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Original Article

Morbidity and Mortality in Late Preterm Newborns Followed in a Neonatal Intensive Care Unit

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ABSTRACT

Background: Neonates born between 340/7-366/7 gestational weeks are considered late preterms with fewer risks, compared to smaller babies and more risks for morbidity and mortality than their term peers. The present study aimed to analyze maternal problems, as well as morbidity and mortality of late preterms followed in the Neonatal Intensive Care Unit.

Methods: A total of 230 neonates' files were analyzed, and demographic characteristics, respiratory, as well as metabolic and maternal problems, were recorded in this study.

Results: Out of 230 neonates, 166 (72, 2%) and 129 (56,1%) newborns were inborn and male, respectively. Moreover, 23 (10%) neonates were born through vaginal delivery. The mean birth weight of the neonates was estimated at 2532.1±540.3 gr. In total, 66, 71, and 93 infants were 34 0/7 and 34 6/7, 35 0/7-356/7, as well as 36 0/7-36 6/7, respectively. The premature rupture of membranes, placenta previa, ablatio placenta were obtained at 9.1% (n=21), 2.2% (n=5), and 3.5% (n=8), respectively.

In addition, preeclampsia (n=24; 10.4%), cholestasis of pregnancy (n=7; 3%), oligohydramnios (n=26; 11.3%), and gestational diabetes mellitus (n=27; 11.7%) were observed in this study. The rates of transient tachypnea of the newborn, respiratory distress syndrome, polycythemia, hypoglycemia, indirect hyperbilirubinemia with intensive phototherapy, and feeding intolerance was estimated at 72.2% (n=166), 7.8% (n=18), 5.6% (n=13), 6.1% (n=14), 4.3% (n=10), and 8.7% (n=20), respectively. Any maternal problems and cholestasis of pregnancy were significantly more likely in 340/7 and 346/7 gestational weeks, compared to others (for any maternal problem and cholestasis of pregnancy: P=0.009 and P=0.012, respectively).

Conclusion: Evaluation of the late preterms as terms may lead to neglecting some problems. Therefore, late preterms should be closely monitored, especially for respiratory problems in terms of intensive care requirements.

Keywords: Late preterm, Maternal problems, Morbidity, Mortality, Newborn

Introduction

Premature birth is considered the baby delivery before 37 completed weeks of gestation. The American Academy of Pediatrics defined infants born before 320/7 weeks as very premature, between 320/7 and 336/7 weeks as moderately premature, and between 340/7and 366/7 weeks as late premature (LP) (10%) (1, 3). Approximately, 100,000 LP neonates are born annually in Turkey (4). Maternal factors, such as preterm labor, preeclampsia, premature rupture of membranes, multiple pregnancies, assisted reproductive techniques, and gestational diabetes can lead to the delivery of LP newborns (5, 6). Although LP newborns face fewer risks, compared to infants born at earlier weeks, they are prone to more risks for morbidity and mortality, compared to term neonates (7-10). This study aimed to determine maternal problems, as well as morbidity and mortality rates of LP babies followed in the neonatal intensive care unit (NICU).

Methods

In this cross-sectional retrospective study, the files of 231 LP neonates were analyzed in a level-3 NICU of the Medistate Hospital, Istanbul, Turkey,

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from November 2011 to September 2020. Moreover, one neonate out of 231 infants diagnosed with the congenital diaphragmatic hernia was excluded from this study. Data, such as demographic characteristics of the infants, respiratory problems, metabolic problems, polycythemia, sepsis, congenital heart disease, and maternal problems were recorded from the patients' files.

Gestational weeks of neonates were evaluated using the last menstrual period, prenatal ultrasonography measurements (11), and new Ballard score (12). Newborns with birth weight less than 10% and more than 90% percentile according to gestational week were considered small and large for gestational age (SGA and LGA, respectively). In addition, babies with a birth weight percentile of 10%-90% were defined as normal (appropriate for gestational age, AGA) (13). Pre-gestational diabetes and gestational diabetes mellitus (GDM) were defined as diabetes diagnosed before pregnancy and hyperglycemia of varying severity during pregnancy, respectively (14). The amniotic fluid index less than 5 cm was accepted as oligohydramnios (15), and the rupture of amniotic membranes more than 18 h before birth was considered prolonged premature rupture of membranes (PPROM) (16). Preeclampsia was diagnosed after the 20th week of pregnancy with high blood pressure, proteinuria, and edema (17). Body mass index was calculated by dividing body weight by the square of height (kg/m2). The level of blood glucose with less than 47 mg/dl in infants was accepted as hypoglycemia (18), monitored at the 1st, 6th, and 24th h after birth. As recommended by the American Academy of Pediatrics (AAP) for LP newborns, patients were evaluated according to symptoms and blood glucose levels and were also treated with intravenous glucose if necessary (19).

Diagnosis of transient tachypnea of the newborn (TTN) was made in infants with tachypnea (respiratory rate ≥60/min), grunting, nasal flaring, and fluid in fissure, increased peribronchial vascularity, increased ventilation on plain radiography, increased anterior-posterior diameter of the chest with excluding other causes of respiratory distress (20). Respiratory distress syndrome (RDS) was diagnosed in babies with respiratory distress, such as tachypnea, retraction, and cyanosis, through air bronchograms and reticulogranular on chest X-ray.

Patients with pH<7 and BE<-12 in a cord or those who obtained blood gas within the first hour of delivery and Apgar score of <5 in the 5th minute were followed with perinatal asphyxia. Clinically, infants with feeding intolerance, hypotonia, and developing or increasing requirement of respiratory support, apnea, bradycardia, tachycardia, body temperature imbalance (hypo-hyperthermia), lethargy, leukocytosis/leukopenia, and thrombocytopenia with procalcitonin >2 ng/ml and C-reactive protein >5 mg/l in the laboratory and/or blood culture positivity were diagnosed with neonatal sepsis (21,22). Hyperbilirubinemia treatments were planned according to phototherapy and exchange transfusion curves of the AAP (23). Polycythemia was defined as venous hematocrit >65%.

Statistical analysis

Statistical analysis was conducted using the SPSS software (version 25). Categorical variables were summarized as numbers and percentages; moreover, continuous variables were defined as mean, standard deviation, and minimum-maximum. Variable relevance to normal distribution was examined by Kolmogorov-Smirnov/Shapiro-Wilk tests. The Chi-square and Fischer's exact tests were used for comparing categorical variables. Furthermore, one-way ANOVA and Kruskal-Wallis tests were employed for normally distributed parameters and parameters without normal distribution, respectively. A p-value less than 0.05 was considered statistically significant within a 95% confidence interval with Ethics Committee approval No: 2020/3.

Results

During the study, 12.7% of all births in the hospital were LP deliveries, and 41.4% of these neonates needed neonatal intensive care. In the same period, out of 231 (34.9%) newborns, 661 patients followed in the unit were LP, and 166 (72.2%) neonates out of 230 LP cases followed and included in the study were born in the NICU in our hospital. Furthermore, 129 (56.1%) patients were male, and 23 neonates were born by spontaneous vaginal delivery with a mean birth weight of 2532.1±540.3 gr .

In total, 66, 71, and 93 neonates were between 340/7 and 346/7, 350/7-356/7, as well as 360/7-366/7 weeks, respectively. Furthermore, 5 (10.8%) and 14 (6.1%) neonates were small and large for gestational age, and 2 (0.9%) newborns who died were followed with perinatal asphyxia (Table 1).

Table 1. Demographic characteristics of all newborns and mothers

	Mean±standart deviation (min-max)
Birth weight (gr)(mean±SD)	2532±540 (1370-4480)
Lenght (cm)(mean±SD)	46.9± 2.9 (40.0-56.0)
Head circumference (cm)((mean±SD)	32.8± 1.9 (28.0-37.0)
Gestational age (week)(mean±SD)	35.1±0.83(34-36)
Maternal age (year)(mean±SD)	30±5(16-45)
Maternal BMI (mean±SD)	26.59±5.39(16.60-44.90)
Lenght of stay (mean±SD)	10±7(1-40)
	n(%)
Inborn	166(72.2)
AGA/LGA/SGA	191/14/25(83.0/6.1/10.9)
VD/CS	23/207(10,0/90,0)
Female/Male	101/129(43.9/56.1)

Note: AGA: appropriate for gestational age, LGA: Large for gestational age, SGA: Small for gestational age, BMI: Body mass index, SD: Standard deviation, VD: Vaginal delivery, CS: Cesarean section

The mean maternal age was obtained at 30.4±4.8 years, and 66 (38.6%) neonates were multiple pregnancy products, 62 and 4 of whom were twins and triplets, respectively. The rate of *in vitro* fertilization pregnancy was 17% (n=39). The incidence rates of PROM (n=21; 9.1%), placenta previa (n=5; 2.2%), ablation of placenta (n=8; 3.5%), preeclampsia (n=24; 10.4%), cholestasis of pregnancy (n=7; 3%), chronic hypertension (n=9; 3.9%), oligohydramnios (n=26; 11.3%), polyhydramnios (n=2; 0.9%), type 1 diabetes mellitus (n=5; 2.2%), type 2 diabetes mellitus (n=3; 1.3%), and GDM (n=27; 11.7%) were also estimated in this study. It should be noted that antenatal steroid was received by 34.8% (n=80) of mothers.

Table 2. Maternal problems of all infants

	n(%)
Any maternal problem	209(90.9)
In vitro fertilization	39(17.0)
Preterm labor	98(42.6)
Cholestasis of pregnancy	7(3.0)
Premature rupture of membranes	21(9.1)
Ablatio placenta	8(3.5)
Placenta previa	5(2.2)
Preeclampsia	24(10.4)
Oligohydramnios	26(11.3)

Any maternal problem: Any maternal problem leading to preterm delivery

TTN was the most common respiratory problem, and 166 (72.2%) neonates were followed with this diagnosis. Moreover, RDS (n=18; 7.8%), polycythemia (n=13; 5.6%), hypoglycemia (n=14; 6.1%), indirect hyperbilirubinemia requiring intensive phototherapy (n=10; 4.3%), vitamin D3 deficiency (n=14; 6.1%), feeding intolerance (n=20; 8.7%), culture-positive sepsis (n=5; 2.2%), and clinical sepsis (n=24 ;10.4%) were diagnosed in this study (Table 3).

Of all, 52 (22.6%) and 67(29.1%) infants required resuscitation at birth and intubation during follow-up, respectively. Regarding congenital heart disease, 12 (5.2%) and 10 (4.3%) neonates were diagnosed with atrial septal defect (ASD) and ventricular septal defect (VSD), respectively; furthermore, ASD and VSD (n=1; 0.4%), as well as aortic stenosis (n=1; 0.4%) were observed in this study. It is worth mentioning that one infant had aortic coarctation. It was statistically significant that the birth weight, as well as the height and head circumference of babies with $34^{0/7}$-$34^{6/7}$ weeks, were lower than those with higher gestational weeks; in addition, the length of hospitalization was higher than those with higher gestational weeks (for both: $P<0.05$). The number of male infants was significantly lower in those with gestational weeks between $34^{0/7}$ and $34^{6/7}$, compared to those with higher gestational weeks ($P<0.05$) (Table 4).

Table 3. Diagnosis of all newborns during NICU course

	N (%)
Resuscitation requirement at birth	52(22.6)
Intubation need during follow-up	67(29.1)
Transient tachypnea of the newborn	166(72.2)
Respiratory distress syndrome	18(7.8)
Hypoglycemia	14(6.1)
Polycythemia	13(5.6)
Jaundice requiring intensive phototherapy	10(4.3)
Feeding intolerance	20(8.7)

Note: NICU: Neonatal intensive care unit

Maternal problems leading to preterm delivery and cholestasis of pregnancy in $34^{0/7}$-$34^{6/7}$ weeks were more statistically significant, compared to neonates with higher gestational weeks (P=0.009 and P=0.012 for the presence of maternal problems and cholestasis of pregnancy, respectively). No difference was considered in terms of the gestational week for other maternal problems, such as *in vitro* fertilization, premature rupture of membrane, ablatio placenta, placenta previa, preeclampsia, and oligohydramnios (P>0.05) as shown in Table 5. Additionally, no difference was observed in terms of TTN, respiratory distress syndrome, sepsis, and metabolic problems according to gestational weeks (P>0.05; Table 6).

Table 4. Comparision of demographic characteristics of infants by gestational week

		$34^{0/7}$-$34^{6/7}$ week	$35^{0/7}$-$35^{6/7}$ week	$36^{0/7}$-$36^{6/7}$ week	p
Birth weight (gr)(mean±SD) (min-max)		2215±337 (1540-2940)	2540±534 (1510-4480)	2680±574 (1570-4440)	<0.001
Lenght (cm)(mean±SD)		45.14±2.25	47.31±2.77	47.79±2.82	<0.001
Head circumference (cm)((mean±SD)		31.75±1.51	32.88±1.78	33.59±1.75	<0.001
Gestational age (week)(mean±SD)		34.20±0.22	35.20±0.20	36.21±0.21	<0.001
Maternal age (year)(mean±SD)		30.35±4.81	36.69±5.54	30.38±4.24	0.894
Maternal BMI (mean±SD)		26.0±4.38	25.96±6.29	27.67±5.21	0.330
Lenght of stay (mean±SD)		11.5±7 (2-32)	8±6 (1-32)	7± 6(2-40)	<0.001
		Tn/n(%)	Tn/n(%)	Tn/n(%)	
Inborn/Outborn		66/47 (71.2)	71/50 (70.4)	93/69 (74.2)	0.849
AGA/LGA/SGA	AGA	66/59 (89.4)	71/57 (80.2)	93/75 (80.6)	
	LGA	66/1 (1.5)	71/7 (9.9)	93/6 (6.5)	0.286
	SGA	66/6 (9.1)	71/7 (9.9)	93/12 (12.9)	
Delivery Tn/VD		66/60 (90.9)	71/61 (85.9)	93/86 (92.5)	0.366
Gender Tn/Male		66/27 (40.9)	71/44 (62.0)	93/58 (62.4)	0.013

Note: AGA: Appropriate for gestational age. LGA: Large for gestational age. SGA: Small for gestational age. BMI: Body mass index. SD: Standard deviation. VD: Vaginal delivery. CS: Cesarean section.Tn: Total number of infants. n: Number of infants

Table 5. Comparision of maternal problems by gestational week

	$34^{0/7}$-$34^{6/7}$ week	$35^{0/7}$-$35^{6/7}$ week	$36^{0/7}$-$36^{6/7}$ week	p
	Tn/n(%)	Tn/n(%)	Tn/n(%)	
Any maternal problem	66/64 (97.0)	71/67 (94.4)	93/78 (83.9)	0.009
In vitro fertilization	66/15 (22.7)	71/9 (12.7)	93/15 (16.1)	0.282
Preterm labor	66/29 (43.9)	71/33 (46.5)	93/36 (38.7)	0.588
Cholestasis of pregnancy	66/5 (7.6)	71/2 (2.8)	93/0 (0.0)	0.012
Premature rupture of membranes	66/10 (15.2)	71/5 (7.0)	93/6 (6.5)	0.131
Ablatio placenta	66/3 (4.5)	71/3 (4.2)	93/2 (2.2)	0.660
Placenta previa	66/2 (3.0)	71/0 (0.0)	93/3 (3.2)	0.318
Preeclampsia	66/8 (12.1)	71/9 (12.7)	93/7 (7.5)	0.491
Oligohydramnios	66/11 (16.7)	71/6 (8.5)	93/9 (9.7)	0.257

Tn: Total number of infants. n: Number of infants

Table 6. Comparision of NICU progress by gestational week

	$34^{0/7}$-$34^{6/7}$ week	$35^{0/7}$-$35^{6/7}$ week	$36^{0/7}$-$36^{6/7}$ week	P
	Tn/n(%)	Tn/n(%)	Tn/n(%)	
Resuscitation requirement at birth	66/18 (27.3)	71/18 (25.4)	93/16 (17.2)	0.262
Intubation need during follow up	66/18 (27.3)	71/25 (35.2)	93/25 (26.9)	0.455
Respiratory distress syndrome	66/5 (7.6)	71/5 (7.0)	93/8 (8.6)	0.931
Transient tachypnea of the newborn	66/45 (68.2)	71/55 (77.5)	93/66 (71)	0.473
Polycythemia	66/6 (9.1)	71/3 (4.2)	93/4 (4.3)	0.358
Hypoglycemia	66/5 (7.6)	71/3 (4.2)	93/6 (6.5)	0.702
Culture positive septicemia	66/3 (4.6)	71/1 (1.4)	93/1 (1.1)	0.291
Clinic septicemia	66/9 (13.6)	71/9 (12.7)	93/8 (8.6)	0.558
Jaundice requiring phototherapy	66/4 (6.1)	71/2 (2.8)	93/4 (4.3)	0.649
Feeding intolerance	66/6 (9.1)	71/5 (7.0)	93/9 (9.7)	0.831

Tn: Total number of infants. n: Number of infants, NICU: Neonatal intensive care unit

Discussion

Maternal problems are important causes of late-preterm delivery with different results due to the socioeconomic status of the family and perinatal follow-up. In Turkey, a study reported maternal problems in LP infants, and the rates of preeclampsia, diabetes, and PPROM were determined at 9.3%, 6.7%, and 8%, respectively (6). Furthermore, the incidence rates of PPROM, diabetes mellitus, and preeclampsia were

estimated at 6.3%, 1.8%, and 7.7%, respectively (24). The rate of preeclampsia and PROM were determined at as 22.3% and 29%, respectively (25). Similarly, in the present study, the rates of PROM and preeclampsia were 9.1% (n=21) and 10.4% (n=24), respectively. Additionally, the incidence rates of placenta previa (n=5; 2.2%), ablation of placenta (n=8; 3.5%), cholestasis of pregnancy (n=7; 3%), chronic hypertension (n=9; 3.9%), oligohydramnios (n=26; 11.3%), polyhydramnios (n=2; 0.9%), type 1 diabetes mellitus (n=5; 2.2%), type 2 diabetes mellitus (n=3; 1.3%), and GDM (n=27; 11.7%) were determined in this study.

Ablation of the placenta, placenta previa, and diabetes may lead to the birth of the SGA neonates. Furthermore, 31% of the late premature SGA newborns had preeclamptic mothers (6). In this study, mothers of 20% of the SGA infants had preeclampsia, and 4% of the mothers had ablatio placenta. In addition, diabetes and cholestasis of pregnancy were observed in 12% and 4% of the mothers, respectively.

Respiratory problems were more common in LP newborns, compared to term peers, and the rate of respiratory distress in LP newborns was estimated at 14.3% (26) that was 46.5% in a study conducted in Turkey (27). Moreover, the rate of hospitalization due to respiratory problems was reported as 76.7% (6), and 84.3% of the patients were hospitalized due to respiratory problems.

The rate of RDS in neonates was reported between 3% and 9% (28). In Turkey, 51 (2.1%) infants with LP in a total of 2,437 infants were diagnosed with RDS (29), and the rate of RDS was reported as 3.6% (6), which was consistent with the findings of our study with the incidence of 3.9%. Feeding intolerance and hypoglycemia in infants with LP were reported at different rates between 65% and 8% in some studies. Additionally, the rate of feeding intolerance was reported as 9.1% in LP infants (24), and the incidence rates of hospitalization due to feeding intolerance and hypoglycemia were reported as 5.3% and 4.7%, respectively (6). In the present study, 8.7% and 6% of infants were hospitalized due to feeding intolerance and hypoglycemia, respectively; in addition, 14.2% of infants diagnosed with hypoglycemia were also SGA in our study. The incidence of perinatal asphyxia was reported as 2.7% (6), and in our study, 3 (0.9%) neonates were diagnosed with perinatal asphyxia, two of them were lost, and one was discharged. The lengths of stay in hospital for LP infants born at 34, 35, and 36 weeks of gestation were reported as 8±7, 3±4, and 3±4 days, respectively (30). Moreover, the hospitalization length of infants was determined as 8.79±5.28 days (6). Additionally, the duration of hospitalization for babies born at 34, 35, 36 gestational weeks were 11.5 (2-32) days, 8 (1-32) days, and 7 (2-40) days, respectively, in this study.

Newborn babies, especially premature ones, are susceptible to infections due to insufficient development of their immune systems and defense mechanisms (31). Incidence of early- and late-onset sepsis is reported in the literature as 0.4% and 0.6%, respectively (32), and the rate of clinical sepsis was reported as 8.2% (23). In a clinical study, the rates of early and late sepsis were 8.3% and 9.7%, respectively (6), without any detection of the culture-positive sepsis. In our study, the culture-positive sepsis was detected in 6 (2.6%) patients; moreover, 1 (0.4%) and 25 (10.8%) neonates were observed with early neonatal sepsis and clinical sepsis, respectively. Evaluation of the LP newborns as term babies may lead to neglecting some problems due to their size resembling some term infants. Therefore, LP newborns should be closely monitored in terms of the need for intensive care, especially for respiratory problems.

Conclusion

Evaluation of the late preterms as terms may lead to neglecting some problems. Therefore, late preterms should be closely monitored, especially for respiratory problems in terms of intensive care requirements.

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Conflicts of interest

None.

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Authors' contributions

FCC planned the study, entered and analyzed data, drafted the manuscript, and revised the final draft. The author read and approved the final manuscript.

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