple pregnancy, and maternal disease as well as birth weight and gestational age in the first visit. We had only a correlation between social interactions with mode of delivery (p= 0.008), problem solving with parental consanguinity (p= 0.013) and NICU admission with communication (p= 0.04).

The frequency of newborns' placement in group 2 – the group of those in need of treatment for obtaining a normal developmental score at 12 months- was more in social interactions (23%) followed by fine movement (21.7%) and communication (20.3%) (Table 3). There was a correlation between birth weight and fine movement (p= 0.02) as well as folic acid consumption and gross movement (p= 0.03) at this time.

Abnormal developmental items in 18 months were respectively gross movements (71.6%), communication (64.9%), fine movement (63.5%), problem solving (56.7%) and social interaction (55.4%) (Table 4).

At the age of 24 months, communication and gross movement's abnormality was found in about two-thirds of studied premature newborns (Table 5).

About a time from 4 months to 24 months, the highest and the lowest prevalence were related to the area of gross movement (77 %) at 12 months and the area of communication (39 %) at 4 months, respectively (Table 2-5).

The results of Related-Samples Friedman's Two-Way Analysis of Variance showed that there is statistically a significant difference between communication four times (Test value=24.427, P < 0.001). Following, pairwise comparisons revealed that there is a significant difference between communication in time 1 and time 4 (Test value= -2.778, P= 0.033). The results of Related-Samples Friedman's showed that statistically there is no significant difference between other developmental items in the four visits; gross movement (Test value= 4.589, P= 0.204), fine movement (Test value= 2.311, P= 0.510), problem solving (Test value= 0.884, P= 0.654) and social interaction (Test value= 1.147, P= 0.776).

Table-2: Frequency distribution of developmental disorders in the studied premature newborns at the first visit

n=77	**The first refer at the age of 4 months**				
Development item	percentile			% Abnormality	Mean ± SD
	Group 1	Group 2	Group 3		
Communication	61	13	26	39	1.64 ±0.87
Gross movements	29.9	22.1	48	70.1	2.18 ± 0.86
Fine movements	41.6	20.8	37.6	58.4	1.96 ± 0.89
Problem solving	41.6	18.2	40.2	58.4	1.98 ± 0.91
Social interactions	51.9	20.4	27.7	48.1	1.80± 0.82

Table-3: Frequency distribution of developmental disorders in the studied premature newborns at the second visit

n=74	The second refer at the age of 12 months				
Development item	percentile			% Abnormality	Mean ± SD
	Group 1	Group 2	Group 3		
Communication	44.6	20.3	35.1	55.4	1.83±0.93
Gross movements	23	13.5	63.5	77	2.31± 0.94
Fine movements	43.2	21.7	35.1	56.8	1.84± 0.94
Problem solving	40.5	12.2	47.3	59.5	1.9± 1.0
Social interactions	44.6	23	32.4	55.4	1.80±0.9

Table-4: Frequency distribution of developmental disorders in the studied premature newborns at the third visit

n=74	The third refer at the age of 18 months				
Development item	percentile			% Abnormality	Mean ± SD
	Group 1	Group 2	Group 3		
Communication	35.1	16.2	48.7	64.9	2.05± 0.98
Gross movements	28.4	10.8	60.8	71.6	2.23± 0.98
Fine movements	36.5	18.9	44.6	63.5	2.00± 0.97
Problem solving	43.3	14.9	41.8	56.7	1.90± 0.98
Social interactions	44.6	18.9	36.5	55.4	1.86± 0.96

Table-5: Frequency distribution of developmental disorders in the studied premature newborns at the fourth visit

n=74	The forth refer at the age of 24 months				
Development item	percentile			% Abnormality	Mean ± SD
	Group 1	Group 2	Group 3		
Communication	32.4	13.5	54.1	67.6	2.12± 0.99
Gross movements	32.4	16.2	51.4	67.6	2.10± 0.98
Fine movements	39.2	20.3	40.5	60.8	1.93± 0.98
Problem solving	44.6	12.1	43.3	55.4	1.90± 1.00
Social interactions	44.6	16.2	39.2	55.4	1.87± 0.97

4- DISCUSSION

The significance of increased survival rates among preterm infants is closely linked to the complications of prematurity and subsequent disturbance of the normal development of infants (13). This study investigated the medical chart of 77 premature infants for 5 developmental items of communication, gross movements, fine movements, problem solving, and social interactions in the age range of 4 to 24 months.

Our study found a relationship between communication skills and NICU admission at the age of 4 months. This suggests that infants who spent time in the NICU may face challenges in developing communication skills. Similar findings were observed in a study by Fernandez et al., which evaluated 134 premature newborns hospitalized in the NICU. Their research identified statistically significant associations between neurological conditions and the duration of NICU stays

($P < 0.001$), indicating that longer NICU admissions may correlate with poorer neurological outcomes (14).

Folic acid deficiency can lead to significant developmental delays and neurological issues, primarily through the elevation of plasma total homocysteine (15). Our findings suggest a correlation between folic acid consumption and improved gross motor skills in children. In a randomized, double blind trial by Kvestad et al., children aged 6 to 30 months who received either placebo or supplements of vitamin B12 and/or folic acid over six months showed improvements in gross motor and problem solving abilities (16). This highlights the importance of adequate folic acid intake for optimal neurodevelopment in young infants.

In a cohort study involving 125 Iranian children aged 12 to 36 months, Shahsavari et al. identified low birth weight in full-term infants as a significant risk factor affecting fine motor skills (17). Their research and our findings demonstrated a correlation between the weight of infants and fine motor abilities, suggesting that lower birth weight may negatively impact the development of this skill.

The frequency of consanguineous mating can vary widely across geographic regions and this practice may increase the risk of inheriting homozygous pathogenic alleles. Such alleles can predispose individuals to developmental disease. A study by Fan et al. examined 607 pediatric patients referred for developmental disorders, revealing that parental consanguinity is relatively common among children facing these problems (18). Our recent study has further suggested that consanguinity has negative effects on child development, particularly in areas like problem solving abilities.

Cavaggioni et al. found a higher incidence of developmental delays in children born via elective cesarean section compared to those born through vaginal delivery (19). Additionally, we observed a correlation between social interactions with mode of delivery in premature newborns. These results are significant for guiding doctors and expectant mothers in making informed choices about delivery methods, especially given the high rates of cesarean section in the country.

Evidence suggests that some developmental disorders in preterm neonates may improve gradually with normal growth. Factors such as early intervention, nurturing environments and supportive care significantly influence outcomes (20, 21). According to our study, the number of patients in group 2 with ASQ scores between -1 SD to -2 SD at 4 months of age did not differ from the scores at 48 months. This could indicate that while some infants may initially show delays, their developmental trajectory stabilizes over time, suggesting a potential for resilience.

Communication abilities are essential for social interaction and cognitive development (22). Our data implies that communication delay can significantly increase in premature newborn from 4 to 48 months (Test value=24.427, $P < 0.001$). The relationship between communication and the postnatal environment is complex and multifaceted. Recognizing the importance of early interventions such as maternal and neonatal health services and regular developmental screening may enhance outcomes for premature infants who are growing.

In the current study, developmental disorders had the highest score in the area of gross movement skills with 77% at the age of 12 months, while the lowest score belonged to the domain of communication at 39% in the 4 months of age. Findings from Baskabadi et al. on 270 Iranian premature infants showed abnormal development in problem solving (57%)

followed by social interactions (33%), minor movements (27.5%), major movements (19.6%) and communication (7.8%) (23), respectively.The various results call for additional research to validate findings across different settings.

4-1. Study Limitations

This study has some limitations. The ASQ relies on parent- reported observations, which can sometimes introduce bias or inaccuracies. However, it is generally regarded as a reliable tool when administered correctly. Unmeasured confounders, such as smoking during pregnancy, and treatment with antenatal steroids before delivery, might have influenced our results. This study was conducted in a single-center setting, indicating the need for multicenter research to enhance the validity and generalizability of the findings.

5- CONCLUSION

Monitoring developmental progress of preterm infants using tools like the ASQ is crucial for identifying those who may need additional support. Understanding risk factors and implementing early intervention strategies can enhance screening programs and continuous follow-ups should be considered in terms of developmental growth of these children.

6- ETHICAL CONSIDERATIONS

Ethical approval was obtained from the local research ethics committee at Shiraz University of Medical Sciences (Project registration number IR.SUMS.MED.REC.1399.461). Written informed consent was taken from the parents of all participating children.

6- CONFLICT OF INTEREST

None.

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