

Late Preterm and Early Term Neonates: A New Group of High Risk Newborn in Neonatology with Varied Complications

Chetan Kumar, Deepak Sharma* and Aakash Pandita

Department of Neonatology, Fernandez Hospital, Hyderabad, India

*Corresponding author: Deepak Sharma, Department of Neonatology, Fernandez Hospital, Hyderabad, India, Tel: +919462270002; E-mail: dr.deepak.rohtak@gmail.com

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Introduction

Moderate preterm, late preterm, and early term neonates are a new group of neonates which have varied complication when compared with moderate term or late term neonates. Moderate preterm and late preterm deliveries—defined, as delivery between 32 0/7 and 33 6/7 weeks and between 34 0/7 and 36 6/7 weeks of gestation, respectively. The early term delivery—defined as delivery between 37 0/7 and 38 6/7 weeks, moderate term delivery between 39 0/7 and 40 6/7 weeks, late term delivery between 41 0/7 and 41 6/7 weeks. The post term defined as 42 0/7 weeks and beyond [1].

Late preterm infants have been termed The Great Imposters. Infants delivered at late preterm and early term gestational age are at disproportionately higher risk for immediate complications like Respiratory Distress Syndrome (RDS), Transient Tachypnea of Newborn (TTNB), neonatal sepsis, neonatal jaundice, hypoglycemia, Neonatal Intensive Care Unit (NICU) admission [2,3], prolonged hospitalization and re-hospitalisation [4,5], major morbidity, death, and increased health care utilization [6]. The long term complications include poor growth, learning disorder, cerebral palsy, development of psychiatric disorders, poor fetal growth and experience mental and physical developmental delay [7-9]. Late preterm and early term may occur as a result of

- Spontaneous /idiopathic early term or preterm labor
- Prelabor Spontaneous Rupture of Chorioamniotic Membranes (PPROM)
- Maternal and fetal conditions needing an iatrogenic delivery or
- Delivery for non-indicated reasons like patient or provider preference [10]

With the time period there have been gradual increases in the prevalence of late preterm and early term delivery in United States. In 1995, the proportions of deliveries at 34 to 36, and 37 to 38 weeks were 6.2%, and 20.6%, respectively which increased to 7.5%, and 29.7%, respectively in 2008. The absolute increases in deliveries in the late preterm (34–36 weeks) and early term delivery 1.3% and 9.1% [11]. The cause of this change has been suggested because of frequent obstetric intervention leading to increase in the proportion of deliveries in one gestational age window with simultaneous reduction of another. The increase in delivery at 37 to 38 weeks' gestational age is the result of a shift away from delivery at 39 weeks or greater gestational age [12]. A recent meta-analysis conducted by Lisonkova et al on deliveries in the United States, Canada, and 26 other European countries found that the prevalence of late preterm birth ranged from 4.4% to 10.0% [13].

Adverse Infant Outcomes Associated With Delivery from 34 to 38 Weeks' Gestation

Respiratory Disorders

The varied respiratory disorders in this unique group of population can be varied and often includes Transient Tachypnea of The Newborn (TTNB), Respiratory Distress Syndrome (RDS), Persistent Pulmonary Hypertension (PPHN), and rarely apnea [14-17]. Of the affected babies, the incidence of respiratory distress requiring mechanical ventilation corresponded with the degree of prematurity: 3.3% of late preterm infants born at 34 weeks' gestation, 1.7% at 35 weeks, and 0.8% at 36 weeks' gestation [18], showing that with decrease in gestational age of delivery the respiratory morbidity increases [19]. The immature lung structure present before moderate term may be associated functionally with delayed intrapulmonary fluid absorption, surfactant insufficiency, and inefficient gas exchange leading to TTNB and RDS [6,20]. Colin et al concluded that preterm birth, even without any significant neonatal respiratory disease, can still have adverse effects on lung growth and development, leading to reduced pulmonary function and increased morbidity [21]. Ghartey et al. reported that the rates of RDS, transient TTN, pneumonia, surfactant use, and ventilation use were more at 37 weeks compared with 39 weeks and showed inverse relationship with increase in gestation [22]. Although majority of these neonates have transient respiratory issues, but few neonates develop persistent pulmonary hypertension of the neonate (PPHN) or severe hypoxic respiratory failure, conditions requiring advanced respiratory support therapies such as nitric oxide, high-frequency ventilation, and Extracorporeal Membrane Oxygenation (ECMO) [17,23]. In long term these neonates have higher risk of respiratory illnesses and re-hospitalizations in infancy and early childhood [24,25]. The detail review on the respiratory morbidity can be studied elsewhere [26].

Neurologic and Metabolic Issues

Late preterm and early term infants are generally considered to be low-risk groups for neurological and metabolic problems but they are important group who are prone to develop various neurological morbidities in long term. The frequency of GMH-IVH is very low in late preterm and early term infants as there is involution of germinal matrix by 34 weeks of gestation [18,27]. Relative to GMH-IVH there are even fewer data on Periventricular Leukomalacia (PVL) in late preterm and early term infants [6,18,28]. There are currently no specific recommendations for screening and neuro imaging of late preterm, or early term infants. The most commonly seen clinical problem in late preterm and early term infants is feeding difficulties. In a systematic review conducted by Teune et al. on the medical and developmental short-term and long-term outcomes of late preterm

infants, showed that 34 % of these late preterm infants had feeding difficulties and was the most common short-term morbidity encountered by this cohort [27]. Feeding issues of these late preterm infants are extensions of maturational development of feeding abilities of the moderately preterm infant [28]. These vulnerable groups are also prone for metabolic complications like hypoglycemia, hypothermia, jaundice, immunologic problems, increased susceptibility to infection hypocalcemia and polycythaemia. The detail review on the neurological and metabolic issues can be studied in various excellent reviews [29].

Long-Term Outcomes

Between 35 and 41 weeks, there is a 5-fold increase in brain volume and this continued active brain maturation occurs during the last few weeks of gestation because of neurogenesis, synaptogenesis, and dendritic arborization. These processes of neural development get interrupted by delivery as the infant is removed the natural protective environment of the uterus [30]. These late preterm and early term infants have more subtle findings of language delay, attention deficits, lower intelligence, behavioural problems, developmental disability, school failure, and academic achievement issues [8,31-34]. The detail review on the long term outcome of these infants can be read elsewhere [35].

Hospital Readmissions

Readmission rates of late preterm infants are 1.5 to 3 times that of term infants [5,33,36]. The most common causes for re-hospitalisation within 2 weeks of life includes jaundice, infection and feeding problems [5,37]. The cause of recurrent hospitalization after two weeks of age included bronchiolitis, pneumonia, fever and gastrointestinal. The incidence of readmission decrease with increases in gestational age [38,39].

Jaundice and Kernicterus

The early discharge of the late preterm and early term places these neonates for higher adverse effect of neonatal jaundice. The high rates for jaundice admissions in late preterm and early term infants can be understood by considering underlying pathophysiology. Late preterm infants and early terms have a decreased capacity to handle unconjugated bilirubin, decreased hepatic uptake, decreased Uridinediphosphoglucuronate Glucuronosyl Transferase (UGT) activity, and increased enterohepatic circulation, delayed postnatal maturation of hepatic bilirubin uptake and bilirubin conjugation, placing them at higher risk for neonatal jaundice. This hepatic immaturity is added by delayed lactogenesis seen in mothers of these infants [40-42]. These all factors add up leading to high chances of jaundice and neonatal jaundice is most common cause of readmission in these infants within two weeks of life [5].

Future directions

Maturation is a continuous process with no specific goals to be achieved. When the late preterm and early term infants are compared with those born before 34 weeks of gestation, these infants are at lower risks for numerous medical problems, but, compared with those born at 39 and 40 weeks' gestation, they are at higher risks for various morbidity and mortality [43-45]. There are many field of investigation and research including cardiovascular and pulmonary systems, nervous system, metabolic, nutrition, breastfeeding and lactation,

immunology and sepsis, renal and genitourinary systems, development pharmacology [46,47].

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