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ORIGINAL ARTICLE

Short-Term Neonatal Outcome in Late Preterm vs. Term Infants

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Abstract

Objective: To determine the short-term neonatal outcomes in late preterm infants (LPI's) as compared to term infants and their association with maternal risk factors.

Study Design: A case control, descriptive study.

Place and Duration of Study: The Aga Khan University Hospital, Karachi, Pakistan, from January to December 2009.

Methodology: The study included 326 late preterm babies (defined as those born between 34⅐ to 37⅐ weeks of gestation) and equal number of term control babies at the Aga Khan University Hospital, Karachi, Pakistan. Data, including obstetric history, maternal complications, neonatal morbidities, etc., was retrieved from patients' medical records. The data was compared with the control group for complications, fetal morbidity and maternal morbidity.

Results: Late preterm infants constituted 10.6% of all deliveries and 77% of all live preterm births during the study period. Respiratory distress syndrome (RDS) (16.5% vs. 0.3%, p < 0.001), growth retardation (24.8% vs. 4%, p < 0.001), hyperbilirubinemia requiring phototherapy (37.9% vs. 11%, p < 0.001), and sepsis (4.9% vs. 0.3%, p < 0.001) were found to be the major morbidities in the study group. The need for resuscitation was 12.7 times higher in the study group as compared to the term babies (21.4% vs. 1.2%, p < 0.001). NICU admissions in the study group were also higher (18.8% vs. 2.4%, p < 0.001). Hypertension (12.5% vs. 1.5%, p < 0.001), diabetes (12.5% vs. 9.2%, p < 0.001), antenatal history of UTI (1.5% vs. 0.3%, p < 0.001), and prolong rupture of membrane (8.9% vs. 4%, p < 0.001) were significant maternal morbidities in the late preterm group.

Conclusion: The late preterm group had greater morbidity, compared to term neonates. Prior awareness of the morbidities associated with late preterm babies is helpful for the health care providers to anticipate and manage potential complications in late preterm infants.

Key Words: *Late preterm birth. Risk factors. Neonatal morbidity.*

INTRODUCTION

Preterm delivery is one of the most important determinants of neonatal morbidity and mortality. The annual number of late preterm deliveries is increasing, persistently, worldwide. The rate of preterm births in the United States increased from 9.1% in 1981 to 12.3% in 2003, an increase of 3.1%, most of which was caused by an increase in the proportion of late preterm births. The foremost reasons are an early deliveries of high risk pregnancy to prevent sudden and unexpected fetal loss and increase in the number of successful artificial reproductive techniques.[1]

The American Academy of Pediatrics and the American College of Obstetrician and Gynecologists define a preterm infant as one who is born before 37th week (259th days) of pregnancy, counting from the first day of last menstrual period.[2] In 2005, the NICHD proposed the definition of late preterm infants as those born between $34^{0/7}$ (239 days) to $37^{6/7}$ weeks (259 days) of gestation.[3] Previously the term “near term” was used for these babies, as these babies are apparently mature and have birth weight comparable to term babies. This create the deceitful imprint that they are almost term, and triage and managed as term babies, although they are physiologically and metabolically less mature than term infants, and have more risks of complications, compared with term babies.

A broad range of neonatal problems have been documented in recent literature on late preterm infants. These problems include feeding difficulties, hypoglycemia, respiratory distress syndrome (RDS), temperature instability, presumed or confirmed sepsis, apnea, hypoglycemia, jaundice, and transient tachypnea of the newborn.[4,5] An understanding of the morbidities associated with late preterm babies is helpful for the healthcare provider to anticipate and manage potential complications in late preterm, and also to improve maternal care, and reduce non-emergency obstetrics decisions.

In developed countries, a lot of work has been done in this vital group of newborns, which demonstrate the high morbidity and mortality associated with late preterm infants.[6,7] In 2000, Kramer *et al*. reported from United States and Canadian data, that these late preterm babies contributed significantly to overall infant and neonatal mortality.[8] In South East Asia, limited work have been done, so far, and only few studies have been published.[9,10] In a resource-poor country like Pakistan, a

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large impact can be made in reducing neonatal morbidity and mortality by providing meticulous care to this late preterm group.

The aim of this study was to determine the short-term outcome of late preterm infants compared with term infants.

METHODOLOGY

Medical records of neonates (late preterm and term), who were born during the period from January to December 2009 at AKUH, Karachi, were reviewed in detail. Neonates were considered as late preterm at $34^{0/7}$ to $36^{6/7}$ and term at $37^{0/7}$ to $40^{0/7}$ weeks of gestation. A total of 428 late preterm infants were born during this period and 102 babies were excluded for not meeting clinical criteria. Exclusion criteria were incomplete medical record, major congenital anomalies, and multiple gestations. The final sample size of 326 neonates in each group was taken in order to detect a difference in morbidity between the study group and term babies, at a significance level of 0.05 with 80% power. Data was retrieved from electronic medical record (eMAR) and by reviewing clinical notes in a structured questionnaire, which entailed information about demographics, obstetric history, and complications during current pregnancy, and neonatal morbidities. Gestational age was calculated on the basis of last menstrual period, or ultrasound, and by postnatal examination (Ballard scoring). The study was carried out after obtaining approval from the institutional ethical review committee.

The definitions of variables were based on pre-set definitions in current literature. Transient tachypnea of newborn was defined as the onset of respiratory distress at the time of birth and within 2 hours after delivery, with tachypnea being the most prominent clinical feature along with chest X-ray findings of fluid in the interlobar fissure.[11] An infant was labeled as having RDS if the baby required oxygen at 6 hours of life, along with an abnormal chest X-ray within 24 hours of birth, consistent with surfactant deficiency. Hypoglycemia was defined as blood sugar < 40 mg/dl in symptomatic or/and < 25 mg/dl in asymptomatic baby.[12] Apnea of prematurity (AOP) was defined as breathing pauses lasting for > 20 seconds or for > 10 seconds associated with bradycardia or oxygen desaturation of < 80 – 85%.[13] Birth weight less than the 10th percentile for gestational age are considered IUGR.[14] The diagnosis necrotizing enterocolitis (NEC) was based on a clinical documentation of signs and symptoms (temperature instability, apnea, abdominal distension, gastric aspirate) along with radiologic evidence (pneumatosis intestinalis, pneumoperitoneum).[15] Patient ductus arteriosus (PDA) was diagnosed clinically on the basis of continuous or systolic murmur in the left sub-clavicular area, associated with hyperactive precordium with wide pulse pressure or bounding pulses. It was labelled echocardiographically significant when the ductal size > 1.5 mm or

Table I: Maternal and neonatal characteristics and associated morbidities.

	Late preterm Mean ± SD / n (%)	Term Mean ± SD / n (%)	Significance p-value
Maternal Characteristics			
Age (years)	29.2 ± 5.00	28.3 ± 4.51	0.012
Diabetes	41 (12.5%)	30 (9.2%)	0.000
Antenatal history of hypertension	41 (12.5%)	5 (1.5%)	< 0.001
PROM	28 (8.9%)	13 (4.0%)	< 0.001
Perinatal depression	12 (3.7%)	2 (0.6%)	< 0.001
Antenatal history of urinary tract infection	5 (1.5%)	1 (0.3%)	< 0.001
Neonates Characteristics and morbidities			
Birth weight (kg)	2.35 ± 0.47	3.12 ± 0.41	< 0.001
Hyperbilirubinemia requiring phototherapy	124 (37.9%)	36 (11.0%)	<0.001
Presumed sepsis	89 (27.2%)	33 (10.1%)	< 0.001
IUGR	81 (24.8%)	13 (4.0%)	< 0.001
Resuscitation	70 (21.4%)	4 (1.2%)	< 0.001
NICU	59 (18.8%)	8 (2.4%)	< 0.001
RDS	54 (16.5%)	1 (0.3%)	< 0.001
Apnea	50 (15.3)	0 (0.0%)	< 0.001
Ventilation	49 (15.0%)	0 (0.0%)	< 0.001
Surfactant	31 (9.5%)		
Fetal distress	28 (8.6%)	4 (1.2%)	0.045
TTN	23 (7.0%)	2 (0.6%)	0.007
Hypoglycemia	17 (5.2%)	3 (0.9%)	0.002
Confirmed sepsis	16 (4.9%)	1 (0.3%)	< 0.001
Formula milk	15 (4.6%)	1 (0.3%)	< 0.001
Managed with I/V fluid bolus	14 (4.3%)	2 (0.6%)	< 0.001
Hyperbilirubinemia requiring exchange transfusion	6 (1.8%)	1 (0.3%)	< 0.001

Table II: Likelihood of neonatal morbidities.

	N (%)	OR 95% CI	p-value
Resuscitation	70 (21.4%)	12.7 (4.10 - 39.1)	< 0.001
RDS	54 (16.5%)	18.7 (2.27 - 153.5)	0.006
NICU admission	59 (18.8%)	3.20 (1.17 - 8.77)	0.024
Hyperbilirubinemia requiring phototherapy	124 (37.9%)	1.84 (1.04 - 3.27)	0.036
Fetal distress	28 (8.6%)	6.14 (1.55 - 24.2)	0.018

the left atrial to aortic root ratio was < 1.4.[16] The study followed clinical practice guideline provided by American Academy of Paediatrics and Bhuttani *et al*. for the diagnosis of hyperbilirubinemia.[17] Physician documented episode of tachycardia / bradycardia, apnea, hypotension, hyper/hypothermia, hyper / hypo-glycemia or any other sign of systemic illness, with or without positive blood culture, was labelled as sepsis.[18,19]

Frequencies of maternal complications were obtained. To determine the association of maternal characteristics and neonatal morbidities between groups, chi-square test was used for categorical variables, and t-test was used for continuous variables. Logistic regression analysis was applied for each of the neonatal morbidities. Logistic regression analysis was used for all dichotomous variables. The results are presented as adjusted odd ratios (OR) with 95% confidence interval (CI). All these analyses were carried out using Statistical Package for Social Sciences (SPSS) version 19.0.

RESULTS

A total of 326 files were reviewed in each group. Results showed that maternal morbidities like hypertension (12.5% vs. 1.5%), diabetes (12.5% vs. 9.2%), antenatal history of UTI (1.5% vs. 0.3%) and prolonged rupture of membrane (28.9% vs. 4.0%) were substantially higher in the late preterm group (Table I). Maternal demographics and pregnancy complications were used as predictors of all neonatal complications. From all the neonatal complications listed in Table I, RDS, NICU admission, fetal distress, hyperbilirubinemia requiring phototherapy and resuscitation were found to be more significant in the late preterm group. The odds of RDS were 18.7 times higher in the late preterm group as compared to the term babies (OR 18.7, CI 2.27 – 153.5, p = 0.006). There was a greater likelihood of hyperbilirubinemia requiring phototherapy in the study population (OR 1.84, CI 1.04 – 3.27, p = 0.036). Likewise, NICU admissions were 3.2 times more in late preterm (OR 3.20, CI 1.17 – 8.77, p = 0.024). The chances of fetal distress and resuscitation were 6.14 and 12.7 times greater in late preterm, respectively. Other significant comorbidities related with the above mentioned neonatal complications were low birth weight and perinatal depression (Table II).

DISCUSSION

The incidence of late preterm births has been increasing globally, with an estimated 15 million babies being born preterm (before 37 completed weeks of gestation). Consistent with data, the rate of preterm birth ranges from 5% to 18% of babies born, and over 60% of preterm births occur in Africa and South Asia.[20] Management of these late preterm infants is becoming a greater component of obstetric care, and late preterm infants are using a significant proportion of the nation's health resources.[21] Accurate estimates of the risks of morbidity and death associated with late preterm births are required to enable healthcare provider and legislators to make informed decisions.

There are pronounced differences in the survival rates of these babies around the world. In low-income settings, half of the babies born at 32 weeks (2 months early) die due to a dearth of reasonable economical care, such as providing warmth, support breast feeding, prevention of infections, and appropriate care for breathing difficulties. In high-income countries, almost all of these babies survive.[22] Until recently, these babies were managed like term babies as these babies are apparently mature and have birth weight similar to term infants. It has been repeatedly stated that late preterm infants have more chances of morbidities, compared to term babies, and careful attention to this group may reduce the overall neonatal and infant morbidity and mortality.[23] There is a scarcity of data from South East Asia and only few studies have been conducted on this issue in this part of the world.[9,10]

Kramer *et al*. showed that late-preterm infants have a mortality rate three times greater than term infants, with the highest risk occurring during the neonatal period.[8] A number of maternal medical conditions, including hypertensive disorders of pregnancy, diabetes and asthma are associated with an increased risk of induced or spontaneous preterm birth.[24] In this study, diabetes mellitus, hypertension, and prolonged repture of membranes (PROM) were seen more frequently in the mothers of late preterm babies. Mendoza *et al*. conducted a large population based study and found that maternal medical conditions are self-determining risk factors for newborn morbidity in late preterm group.[23] Another population based cohort study showed that there was increased prevalence of chorioamnionitis, hypertension and PROM in the preterm group.[8]

Data published by Wang *et al*. about the clinical outcomes of late preterm babies, found that temperature instability, respiratory distress, hypoglycemia and

jaundice occurred significantly in late preterm babies.[22] There is also significant increase in NICU admissions and need of ventilator support, which increases the overall financial burden. Reports from USA stated nearly three times the cost in treatment of late preterm neonates.[25] Various other studies from this cohort of infants have been conducted.[3,12] Recently, a prospective study from India supported the present findings and demonstrated the morbidities of late preterm group which has been previously underestimated.[10] Results from the current study suggest that maternal morbidities like hypertension, diabetes, and antenatal history of UTI and rupture of membrane were substantially higher in the late preterm group. RDS, NICU admission, fetal distress, hyperbilirubinemia requiring phototherapy and resuscitation were more significant in late preterm babies. Further research is desirable to confirm this notion.

This study included several limitations that should be addressed. Data were obtained from electronic medical record (eMAR) database that was not necessarily designed for research. Data on the eMAR is also prone to clerical errors, misclassification, coding bias rates for financial gains as health care is self-financed at the study centre. Also, much of the design of this study was based on file review in which the physician's final diagnosis also has a tendency for bias. Physician bias can take many forms. However, combining these data sources does improve accuracy over using the data sources alone.

The findings of this study would also help healthcare providers during antenatal counselling of late preterm group. Further research is required that should focus on addressing the other areas like long-term morbidity, mortality, and healthcare disbursement, and comparing these risks with the benefits of early deliveries.

CONCLUSION

The late preterm group had greater morbidity, compared to term neonates. Prior awareness of the morbidities associated with late preterm babies is helpful for the health care providers to anticipate and manage potential complications in late preterm infants.

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