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Original Article

Paediatrics Section

Morbidity and Mortality Pattern in Late Preterm Infants at a Tertiary Care Hospital in Jammu & Kashmir, Northern India

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ABSTRACT

Introduction: The morbidity and mortality pattern in late preterm infants is higher than term infants (gestational age ≥ 37 weeks). The main reason behind that is the relative physiologic and metabolic immaturity, though there is no significant difference in the weight or the size of the two groups.

Aim: The present study was undertaken to study the incidence, early neonatal morbidity and mortality (within first 7 days of life) in late preterm infants (34 – 36 6/7 weeks).

Materials and Methods: It was a hospital based prospective study conducted from April 2012 to March 2013. The study was conducted in the Department of Paediatrics and Neonatology at G.B. Pant General Hospital and Department of Gynaecology and Obstetrics L.D hospital and G.B. pant general hospital, (associated hospitals of Government Medical College, Srinagar).

Results: A total of 4100 neonates were included in the study. Incidence of late preterm neonates was 11.58 %. Three hundred sixty five (76.8%) of late preterm and 965 (28.3%) of term infants had at least one of the predefined neonatal conditions. Late preterm infants were at significantly higher risk for overall morbidity due to any cause ($p<0.0001$), respiratory morbidity ($p<0.0001$), mechanical ventilation ($p=0.0002$), jaundice ($p<0.0001$), hypoglycaemia ($p<0.0001$), and sepsis ($p<0.0001$) Perinatal asphyxia ($p= 0.186$). Early neonatal mortality in late preterm neonates was 2.5% or 25/1000 live births.

Conclusion: Compared with term infants, late preterm infants are at high risk for overall morbidity, respiratory morbidity, and need of mechanical ventilation, jaundice, hypoglycaemia & sepsis. They also have a higher mortality as compared to term neonates.

Keywords: Hypoglycaemia, Jaundice, Sepsis

INTRODUCTION

Late preterm infants – The American Academy of Paediatrics (AAP), American College of Obstetrics and Gynaecology (ACOG) and National Center for Health Statistics (NCHS) define late preterm birth as the delivery of an infant from 34 weeks to 36 weeks and 6 days of gestation (i.e., 239 to 259 days after the first day of the LMP) [1]. They account for 9.1% of all births and three-quarter of all preterm births [2].

The morbidity and mortality pattern in late preterm infants is higher than term infants (gestational age ≥ 37weeks). The main reason behind that is the relative physiologic and metabolic immaturity, though there is no significant difference in the weight or the size of the two groups. The late preterm infants are at twice to thrice increased risk of morbidities like hypoglycaemia, poor feeding, jaundice, infection and re-admission rates after initial hospital discharge [3-6]. The infant mortality rate during first year of life for late-preterm infants is on an average four-fold higher than that for term infants [7-10].

During the past few years proportion of late-preterm births has increased. The reason for the increase in late-preterm births during the last decade is not well understood. One hypothesis is that it may be attributable, in part, to increased use of reproductive technologies and, as a result, an increase in multi fetal pregnancies. Another hypothesis is that advances in obstetric practice have led to an increase in surveillance and medical interventions during pregnancy, as a result, at risk infants like those of intrauterine growth restrictions, fetal abnormalities and anomalies can be identified earlier and hence delivered earlier [11-15].

Apnea occurs more frequently among late preterm infants than term infants. The incidence of apnea in late preterm infants is reported to be between 4% and 7% compared with 1% to 2% at term.

Immature liver glycogenolysis, hormonal dysregulation, and inefficient hepatic glycogenesis and ketogenesis predispose preterms for developing sympotomatic hypoglycaemia [16]. Also, late-preterm infants have increased chances of developing hyperbilirubinaemia because feeding difficulties that predispose them to an increase in enterohepatic circulation, decreased stool frequency, and dehydration [17,18]. Late-preterm infants are also more vulnerable to develop various respiratory morbidities including transient tachypnea of the newborn, respiratory distress syndrome, pneumonia, and pulmonary hypertension. Most common factor responsible for late preterm birth is preterm labour (45%) [19-21].

MATERIALS AND METHODS

The study was conducted in the Department of Paediatrics and Neonatology at G.B. Pant General Hospital and Department of Gynaecology and Obstetrics Lalla Ded (L.D) Hospital and G.B. pant Hospital, (associated Hospitals of Government Medical College, Srinagar). It was a Hospital based Prospective study conducted from April 2012 to March 2013.

Study group & inclusion criteria: The study group included live born late preterm as well as term babies neonates who fulfilled the inclusion criteria delivered in the Department of Obstetrics and Gynaecology L.D hospital and G.B. Pant General Hospital during the study period. Term infants were taken as control. Gestational age was assessed by maternal last menstrual period and New Ballard score. All infants enrolled in study were followed for first seven days of life for any morbidity and mortality. Late preterm neonates and term neonates who needed admission were admitted in the neonatology section at G.B. pant Hospital and L.D. hospital.

Exclusion Criteria: Infants with major congenital anomalies and those with clinically identified chromosomal syndromes were excluded from the study.

Neonates in study group who needed admission were evaluated in the Neonatology section of G.B. pant Hospital and L.D. Hospital.

Relevant history was recorded which would include order of birth, sex of baby, address, gestational age, place of delivery, mode of delivery (Vaginal, Caesarean), date and time of delivery, Apgar score at 1 minute and 5 minutes of birth, need for resuscitation, presence of maternal fever and prolonged rupture of membranes. The examination included determination of gestational age (maternal last menstrual period, New ballard score), weight of baby, muscle tone and activity, colour, respiratory rate, respiratory distress (nasal flaring, intercostal/sub costal retractions, grunt) and heart rate. Systemic examination was done and recorded. The chest x-ray was done as and when needed. CBC, serum billuribin (total, direct, indirect), arterial blood gas, serum electrolytes, KFT, serum calcium, serum magnesium, blood group of mother and baby. These investigations were done at admission, day 3, day 7 and in between as and when indicated except blood sugar which was done 6 hourly for first 24 hours of life followed by 12 hourly upto 72 hours of life. Blood sugar was done by Glucostick method & any abnormal values if found were sent to laboratory for confirmation by Glucose oxidase method. Blood culture and sensitivity was done in suspected cases of septicaemia. Mechanical ventilation was used as and when indicated. The neonates were followed upto 7 days of their life.

STATISTICAL ANALYSIS

All data collected was analysed using SPSS and Graphpad instat software. Neonatal morbidities were compared between late preterm and term infants. Chi-square test or Fishers exact test were used for statistical analysis. The *p*-value <0.05 was considered significant.

Hypoglycaemia: Defined as a blood glucose level less than 40 mg/dl in first 24 hours & less than 45 mg/dl after 24 hours [22].

Jaundice: Clinically visible jaundice requiring phototherapy/exchange transfusion as per hour specific total serum biluribin (TSB) nomogram (AAP chart). Criteria for 35 weeks were used for infants with 34 weeks gestation.

Sepsis: Probable sepsis: Positive septic screen (two of the five parameters namely, TLC <5000/mm^3 or >15000/ mm^3, I/T immature to total polymorph ratio of ≥0.2, absolute neutrophil count less than 1750/mm^3 or >7200/mm^3, C reactive protein > 1 mg/dL, platelets <1 lac/mm^3), or proven sepsis: Isolation of pathogens from blood or CSF [23].

Respiratory Distress: Sustained respiratory distress for more than 2 hours after birth (RR > 60/min) accompanied by grunting, flaring, tachypnea, retractions, or supplemental oxygen requirement [24].

Perinatal Asphyxia: American Academy of Paediatrics (AAP) and American College of Obstetrics and Gynaecology(ACOG) definition of perinatal asphyxia which included infants with Profound metabolic or mixed acidemia (pH < 7.00) in an umbilical arterial blood sample, apgar score of 0-3 > 5 min after birth, neonatal encephalopathy (e.g., seizures, coma, hypotonia) and multiple organ involvement (kidney, lungs, liver, heart, intestines) [25].

Mechanical Ventilation: The initiation of mechanical ventilation is based on clinical condition of infant and evaluation of blood gases. Mechanical ventilation was used when pco_2 rises acutely above 55 to 65 mm Hg and pH decreases to <7.25- 7.20 [26].

Any other clinical or metabolic complication if identified was defined on the basis of criteria outlined for it in Standard Textbooks of Neonatology (Avery`s Diseases of Newborn & Cloherty`s Manual of Neonatal Care). Any neonatal complications if identified were managed as per standard protocols outlined for these conditions.

RESULTS

The study was conducted over a period of one year from April 2012 to Mar 2013. The study group included live born neonates delivered in Department of Obstetrics and Gynaecology LD hospital & GB pant general hospital. During this period a total of 4100 neonates were included in study out of these 3400 (82.92%) were term babies while as 673 (16.41%) were preterm babies, among these preterm babies 475 babies (70.57%) were late preterm neonates (gestation age 34 0/7 – 36 6/7 weeks) while as 198 babies were born at gestational age of < 34 weeks. Out of the 3400 term babies 965 (28.38%) babies were admitted for various morbidities while among 475 late preterm babies 365 (76.84%) were admitted.12 Late preterm babies expired during this period (mortality = 25/1000 live births) while 40 term babies expired during this period (mortality = 11/1000 live births), 27 were excluded due to major congenital malformations. Incidence of late preterm neonates was 11.6% or 116 per thousand live births. Baseline variables of the study population are given in [Table/Fig-1].

Overall morbidities were significantly higher (76.8% compared to 28.3%) in late preterms as compared to term babies. Jaundice (41.6% compared to 15.3%), Hypoglycaemia (16% compared to 6.5%), Respiratory morbidities (11.2% compared to 2.1%), sepsis (4.8% compared to 1.53%), Perinatal asphyxia (2.9% compared to 1.9%) were all significantly higher in late preterm babies as compared to term babies. A 3.7% of late preterm babies required mechanical ventilation as compared to only 1.3% of term babies.

The mortality in late preterm babies (25/1000 live births) was also significantly higher than term babies (11/1000 live births).

Variable		Late preterm (n = 475)	Term (n = 3400)
Gestation (wks) mean (SD)		34.8 (±0.78)	38.6 (±0.8)
Birth weight (Kg) Mean (SD)		2.4 (±0.6)	2.8 (±0.6)
Male/female		M=257 (54.1%) F=218 (45.9%)	M=1752 (51.5%) F=1648 (48.5%)
Weight for gestation	AGA	385 (81.05%)	2911 (85.6%)
	SGA	56 (11.7%)	186 (5.47%)
	LGA	34 (7.1%)	310 (9.44%)
Mode of delivery	Vaginal	163 (34.3%)	2103 (61.8%)
	Cesarean	312 (65.7%)	1297 (38.1%)
Singleton pregnancy		386 (81.2%)	3381 (99 %)

[Table/Fig-1]: Baseline Variables of the study population

Morbidity	Late Preterm	Term	p-value
Yes	365	965	<0.0001
No	110	2435	

[Table/Fig-2]: Overall morbidity among late preterm and term neonates

The above [Table/Fig-2] shows that morbidity was higher in late pretems than that of term babies with statistical significant difference between them.

Jaundice	Late Preterm	Term	p-Value
Yes	198	520	<0.0001
No	277	2880	

[Table/Fig-3]: Comparison of Jaundice between late preterm and term neonates

The above [Table/Fig-3] shows that there is a statistical significant difference of development of jaundice between late preterms and term babies.

Respiratory morbidity	Late Preterm	Term	p-Value
Yes	53	73	<0.0001
No	422	3327	

[Table/Fig-4]: Comparison of respiratory morbidity between late preterm and term neonates

The above [Table/Fig-4] clearly shows that respiratory morbidity was more in late preterms than those of term babies.

	Died	Alive	p-value
Late preterm	12	463	0.02
Term	40	3360	

[Table/Fig-5]: Comparison of mortality between late preterm and term neonates

As depicted above out of 3400 term babies death occurred in 40 (11/1000 live births) neonates and out of 475 late preterm neonates death occurred in 12 (25/1000 live births) neonates [Table/Fig-5].

DISCUSSION

The study group included 4100 live born neonates delivered in the Department of Obstetrics and Gynaecology L.D Hospital and G.B. Pant General Hospital during the study period (Apr 2012 to Mar 2013). The purpose of our study was to study the incidence of late preterm delivery, early neonatal morbidity and mortality in late preterm and term neonates.

The incidence of late preterm neonates in our study was 11.6% or 116 per 1000 live births. In our study 365 (76.8%) late preterm neonates and 965 (28.3%) term neonates were admitted. Statistically overall morbidity was found significantly higher in late preterm neonates as compared to term neonates (OR=8.37, 95% CI (6.68-10.5), p-value= <0.0001). Srinivasmurki et al., found overall morbidity significantly higher in late preterm neonates (70.8%) as compared to term neonates (29.1%) (P<0.001, adjusted OR: 5.5, 95% CI: 4.2-5.1) [21].

Jaundice was most common morbidity in our study. In our study, 198 (41.6%) late preterm neonates and 520 (15.3%) term neonates were admitted with jaundice. Statistically jaundice was found significantly higher in late preterm neonates as compared to term neonates (p-value< 0.0001, OR = 3.96, 95% CI (3.23– 4.86). Wang et al., did a study in which they found jaundice in 54.4% late preterm neonates and 37.9 % term neonates (OR 1.95, 95% CI (1.04–3.67), p-value < 0.027) [5]. Due to relative deficiency of uridinediphosphoglucuronate-glucuronosyl transferase there is more chance of hyperbilirubinaemia among late-preterm infants than term infants [27]. Also, late-preterm infants have increased chances of developing hyperbilirubinaemia because feeding difficulties that predispose them to an increase in enterohepatic circulation, decreased stool frequency, and dehydration [17,18].

In our study, hypoglycaemia occurred in 76(16%) of late preterm neonates and 221(6.5 %) of term babies. Statistically hypoglycaemia was found significantly higher in late preterm neonates as compared to term neonates (p-value=0.0001, OR =2.74, 95% CI = (2.07 - 3.63) [Table/Fig-6]. Araújo BF, Zatti H et al., found that late-preterms were statistically more likely to be subject to hypoglycaemia as compared to term neonates [28]. Preterm infants are at increased risk of developing hypoglycaemia after birth, because they have immature hepatic glycogenolysis and adipose tissue lipolysis, hormonal dysregulation and deficient hepatic gluconeogenesis and ketogenesis. Statistically respiratory morbidities were found significantly higher in late preterm neonates as compared to term neonates (p-value <0.0001, OR=5.72, 95% CI (3.96-8.27). Hendricks-Muñoz KD et al., found a Respiratory Distress Syndrome (RDS) in 9%, 4%, 3%, in 34-week, 35-week, 36-week as compared to 0.7%, 0.2% and 0% in 37-week, 38 to 39 week, and 40-week gestational age neonates (p < 0. 001) [29]. Statistically need of mechanical ventilation was found significantly higher in late preterm neonates as compared to term neonates (p-value =0.0002, OR=2.94, 95%CI (1.69-5.12) [Table/Fig-7]. Gilbert et al., found that

Hypoglycemia	late Preterm	Term	Odds ratio	95% CI	p-value
Yes	76	221	2.74	2.07-3.63	<0.0001
No	399	3179			

[Table/Fig-6]: Comparison of hypoglycemia between late preterm and term neonates

Mechanical Ventilation	late Preterm	Term	Odds ratio	95% CI	p-value
Yes	18	45	2.94	1.69-5.12	0.0002
No	457	3355			

[Table/Fig-7]: Comparison of need of mechanical ventilation between late preterm and term neonates

3.4% late preterm neonates as compared to 0.9% term neonates needed mechanical ventillation [30].

In our study, out of 475 late preterm neonates death occurred in 12 neonates (2.5% OR 25 per 1000 live births) and out of 3400 term neonates death occurred in 40 neonates (11 per 1000 live births). Statistically mortality was found significantly higher in late preterm neonates as compared to term neonates (OR = 2.17, P= 0.02). Celik IH et al., found a mortality rate of 2.1% or 21 per thousand live births [31]. They also found mortality in late preterm significantly higher as compared to term neonates (p<0.001).

LIMITATION

If sample size was more the results would have been more conclusive.

CONCLUSION

To conclude our study revealed that late-preterm neonates have significantly higher risk of morbidity and mortality compared with term newborns. Greater concern and attention is required for the care of this ignored, at risk population. The results of present study lay strong importance for timely and judicious decision making while considering a preterm delivery and also suggest the need of the anticipatory clinical guidelines and preparedness in terms of staff, equipment and proper infrastructure for the care of such late preterm infants.

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