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Neurodevelopmental problems and factors affecting neurological morbidity of very low birth weight premature infants

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Summary

Aim: To evaluate neurodevelopmental outcome of premature infants born with a gestational age less than 32 weeks and /or very low birth weight (<1500gr) at the adjusted age of three years.

Material and Method: In this study, neurodevelopmental characteristics (Denver II Developmental screening Test, DDST II) and neurological sequelaes (Amiel Tison) were examined retrospectively.

Results: Seventeen hundred infants were evaluated at a mean age of 35.8±2.3 months (27-2). There were 57 female and 60 male patients and mean birth weight and gestational age were 1271+22,09 gr and 31+2.1 weeks, respectively. Most important acute morbidities included respiratory distress syndrome (RDS) (21%), bronchopulmonary dysplasia (BPD) (% 8), severe retinopathy of prematurity (ROP) (5%), sepsis (21%), severe intraventricular hemorrhage (IVH) (7%) and an Apgar score of <6 (24%) . 9.4% of the patients had major neurological sequelae; ten cases had cerebral palsy, five had hydrocephalus and two had blindness. Denver II Developmental Screening Test was abnormal in 23% cases.

Conclusions: Our neurodevelopmental assessment results were similar to the literature. One of the most important risk factors in neurodevelopmental retardation was transport. *(Turk Arch Ped 2011; 46: 199-206)*

Key words: Prematurity, neurodevelopmental outcome, Denver Developmental Screening Test, cerebral palsy

Introduction

Neurodevelopmental disorders observed in premature infants in long-term follow up are multifactorial and are affected by problems of prenatal and neonatal periods. It has been reported in the literature that socioeconomic and sociocultural levels also affect the development in addition to maternal and infantile problems (1).

Neurodevelopmental disorders are classified as severe and mild neurologic sequelae. Severe neurologic sequelae include cerabral palsy (CP), mental retardation, blindness, deafness, hydrocephaly and convulsion. Mild neurologic sequelae include adaptation and balance disorders, myopia, mild hearing deficit, difficulty in perception and behavioral problems (2).

There are many studies about long-term follow up and problems of very low birth weight (VLBW) infants in the literature. In developed countries, neurodevelopmental retardation is specifically perceived as a public health problem and preventive measures, treatment programs, close multi-centered monitoring are put at forefront and the aim is to gain the infant as a healthy individual for the community. In our country, the number of units giving service on this area and the number of published results are very limited. The support of the Social Security Institution for these patients began in 1998 (3).

In this study, we showed the neurodevelopmental problems and the factors affecting the prognosis in very low birth weight infants at the adjusted age of three and examined the compliance of the patients to the follow-up and cure programs and the results of family support.

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Material and Method

In this study, neurodevelopmental evaluation of 117 infants with a birth weight of 1500 g or lower and a gestational age of 32 weeks or less according to the new Ballard score (4) who were born in the Ministry of Health Bakırköy Women's and Children's Diseases Hospital in 2002 or who were born in another hospital and referred to our hospital and were followed up in the outpatient clinic following hospitalization in 2nd and 3rd level intensive care units. During the evaluation, adjusted age was calculated according to the formula of gestational week- (40-GW).

Multiple pregnancies, patients who were referred to another hospital because there was no empty bed in our intensive care unit and patients who died during hospitalization or during follow-up were not included in our study group. Prenatal, perinatal and postnatal risk factors of these high-risk premature infants who constituted our study group were obtained from the computer database of our unit and from patient files. These included birth weight, GW, mode of delivery, diagnoses made (bronchopulmonary displasia (BPD) (5), intracranial bleeding (ICB) (6), nectotizing enterocolitis (NEC) (7), respiratory distress syndrome (RDS), sepsis, meningitis), follow-up in the intensive care unit, respiratory support and history of prenatal steroid use. The study was started in January 2005 after obtaining ethics committee approval (06.20.2005/96). The families were contacted by phone. On the day of appointment, the child and the family were seen together and consent was obtained for all tests and evaluations.

In our double-blind study, general physical examination and Modified Amiel-Tison assessment test (8) were done by the same pediatrician. Denver II Developmental Screening Test (9) (DGTT II) was performed by a pedagogue who was not aware of the child's problems during the newborn period and during the follow-up period afterwards. These two investigators evaluated all infants without being aware of each other's results. The results were explained after analysis in the computer.

According to the findings on neurological examination the patients were evaluated in three groups (normal, mild neurological sequela and severe neurological sequela).

Children with severe neurological sequela were evaluated by a pediatric neurologist and necessary referrals were done (physical therapy, special education). In addition, cranial imaging was ordered in children with severe neurological sequela to confirm the diagnosis.

For evaluation of hearing, brain stem auditory evoked response (BAER) test was performed by the same audiologist.

Ophtalmologic examination of premature infants was performed by the same faculty member in the 4-8th week after birth according to the International ROP screening criteria in İstanbul University Medical Faculty Department of Ophtalmology Retina Unit (10). Screening results were obtained from outpatient follow-up files. Factors affecting the neurodevelopmental prognosis were recorded.

A scoring system was established for classification of socioeconomic levels and education levels of the families. Income level, education level of the parents, occupation of the parents, status of residence, the number of rooms in the house, the level of residence, heating status, consanguineous marriage, number of children and the total population in the house were questined for scoring. Families below the standard deviation were classified as having a poor socioeconomic level, families above the standard deviation were classified as having a high socioeconomic level and the others were classified as having a moderate socioeconomic level. In statistical evaluation, scores below -2SD were considered to be poor and the others were considered to be high.

Statistical analyses were done using qui-square test, Student's t-test, Man Whitney U test and SPSS (Statistical Program in Social Science) computer package program. A p value <0.05 was considered to be significant.

The mean values of the study group were expressed as±standard deviation.

Results

310 infants ≤32 weeks and/or ≤1500 g from inside and outside our hospital were hospitalized in our 2nd and 3rd level neonatal intensive care unit for follow-up, investigation and treatment between Januray 2002 and December 2002. 33 infants who died during the neonatal period (0-28 days) and post-neonatal period, 21 infants born to multiple pregnancy and 17 infants who were referred to another center because there was no empty bed in our unit were not included in the study. 108 patients could not be reached because their phone numbers and addressed had changeed. 14 patients did not accept the evaluation. Consequently, 117 very low birth weight infants were included in the study group.

Data were obtained from the computer database, hospital files and outpatient follow-up forms. Whether the data of the subjects who could not be reached and who did not accept the evaluation (Group 2) were different form the study group (Group 1) and their statistical comparability were questioned and the following result were found:

The birth weights of the patients who could not be reached were between 750 g and 1895 g (mean: 1240±234,38). Gestational age was more than 30 weeks in 83 subjects (68%) and less than 30 weeks in 39 subjects (32%). 62 patients were female (50.8%) and 60 patients were male (49.2%). Delivery mode was cesarean section in 79 subjects (64.8%) and vaginal delivery in 43 subjects (35.2%). Intrauterine growth in the premature infanst was evaluated as follows: 84 infants (68.9%) were appropriate for gestational age (AGA) and 38 infants (31.1%) were small for gestational age (SGA). 16 infants (13.1%) had an APGAR score of 6 and lower in the 5th minute.

When the two groups were compared, being AGA and SGA was statistically insignificant ($p>0.05$). There was no statistically significant difference in terms of apgar score in

Table 1. Prenatal and postnatal risk factors in the neonatal period				
Variable	(+)		(-)	
	n	%	n	%
Prenatal steroid	37	31.6%	80	68.4%
Follow-up in the intensive care unit	39	33.3%	78	66.7%
Mechanical ventilation	35	29.9%	82	70.1%
RDS	24	20.5%	93	79.5%
Surfactant	19	16.2%	98	83.8%
BPD	9	7.7%	108	92.3%
≥Grade III ROP	6	5.1%	111	94.9%
Sepsis	24	20.5%	93	79.5%
≥Stage III ICB	8	6.8%	109	93.2%
Transport	33	28.2%	84	71.8%

RDS: Respiratory distress syndrome, BPD: Bronchopulmonary dysplasia, ICB: Intracranial bleeding, ROP: Retinopathy of prematurity

Table 2: Denver II Developmental Screening Test Results.		
Area	**Normal (n%)**	**Abormal (n%)**
Language	90 (76.9%)	27 (23.1%)
Fine Motor	102 (87.2%)	15 (12.8)
Gross Motor	105 (89.7%)	12 (10.3%)
Individual-Social	102 (87.2%)	15 (12.8)
Total	85(72.6%)	32(27.4%)

the fifth minute, rates of stay in the intensive care unit, NEC, sepsis, meningitis and ICB rates (p>0.05).

According to these results, the patient groups who could be reached and could not be reached were similar to each other.

57 infants were female (48.7%) and 60 infants were male (51.3%) in the study group composed of VLBW premature infants. 36 infants were born by spontaneous normal vaginal delivery (30.8%) and 81 infants were born by C/S (69.2%). The chronological age of the infants was between 33 months and 45 months (mean: 32.8±2.26). Their adjusted age was between 27 months and 42 months (mean: 35.8±2.39 months). Their birth weight was between 700 g and 1800 g (mean: 1271±226.09 g) and gestational age was between 25 weeks and 36 weeks (mean: 31±2.16).

80 infants in our study group (68.4%) were AGA and 37 infants (31.6%) were SGA. Prenatal and postnatal risk faktors of the premature infants are shown in Table 1.

Modified Amiel-Tison neurological examination method revealed normal neurological findings in 102 subjects (87.2%), strabismus in 4 subjects (3.4%) and severe neurological sequela in 11 subjects (9.4%). 10 of these subjects had cerabral palsy (CP), 5 had spastic diplegia and 5 had spastic tetraplegia. Blindness as a severe neurological sequela was defined in two subjects. One of them had spastic tetraparesia at the same time.

Cranial imaging was performed in 8 patients with severe neurological abnormality. Since blindness was the severe neurological sequela in two subjects and the family of one patient did not give consent for imaging test, cranial imaging was not performed in the three other patients. Periventricular leucomalacia (PVL) was found in three patients and ventricular enlargement was found in 5 patients. Ventriculoperitoneal shunt was placed in three infants who developed hydrocephaly following ICB at a mean age of three months.

Denver II developmental screening test revealed that 85 of 117 patients (72.6%) were normal for their age and 32 (27.4%) were retarded for their age. When the parts of Denver II test were evaluated, 90 patients (76.9%) were found to be appropriate for their age in language and 27 (23.1%) were found to be delayed. In Denver II motor test, 102 (7.2%) patients were found to be appropriate for their age and 15 patients (12.8%) were found to be delayed. In the gross motor skill test, 105 patients (89.7%) were found to be appropriated for their age and 12 patients (10.3%) were found to be delayed. Individual social test revealed that 102 patients (87.2%) were appropriate for their age and 15 (12.8%) were found to be delayed (Table 2).

We could perform BAER test in 70 (59%) of 117 subjects in the study group. Mild hearing deficit was found in 8 of them (11%).

Etiological risk factors, developmental test results and treatment findings of the patients who had a diagnosis of cerabral palsy are summarized in Tablo 3.

The etiological relation between prenatal and postnatal risks for poor prognosis in VLBW infants with neurological abnormality and developmental retardation was investigated. There was a significant relation between gestational week and neuromotor retardation. While developmental retardation was found in 19% of the subjects with a gestational age of more than 30 weeks, the same rate was found to be 39% in the subjects with a gestational age less than 30 weeks (p=0.033). No correlation was found between birth weight and being SGA and developmental retardation. Male gender was a significant risk factor for developmental retardation (p=0.024). While neurodevelopmental retardation was found in 10 of 37 subjects who received steroid prenatally, 27 subjects had an appropriate neurodevelopment

for their age. There was no significant relation between prenatal steroid use and neurodevelopmental retardation (p>0.05). Denver II test revealed retardation with a rate of 50% in subjects with an APGAR score of 6 or lower in the 5th minute (p<0.05). The relation between demographic properties and Denver DST II is summarized in Tablo 4.

While neurodevelopmental retardation was found in 41% of 39 preterm infants followed up in the intensive care unit (p=0.927), this rate was found to be 87% in infants defined to have BPD (p=0.02).

While neurodevelopmental retardation was found in 50% of 24 patients who had sepsis (p=0.009), this rate was found to be 75% in patients with stage III and higher ICB (p=0.005). 45% of the patients who were referred after birth from another hospital were affected neurodevelopmentally (p=0.01). The relation between neonatal problems and Denver DST II is shown in Table 5.

When maternal education levels were evaluated, three mothers (2,6%) had no education, 85 mothers (72.6%) had elementary-school education, 26 mothers (22.2%) had high-school education and three mothers (2.6%) had university education. One of the fathers (0,9%) had no education, 78 (66.6%) had elementary-school education, 26 (22.2%) had high-school education and 12 (10.3%) had university education. No significant relation was found between the education level of the parents and developmental retardation. There was also no significant relation between socioeconomic level and neurodevelopmental retardation (p>0.05) (Table 6).

Discussion

In the long-term follow up of preterm infants, severe neurological sequelae include CP, mental retardation,

Table 3. Summary of 10 subjects defined to have cerebral palsy

Name	BW	GW	Apgar	KICB	Sepsis	Menj.	Hydrocephaly	Abormal DDST	Abormal Amiel Tison	Rehabilitation
S.C.*	1170	28	5	G III	-	-	–	+	Sequela+Disability	Since 1 year of age
İ.D.	890	27	5	-	+	-	-	+	Sequela+ Disability	Since 1 year of age
M.K.**	1100	29	5	G III	-	-	+	+	Sequela+Disability	Since 2 years of age
G.A.**	930	35	9	--	+	+	+	+	Sequela+Disability	Since 6 months of age
A.K.	1290	28	7	G IV	-	-	+	+	Sequela+Disability	Since 1 year of age
S.G.	1260	29	5	GIII	+	-	+	+	Sequela+Disability	Since 2 years of age
G.K.	1260	27	5	--	-	-	-	+	Sequela+Disability	Referred at the age of 3
B.K.**	1400	28	5	G III	-	+	+	+	Sequela+Disability	Since 2 years of age
V.B.*	900	29	5	--	+	-	-	+	Sequela+Disability	None
A.O.*	980	28	7	---	-	+	-	+	Sequela+Disability	Since 1 year of age

*Periventricular leucomalacia was found in these patients.
M.K, G.A, B.K : Patients in whom shunt was placed
BW: Birth weight, GW : Gestational week, ICB: Intracranial bleeding, DDST: Denver developmental screening test

Table 4. Comparison of Denver DST II according to demographic properties

Variable	Denver DST II			
	Normal n %	Abormal n %	Total n %	p
Female	47 (40.2)	10 (8.5)	57 (48.7)	0.024
Male	38 (32.5)	22 (18.8)	60 (51.3)	
AGA	56 (47.9)	24 (20.5)	80 (68.4)	0.382
SGA	29 (24.8)	8 (6.8)	37 (31.6)	
Gestational Week				
<30	28 (60.9)	18 (39.1)	46 (100)	0.033
≥30	57 (80.3)	14 (19.7)	7 (100)	
<1000 g	8 (67.1)	9 (32.9)	17 (14.5)	0.229
1001-1500 g	77 (77)	23 (23)	100 (85.5)	
Prenatal steroid History	27 (23.1)	10 (8.5)	37 (31.6)	1.0
APGAR				
<6	13 (50)	13 (50)	26 (100)	0.005
>6	72 (79.1)	19 (20.9)	91 (100)	

AGA: appropriate for gestational week, SGA: Small for gestational week

Table 5. Relation between neonatal problems and Denver DST II

Variable	Denver DST II			
	Normal n%	Abormal n%	Total n%	p
ICU monitoring				
No	62 (53.3)	16 (13.7)	78 (66.7)	0.027
Yes	23 (19.7)	16 (13.7)	39 (33.3)	
BPD				
No	83 (70.9)	25 (21.4)	108 (92.3)	0.02
Yes	2 (1.7)	7 (6)	9 (7.7)	
Sepsis				
No	73 (62.4)	20 (17.1)	93 (79.4)	0.009
Yes	12 (10.3)	12 (10.3)	24 (20.5)	
ICB				
No or Grade I-II	83 (70.9)	26 (22.2)	109 (93.2)	0.005
Yes Grade III-IV	2 (1.7)	6 (5.1)	8 (6.8)	
ROP				
No or Grade I-II	82 (70.1)	29 (24.8)	111 (94.9)	0.343
Yes Grade III-IV	3 (2.6)	3 (2.6)	6 (5.1)	
Transport				
No	67 (57.3)	17 (14.5)	84 (71.8)	0.01
Yes	18 (15.4)	15 (12.8)	33 (28.2)	

ICU : Intensive Care Unit, BPD: Bronchopulmonary dysplasia, ICB: Intracranial bleeding, ROP: Retinopathy of prematurity

Table 6. Relation between socioeconomic level and DDST II

Socioeconomic level	Denver II DST			
	Normal	Abormal	Total	p
Low (n%)	10 (8.5)	5 (4.3)	15 (12.8)	
Normal (n%)	75 (64.1)	27 (23.1)	102 (87.2)	0.550
Total (n%)	85 (72.6)	32 (27.4)	117 (100)	
Maternal education level				
Elementary(n%)	65 (55.6)	23 (19.7)	88 (75.2)	
Highschool-University (n%)	20 (17.1)	9 (7.7)	29 (24.8)	0.635
Total (n%)	85 (72.6)	32 (27.4)	117 (100)	

convulsion, blindness, hydrocephaly and deafness; the incidence has been reported to be 7-30% (11-14). The most common severe neurological disorder is CP. Its incidence has been reported to be 7.5% in preterm infants with a birth weight of <1500 g (15) and 4-14% in infants with a birth weight of 1000-1500 g (1). Hack et al. (13) reported the incidence of CP to be 15% in infants with a birth weight of <1000 g. In a study performed by Kerimoğlu et al. (14) in our hospital, 262 VLBW infants were examined at a mean age of 27 months and CP was found with a rate of 6.03%. We found the rates of severe neurological sequela and CP to be 9.4% and 8.5%, respectively in a study we performed in a similar group. Our results were compatible with the rates reported in the literature. Among patients with severe neurological disorder, 5 (4.2%) had spastic diplegia and 5 (4.2%) had spastic tetraplegia. 5 of the patients with CP had hydrocephaly at the same time and 2 (1.7%) had blindness related to retinopathy. 72.6% of 117 high-risk preterm infants were found to be normal with Denver Developmental Screening Test and 25.4% were found to be abnormal. Pathologic results were obtained with a rate of 23.1% in language test, 12.8% in fine motor skill test, 10.3% in gross motor skill test and 12.8% in individual social development.

In our study, prenatal steroid use as one of the perinatal risk factors affecting the morbidity in infants was evaluated. Kesiak M. et al. (15) performed a study in which they examined the negative effects of prenatal steroid use on the growth and development of the brain. They reported that use of a single dose of betamethasone was safe for the nervous system of the newborn and decreased the rate of mortality and the incidence of ICB. Rajadurai et al. (16) reported that prenatal single dose steroid adinistered to women with premature labour was highly efficient in decreasing the rates of RDS, ICB, neonatal mortality and the incidence of CP. In our study, prenatal steroid was administered to 37 pregnant women (31.6%). No difference could be found in terms of

Denver II scores between VLBW infants with and without prenatal steroid administration. Prenatal steroid was used in 2 of our 10 subjects with CP (20%).

In our study, birth weight, GW and gender as factors related to the infant which affect the neurodevelopmental prognosis were examined. In the literature, it has been reported that the rate of developmental sequela increased, as birth weight and GW decreased (17). In contrast, Thompson et al.(18) found no difference between infants with a birth weight of <1000 g and infants with a birth rate ≥1000 g in terms of developmental retardation. In our study, it was observed that birth weight did not affect Denver II results and this was attributed to the low number of subjects with a birth weight of 1000 g and less (17/ 14.5%). When Lya et al. (19) evaluated 555 preterm infants with a gestational age less than 32 weeks at the age of two, they found the rate of neuromotor retardation to be 60% in infants with a gestational age of less than 24-25 weeks, 16.6% in infants with a gestational age of 26-27 weeks, 22% in infants with a gestational age of 28-29 weeks and 15.5% in infants with a gestational age of 30-31 weeks. In our study, 46 subjects (39.3%) had a gestational age of 30 weeks and less and the rate of abnormal Denver II was found to be significantly high ($p<0.05$) (Table 4). Although there are limited number of studies examining the effects of gender, it has been reported that male infants have a higher risk compared to female infants in terms of development (13,20,21). In our study, the frequency of abnormal Denver DST II was found to be significantly high in male infants ($p<0.05$).

Malnutrition can cause persistent changes in various organs in periods when cell growth is critical in the fetus. Fetal brain development is also affected. In a study, it was suggested that birth weight and cognitive function were related (22). There are studies which suggested that Bayley scores of preterm SGA infants were lower (23). In contrast, Latal-Hajnal et al. (24) reported that being SGA at birth was not related to poor neurodevelopmental prognosis in their study. Our study included 37 (31.6%) preterm SGA infants, but no relation could be found between developmental retardation and being SGA (Table 4).

It is known that the value in the 5th minute is more significant compared to the value in the first minute in evaluation of APGAR score used for urgent assessment of the newborn in the delivery room in determining the mortality rate and neurological status. Karin et al. (25) found the rate of CP to be 1.3% in infants with an APGAR score of 4-6 in the 5th minute, 5.1% in infants with an Apgar score of 0-3 in the 5th minute and 22% in infants with an APGAR score of 0-3 in the 15th minute. Behnke et al. (26) could not find a difference between APGAR score and Bayley score in their study. In our study, no relation was found between the APGAR score in the first minute and neurodevelopmental retardation, but APGAR score in the 5th minute had a statistically significantly negative effect on neurological development ($p<0.05$).

Problems experienced by preterm infants in the acute period affect neurological diseases negatively. These include ICB, BPD, need for mechanical ventilation, sepsis and retinopathy of prematurity.

When Piecuch et al. (27) evaluated preterm infants with a birth weight of <1000 g at the age of 55 months, they found the risk of developmental sequela to be 39% and showed that this was related to the degree of ICB, BPD, PVL and social risks. In another study, CP was reported in all preterm infants with stage III and stage IV ICB (28). CP, poor motor status and significant sensory disorders were also reported in perterm infants with severe ICB (29). Gleissner et al. (30) emphasized the importance of being referred from a hospital among risk factors of ICB in 3721 preterm infants in a cohort study. In our study, 8 subjects (6.8%) had stage ≥III ICB; 6 of them (75%) had neurodevelopmental abnormality and spastic diplegia was defined in 5 subjects. Hydrocephaly developed in 5 of 10 infants with a diagnosis of cerebral palsy (Table 3) and a significant relation was observed between ICB and neurodevelopmental sequela in our study.

Bronchopulmonary displasia is a condition predisposing to neurodevelopmental sequela because of many risk factors including prolonged ventilation, oxygen treatment, hypoxia, apnea, tendency to infection, ICB and side effects of steroids. Majnemer et al. (31) compared 27 preterm infants with 27 control infants who were similar in terms of gestational age, birth weight and gender. They reported the risk of neurological sequela to be significantly high (71%) in the group with a diagnosis of BPD and 19% in the control group. In another study, neurological results of 78 preterm infants with BPD were compared with 78 infants with similar birth weights. It was found that the rates of neurodevelopmental retardation were higher in the group with a diagnosis of BPD, though not statistically significantly (32). In the study performed by the authors in VLBW infants with BPD at the age of 21-42 months, neurodevelopmental retardation was found with a rate of 32%. The rate of abnormal DDST II was reported to be 6% in the control group with similar characteristics ($p=0.01$) (33). In our study group, 9 subjects had BPD (7.7%). Developmental retardataion was defined in 7 of them (77.7%).

Sepsis is a condition which is observed with a high rate in preterm infants. In the literature, one study reported that 20-30% of the preterm infants with sepsis were complicated with bacterial meningitis and 25% of these subjects were lost and 27% developed severe neurological disorder (34). In another study in which the prognosis of 320 newborn infants with sepsis was investigated, death was observed in 27% and moderate and severe neurological sequela was observed in 20% who survived. In the group with meningitis mental retardation was reported with a rate of 100% (35). In our study, sepsis was defined in 24 subjects (20.5%) and 5 of them (20%) had meningitis at the same time. In 12 of the subjects with sepsis, DDST II results were abnormal and the relation was significant ($p<0.009$).

There are limited number of studies examining the relation between retinopathy of prematurity and developmental prognosis of preterm infants. Msall et al. (36)

reported that the stage of ROP is effective in determining functional problems at the age of 5.5 years in the ralation between ROP and the results of neurological examination. The most severe complication of ROP is blindness and its incidence has been reported to be 0.1-15%. In our study, blindness developed in two subjects (1.7%). One of them had spastic tetraplegia at the same time. No statistical significance was found between blindness and DDST II abnormality (p=0.34).

Hearing could be evaluated in 70 (59%) patients with BAER method; hearing deficit was found in 8 subjects (11%). Deafness was not found. Korkmaz et al. (12) found similar results with our data in the study they performed in 18 preterm infants at the age of 12-18 months. In the literature, deafness was reported with a rate of 0.1-15% (1,12).

Currently many studies have shown that transport of the newborn from the center to another hospital increases the morbidity rate especially in preterm infants (37). It has been reported that transport of high risk infants (28 GW and less than 1000 g) in the mother's abdomen and delivery in a third level hospital affects the prognosis positively (37). In another study, the positive effects of regional organization on safe newborn transport was emphasized (38). In our study, 10 of 11 subjects (90%) who had severe neurological anomaly had been transported to our hospital in the postnatal period.

It has been suggested that preterm infants are more sensitive against enviromental factors compared to term infants. Kuperus at al. (39) reported that the cognitive development of VLBW preterm infants carrying high biological risk was affected by enviromental factors with a higher rate during the periods between tha ages of 1, 3 and 6 years and the cognitive functions of the infants growing in an enviroment rich in stimuli could catch up with the peers even if they carry a high risk. It has been reported in the literature that factors related to socioeconomic status including family structure, income level, education level of the parents and health state of the parents have significant effects on development (40-42). Resnick et al.(41) emphasized in their study that maternal education level below high school and the mother's marital status being divorced were significant factors for cognitive development in preterm infants with a birth weight of >1000 g. Vohr et al. (43) suggested that sociodemographic factors had limited effects on the development in the first year, but these factors were rather significant at the age of five and even change and improved the possible effects of preterm birth on the development in infants with higher socioeconomic level. In our study group, there was no relation between maternal education level and developmental delay. In our study group three mothers had university education (2.5%), 26 mothers had high-school education (22.2%) and 88 mothers had elementary school education (75.2%). When the socioeconomic levels of the families were classified, 14 families (12%) were found to be below the standard deviation. No statistical relation was found between families with low socioeconomic level and DDST II results. Our study group generally consisted of families with a low education and a low socioeconomic level. In spite of this, we found that the parents made great efforts for their children's development, spent much time with them and did not delay their follow up and treatments even if they had to force their possibilities. 8 of 11 subjects with severe neurological sequela were found to be brought to the outpatient clinic regularly for follow up and continued curative programs, one subject was found to be directed during the study and one subject was found to reject the curative program. We attributed this result to the families' protective attitudes and fear of loss related to the problems they experienced.

Consequently, VLBW infants carry a higher risk compared to the infants born with a gestational age more than 32 weeks and with a birth weight greater than 1500 g and compared to term infants in terms of developmental problems. Determination of developmental problems with prior prediction, appropriate rehabilitation of the subjects and planning of treatment are very important in terms of preventing disabilities. There are studies which showed that the development of VLBW preterm infants had an average course at the beginning and decreased below the average at the age of 5-6 years (42,43).

In our study, we investigated the neurodevelopmental course of preterm infants at the age of three. However, considering that these results are not the last results showing the prognosis, we are planning to evaluate these subjects at the age of 6-7 years in terms of cognitive and fine motor functions.

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