THE MEDICAL BULLETIN OF
SISLI ETFAL HOSPITAL

DOI: 10.14744/SEMB.2020.06881
Med Bull Sisli Etfal Hosp 2020;54(3):337–345

Original Research

Midterm Neuromotor Development Results of Preterm Babies less than 34 Weeks Gestational Age

Ali Bulbul,[1] Dilek Kabakci Kaya,[1] Gulperi Yagar Keskin,[1] Gulsen Kose,[2] Lida Bulbul,[3] Gizem Kara Elitok,[1] Ebru Ayyildiz,[1] Evrim Kiray Bas,[1] Sinan Uslu[1]

[1]Department of Pediatrics, Division of Neonatology, University of Health Sciences Turkey, Sisli Hamidiye Etfal Teaching and Resarch Hospital, Istanbul, Turkey
[2]Department of Pediatrics, Division of Pediatric Neurology, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey
[3]Department of Pediatrics, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, University of Health Science, Istanbul, Turkey

Abstract

Objectives: This study aimed to evaluate the neuromotor development of premature babies and to determine the risk factors affecting neuromotor development in the middle time (3 years).

Methods: All babies with ≤34 weeks gestational age and born between 2011-2014 and hospitalized in our neonatal clinic were included in this study. Prenatal, perinatal and postnatal features of the babies were recorded. Consent was obtained from the families who had an outpatient follow-up and agreed to participate in this study. Neurological examination and Denver II Developmental Screening Test (DDST-II) were applied to babies and their results were recorded. Factors affecting neurodevelopment were evaluated.

Results: Complete data for 96 of the study infant were obtained. Fifty (52.1%) of the cases were female. The mean birth weight was 1542±518 grams. The mean corrected age was 20.9±10.7 months at the time of the examination. It was found cerebral palsy in 11 babies (11.5%) with the neurological examination and developmental retardation in 15 babies (15.6%) with DDST-II. Low birth weight, a gestational period of 25-26 weeks, Apgar score at 5th minute <7 were found to be the main risk factors for cerebral palsy and abnormal DDST-II result ($p<0.05$). In babies with abnormal neurological examination, the frequency of bronchopulmonary dysplasia, sepsis and intraventricular hemorrhage were found to be high ($p<0.05$), and in babies with abnormal DDST-II results the frequency of respiratory distress syndrome, bronchopulmonary dysplasia and sepsis were found to be high ($p<0.05$).

Conclusion: In our study, abnormal neurological examination rate was found 11.5% in preterm infants with gestational age ≤34 weeks, and the rate of abnormal DDST-II was found 15.6%. The main factors affecting neuromotor development were gestational week, birth weight and 5th minute Apgar score. The frequency of bronchopulmonary dysplasia, sepsis and intraventricular hemorrhage in babies with abnormal neurological examination, and the frequency of respiratory distress, bronchopulmonary dysplasia and sepsis were found to be high in babies with abnormal DDST-II.

Keywords: Premature; neuromotor development; morbidity.

Please cite this article as "Bulbul A, Kabakci Kaya D, Yagar Keskin G, Kose G, Bulbul L, Kara Elitok G. Midterm Neuromotor Development Results of Preterm Babies less than 34 Weeks Gestational Age. Med Bull Sisli Etfal Hosp 2020;54(3):337–345".

Mortality rates in preterm infants have decreased significantly thanks to the improvements in service provision in neonatal intensive care units, especially in surfactant and antenatal steroid treatment.[1, 2] It has been recently reported that average survival rate of babies born at 25th gestational week is 56%, and the survival rate in babies born at 22nd-25th gestational weeks gradually increases with improved health care services.[3] The increase in survival rates and premature

Address for correspondence: Ali Bulbul, MD. Saglik Bilimleri Universitesi, Sisli Hamidiye Etfal Egitim ve Arastirma Hastanesi Neonatoloji Bolumu Cocuk Sagligi ve Hastaliklari Klinigi, Istanbul, Turkey
Phone: +90 505 265 44 25 **E-mail:** drbulbul@yahoo.com

Submitted Date: March 03, 2020 **Accepted Date:** May 27, 2020 **Available Online Date:** September 04, 2020

births has not been accompanied by a decrease in long-term neurodevelopmental retardation. Survived premature babies constitute an important risk group for neurodevelopmental problems, such as cerebral palsy (CP) and mental retardation (MR). Especially neonates and extremely low- birth weight (ELBW) newborns constitute a high risk group for neurodevelopmental retardation. Today, it is accepted that the success criteria of neonatal intensive care units worldwide are related to neurodevelopmental outcomes.[4]

The incidence of CP in pretem babies is higher than term babies.[5] In the United States, preterm babies constitute approximately 45% of the children with cerebral palsy, 35% of the children with visual impairment and 25% of children with cognitive impairment or hearing impairment.[6] In addition, problems in domains of cognitive functions, language, attention and behavior that affect the success of school performence may emerge in preterm infants during childhood. [7] In studies performed, CP, MR, blindness, deafness and hydrocephalus have been accepted as major neurological sequelae.[7, 8] The minor neurological sequelae affecting higher number of the premature children include delayed speech, learning difficulties, perception problems, attention disorders, and behavioral problems. Minor neurological disorders are generally not detected until school age.[9]

Long-term follow-up of babies at appropriate intervals and suitable methods according to the risks detected in the prenatal period; allows early detection of morbidity, taking necessary precautions and planning treatments.

In our study, our primary objective was to determine the risk factors affecting the neuromotor development of the babies born at ≤34 gestational weeks in our hospital between 2011-2014, and hospitalized in our Neonatal Clinic. Our second objective was to investigate the mid-term (first 3 years of life) evaluation of neuromotor development of babies using neurological examination and Denver II Developmental Screening Test (DDST-II).

Methods

A prospective, cross-sectional study was planned. This study was carried out in two stages. In the first stage, all babies born at ≤34 gestational weeks between 2011-2014 in our hospital, and hospitalized in the Neonatal Intensive Care Unit were included in this study. Information of the babies during hospitalization was recorded. In the second stage, our patients who attended the control visits at outpatient clinics were informed about this study and invited to our hospital for neurological examination and application of Denver II Developmental Screening Test. This study was completed with the patients who agreed to participate in this study.

Exclusion Criteria

Babies born in an external center, babies born in our hospital and referred to an external center, infants lost during hospitalization, cases with major congenital anomalies (e.g., cyanotic congenital heart disease, neural tube defect) and congenital metabolic disease were excluded from this study.

Data Collection:

Ethical approval for this study was obtained from the Sisli Hamidiye Etfal Training and Research Hospital Ethics Committee (05/06/2014-317).

In the first stage, the characteristic features of the babies whose data can be accessed were scanned from the patient registry files and the electronic database of the neonatal intensive care unit.

Information about gestational age, gender, birth weight, height and head circumference; 1st and 5th min Apgar scores, type of delivery, length of hospital stay, oxygenation status of the patients, resuscitation applied at birth (if any), duration of adherence to mechanical ventilator, and CPAP (Continuous Positive Airway Pressure) application time, use of surfactant, caffeine, and antibiotic therapy (if any), whether or not the patient had been diagnosed as respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), sepsis, necrotizing enterocolitis (NEC) and intraventricular bleeding (IVC), and received postnatal steroids for bronchopulmonary dysplasia have been recorded.

In the second stage, the families of the babies who could be reached and accepted to participate in this study were informed about this study, and the families were called for control. The cases brought to the Well Child Outpatient Clinic and undergoing neurodevelopmental evaluation constituted the study group. Voluntary consent forms were obtained from the families, then, the neurological examination and DDST-II tests were performed. Neurological examination was performed by a pediatrician. Patients with pathological findings were reevaluated by the pediatric neurologist. DDST-II test was applied by the certified Child Development Specialist. The cases with abnormal neurological examination and DDST-II results were followed up by the pediatric neurology and child development specialist.

Mid-term Results: Babies whose corrected age did not exceed three years (36 months) were included in this study.

Statistical Analysis

IBM SPSS Statistics 22 program was used for statistical analysis of the information obtained from this study. While evaluating the study data, the fitness of the parameters to

normal distribution was evaluated with the Shapiro- Wilks test. While evaluating the study data, descriptive statistical methods (mean, standard deviation, frequency) were used. Regarding quantitative data Oneway Anova test was used for intergroup comparison of the parametres with normal distribution. Tukey test was employed to determine the group that caused the difference. Student's t-test was used for comparisons of normally distributed parameters between two groups, and Mann- Whitney U test was used for comparisons of non-normally distributed parameters between two groups.

In the comparison of qualitative data, Chi-square test, Fisher's Exact Chi-Square test and Continuity (Yates) Correction were used. Pearson correlation analysis was used to examine the relationships between parameters that show normal distribution. Significance was evaluated at the level of $p<0.05$.

Results

The data of the cases that meet the study criteria, patients without missing data who were brought to the outpatient clinic of our Newborn Clinic for examination within the period determined were recorded. Flow diagram of this study is given in Figure 1. The prenatal, natal and postnatal features of the patients included in this study and their demographic features during hospitalization in the neonatal period are presented in Table 1. There were 51 (53.1%) mothers who received antenatal steroid treatment; it was found that 29 of them (30.2%) were administered a single dose and 22 of them (22.9%) were on full cure steroid treatment. The chronological ages of the babies ranged between 5 and 39 months, and the mean chronological age was 22.1±9.7 months, and the adjusted age was 20.9±10.7 months. Neurological examination and DDST-II results of the cases are presented in Table 2. Based on neurological examination findings, 11 patients were diagnosed with cerebral palsy.

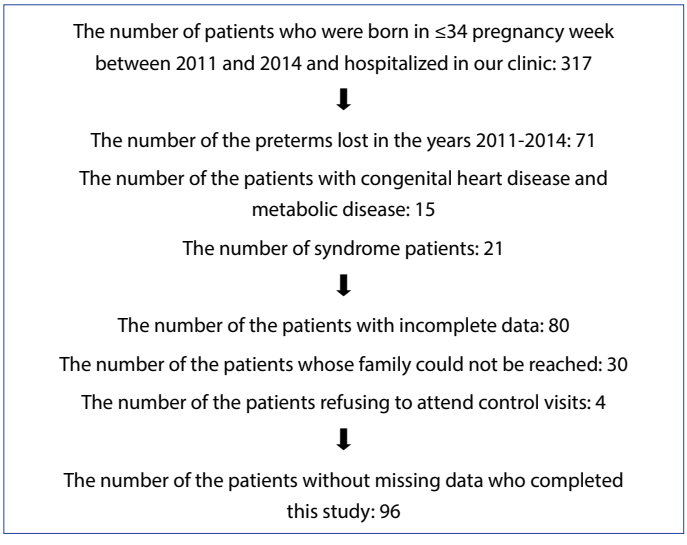

Figure 1. Flow diagram of the study.

The evaluation of the risk factors of the patients and the results of the neurological examination are presented in Table 3. There was a significant relationship between abnormal neurological examination findings, low- birth weight and gestational week (p=0.02, p=0.03). According to the results of the neurological examination, a statistically significant difference was found between the distributions of the gestational weeks (p=0.031). As a result of the pairwise comparisons made to determine the gestational week that caused the difference, the higher number of babies with abnormal neurological examination findings had been delivered between 25th and 26th gestational weeks. The incidence of BPD, sepsis and IVC was higher in patients with abnormal neurological examination findings (p=0.009, p=0.009, p=0.026).

Any significant difference was not found between the frequency of RDS and NEC among patients with abnormal and normal neurological examination findings. Requirement for mechanical ventilator was found to be significantly higher in patients with abnormal neurological examination findings (p=0.01). Duration of oxygen therapy and CPAP application time were increased in patients with abnormal neurological examination findings (p=0.01, p=0.024).

The comparison of DDST-II results with the demographic characteristics of the cases is presented in Table 4. There was a significant relationship between abnormal DDST-II results and low- birth weight and gestational week (p=0.001, p=0.002). As a result of the pairwise comparisons made to determine the gestational week that caused the difference, higher number of the babies born between 25th-26th gestational weeks was found to have abnormal DDST-II results. No significant correlation was found between abnormal DDST-II results, weight groups (SGA, AGA, LGA), mode of delivery and gender of babies.

The frequency of RDS, BPD and sepsis were found to be higher in patients with abnormal DDST-II results (p=0.028, p=0.001, p=0.014). No significant difference was found between the frequency of NEC and IVC among patients with abnormal or abnormal DDST-II results (Table 4). In patients with abnormal DDST-II results, requirement for mechanical ventilation was found to be significantly higher (p=0.05). Frequency of surfactant treatment in patients with abnormal DDST -II results was higher than patients with normal DDST-II results (p=0.028).

Table 1. The prenatal, natal and postnatal features of the cases and their demographic characteristics during hospitalization in the neonatal period

	Mean±SD	Lower and upper limits
Birth weight, g	1542.1±518.5	625-2950
Gestational weeks	**n**	**%**
25-26	11	11.5
27-28	5	5.2
29-30	19	19.8
31-32	42	43.8
33-34	19	19.8
Antenatal steroid use	51	53.1
Apgar score, (1. min <7)	54	56.3
Apgar score (5. min <7)	12	12.5
Mode of delivery, cesarean	86	89.4
Diagnoses at hospitalisation		
Respiratory Distress Syndrome	27	28.1
Bronchopulmonary Dysplasia	20	20.8
Mild	17	17.7
Moderate	3	3.1
Sepsis	20	20.8
Necrotizing Enterocholitis	25	26
Stage 1	20	20.8
Stage 2	5	5.2
Intraventricular bleeding	24	25
Stage 1	16	16.6
Stage 2	4	4.2
Stage 3	4	4.2
Treatments administered at admission		
Oxygen support	88	91.7
Mechanical ventilation support	42	43.8
Continuous positive airway pressure	68	70.8
Surfactant	27	28.1
Caffeine	45	46.9
Antibiotics	88	91.7
Steroid therapy with the indication of bronchopulmonary dysplasia		
Once	15	15.6
Twice	5	5.2
Characteristic features of hospital stay	**Mean±SD**	**Lower and upper limits**
Length of hospital stay, days	40±28.9	5-166
Oxygen requirement time, days	20.1±27.3	1-166
Duration of mechanical ventilation, days	10.5±17.4	1-83
Duration of CPAP application, days	5.6±6.3	1-33
Duration of antibiotherapy, days	14.3±11.8	3-74

SD: Standard deviation.

Table 2. Midterm (for a period of three years) results of neurological examination, and DDST-II tests of the cases

	n	%
Neurological examination results		
Normal	85	88.5
Abnormal	11	11.5
DDST-II		
Normal	81	84.4
Abnormal	15	15.6
Distribution of DDST-II test results		
Abnormal Personal–Social Development	4	4.2
Abnormal fine motor development	6	6.3
Abnormal development of language	5	5.2
Abnormal gross motor development	9	9.4

DGTT-II: Denver II Developmental Screening Test.

Discussion

In recent years, through the developments in perinatology and neonatal intensive care services, the life span of premature babies has increased significantly.[10] Despite all these favourable advances, the number of premature and LBW babies could not be reduced. Premature babies, especially very and extremely preterm babies, constitute a significant risk group for neurodevelopmental problems, such as cerebral palsy and mental retardation. In the USA, preterm infants constitute 45% of children with CP, 35% of the visually impaired and 25% of the children with impaired hearing and cognitive functions.[6]

CP is a non-progressive disease of the central nervous system, which occurs when prenatal and perinatal events affect the developing brain tissue, including posture and movement disorders.[11] In studies conducted on the frequency of cerebral palsy by gestational week, the highest rate has been reported in patients who were born at the 22nd gestational week (21.7%) and at the 23rd gestational week (17.8%), while in 4.%, and 0.7 % of the babies born at the 33th, and 34th gestational weeks, respectively.[12, 13] The incidence of CP was 14.2% at the age of six in the evaluation of these 183 preterm children regardless of their gestational weeks at birth.[14] In our country, the incidence of CP in premature babies was determined to be between 8.5-24.2%.[15, 16] In our study, it was seen that the frequency of CP was similar to the results reported in our country.

In a study in which neurological evaluation was performed using DDST-II tests, in babies with abnormal DDST-II results, the frequency of severe RDS and requirement for surfactant was significantly higher.[17] Similarly, in our study, higher rates were found in babies with abnormal DDST-II results. BPD plays a significant role in clinical diseases that nega-

Table 3. Evaluation of neurological examination results, and risk factors of the cases

	Neurological examination results		p
	Normal n=85	Abnormal n=11	
	Mean±SD		
Birth weight, g	1598.8±503.9	1103.8±427.8	<0.001
Gestational weeks	30.9±2.3	28.6±2.6	0.003
	n (%)	n (%)	
Gestational weeks		0.031	
25-26	7 (7.3)	4 (4.2)	
27-28	4 (4.2)	1 (1)	
29-30	16 (16.7)	3 (3.1)	
31-32	39 (40.6)	3 (3.1)	
33-34	19 (19.8)	0 (0)	
Apgar score (1st min <7)	44 (45.8)	10 (10.4)	0.021
Apgar score (5th min <7)	7 (7.3)	5 (5.2)	0.004
Bronchopulmonary dysplasia	14 (14.6)	6 (6.3)	0.009
Sepsis	14 (14.6)	6 (6.3)	0.009
Intraventricular bleeding	18 (18.8)	6 (6.3)	0.026
Requirement for mechanical ventilation	32 (33.3)	10 (10.4)	0.001
Surfactant treatment	21 (21.9)	6 (6.3)	0.069
Duration of oxygen therapy	15.5±19.4 (7)	52.8±47.9 (40)	0.001
Duration of CPAP application	5.3±6.4 (3)	7.7±5.3 (6)	0.024

CPAP: Continuous Positive Airway Pressure.

Table 4. Evaluation of the factors effective on DDST-II results

	DDST-II test results		p
	Normal n=81	Abnormal n=15	
	Mean±SD		
Birth weight g	1616.4±497	114.9±456.8	0.001
Gestational weeks	31±2.2	28.5±2.8	0.001
n (%)			
Gestational weeks			0.002
25-26	5 (5.2)	6 (6.3)	
27-28	4 (4.2)	1 (1)	
29-30	15 (15.6)	4 (4.2)	
31-32	39 (40.6)	3 (3.1)	
33-34	18 (18.8)	1 (1)	
Apgar score (5th min <7)	6 (6.3)	6 (6.3)	0.003
Respiratory distress syndrome	19 (19.8)	8 (8.3)	0.028
Bronchopulmonary displasia	11 (11.5)	9 (9.4)	0.001
Sepsis	13 (13.5)	7 (7.3)	0.014
Requirement for mechanical ventilation	30 (31.3)	12 (12.5)	0.005
Surfactant treatment	19 (19.8)	8 (8.3)	0.028

DDST-II: Denver II Developmental Screening Test; SD: Standard deviation.

tively affect neurodevelopmental prognosis. In studies conducted in preterm infants in our country, the frequency of BPD has been reported to range between 13.1% and 30%.[17, 18] The BPD is thought to negatively affect growth and development because it impairs nutrition, causes frequent lung infections and increases the frequency of hospitalizations.

In the study conducted by Kavuncuoğlu et al.,[19] patients with and without the diagnosis of BPD were compared, and abnormal DDST-II results were detected in 32%, and 6% of the patients diagnosed with BPD and the patients in the control group, respectively. However, there was no difference in the development of CP among patients with BPD. Similarly, in our study, the frequency of BPD was high in patients who were abnormal as a result of DDST-II. In our study, the frequency of BPD was found to be significantly higher in patients with CP.

Use of antenatal steroids in preterm infants reduces the incidence of RDS mortality, NEC and IVC.[20, 21] However, some studies have reported that the use of antenatal steroids causes cystic developments in white matter.[22] It has been reported that the administration of single-cycle antenatal steroids in preterm infants is a safe procedure regarding the nervous system of the newborn and an effective method in preventing the development of cerebral palsy and decreasing the frequency of death and IVC.[23] It has been reported that there is no significant relationship between abnormal DDST-II results and antenatal steroid administration.[15] Similarly, in our study, no statistically significant relationship was found between abnormal DDST-II results and antenatal steroid administration.

Based on the results of metaanalysis, it was seen that the use of systemic postnatal dexamethasone reduced the frequency of BPD, but its use was limited due to the neurocognitive side effects it may cause. When early and late term postnatal steroid use was evaluated separately, it was suggested that early steroid use increases the risk of CP. Thus, recommendations did not favour its use. However, its long-term use has been suggested because it does not significantly increase the risk of development of neurological sequelae in the long-term, so its limited use has been recommended due to its side effects.[24] The results of this study on the effects of postnatal steroid use on neuromotor development are contradictory and there is no clear consensus.

When the neuromotor development of 2-year-old babies who received postnatal systemic dexamethasone treatment was evaluated, the incidence of neuromotor dysfunction was reported to decrease by 40 percent.[25] In another study, 366 of the 2358 premature babies were administered postnatal systemic corticosteroid treatment, and as a result of this study, a reduction of 2.0 points in the mental development index and a 40% increase in CP risk in each 1 mg/kg dose of steroid administered.[26] In a study in which premature babies were evaluated at the age of seven, in patients with BPD who received postnatal steroids in the early and late periods; it was reported that there was no difference concerning the frequency of CP and behavioral disorders between both groups.[27] In our study, 20 (20.8%) patients diagnosed with BPD received late postnatal steroid (dexamethasone) treatment. There was no significant difference between patients with CP and patients with normal neurological examination findings in terms of steroid treatment.

Infections have been shown to negatively affect neurodevelopmental prognosis in very-low-birth-weight (VLBW) preterm infants.[28] The main mechanism causing developmental disorders in sepsis is white matter damage that arises from the effects of inflammatory cytokines induced by infections in the perinatal and postnatal periods.[29] In our study, the incidence of sepsis was found to be higher in patients with CP. In the study conducted by Sütçüoğlu et al.,[17] when the babies were evaluated at the age of two, the detection rate of abnormal DDST-II results was found to be statistically significantly higher when compared with the patients who did not have sepsis. In accordance with the other studies cited herein, the frequency of sepsis was found to be higher in patients with abnormal DDST-II results. It has been reported that the development of stage ≥3 NEC in preterm babies with a birth weight below 1000 g is an independent risk factor for developmental problems seen in 18-22 months of life.[30] In our study, unlike the literature, there was no significant relationship between NEC and abnormal neurological examination and abnormal DDST-II results. This situation can be explained that the babies in our study had a higher gestational week at birth.

One of the most significant factors contributing to the unfavourable neurodevelopmental prognosis is considered as intraventricular bleeding. Psychiatric problems and dysfunction in management functions are seen in approximately 1/3 of infants with stage 3 and 4 intraventricular bleeding.[31, 32] In a study in which 128 VLBW babies in our country were evaluated in adjusted 12-18 months, the detection rate of IVC was found to be statistically significantly higher in patients diagnosed with CP.[33] In our study, there was a positive relationship between the frequency of IVC and the diagnosis of the CP.

In babies with a birth weight below 1250 g, caffeine treatment has been shown to shorten their stay in mechanical ventilation and reduce the incidence of BPD in these ba-

bies.[34] A total of 2006 babies with birth weights between 500-1250 grams, were evaluated at corrected 18-21 years of age and at the age of five months; higher survival rate was detected for babies who used caffeine and any significant difference in terms of neurodevelopmental retardation was not reported between both groups.[35, 36] In our study, there was no positive effect of caffeine treatment on neurological development.

As the gestational weeks at birth and birth weight decrease, the rate of neurodevelopmental retardation increases. In a study where babies were evaluated at the age of 2.5, CP was detected in 7% of the babies born at a gestational age less than 27 weeks and in 0.1% of term babies.[37] In our study, the mean gestational age at birth and birth weight of the patients diagnosed with CP were significantly lower as expected. In our study, the mean gestational week at birth and birth weight were found to be significantly lower in babies with abnormal DDST-II results.

It has been reported that unfavourable neurodevelopmental prognosis in VLBW infants is associated with male gender, and the incidence of moderate to severe CP is higher in males.[38] In a study conducted in our country, the male gender was found to be a significant risk factor for abnormal neurodevelopment based on the evaluation of DGTT-II results.[15] However, similar to our study, it was observed in different studies that there was no relationship between male gender and abnormal DDST-II results.[33]

In a study evaluating premature babies with DDST-II, there was no relationship between 1st minute Apgar scores and abnormal DDST-II results, while a statistically significant relationship was found between the 5th minute Apgar scores and abnormal DDST-II results.[15] In our study, there was no relationship between 1st minute Apgar scores and abnormal DDST-II results, whereas 5th minute Apgar scores were found to be significantly lower in cases with abnormal DDST-II results.

In our study, the neurodevelopmental evaluation was performed with the neurological examination and DGTT-II tests. In abnormal neurological examination, findings can be detected in 58% preterm babies at the age of 2.5.[37] In our study, the low detection rate of abnormal neurological examination results can be explained by that our babies were born at higher gestational weeks.

In a study with 367 VLBW infants with a corrected age of 15 months, abnormal DDST results were detected in 10.9% of these cases. In addition, retardation was reported in the personal-social development domain in 7.1%, in the fine motor domain in 7.9%, in language domain in 8.8% and in the gross motor domain in 10.7% of the cases.[39] In our country, DDST-II test was performed in VLBW infants with a corrected age of 12-18 months, and retardations were detected in the personal-social domain in 7-13%, in fine motor domain in 9.4-13%, in language domain in 7.8-23.1%, and in gross motor domain in 10.3-12.5% of the cases. In our study, it was thought that the rates of abnormal conditions detected in the domains of personal-social, fine motor, language and gross motor functions were lower than the incidence rates reported in our country, and this situation could have a positive reflection on the developing newborn health care of babies.

Conclusion

In conclusion, in our study, abnormal neurological examination findings, and DDST-II test results were found in 11.5% and 15.6% of preterm infants born at <34th gestational weeks, respectively. The main factors affecting neuromotor development were gestational week, birth weight and the 5th min Apgar scores. Higher frequency of the BPD, sepsis and IVC were found in babies with abnormal neurological examination findings, while the frequency of RDS, BPD and sepsis was higher in babies with abnormal DDST-II results. It was found that the babies who had abnormal neurological examination findings and DDST-II results required mechanical ventilator and oxygen therapy and prolonged adherence to a mechanical ventilator.

Disclosures

Ethics Committee Approval: Sisli Hamidiye Etfal Training and Research Hospital Ethics Committee (05/06/2014-317).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – A.B., S.U.; Design – A.B., S.U.; Supervision – L.B., G.K.E.; Materials – D.K., G.Y.K., E.A.; Data collection &/or processing – D.K., G.Y.K., E.A.; Analysis and/or interpretation – L.B., G.K.E.; Literature search – E.K.B., D.K.; Writing – A.B., G.K.; Critical review – G.K., E.K.B.

References

1. Field DJ, Dorling JS, Manktelow BN, Draper ES. Survival of extremely premature babies in a geographically defined population: prospective cohort study of 1994-9 compared with 2000-5. BMJ 2008;336:1221–3. [CrossRef]
2. Horbar JD, Carpenter JH, Badger GJ, Kenny MJ, Soll RF, Morrow KA, et al. Mortality and neonatal morbidity among infants 501 to 1500 grams from 2000 to 2009. Pediatrics 2012;129:1019–26.
3. Dani C, Poggi C, Romagnoli C, Bertini G. Survival and major disability rate in infant born at 22-25 weeks of gestation. J Perinat Med 2009;37:599–608. [CrossRef]
4. Stephens BE, Vohr BR. Neurodevelopmental outcome of the premature infant. Pediatr Clin North Am 2009;56:631–46. [CrossRef]
5. Hirvonen M, Ojala R, Korhonen P, Haataja P, Eriksson K, Gissler M,

et al. Cerebral palsy among children born moderately and late preterm. Pediatrics 2014;134:e1584–93. [CrossRef]
6. Allen MC. Neurodevelopmental outcomes of preterm infants. Curr Opin Neurol 2008;21:123–8. [CrossRef]
7. Vohr BR. Neurodevelopmental outcomes of extremely preterm infants. Clin Perinatol 2014;41:241–55. [CrossRef]
8. Saigal S, Rosenbaum P, Stoskopf B, Hoult L, Furlong W, Feeny D, et al. Comprehensive assessment of the health status of extremely low birth weight children at eight years of age: comparison with a reference group. J Pediatr 1994;125:411–7. [CrossRef]
9. Weindrich D, Jennen-Steinmetz C, Laucht M, Schmidt MH. Late sequelae of low birthweight: mediators of poor school performance at 11 years. Dev Med Child Neurol 2003;45:463–9. [CrossRef]
10. Doyle LW; Victorian Infant Collaborative Study Group. Evaluation of neonatal intensive care for extremely low birth weight infants in Victoria over two decades: II. Efficiency. Pediatrics 2004;113:510–4. [CrossRef]
11. Korzeniewski SJ, Birbeck G, DeLano MC, Potchen MJ, Paneth N. A systematic review of neuroimaging for cerebral palsy. J Child Neurol 2008;23:216–27. [CrossRef]
12. Ishii N, Kono Y, Yonemoto N, Kusuda S, Fujimura M; Neonatal Research Network, Japan. Outcomes of infants born at 22 and 23 weeks' gestation. Pediatrics 2013;132:62–71. [CrossRef]
13. Marret S, Ancel PY, Marpeau L, Marchand L, Pierrat V, Larroque B, et al; Epipage Study Group. Neonatal and 5-year outcomes after birth at 30-34 weeks of gestation. Obstet Gynecol 2007;110:72–80. [CrossRef]
14. Stoll BJ, Hansen NI, Bell EF, Shankaran S, Laptook AR, Walsh MC, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. Pediatrics 2010;126:443–56. [CrossRef]
15. Göçer C, Kavuncuoğlu S, Arslan G, Ertem İ, Özbek S, Öztüregen E, et al. Neurodevelopmental problems of very low birth weight premature infants and factors affecting neurological morbidity. Türk Ped. Arş 2011;46:207–14. [CrossRef]
16. Erdem G, Erdoğan Bakar E, Yiğit Ş, Turanlı G. Hacettepe Üniversitesi Hastanesi Yenidoğan Yoğun Bakım Ünitesi'nde izlenen prematüre bebeklerin nörogelişimsel izlemi. Çocuk Sağlığı ve Hastalıkları Dergisi 2006;49:185–92.
17. Sütçüoğlu S, Dikerler A, Halıcıoğlu O, Akkaya Mİ, Öztürk C, Akman SA, Özer E. Neurodevelopmental follow-up results in very low birth weight premature infants and influential factors. İzmir Dr. Behçet Uz Çocuk Hastanesi Dergisi 2012;2:94–101. [CrossRef]
18. Özkan H, Köksal N, Çetinkaya M, Canıtez Y. Bronkopulmoner displazide risk faktörleri. Güncel Pediatri 2008;6:66–71.
19. Kavuncuoğlu S, Aldemir EY, Altuncu E, Arduç A, Alpaslan S, Arslan G, et al. Bronkopulmoner displazili hastalarımızın uzun dönem izleminde somatik büyüme, akciğer sorunları ve nörogelişimsel özelliklerinin irdelenmesi. Türk Ped Arş 2008;43:17–23.
20. Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2017;3:CD004454.
21. Poryo M, Boeckh JC, Gortner L, Zemlin M, Duppré P, Ebrahimi-Fakhari D, et al; PROGRESS study consortium and NGFN - Nationales Genomforschungsnetz Deutschland. Ante-, peri- and postnatal factors associated with intraventricular hemorrhage in very premature infants. Early Hum Dev 2018;116:1–8. [CrossRef]
22. Ghotra S, Vincer M, Allen VM, Khan N. A population-based study of cystic white matter injury on ultrasound in very preterm infants born over two decades in Nova Scotia, Canada. J Perinatol 2019;39:269–77. [CrossRef]
23. Rajadurai VS, Tan KH. The use and abuse of steroids in perinatal medicine. Ann Acad Med Singapore 2003;32:324–34.
24. Doyle LW, Ehrenkranz RA, Halliday HL. Early (< 8 days) postnatal corticosteroids for preventing chronic lung disease in preterm infants. Cochrane Database Syst Rev 2014;CD001146. [CrossRef]
25. Yeh TF, Lin YJ, Huang CC, Chen YJ, Lin CH, Lin HC, et al. Early dexamethasone therapy in preterm infants: a follow-up study. Pediatrics 1998;101:E7. [CrossRef]
26. Wilson-Costello D, Walsh MC, Langer JC, Guillet R, Laptook AR, Stoll BJ, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Impact of postnatal corticosteroid use on neurodevelopment at 18 to 22 months' adjusted age: effects of dose, timing, and risk of bronchopulmonary dysplasia in extremely low birth weight infants. Pediatrics 2009;123:e430–7. [CrossRef]
27. Wilson TT, Waters L, Patterson CC, McCusker CG, Rooney NM, Marlow N, et al. Neurodevelopmental and respiratory follow-up results at 7 years for children from the United Kingdom and Ireland enrolled in a randomized trial of early and late postnatal corticosteroid treatment, systemic and inhaled (the Open Study of Early Corticosteroid Treatment). Pediatrics 2006;117:2196–205.
28. Murphy DJ, Sellers S, MacKenzie IZ, Yudkin PL, Johnson AM. Case-control study of antenatal and intrapartum risk factors for cerebral palsy in very preterm singleton babies. Lancet 1995;346:1449–54.
29. Adams-Chapman I, Stoll BJ. Neonatal infection and long-term neurodevelopmental outcome in the preterm infant. Curr Opin Infect Dis 2006;19:290–7. [CrossRef]
30. Hintz SR, Kendrick DE, Stoll BJ, Vohr BR, Fanaroff AA, Donovan EF, et al; NICHD Neonatal Research Network. Neurodevelopmental and growth outcomes of extremely low birth weight infants after necrotizing enterocolitis. Pediatrics 2005;115:696–703. [CrossRef]
31. Indredavik MS, Vik T, Evensen KA, Skranes J, Taraldsen G, Brubakk AM. Perinatal risk and psychiatric outcome in adolescents born preterm with very low birth weight or term small for gestational age. J Dev Behav Pediatr 2010;31:286–94. [CrossRef]
32. Whitaker AH, Feldman JF, Lorenz JM, McNicholas F, Fisher PW, Shen S, et al. Neonatal head ultrasound abnormalities in preterm infants and adolescent psychiatric disorders. Arch Gen Psychiatry 2011;68:742–52. [CrossRef]
33. Long-term follow-up of very low birth weight infants at Hacettepe

University İhsan Doğramacı Children's Hospital during 2003-2006 period. Çocuk Sağlığı ve Hastalıkları Dergisi 2009;52:101–12.
34. Davis PG, Schmidt B, Roberts RS, Doyle LW, Asztalos E, Haslam R, et al; Caffeine for Apnea of Prematurity Trial Group. Caffeine for Apnea of Prematurity trial: benefits may vary in subgroups. J Pediatr 2010;156:382–7. [CrossRef]
35. Schmidt B, Roberts RS, Davis P, Doyle LW, Barrington KJ, Ohlsson A, et al; Caffeine for Apnea of Prematurity Trial Group. Long-term effects of caffeine therapy for apnea of prematurity. N Engl J Med 2007;357:1893–902. [CrossRef]
36. Schmidt B, Anderson PJ, Doyle LW, Dewey D, Grunau RE, Asztalos EV, et al; Caffeine for Apnea of Prematurity (CAP) Trial Investigators. Survival without disability to age 5 years after neonatal caffeine therapy for apnea of prematurity. JAMA 2012;307:275–82.
37. Serenius F, Källén K, Blennow M, Ewald U, Fellman V, Holmström G, et al; EXPRESS Group. Neurodevelopmental outcome in extremely preterm infants at 2.5 years after active perinatal care in Sweden. JAMA 2013;309:1810–20. [CrossRef]
38. Hintz SR, Kendrick DE, Vohr BR, Kenneth Poole W, Higgins RD; Nichd Neonatal Research Network. Gender differences in neurodevelopmental outcomes among extremely preterm, extremely-low-birthweight infants. Acta Paediatr 2006;95:1239–48. [CrossRef]
39. Schendel DE, Stockbauer JW, Hoffman HJ, Herman AA, Berg CJ, Schramm WF. Relation between very low birth weight and developmental delay among preschool children without disabilities. Am J Epidemiol 1997;146:740–9. [CrossRef]