

DEMOGRAPHIC CHARACTERISTICS AND SHORT-TERM FOLLOW-UP OUTCOMES OF EXTREMELY LOW BIRTH WEIGHT INFANTS

AŞIRI DÜŞÜK DOĞUM AĞIRLIKLIL BEBEKLERİN DEMOGRAFİK ÖZELLİKLERİ VE KISA DÖNEM İZLEM SONUÇLARI

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ABSTRACT

Introduction and Objective: Mortality of preterm infants has been decreased with recent developments in the neonatal intensive care units (NICU). This decrease is prominent especially in the extremely low birthweight (ELBW) preterm infants group. Intensive care unit short-term outcomes, features of the intensive care follow-up, the treatment, incidence and severity of comorbidity differ in this group than the others. Results of the data for this patient group is important to set the patient treatment and follow-up protocols. We aimed to present the data of ELBW preterm infants who are discharged from our NICU which is the largest one in Turkey.

Material and Methods: In this retrospective study, ELBW preterm infants who were followed-up at our Neonatology outpatient clinic of our hospital between January-2009 and July 2010 are included. Perinatal demographic features, intensive care follow-up features, short-term outcomes and comorbidities are recorded.

Results: A hundred and fifty-four ELBW preterm infants were included to the study. Among 113 survived ELBW preterm infants in the NICU mean gestational week, mean birth weight and mean maternal age were 26.9±1.8 weeks, 853±60 g and 27.7±5.6 years, respectively. During the hospitalization, patent ductus arteriosus (PDA) was observed in 53.9%, necrotizing enterocolitis (NEC) in 9.7%, pneumothorax in 5.5%, pulmonary hemorrhage in 9.8%, severe intracranial hemorrhage (stage 3 and 4) 21.4% and hydrocephalus requiring shunt operation was in 3.5% of the neonates. Retinopathy of prematurity (ROP) requiring treatment was observed in 23%. Bronchopulmonary dysplasia (BDP) was found to be 30.3% of the patients whereas only eight patients (8%) required home-oxygen treatment.

Conclusion: This first wide series data presented in our country in ELBW premature neonates indicates that special treatment and follow-up policies should be set for the related comorbidities in the era of low mortality.

Key words: Extremely low birthweight, neonatal intensive care unit, premature

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ÖZET:

Giriş ve Amaç: Yenidoğan ünitelerinde son yıllarda görülen gelişmelerle birlikte preterm bebeklerde mortalite azalmıştır. Bu azalma özellikle aşırı düşük doğum ağırlığı (ADDA) olan bebek grubunda belirgindir. Bu grubun yoğun bakım kısa dönem sonuçları, yoğun bakım izlem ve tedavi özellikleri, eşlik eden morbidite sıklığı ve şiddeti diğer hasta gruplarından belirgin derecede farklıdır. Bu hasta grubunun verilerinin ortaya konması hasta tedavi ve izlem protokollerinin oluşturulması açısından önem arz etmektedir. Ülkemizin en büyük yenidoğan yoğun bakım servisine sahip olan ünitemizin aşırı düşük doğum ağırlıklı hasta grubunun verilerinin ortaya konmasını amaçladık.

Gereç ve Yöntemler: Bu retrospektif çalışmada, hastanemiz yenidoğan kliniğinde Ocak 2009-Temmuz 2010 tarihleri arasında izlenen, ADDA prematüre bebekler alınmıştır. Perinatal demografik özellikler ile yoğun bakım izlem özellikleri, kısa dönem izlem sonuçları ile eşlik eden morbiditeler kaydedilmiştir.

Bulgular: Yüz elli dört ADDA prematüre bebek çalışmaya alındı. Kırkbir hasta (%26.6) izlem sırasında kaybedildi. Yoğun bakım izlemleri yapılan 113 ADDA prematüre bebeğin ortalama gebelik haftası 26.9±1.8 hafta, ortalama doğum ağırlığı 853±60 gram, ortalama anne yaşı 27.7±5.6 yıl idi. Hastaların izlemlerinde %53.9 patent duktus arteriozus (PDA), %9.7 nekrotizan enterokolit (NEK), %21.4 ciddi İntrakraniyal Kanama [(İKK);evre 3,4], şant operasyonu gereken hidrosefali ise %3.5 olarak gözlemlendi. Tedavi gerektiren prematüre retinopatisi (ROP) %23 gözlemlendi. Bronkopulmoner displazi(BPD) ise %30.3 oranında gözlemlendi.

Sonuçlar: Çalışmamızda ortaya konan ADDA prematüre bebeklere yönelik ülkemizden yayınlanan bu ilk geniş serili veriler bu grupta mortalitenin düşük seyretmesinin yanında yüksek oranda eşlik eden morbiditelere yönelik tedavi ve takip politikalarının düzenlenmesi gerekliliğini ortaya koymuştur.

Anahtar Kelimeler: Aşırı düşük doğum ağırlığı, yenidoğan yoğun bakım

INTRODUCTION

Infant mortality has been seriously decreased in our country with the advances in neonatal intensive care in parallel to the developments in the world in the last decade. A marked improvement is seen, especially in the survival rates in the patient group having a risk of gestational week and birth weight (1-3). The rates of morbidity and mortality of very low birth weight (VLBW) and extremely low weight birth (ELBW) infants in the neonatal intensive care units (NICU) statistics are important indicators for the intensive care standards of a NICU. Mostly, increased morbidity features of the survivor ELBW infants appear as crucial problems. Morbidities such as BPD, NEC and ROP are known to be observed more commonly in this patient group (4-6). In

addition, ELBW infants are a group of patients who were born in much earlier weeks and required more attentive care. The various ventilatory support characteristics of much more immature lungs, total parenteral nutrition (TPN) requirements, high growth rates, need of a longer time for hospitalization, increased familial and social problems with increased complications necessitate different care standards. Support of the preparations for discharge, completion of the family education and providing follow-up conditions requiring a multidisciplinary approach after the discharge critical considerations in ELBW patient group (7,8). Reporting the statistics of this group of patients is important to show the characteristics of the staying in the NICU and the stage in which they are in the follow-up after the discharge. In this study, we ai-

med to present NICU characteristics and obtained short-term outcomes of the ELBW preterm infants who were followed-up in our NICU.

MATERIAL AND METHODS

In this retrospective study, ELBW infants, who were followed-up in the NICU of our hospital between January 2009 and July 2010 were included. Maternal risk factors and maternal demographic characteristics (gestational week, maternal age, pregnancy number, additional maternal disease, and delivery route) were recorded. The infants of the mothers who received betamethasone within 24 hours before the delivery, were accepted to be administered antenatal steroids. The gestational weeks were defined according to the last menstruation date of the mothers or to the findings of the ultrasonography performed in the first trimester. Birth weight and hour of the delivery were detailed from the files. APGAR scores of 1-5 minutes and whether there was a need for an aggressive resuscitation during the delivery were recorded. Respiratory problems, surfactant treatment, type and duration of the ventilation support, cardiological evaluation outcomes, treatment applications for PDA, presence of clinic or culture-positive sepsis and the nutritional problems encountered during the hospitalization were recorded in the follow-up period in the NICU. TPN support administered during the hospitalization and enteral nutrition features were also recorded. Comorbidities of the patients may accompany during the follow-up such as BPD, NEC, ICH and ROP were recorded. The diagnosis of NEC was established in line with the Bell classification, while BPD diagnosis was made according to criteria by Jobe & Bancalari (9,10). Echocardiographic examination are performed at 48 to 96 hours of life. The definition of hemodynamically significant PDA in our center was based on clinical signs (tachycardia of more than 160 beats per minute, presence of a murmur, bounding pulses) and echocardiographic finding of a ductal size > 1.5 mm or left atrial to aortic root ratio > 1.5, as published elsewhere, left-to-right shunting of blood, end-diastolic reversal of blood flow in the aorta, or poor cardiac function (11). Cranial ultrasound examination for the diagnosis and sta-

ging of ICH was carried out by an experienced radiologist on postnatal 5, 14, 28 day of babies life, respectively (12). While diagnosis, treatment and follow-up of ROP were performed by an experienced ophthalmologist.

RESULTS

A hundred and fifty-four ELBW infants were included in the study. Forty-one (26.6%) of the patients died during their hospitalization. Thirty of these 41 patients died in the early neonatal period (≤ 7 days). The main causes of death of these patients were ICH (n=8), pulmonary hemorrhage (n=8), immaturity (n=3) and sepsis (n=10); respectively. The other 11 patients died after one week of their hospitalization. Sepsis, pneumonia and NEC were the three important causes of death. The mean gestational week, birth weight and maternal age of remaining 113 ELBW preterm infants were as 26.9 ± 1.8 weeks, 853 ± 60 g and 27.7 ± 5.6 years, respectively. Demographic and maternal data of the patients are shown in Table 1.

Table 1. Perinatal demographic characteristics of extremely low birth weight infants

Maternal age, mean \pm SD (year)	27.7 \pm 5.6
Gestational age, mean \pm SD (week)	26.9 \pm 1.8
Birth weight, mean \pm SD (g)	853 \pm 60
Male, n (%)	51 (45.1)
Delivery by caesarean section, n (%)	81 (71)
Prenatal Steroid, n (%)	88 (77.7)
Early membrane rupture > 18 hours, n (%)	21 (18.8)
APGAR 1. minute, mean (Min-max)	5 (1-8)
APGAR 5. minute, mean (Min-max)	7 (8-9)
Entubation need during the delivery, n (%)	71 (62.8)
Respiratory distress syndrome, n (%)	86 (75.9)

There was a need for resuscitation in the delivery room in 62.8% of the patients. The mean duration of the mechanical ventilation was 7.6 ± 2.5 days, and the mean duration of continuous positive airway pressure (CPAP) support was 6.7 ± 6.3 days for hospitalized patients. The

mean length of hospitalization was 80.3±25.8 days for the patients admitted to NICU and survived. When the patients were evaluated in terms of the premature morbidity, PDA was found in 53.9%, NEC in 9.7%, pulmonary hemorrhage in 9.8%, severe ICH (stages 3,4) in 21.4%, hydrocephalus required shunt surgery in 3.5%, ROP required treatment in 23%, BPD in 30.3 % and culture positive late neonatal sepsis in 43.3% (Table 2).

Table 2. Comorbidity characteristics of extremely low birth weight infants

Pneumothorax, n (%)	6 (5.5)
Pulmonary hemorrhage, n (%)	11 (9.8)
Need for intubation in the first three days, n (%)	68 (62.4)
Mechanical ventilation duration, mean ± SD (days)	7.6± 2.5
n-CPAP duration, mean ± SD (days)	6.7 ± 6.3
Oxygen requirement duration, mean ± SD (days)	47 ± 35.6
Bronchopulmonary dysplasia ³ , n (%)	34 (30.3)
Patent ductusarteriosus, n (%)	61 (53.9)
Intracranial hemorrhage ¹ , n (%)	23 (21.4)
Hydrocephalia, n (%)	16(14.1)
Need for ventriculoperitoneal shunting, n (%)	4 (3.5)
Necrotizing enterocolitis, n (%)	11 (9.7)
Premature retinopathy ² , n (%)	26 (23)
Discharge weight, mean ± SD (g)	2200 ± 2014
Sent to home-oxygen treatment, n (%)	8 (7.2)
Hospitalization, mean ± SD (gün)	80.3 ± 25.8

¹Stage 3-4 Intracranial hemorrhage, ² Premature retinopathy required laser therapy, ³Oxygen requirement in the week 36

DISCUSSION

A significant increase has been noted in survival rates of ELBW infants with the improvements in perinatal and neonatal intensive care conditions in the last three deca-

des (13). The survival rate of ELBW preterm infants has increased to 75% in 1990s from 25% in 1970s (14). On the other hand, special prematurity related problems such as NEC, BPD, IVH and PDA have become more common with the increased survival rates. These morbidities and their ongoing complications are known to affect the life quality and healthy development of the infant both in the NICU and post-discharge follow-up periods (6).

Prematurity and associated problems are accounted for an important part of the work load of NICUs worldwide. The rate of the premature birth differs between the countries and regions. In a conducted study, this rate was reported as 12.7 per hundred live births (15). Besides this, the birth rate of ELBW infants is around 3-4 per 1,000 live births (16). This rate is around 1% among hospitalized patients in our NICU. This was interpreted to be caused by that our unit is a tertiary center in which pregnant referral and follow-up are performed.

The most significant morbidity in ELBW infants is ICH followed by the posthemorrhagic hydrocephalus. Severe IVH is seen between 7% and 23% in ELBW infants inversely proportional to the gestational week. Posthemorrhagic hydrocephalus develops in one-third of the infants with severe IVH and 15% of these have been reported to be shunted (13). Serious neurodevelopmental problems have been reported in follow-up of the patients with posthemorrhagic hydrocephalus required shunting (13). In our patient group, posthemorrhagic hydrocephalus (14.1%) and associated shunt (3.5%) were found to be consistent with the literature.

Respiratory problems are an important cause of morbidity and mortality in the premature infants. Starting with the admission of the infant to the NICU, the respiratory treatment continues almost until the discharge. Respiratory problems during their follow-up and treatment continue, also in the follow-up after the discharge in some patient groups at risk (4).

RDS incidence differs between 86% and 98% in ELBW infants (15). On the other hand, RDS diagnosis, indications of surfactant therapy and its rate of use may differ from each other in line with the practices of the NICUs. The incidence of RDS was around 76% in the

ELBW infants hospitalized in our unit. Our respiratory support duration results demonstrated that rapid extubation and CPAP application were preferred even for these patients.

Pulmonary air leak problems are occasionally seen in the ELBW patient group who are intensively receiving mechanical ventilation. Pneumothorax rate in ELBW patient group was 5.5 % in our unit. Pneumothorax was observed together with pneumomediastinum in one patient.

The diagnosis and staging of BPD are made according to the gestational week, postnatal age, week of discharge and the type of the ventilation support (13). However, it can be characterized with the oxygen need of premature infants and continuation of the ventilation support. Both BPD itself and secondary respiratory problems result in problems requiring intensive follow-up during and after the intensive care (4).

BPD is seen in about half of the patients in ELBW group (17). The incidence of BPD may markedly differ between the units. This is caused by some factors such as using different diagnostic criteria, the difference in the perception of the need for oxygen, different therapies, follow-up rates of the infants at risk and the mortality differences of ELBW infants. BPD incidence was found as 30.3% among ELBW preterm infants in our unit. This lower rate than the literature was attributed to the rapid extubation and early CPAP applied in our practice. Considering the number of the patients discharged with the home oxygen therapy (n=8, 7%), low rate of severe BPD can be thought to support this thesis.

Retinopathy of prematurity is the main cause of the visual problems in preterm neonates (18). Increased survival rate of the low birth-weight infants in the developing countries, has given prominence to ROP (19,20). The incidence and severity of ROP have shown differences in the developing countries by years (20,21). The incidence and severity of ROP are inversely proportional to the gestational week and birth weight. Therefore; the infants under 1.000 g are at the highest risk (19-21).

In a single center study from Brasil, one of the developing countries, incidence of ROP was 48.9% in ELBW

preterm infants. In this group, incidence of the patients considered to have severe ROP and requiring treatment was 17% in ELBW group, while this rate decreased to 2.3% in the infants born above 1,000 g (20). In our unit, the rate of ROP in the infants under 1,000 g required intervention was 23% in this study group.

Necrotizing enterocolitis is the most important gastrointestinal problem in the neonatal period with a multifactorial etiology. Many explanatory causes have been proposed such as the intestinal immaturity, insufficient antioxidant response of the premature and insufficiency in regulation of the intestinal circulation and presence of accompanying sepsis (23).

Necrotizing enterocolitis incidence is inversely proportional to the gestational week (24). Mainly, the infants born under 1.500 g are at risk, although this risk significantly increases for the babies born under 28 weeks and 1.000 g (5). The incidences differ in LBW patient group between 6% and 10% (25). In our patient group, NEC was observed in 11 patients (9.7%) which is similar with the literature. However, this number increases to 19 (12.3%) when the patients diagnosed with NEC and lost are added.

In conclusion, our ELBW preterm infants showed that the rates of morbidity and mortality for developed countries have been caught with a proper neonatal care. The morbidities observed in these patients and high requirement for special treatments are important to understand that this group of patients are specific to develop special follow-up policies. Revealing the data of ELBW infants with follow-up and neurodevelopmental outcomes nationwide are believed to guide the national health policies to be implemented.

REFERENCES

1. Lucey JF, Rowan CA, Shiono P, Wilkinson AR, Kilpatrick S, Payne NR, et al. Fetal infants: the fate of 4172 infants with birthweights of 401 to 500 grams: the Vermont Oxford Network experience (1996-2000). *Pediatrics* 2004;113(6):1559-66.
2. Meadow W, Lee G, Lin K, Lantos J. Changes in mortality for extremely low birthweight infants in the 1990s: implications for treatment decisions and resource use. *Pediatrics* 2004;113(5):1223-9.

3. Türkiye Neonatal Mortalite Çalışma Grubu. Türk Neonatoloji Derneği Bülteni 2009; 20:22-8.
4. Yurttutan S, Korkmaz A, Yiğit Ş, Yurdakök M, Tekinalp G. Bronkopul monerdisplazili bebeklerin kısa ve uzun süreli izlemi: on yıllık deneyim. Çocuk Sağlığı ve Hastalıkları Dergisi 2011;54(1):1-15.
5. Sari FN, Dizdar EA, Oguz S, Erdeve O, Uras N, Dilmen U. Oral probiotics: Lactobacillus sporogenes for prevention of necrotizing enterocolitis in very low-birth weight infants: a randomized, controlled trial. Eur J Clin Nutr 2011;65(4):434-9.
6. Schmidt B, Asztalos EV, Roberts RS, Robertson CM, Sauve RS, Whitfield MF. Impact of bronchopulmonary dysplasia, brain injury, and severe retinopathy on the outcome of extremely low-birth-weight infants at 18 months: results from the trial of indomethacin prophylaxis in preterms. JAMA 2003;289(9):1124-9.
7. Erdeve O. Aile merkezli bakım ve yenidoğan yoğun bakım ünitesi tasarımında ailenin yeri. Gülhane Tıp Dergisi 2009;51(3):199-203.
8. Korkmaz A, Canpolat FE, Armangil D, Anlar B, Yiğit Ş, Yurdakök M, et al. Hacettepe Üniversitesi İhsan Doğramacı Çocuk Hastanesi 2003-2006 dönemi çok düşük doğum ağırlıklı bebeklerin uzun süreli izlem sonuçları. Çocuk Sağlığı ve Hastalıkları Dergisi 2009;52(3):101-12.
9. Bell MJ, Ternberg JL, Feigin RD, Keating JP, Marshall R, Barton L, et al. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. Ann Surg 1978;187(1):1-7.
10. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. Am J Respir Crit Care Med 2001;163(7):1723-9.
11. El Hajjar M, Vaksmann G, Rakza T, Kongolo G, Storme L. Severity of the ductal shunt: a comparison of different markers. Arch Dis Child Fetal Neonatal Ed 2005;90(5):F419-F22.
12. Canpolat FE, Yurttutan S. Cranial Ultrasonography in Neonatal Intensive Care Unit: Neonatologists' Perspective. Medical Journal of Islamic World Academy of Sciences 2011;19(3):117-20.
13. Adams-Chapman I, Hansen NI, Stoll BJ, Higgins R; NICHD Research Network. Neurodevelopmental outcome of extremely low birthweight infants with posthemorrhagic hydrocephalus requiring shunt insertion. Pediatrics 2008;121(5):e1167-77.
14. Kilbride HW. Effectiveness of neonatal intensive care for extremely low birth weight infants. Pediatrics 2004;114(5):1374-5.
15. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, et al. Births: final data for 2005. Natl Vital Stat Rep 2007;56(6):1-103.
16. Doyle LW. Victorian Infant Collaborative Study Group. Evaluation of neonatal intensive care for extremely low birthweight infants in Victoria over two decades: I. Effectiveness. Pediatrics 2004;113(3 pt 1):505-9.
17. Kobaly K, Schluchter M, Minich N, Friedman H, Gerry Taylor H, Wilson-Costello D, et al. Outcomes of extremely low birthweight (<1 kg) and extremely low gestational age (<28 weeks) infants with bronchopulmonary dysplasia: effects of practice changes in 2000 to 2003. Pediatrics 2008;121(1):73-81.
18. Purohit DM, Ellison RC, Zierler S, Miettinen OS, Nadas AS. Risk factors for retrolental fibroplasia: experience with 3,025 premature infants. National Collaborative Study on Patent Ductus Arteriosus in Premature Infants. Pediatrics 1985;76(3):339-44.
19. Gilbert C. Retinopathy of prematurity: a global perspective of the epidemics, population of babies at risk and implications for control. Early Hum Dev 2008;84(2):77-82.
20. Aydemir O, Sarikabadayı YU, Aydemir C, Tunay ZO, Tok L, Erdeve O, et al. Adjusted poor weight gain for birth weight and gestational age as a predictor of severe ROP in VLBW infants. Eye 2011;25(6):725-9.
21. Phelps DL. Retinopathy of Prematurity. In: Martin RJ, Fanaroff AA, Walsh CM (eds). Neonatal-Perinatal Medicine Disease of The Fetus and Infants. 9th ed. St. Louis, Missouri: Elsevier/Mosby 2011:1764-9.
22. Fortes Filho JB, Eckert GU, Prociyanoy L, Barros CK, Prociyanoy RS. Incidence and risk factors for retinopathy of prematurity in very low and in extremely low birthweight infants in a unit-based approach in southern Brazil. Eye (Lond) 2009;23(1):25-30.
23. Hsueh W, Caplan MS, Qu XW, Tan XD, De Plaen IG, Gonzalez-Crussi F. Neonatal necrotizing enterocolitis: clinical considerations and pathogenetic concepts. PediatrDevPathol 2003;6(1):6-23.
24. Beeby PJ, Jeffery H. Risk factors for necrotising enterocolitis: the influence of gestational age. Arch Dis Child 1992;67(4 spec No):432-5.
25. Uauy RD, Fanaroff AA, Korones SB, Phillips EA, Phillips JB, Wright LL. Necrotizing enterocolitis in very low birthweight infants: bio demographic and clinical correlates. National Institute of Child Health and Human Development Neonatal Research Network. J Pediatr 1991;119(4):630-8.