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The Tiny Tricksters: Differences between Late Preterm and Term Neonates

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Abstract

Introduction: Preterm births are increasing globally, estimated at an annual incidence of 15 million. Of these, about 80% are moderate and late preterm births occurring between 32-37 weeks of gestation. Though large in size they have much more morbidity and mortality compared to their term counterparts. *Methods:* Retrospective case control study conducted in a referral perinatal centre in South India during the period January 2011 to June 2013. Inborn late preterms (LPT) were cases and term babies born during the same period were controls. Maternal and neonatal demography, morbidity and mortality data were collected. Means and standard deviations were used to compare numerical variables between case and control groups using Student's *t* test and the Mann-Whitney test; Pearson's chi-square was used for categorical variables. *Results:* A total of 1933 babies were included in the study of which 233 (12%) were late preterms. Elderly mothers, conceived with ovulation induction, multiple gestation and with antenatal complications had significantly higher number of LPT births. There were more CS and PROM noted. Parity and newborn gender did not show significant differences. There were larger numbers of small and large for gestational age babies among the late preterms. NICU admissions, phototherapy, sepsis treatments, respiratory distress, hypoglycemia, duration of hospital stay and cost of stay, mortality and readmission rates were higher among the LPT babies. *Conclusion:* Late preterms had a longer and more morbid course after delivery as compared to their term peers. They represent a high risk group which may go unrecognized.

Keywords: Late Preterms; Morbidity.

Introduction

Globally there has been an increase in delivery of preterm babies, contributed mainly by birth of late preterms, defined as babies born between 34^0 to 36^6 weeks gestation [1]. Current global estimates show that around 15million babies are born before 37weeks of gestation and this number is increasing. It has been consistently shown that more than 80% of these preterm births occur between 32-37weeks of gestation which is seen across all countries but is more pronounced in Asian and African countries [2]. India has the largest number of preterm births in the world [3]. Prematurity is not only the most common cause of neonatal death but also the second most common cause of under five deaths. Though late preterms resemble term babies in size, they are dramatically different in morbidity, mortality and financial burden on the parents. These large sized babies are relatively immature physiologically and are at risk for hypothermia, jaundice, hypoglycaemia, poor feeding and infections [4]. These infants are also at increased risk of death during infancy [5]. Careful attention to basic newborn care like warmth, breastfeeding, prevention of infections, aggressive treatment of hyperbilirubinemia will reduce a lot of the morbidity and mortality amongst these babies. Three quarters

of these babies can be saved with the present application of cost-effective treatments [3].

Materials and Methods

This retrospective case-control study was done in a tertiary care hospital in South India, the obstetric and neonatal units of which are regional referral centres for perinatal care. Relevant data for all the babies admitted between January 2011 to June 2013 was collected from the hospital records. Late preterms were taken as babies born between 34^{+0} to 36^{+6} weeks of gestation. Term babies born during the same period were taken as controls.

Maternal details like age, type of conception, parity, antenatal complications, antenatal steroids, labour and mode of delivery were collected. Neonatal details like date of birth, sex, birth and discharge weight, gestational age, growth, morbidities, NICU admissions, length of hospital stay etc were collected. A cost analysis of discharge bills was also done.

The relevant data was entered in the excel sheet and analysed by using the SPSS software.

Discrete and continuous variables were analysed using the Pearson Chi square test. Linear by linear association test was done to study the correlation between the late preterm group and the morbidities. p value was calculated using the Fisher's exact test and a value of <0.05 was considered significant.

Results

In the study period of 21/2 years there were a total of 2565 deliveries of which 233 were late preterm babies. This was 9.08% of all deliveries and 12% of the study group. Term babies were 1760 and they were taken as the comparison group. It was noted that mothers who were more than 30yrs had conceived by assisted reproduction like ovulation-induction and IVF were more likely to have late preterm babies (9.4% vs 3.4%). More late preterm mothers had received steroids (0.9% vs 0). The late

Table 1: Maternal demographic features

Factor	Term (%) n=1760	Late preterm (%) n=233	p value
Maternal age			
≤20yrs	222(12.6)	26(11.2)	
21-30yrs	1372(78)	173(74.2)	0.022
>30yrs	166(9.4)	34(14.6)	
Type of conception			
Spontaneous	1699 (96.5)	211 (90.6)	
Ovulation-induction	55 (3.1)	21 (9.0)	<0.01
IVF	6 (0.3)	1 (0.4)	
Type of pregnancy			
Singleton	1719(97.7)	205(88)	<0.01
Multiple	41(2.3)	28(12)	
Parity			
Primigravida	832(47.3)	110(47.2)	
Multigravida	928(52.7)	123(52.8)	0.986
Antenatal complications			
Yes	420(23.9)	98(42.1)	<0.01
No	1340(76.1)	135(57.9)	
Mode of delivery			
Vaginal	1226(69.7)	139(59.7)	0.002
Caesarean	534(30.3)	94(40.3)	
Labour			
Spontaneous	1532(87)	215(92.3)	0.023
Induced	228(13)	18(7.7)	
PROM			
Yes	30(1.7)	33(14.2)	<0.01
No	1730(98.3)	200(85.8)	
Antenatal steroids			
Yes	0(0)	2(0.9)	NA
No	100(1760)	231(99.1)	

preterm babies were either small (13.3% vs 8.2%) or large (3.9% vs 1.8%) for gestational age as compared to term babies. The most common cause for late preterm birth was unexplained preterm (74.7%) followed by multiple gestation (11.2%), severe PIH (6%), IUGR (1.7%), fetal distress (1.7%), antepartum haemorrhage (1.7%) and PROM (0.9%). Late preterm babies were also more likely to develop Respiratory Distress Syndrome (RDS) as compared to term babies. Interestingly it was also observed that babies whose mothers received antenatal steroids did not have RDS as compared to the babies whose mothers did not receive steroids. None of the babies in the term group had RDS. The average duration of hospital stay was around 7 days in a late preterm baby as compared to 5.2 days in a term baby with direct medical cost being almost double in the late preterm group (Rs 3533.37 vs 1640.87). Readmissions to our hospital was more in the late preterms. Dropouts were high but similar in both groups.

Table 2: Newborn demographic features

Characteristic	Term(%) n=1760	Late preterm(%) n=233	p value
Gender			
Male	902(51.3)	139(59.7)	0.016
Female	858(48.8)	94(40.3)	
Mean birth weight (gms)	3019.86(433.9)	2398.72(457.5)	<0.01
Mean gestational age (wks)	38.93(1.02)	35.68(1.04)	<0.01
Growth			
Appropriate	1584(90)	193(82.8)	
Small	145(8.2)	31(13.3)	<0.001
Large	31(1.8)	9 (3.9)	

Table 3: Morbidity differences between term and late preterm neonates

Factor	Term (%) n=1760	Late preterm(%), n=233	p value
NICU admission			
Yes	149(8.5)	90(38.6)	<0.01
No	1611(91.5)	143(61.4)	
Phototherapy			
Yes	152(8.6)	67(28.8)	<0.01
No	1608(91.4)	166(71.2)	
At risk of sepsis			
Yes	29(1.6)	173(74.2)	<0.01
No	1731(98.4)	60(25.8)	
Suspected sepsis			
Yes	6(0.3)	5(2.1)	<0.01
No	1754(99.7)	228(97.9)	
Culture positive sepsis			
Yes	6(0.3)	3(1.3)	
No	1754(99.7)	230(98.7)	0.023
Respiratory distress			
Yes	16(0.9)	12(5.2)	
No	1744(99.1)	221(94.8)	<0.01
TTN			
Yes	37(2.1)	18(7.7)	<0.01
No	1723(97.9)	215(92.3)	
RDS	0	4(1.7)	
Perinatal depression			
Yes	30(1.7)	5(2.1)	
No	1730(98.3)	228(97.9)	0.630
Congenital anomalies			
Yes	71(4)	20(8.6)	
No	96(1689)	213(91.4)	0.002

Congenital heart disease			
Yes	15(0.9)	6(2.6)	
No	1745(99.1)	227(97.4)	0.029
Feeding difficulty			
Yes	20(1.1)	6(2.6)	0.069
No	1740(98.9)	227(97.4)	
Hypoglycaemia			
Yes	12(0.7)	5(2.1)	0.04
No	1748(99.3)	228(97.9)	
Duration of hospital stay(avg days)	5.23	7.01	<0.01
Mean direct medical cost/baby (Rs)	1654.80	3533.37	<0.01
Mortality			
Yes	4(0.2)	3(1.3)	0.010
No	1756(99.8)	230(98.7)	
Rate of readmission			
Yes	107(6)	20(8.6)	
No	848(48.2)	100(43)	0.026
Lost to follow up	805(45.7)	113(48.5)	

Discussion

This was a retrospective study done in a medical college hospital which is a regional perinatal referral centre. The purpose of this study was to study the obstetric profile of mothers giving birth to late preterm babies and morbidity, mortality and Difference in cost of care between late preterm and term babies.

The incidence of late preterm births across the world ranges from 5-18%, though some have reported higher incidences [6]. In our study it was 12% which is similar to the one found by Ghulam Nabi et. al. [7].

The late preterm group had more mothers above 30yrs of age as compared to in the term group (14.6% vs 9.4%). According to Trilla et. al. women with medically indicated late preterm births were older compared to those with spontaneous late preterm births [8]. Tepper et al found that extremes of reproductive age were associated with late preterm birth [9]. However, Nawfal et. al. [10] found no significant difference in the mean maternal age between the term and late preterm babies.

In our study in the late preterm group a higher percentage of mothers had conceived by assisted reproductive techniques (ART) as compared to the term group (9.4% vs 3.4%). Tepper et. al. [9] found that in their study group 7% of the babies were born late preterm in the ART group as compared to 4.3% in non-ART group. Xu et. al. showed in their study that preterm birth rate is one and a half fold higher in ART mothers than non-ART mothers [11] though they have not divided the preterm group further into late preterm and early preterm. They have also shown that preterm birth rate of even singletons is high after assisted reproductive method. This was further corroborated in a study done by Zhu et al who found that the risk of preterm birth was higher in ART group with poorer neonatal outcomes [12]. In light of these findings it should probably be assumed that pregnancy resulting from ART should be considered to be at high risk for late preterm deliveries.

Incidence of multiple births were high in the present study (12% vs 2.3%). Bassil et al found that the strongest associated risk factor for late preterm birth was multi-fetal pregnancy [13].

In our study mothers who had an antenatal complication were more likely to have late preterm birth (42.1% vs 23.9%). Trilla et. al. [8] also showed similar findings. Engle found that maternal chorio-amnionitis, hypertension and premature rupture of membranes are statistically proven contributors to late preterm birth and adverse neonatal outcome [14]. The antenatal complications seen in our study group were gestational diabetes mellitus, hypertensive disorder of pregnancy, anemia, oligohydramnios, cervical incompetence, abruptio placentae, placenta previa, polyhydramnios. Dey et. al. found higher incidences of maternal hypertensive disorder and anemia in their study group [15]. Late preterm group also had more incidence of premature rupture of membranes [14.2% vs 1.7%] which was seen by others as well [15,16].

There was increased incidence of caesarean birth in the late preterm group (40.3% vs 30.3%) which was also seen by Rojas [17]. Engle and Kominiarek stated that majority of the late preterm births were due to improper timing of the elective caesarean deliveries

[18]. However we found that this was not a problem in our series. Most of our late preterms were delivered to mothers who were in labour and there were more emergency caesarean sections than elective caesarean section.

There was no significant gender difference between the two groups. Late preterm babies had lower birth weight as compared to term babies which is expected. But there were more number of small and large for gestational age babies in the late preterm group. (SGA 13.3% vs 8.2%, LGA 3.9% vs 1.8%). Increase in LGA in our study could be due to the high numbers of gestational diabetic mothers delivered here being a perinatal referral centre. Haroon et al found that 24.8% of their babies were growth retarded [16].

Morbidities were as high as 88% in late preterm babies as compared to 18.5% of term babies. Ghulam [7] found that 77% of late preterm babies had any morbidity as compared to 28.3% of term babies. In a study by Femitha et al 42.4% and 20.8% of babies had major and minor morbidity in the late preterm group as compared to 8.4% and 6.8% of term babies [19]. Wagh et al reported that 85% of late preterm neonates had morbidities as compared to 16.3% of term neonates [20].

38.6% of late preterm babies were admitted to NICU as compared to 8.5% of term babies in this study. According to Garcez C et. al. 34.5% of late preterm neonates were admitted to NICU [21]. Araújo et. al. reported that in their study group 54% of late preterm neonates had required NICU admission [6].

The most common morbidities in our study group were risk of sepsis (74.2%) followed by jaundice (28.8%) and respiratory morbidities(14.6%). The incidence of at risk of sepsis could be high in our study group due to department protocol of considering unexplained late preterms at risk of sepsis. According to Wagh et al the most common morbidities were jaundice followed by hypoglycaemia, respiratory morbidities and sepsis [20]. Ghulam [7] found that the most common morbidity was jaundice followed by respiratory morbidity, sepsis, hypoglycaemia and need for mechanical ventilation while Modi et. al. [22] found the common morbidities to be respiratory distress syndrome followed by jaundice and sepsis.

Wang et. al. [4] found almost 54.4% of the late preterm babies had jaundice requiring phototherapy while according to Adamkin there is an eight fold increased risk of developing jaundice with total bilirubin being more than 20mg/dl in a newborn born at 36weeks as compared to the one born between 41-42weeks (23). Marrocchella et. al. found that 25.35% of late preterm babies had jaundice which was significantly higher when stratified for gestational age as compared to term babies [24]. According to Engle et al late preterm infants were 2 times more likely than term infants to have significantly elevated bilirubin values and significantly higher values on days 5 and 7 after birth [14] which was due to immature gastrointestinal system and lower concentration of uridine diphosp-hoglucuronate glucuronyltransferase. Modi et. al. [22] found that late preterm babies were at 2.8times higher risk of developing jaundice compared to term babies. Whyte recommends that late preterm infants should have an assessment for jaundice within 48hrs of birth and should be repeatedly evaluated within the first 10days [25] which is similar to a recommendation by Olusanya et. al. [26] which states that all late preterm infants discharged before 48hrs should be evaluated for jaundice within 1-2days.

The risk of respiratory morbidities is also very significant in late preterm babies.

Ghulam Nabi [7] found respiratory morbidity in 11% of late preterm babies as compared to 2% of term babies. Modi et. al. [22] found respiratory distress syndrome in 44% of late preterm babies as compared to 17% of term babies. Mally et. al. found incidence of respiratory distress syndrome to be 9%, 4% and 3% in 34weeker, 35weeker and 36weeker respectively as compared to 0.7%, 0.2% and 0% in 37weeker, 38-39weeker and 40weeker respectively [27] while de Araújo [6] found RDS in 7.3%, 2.9% and 1.1% of 34weeker, 35weeker and 36weeker respectively. Nawfal [10] found RDS in 3.9% of late preterm babies as compared to 0.1% of term babies.Femitha et. al. [19] found respiratory morbidity in 12.4% of late preterm babies as compared to 5.6% of term babies. We found RDS in 1.7% of late preterm babies as compared to 0% of term babies. We also interestingly found in the late preterm group that mothers who had received antenatal steroids, those babies did not have RDS as compared to late preterm babies whose mothers did not receive steroids.

The incidence of TTN was also high in late preterm babies (7.7% vs 2.1%) compared to term babies. Garcez et. al. [21] found TTN in 40.1% of late preterm babies while de Araújo et. al. [6] found TTN in 36.6%, 28.8% and 17.9% of 34weeker, 35weeker and 36weeker respectively. Nawfal [10] found TTN in 6.9% of late preterm babies as compared to 1.6% of term babies.

In our study a total of 74.2% of late preterm babies were considered at risk of sepsis while 2.1% of babies had suspected sepsis as per clinical features and 1.3% of babies had culture positive sepsis. Garcez [21] found early sepsis in 10.7% of late preterm babies

and Modi et. al. [22] found sepsis in 16.67% of late preterm babies as compared to 6.25% of term babies but they had clubbed all late preterms with sepsis, pneumonia and meningitis in a single group. Femitha [19] found sepsis in 20.8% of late preterm babies as compared to 5.2% of term babies. As per Engle [14] 30% of late preterm babies were evaluated for sepsis while as per Wang et. al. [4] late preterm babies were 3times more likely to be evaluated for sepsis.

Late preterms were also more depressed (2.1% vs 1.7%) and required some resuscitation at birth. de Araújo [6] found that 26.8%, 21.4% and 12.6% of babies at 34weeks, 35weeks and 36weeks required resuscitation at birth. Ghulam Nabi et. al. [7] found perinatal asphyxia in 2.9% of late preterm babies as compared to 1.9% of term babies while Boyle et al(28)found that 17.5% of late preterm babies required resuscitation at birth. It has also been seen in the late preterm group itself that the risk of perinatal depression was higher in those born by elective caesarean section as those compared to those born vaginally 41.4% vs 24% respectively [28]. The risk of resuscitative procedures at birth increases as the gestation drops from 41weeks to 34weeks [29].

The risk of congenital anomalies in late preterm babies was seen to be almost double that seen in term babies 8.6% vs 4% including more congenital heart disease (2.6% vs 0.9%). Boyle et alfound congenital anomalies in 2.9% of late preterm babies as compared to 1.2% of term babies [30].

The incidence of feeding difficulty in late preterm babies was 2.6% as compared to 1.1% in term babies which was not statistically significant but would still increase the maternal stress and the possible duration of hospital stay. Wang et. al. [4] found that 76% of late preterm babies with feeding difficulties had delayed discharge as compared to 28% of term babies. Boyle et. al. [30] found that only 64.2% of late preterm babies were fed breast milk as compared to 72.2% of term babies.

Hypoglycaemia was seen in 2.1% of late preterm babies as compared to only 0.7% of term babies. Ghulam Nabi et. al. [7] found hypoglycaemia in 16% of late preterm babies as compared to only 6.5% of term babies while Modi et. al. [22] found hypoglycaemia in 2.87% of late preterms as compared to 0.89% of term babies. Wagh et. al. [20] reported hypoglycaemia in 23.5%, 40.7% and 28.3% babies at 34weeks, 35weeks and 36weeks respectively while Garcez et. al. [21] reported hypoglycaemia in 21.5% of late preterm babies.

There was a significant difference in the mean weight at discharge between the two groups. According to Jaiswal et. al. [31] 11% of late preterm babies had >10% weight loss at re-admission. Most of the studies report feeding difficulties in the late preterm group.

On an average the duration of mean hospital stay was 7 days in late preterm babies as compared to 5 days in term babies. Early discharge within 72 hrs is rare in our hospital setup. while Garcez et. al. [21] found that the average length of stay was 12days in late preterm babies. Wang et. al. [4] found that late preterm infants were likely to have more morbidities and were hence likely to have delayed discharge as compared to a term infant.

The mean direct medical cost incurred by the late preterm infants was approximately twice (Rs 3533 vs Rs 1654) that of term babies. Wang et. al. [4] also found that there was a significant difference in the median cost incurred by late preterm infant as compared to a term infant and that the nursery costs came down with each week gained beyond 34weeks gestational age. According to Khan et. al. [32] moderate and late preterm birth is associated with significantly increased economic costs over the first 2yrs of life while according to Goyal et. al. [33] discharge of late preterm infants born by vaginal delivery within 48hrs had decreased from 71% to 40% from 1995 to 2000 in US.

In our study 1.3% of the babies died in the late preterm group as compared to 0.2% of term babies. According to Modi et. al. [22] 13.79% of babies died in late preterm group as compared to 6.25% of babies in term group which was also corroborated by Ghulam Nabi et. al. [7] who found neonatal mortality rate as 25 per 1000 live births in the late preterm group as compared to 11 per 1000 live births in the term group de Araújo et. al. [6] found that 7.3%, 3.8% and 2.1% of babies died at 34weeks, 35weeks and 36weeks respectively.

Late preterm babies were often re-admitted (8.6% vs 6%). Oddie et. al. [34] found that infants between 35-37weeks of gestation were 1.7 times more likely to be re-admitted. Wang et. al. [4] found that late preterm infants were 4times more likely to be re-admitted while Tomashek et. al. [35] found that late preterm infants were 1.8 times more likely to be re-admitted.

Conclusion

Late preterms are at risk of increased morbidity and unfavourable outcomes. Proper timing of delivery is important in avoiding unnecessary late preterm births. They have longer hospital stays and higher expenses. Most of the preterm births are late

preterms where simple interventions will go a long way in ensuring survival and thus bringing down infant mortality rate.

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