ORİJİNAL ARAŞTIRMA ORIGINAL RESEARCH
DOI: 10.5336/healthsci.2020-79647

One-year Neurodevelopmental Outcomes of Term and Preterm Infants at Risk: A Retrospective Study

Riskli Prematüre ve Zamanında Doğan Bebeklerin Bir Yıllık Nörogelişimsel Takibinin Sonuçları: Retrospektif Bir Çalışma

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ABSTRACT Objective: The aim of this study was to compare motor, cognitive and gross motor development of preterm and term infants with mild-moderate risk factors and typically developing peers. **Material and Methods:** Forty preterm and 20 term infants with mild to moderate risk factors and 25 typical peers as controls were included in this study. Alberta Infant Motor Scale (AIMS) and Bayley Scales of Infant and Toddler Development-II (BSDI-II) were used at 3., 6., 9., 12. months to assess their motor and cognitive development. Control group was assessed only at 12 months of age. **Results:** Between the 3. and 12. month of gestational age, within-groups measurements in both cognitive and motor ($p<0.001$) development scores of BSDI-II were significantly increased in preterm and term infants. At 12 month, the median motor-cognitive development score of BSDI-II of the preterm and term infants at risk and control group were similar ($p>0.05$). There was no differences in AIMS scores between preterm and term group ($p>0.05$). However, the AIMS scores in infants at risk was statistically lower than the control group at the age of 12 months ($p<0.05$). Also, there was a significantly positive correlation between the AIMS and motor-cognitive development score of the BSDI-II scale in infants at risk at 9 and 12 months of corrected age ($p<0.05$). **Conclusion:** In infants at risk, delay in gross motor development may be observed in the first year of their life compared to their typical peers. In terms of motor and cognitive development, we could comment that, infants at risk should be followed for a longer period.

Keywords: Premature; infant; development; risk

ÖZET Amaç: Bu çalışmanın amacı, hafif veya orta derece risk faktörü olan prematüre ve zamanında doğan bebeklerin ve sağlıklı yaşıtlarının motor, bilişsel ve kaba motor gelişimlerini karşılaştırmaktır. **Gereç ve Yöntemler:** Bu çalışmaya, hafif ila orta derecede risk faktörleri olan 40 prematüre doğan, 20 zamanında doğan bebek ile 25 zamanında doğan ve risk faktörü olmayan bebek dâhil edildi. Alberta İnfant Motor Skalası (AIMS) ve Bayley Bebek ve Küçük Çocuklar İçin Gelişim Ölçeği-II (Bayley-II) 3, 6, 9 ve 12. aylarda riskli bebeklerin motor ve bilişsel gelişimlerini değerlendirmek için kullanıldı. Kontrol grubu sadece 12 aylıkken değerlendirildi. **Bulgular:** 3-12. aylar arasında riskli bebeklerin grup içi Bayley-II motor ve kognitif gelişim puanları anlamlı derecede arttı ($p<0,001$). On ikinci ayda riskli bebeklerin Bayley-II ortanca motor-bilişsel gelişim skorlarıyla kontrol grubundaki bebeklerin skorları birbiriyle benzerdi ($p>0,05$). Prematüre ve zamanında doğan riskli bebekler arasında AIMS skorları açısından fark yoktu ($p>0,05$). Bununla birlikte, riskli bebeklerin 12. aydaki AIMS skorları, kontrol grubuna göre istatistiksel olarak daha düşüktü ($p<0,05$). Ayrıca düzeltilmiş 9. ve 12. aylarda riskli bebeklerde AIMS skoru ile Bayley-II ölçeğinin motor-bilişsel gelişim puanları arasında anlamlı derecede pozitif korelasyon vardı ($p<0,05$). **Sonuç:** Riskli bebeklerde yaşamlarının ilk yılında, tipik gelişim gösteren yaşıtlarına kıyasla kaba motor gelişimde gecikmeler gözlenebilir. Motor ve bilişsel gelişim açısından risk altındaki bebeklerin daha uzun süre takip edilmesi önerilmektedir.

Anahtar Kelimeler: Prematüre; bebek; gelişim; risk

Infants at risk are defined as infants whose negative environmental and biologic factor history is likely to cause neurodevelopmental problems.[1] Accordingly, infants with a neurological problem due to intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), hypoxic ischemic encephalopathy (HIE), intrauterine growth retardation, born less than 1,500 g and born before 32 weeks are included in the infants at risk.[2] Infants whose gestational age is less than 37 weeks are referred to as preterm infants.[3]

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Peer review under responsibility of Turkiye Klinikleri Journal of Health Sciences.

Received: 20 Oct 2020 ***Received in revised form:*** 01 Feb 2021 ***Accepted:*** 03 Feb 2021 ***Available online*:** 04 Mar 2021

Preterm infants are considered at risk about their motor and cognitive development, leads to be monitored in the early life.[4] Infants with a history of moderate to severe IVH especially grade 3-4 are at major risk for neurodevelopmental problems. While grade 1-2 mild IVH does not create major deficit in the early period, some researches suggest a risk for developmental problems.[5,6]

One of the most common problems encountered during the neonatal period is HIE.[7,8] HIE is associated with insufficient oxygenation and perfusion of the infant brain. Approximately 90% of infants had low Apgar score in the first minute. Also mortality and morbidity have been found 76%, 82% and 80% respectively in infants with the Apgar score of 0, 1, 2.[8]

Another problem encountered during the neonatal period is respiratory problems. Neonatal early interventions increased the survival ratio of infants with respiratory problems. However, infants who have pulmonary problems like bronchopulmonary dysplasia, diaphragmatic hernia, persistent pulmonary hypertension and treatments which are used to treat these patients enhance the risk of long-term physical and neurodevelopmental complications.[9] Perinatal risk factors and these problems in neonatal period may lead to neurodevelopmental problems in their future life.[10] So, it is important to follow the cognitive and motor development of infants at risk in order to detect, prevent or minimize the problems they may cope. In children with corrected age of 12 months, environmental factors have less impact on performance and biomedical problems (such as oxygen support for chronic lung disease) are eliminated. The cognitive development, gross motor development and language/speech skills can be evaluated in this period.[10] Therefore, the assessment of cognitive and motor functions, particularly at this time, allows early intervention to improve long-term outcomes.

The aims of the study were to: 1) Describe the developmental profile of preterm and term infants at risk and compare cognitive, motor and the gross motor development with their typical peers at the age of 12 months of corrected age; 2) Explore the correlation between the cognitive and gross motor development in infants at risk.

MATERIAL AND METHODS

PARTICIPANTS

This research was planned as a retrospective study. 40 preterm and 20 term infants with mild to moderate risk factors and complete the developmental assessments at 3, 6, 9 and 12 months of corrected age, between the years 2014-2017 were included in this study. This study was done in Gazi University Department of Physiotherapy and Rehabilitation. The control group consists of 25 healthy infants born at term age (37 0/7 to 41 6/7 weeks) and who had completed the developmental assessments at 12 months of their chronological age. The healthy infants included in the study consisted of infants who showed normal development according to the Denver Developmental Screening Test-II, did not have perinatal risk factors and neonatal intensive care unit stay after birth and were followed up by the Department of Pediatrics of Gazi University Faculty of Medicine Hospital.[11] The exclusion criteria for risky infants were; having major risk factors such as PVL, grade 3-4 IVH, infants with a genetic syndrome and a major congenital anomaly. Ethics Committee of Gazi University approved this study with the approval number 77082166-302.08.01 (approval date: 10.08.2017) and this study was performed in accordance with the Declaration of Helsinki.

PROCEDURE

The gross motor and cognitive performances of the infants were assessed every 3 months of their corrected age of between the 3 and 12 months by a 5 years experienced pediatric physiotherapist and neuropsychologist with 20 years of experience in the field. During the first assessment, which was done in the mornings, both preterm and term group received follow-up with a standard home centered early intervention program, which was structured according to the needs of every infant by a 20 years experienced physiotherapist in pediatric rehabilitation. The early intervention program was based on functional, goal oriented and family-centered approaches.[12,13] This program was individually prepared for each infant's needs. The program was implemented by the family in their home environment. Moreover, programs were checked every three months face to face and revised accordingly. Daily log was used for a better follow-up of the home program. The control group was assessed only at the 12 month of corrected age by the same staff.

ASSESSMENTS

Socio-demographic data and medical histories were recorded from the hospital epicrisis report. Gestational age, birth weight, length of hospital stay, pregnancy (multiple), delivery (spontaneous or cesarean section), Apgar score, status of oxygen uptake, presence of IVH grade 1-2, respiratory distress syndrome (RDS), grade 1-2 HIE and sepsis were recorded.

Gross motor development was assessed with the Alberta Infant Motor Scale (AIMS) and the permission to use AIMS was previously obtained. AIMS is an observational assessment scale developed to assess gross motor development in infants up to 18 months of age. The test contains a total of 58 items and evaluates the babies in four positions (supine, supine, sitting and standing). Each position has its own score and the total score is the sum of the scores obtained from these four positions.[14] The cut-off score of AIMS for 3, 6, 9 and 12 months was determined as 11, 26, 43, and 53, respectively. These scores are equal to the 50. percentile in AIMS developmental curve graph.

The Bayley Scales of Infant and Toddler Development-II (BSID-II) scale was used to assess motor and cognitive development. BSID- II is designed to assess the developmental function of children aged 1-42 months. The assessment was made by an experienced psychologist in the field of pediatrics who has BSID certificate. BSID-II consists of two subscales as Cognitive Development Scale (CDS) and Motor Development Scale (MDS). CDS measures the language, social skills, paying attention to objects etc. and the MDS measures the child's ability to climb, jump, hold or use things using large and small muscle groups.[15] The cut off composite score of BSID-II were determined as 85 point for all months.

All the evaluations were performed in a room which has appropriate lighting, temperature and sound 1 hour after the baby was fed in the morning. Physiotherapists with 4 to 10 year experience in the pediatric rehabilitation performed the AIMS assessments. Then, a psychologist with a 20 year of experience in the pediatric psychology performed the BSID-II to assess the developmental function of the infants.

STATISTICAL ANALYSIS

Statistical analyses were conducted using the SPSS, version 22 for windows (SPSS Inc., Chicago, Ilinois, USA). To determine whether the data were normally distributed, visual methods like histogram and analytical methods like Shapiro-Wilk test were used. Student's t-test or Mann-Whitney U test was used according to the normal distribution of the data in pairwise comparisons. One way ANOVA or Kruskal-Wallis tests were conducted to compare groups (preterm, term, control). Bonferroni correction was used in pairwise comparisons. According to the distribution of the data, repeated measure ANOVA or Friedman test were used in dependent variables analyzed more than twice.

When both variables were normally distributed, correlation coefficients and statistical significance were calculated using the Pearson test. On the other hand, Spearman test was used when both variables were not normally distributed. Correlation coefficients were accepted weak between 0-0.24, moderate between 0.25-0.49, strong between 0.50-0.74, and very strong between 0.75-1.00. Statistical significance was determined as $p<0.05$.

RESULTS

Fourty preterm infants with gestational age of 31.7±2.7 weeks with mild to moderate risk factors, 20 term infants with gestational age of 38.5±1.1 weeks with mild to moderate risk factors and 25 their typical peers as healthy controls were included in this study. Gestational ages and birth weights were significantly lower in the preterm infants compared to terms and healthy controls ($p<0.001$). Also, length of hospital stay, cesarean section rate, oxygen uptake rate, multiple pregnancy rate differed significantly from term and control group ($p<0.05$). There was no statistically significant difference in Apgar score 1 and 5 minutes scores between preterm and term group but this group's scores were significantly lower

TABLE 1: Delivery and infant characteristics.

Participant characteristics	Preterm n=40	Term n=20	Control n=25	p value
Gestational age: Weeks, Mean±SD	31.7±2.7	38.5±1.1	38.8±1.1	<0.001*
Birth weight: Grams, Mean ±SD	1,628±549	3,207±591	3,173±440	<0.001*
Male: n (%)	19 (47.5)	12 (60)	13 (52)	0.659
Length of hospital stay: Days, median (IQR)	38 (18-57)	10 (9-19)	0 (0-0)	<0.001*
Apgar score 1 min, median (IQR)	7.5 (6-9)	6 (4.5-8)	10 (10-10)	<0.001*
Apgar score 5 min, median (IQR)	9 (8-10)	8.5 (7-10)	10 (10-10)	<0.001*
Cesarean section: n (%)	35 (87.5)	11 (57.9)	17 (68)	0.031*
Oxygen uptake: n (%)	26 (66.7)	7 (43,8)	0 (0)	<0.001*
Multiple pregnancy: n (%)	15 (37,5)	0 (0)	4 (16)	0.003*
HIE: n (%)	1 (2.5)	11 (55)	0 (0)	<0.001*
IVH I-II: n (%)	4 (10)	4 (20)	0 (0)	0.390
Sepsis: n (%)	4 (10)	2 (10)	0 (0)	0.660
RDS: n (%)	17 (42.5)	3 (15)	0 (0)	0.033*
Hyperbilirubinemia: n (%)	1 (2.5)	0 (0)	0 (0)	0.684
PDA: n (%)	3 (7.5)	0 (0)	0 (0)	0.289
Maternal age	26.4±3.9	27.4±3.9	26±3.2	0.457

SD: Standart deviation; IQR: Interquartile range; HIE: Hypoxic ischemic encephalopathy; IVH: Intraventricular hemorrhage; RDS: Respiratory distress syndrome; PDA: Patent ductus arteriosus; *p<0.05.

than control group (p<0.001). While HIE rate was significantly higher in term infants (p<0.001), RDS rate was higher in preterm infants (p<0.05) (Table 1).

CDS in BSDI-II was recorded as 77 (73-80), 80 (77-83), 83 (80-87), 87 (85-90.5) and for the months 3., 6., 9., and 12., respectively in preterm infants. MDS in BSDI-II was recorded as 75 (72-80), 80 (77-83), 84 (80-86), 87.5 (83,5-90) for the months 3., 6., 9., and 12., respectively in preterm infants.

Also, in term infants, CDS was measured as 75 (72-77), 80 (77-80), 83 (80-87), 87 (84-90) and for the months 3., 6., 9., and 12., respectively. MDS was measured as 73 (70-79), 77 (75-82), 82 (79-85), 88 (80-91) for the months 3., 6., 9., and 12., respectively. Within groups measurements between 3. and 12. month of gestational age, in CDS (p<0.001) and MDS in BSID-II (p<0.001) were significantly increased in preterm and term groups.

There were no differences in preterm, term and healthy controls in cognitive and MDS of BSID- II scales at the 12 months of corrected age (p>0.05). There was also no difference in gross motor function in preterm and term group (p>0.05). However, preterm and term group recorded statistically lower scores than their typical peers in gross motor function at the age of 12 months of corrected age (p<0.05) (Table 2).

Although there was no correlation between the AIMS score and BSID-II MDS in 3rd and 6th months (p>0.05), there was a positive correlation in the 9th and 12th months (p<0.001). CDS of BSID-II was significantly correlated with the AIMS score in the 9th and 12th months (p<0.05) (Table 3).

TABLE 2: Cognitive, motor (BSID-II) and gross motor development (AIMS) of the groups at 12 month of corrected age.

Measure	Preterm n=40	Term n=20	Control n=25	p value
BSID-II CDS	87 (85-90.5)	87 (84-90)	87(85-93)	0.290
BSID-II MDS	87.5 (83.5-90)	88 (80-91)	88 (88-90)	0.544
AIMS Total score	53 (48-55)	52 (47-53)	55 (52-58)	0.004*

BSID-II: Bayley Scales of Infant and Toddler Development II; CDS: Cognitive Development Scale; MDS: Motor Development Scale; AIMS: Alberta Infant Motor Scale; *p<0.05.

TABLE 3: Correlation between BSID-II motor, cognitive ındex and AIMS score in preterm and term infants at risk (preterm+term) (n=60).

BSID- II MDS months	p value	r value
3rd	0.822	0.030
6th	0.177	0.176
9th	<0.001*	0.508
12th	<0.001*	0.570
BSID- II CDS months	**p value**	**r value**
3rd	0.785	0.036
6th	0.055	0.249
9th	0.001*	0.434
12th	0.004*	0.454

BSID-II: Bayley Scales of Infant and Toddler Development II;
CDS: Cognitive Development Scale; MDS: Motor Developmnet Scale; *p<0.05.

DISCUSSION

The aim of the present study was to describe the developmental profile of the preterm and term infants at risk and compare the cognitive, motor and gross motor development in preterm, term infants and their typical peers at the age of 12 months corrected age. Between 3. and 12. months, there was a regular increase in motor and cognitive scores of BSID-II in preterm and term infants at risk. Preterm and term infants had similar cognitive and MDS in BSID-II compared to their typical peers at 12. month. The median cognitive and MDS in BSID-II was over 85 and it is recorded that these infants were within the range of normality score at the age of 12 months.

In a study evaluating the preterm and term infants with BSID-II cognitive development index reported that preterm infants reached optimal scores in contrast to term infants.[16] In another study done by Coletti et al., it was recorded that both very preterm and late pretem infants had optimal scores in the normal range in BSID-III, without significant differences between the groups.[17] In their study Morag et al. longitudinally assessed the neurodevelopmental outcomes of infants born preterm and compared with term infants. They stated that developmental scores were similar according to their corrected age scores.[18] In their study, Kaya Kara et al. screened the neuromotor development outcomes of premature infants for 1 year. In this study, premature infants were evaluated with BSID-III and Neuro-sensory Motor Development Assessment (NSMDA) and stated that the motor development results of premature infants evaluated with BSID-III were above the cut-off score of 85.[19] In a study of the same author, motor development was evaluated with NSMDA and cognitive and language development with BSID-III. BSID-III motor, cognitive and language development in infants at risk followed for 1 year were found to be above 85, which is the cut-off score.[20] Our study was similar to the studies with 1-year follow-up. On the other hand, in the follow-up studies conducted at 2 years and over, preterm infants had lower scores on cognitive development when compared to term infants.[21,22] In our study, we included the infants with mild to moderate risk factors. This may reduce the difference between preterm and term infants in cognitive and MDS of BSID-II. Therefore, excluding the negative effects of major risk factors on development may enable preterm and term infants at risk to catch up with their typical peers at the 12 months of corrected age.

Preterm and term infants had lower scores in gross motor development when comparing to their typical peers at 12 months of corrected age in our study. In a study of Pin et al. compared the preterm and term control children in term of gross motor development and they found that preterm infants demonstrated less progression in AIMS total score at 12 months corrected age. They also concluded that preterm infants show lack of rotation and fluency in their movements.[23] In another study, Wang et al. showed significant differences in postural control, by using the AIMS between full term and preterm infant at 12 months corrected age.[24] In a study, Restiffe et al. found that preterm infants' mean scores were lower than those of term infants during follow-up. They observed the differences in scores between the 8th to the 11th months of age. Also they stated that the difference gradually decreased from the 12th up to the 16th month.[25] Conversely, Souza et al. showed no difference between preterm and term control groups in the AIMS at 12 months, but they found that the preterm group presented slower gait acquisition.[26] Similar studies and our study shows that preterm infants at risk cannot complete their gross motor development compared to their typical peers by the first year of age. Particularly in the standing subscale of AIMS infants at risk had lower score and they did not achieve to walk independently. Since the beginning of independent walking is considered to be normal up to 18 months of age, we think that it may be important for these infants to keep track of their walking time up to 18 months. Another important point about our study was that, while there was no difference between the groups in the motor scores evaluated with BSID-II, there was a difference between the groups in the gross motor score evaluated with AIMS. In the BSID-II motor section, both gross and fine motor skills are evaluated together and a total score is obtained. We think that there is no difference between the groups in BSID-II total motor score due to the high scores in fine motor skills. For this reason, we believe that motor development areas should be evaluated separately in future studies. Also, due to the correlation between BSID-II motor development index and the AIMS, we have concluded that AIMS can be used for routine examinations as it is based on easy administration, short duration and observation in the first months of the life.

One of the theoretical approaches in infant development is the embodied cognition approach. This approach claim that cognitive and motor development are strongly connected.[27] In addition, this approach state that, children learn and develop cognitive skills by constantly interacting with the environment. As children interact with environment, they receive information about the environment and generate new information from the perceived information, so the cognitive process continues.[27,28] In this sense, fine mobility and gross motor development are necessary for a better cognitive process. In many studies, the correlation between the early motor development and later cognitive skills were investigated but the information about early cross-sectional relations is still scarce.[29,30] In this study, we recorded a link between the gross motor and cognitive development at 9 and 12 months of corrected age in infants at risk. We concluded that the improvement in the mobility from the 9 months of corrected age might be important for the cognitive development. This period includes the crawling and standing so the child may have more chance to explore the environment.

The present study has some limitations. We didn't classify the preterm group as early preterm or late preterm. Such classification of preterm infants at risk in future studies may provide more detailed information about the development of preterm infants. The second limitation is that the present study ended up with a rather limited number of term infants at risk due to lost contact during the follow-up, and therefore further studies should aim to include more term infants.

CONCLUSION

In conclusion, the preterm and term infants at risk showed similar results in cognitive and MDS of BSID-II compared to the control group. However, the gross motor development was lower than their typical peers. In terms of cognitive and gross motor developments, these infants should be followed for a longer period.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Umut Apaydın, Bülent Elbasan**; Design:*** *Kıvılcım Gücüyener, Şebnem Soysal Acar, Bülent Elbasan;* ***Control/Supervision:*** *Kıvılcım Gücüyener, Bülent Elbasan;* ***Data Collection and/or Processing:*** *Ramazan Yıldız, Erkan Erol, Ayşe Yıldız, Umut Apaydın;* ***Analysis and/or Interpretation:*** *Ramazan Yıldız, Umut Apaydın;* ***Literature Review:*** *Ayşe Yıldız, Umut Apaydın;* ***Writing the Article:*** *Ayşe Yıldız, Ramazan Yıldız, Erkan Erol, Umut Apaydın;* ***Critical Review: B****ülent Elbasan, Kıvılcım Gücüyener, Şebnem Soysal Acar;* ***References and Fundings:*** *Kıvılcım Gücüyener, Şebnem Soysal Acar, Bülent Elbasan;* ***Materials:*** *Kıvılcım Gücüyener, Bülent Elbasan, Şebnem Soysal Acar.*

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