



## ORIGINAL RESEARCH

### REHOSPITALIZATION RATES OF INFANTS OF LESS THAN 32 WEEKS GESTATION IN THE FIRST YEAR OF LIFE

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#### ABSTRACT

**Objective:** Preterm infants are at increased risk of rehospitalization after nursery discharge. We aimed to investigate the perinatal and environmental risk factors associated with increased risk of rehospitalization and determine the causes and duration of the rehospitalizations.

**Methods:** Hospital records of infants of gestational age of less than 32 weeks (n=73) discharged from the neonatal intensive care unit at Marmara University Hospital between the period of 1998-2002 and 100 full-term infants born in the same hospital were reviewed retrospectively.

**Results:** Thirty-two (53%) preterm infants were rehospitalized during- follow up period and 12 (20%) infants were readmitted more than once, whereas 5% of full-term infants were rehospitalized in the first year of life (p>0.5) and perinatal problems such as respiratory distress syndrome, bronchopulmonary dysplasia, intraventricular hemorrhage (p>0.5). Extremely low birth weight infants (ELBW) had a higher risk of rehospitalization (85.7% versus 14.3%), (p=0.02). In full-term infants, hyperbilirubinemia, in preterm infants prematurity anemia, respiratory illness, urinary tract infections were the most common reasons for rehospitalization.

**Conclusion:** In conclusion, preterm infants continue to be confronted by new problems after discharge from hospital and the incidence of rehospitalization is high.

**Keywords:** Rehospitalization, Preterm, Prematurity anemia

### DÜŞÜK DOĞUM AĞIRLIKLIL YENİDOĞANLARDA YAŞAMLARININ İLK BİR YILINDA REHOSPİTALİZASYON ORANLARI

#### ÖZET

**Amaç:** Preterm bebekler taburculuk sonrasında tekrar hastaneye yatış açısından risk altındadırlar. Bu çalışmada rehospitalizasyon riskini arttıran perinatal faktörleri, rehospitalizasyon nedenlerini, ortalama süresini belirlemeyi amaçladık.

**Yöntem:** Marmara Üniversitesi Hastanesi Yenidoğan Yoğunbakım Ünitesinde 1998-2002 arasında izlenmiş olan gestasyon yaşı 32 haftadan düşük 73 yenidoğanın ve 100 term yenidoğanın kayıtları retrospektif olarak incelendi.

**Bulgular:** Bir yıllık takip süresinde preterm yenidoğanların %53'ü (n=32) en az bir kez, %20'si (n=12) birden fazla kez, term yenidoğanların %5'i (n=5) rehospitalize edilmiştir. Rehospitalize edilmiş yada edilmemiş olan yenidoğanların sepsis, intravenriküler kanama, bronkopulmoner displazi, respiratuar distres sendromu gibi perinatal faktörleri, gestasyon yaşı, doğum ağırlığı, cinsiyeti benzer saptanmıştır. Çok düşük doğum ağırlıklı olmak hastaneye yatış için riski bulunmuştur (85.7% karşılık 14.3%), (p=0.02). Prematürelde en sık rehospitalizasyon nedenleri prematürite anemisi, solunum sistemi hastalıkları ve idrar yolu enfeksiyonu olmakla beraber term yenidoğanlarda en sık neden sarılık olarak saptanmıştır.

**Sonuç:** Preterm doğanlar taburcu edildikten sonra tekrar hastaneye yatışa sebep olabilecek değişik sağlık sorunları ile karşılaşmaktadır ve tekrar yatış oranları yüksektir.

**Anahtar Kelimeler:** Rehospitalizasyon, Preterm, Prematüre anemisi

#### INTRODUCTION

The survival of premature infants has increased dramatically in the last decade. However, prolonged hospitalization and long-term morbidities are still important problems<sup>1</sup>. Birth weight, presence of respiratory distress syndrome (RDS) requiring mechanical ventilation and bronchopulmonary dysplasia (BPD) are the most powerful predictive factors affecting the duration

of neonatal intensive care (NICU) stay<sup>1</sup>. Very low birth weight (VLBW) infants are also at increased risk of repeated hospitalization after their initial neonatal stay. A previous study found that VLBW infants were readmitted due to respiratory illness in %11-33 of cases<sup>2</sup>. VLBW infants with chronic lung disease (CLD) have an even higher risk of severe pulmonary infections<sup>3,4,5</sup>. Treatment with surfactant increases survival rates but does not

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lower risk of CLD<sup>4</sup>. Respiratory syncytial virus (RSV) prophylaxis with palivizumab has been found to decrease hospitalization due to RSV<sup>6,7</sup>. We reviewed the outcomes of VLBW infants discharged from Marmara University Hospital over a 4 year period. The incidence, duration and causes of rehospitalization were determined. We also investigated perinatal and environmental risk factors leading to rehospitalization.

## METHODS

Hospital records of all (n=73) surviving infants of gestational age of less than 32 weeks cared for in NICU at Marmara University Hospital and 100 full-term infants born in the same hospital were reviewed retrospectively. Sixty of the premature infants and all of the full-term neonates came to their follow up appointments until 1 year of age. Perinatal and environmental risk factors for rehospitalization were analyzed. Gestational age for these infants was determined from maternal dates of the last menstrual period. The gestational age of infants of >28 weeks' gestation was confirmed by Ballard examination. RDS was defined by clinical findings of respiratory distress and typical radiological findings. All preterm infants with RDS received early surfactant therapy. CLD (BPD) was defined as an oxygen requirement greater than room air at the 36th postconceptional week. Brain ultrasound was done at the first, third, seventh and twenty-first day of life. Intraventricular hemorrhage (IVH) was graded according to Papille's classification<sup>8</sup>. Sepsis was defined by clinical symptoms and positive blood culture. Prematurity anemia was defined as the normocytic, normochromic anemia accompanying low erythropoietin concentrations in premature infants. The preterm infants of less than 1000 grams and 28 weeks gestational age received 1200 U/kg erythropoietin three times a week for two weeks<sup>9</sup>. The erythrocyte transfusions were given according to the guidelines<sup>10</sup>. RSV prophylaxis with palivizumab was administered to preterm infants according to the recommendations of the American Academy of Pediatrics<sup>11</sup>. Environmental risk factors such as crowded housing, siblings at school, smokers in the household, season at NICU discharge and use of RSV prophylaxis were investigated. The infants were followed up monthly, at each follow up visit, information was obtained regarding hospitalization. The infants' age, cause and duration of rehospitalization were determined. Full-term and preterm infants were compared regarding the rate of hospital admission. Preterm

infants with and without rehospitalization were compared to determine perinatal and demographic factors associated with hospital readmission.

Statistical analysis: The differences between the infants with or without rehospitalization in the discrete variables such as sex, multiple gestation and presence of perinatal and environmental risk factors were compared by chi-square test. The differences in continuous variables were analyzed by student's t-test.

## RESULTS

Thirty-two (53%) preterm infants were rehospitalized during the follow up period and 12 (20%) infants were readmitted more than once, whereas 5% of the full-term infants were rehospitalized in the first year of life (p<0.05) (Table I). Perinatal problems such as respiratory distress syndrome, bronchopulmonary dysplasia (BPD), intraventricular hemorrhage were not found to be different in these patients (p>0.05). Eight of the preterm infants developed BPD. Two of them were rehospitalized due to respiratory problems. Extremely low birth weight infants had a higher risk of rehospitalization (85.7% versus 14.3%) (p=0.02). Infants who had a smoker in the household (8%) seemed to have a higher risk of rehospitalization (71.4% versus 56.4%) but this was not statistically significant either (p=0.68). Preterm infants with rehospitalization were similar for the other environmental risk factors such as the number of household person, siblings at daycare or school, palivizumab administration (p>0.05) (Table II). Thirty-three (56%) of the premature infants received RSV immunoprophylaxis with palivizumab. Eighteen (54%) premature infants who received RSV prophylaxis were rehospitalized. Respiratory problems (n=6), blood transfusion (n=7), infection (n=4), hyperbilirubinemia (n=1) were the causes of the rehospitalization in this group. Total number of preterms rehospitalized due to respiratory problems was 10 (17%). Nine of these infants were screened for RSV antigen in the nasopharyngeal aspirate and 3 (33%) of them were found to be positive. Six of 10 pulmonary related rehospitalized preterm infants had received palivizumab prophylaxis and 3 of 6 had RSV infection. Anemia of prematurity (39%, n=17), respiratory illness (24%, n=10), urinary tract (24%, n=10) infections are the most common reasons for rehospitalization in premature infants, whereas hyperbilirubinemia (4%, n=4) is the most common reason for rehospitalization in full-term infants (Table III).

**Table I:** Demographic findings

Clinical characteristics	Rehospitalized (n=32)	Not rehospitalized (n=28)	p value
Gestational age (weeks)	30.4±1.7	30.7±1.5	0.54
Birth weight (grams)	1384±349	1430±248	0.57
Birth weight <1000 grams (n=7)	6	1	0.02
Sex (M/F)	20/12	12/16	0.19
Multiple gestation (n=20) (twin and triplet)	9	11	0.41

**Table II:** Risk factors for rehospitalization

Risk factors	Rehospitalization % (n)	p value
Smoker in the household		
yes	71.4% (5)	0.68*
no	56.4% (22)	
Household		
>4 person	54.5% (6)	0.88**
≤4 person	57.1% (16)	
Siblings at daycare or school		
yes	54.5% (6)	0.90**
no	56.7% (17)	
Palivizumab administration		
yes	54.5% (18)	0.83
no	51.9% (14)	

\* Fisher's exact test

\*\* Chi-square test

**Table III:** Causes and duration of hospitalization

Rehospitalization number	Causes of rehospitalization	N (%)	Duration (days)
Preterm (n=44)	Anemia treatment	17 (39%)	1
	Respiratory Problems	10 (24%)	2.6
	Hyperbilirubinemia	2 (5%)	3
	Infection	11 (25%)	7
	UTI	10	
	Shunt	1	
	Hernia operation	3 (7%)	4
Term (n=5)	Hyperbilirubinemia	4 (4%)	3
	Infection	1 (1%)	7

## DISCUSSION



In this study 53% of VLBW were rehospitalized after their initial neonatal stay. It has been reported that 72% of extremely low birth weight (ELBW) infants were readmitted in the first 2 years of life<sup>4</sup>. 58%-67% of infants with BPD were rehospitalized in other studies<sup>4,12</sup>.

The incidence of chronic lung disease (CLD) in our population was 12% (9/73) which is comparable to previous reports<sup>13</sup>. The frequency of neonatal CLD is likely to increase due to the increasing survival of VLBW infants despite therapeutic advances including exogenous surfactant therapy, antenatal steroids, dexamethasone therapy for CLD and improved postnatal ventilatory and nutritional support. VLBW infants with CLD have diminished pulmonary reserve and prematurity itself may alter the long term development of the lung. We found that the transfusion for prematurity anemia of prematurity, respiratory illness and UTI were the most common reasons for rehospitalization.

The high readmission rate due to respiratory problems in preterm infants may have been due to poor pulmonary reserve induced by prematurity. Respiratory infections have a higher mortality and morbidity in this high risk group. Eight of the preterm infants developed BPD and two of them were rehospitalized due to respiratory problems in our study group. As the sample size is very small, no statistical relation was found between BPD and rehospitalization. None of our patients were discharged home on oxygen therapy (HOT) because management of these patients at home would not be possible without having adequately trained health care personnel at the patients' home. In developed countries, discharging home on oxygen therapy is a common practice, which is good for improved parent-infant interactions, and provides substantial cost savings<sup>4</sup>. Supportive services, both medical and social, have to be available before HOT becomes possible in developing countries.

RSV is the leading cause of lower respiratory illness in children. IMPact trial has shown that monthly palivizumab therapy reduces the incidence of hospitalization because of RSV infection by 55%. Fifty-six percent of VLBW infants have received palivizumab for RSV prophylaxis in our study. In our study, 10 (17%) infants were rehospitalized due to respiratory illness, but only 3 of 6 who had received palivizumab had RSV infection. The rehospitalization rate due to respiratory illness and the percentage of RSV as the etiologic agent in

these infections were found to be lower than the rates reported in the literature<sup>2</sup>. In our study, all parents were counseled to protect infants from exposure to tobacco smoke, thus only 8% of the parents' of premature infants smoked in the house. Counseling regarding the environmental risk factors might decrease thr repeated hospitalizations of high risk infants.

The normocytic, normochromic anemia accompanying low erythropoietin (Epo) concentrations, commonly affecting infants less of than 32 weeks gestation is called prematurity anemia<sup>10,14,15</sup>. Readmission for red cell transfusion prematurity anemia is the most common reason for rehospitalization in our study. Multiple clinical trials evaluating the use of Epo to prevent and treat anemia in preterm infants have been published in recent years and have reported a variety of results<sup>8,16</sup>. In some studies Epo with supplemental iron therapy and institution of strict transfusion guidelines have decreased the transfusion requirement of VLBW infants<sup>17-21</sup>. Whereas a multicentered study with a larger sample size of infants (n=241) less than 1250 grams failed to show any difference in transfusion requirements and thus did not support routine use of Epo<sup>14,22</sup>. Early Epo and iron therapy with a small sample size (n=27) was found to be not effective in decreasing the need for transfusion due to high phlebotomy losses for laboratory analysis in a study reported from Turkey<sup>23</sup>. Although in our unit we use human recombinant erythropoietin starting in the first week of life and institute rigorous and standardized transfusion guidelines, 39% of the rehospitalizations was related to the transfusion requirement after discharge. This may be due to the failure to decrease phlebotomy losses and the absence of microblood sampling techniques in our hospital.

In our study, full-term infants had a significant lower rehospitalization rate. It has been recognized that hyperbilirubinemia requiring phototherapy is the most commonly reported readmission diagnosis in term infants<sup>24</sup>. Similarly hyperbilirubinemia was the most common reason for the rehospitalization of full- term infants in our study. Hyperbilirubinemia is an important clinical problem since severe jaundice and even kernicterus can occur in some full-term healthy newborns. Thus the recognition and close follow up of jaundice is necessary. In conclusion, VLBW infants continue to be confronted by new problems after discharge from the hospital, thus a close follow up of the developmental milestones,



pulmonary problems and nutritional and metabolic needs of these high risk infants is necessary. This is an institution- based study on the provision of care and the outcome of high risk infants that determines the causes and duration of rehospitalization. Population-based national data provide a more accurate view and assist in allocating health resources. National data collection by clinical networks is necessary to properly determine the current outcome and problems of high risk infants.

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