

## Evaluation of very low birth weight infants in the neonatal intensive care unit of a university hospital

*Bir üniversite hastanesi yenidoğan yoğun bakım ünitesinde izlenen çok düşük doğum ağırlıklı bebeklerin değerlendirilmesi*

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### ABSTRACT

**Objective:** Neonates with birth weights below 1500 g who were cared for in the neonatal intensive care unit of Fatih University Hospital were retrospectively examined in order to define their rates of morbidity and mortality.

**Methods:** This study was conducted on 72 premature infants divided into two groups: those with birth weights below 1000 g (31 infants) and those above 1001 g (41 infants). Data on these infants were recorded and statistically evaluated. Birth weights ranged from 670 g to 1500 g and gestational weeks varied between 25 and 35 weeks.

**Results:** In our study, the mortality rate of infants with extremely low birth weights was 7.6%. Durations of oxygen and antibiotic therapies were found to be significantly longer in the infants with birth weights of 1000 g or less ( $p < 0.01$ ). The most common diseases in all the groups were retinopathy of prematurity, occurring in 54.2% ( $n=39$ ); broncho-pulmonary dysplasia (BPD) in 51.4% ( $n=37$ ); and intraventricular hemorrhage (IVH) in 34.5% ( $n=20$ ). Incidence of chronic pulmonary disease and retinopathy of prematurity (ROP) was found to be statistically significant in the infants with birth weights of 1000 g or less ( $p < 0.01$ ).

**Conclusion:** Because mortality rate is low but rates of ROP, IVH and BPD are high in this unit, risk factors of these diseases should be well assessed and necessary measures should be taken in order to increase quality of life in the long term for the infants with extremely low birth weights.

**Key words:** premature, infant, mortality, morbidity

### ÖZET

**Amaç:** Şubat 2007 ile Şubat 2013 tarihleri arasında Fatih Üniversitesi Hastanesi yenidoğan yoğun bakım ünitesinde takip edilen doğum ağırlıkları 1500gr ve altı bebeklerin hastalık ve ölüm oranlarını belirlemek amacıyla hastalar retrospektif olarak incelendi.

**Yöntemler:** Çalışma doğum kilosu 1000 gram ve daha az (31 bebek), 1001-1500 gram arası (41 bebek) olarak ikiye bölünen 72 prematüre bebek ile yapılmıştır. Bu bebeklerin verileri dosyalardan kaydedilip, istatistiksel olarak değerlendirildi. Bebeklerin doğum ağırlıkları 670 ile 1500 gram arasında, doğum haftaları 25 ile 35 hafta arasında değişmekteydi.

**Bulgular:** Çalışmamızda çok düşük doğum ağırlıklı bebeklerin ölüm oranı %7,6 idi. 1000gr ve altı bebeklerde oksijen ve antibiyotik tedavi süreleri anlamlı olarak uzun bulundu ( $p<0,01$ ). Bütün çalışma grubunda en sık görülen hastalıklar %54,2 (39) prematüre retinopatisi (ROP), %51,4 ( $n=37$ ) bronkopulmoner displazi (BPD), %34,5 ( $n=20$ ) intraventriküler hemoraji (İVH) idi. 1000 gr altı bebeklerde kronik akciğer hastalığı ve prematüre retinopatisi (ROP) görülme oranları istatistiksel olarak anlamlı bulundu ( $p<0,01$ ).

**Sonuç:** Ünitimizde mortalite oranımız düşük, ancak ROP, İVH, BPD oranlarımızın yüksek olması nedeniyle bu hastalıkların risk faktörlerinin iyi değerlendirilerek önlemlerin alınması ve böylece çok düşük ağırlıklı prematüre bebeklerimizin uzun dönemde yaşam kalitelerinin artırılması gerektiğini düşünmekteyiz.

**Anahtar kelimeler:** Prematüre, yenidoğan, mortalite, morbidite

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## INTRODUCTION

In recent years, advances in technology and the widespread implementation of assisted reproductive techniques have led to an increase in preterm births and have resulted in an increase in the number of infants in neonatal intensive care units [1]. The survival rates of preterm infants have increased steadily owing to increased steroid use, especially in the prenatal period, advancements in intensive care units, widespread use of post-natal surfactant and ventilation therapies, and introduction of new-generation antibiotics. In Turkey, preterm infant mortality has been reported to be between 16.5% and 30% [2].

Although mortality in this population has decreased, it is important to strive for decreased morbidity as well. Even more crucial than bringing down the mortality due to preterm birth is the prevention of various complications due to early birth so that these infants can live normal lives without sequelae [3- 6 ]. For this reason, we examined 78 preterm infants hospitalized between 2007 and 2013 in the Fatih University Neonatal Intensive Care Unit with a gestation age of 25-36 weeks in terms of mortality and morbidity incidence for conditions such as RDS, ROP, IVH, NEC, BPD, and PDA. We discuss the results of our study in the context of results from existing literature.

## METHODS

Seventy-eight preterm infants hospitalized in the Fatih University Neonatal Intensive Care Unit with a gestation age (GW) of 25-36 weeks were examined in terms of mortality and morbidity. Three preterm infants died owing to major congenital abnormalities, and three others died owing to very early gestational age (e.g., 22 GW). These six preterm infants were included in the mortality evaluation but were excluded from the morbidity evaluation. The demographic characteristics of these babies were recorded from files. They were evaluated statistically by dividing them into two groups as follows: infants weighing less than 1000 g and infants weighing more than 1000 g (table 1).

Gestational week values were calculated using the modified Ballard method and considering the date of the last menstrual period. Intrauterine growth was assessed using the Lubchenco curve.

Those who were >90th percentile in birth weight were considered to have high birth weight according to the gestational week, while those <10th percentile were considered to have low birth weight (LBW) according to the gestational week. Those between the 10th and 90th percentile were considered to have normal birth weight according to the gestational week. The babies with an Apgar score of 7 at the fifth minute were considered as asphyxia births. Sepsis was diagnosed according to the clinical symptoms of tachypnea, tachycardia, prolongation of the peripheral capillary refill time, cutis marmoratus, and presence of sclerotization. RDS was diagnosed according to clinical data and lung x-rays . ROP was diagnosed based on the international ROP classification [7]. IVH was evaluated from ultrasound findings according to the Papile classification [8]. NEC was graded using the modified Bell classification scheme [9]. BPD was identified as the continuation of oxygen demand on the 28th postnatal day or the 36th postconception week [10].

## Statistical analysis

A software application called Statistical Package for Social Sciences (SPSS) 15.0 for Windows was used for statistical analysis. Descriptive statistical methods such as average and standard deviation were used for quantitative data. Student's t test was employed to compare normally distributed parameters between the groups, and the Mann Whitney U test was used to compare non-normally distributed parameters between the groups. Fisher's exact test and continuity correlation (Yates) tests were used to compare qualitative data. Values of  $p < 0.05$  were considered statistically significant.

## RESULTS

This study was conducted between October 2007 and January 2013 with 78 preterm infants. Three preterm infants died owing to major congenital abnormalities, and three others died owing to very early gestational age (e.g., 22 GW) within the first 24 h. While mortality was assessed for all 78 preterm infants, morbidity was assessed for 72 premature babies, of which 31 (43.1%) had birth weights of 1000 g or less and 41 (56.9%) had birth weights of 1001-1500 g. The birth weights of the infants ranged from 670 g to 1500 g, and the average birth weight was  $1171.94 \pm 246.71$  g. Birth weeks ranged

from 25 to 35, and the average was  $29.64 \pm 2.45$  weeks. The mortality rate was 7.9%.

The average birth week of the infants with birth weights of 1001-1500g was significantly higher than that of the infants with birth weights of 1000

g or less ( $p < 0.01$ ). However, there were no statistical differences in birth weight according to gender, delivery method, and gestational week between the groups ( $p < 0.05$ ) (Table 1).

**Table 1.** Demographic and clinical characteristics of patients according to birth weight

	Birth Weight		p
	$\leq 1000$ g	1001-1500 g	
	Mean $\pm$ SD	Mean $\pm$ SD	
Gestational Age	27.90 $\pm$ 1.53	30.95 $\pm$ 2.18	0.001**
	n (%)	n (%)	
AGA	25 (80.6%)	32 (82.1%)	
SGA	6 (19.4%)	7 (17.9%)	<0.05
Sex			<sup>3</sup> 1,000
	Female	21 (51.2%)	
	Male	20 (48.8%)	
Delivery Method			<sup>3</sup> 1,786
	Normal	0 (0%)	
	Section	41 (100%)	
Multiple Pregnancy	12 (38.7%)	13 (33.3%)	<sup>4</sup> 0.182
Maternal Preeclampsia	8 (25.8%)	9 (22%)	<sup>3</sup> 0.919
premature rupture of membranes (PROM)	2 (6.5%)	9 (22%)	<sup>4</sup> 1.000
Maternal Diabetes	3 (9.7%)	3 (7.3%)	<sup>4</sup> 1.000
Antenatal Steroids	30 (96.8%)	38 (92.7%)	<sup>4</sup> 0.629
Ventilator T. Duration (days)	8.2 $\pm$ 8.1 (5)	5.1 $\pm$ 2.5 (3.5)	0.140
O <sub>2</sub> Duration (days)	39.7 $\pm$ 19.7(31.5)	24.7 $\pm$ 16.1(20.5)	0.014*
Sepsis	11 (36.7%)	9 (22%)	<sup>3</sup> 0.274
Antibiotic Duration (days)	34.4 $\pm$ 17.4 (35)	22.4 $\pm$ 19.9 (20)	0.002**

AGA: Appropriate for Gestational Age, SGA: Small for Gestational Age

<sup>1</sup>Student t test (Yates), <sup>2</sup>Mann-Whitney U test, <sup>3</sup>Continuity, <sup>4</sup>Fisher's Exact test, \* $p < 0.05$ , \*\* $p < 0.01$

In addition, there were no statistical differences between the groups in terms of maternal risk factors triggering premature birth, such as multiple pregnancy, gestational diabetes, maternal preeclampsia, in vitro fertilization, and early membrane rupture ( $p < 0.05$ ).

There were no significant differences between the groups in terms of the antenatal steroid administration and ventilator supportive therapy time ( $p < 0.05$ ). However, infants with birth weights of 1000 g or less received RDS and O<sub>2</sub> for significantly longer durations than did infants with birth weights of 1001-1500 g ( $p < 0.05$ ). Because preterm infants with birth weights  $< 1000$  g received oxygen for an average of 31.5 days more than did infants with birth weights  $> 1000$ g, the incidence of

BPD was significantly higher in the smaller infants ( $p < 0.05$ ).

Although there was no statistical difference between the groups with regards to sepsis, the duration of antibiotic use in the infants with birth weights  $< 1000$ g was significantly longer ( $p < 0.05$ ).

When both groups were compared in terms of morbidity, there was no statistical difference in the incidence of PDA, NEC, IVH from cranial complications, convulsion, hydrocephalus, or leukomalacia ( $p < 0.05$ ). However, the incidence of RDS, BPD, ROP, and inguinal hernia was significantly higher in preterm infants with birth weights of  $< 1000$ g ( $p < 0.05$ ), but there was no difference in ROP classification ( $p < 0.05$ ) (Table 2).

**Table 2.** Disease ratios of the cases

	Birth Weight		p
	≤ 1000 g	1001-1500 g	
	n (%)	n (%)	
RDS	22 (71%)	20 (48%)	0.099
Bronchopulmonary Dysplasia	23 (74.2%)	14 (34.1%)	0.002**
PDA (+)	4 (12.9%)	2 (4.9%)	0.392
Inguinal Hernia	8 (25.8%)	2 (4.9%)	0.016*
NEC	2 (6.5%)	2 (4.9%)	1.000
ROP (+)	23 (74.2%)	16 (39%)	0.006**
ROP	Mild	7 (30.4%)	7 (43.8%)
	Severe	16 (69.6%)	9 (56.3%)
Intraventricular Hemorrhage	11 (44%)	9 (27.3%)	0.294
Convulsions	1 (3.2%)	1 (2.4%)	1.000
Periventricular leukomalacia	3 (12%)	4 (12.1%)	0.695
Hydrocephalus	1 (4%)	2 (6.1%)	0.732

RDS: Respiratuar distress syndrome, PDA: Patent ductus arteriosus, ROP: Retinopathy of prematurity, \*p<0.05, \*\*p<0.01

## DISCUSSION

Owing to recent developments in antenatal care and neonatal intensive care conditions, the perinatal mortality rate of LBW premature infants with birth weights of 1500 g or less has decreased, particularly in developed countries [7]. The mortality rate of these infants ranges from 10% to 60%, depending on the country's development level [11,12]. While the mortality rate in LBW infants ranged from 16.5% to 30% in various studies conducted in Turkey, the mortality rate was reported to be between 10% and 54% in a multicenter study conducted by the Turkish Neonatology Society [13]. In our current study, the mortality rate was 7.9%. We believe that the mortality rate in our study was lower than those in previously reported studies because all pregnant women in our study were under follow-up (given that our hospital is a private hospital), antenatal steroid use was high (94.4%), most births were cesarean deliveries (97.2%), number of nurses was adequate (one nurse for two infants), sepsis rate was low, and technological facilities available in our hospital were adequate.

Owing to maternal and fetal factors, multiple pregnancy negatively affects gestational age and birth weight [14]. Several studies have shown that the occurrence rate of LBW owing to multiple pregnancy is between 20.4% and 31.2% [15,16]. The

rate of multiple pregnancy was 35.7% in the current study, which is consistent with that in the literature.

In our study, LBW infants were investigated in terms of maternal risk factors, and we found that the most common risk factor was preeclampsia, with an occurrence rate of 23.6%. This result is consistent with data from the National Institute of Child Health and Human Developmental (NICHD)-Neonatal Network [17].

Various studies have reported that antenatal steroids decrease mortality rate, RDS, NEC, and IVH rates in LBW infants [18]. According to the NICHD Neonatal Research Network, antenatal steroid use has increased in recent years and was as high as 71% in 1996. Depending on the region, the rate of antenatal steroid use in Turkey is 8%-55.6% [19,20]. In the current study, the rate of antenatal steroid use was 94.4%. This value is higher than those reported in other studies conducted in Turkey, but it is similar to the rates reported in developed countries [17].

The RDS development rate in LBW infants has been reported to be between 44% and 73% in international studies [21,22]. In Turkey, this rate ranges from 36% to 47% [23,24]. In parallel with these data, in the current study, 58.3% of LBW infants developed RDS, and 51.4% of those infants were given surfactant. While the rate of surfactant application in Turkey ranges between 20% and 40%,



the corresponding figure for developed countries is 57% [21-24]. Our surfactant application rate was higher than previous rates reported in our country.

IVH occurs in 20% of VLBW infants, and most of those cases are stage 1-2 hemorrhage [25]. Intraparenchymal hemorrhage is seen in 5%-11% of such infants [25]. The occurrence frequency of Stage 3-4 hemorrhage ranges from 6.4% to 20% in Turkey [23,24]. The IVH rate of infants with a birth weight of 1500 g or less was 34.5% in the current study. In addition, this rate was 44% in infants with birth weights of 1000 g or less and 27% in infants with birth weights of 1001 g or more. In our opinion, these rates are much higher than those reported in other studies because the number of infants with birth weights of 1000 g or less was greater in the previous studies. Convulsion was detected in 2.8% of the infants in this study, all of whom had IVH.

Retinopathy of prematurity (ROP) is an important problem for at-risk premature infants, and it may cause vision disorders, including blindness. ROP development in Turkey ranges from 23% to 56.2% [26,27], and in the current study, it was 54.2%, which is consistent with the literature. The ROP rate in this study was 74.2% in infants with birth weights of 1000 g or less and 39% in infants with birth weights of 1001-1500 g, which represents a significant difference. It has been reported that 35.9% of patients have stage 3 or higher ROP, which requires surgical treatment. Most of these patients (69.6%) have birth weights of 1000 g or less. ROP rates in infants with birth weights of 1000 g or more are generally higher in developing countries [28-30].

NEC is another crucial disease observed in infants with low birth weights, and its occurrence rate has been reported to be 6%-28% [31]. In the current study, the NEC rate was 5.6%, which is somewhat lower compared to data from other Turkey-based studies [2,20-24]. We ascribe the lower NEC rate in our study to the fact that the premature infants were fed breast milk and because of the high rate of antenatal steroid use (94.4%). It has been reported that prenatal use of steroids decreases mortality and morbidities such as RDS, NEC, and IVH in premature infants [32]. All NEC cases in our study were stage 1. There was no significant difference between

infants with birth weights of 1000 g or less and other infants in terms of NEC development.

Sepsis is a frequent cause of mortality in premature infants [33]. It adversely affects neurodevelopment in the late period. Therefore, its early diagnosis and treatment are crucial. The incidence of sepsis has been reported to be 20%-60% in Turkey as well as worldwide. [20,23,34]. In the current study, the incidence of sepsis was 28.2%. These patients were clinically diagnosed with sepsis. Blood culture positive for sepsis was observed in only one patient. Because there was an adequate number of nurses and fewer incubators in our unit, the incidence of sepsis was lower; therefore, the mortality rate was lower.

Another important disease common in premature infants is PDA, and according to NICHD data, its incidence is 30%. In the current study, the incidence of PDA was 8.3%, which is lower than the above mentioned value. There was no significant difference in the incidence of PDA between the groups in our study. Inguinal hernia is a major surgical problem, especially in infants with birth weights of 1000 g or less. Its incidence rate is 10%-25% in premature babies. The incidence of inguinal hernia in our study was 13.8%, and it was significantly higher in the infants with birth weights of 1000 g or less. All patients with inguinal hernia were operated on one day before discharge, and there were no complications.

While the incidence of BPD has been reported to be between 2.5% and 10.5% in Turkey, the NICHD reports it to be 23% [12,19,21,23,24,34]. In our study, BPD incidence stood at 51.4%, and all cases were stage 1. We believe that this rate was higher in our study because of the low mortality rate and greater number of infants with birth weights of 1000 g or less.

In conclusion, the mortality rate in our study was lower than those in previous studies. This is most likely because the infants in our study had lower sepsis rates, which can be attributed to good prenatal follow-up of at-risk infants, high rate of antenatal steroid use, and the presence of a sufficient number of experienced intensive care unit nurses in our hospital. However, because the occurrence of diseases such as BPD, ROP, and IVH was higher

in the infants in this study, we believe that it is necessary to identify and focus on all risk factors affecting morbidity during follow-up to ensure that the patients can be reintegrated into society without sequelae.

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