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The ratio of mortality and morbidity in very low birth weight infants in a public hospital

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Summary

Aim: Patients were retrospectively analysed to determine mortality and morbidity rates in very low birth weight infants in the neonatal intensive care unit (NICU) in our hospital.

Material and Method: In this study 94 very low birth weight premature babies who were hospitalized in our NICU in the last two years and were compatible with our study criteria were evaluated. The input data (gestational age, birth weight, perinatal risk factors, hospital stay, surfactant therapy, mechanical ventilation strategies, respiratory distress syndrome, intraventricular hemorrhage, periventricular leukomalacia, necrotizing enterocolitis, chronic lung disease and retinopathy of prematurity) of these babies were recorded and analyzed statistically.

Results: In our study the mortality ratio of very low birth weight babies was found to be 25.5%. The most common maternal risk factor was preeclampsia/eclampsia (%26.3) which was compatible with the data of NICHD Neonatal Network Group.

The ratio of RDS was found to be 100% in group 1, 93.8% in group 2, 78.3% in group 3 and 47.6% in group 4. There was no significant difference between RDS(+) and RDS(-) groups in terms of gender distribution (p=0,191). However probability of RDS in male premature babies was found to be 1.81 fold (0.74-4.42) higher than female premature babies.

Conclusions: We expect that the mortality ratio which we found to be 25.5% in our NICU will improve parallel to the improvements in prenatal care, decrease in neonatal infections which we frequently face because of deficient prenatal care and improvement in transportation conditions as well as with an increase in steroid usage. *(Turk Arch Ped 2011; 46: 137-43)*

Key words: Newborn, prematurity, very low birth weight, mortality, morbidity

Introduction

Although neonatal mortality rate has decreased markedly worldwide due to advanced technology, new drugs and increased knowledge, it still maintains its significance (1). In the whole world, neonatal mortality is compatible with the rule of 2/3 among infant deaths; 2/3 of infant deaths occur in the first month, 2/3 of these deaths occur in the first week and 2/3 of these deaths occur in the first day. 30% of neonatal deaths are related to perinatal asphyxia, 30% are related to infections, 25% are related to preterm birth and 10% are related to congenital malformation. Low birth weight is the most significant risk factor for neonatal mortality (2,3).

Very low birth weight (VLBW; <1500 g) premature babies who constitute 25-30% of preterm births is a group with a high morbidity and mortality rate due to different and severe postnatal problems. A marked increase in survival rates of VLBW infants has been observed due to advances in perinatal and neonatal care especially in the last 20 years. Steroid use in pregnant women with a risk of preterm delivery, prevention of respiratory distress syndrome (RDS), surfactant use in treatment of RDS and new practices in mechanical ventilation therapy are among the most significant innovations (4-9).

Establishment of neonatal intensive care units in the early 1970's caused the survival rate of VLBW babies to increase from 50% to 80% (4,10,11). However,

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approximately half of the babies born at 25th gestational week in developed countries die despite all these improvements. Even in developed countries, the morbidity rate as well as mortality rate is rather high in VLWB preterm babies (12). While most of the studies conducted on these subjects reflect the results of developed countries, very few data are available in developing countries.

In this study, we aimed to evaluate the morbidity and mortality rates retrospectively in VLBW preterm babies followed up in the neonatal intensive care unit in our hospital in the last two years. In addition, our data and the data reported in developed countries previously were compared.

Material and Method

After obtaining approval from the ethics committee, the morbidity and mortality rates were examined retrospectively by screening the files of VLBW preterm babies internalized in the NICU in our hospital in the last two years. A total of 94 newborns comprising of babies born live in the obstetrics clinic of our hospital with a birth weight of 1500 g or lower and babies born in external centers and referred to our NICU in the first 7 days. Subjects with fatal congenital anomalies and who were born in external centers and referred to our NICU after the first 7 days were not included in the study.

Gestational age was determined by obstetric measurements (date of the last menstruation, established obstetric variables and ultrasonography (USG)) and New Ballard examination as completed gestational week (13,14). New Ballard examination was used especially in cases where maternal and gestational data were not known fully. Growth retardation at birth (SGA; birth weight lower than the 10th percentile according to gestational age) was evaluated according to growth curves defined by Lubchenco (15).

Patients included in our study were divided into four groups according to birth weight. Patients <750 g constituted group 1, patients with a birth weight of 750-1000 g constituted group 2, patients with a birth weight of 1000-1250 g constituted group 3 and patients with a birth weight of >1250 g constituted group 4. Morbidity and mortality rates were compared between these groups.

Statistical analyses in this study were done using NCSS 2007 package program. In evaluation of the data, single-tail variance analysis was used for comparison between groups, Tukey multiple comparison test was used for subgroup comparisons, independent t test was used for comparison of paired groups and chi-square test was used for comparison of qualitative data in addition to definitive statistical methods (mean, standart deviation). A p value of <0.05 was considered to be significant.

Table 1. Distribution of the patients by birth weight

			n	%
Birth weight	Group 1	250-500 gr	3	3.2
		501-750 gr	10	10.6
	Group 2	751-1000 gr	16	17
	Group 3	1001-1250 gr	23	24.5
	Group 4	>1250 gr	42	44.7

Results

Among the VLWB babies treated in our NICU in our hospital in the last two years, 94 subjects compatible with the study criteria were included in the study. These subjects were divided into groups according to birth weight (Table 1). The data were recorded and statistical analysis was performed.

70% of the patients (74.5%) were born in our hospital and 24 (25.5%) were referred from external centers. When the birth place distributions were compared between the patients who died and who survived, no statistically significant difference was observed between the two groups (p=0.25).

26 of 94 subjects were born from multiple pregnancies. When the distributions of multiple pregnancies were compared between the patients who died and who survived, no statistically significant difference was observed between the two groups (p=0.74).

50 of our patients (53.2%) were male and 44 (46.8%) were female. 16 of the patients who died were male and 8 were female. When the gender distributions between the patients who died and who survived were compared, no statistically significant difference was observed between the two groups (p=0.13). However, the mortality risk in male babies was found to be 2.12 fold (0.8-5.58) higher than female babies.

Mean birth weight of our patients was found to be 1145.21 g. When the mortality rates of the groups were compared, a statistically significant difference was observed (p=0.0001). The mortality rate in group 3 and group 4 was observed to be lower compared to the other groups (Table 2).

When the mean durations of mechanical ventilation (MV) were compared, a statistically significant difference was observed between the groups (p=0.001). The mean MV times in group 1 were found to be statistically significantly lower than the mean MV times in group 3 (p=0.016). Similarly, the mean MV times in group 3 were found to be statistically significantly lower than the mean MV times in group 4 (p=0.001) (Table 2).

The mean gestational weeks in the patients who died were found to be statistically significantly lower than the mean gestational weeks in the patients who survived (p=0.0001). The mean birth weight values in the patients who died were found to be statistically significantly lower than the mean birth weight values in the patients who survived (p=0.0001). The mean hospitalization times in the patients who died were found to be statistically

significantly lower than the mean hospitalization times in the patients who survived (p=0.0001). The mean MV times in the patients who died were found to be statistically significantly lower than the mean MV times in the patients who survived (p=0.002) (Table 3).

Among all patients, a statistically significant difference was found between the groups in terms of intrauterine growth retardation (IUGR) (p=0.002). The rate of IUGR was observed to be low in group 3 and group 4. There was no statistically significant difference between the patients who died and who survived in terms of IUGR distribution (p=0.344).

A statistically significant difference was observed between the groups in terms of presence of respiratory distress syndrome and surfactant use (p=0.0001). The rate of RDS positivity in group 4 was observed to be low. The rate of surfactant use was found to be low in group 4. (Table 2).

A statistically significant difference was observed between the patients who died and who survived in terms of presence of RDS and surfactant use (p=0.0001). The rate of RDS positivity was found to be higher in the patients who died (24 (100%)) compared to the patients who survived (42 (60%)). The possibility of RDS in male babies was found to be 1.81 fold 80,74-4,42) higher than female babies (Table 4).

The mean gestational week and birth weights in the RDS (+) group were found to be statistically significantly lower compared to the ones in the RDS(-) group (p=0,0001). No statistically significant difference was found between the RDS(+) and RDS(-) groups in terms of hospitalization time (p=0.43). Mean MV time in the RDS(+) group was found to be statistically significantly higher compared to the RDS(-) group (p=0.0001) (Table 5). In only 17 of our patients (18.1%) prenatal steroid was administered.

Table 2. Comparison of the patient groups in terms of morbidity and mortality rates

	<750 gr n:13		751-1000 gr n:16		1001-1250 gr n:23		>1250 gr n:42		p
RDS (+)	13	100.0%	15	93.8%	18	78.3%	20	47.6%	χ^2:20.7
RDS (-)	0	0.0%	1	6.3%	5	21.7%	22	52.4%	p=0.0001
Surfactant (+)	13	100.0%	15	93.%	18	78.3%	20	47.6%	χ2:20.7
Surfactant (-)	0	0.0%	1	6.3%	5	21.7%	22	52.4%	p=0.0001
CLD (+)	0	0.0%	2	12.5%	5	21.7%	1	2.4%	χ^2:8.73
CLD (-)	13	100%	14	87.5%	18	78.3%	41	97.6%	p=0.033
IVB (+)	7	53.8%	4	25.0%	1	4.3%	1	2.4%	χ^2:25.4
IVB (-)	6	46.2%	12	75.0%	22	95.7%	41	97.6%	p=0.0001
PVL (+)	1	7.7%	1	6.3%	5	21.7%	1	2.4%	χ^2:7.31
PVL (-)	12	92.3%	15	93.8%	18	78.3%	41	97.6%	p=0.063
NEC (+)	0	0.0%	0	0.0%	2	8.7%	0	0.0%	χ^2:6.3
NEC (-)	13	100.%	16	100.0%	21	91.3%	42	100.0%	p=0.098
ROP (+)	1	7.7%	2	12.5%	3	13.0%	1	2.4%	χ^2:3.2
ROP (-)	12	92.3%	14	87.5%	20	87.0%	41	97.6%	p=0.361
Surviving	1	(7.7%)	8	(50%)	21	(91.3%)	40	(95.2%)	χ^2:48.4
Lost	12	(2.3%)	8	(50%)	2	(8.7%)	2	(4.8%)	p=0.0001
Duration of hospitalization	8.31±24.86		30.81±33.44		41.74±24.92		24.9±9.93		p=0.0001
Duration of MV	1.77±1.48		4.81±4.94		6.87±8		1.98±2.64		p=0.001

RDS: Respiratory distress syndrome, CLD: Chronic lung disease, IVB: Intraventricular bleeding, PVL: Periventricular leucomalacia, NEC: Necrotizing enterocolitis, ROP: Retinopathy of prematurity, MV: Mechanical ventilation

Table 3. Comparison of the patients who died and who survived

	Surviving n:70	Exitus n:24	T	p
Gestational age	30.61±2.05	26±2.06	9.52	0.0001
Birth weight	1263.57±192.51	800±268.73	7.79	0.0001
Duration of hospitalization	36.64±20.84	1.75±1.75	13.86	0.0001
Duration of MV	4.27±5.81	1.75±1.75	3.23	0.002

Table 4. Mortality rates by presence of RDS and surfactant use.

	Surviving		Exitus		
RDS (+)	42	60.0%	24	100.0%	χ^2:13.6
RDS (-)	28	40.0%	0	0.0%	p=0.0001
Present	42	60.0%	24	100.0%	χ^2:13.6
Not present	28	40.0%	0	0.0%	p=0.0001

RDS: Respiratory distress syndrome

There was no statistically significant difference between patient groups in terms of retinopathy of prematurity (ROP) (p=0.36). When ROP distributions in the patients who died and who survived were examined, no statistically significant difference was found between the two groups (p=0.11) (Table 2).

No statistically significant difference was observed between the groups in terms of presence of necrotizing enterocolitis (NEC) (p=0.10). There was no statistically significant difference between the patients who died and who survived in terms of presence of NEC (p=0.42) (Table 2).

No statistically significant difference was observed between the groups in terms of intraventricular bleeding (IVB) (p=0.0001). The rate of IVB in group 3 and 4 was observed to be low.

Table 5. Comparison of the patients who developed RDS and who did not develop RDS

	RDS (+) n:66	RDS (-) n:28	t	p
Gestational week	28.39±2.63	31.89±1.69	-6.48	0.0001
Birth weight	1063.03±305.92	1338.93±133.20	-6.09	0.0001
Duration of hospitalization	28.64±27.53	25.61±9.31	0.79	0.430
Duration of MV	5.11±5.57	0.14±0.53	4.69	0.0001

RDS: Respiratory distress syndrome, MV: Mechanical ventilation

Table 6: Morbidity and mortality rates of all patients

		n	Morbidity rate %	Mortality rate n (%)
IUGR	IUGR (+)	14	14.9%	5 (35.7%)
	IUGR (-)	80	85.1%	
RDS	RDS (+)	66	70.2%	24 (36.4%)
	RDS (-)	28	29.8%	
Survanta	Present	66	70.2%	24 (36.4%)
	Not present	28	29.8%	
ROP	Present	7	7.4%	0 (0%)
	Not present	87	92.6%	
NEC	Present	2	2.1%	1 (50%)
	Not present	92	97.9%	
IVB	Present	13	13.8%	13 (100%)
	Not present	81	86.2%	
CLD	Present	8	8.5%	0 (0%)
	Not present	86	91.5%	
PVL	Present	8	8.5%	0 (0%)
	Not present	86	91.5%	
Result	Surviving	70	74.5%	
	Exitus	24	25.5%	

Note: Some of the subjects have multiple morbidities.

IUGR: Intrauterine growth retardation, RDS: Respiratory distress syndrome, CLD: Chronic lung disease, IVB: Intraventricular bleeding, PVL: Periventricular leucomalacia NEC: Necrotizing enterocolitis, ROP: Retinopathy of prematurity

A statistically significant difference was observed between the groups in terms of intraventricular bleeding (IVB) (p=0.0001). The rate of IVB in group 3 and group 4 was observed to be low. When the patients who died and who survived were compared in terms of IVB positivity, a statistically significant difference was observed (p=0.0001). The rate of IVB positivity (13 (54.2%)) in the patients who died was found to be higher compared to the patients who survived (0 (0.0%)) (Table 2).

A statistically significant difference was observed between the groups in terms of presence of chronic lung disease (CLD) (p=0.03). The rate of CLD was observed to be low in group 4. No statistically significant difference was observed between the patients who died and who survived in terms of presence of CLD (p=0.08) (Table 2).

No statistically significant difference was observed between the groups in terms of presence of periventricular leucomalacia (PVL) (p=0.06). No statistically significant difference was observed between the patients who died and who survived in terms of presence of periventricular leucomalacia (PVL) (p=.08) (Table 2).

A statistically significant difference was observed between the groups in terms of mortality rates (p=0.0001). The mortality rate was observed to be low in group 3 and group 4 (Table 2).

The morbidity and mortality rates of all patients are shown in table 6. The morbidity rates in the patients groups are shown in Figure 1. When the disease-free survival rates were examined, a statistically significant difference was observed between the groups (p=0.0001). The disease-free survival rate was observed to be high in group 4 (Table 7).

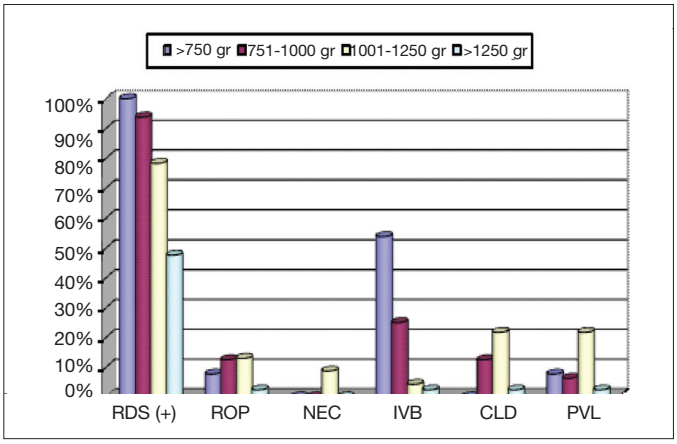

Figure 1: Morbidity rates in the patient groups.

RDS: Respiratory distress syndrome, CLD: Chronic lung disease, IVB: Intraventricular bleeding, PVL: Periventricular leucomalacia, NEC: Necrotizing enterocolitis, ROP: Retinopathy of prematurity

Table 7. The disease-free survival rate in our patient groups.

	<750 gr	751-1000 gr	1001-1250 gr	>1250 gr	
Disease-free survival (+)	5 38.5%	10 62.5%	13 56.5%	39 92.9%	p=0.0001

Discussion

Preterm birth is still a significant reason of morbidity and mortality in the perinatal, neonatal and postnatal periods. Very low birth weight infants who constitute approximately 25-30% of preterm births is a group with a high morbidity and mortality rate because of postnatal problems which have a different and severe course. Specifically, in the last 20 years, a marked increase in the survival rates of very low birth weight infants has been observed due to advances in perinatal and neonatal care. Prenatal steroid use in pregnant women who have a risk of preterm delivery, prevention of RDS, surfactant administration for treatment of RDS and new practices in mechanical ventilation therapy are the most significant ones among these innovations (4-9).

In our study, the mortality rate in very low birth weight infants was found to be 25.5%. When studies from underdeveloped and developing countries were examined, the mortality rate in very low birth weight infants followed up in neonatal intensive care units was found to be 17% in Singapour, 34% in Malesia and 30% in India (16).

The most significant factors determining the chance of survival in preterm babies are birth weight and gestational week (12). In our study, a statistically significant difference was found between the patients who died and who survived in terms of mean birth weight ($p<0.05$) (Table 3). As the birth weight increased, the mortality rate decreased and this difference was found to be statistically significant ($p<0.05$). The mortality rate was found to be low in group 3 and 4 (Table 2).

According to the data of National Institute of Child Health and Human Developmental(NICHD)-Neonatal Network the mortality rate which was found to be 66% in newborns between 501 and 750 g in 1988 was observed to be decreased to 48% in 1996. The mortality rate decreased from 34% to 14% in newborns with a birth weight of 751-1000 g, from 13% to 6% in newborns with a birth weight of 1001-1250 g and from 7% to 3.5% in newborns with a birth weight of 1251-1500 g (17). In a study performed by Atasay et al.(18) in 2003, the mortality rate of VLBW preterm babies was found to be 16.5% and the mortality rates by body weights were found to be 80.7%, 20.1%, 8.9% and 5.3%, respectively for <750 g, 750-1000 g, 1001-1250 g and 125-1500 g . When compared with these data, our mortality rates in babies below 1000 g were found to be higher and the mortality rates in babies above 1000 g were found to be lower.

While the mean gestational age in the patients who died was found to be 26 weeks, it was 30,6 weeks in the patients who survived. The mortality rates by gestational week were found to be 100%, 90%, 30.7%, 10%, 3.0% and 0%, respectively for 22-24, 25-26, 27-28, 29-30, 31-32 and 33-34 gestational weeks. When these rates were compared with the 2007 mortality rates found in a multi-center study comprising of data from 31 neonatal intensive care units performed by the Turkish Neonatology Association, they were found to be higher for 22-24, 25-26 and 27-28 gestational weeks and lower for 29-30 and 31-32 gestational weeks (19).

Although gestational week and birth weight are considered to be the most important determinants of morbidity and mortality rates and are found to be related to the mortality rate in many studies, gestational week is considered to be more significant, since it will give a more accurate information about the structure of the neonate. However, gestational week may not reflect the truth, if prenatal monitoring has not been performed appropriately and if early ultrasonography has not been performed. Therefore, use of birth weight is considered to be more practical, since it can be easily determined and is objective (20).

The mortality rate was found to be 32% in male subjects and 18.2% in female subjects. This difference was not statistically significant. Our data in terms of this point are not compatible with the literature. Many studies have shown that the mortality risk is increased in preterm babies (21). In our study, the mortality risk in male babies was found to be 2,12 fold (0,8-5,58) higher compared to female babies. Similarly, in the reports of NICHD Neonatal Research Network Group, the mortality rate in male babies were noted to be higher than female babies by the same birth weight and gestational week (17).

It is known that administration of prenatal steroid treatment in pregnant women with a risk of preterm delivery decreases the risk of RDS, intracranial bleeding and the mortality rate. According to the data of NICHD Neonatal Research Network, prenatal steroid use increased from 16% in 1988 to 71% in 1996. In the Vermont-Oxford Network studies, this rate was found to be 24% in 1991 and 72% in 1999. In our study, prenatal steroid could be used only in 18.1% of the mothers with preterm delivery. We believe this low rate is up to the fact that only 66% of the pregnant women whose deliveries took place in our hospital had been monitored regularly.

The most common maternal risk factors were preeclampsia/eclampsia (26.3%) and our results were compatible with the data of NICHD Neonatal Network Group (17). The frequency of RDS increases as the gestational week and birth weight decrease (22). While RDS is seen in 50-85% of the babies at the 26-28th gestational week, the frequency decreases to 4% in babies at the 30-31st gestational week, 10-15% in babies at the 34th week and 1% in babies at the 36th week (23).

In our study, the frequency of RDS was found to be 100% in babies with a birth weight of 500-750 g, 93.8% in group 2, 78.3% in group 3 and 47.6% in group 4. These results were compatible with the results of the study performed by Hack et al. (17). No statistically significant difference was observed between the RDS (+) and RDS(-) groups in terms of gender distribution ($p=0.191$). However, the risk of RDS in male babies was found to be 1,81 fold (0,74-4,42) higher compared to female babies. The frequency of RDS in male babies was noted to be higher compared to female babies in the literature (22).

We face with severe morbidities including severe IVB, NEC, PVL and CLD with an increasing rate which is

related to decreased mortality rate in VLBW newborns. In the 6-year-follow up of the centers of American National Child and Human Development Neonatal Working Groups, the mortality rates in VLBW newborns decreased markedly, while the increase in the morbidity rates drew attention. The rate of severe morbidity which was 27% in 1991 increased to 30% in 1996 due to increase in chronic lung disease (9% in 1991, 23% in 1996) (14). The frequency of severe intracranial bleeding was reported to be 8.4% in 1991 and 11% in 1996. The frequency of NEC was reported to be 4.5% in 1991 and 5% in 1996 (17).

In USA, 7500 new diagnoses of CLD are made each year and 10% of these babies are lost with complications in the first year (24). Increase in use of surfactant and in the quality of intensive care services have decreased the risk of CLD on one side and increased the survival rates of more risky babies and led to relative increase in the frequency of CLD on the other side (24). According to NICHD data, no decrease in the frequency of CLD (23%) has been observed, although the survival rates have increased (17). The frequencies of CLD in the centers in our country have been reported to be 2,3-10.5% (21). In our study, the rate of CLD was found to be 8.5% which was compatible with the data of our country. Tha fact that the frequency of CLD in group 3 was higher than group 2 was related to the markedly high mortality rate in group 2.

Although the frequency of periventricular (PV)-IVB and PVL has gradually decreased in the last 20-30 years, the frequency of severe PV-ICB in babies below 1500 g is still being reported to be 5,6-11.6%. This rate is 26% in babies between 500 g and 750 g and 12% in babies between 750 g and 1000 g. In the same study, the frequency of PVL was reported to be 5% in babies below 1500 g (7% in babies of 500-1000 g) (25). In our country, Köksal et al.(26) reported the frequency of PV-ICB in 120 babies who weighed below 1500 g to be 15% in 2002. In our study, a statistically significant difference was observed between the groups in terms of presence of IVB (p=0.0001). The rate of presence of IVB was observed to be low in group 3 and group 4. This rate is higher compared to NICHD data and compatible with the results of the study performed by Köksal et al.(26) in 2002.

The frequency of necrotizing enterocolitis increases with decreasing birth weight and decreasing gestational age. Wilson et al. (27) evaluated 148 patients with NEC and observed the highest rates (42%) in babies who were below 1000 g. The frequency of NEC was found to be 39.0% in babies with a birth weight of 1000-1500 g, 3.8% in babies with a birth weight of 1501-2000 g and 0.11% in babies with a birth weight above 2500 g. Grade III-IV necrotizing enterocolitis was observed only in 2 subjects (2.1%) and this rate was lower than the rate found by NICHD Neonatal Research Network in 1996 (17). No statistically significant difference was found between the groups in terms of presence of necrotizing enterocolitis (p=0.010). This was related to the low number of subjects.

Recently, both retrospective and prospective studies have reported the frequency and severity of ROP in a wide range varying from hospital to hospital and from population to population (28-42). There are limited number of prospective, multicenter studies performed in different populations. In our study, the frequency of Grade III and higher ROP was found to be 7.4% and this rate was 11.5% in the patients with a birth weight below 1250 g. Both rates are compatible with the data of the literature. No statistically significant difference was observed between the patient groups in terms of ROP distribution (p=0.361). This was attributed to the low number of subjects.

In our study, sever disease-free survival rate was found to be 71.3%. A statistically significant difference was observed between the groups in terms of disease-free survival distribution (p=0.0001). In group 4, the disease-free survival rate was found to be high.

We believe that the mortality rate which was found to be 25.5% in our unit will improve with improvement in prenatal care conditions, increase in steroid use, decrease in early neonatal infections which are observed frequently due to deficient prenatal care and improvement of transportation conditions.

Conflict of interest: None declared.

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