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Comparison of Perinatal Outcomes in Late Preterm Spontaneous and Indicated Preterm Birth Neonates

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Abstract

Objective: We aimed to compare the perinatal outcomes in late preterm spontaneous and indicated birth neonates. Methods: We studied 289 late preterm births, classified as either aspontaneous late preterm birth (sLPTB) group (preterm labor with intact membranes and preterm premature rupture of membranes) or an indicated late preterm birth (iLPTB) group (hypertensive disorder in pregnancy, placental causes, and maternal diseases), according to the delivery indication. We then compared the maternal and neonatal characteristics and perinatal outcomes, including the Apgar score, admission to the neonatal intensive care unit (NICU) or special care nursery (SCN), duration of NICU stay, and the rate of composite morbidity (antibiotic use, hypoglycemia, hypocalcemia, hyperbilirubinemia requiring phototherapy, respiratory support, and respiratory distress syndrome). Results: A total of 198 neonates were in the sLPTB group and 91 were in the iLPTB group. In spite of greater gestational age at the time of delivery in the iLPTB group, the mean birth weight was lower than that in the sLPTB group. Additionally, the iLPTB group showed lower Apgar scores, and higher rates of NICU or SCN admission, respiratory support, and hypoglycemia, but there was no difference in the rate of composite morbidity between the two groups. Conclusion: iLPTB neonates had lower birth weights despite greater gestational age than those in the sLPTB group, but there was no difference in the rate of composite morbidity between the two groups.

Keywords

Composite Morbidity, Indicated Preterm Birth, Late Preterm Birth, Perinatal Outcomes, Spontaneous Preterm Birth

1. Introduction

Late preterm births are defined as births at a gestational age between 34 weeks and 36 weeks, 6 days, and comprise nearly 74% of all preterm deliveries and approximately 8% of total deliveries [1] [2]. Although the incidence of preterm-related morbidity decreases after 34 weeks of gestation [3], previous studies show that late preterm neonates have higher rates of morbidity, such as feeding difficulty, jaundice, hypoglycemia, temperature instability, apnea, respiratory distress, and mortality, compared to full-term births [3] [4]. Moreover, a recent study showed that antenatal administration of betamethasone reduces neonatal respiratory morbidity in late preterm births [5]. However, most obstetrical providers tend to stop the administration of antenatal corticosteroids and tocolytics and deliver fetuses with suspected compromised intrauterine status or poor maternal conditions after 34 completed weeks, rather than continuing a high-risk pregnancy [6]. In addition, compared to studies on outcomes in latepreterm and full-term neonates, there have been few reports on latepreterm births according to the indications for delivery [7]-[11], particularly in Korea. Thus, we aimed to compare late preterm perinatal outcomes in spontaneous and indicated late preterm birth neonates.

2. Materials and Methods

This was a retrospective study of singleton late preterm births between January 2011 and December 2014 from our third-party referral center. We identified patients and collected clinical information from electronic medical records. We included late preterm births that were delivered between a gestational age of $34^{0/7}$ and $36^{6/7}$. We excluded multiple pregnancies, major structural anomalies (especially congenital heart anomalies), chromosomal anomalies, and stillbirths.

The spontaneous late preterm birth (sLPTB) group included preterm labor with intact membranes (PTL) and preterm premature rupture of membranes (PPROM); the indicated late preterm birth (iLPTB) group included hypertensive disorders such as gestational hypertension, preeclampsia and superimposed preeclampsia, placental causes (placental abruption, placental previa), fetal causes (intrauterine growth restriction, oligohydramnios, fetal distress), and maternal medical diseases, including cardiopulmonary or rheumatic diseases. We classified our study subjects into spontaneous and indicated preterm birth groups according to the direct reason for preterm delivery. A combination of PTL and PPROM cases were categorized by preceding events. We assessed maternal and neonatal characteristics including age, parity, gestational age at delivery, mode of delivery, birth weight, and gender. Additionally, we reviewed the Apgar score at 1 and 5 minutes after each birth, admission to the neonatal intensive care unit (NICU) or special care nursery (SCN), duration of NICU stay, and the rate of composite morbidity. Composite morbidity is defined as having more than one of the following: antibiotic use, hypoglycemia, hypocalcemia, hyperbilirubinemia requiring phototherapy, respiratory support, and respiratory distress syndrome (RDS). Criteria for NICU or SCN admission were as follows: gestational ageless than 35 weeks, birth weight less than 2.3 kg, or need for close observation by a neonatologist. The indications for anti-

biotic use were as follows: cases of PPROM, maternal fever, or suspicion of perinatal acquired infection. After confirmation of a negative culture test, antibiotics were stopped. Hypoglycemia was defined as plasma glucose less than 40 mg/dL, and hypocalcemia as an ionized calcium concentration of less than 4 mg/dL. Respiratory support was defined as the use of a mechanical ventilator or continuous positive airway pressure (CPAP). RDS was defined as the presence of diagnostic radiographic chest findings, plus one or more clinical signs of respiratory distress, including respiratory grunting, retracting, and increased oxygen requirement (fraction of inspired oxygen greater than 0.4), or the administration of exogenous pulmonary surfactant.

We then compared maternal and neonatal characteristics and perinatal outcomes in the two groups. This study used Pearson's chi-squared (χ^2) test for categorical variables and Student's t-test for continuous variables. Statistical analysis was performed using SPSS software, version 19.0 (SPSS Inc., Chicago, IL, USA). This study was approved by the institutional review board (IRB) of Kyungpook National University Hospital and Kyungpook National University School of Medicine, South Korea (IRB No. 2016-04-005).

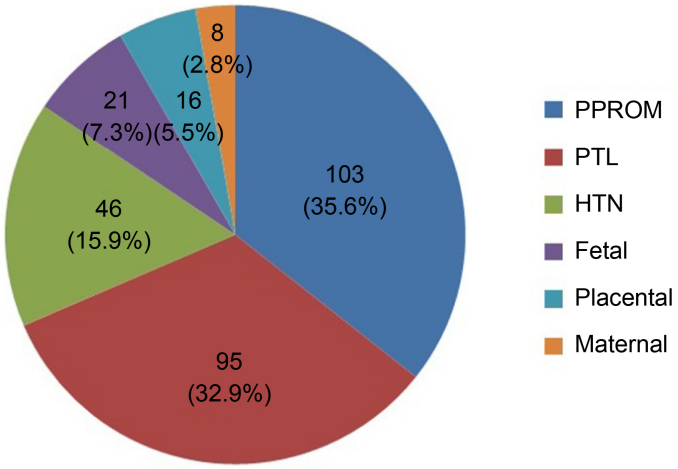
3. Results

Among 509 singleton preterm births during the study period, 65.6% (334 of 509) were late preterm births. We excluded 43 cases with major fetal anomalies, which could affect perinatal outcomes, and two stillbirths. Finally, we included 289 singleton late preterm births.

Among the 289 neonates in this study, 198 (68.5%) were in the spontaneous preterm birth group, and 91 (31.5%) were in the indicated group. Indications for late preterm births are shown in Figure 1. In the spontaneous group, 103 (35.6%) cases had PPROM and 95 (32.9%) had PTL. In the indicated group, hypertensive disorders accounted for most cases, followed by fetal indications, placental causes, and maternal causes, respectively (Figure 1).

There were several differences in maternal and neonatal baseline characteristics (Table 1). In the iLPTB group, maternal age was greater (31.97 ± 4.40 years vs. 33.48 ± 4.03 years, $p = 0.006$), and gestational age at delivery was also significantly greater compared to that of the sLPTB group (35.2 ± 0.8 weeks vs. 35.6 ± 0.8 weeks, $p < 0.001$). Furthermore, there were significant differences between the iLPTB and sLPTB groups in the percentage of neonates who reached a complete gestational age of 36 weeks at delivery, as well as in the mean gestational age at delivery (Table 1). There was no difference in the rate of nulliparity between the groups, but the rate of cesarean delivery was significantly higher in the iLPTB group (43.4% vs. 89.0%, $p < 0.001$). The mean birth weight in the iLPTB group was less than that in the sLPTB group (2.46 ± 0.35 kg vs. 2.26 ± 0.47 kg, $p < 0.001$).

The perinatal outcomes in both groups are shown in Table 2. The iLPTB group was associated with a lower Apgar score and a higher rate of NICU or SCN admission compared to the sLPTB group (70.0% vs. 81.3%, $p = 0.046$). In addition, there was a



PPROM: preterm premature rupture of membranes
PTL: preterm labor with intact membranes
HTN: hypertensive disorders such as gestational hypertension, preeclampsia and superimposed preeclampsia

Figure 1. Indications for late preterm birth.

Table 1. Comparison of maternal and neonatal characteristics between spontaneous and indicated late preterm births.

	Spontaneous (n = 198)	Indicated (n = 91)	P value
Maternal characteristics			
Age (year)*	31.97 ± 4.40	33.48 ± 4.03	0.006
GAD (week)*	35.2 ± 0.8	35.6 ± 0.8	<0.001
GAD (weeks)			
34 weeks	71 (35.9)	16 (17.6)	
35 weeks	76 (38.4)	27 (29.7)	<0.001
36 weeks	51 (25.8)	48 (52.7)	
Nulliparity (%)	109 (55.1)	50 (54.9)	0.987
Diabetes (%)	19 (9.6)	10 (11.0)	0.714
Delivery mode			
Spontaneous vaginal delivery (%)	102 (51.5)	10 (11.0)	
Vacuum delivery (%)	10 (5.1)	0 (0)	<0.001
Cesarean section (%)	86 (43.4)	81 (89.0)	
Neonatal characteristics			
Birth weight (kg)*	2.46 ± 0.35	2.26 ± 0.47	<0.001
Male (%)	116 (58.6)	43 (47.3)	0.072

GAD: gestational age at delivery; *mean ± standard deviation.

difference in NICU admission rates for neonates who reached 36 complete weeks of gestation (41.2% vs. 75.0%, $p < 0.001$). However, there was no statistically significant difference in the duration of NICU stay (11 days vs. 12 days, $p = 0.271$).

Table 2. Comparison of perinatal outcomes between spontaneous and indicated late preterm births.

	Spontaneous (n = 198)	Indicated (N = 91)	P value
Perinatal morbidity			
Apgar score below 4 at 1 min (%)	4 (2.0)	9 (10.0)	0.003
Apgar score below 7 at 5 min (%)	3 (1.5)	6 (6.7)	0.020
Admission to NICU or SCN (%)	139 (70.0)	74 (81.3)	0.046
34 weeks	67 (94.4)	15 (93.8)	0.924
35 weeks	51 (67.1)	23 (85.2)	0.073
36 weeks	21 (41.2)	36 (75.0)	<0.001
Duration of NICU stay (day)*	11 (2-56)	12 (2-366)	0.271
Composite morbidity	104 (52.5)	55 (60.4)	0.209
Antibiotics (%)	75 (37.9)	28 (30.8)	0.241
Hypoglycemia	3 (1.5)	9 (9.9)	0.001
Hypocalcemia	7 (3.5)	2 (2.2)	0.543
Phototherapy (%)	73 (36.9)	28 (30.8)	0.312
Respiratory support (%)	20 (10.1)	17 (18.7)	0.043
Ventilator	14 (7.1)	13 (14.3)	
Nasal CPAP	6 (3.0)	4 (4.4)	
Respiratory distress syndrome	12 (6.1)	10 (11.0)	0.142
Perinatal mortality			
Neonatal death (%)	0 (0.0)	0 (0.0)	-

NICU: neonatal intensive care unit; SCN: special care nursery; CPAP: continuous positive airway pressure.

Lastly, there was no difference in the rate of composite morbidity between the two groups (52.5% vs. 60.4%, $p = 0.209$). However, the rate of hypoglycemia was higher in the iLPTB group (1.5% vs. 9.9%, $p < 0.001$), with no significant difference in the rate of gestational diabetes mellitus (GDM). Even though there was no difference in the rate of RDS between the groups, the rate of respiratory support was higher in the iLPTB group (10.1% vs. 18.7%, $p = 0.043$).

4. Discussion

Similar to the results of previous studies, we found that sLPTB accounted for about 70% of all late preterm births and iLPTB for the remaining 30% in our study group [2] [12]-[14]. In addition, we found that despite a greatergestational age and higher proportion of 36 complete weeks of gestation in the iLPTB group, the mean birth weight was significantly less in the iLPTB group compared to that in the sLPTB group. In terms of perinatal outcomes, there was no difference in the rate of composite morbidity between the two groups, but the iLPTB group showed higher rates of NICU admission, hypoglycemia, and respiratory support.

Kase *et al.* reported that medically-indicated preterm birthshada significantly higher

rate of small for gestational age (SGA) infants compared to the spontaneous preterm birth group in chronic hypertensive women, but there was no difference in perinatal outcomes between the two groups [8]. However, another study reported that iLPTB increased the risk of NICU admission and respiratory disorders in neonates in comparison with sLPTB in twin pregnancies without any differences in gestational age at delivery or birth weight in twin late preterm births [7]. Our study showed that poorer intrauterine environment in the iLPTB group may induce lighter birth weight and be associated with higher rates of several adverse perinatal outcomes (NICU admission, hypoglycemia, and respiratory support), but there was no difference in the rate of composite morbidity and severe adverse perinatal outcomes, such as RDS or longer stay in the NICU.

There was no difference in the rate of RDS between the two groups, but the rate of respiratory support was significantly higher in the iLPTB group, and was also associated with a higher rate of cesarean section in our study. A large population-based study from Nova Scotia showed that late preterm infants born by cesarean section without labor have an increased risk of adverse perinatal outcomes, such as need for resuscitation, total parenteral nutrition, transient tachypnea, hypoglycemia, necrotizing enterocolitis, and RDS or apneic spells [8]. Similarly, there have been reports that late preterm infants delivered without a definitive indication or spontaneous labor had higher neonatal mortality rates, suggesting that spontaneous labor may be a positive prognostic factor in late preterm births [11]-[15]. An endogenous steroid surge during spontaneous labor would likely reduce the risk of fetal respiratory complications in late and term infants [16]. Therefore, higher rates of cesarean section in iLPTB would be associated with an increased respiratory support rate.

Metabolic morbidities, such as neonatal hypoglycemia, hypocalcemia, or hyperbilirubinemia requiring phototherapy, are more common in late preterm births compared to full term births [3]. Our results show that the rate of hypoglycemia was higher in the iLPTB group than in the sLPTB group, without differences in the GDM rate [17] [18]. Since high-risk neonates are more susceptible to hypoglycemia [19], close attention should be paid to screening neonatal hypoglycemia in late preterm births, especially in indicated late preterm births.

There are several limitations in our study. We could not evaluate important composite morbidities, such as bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), and mortality rate, due to uncertainty of these diagnoses and the small study sample size. In addition, we evaluated the rate of antibiotic use rather than the rate of sepsis, because clinical symptoms, such as tachypnea or respiratory difficulty, induced the administration of antibiotics before culture test results.

5. Conclusion

In conclusion, there was no difference in composite morbidity between the spontaneous and indicated groups. However, indication for delivery in late preterm birth might

influence several perinatal outcomes (NICU admission, hypoglycemia, and respiratory support); therefore, obstetrical providers should individualize the management of late preterm deliveries.

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