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Characteristics of Term Neonates Admitted to the Neonatal Intensive Care Unit: A Single-center Experience

Yenidoğan Yoğun Bakım Ünitesine Yatırılan Term Yenidoğan Bebeklerin Özellikleri: Tek Merkez Deneyimi

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Abstract

Objective: Considerable research has been reported about the problems of preterm neonates admitted to the neonatal intensive care unit (NICU); however, the number of studies examining the problems of term neonates is limited. Thus, this study examined the problems of term neonates admitted to the NICU.

Materials and Methods: The demographic and clinical characteristics of mothers and term neonates admitted to the NICU between January 1, 2015, and December 31, 2020, were retrospectively examined from the medical records. Neonates with major congenital anomalies, diagnosed with genetic syndromes, or referred to another hospital for any reason were excluded from the study. Categorical variables are expressed as n and percentage (%) and numerical variables as median (25^{th}-75^{th} percentile) values.

Results: In total, 1,221 term neonates were enrolled, of which 349 (28.6%) were referred from other centers. The mean gestational age of the infant was 38 weeks (37-39) and the median birth weight was 3.560 g (3,210-3,672). The most common reason for admission to hospital was respiratory distress (n=399, 32.7%), followed by neonatal jaundice (n=370, 30.3%), infections (n=181, 14.8%), hypoxic-ischemic encephalopathy (HIE) (n=98, 8%), hypoglycemia (n=40, 3.3%), small for gestational age (n=25, 2%), poor feeding (n=16, 1.3%), and others (n=92, 7.6%). The median length of hospital stay was 5 (3-8) days. The mortality rate was calculated as 1.1%. Mortality occurred in seven neonates due to infection during the study and in seven due to HIE.

Conclusion: Term neonates represent a significant proportion of patients admitted to the NICU. In light of admission causes, various antenatal practices may help reduce the admission frequency of these neonates.

Öz

Amaç: Yenidoğan yoğun bakım ünitesine (YYBÜ) yatırılan preterm bebeklerin sorunları ile ilgili çok sayıda araştırma bulunmakta iken, literatürde term bebeklerin sorunlarını inceleyen kısıtlı sayıda çalışma bulunmaktadır. Bu çalışmada hastanemizin YYBÜ'de yatan term bebeklerin sorunları incelenmiştir.

Gereç ve Yöntemler: 1 Ocak 2015 ile 31 Aralık 2020 tarihleri arasında YYBÜ'de yatan term bebeklerin ve annelerinin demografik ve klinik özellikleri tıbbi kayıtlardan geriye dönük olarak incelendi. Majör konjenital anomalisi olan, genetik sendrom

tanısı alan ve herhangi bir nedenle başka bir hastaneye sevk edilen bebekler çalışma dışı bırakıldı. Kategorik değişkenler frekans (n) ve yüzde (%) olarak, nümerik değişkenler ise ortanca (25 persantil-75 persantil) olarak verildi.
Bulgular: Çalışmaya 1,221 term bebek dahil edildi. Bu bebeklerin 349'u (%28,6) diğer bir sağlık merkezinden sevk ile yatırılmıştı. Çalışmaya alınan bebeklerin ortanca gebelik haftası 38 hafta (37-39), bebeklerin ortanca doğum ağırlığı 3,560 g (3.210-3.672) idi. Hastaneye yatış nedenleri değerlendirildiğinde, en sık nedenin solunum sıkıntısı (n=399, %32,7) olduğu görüldü. Bunu sırası ile yenidoğan sarılığı (n=370, %30,3), enfeksiyonlar (n=181, %14,8), hipoksik-iskemik ensefalopati (HİE) (n=98, %8), hipoglisemi (n=40, %3,3), düşük doğum ağırlığı (n=25, %2), beslenme sorunları (n=16, %1,3) ve diğer nedenler (n=92, %7,5) takip ediyordu. Ortanca hastanede yatış günü 5 (3-8) idi. Çalışma süresince yedi bebeğin yenidoğan enfeksiyonu olduğu, yedi bebeğin de HİE nedeni ile eksitus olduğu görüldü ve mortalite oranı %1,1 olarak belirlendi.
Sonuç: Günümüzde YYBÜ'de yatan hastaların önemli bir kısmını term bebekler oluşturmaktadır. Yatış nedenleri göz önüne alındığında bazı antenatal uygulamaların ve ebeveyn eğitiminin bu bebeklerin yatış sıklığını azaltmada yardımcı olabileceği düşünülmüştür.

Introduction

The neonatal period is one when the baby endeavors to adapt to extrauterine life, and when marked physiological changes occur. A significant proportion of deaths in the first year of life are observed during this time when the baby is most defenseless (1). The fact that three out of four deaths in the neonatal period occur in the first week of life heightens the importance of the care provided for the baby (2). Infant death rates are one of the criteria used to determine countries' level of development and also reflect the accessibility and effectiveness of health services.

Prematurity and low birth weight are the most important risk factors for neonatal morbidity and mortality. Numerous studies have therefore examined the problems of preterm babies. However, analysis of all neonatal intensive care unit (NICU) admissions shows that term babies constitute more than 50% of such infants (3). A study from Ireland reported that 54% of babies admitted to the NICU had birth weights of 2,500 g or more (4). Similarly, term babies were reported to constitute 60% of admissions to the NICU in the UK in 2012-2013 (3). In addition to the potential complications and high treatment costs associated with admission to the NICU, the separation of the mother and neonate after birth damages mother-infant bonding, reduces the physiological benefits of bonding, and disrupts the feeding of the infant (5).

The purpose of this study was to evaluate the clinical and demographic characteristics and the reasons for admission of term neonates in our hospital, which has one of the largest tertiary NICUs in its region.

Materials and Methods

Term neonates (≥37 birth weeks) admitted to the NICU of the university hospital between 1 January 2015, and 31 December 2020, were included in this retrospective, cross-sectional study. Medical records of mothers during pregnancy and babies' detailed NICU admission records were examined in detail. When identifying the reasons for babies' admission, a single basic cause of admission to the hospital was recorded. Babies with major congenital anomalies, diagnosed with genetic syndromes, or referred to another hospital for any reason were excluded from the study. Ethical committee approval was received before the study commenced from Aydın Adnan Menderes University (decision no: 11, date: 22.04.2021).

Definitions

Gestational age was calculated based on the date of the last menstrual cycle and/or fetal ultrasound measurements performed in the first trimester. Babies with birth weights below the 10th percentile for the birth week were defined as small for gestational age (SGA) (6). Respiratory distress was defined as tachypnea commencing immediately after birth, contraction in the respiratory muscles and use of auxiliary respiratory muscles, grunting, cyanosis, apnea, or oxygen requirement. Respiratory distress syndrome (RDS) was diagnosed based on cyanosis, tachypnea (respiratory rate >60 breaths/min), intercostal retractions, grunting, a diffuse reticulogranular appearance, and air bronchograms on chest X-rays, starting in the first hours after birth and exceeding 24 h in duration. Transient tachypnea of the newborn (TTN) was diagnosed with grunting and tachypnea commencing in the first 6 h after birth

and lasting at least 12 h, together with a pronounced pulmonary vascular bed on lung X-rays, increased aeration, perihilar fullness, and fluid in fissures (7). Pneumonia was diagnosed in the presence of typical lung X-ray findings in respiratory difficulty accompanied by acute phase reactant elevation (7). Meconium aspiration syndrome (MAS) was diagnosed based on amniotic fluid being stained with meconium and an increased oxygen requirement, together with the absence of any pathology capable of causing respiratory difficulty and/or observation of typical radiological changes on chest X-rays (8). Hypoglycemia was defined as venous blood glucose lower than 47 mg/dL (9). Hypoxic-ischemia encephalopathy (HIE) was diagnosed based on Apgar scores of less than 5 at 5 minutes and 10 minutes, presence of marked metabolic acidosis (pH <7.0 or base deficit <12 mmol/L, or both together) in blood gas taken from umbilical cord blood or in the first hour after birth, the observation of neurological findings such as seizure, and multiple organ failure (10). Chorioamnionitis was diagnosed based on maternal body temperature elevation plus at least two or more of the following: maternal leukocytosis (>15,000 cells/mm^3), maternal tachycardia (>100 beats/min), fetal tachycardia (>160 beats/min), uterine tenderness or purulent amniotic fluid (11). Infection was diagnosed as a pathological process caused by the invasion of normally sterile tissue or fluid or body cavity by pathogenic or potentially pathogenic organisms. Neonatal sepsis diagnosed as, presence of clinical signs and symptoms of infection (hypotension, seizure, increase oxygen requirement, apnea, intercostal retraction, tachypnea, weak pulse, delayed capillary refill, bradycardia or tachycardia, irritability, hypotonia, lethargy, feed intolerance) and abnormal laboratory results (increased C-reactive protein, leukocytosis or leukopenia, thrombocytopenia, elevated immature: total neutrophil ratio) with or without the presence of positive blood culture (12). Neonatal jaundice was evaluated in line with Turkish Neonatal Society protocols (13).

Statistical Analysis

Statistical analyses were performed using SPSS version 19 software (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.). Descriptive statistics (kurtosis and skewness), visual methods (histograms), and analytical tests (Shapiro-Wilk test) were employed to determine the normal distribution of numerical variables. Categorical data were presented as n and %, and numerical data were mean ± standard deviation if normally distributed, and as median values (25-75%) if non-normally distributed. Spearman's correlation test was used for non-normally distributed data. A p-value less than 0.05 was considered statistically significant.

Results

A total of 3,439 neonates were admitted to the NICU during the study period, of which 1,855 (54%) were term. Six hundred thirty-four infants were excluded from the study, and 1,221 term infants were enrolled (Figure 1). The demographic and clinical characteristics of the neonates and mothers included in the study are presented in Tables 1 and 2. The median age of the mothers was 29 (25-33) years, and 91.8% had received regular prenatal follow-up. In addition, 70.2% of births were by cesarean delivery, and 98% of babies were singletons. The babies' median birth weight was 3,560 g (3,210-3,672) and median gestational age was 38 weeks (37-39). Six hundred eighty-three babies (55.9%) were boys (male: female ratio 1.2). Three hundred forty-nine (28.6%) babies were referred from another hospital.

Forty-nine percent of babies were admitted within the first 24 h after birth. Respiratory distress was the most frequent reason for admission (32.7%). TTN was the most common respiratory morbidity (55.6%). The other causes of the admission in respiratory distress group were pneumonia (27.6%), RDS (7%), pneumothorax (6.8%), and MAS (3%). The median admission time among neonates with respiratory morbidity was postnatal 1 (1-3) day. Mechanical ventilation requirement of these neonates was 85%, and 15.1% received surfactant therapy. The median length of stay of the hospital was 5 (3-8) days in respiratory distress group.

The second most common cause of admission to the NICU was neonatal jaundice (30.3%). The median time of admission of babies with jaundice was postnatal 3 (1-5) days. ABO incompatibility was present in 32.4% of these infants, Rh incompatibility in 12.1%, ABO and Rh incompatibility in 2.4%, subgroup incompatibility in 1.9%, glucose 6-phosphate dehydrogenase deficiency in 1.9%, and other causes in 49.3%. The median length of stay in NICU was 3 (2-5) days in

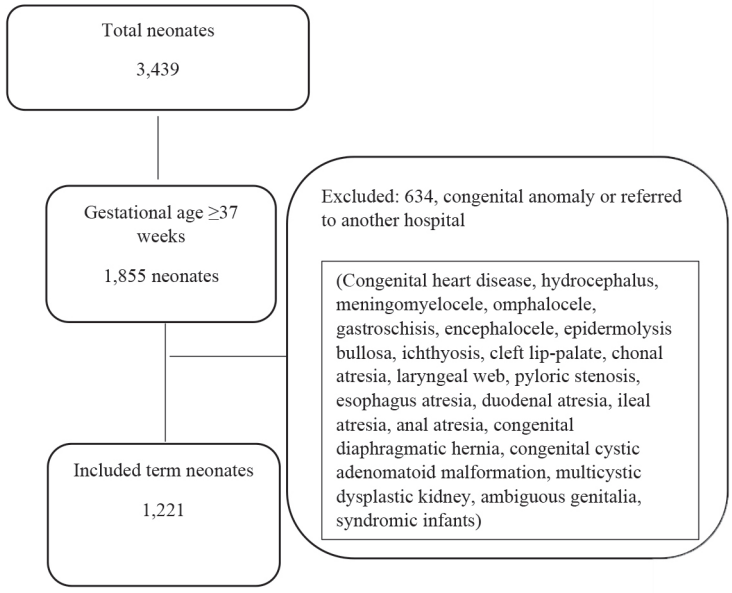

Figure 1. Diagram of inclusion and exclusion

Table 1. The demographic and clinical characteristics of mothers

Variable	n	%
Maternal age (years)		
<18	40	3.4
18-34	935	76.6
≥35	245	20
Parity		
Primipara	455	37.2
Multipara	766	62.8
Assisted reproductive technology	10	0.8
Regular prenatal care	1,121	91.8
Twin status	25	2
Diabetes	171	14
With insulin	39	3.2
Preeclampsia	60	4.9
Hyperthyroidism	3	0.2
Hypothyroidism	86	7
Placenta previa	22	1.8
Placental abruption	5	0.4
Premature rupture of membrane	44	3.6
Chorioamnionitis	13	1
Cardiac disease	11	0.9
Autoimmune disease	11	0.9

neonates with jaundice. Seven neonates (1.9%) with jaundice were treated with exchange transfusion. Kernicterus developed in one baby who was treated with exchange transfusion with a diagnosis of glucose 6-phosphate dehydrogenase deficiency.

One hundred eighty-one (14.8%) neonates were followed up due to neonatal infection. Blood culture positivity was observed in 51 (28.1%) of these infants. The most commonly isolated microorganisms were *Staphylococcus aureus* (21.5%), coagulase-negative *staphylococci* (21.5%), *Escherichia coli* (19.6%) and *Klebsiella pneumoniae* (16.6%).

Ninety-eight (8.1%) of term neonates were admitted with diagnoses of HIE. Sixty-one (62.2%) of these neonates were started on hypothermia therapy. Eighty-seven (88.8%) of the babies with HIE were referred from another hospital, and 62 (63.2%) were born by vaginal delivery. The mean length of hospitalization among these patients was 7 (5-11) days.

Forty patients (3.3%) were admitted due to hypoglycemia, 25 (2.0%) due to SGA, 16 (1.3%) due to feeding problems, and 92 (7.6%) for other reasons (neonatal abstinence syndrome, social indication, admission for some diagnostic tests, cardiac arrhythmia, etc.).

Seven neonates with HIE and seven neonates with sepsis died during the study period and the mortality rate was 1.1%.

Table 2. The demographic and clinical characteristics of term neonates

Variable	n	%
Sex		
Male	683	55.9
Gestational age at birth (weeks)		
37-38	319	26.1
38-39	535	43.8
39-40	215	17.7
40-41	114	9.3
41-42	25	2
≥42	13	1.1
Birth weight (g)		
<2,500	92	7.5
2,500-3,990	1,050	86
≥4,000	79	6.5
Mode of delivery		
Cesarean delivery	858s	70
Postnatal age at admission (days)		
<24 h	599	49
24 h-1 week	366	30
1 week-2 weeks	103	8.5
≥2 weeks	153	12.5
Reason for admission		
Respiratory distress	399	32.7
Jaundice	370	30.3
Infection	181	14.8
HIE	98	8
Hypoglycaemia	40	3.3
SGA	25	2
Poor feeding	16	1.3
Others	92	7.6

HIE: Hypoxic ischemic encephalopathy, SGA: Small for gestational age

The length of stay in NICU was longer among babies with neonatal infection, HIE, and hypoglycemia than in babies admitted for other reasons (p<0.001) (Table 3). Besides, there was no correlation between the gestational age and length of stay in NICU (r=0.041, p=0.154).

Table 3. Length of stay in a neonatal intensive care unit

Reason for admission	Length of stay (days)	p*
Respiratory distress	5 (3-8)	<0.001**
Jaundice	3 (2-5)	
Infection	7 (4-9)	
HIE	7 (5-11)	
Hypoglycaemia	7 (4-9)	
SGA	4 (3-8)	
Poor feeding	3 (2-4)	
Others	4 (2-7)	

HIE: Hypoxic ischemic encephalopathy, SGA: Small for gestational age
Data were given as median (25-75 percentile)
*Kruskal-Wallis test, **Infection, HIE, and hypoglycemia vs. the other diagnoses

Discussion

Although term babies are regarded as being at low risk of admission to the NICU, 5-18% of these babies are admitted to intensive care (14). Consistent with previous studies, the present study showed that term neonates constituted more than half of NICU admissions (3). An epidemiological study from the USA performed in 2007-2012 reported that babies with a birth weight exceeding 2,500 g constituted more than half of NICU admissions (15). Overall, 1,221 term neonates had been included in the study period. Among them, male neonates were a little more than female neonates, which is consistent with the previous studies (16,17). It was reported that male neonates born at all birth weights had higher mortality rates up to 18 years of age than female neonates (18). The study by Ito et al. (19) reported that the mortality rates of male neonates are higher than the mortality rates of female neonates because of the higher incidence of respiratory and gastrointestinal diseases in male neonates. Moreover, cultural factors could lead to males receiving more consideration from parents than females.

In the present study, the most common cause of admission to NICU was respiratory distress consistent with literature data (16). A cohort study investigating risk factors in NICU admissions in babies with gestational ages exceeding 36 weeks reported that respiratory morbidity represented 49.3% of reasons for admission (20). In the present study, 74% of babies admitted due to respiratory morbidity were born before 39 weeks, 76% were born by cesarean delivery. This may be attributable to antenatal risk factors such as diabetes, preeclampsia, and infection being more frequent among mothers of babies

born before the 39th week of pregnancy and the greater prevalence of cesarean deliveries in births occurring before that week. Horowitz et al. (21) reported an increased incidence of admission due to respiratory distress in births before 39 weeks, and a greater incidence of cesarean delivery among these neonates. The risk of respiratory distress in neonates born by elective cesarean delivery, cesarean delivery performed after the onset of labor, and neonates born by the vaginal delivery equalized in the 39th week (22). Elective cesarean delivery is therefore recommended in the 39th week (23). We think it is important for such information to be provided to parents scheduled for cesarean delivery. In addition, there are many advances to reduce the incidence and severity of respiratory distress including ensuring lung maturation with prenatal steroids, follow-up of high-risk pregnancies in tertiary perinatal centers, and non-invasive mechanical ventilation techniques. In the present study, non-invasive mechanical ventilation support was given to 30% of the neonates' admissions due to respiratory distress which is consistent with previous studies (24).

Neonatal jaundice was the second most frequent reason for admission to NICU, at a rate of 30.3% in this study. The rate of admission to the NICU due to indirect hyperbilirubinemia has increased following the shortening of postpartum hospital stay (25). Indirect hyperbilirubinemia is one of the most common neonatal problem and can give rise to severe conditions such as kernicterus (26). Exchange transfusion was performed in one patient diagnosed with glucose 6-phosphate dehydrogenase deficiency in the present study, but due to late presentation, kernicterus development could not be prevented. A retrospective cohort study from the UK reported that birth after the 37th gestational week increased the incidence of admission to intensive care due to jaundice (3). Before discharge, it is important for parents to be informed about neonatal feeding and jaundice, particularly in the presence of risk factors, and concerning when the baby should be brought for control examination (13).

In the present study, 14.8% of neonates were admitted due to neonatal infections. Neonatal infections are still an important cause of morbidity and mortality in the neonatal period in both developed and developing countries (27). Yang and Meng (16) reported a rate of 6.5% for admission to the NICU among term babies because of neonatal infections. Despite all the many advances in the field of neonatology, neonatal infections retain their clinical importance because there is no finding entirely showing infection, and due to the lack of a specific marker showing neonatal infection. Rapid initiation of empiric antibiotic therapy in case of suspected infection can be life-saving. Antenatal prophylaxis, hand washing, using an aseptic technique during invasive procedures, infection control education of all staff, and the determination of hospital infectious agents and sensitivity rates play a leading role in infection control policies. In the present study, seven babies died due to neonatal sepsis. Eighty-five percent of these babies had been referred to our NICU from another hospital. Therefore, we think that this situation may have caused a delay in the initiation of empirical antibiotic therapy and appropriate treatment.

The incidence of HIE is 1.5 per 1,000 live births in developed countries (28). According to Turkish Neonatal Society HIE Working Group data, the incidence of HIE in babies with gestational ages >37 weeks is 2.6 per 1,000 live births (29). In the present study, 8.1% of babies were admitted due to HIE. It was noteworthy that 90% of the babies in this patient group had been referred from other hospitals, and that while the rate of vaginal delivery among all babies was 29.8%, the rate was 63% in these infants. Martinez-Biarge et al. (30) reported a higher risk of HIE in vaginal births compared to elective cesarean births. A similar risk of HIE has been reported in operative vaginal deliveries and emergency cesarean section with full cervical dilation (31). In the present study, none of the neonates treated with hypothermia were born by elective cesarean section. The study investigating the intrapartum risk factors for HIE reported that operative vaginal delivery (2.34) and emergency cesarean section (2.17) were both associated with an increased risk of encephalopathy compared to spontaneous vaginal delivery (32). In addition, considering the heterogeneity of the etiological causes and possible relations with the antepartum period, elective cesarean delivery is not recommended to reduce the risk of asphyxia (33). Due to the lack of data on an operative vaginal delivery, no comment could be made on this subject

in the present study. Seven babies died from HIE in this study. Identifying at-risk pregnant, intrauterine transport of infants, appropriate antenatal care of the mother, and the provision of periodic neonatal resuscitation program training sessions for health personnel can all be effective in reducing perinatal asphyxia-related mortality (34,35).

The fact that one-third of the term neonates admitted to the NICU were followed up less than three days suggests that the admission criteria for term babies need to be reviewed in this study. In a cohort study in which 19 NICUs were examined retrospectively, babies born at gestational weeks between 35-42 and admitted to the NICU were investigated, and no identifiable cause was found in 10.8% of patients (36). In addition, intensive care admission can be prevented by various antenatal procedures in some term babies. Considering that admitting babies to the NICU represents a significant source of anxiety for families, babies being followed up in the same room with their mothers, if babies expected to be admitted for short periods, will contribute to bonding between mother and the baby and maintenance of feeding of infant (37).

The present study had a few limitations. The study involves results from a single-center it reflects data from the local region, and the results may not, therefore, be capable of being generalized to the entire population. Moreover, kernicterus developed in one baby in this study. Since kernicterus can also be diagnosed at post-discharge follow-up, our findings may not reflect the true results. In addition, this study was unable of measuring results beyond the NICU admissions.

Conclusion

Term neonates represent a significant proportion of admissions to the NICU. This study reported the clinical characteristics and reasons for admission of term babies. In light of the reasons for admission of term neonates, we think that various antenatal measures and parental education may help reduce the incidence of admission among these babies. We think that evaluation of the reasons for term neonate admissions and the measures to be taken to reduce the rate of admission of these babies in our country, in which the number of NICU beds is critical, is a matter of considerable importance. Reducing the incidence of hospitalization of term neonates will reduce morbidity and complications during admission and lower costs, as well as preventing the adverse consequences of separating mother and baby.

Ethics

Ethics Committee Approval: Ethical committee approval was received before the study commenced from Aydın Adnan Menderes University (decision no: 11, date: 22.04.2021).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: A.A., D.İ.G., A.B.A., G.E., Design: A.A., D.İ.G., A.B.A., G.E., Supervision: A.A., D.İ.G., G.E., Data Collection or Processing: A.A., D.İ.G., G.E., M.K.T., Analysis or Interpretation: A.A., D.İ.G., G.E., M.K.T., Literature Search: A.A., D.İ.G., G.E., M.K.T., Writing: A.A., D.İ.G., G.E., M.K.T., Critical Review: A.A., D.İ.G., G.E., M.K.T.

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