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Original Article

The Most Common Causes of Morbidity and Mortality in Late Preterm Infants: 8-year Single-center Experience

Geç Prematüre İnfantlarda En Yaygın Morbidite ve Mortalite Nedenleri: 8 Yıllık Tek Merkez Deneyimi

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ABSTRACT

Objective: Late preterm infants are immature regarding respiratory, metabolic, neurological, and immunological features and have a high risk for morbidity and mortality. Therefore, it is aimed to draw attention to the problems that may develop in newborn care by scanning all hospitalization and mortality rates of late preterm infants.

Method: In this retrospective study, late preterm infants hospitalized in a tertiary university hospital between January 1, 2007, and December 31, 2014, having the study admission criteria, were enrolled.

Results: A total of 1,088 late preterm infants were included in the eight-year study period. According to their gestational weeks, the infants were divided into three main groups; 31.4% (n=342) were in group 1 (340/7-346/7), 30.6% (n=333) were in group 2 (350/7-356/7), 38% (n=413) were in group 3 (360/7-366/7). The most common causes for admission to the neonatal intensive care unit were hyperbilirubinemia, suspected sepsis and infections, respiratory morbidities, poor feeding, and hypoglycemia; reasons for rehospitalization included jaundice, infections, suspicion of sepsis, and poor feeding. In addition, neonatal transient tachypnea, apnea, hypoglycemia, early-onset sepsis, healthcare-associated infection were most common in those born at 34-346/7 gestational weeks; respiratory distress syndrome, pneumonia, late-onset sepsis were most frequently in those born at 35-356/7 gestational weeks.

Conclusion: As a result, late preterm infants are at risk for respiratory disorders, sepsis, jaundice, and metabolic problems; the need for intervention increases as gestational age decreases. The delivery timing should be planned with these problems in mind, and the follow-up and treatment of late preterm infants should be carried out accordingly.

Keywords: Preterm birth, gestational age, late premature, morbidity, mortality

ÖZ

Amaç: Geç preterm bebekler solunum, metabolik, nörolojik ve immünolojik açıdan olgunlaşmamış olup morbidite ve mortalite açısından yüksek risk taşırlar.

Yöntem: Bu retrospektif çalışmaya, üçüncü basamak bir çocuk hastanesi yenidoğan yoğunbakım ünitesinde, 1 Ocak 2007 ile 31 Aralık 2014 tarihleri arasında yatırılan ve çalışma kriterlerine uygun geç prematüre bebekler dahil edildi.

Bulgular: Sekiz yıllık süreyi kapsayan çalışmaya toplam 1,088 geç prematüre bebek dahil edildi. Bebekler gebelik haftalarına göre üç ana gruba ayrıldı. Grup 1, 342 (%31,4) geç pretermden oluşup 34-346/7gebelik haftasında doğan, grup 2, 333 (%30,6) geç pretermden oluşup 35-356/7 gebelik haftasında doğan, ve grup 3, 413 (%38) geç pretermden oluşup 36-366/7 gebelik haftasında doğanlar idi. Yenidoğan yoğun bakım ünitesine en sık başvuru nedenleri hiperbilirubinemi, şüpheli sepsis ve enfeksiyonlar, solunumsal morbiditeler, yetersiz beslenme ve hipoglisemi olup; yeniden hastaneye yatış nedenleri arasında sarılık, enfeksiyonlar, şüpheli sepsis ve kötü beslenme vardı. Yenidoğan geçici takipnesi, apne, hipoglisemi, erken başlangıçlı sepsis, sağlık hizmeti ilişkili enfeksiyon 34-346/7 gebelik haftasında doğanlarda yaygın olup; respiratuvar distress sendromu, pnömoni, geç başlangıçlı sepsis en sık 35-356/7 gebelik haftasında doğanlarda idi.

Sonuç: Sonuç olarak geç prematüreler solunumsal rahatsızlıklar, sepsis, sarılık ve metabolik problemler açısından risk altında olup; gebelik yaşı azaldıkça müdahale ihtiyacı artar. Doğum zamanı bu sorunlar göz önünde bulundurularak planlanmalı ve geç prematüre bebeklerin takip ve tedavisi buna göre yapılmalıdır.

Anahtar kelimeler: Erken doğum, gebelik haftası, geç prematürite, morbidite, mortalite

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INTRODUCTION

Late preterm infants have attracted attention for the last 20 years since they comprise approximately 80% of all births and have a higher risk of short- and long-term morbidity and mortality than term infants[1]. Late preterm birth rates in the United States increased from 6.82% to 7.09% between 2014 and 2016, accounting for approximately 72% of all preterm births[2].

Preterm labor, premature rupture of membranes, the increasing occurrence of multiple births due to assisted reproductive technologies, advanced maternal age, maternal obesity, and maternal and physician concern about complications such as hypoxic-ischemic encephalopathy and birth traumas in advanced gestational weeks are all possible contributors to the rising incidence of late preterm birth[3-5].

Although late preterm infants have a better prognosis and survival rate than premature infants, they are more likely to develop respiratory complications, infections, feeding issues, hyperbilirubinemia, hypothermia, and hypoglycemia[6]. In addition, the duration of hospitalization and readmission rates after discharge are two to three times higher in late preterm infants than in term infants, resulting in increased healthcare costs and, ultimately, a public health problem[7].

The aim of this retrospective study, which was planned considering these problems of late premature, was to evaluate the clinical and laboratory findings, the leading indications of hospitalization, the cause and rate of mortality in all infants at $34^{0/7}$-$36^{6/7}$ gestational weeks in our neonatal intensive care unit (NICU). In addition, it was planned to compare our results with national and international studies, explain the reasons for their differences, and emphasize all the problems that may develop in late preterm babies to attract the attention of pediatricians and obstetricians.

MATERIALS and METHODS

This study was conducted in a tertiary university hospital. The study included 1,088 late preterm infants born between $34^{0/7}$ and $36^{6/7}$ weeks admitted to the NICU between January 1, 2007, and December 31, 2014.

The patients were divided into three main groups: infants born at $34^{0/7}$-$34^{6/7}$ were classified as group 1, infants born at $35^{0/7}$-$35^{6/7}$ were classified as group 2, and infants born at $36^{0/7}$-$36^{6/7}$ were classified as group 3.

Definitions

Late premature: According to World Health Organization, the American Academy of Pediatrics (AAP), and the American College of Obstetrics and Gynecology (ACOG), infants born between $34^{0/6}$ weeks of gestation and $36^{6/7}$ weeks from the mother's last menstrual cycle were considered late preterm [8-10].

Respiratory disorders: Tachypnea (respiratory rate >60/min), suprasternal-intercostal-subcostal retractions, groaning, cyanosis, apnea, or oxygen requirement were all considered signs of postpartum respiratory distress. Respiratory distress syndrome (RDS) was defined as cyanosis, tachypnea, intercostal retractions, persistent or progressive groaning for 48-96 hours of life, and diffuse reticulonodular appearance and air bronchogram on chest X-ray[11]. Pneumonia was defined as respiratory distress with cough, fever, malnutrition, pathological clinical and respiratory findings, evidence of infiltration-consolidation, reticulonodular appearance with air bronchograms, and pleural fluid seen in X-ray[12]. Transient tachypnea (TTN) of the newborn was defined as pulmonary vascular prominence, increased lung aeration, and fluid in the fissures on the chest X-ray accompanied by tachypnea and moderate respiratory distress that started shortly after birth and generally resolved within 3-5 days[13]. Apnea was defined as a 20-second or more prolonged decrease in oxygen saturation and respiratory arrests accompanied by bradycardia [14].

Hypoglycemia: According to AAP guidelines, the lower limit for low blood sugar in an asymptomatic late preterm infant was accepted as 25 mg/dL in the first four hours of life and 35 mg/dL between 4-24 hours. The lower limit of blood glucose was accepted after 24 hours as 47 mg/dL[15].

Hypocalcemia: Serum calcium value <7 mg/dL was accepted as hypocalcemia[16].

Hyperbilirubinemia: According to the Bhutani nomogram, late preterm infants who required phototherapy were included [17].

Neonatal sepsis: The presence of at least three of the following clinical findings, such as bradycardia or tachycardia, hypotension, hypotonia, seizure, apnea, tachypnea, cyanosis, respiratory distress, deterioration of skin color and perfusion, malnutrition, irritability, lethargy, and the presence of positive blood or other cultures, was defined as neonatal sepsis. Sepsis detected in the first three days of life was considered early neonatal

sepsis and noticed after the 4th day of life was considered late-onset neonatal sepsis. Nosocomial sepsis was defined as a late preterm infant with signs of infection 48-72 hours after hospitalization or rehospitalization within the previous ten days [18].

Infants referred to another center after birth whose file information was lacking from the study were excluded.

Patients' data were collected from medical records, including prenatal problems, mothers' age, type of delivery, gestational week, birth weight, gender, indications of hospitalization, all physical examination-clinical-laboratory-radiological findings, causes, and rates and reasons for rehospitalization and mortality.

Statistical Analysis

The late preterm infants were divided into three groups based on their gestational weeks, and the statistical analyses were performed on these groups' axis. The Kruskal-Wallis scale was used to compare numerical values according to gestational week groups. Statistical analysis was performed using SPSS Statistical Software (version 20; SPSS, Chicago, IL, USA). Categorical variables were presented with frequency and percentage, while numerical variables were presented using tables as (mean ± SD) or (median) range (minimum, maximum). The Spearman's Rho correlation test was used to determine the correlations between numerical variables, and p values corresponding to the correlation values were obtained. A multivariate logistic regression model was designed to investigate the effect of the variables on the gestational week. In addition, a chi-square test and post-hoc analysis were used to investigate the association level among variables, with significance set to $p<0.05$.

This study was approved by the Necmettin Erbakan University, Meram Faculty of Medicine Ethics Committee for Non-pharmaceutical and Medical Device Research (decision no: 2015-282, date: 16.09.2015).

RESULT

Comparison of Demographic Data and Clinical Features of Three Late Preterm Groups

During these eight years, 1,088 late preterm infants hospitalized in the NICU were included in the study. According to their gestational weeks, the infants were divided into three main groups; 31.4% (n=342) were in group 1 ($34^{0/7}$-$34^{6/7}$), 30.6% (n=333) were in group 2 ($35^{0/7}$-$35^{6/7}$), 38% (n=413) were in group 3 ($36^{0/7}$-$36^{6/7}$). Of the 1,088 infants, 53.7% (n=584) were male, 45.9% (n=499) were female, and the remaining 5 (0.4%) infants had ambiguous genitalia. The male gender was more dominant at all gestational weeks (%55 in group 1; %50.7 in group 2, %55 in group 3). Among all late premature, the rate of cesarean section (C/S) was as high as 85.9% (n=934). When each gestational week was evaluated separately, C/S deliveries were statistically higher than spontaneous vaginal deliveries (SVD) (p=0.001).

While 84.6% (n=921) of all pregnancies were spontaneous, 15.4% (n=167) were accomplished via assisted reproductive techniques (ART). In addition, the majority of ART pregnancies were born at $34^{0/7}$-$34^{6/7}$ gestational weeks, whereas spontaneous pregnancies were born at $36^{0/7}$-$36^{6/7}$ gestational weeks. The distinction was statistically significant (p=0.003).

The multiple pregnancy rate among all groups was 20.6% (n=224). Of these, 17% (n=184) were twin pregnancies, and 3.6% (n=40) were triplet pregnancies. While the majority of triplet pregnancies were born at $34^{0/7}$-$34^{6/7}$ gestational weeks, there were no triplet births at $36^{0/7}$-$36^{6/7}$ gestational weeks. Regarding multiple pregnancies, the difference between gestational week groups was significant (p=0.012).

Post-hoc analysis revealed a statistically significant difference between groups 1 and group 3 regarding C/S delivery, while a statistically significant difference between group 1- group 3 and group 2- group 3 for ART and multiple pregnancies. The epidemiological characteristics of all three groups are summarized in Table 1.

Comparison of Three Late Preterm Groups' Reasons for Admission to the NICU

The most common reasons for admission to the NICU for all late preterm infants were jaundice, suspected or proven sepsis or another infectious disease, respiratory disorders, malnutrition, and hypoglycemia (detailed in Table 2).

Among the respiratory diseases, TTN and apnea were more common in group 1 than in those group 2 and group 3 (8.4%, n=29; 5%, n=17, respectively), while RDS and pneumonia were more common in group 2 than in those group 1 and group 3 (6.3%, 21; 12.6%, n=42, respectively). There was a statistically significant difference between the groups regarding apnea and RDS (p=0.032, p=0.009, respectively).

Table 1. The comparison of demographic data and clinical features of three groups				
	Group 1 ($34^{0/7}$-$34^{6/7}$)	**Group 2 ($35^{0/7}$-$35^{6/7}$)**	**Group 3 ($36^{0/7}$-$36^{6/7}$)**	**p-value**
Demographic data				
Number, n(%)	342 (31.4%)	333 (30.6%)	413 (38%)	
Gender, n (%)				
Male	188 (55%)	169 (50.7%)	227 (55%)	
Female	154 (45%)	164 (49.3%)	186 (45%)	
Type of delivery				
C/S ratio, n(%)	308 (90%)	289 (86.8%)	338 (81,8%)	0.001[b]
SVD ratio, n(%)	34 (10%)	44 (13.2%)	75 (18.2%)	
The mean duration of hospitalization days (mean ± SD)	11.49±13.6	10.39±15.2	9.21±14.3	>0.05
Method for achieving pregnancy, n(%)				
Spontaneous	278 (81,3%)	276 (82,9%)	367 (88.9%)	0.003[b,c]
ART	64 (18.7%)	57 (17.1%)	46 (11.1%)	
Multiple pregnancy ratio, n (%)	78 (23%)	72 (21.6%)	72 (17.6%)	0.012[b,c]

n: Number, C/S: Cesarean section, SVD: Spontaneous vaginal delivery, SD: Standard deviation, ART: Assisted reproductive techniques

[b]statistically significant difference between group 1-3 (p=0.001 for C/S; p=0.002 for ART; p<0.000 for multiple pregnancy)

[c]statistically significant difference between group 2-3 (p=0.01 for ART; p=0.002 for multiple pregnancy

Table 2. Reasons for NICU admission in late preterm infants	
Indications of NICU admission	**n (%)**
Jaundice	578 (53.1%)
Suspected sepsis	573 (52.6%)
Hypoglycemia	319 (29.3%)
Pneumonia	116 (10.7%)
RDS	42 (3.9%)
TTN	84 (7.7%)
Apnea	34 (3.1%)
Hypocalcemia	344 (31.6%)

NICU: Neonatal intensive care unit, RDS: Respiratory distress syndrome, TTN: Transient tachypnea of the newborn

In total, 53.4% (n=581) of infants had sepsis. Early-onset sepsis was observed in 69.9% (n=406) of the cases, nosocomial sepsis was observed in 23.2% (n=135), and late-onset sepsis was observed in 6.9% (n=40) cases. The risk of early-onset and nosocomial sepsis was inversely proportional to gestational week. Late-onset neonatal sepsis was detected in group 2, with the highest percentage. However, a statistically significant difference was found in early-onset sepsis between gestational weeks (p<0.01). Blood cultures were positive in 18.2% (n=106) of late preterm infants with sepsis, and other (urine- bronchoalveolar lavage- cerebrospinal fluid-wound) cultures were positive in 7.7% (n=45). Antibiotics were administered to 81.7% (n=475) of the infants. The most common agents detected in patients with early-onset sepsis were coagulase-negative *Staphylococcus* CoNS (n=24), *Klebsiella pneumonia* (n=10), and *Staphylococcus aureus* (n=5). The most common agents noticed in patients with late-onset sepsis were CoNS (n=34), S*taphylococcus aureus* (n=10), and *Klebsiella pneumonia* (n=5). Furthermore, *Staphylococcus*, *Klebsiella*, and *Pseudomonas* species were the most common pathogens of nosocomial infections.

Hypoglycemia and hypocalcemia were seen at the highest percentage in group 1 (35.7%, n=122; 35.4%, n=121, respectively). Hypocalcemia was observed, particularly on the second or third postnatal days, with no systemic findings. There was a statistically significant difference between the weeks of gestation for both conditions (p<0.001, p=0.003, respectively).

Jaundice requiring phototherapy was observed in 53.1% (n=578) of all infants. The highest rate of jaundice was observed in group 1 and was statistically significant (p=0.043). Jaundice was reported in the first seven days of life, particularly in the 2-5. days. Twenty-one babies required exchange transfusions.

There was a statistically significant difference between groups 1-3 in terms of RDS, apnea, hypoglycemia, hypocalcemia, early-onset sepsis, and jaundice in the post-hoc analysis. In addition, while there was a statistically significant difference in hyperbilirubinemia

between groups 1 and 2, there was a significant difference between groups 2 and 3 in RDS and hypocalcemia.

Sixty-nine (6.3%) late preterm infants were readmitted to the hospital after discharge. Although there was no statistically significant difference in gestational weeks, group 1 had the highest readmission rate (p>0.05). Jaundice and infectious disease were the leading causes of rehospitalization.

In total, seventy-seven (7.07%) late preterm infants died. Group 2 had the highest mortality percentage for the 34th gestational week; however, there was no statistically significant difference among the three groups. The most significant reasons for mortality were congenital anomalies and sepsis (respectively %44.1, n=34; %22, n=17). Other causes of death included hydrops fetalis, asphyxia, and complete atrioventricular block (AV block). The reasons and rates of hospitalization according to gestational weeks are summarized in Table 3.

DISCUSSION

Extensive clinical studies evaluating the differences among late preterm infants according to their gestational week were limited. Therefore, in this descriptive study, we compared 1,088 late preterm infants. Certain differences were found in these study as; while TTN, apnea, hypoglycemia, early-onset sepsis, and nosocomial sepsis were most common in those born at 34-34$^{6/7}$ weeks of gestation, RDS, pneumonia, and late-onset sepsis were most common in those born at 35-35$^{6/7}$ gestational weeks. Compared to other groups, those born at 36 weeks of gestation had lower rates of these morbidities.

Late preterm infants constituted 21.6% of all infants needing NICU and 51.8% of the premature group in our 8-year retrospective study. While the rate of late preterm birth was 9.6% in a recent 3-year survey[19], this rate was 21.6% in our study. It is thought that the rates vary according to the region where the high-risk pregnancy centers are located, as well as the differences in patients.

As stated in most studies in the literature, it was observed that C/S proportions were high in our research, and C/S percentages increased as the gestational week decreased[19-21]. In addition, studies have stated that increased multiple pregnancy rates with ART contribute to preterm birth[22,23]. Refuerzo et al.[24] observed that the mean week of birth was 35.3 weeks in twins and 32.2 weeks in triplets, and the rate of late prematurity in twins was 50%. Similar to the reports, multiple births were observed to occur at earlier gestational weeks in our study. In addition, triplet pregnancy was at the highest rate at 34th gestational weeks, supporting that

Table 3. Comparison of the reasons for admission to NICU between the three groups

Indications of NICU admission	Group 1 n=342 (34$^{0/7}$-34$^{6/7}$)	Group 2 n=333 (35$^{0/7}$-35$^{6/7}$)	Group 3 n=413 (36$^{0/7}$-36$^{6/7}$)	p-value
RDS	16 (4.7%)	21 (6.3%)	5 (1.2%)	**0.009**[b,c]
TTN	29 (8.4%)	24 (7.2%)	31 (7.5%)	>0.05
Apnea	17 (5%)	8 (2.4%)	9 (2.2%)	**0.032**[b]
Pneumonia	34 (10%)	42 (12.6%)	40 (9.6%)	>0.05
Hypoglycemia	122 (35.7%)	97 (29.1%)	100 (24.1%)	**<0.001**[b]
Hypocalcemia	121 (35.4%)	115 (34.5%)	108 (26.1%)	**0.003**[b,c]
Early-onset sepsis	140 (41%)	131 (39.3%)	135 (32.7%)	**0.012**[b]
Late-onset sepsis	8 (2.3%)	16 (4.8%)	16 (3.9%)	>0.05
Nosocomial sepsis	49 (14.3%)	39 (11.7%)	47 (11.4%)	>0.05
Jaundice	203 (59.4%)	159 (47.8%)	216 (52.3)	**0.043**[a,b]
Rehospitalization	26 (7.6%)	19 (5.7%)	24 (5.8%)	>0.05
Mortality	24 (7.01%)	24 (7.2%)	29 (7.02)	>0.05

NICU: Neonatal intensive care unit, RDS: Respiratory distress syndrome, TTN: Transient tachypnea of the newborn

[a]statistically significant difference between group 1-2 (p=0.003)

[b]statistically significant difference between group 1-3 (p=0.004 for RDS; p=0.036 for apnea; p<0.000 for hypoglycemia; p=0.004 for hypocalcemia; p=0.02 for early-onset sepsis; p=0.031 for jaundice)

[c]statistically significant difference between group 2-3 (p<0.000 for RDS; p=0.005 for hypocalcemia)

the number of fetuses was significantly associated with prematurity.

Late preterm babies are more prone to complications such as heat instability, hypoglycemia, respiratory distress, apnea, jaundice, and feeding difficulties than term babies[25]. According to a study by Hakan et al.[19], the most common problems of late preterm infants were respiratory distress (49%) and indirect hyperbilirubinemia (21%). In our study, however, jaundice and sepsis were the leading causes of hospitalization, followed by respiratory diseases.

Late preterm babies are more likely than term babies to develop apnea, TTN, RDS, pneumonia, pulmonary hypertension, and respiratory failure due to being born with lung and ventilation center immaturity[26,27]. In our study, pneumonia, TTN, and RDS were the most common causes of respiratory morbidity, as reported in the literature. The occurrence and severity of respiratory distress decreased as gestational age increased, with the highest at 34 weeks and the lowest at 39 weeks[5].

In the literature, antenatal corticosteroid administration decreased the incidence of RDS in extremely premature infants, but the same result was not observed in late preterm infants[28]. However, the rate of RDS was lower in our study than in the literature; 50% of these infants were born at the 35th gestational age. This was attributed to infants born at the 35th gestational week receiving fewer antenatal corticosteroids than infants born at the 34th gestational week. Although the rates of RDS were significantly lower in those born at 36 weeks of gestation compared to 34 and 35 weeks of gestation, the findings indicated that prophylaxis in late preterm infants remains necessary.

TTN and other respiratory problems are caused by prematurity and performing a cesarean delivery before labor begins. TTN rates ranged between 3.9% and 9.9%, decreasing as the gestational week increased[5]. TTN rates were reported to be low in our report, which was attributed to the late prematurity of all infants included in the study, as well as the fact that respiratory distress persisted for more than 24 hours in the majority of infants, necessitating the early initiation of empirical antibiotic therapy with the diagnoses of suspected sepsis/pneumonia. In addition, TTN was highest in infants born at 34 weeks of gestation and lowest in infants born at 35 weeks, contrary to the literature. The possible reason was that infants born at the 35th gestational week had more severe respiratory diseases than TTN.

In our research, pneumonia rates were reported to be greater than the general literature and comparable to data from our country[19,29-31]. These rates were related to the monitoring of complicated infants. Apnea is caused by an immature neurological system, physiological immaturity of the respiratory system, and a lack of coordination between feeding, swallowing, and breathing[29]. According to a meta-analysis, the incidence of apnea in late preterm infants was 0.9% and 0.05% in term infants and decreased as gestational age increased[32]. In this study, ten percent of late preterm infants have significant prematurity apnea. Half of them were born at 34 weeks, statistically higher than those at 36 weeks. This rate was consistent with the literature and was attributed to the apparent physiological immaturity as the gestational week declines.

The risk of hypoglycemia was increased in late preterms because of insufficient glycogen stores, particularly in challenging conditions such as hypothermia, sepsis, and feeding difficulties. The incidence of hypoglycemia is known to enhance inversely with gestational age[33]. The incidence of hypoglycemia in late preterm infants is approximately three times higher than in term infants, according to studies similar to ours.[34-36]. In our study, the rate of hypoglycemia was significantly higher at the 34th gestational week, particularly compared with the 36th gestational week; as the gestational week increased, the rate of hypoglycemia decreased. These findings were generally consistent with previous research.

Similar to Picone et al.[37], hypocalcemia was observed mainly on the second or third postnatal days, with no systemic findings, in our study. Furthermore, hypocalcemia decreased as the gestational week increased, with the lowest incidence in those born at the 36th gestational week. This situation was similar to the literature and was attributed to the insufficiency of parathormone secretion due to incomplete parathyroid development.

Likewise to our findings, the rates of jaundice in late preterm infants were significantly higher in the literature [5,38]. Similar to the literature, jaundice was most common between the second and fifth days of life. Those born at the 34th gestational week had the highest rate, compared with the 35th and 36th gestational weeks. However, contrary to popular opinions in this study, those born at the 35th gestational week had the lowest percentage of jaundice.

Early-onset neonatal and nosocomial sepsis are frequent in late preterm infants and are significant

causes of morbidity and mortality. The probability of culture positivity increases as gestational age decreases. The rate of clinical sepsis was 10% in the study by Hakan et al.[19], and a quarter of patients had positivity in the blood culture. Our study's blood culture positivity rate was 18.2%, higher than the literature. The rate of sepsis increased 33 times in the premature birth group in McIntire and Leveno's[39] studies, where sepsis screening was performed at 34 and 39 weeks of gestation. In our study, the incidence of sepsis was reported to be high in late preterm infants, which was consistent with the literature. Our study's high rates of sepsis were associated with being a developing country, the patients' poor financial and living conditions, intensive follow-up of high-risk pregnancies and infants, and accepting many referrals from various centers. Similar to the literature, it was observed that the probability of early-onset sepsis and nosocomial sepsis increased as the gestational week decreased. On the other hand, late-onset sepsis was highest in those born at the 35th gestational week and lowest in those born at the 34th gestational week. This situation was related to the predominance of early-onset and nosocomial sepsis in the types of sepsis seen at 34 weeks of gestation.

There have been a few studies on the agents that cause sepsis in late preterm infants[19,40]. While group B *Streptococcus* and *Escherichia coli* are the most common pathogens in early-onset sepsis in developed countries[41], *Escherichia coli* is uncommon as a causative agent in our study, and group B *Streptococcus* was not observed.

In this report, the most common agent in early-onset sepsis was CoNS, followed by *Klebsiella pneumonia* and *Staphylococcus aureus*. The most common agent in late-onset sepsis was CoNS, followed by *Staphylococcus aureus* and *Klebsiella pneumonia*. *Staphylococci, Klebsiella, Pseudomonas, Enterococci,* and *Candida* species were causative agents in nosocomial sepsis. Bacteria that caused death were Gram-negative agents in early and late-onset sepsis, consistent with neonatal sepsis cases in the literature[42].

The length of hospital stay is inversely proportional to gestational week (e.g., 6-11 days, 4-6 days, and 3-4 days in infants born at 34th, 35th, and 36th weeks, respectively) [43]. In a study conducted in Spain, the mean length of hospital stay for late preterm infants were six days and 2.8 days for term infants, with a statistically significant difference[44]. Similarly, prematurity was reported to affect our study's length of hospital stay substantially. Furthermore, it was noticed that following complicated infants, receiving more referrals, and avoiding early infant discharge as much as possible increased hospitalization rates.

Despite the high morbidity risks, late preterm infants are typically cared for in the healthy infant neonatal unit after birth and discharged from the hospital at 2-3 days of age, which increases hospital readmission rates. As a result, understanding the causes and risks of morbidity in late preterm infants is critical for post-discharge follow-up and preventing complications. According to the literature and our findings, the hospital readmission rate in late preterm infants is 1.5-3 times higher than in term newborns[7,44]. The lower hospital readmission rates in our study compared to other studies in the literature were attributed to the avoidance of early discharge in late preterm babies in our unit. Similar to the literature, in our study, the highest readmission rate was observed at 34 weeks of gestation, and as the week of gestation increased, the readmission rate decreased. Jaundice was the most common reason for hospital readmission, followed by infections, suspicion of sepsis, and malnutrition[26,45].

In the study of Karnati et al.,[5] late preterm infants were approximately four times more likely than term infants to die from congenital malformations, neonatal bacterial sepsis, and placental, cord, and membrane complications in infancy. A recent study conducted in Spain showed that 1-year mortality rates were higher in late preterm infants than in term infants[44]. Our study's mortality rate among all late preterm infants was 7%. Although the rates are very similar during the gestational weeks, infants born at the 35th gestational week have the highest mortality rate; infants born at the 34th gestational week have the lowest rate. According to the literature, the death rate decreases as the gestational week increases, but the rates were nearly equal in our study. This rate was attributed to the fact that most patients who died had congenital malformations rather than late prematurity. And these infants were mainly born at 35 and 36 weeks of gestation.

Study Limitations

Several considerations should be noted when interpreting the results. First, this was a single-center retrospective study with inherent limitations compared to randomized clinical trials. Due to the retrospective review of medical records, we had limited access to perinatal data. However, we believe it is a good sample size as it is an 8-year study with 1,088 cases. Furthermore,

while late preterm and term babies have been compared in the literature, late preterm infants were compared within themselves in our research, and similar studies are still scarce.

CONCLUSION

Numerous short-term complications have been observed in late preterm infants, including respiratory distress, hyperbilirubinemia, feeding intolerance, hypoglycemia, and sepsis. Since of morbidities and a high readmission rate after discharge, these infants have a prolonged hospital stay. As a result, discharge planning and follow-up are crucial to reducing re-admission rates of late preterm infants, who are a greater risk group, and promoting healthy growth and development. Furthermore, new approaches must be developed to reduce the off-label C/S ratio. Premature births are thought to be preventable in this manner.

Ethics

Ethics Committee Approval: This study was approved by the Necmettin Erbakan University, Meram Faculty of Medicine Ethics Committee for Non-pharmaceutical and Medical Device Research (decision no: 2015-282, date: 16.09.2015).

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Author Contributions

Surgical and Medical Practices: E.C., Concept: R.Ö., Design: R.Ö., Data Collection or Processing: E.C., Analysis or Interpretation: R.Ö., Literature Search: E.C., Writing: E.C.

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