THE LATE PRETERM INFANT - EVIDENCE IS NOT REASSURING

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Abstract: *Late preterm infants (LPI) are representing the largest category of preterm infants and their number is continuously increasing due to multiple factors. Evidence is suggesting that LPI must be considered an at risk category of newborns. Aim: The papers aims to present the reported evidence regarding short and long term risks of LPI. Material and methods: The literature was search for relevant papers and reviews outlining neonatal and postneonatal complications associated with late preterm delivery. Results: The authors are presenting epidemiological data, etiology, neonatal morbidity, neonatal mortality, and recent data about long term risks of LPI. Conclusion: More and more evidence suggest that late preterm birth has not only increased neonatal morbidity and mortality but also increased risks for unfavourable long term prognosis. Efforts should be done by professional to decrease the rate of late preterm delivery and to improve LPI outcome.*

INTRODUCTION

Prematurity - defined as birth before 37 weeks of gestation - and its complications are still the leading cause of death during the neonatal period. (1-4) In the latest years, due to advances in modern neonatology and obstetrics threshold of viability limits were continuously challenged, more and more extremely preterm infants surviving.(5) While focusing on improving survival of very preterm infants, evidence gathered about the vulnerability of another category of preterm infants, those delivered near term, so called "moderate premature infants" or "near term infants".

Long time ignored by both obstetricians and neonatologists, preterm infants born between 34 weeks 0 days to 36 weeks 6 days are looking very similar to term infants but demonstrate particularities, vulnerabilities, and pathology characteristic to preterm infants, as reported by studies published after the year 2000. Therefore, experts decided to abandon the former terminology and introduced the term of "late preterm infant" (LPI) in order to more clearly underline the fact they are preterm infants and to warn about their increased risk of short and long term complications due to immaturity.(6)

The experts have turned their attention towards this category of preterm infants not just because of the risks, but also because an increased rate of late preterm delivery was signalled all over the world, especially in industrialized countries.(2,7,8) Recommendations and special protocols are needed in order to improve LPI outcome, both during neonatal period and on long term since more and more late prematurity is recognized as a public health problem.(9)

PURPOSE

The aim of this paper is to review and present the most recent reported evidence regarding short and long term risks of LPI.

MATERIALS AND METHODS

The literature was searched for relevant papers and reviews outlining neonatal and postneonatal complications associated with late preterm delivery.

RESULTS AND DISCUSSIONS

Epidemiology

Late preterm infants are representing the highest proportion of the preterm infants - 63.2-79% (2,10,11) - and about 6% of all live births (2), while the global rate of prematurity is around 8%.(3) The proportion of LPI is increasing with decreased gestational age (GA): 19.8% LPI born at 34 weeks, 26.3% at 35 weeks, and 53.8% at 36 weeks gestation, as reported by Gázquez Serrano et al.(3) Also, due to perinatal complications, LPI representing around 20-25% of the admission in neonatal intensive care units (NICU).(3,12) Increased number of LPI is seen mostly in tertiary neonatal centers and in industrialized countries, and this is explained by the rising number of induced births due to maternal or fetal considerations.(13)

Etiology

Multiple circumstances are contributing to the increased rate of late preterm delivery reported in the latest years worldwide. Labor induction or elective cesarean section due to maternal and/or fetal medical reasons is reported by some authors as the main determinant of increased rate of late prematurity (2) as a result of an improved recognition and management of at risk pregnancies.(8,14). Other important contributors to increased rate of LPI are: increased number of pregnancies after assisted conception and, potentially multiple pregnancies as a result of this methods, increased recognition of conditions at risk for preterm delivery or complications as thrombophilia, increased number of scheduled cesarean sections without a clear maternal or fetal indication, increased number of elective cesarean sections performed at patient request, incorrect appreciation of GA, increased maternal age (associated with increased rate of prepartum and intrapartum complications).(2,3,15) Available data suggests that 6.1-23.2% of the late preterm deliveries have no valid indication or are avoidable births.(16-19) In a study of 3.483.496 deliveries of singletons, Reddy et al. (19) reported 292.627 late preterm

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deliveries of which 76.8% were spontaneous or with medical or obstetrical indication, while no indication was found in 23.2% cases and warned that neonatal morbidity and mortality was increased in infants delivered without indication compared to LPI spontaneously born.

Conditions known to carry an increased risk for spontaneous preterm delivery are responsible for a great part of late preterm deliveries: spontaneous preterm rupture of amniotic membrane, chorioamnionitis, multiple pregnancy, maternal hemorrhages, abruptio placentae, pregnancy-induced hypertension and eclampsia, pre-existent or gestational diabetes, maternal age under 20 years, oligohydramnios, lack of prenatal care, smoking, drug abuse, history of preterm delivery, multiparity, reduced interval between pregnancies.(2,3,20-24)

Neonatal pathology

Neonatal morbidity risk

Immaturity of the all organs and systems and circumstances causing or associated to preterm delivery are increasing significantly the neonatal morbidity risk in LPI compared to term infants. The reported neonatal morbidity risk is 2-9 times higher than in term infants (2,15,20,25,26), increasing as GA decreases. (27) Shapiro-Mendoza et al. (27), in a large study comprising 26.170 LPI compared to 377.638 term infants reported that LPI has a 22.2% morbidity rate as compared to 3% in term infants, a relative risk for morbidity two fold increased for every week decrease in GA, a relative risk for morbidity of 20.6 at 34 weeks and of 10.2 at 35 weeks gestation. Association with intrauterine growth restriction increases even more the neonatal morbidity and mortality risks.(28)

Respiratory conditions

Between 27 and 36 weeks gestation the pulmonary alveoli are in the saccular developmental stage (before the alveolar stage), a transitional stage towards complete maturation of the alveoli. Primitive alveoli of this stage are more and more efficient as gas exchange chambers. Still, even near term, alveoli can be insufficient in terms of number and quality for sustained pulmonary functioning. Maintaining functional residual pulmonary capacity is affected by pulmonary compliance, low pulmonary volumes, reduced mobility of the airways, and increased compliance of the thoracic cage.(20,29) At 34 weeks gestation, the pulmonary volume is representing only 47% of the pulmonary volume of a term infant (20) and gas exchange surface is increasing 30 times from 36 to 40 weeks gestation.(30) A reduced inflammatory stimulus may accelerate pulmonary maturation but more intense inflammation, causing severe inflammatory lesions of the alveolar-capillary unit, may induce serum protein leakage into the airways and surfactant inactivation, predisposing to respiratory distress syndrome.(20) Maturation of surfactant system also occurs during this period, ensuring the alveolar stability and preventing alveolar collapse during expiration and hyperinflation during inspiration.(30)

Respiratory complications are the prime morbidities of LPI.(17,22,31-33) Structural and functional immaturity of the lung increases the risk for difficult adaptation immediately after birth and for respiratory conditions:

- transient tachypnea of the newborn (delayed resorption of the fetal pulmonary fluid), mostly in infants delivered by cesarean section and precipitated labor;(13) occurring in 6.4% LPI compared to 0.3% in term infants;(34) an increased risk for severe hypoxemic respiratory failure (malignant transient tachypnea of the newborn) was reported in LPI;(13)
- respiratory distress syndrome (secondary to quantitative and/or qualitative surfactant deficiency), the most severe acute respiratory complication of prematurity; frequency of 10.5% in LPI compared to 0.3% in term neonates;(34)
- apnea (due to a biphasic ventilatory response to hypoxia); occurring in 4-7% of LPI versus 1-2% of term newborns;(15)
- sudden infant death syndrome (due to increased immaturity of the autonomous nervous system overlapping respiratory immaturity).(13,20,30,35)

Respiratory morbidity can be negatively influenced by prenatal conditions as intrauterine growth restriction, low birth weight, cesarean section delivery, maternal diabetes, hypertension, and eclampsia.(20)

Cardiovascular conditions

Functional cardiovascular immaturity may delay transition from fetal to adult circulation, with persistence of the fetal communications - foramen ovale, ductus arteriosus - and persistent high pulmonary vascular resistances. Frequently, this leads to persistent pulmonary hypertension and usually complicates respiratory conditions (transient tachypnea of the newborn, respiratory distress syndrome, meconium aspiration, air-leak syndromes). Persistent elevation of the pulmonary artery pressure with right-to-left shunt and hypoxemia may evolve towards acute hypoxemic cardiorespiratory failure.(13,15) Delayed parasympathetic maturation predisposes LPI to bradycardia.(35)

Neurological influences

Maturity of the nervous system is crucial for the functioning of all organs and systems. Brain development is substantial and rapid during the last weeks before birth: at 35 weeks gestation brain weighs only two thirds of the weight at term, at 36 weeks brain volume is only 60% of the volume at term, the volume of white matter increases 5 times during the last 6-8 weeks of pregnancy, 25% of cerebellum development occurs between 34 and 40 weeks, and up to term the cerebral cortex almost doubles its volume due to huge number of connections between nervous cells and different cerebral areas.(6,9,20,36,37) Preterm infant brain is characterized by anatomic and functional immaturity. Reduced number of giri and sulci, ongoing myelination and cortical neuronal migration, immature white matter, incomplete sinaptogenesis and dendritic arborization are explaining the increased risk of LPI for white and gray matter lesions associated with hypoxia and ischemia.(9,20) Incomplete brain development at birth is also incriminated as an important risk factor for long term developmental, neurological, behavioral and psychiatric abnormalities.(9,20)

During the neonatal period, immaturity of the nervous system is associated with poor regulation of the states, disorganized, unpredictable behavior, and irritability to stimulation.(38) Immaturity of the nervous centers of the brainstem is responsible for the increased risk for apnea, disorganized suck-swallow-breathe pattern, and sleeping difficulties.(39) Hypoxia and ischemia at birth or secondary to severe cardiorespiratory conditions may lead to intraventricular hemorrhage and/or periventricular leukomalacia. The rates of intraventricular hemorrhage are low in PTI but higher than in term infants (0.2-1.4%) (31,34,40) but, same as for periventricular leukomalacia, the real rates are practically unknown since routine head ultrasound is not performed in LPI.(20) The risk for periventricular leukomalacia is three times higher than in term infants.(31,41) Some studies also reported an increased risk for neonatal vascular cerebral infarct in LPI, associated with fetal distress and cardiac congenital defects.(42-44)

Birth hypoxia

The last weeks of gestation are representing a critical developmental period for the maturation of all systems and organs. Biochemical and hormonal changes associated with spontaneous birth are determinant for an adequate transition to extrauterine life.(45) Preterm delivery occurs before maturation

of these processes is finished, therefore respiratory and hemodynamic transition to extrauterine life is affected. Increased need for resuscitation at birth (46% compared to 28% in term infants, $p<0.001$), lower Apgar scores, and increased need for oxygen (32% versus 22%, $p<0.001$) and for respiratory support (1 in 7 LPI) are reported in LPI.(45) The need for resuscitation procedures at birth increases in association with multiparity, multiple pregnancy, maternal hypertension, delivery by cesarean section, low birth weight, and male gender.(3,45)

Hypothermia

After birth, the response to cold is dependent on GA, birth weight, quantity of brown and white fat, and hypothalamic maturation.(15,46) Brown fat accumulation and maturation is maximum at term.(15) Preterm infants lack sufficient quantities of hormones implied in brown fat metabolism - prolactin, leptin, norepinephrine, cortisol, triiodothyronine - and have a reduced capacity to generate heat compared to term infants.(47) Physical characteristics of the LPI are predisposing to heat loss: increased body surface to weight ratio, immature epidermal barrier, reduced flexion due to hypotonia.(15,26,48) In cold environment, LPI can lose 1^0C per minute.(6,49) All these factors are contributing to a nine fold increased risk for hypothermia in LPI.(32)

Gastrointestinal problems

The digestive tract is developing throughout the entire pregnancy but maturation occurs only in the third trimester. Infant born late preterm have decreased intestinal peristalsis, reduced control of the esophageal sphincter, reduce acidic gastric secretions, low pancreatic enzymatic activity, underdeveloped intestinal villi, reduced lactase activity, reduced secretion of bile salts compared to term infants but has a good tolerance of maternal milk.(6,15,26,50,51) All these are affecting nutrients digestion and absorption (50) in an infant with increased nutritional and energy needs compared to term infant.(52) Achievement of nutritional need is impeded also by breastfeeding difficulties.(40,53-56) Multiple factors are influencing breastfeeding: poor coordination of sucking with deglutition and breathing (maturation occurs at around 35 weeks gestation), low oral motor tone, insufficient pressure, poor regulation of states (with sudden transition from an under aroused, sleepy child to an over aroused, fussy and reluctant one), rapid tiredness.(2,6,10,48,50,55-57) Medical conditions at birth also impede breastfeeding initiation and success due to frequent separation of child from his mother. Poor breast attachment and suck are interfering with lactogenesis, aggravating breastfeeding even more (54-56,58) completing a vicious circle that results in increased risk for marked decrease of body weight during the first days of life (physiologic weight loss), slow weight gain, hypoglycemia, hyperbilirubinemia (with increased risk for kern icterus and breastfeeding jaundice), dehydration, and breastfeeding failure.(6,48,52) Complications arising from feeding difficulties are increasing the risk for readmission after discharge from maternity hospital.(32,59) Poor suck-swallow-breathe coordination increases the risk for apnea and aspiration syndrome.(15)

Hypoglycemia

Clinically significant hypoglycemia, reflecting an unbalance between glucose and alternative resources intake and utilization, may occur in circumstances affecting glucose control and regulation.(56) Unfortunately, there is no specific plasmatic glucose concentration or duration of hypoglycemia that can predict the occurrence of permanent neurological lesions in newborns at risk, as LPI are, therefore glucose concentration monitoring is mandatory in these neonates.(56) Lower glycogen stores, immature hepatic glycogenolysis, immature brown fat lipolysis, hormonal imbalances, reduced hepatic gluconeogenesis, deficient ketogenesis, feeding difficulties, and increased incidence of perinatal conditions (hypothermia, birth asphyxia, respiratory distress, infections, etc.) are predisposing LPI to hypoglycemia.(2,15,20,48) The risk of hypoglycemia is inversely correlated with GA (15) and three times higher in LPI compared to term infants.(32,48,60)

Jaundice

Neonatal jaundice is occurring more often and is more prolonged in LPI compared to term infants.(2,15,20,48) Also, LPI are more frequently presenting significant hyperbilirubinemia (32,62) and have an increased risk for severe jaundice (kern icterus) (62) - bilirubin levels > 20 mg/dl are occurring 8 times more often in LPI compared to term infants.(48) Increased bilirubin load and immature bilirubin metabolism - deficient bilirubin uptake, insufficient bilirubin conjugation, deficient bilirubin binding to albumin, low albumin concentrations - are partially responsible for this increased risks. Feeding difficulties and in some circumstances maternal conditions (as, for example, obesity, diabetes, cesarean delivery, hypertension) are delaying lactogenesis II.(54,55,58,63-65) Insufficient breast emptying and stimulation are interfering with the offer-demand response of lactation, the result being a continuous decrease of milk supply.(58) Excessive weight loss, in absence of nutritional supplementation, contributes to jaundice intensification and prolongation, interfering with bilirubin clearance. Increased betaglucuronidase concentrations in breast milk and gut are releasing bilirubin from conjugated compounds and reduced intestinal motility favors bilirubin recirculation into entero-hepatic circulation, inhibiting bilirubin elimination.(9,48,66) Dehydration and associated hypernatremia are increasing the risk of bilirubin toxicity and kern icterus. In USA, kern icterus was reported almost exclusively in LPI.(9,15,67,69)

Infections

Late preterm infants have immature defence against infections due to structural and functional cutaneous and mucous barriers, immature and/or deficient immune responses, umoral and cellular deficiency, lower concentrations of immunoglobulins, cytokines, fibronectin, deficient functioning of antibodies.(2,6,48) Other factors increasing the risk for neonatal infections are the premature birth itself (often associated with chorioamnionitis and neonatal sepsis), increased need for resuscitation at birth, increased rates of perinatal pathology imposing admission to neonatal intensive care units and/or invasive diagnostic and therapeutic procedures, low birth weight, cesarean section delivery.(26,40,69,70) Increased rates of neonatal sepsis compared to term infants is reported by many studies (48,70), increasing the neonatal mortality rate.(70,71) Careful evaluation of the risk factors for neonatal infections in LPI is recommended for early identification of at risk infants, early treatment, and improved outcome.(72) Due to unspecific simptomatology and immunological characteristics, LPI are frequently evaluated for sepsis and more often exposes to antibiotic therapy during the first days of life compared to term infants.(15,27)

Other problems

Hepatic and renal functional immaturity may modify drugs metabolism and elimination. Hepatic and renal dysfunction or failure may occur secondary to severe perinatal conditions (birth asphyxia, hypoxic-ischemic encephalopathy, respiratory distress syndrome, persistent pulmonary hypertension, hypothermia, cholestasis, etc.), complicating the clinical development and increasing the mortality risk.(6)

Late preterm infants have also an increased risk for electrolytic disturbances, mostly hypocalcemia.(2)

Readmission during neonatal period is more frequent

in LPI compared to term infants due to suspected sepsis, feeding difficulties, and intense jaundice.(3,26,27,54,56,59)

Neonatal mortality risk

Infants born late preterm have an increased neonatal mortality risk compared to term infants - 1.7-9.1.(15,22,71,73-76) Association with intrauterine growth restriction increases the neonatal mortality rate up 44 times compared to term infants with appropriate for gestational age birth weight.(78) Congenital malformations and birth from a multiple pregnancy are also risk factors for increased neonatal mortality.(20,52) Same as neonatal morbidity, neonatal mortality of LPI increased with decreased GA.(15)

Long term outcome

The most worrisome aspect related to late preterm delivery for the long term outcome is the immaturity of the central nervous system. Exposure to extrauterine life in a moment of rapid and complex brain development is not without risks, as studies in the latest years have shown. On long term, compared to term infant, LPI has an increased risk for delayed general growth and development (lower weight and height in the first two years of life) (26,41,78), often associated with increased metabolic risks into adulthood: hyperglycemia, abnormal lipidic prophile, arterial hypertension.(26,79)

Many studies have reported increased rates of neurological and cognitive deficits and conditions: cerebral palsy, seizures, mental retardation, lower academic performances, neurocognitive functioning deficiencies, reading and speech difficulties.(6,31,41,78,80) As in smaller preterm infants, the incidence of neurodevelopmental effects is increased as GA is decreasing.(41,78) Neurosensorial deficits (hearing and ophthalmologic) are often reported with rates similar to those of 30-33 weeks gestation preterm infants.(26,41,78,81) Infants born late preterm are also at increased risk for behavior and psychiatric conditions: internalization and attention deficits, attention deficit - hyperactive disorder (ADHD), autism spectrum disorders, emotional problems, social difficulties (26,41,78,79,82,83), schizophrenia.(78,83) Social and financial difficulties reported in LPI are related to lower academic performances, lower social positions and incomes.(78)

Perinatal complications and delayed growth and development of LPI are incriminated for the increased risk of medical conditions in childhood: respiratory infections, asthma, and diabetes.(20,41,78,83,84)

Studies are also reporting that the increased risk for mortality persists after the neonatal period.(84) A meta-analysis found the LPI have a 5.9 fold increased risk for mortality during the first year of life compared to term infants.(31)

CONCLUSIONS

Obstetricians, neonatologists, and pediatricians must inform parents about the increased vulnerability, short and long term morbidity and mortality risks associated with late preterm delivery. Also, compliance to experts' recommendation to avoid elective delivery before 39 weeks gestation in well-dated pregnancies is expected to reduce the rate of late preterm births.(20,85) Revision of protocols regarding pregnancies at risk for preterm delivery and continuous improvement of the management of these pregnancies is also expected to decrease the number of LPI. Extended prophylactic corticosteroid administration beyond 34 weeks gestation as well as tocolysis for preterm labor (whenever feasible) may help to decrease the incidence and severity of respiratory distress syndrome, the most frequent and severe complication of prematurity. Prompt recognition and treatment of conditions associated with late prematurity may prevent short and long term complications. Safe discharge from maternity hospital, preferably no sooner than 48 hours after delivery for LPI without complications may prevent readmissions. Collaboration with family physician is mandatory due to high rates of feeding difficulties, prolonged jaundice, and increased risk for infections in LPI. Also, a careful monitoring of growth, development, and neurological development may identify in time long term complications of late preterm birth, allowing early intervention and improved outcome.

REFERENCES

1. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet. 2015;385:430-440.
2. Machado Jr. LC, Passini Jr. R, Rodrigues Machado Rosa I. Late prematurity: a systematic review. J Pediatr (Rio J). 2014;90(3):221-231.
3. Gázquez Serrano IM, Arroyos Plana A, Díaz Morales O, Herráiz Perea C, Holgueras Bragado A. Antenatal corticosteroid therapy and late preterm infant morbidity and mortality. An Pediatr (Barc). 2014;81(6):374-382.
4. Committee on Obstetric Practice. ACOG committee opinion No. 404 April 2008. Late-preterm infants. Obstet Gynecol. 2008; 111(4):1029-1032.
5. Seaton SE, King S, Manktelow BN, Draper ES, Field DJ. Babies born at the threshold of viability: changes in survival and workload over 20 years. Arch Dis Child Fetal Neonatal Ed. 2013;98:F15-F20.
6. Raju TN. The problem of late-preterm (near term) births: a workshop summary. Pediatr Res. 2006;60(6):775-776.
7. Yoder BA, Gordon MC, Barth Jr WH. Late-preterm birth: does the changing obstetric paradigm alter the epidemiology of respiratory complications? Obstet Gynecol. 2008;111:814-822.
8. Davidoff MJ, Dias T, Damus K, Russell R, Bettegowda VR, Dolan S, et al. Changes in the gestational age distribution among U.S. singleton births: impact on rates of late preterm birth, 1992 to 2002. Semin Perinatol. 2006;30:8-15.
9. Bhutani VA. Late Preterm Births: Major Cause of Prematurity and Adverse Outcomes of Neonatal Hyperbilirubinemia. Indian Pediatrics. 2012;49:704-705.
10. McIntire DD, Leveno KJ. Neonatal mortality and morbidity rates in late preterm births compared with births at term. Obstet Gynecol. 2008;111:35-41.
11. Guasch XD, Torrent FR, Martínez-Nadal S, Cerén CV, Saco MJ, Castellví PS. Late preterm infants: a population at underestimated risk. An Pediatr (Barc). 2009;71:291-298.
12. McCall E, Craig S. Neonatal Intensive Care Outcomes Research and Evaluation (NICORE) Steering Group. Neonatal Care in Northern Ireland 2006. Belfast, Northern Ireland: Neonatal Intensive Care Outcomes Research and Evaluation Group; 2009.
13. Jain L. The Late Preterm Infant. Neonatology Today. 2007;2(5):1-14.
14. Joseph KS, Allen AC, Dodds L, Vincer MJ, Armson BA. Causes and consequences of recent increases in preterm birth among twins. Obstet Gynecol. 2001;98:57-64.
15. Engle WA, Tomashek KM, Wallman C. Committee on Fetus and Newborn, American Academy of Pediatrics. Late preterm infants: a population at risk. Pediatrics. 2007;120(6):1390-1401.
16. Laughon SK, Reddy UM, Sun L, Zhang J. Precursors for late preterm birth in singleton gestations. Obstet Gynecol. 2010;116(5):1047-1055.
17. Loftin RW, Habli M, Snyder CC, Cormier CM, Lewis DF,

Defranco EA. Late preterm birth. Rev Obstet Gynecol. 2010;3(1):1-9.
18. Holland MG, Refuerzo JS, Ramin SM, Saade GR, Blackwell SC. Late preterm birth: how often is it avoidable?. Am J Obstet Gynecol. 2009;201(404):e1-4.
19. Reddy UM, Ko CW, Raju TN, Willinger M. Delivery indications at late preterm gestations and infant mortality rates in the United States. Pediatrics. 2009;124(1):234-240.
20. Kugelman A, Colin AA. Late Preterm Infants: Near Term But Still in a Critical Developmental Time Period. Pediatrics. 2013;132:741-751.
21. Selo-Ojme DO, Tewari R. Late preterm (32-36 weeks) birth in a North London hospital. J Obstet Gynaecol. 2006;26:624-626.
22. Khashu M, Narayanan M, Bhargava S, Osiovich H. Perinatal outcomes associated with preterm birth at 33 to 36 weeks' gestation: a population-based cohort study. Pediatrics. 2009;123(1):109-113.
23. Dietz PM, England LJ, Shapiro-Mendoza CK, Tong VT, Farr SL, Callaghan WM. Infant morbidity and mortality attributable to prenatal smoking in the U.S. Am J Prev Med. 2010;39(1):45-52.
24. Langenveld J, Ravelli AC, van Kaam AH, van der Ham DP, van Pampus MG, Porath M, et al. Neonatal outcome of pregnancies complicated by hypertensive disorders between 34 and 37 weeks of gestation: a 7 year retrospective analysis of a national registry. Am J Obstet Gynecol. 2011;205 (6):540.e1-e7.
25. Bird MT, Bronstein JM, Hall RW, Lowery CL, Nugent R, Mays GP. Late Preterm Infants: Birth Outcomes and Health Care Utilization in the First Year. Pediatrics. 2010;126:e311-e319.
26. Santos IS, Matijasevich A, Silveira MF, Sclowitz IK, Barros AJ, Victora CG, et al. Associated factors and consequences of late preterm births: results from the 2004 Pelotas birth cohort. Paediatr Perinat Epidemiol. 2008;22:350-359.
27. Shapiro-Mendoza CK, Tomashek KM, Kotelchuck M, Barfield W, Nannini A, Weiss J, et al. Effect of late-preterm birth and maternal medical conditions on newborn morbidity risk. Pediatrics. 2008;121(2):e223-232.
28. Mathews TJ, MacDorman MF. Infant mortality statistics from the 2006 period linked birth/infant death data set. Natl Vital Stat Rep. 2010;58(17):1-31.
29. Langston C, Kida K, Reed M, Thurlbeck WM. Human lung growth in late gestation and in the neonate. Am Rev Respir Dis. 1984;129(4):607-613.
30. Smith LJ, McKay KO, van Asperen PP, Selvadurai H, Fitzgerald DA. Normal development of the lung and premature birth. Paediatric Resp Rev. 2010;11(3):135-142.
31. Teune MJ, Bakhuizen S, Gyamfi Bannerman C, Opmeer BC, van Kaam AH, van Wassenaer AG, et al. A systematic review of severe morbidity in infants born late preterm. Am J Obstet Gynecol. 2011; 205(4):374.e1-e9.
32. Wang ML, Dorer DJ, Fleming MP, Catlin EA. Clinical outcomes of near-term infants. Pediatrics. 2004;114(2):372-376.
33. Young PC, Korgenski K, Buchi KF. Early readmission of newborns in a large health care system. Pediatrics. 2013;131(5):e1538-1544.
34. Bastek JA, Sammel MD, Paré E, Srinivas SK, Posencheg MA, Elovitz MA. Adverse neonatal outcomes: examining the risks between preterm, late preterm, and term infants. Am J Obstet Gynecol. 2008;199(4):e1-e8.
35. Hunt CE. Ontogeny of Autonomic Regulation in Late Preterm Infants Born at 34-37 Weeks Postmenstrual Age. Semin Perinatol. 2006;30:73-76.
36. Kinney HC. The near-term (late preterm) human brain and risk for periventricular leukomalacia: a review. Semin Perinatol. 2006;30:81-88.
37. Adams-Chapman I. Neurodevelopmental outcome of the late preterm infant. Clin Perinatol. 2006;33(4):947-964.
38. Jain L. School outcome in late preterm infants: a cause for concern. J Pediatr. 2008;153(10):25-31.
39. Darnall RA, Ariagno RL, Kinney HC. The late preterm infant and the control of breathing, sleep and brainstem development: a review. Clin Perinatol. 2006;33(4):883-914.
40. Melamed N, Klinger G, Tenenbaum-Gavish K, Herscovici T, Linder N, Hod M, et al. Short-term neonatal outcome in low-risk, spontaneous, singleton, late preterm deliveries. Obstet Gynecol. 2009;114(2Pt1):253-260.
41. Petrini JR, Dias T, McCormick MC, Massolo ML, Green NS, Escobar GJ. Increased risk of adverse neurological development for late preterm infants. J Pediatr. 2009;154(2):169-176.
42. Bruno CJ, Beslow LA, Witmer CM, Vossough A, Jordan LC, Zelonis S, et al. Hemorrhagic Stroke in Term and Late Preterm Neonates. Arch Dis Child Fetal Neonatal Ed. 2014;99(1):F48-F53.
43. Armstrong-Wells J, Johnston SC, Wu YW, Sidney S, Fullerton HJ. Prevalence and predictors of perinatal hemorrhagic stroke: results from the Kaiser pediatric stroke study. Pediatrics. 2009;123:823-828.
44. Wu YW, Escobar GJ, Grether JK, Croen LA, Greene JD, Newman TB. Chorioamnionitis and cerebral palsy in term and near-term infants. JAMA. 2003;290:2677-2684.
45. de Almeida MF, Guinsburg R, da Costa JO, Anchieta LM, Freire LM, Junior DC. Resuscitative procedures at birth in late preterm infants. J Perinatol. 2007;27:761-765.
46. Sedin G. Physical environment. Part 1: the thermal environment of the newborn infant. In: Martin RJ, Fanaroff AA, Walsh MC (eds.). Fanaroff and Martin's Neonatal-Perinatal Medicine. 8th ed. Philadelphia, PA: Mosby Elsevier; 2006. p. 585-597.
47. Symonds ME, Mostyn A, Pearce S, Budge H, Stephenson T. Endocrine and nutritional regulation of fetal adipose tissue development. J Endocrinol. 2003;179:293-299.
48. Stuckey-Schrock K, Schrock SD. Late preterm infants may look like their full-term counterparts, but they face many more challenges. Here's what to keep in mind. The Journal of Family Practice. 2013 62(4):E3-E8.
49. Fowlie PW, McGuire W. ABC of preterm birth. Immediate care of the preterm infant. BMJ. 2004;329:845-848.
50. Femitha P, Vishnu Bhat B. Early Neonatal Outcome in Late Preterms. Indian J Pediatr. 2012;79(8):1019-1024.
51. Neu J. Gastrointestinal maturation and feeding. Semin Perinatol. 2006;30:77-80.
52. Refuerzo JS, Momirova V, Peaceman AM, Sciscione A, Rouse DJ, Caritis SN, et al. the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Neonatal Outcomes in Twin Pregnancies Delivered Moderately Preterm, Late Preterm and Term. Am J Perinatol. 2010;27(7):537-542.
53. Escobar GJ, Greene JD, Hulac P, Kincannon E, Bischoff K, Gardner MN. Rehospitalisation after birth hospitalisation: patterns among infants of all gestations. Arch Dis Child. 2005; 90(2):125-131.
54. Radtke JV. The paradox of breastfeeding-associated morbidity among late preterm infants. J Obstet Gynecol Neonatal Nurs. 2011;40:9-24.

55. Walker M. Breastfeeding the Late Preterm Infant. JOGNN. 2008;37:692-701.
56. Adamkin DH. Feeding problems in the late preterm infant. Clin Perinatol. 2006;33(4):831-837.
57. Geddes DT, Kent JC, Mitoulas LR, Hartmann PE. Tongue movement and intra-oral vacuum in breastfeeding infants. Early Human Development. 2008;84(7):471-477.
58. Meier PP, Furman LM, Degenhardt M. Increased Lactation Risk for Late Preterm Infants and Mothers: Evidence and Management Strategies to Protect Breastfeeding. J Midwifery Womens Health. 2007;52:579-587.
59. Natile M, Ventura ML, Colombo M, Bernasconi D, Locatelli A, Plevani C, et al. Short-term respiratory outcomes in late preterm infants. Italian Journal of Pediatrics. 2014:40:52
60. Jensen A. Late preterm babies – their problems and care. Infant. 2011;7(4):126-130.
61. Sarici SU, Serdar MA, Korkmaz A, Erdem G, Oran O, Tekinalp G, et al. Incidence, course, and prediction of hyperbilirubinemia in near-term and term newborns. Pediatrics. 2004;113:775-780.
62. Bhutani VK, Johnson LH, Maisels MJ, Newman TB, Phibbs C, Stark AR, et al. Kernicterus: Epidemiological strategies for its prevention through systems-based approaches. J Perinatol. 2004;24:650-662.
63. Rasmussen KM, Kjolhede CL. Prepregnant overweight and obesity diminish the prolactin response to suckling in the first week postpartum. Pediatrics. 2004;113:e465-e471.
64. Dewey KG, Nommsen-Rivers LA, Heinig MJ, Cohen RJ. Risk factors for suboptimal infant breastfeeding behavior, delayed onset of lactation, and excess neonatal weight loss. Pediatrics. 2003;112:607-619.
65. Arthur PG, Smith M, Hartmann PE. Milk lactose, citrate, and glucose as markers of lactogenesis in normal and diabetic women. Journal of Pediatrics Gastroenterology and Nutrition. 1989;9:488-496.
66. Gartner LM. Breastfeeding and Jaundice. Journal of Perinatology. 2001;21:S25-S29.
67. American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia. Clinical Practice Guideline: Management of Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation. Pediatrics. 2004;114:297-316.
68. Maisels MJ, Bhutani VK, Bogen D, Newman TB, Stark AR, Watchko JF. Hyperbilirubinemia in the newborn infant > or =35 weeks' gestation: an update with clarifications. Pediatrics. 2009;124:1193-1198.
69. Dani C, Corsini I, Piergentili L, Bertini G, Pratesi S, Rubaltelli FF. Neonatal morbidity in late preterm and term infants in the nursery of a tertiary hospital. Acta Paediatr. 2009;98:1841-1843.
70. Cohen-Wolkowiez M, Moran C, Benjamin DK, Cotten MC, Clark RH, Benjamin DKJr, et al. Early and Late Onset Sepsis in Late Preterm Infants. Pediatr Infect Dis J. 2009;28(12):1052-1056.
71. Kramer MS, Demissie K, Yang H, Platt RW, Sauve R, Liston R. The contribution of mild and moderate preterm birth to infant mortality. Fetal and Infant Health Study Group of the Canadian Perinatal Surveillance System. JAMA. 2000;284(7):843-849.
72. Stocker M, Berger C, McDougall J, Giannoni E, Taskforce for the Swiss Society of Neonatology and the Paediatric Infectious Disease Group of Switzerland. Recommendations for term and late preterm infants at risk for perinatal bacterial infection. Swiss Med Wkly. 2013;143:w13873.
73. Oddie SJ, Hammal D, Richmond S, Parker L. Early discharge and readmission to hospital in the first month of life in the Northern Region of the UK during 1998: a case cohort study. Arch Dis Child. 2005;90:119-124.
74. Machado LCJr, Passini RJr, Rosa IR, Carvalho HB. Neonatal outcomes of late preterm and early term birth. Eur J Obstet Gynecol Reprod Biol. 2014;179:204-208.
75. Araújo BF, Zatti H, Madi JM, Coelho MB, Olmi FB, Canabarro CT. Analysis of neonatal morbidity and mortality in late-preterm newborn infants. J Pediatr (Rio J). 2012; 88:259-266.
76. Tomashek KM, Shapiro-Mendoza CK, Davidoff MJ, Petrini JR. Differences in mortality between late preterm and term singleton infants in the United States, 1995–2002. J Pediatr. 2007;151(5):450-456.
77. Pulver LS, Guest-Warnick G, Stoddard GJ, Byington CL, Young PC. Weight for gestational age affects the mortality of late preterm infants. Pediatrics. 2009;123(6):e1072-1077.
78. Moster D, Terje Lie R, Markestad T. Long term medical and social consequences of preterm birth. N Engl J Med. 2008;359(3):262-273.
79. Victora CG, Adair L, Fall C, Hallal PC, Martorell R, Richter L, Sachdev HS. Maternal and Child Undernutrition Study Group: Maternal and child undernutrition: consequences for adult health and human capital. Lancet. 2008;371:340-357.
80. Himmelmann K, Hagberg G, Beckung E, Hagberg B, Uvebrant P. The changing panorama of cerebral palsy in Sweden. IX. Prevalence and origin in the birth-year period 1995–1998. Acta Paediatr. 2005;94:287-294.
81. Baron IS, Erickson K, Ahronovich MD, Coulehan K, Baker R, Litman FR. Visuospatial and verbal fluency relative deficits in 'complicated' late-preterm preschool children. Early Hum Dev. 2009;85(12):751-754.
82. Talge NM, Holzman C, Wang J, Lucia V, Gardiner J, Breslau N. Late-preterm birth and its association with cognitive and socioemotional outcomes at 6 years of age. Pediatrics. 2010;126(6):1124-1131.
83. Lindstrom K, Lindbald F, Hjern A. Psychiatric morbidity in adolescent and young adults born preterm: a Swedish national cohort study. Pediatrics. 2009;123(1):e47-53.
84. Crump C, Sundquist K, Sundquist J, Winkleby MA. Gestational age at birth and mortality in young adulthood. JAMA. 2011;306(11):1233-1240.
85. American College of Obstetricians and Gynecologists. ACOG practice bulletin No. 10: clinical management guidelines for the obstetrician gynecologist. Induction of labor; 1999.