

Late-preterm birth – neonatologist's point of view. Part 1

ANITA CHUDZIK¹, PAWEŁ KRAJEWSKI³, JAROSŁAW KALINKA^{2,3},
MICHAŁ SKOCZYLAŚ², MAŁGORZATA POKRZYWNICKA¹

Abstract

In the last twenty years the number of preterm births is still increasing, but the biggest group of them are late-preterm newborns (34^{0/7}-36^{6/7} weeks' gestation). For many years late-preterm newborns have been treated as normal healthy newborns but many researches revealed that obstetricians and neonatologists should change their attitude to late-preterm newborns and pay more attention on them. Late-preterm newborns (LPN) are at an increased risk of morbidity and mortality during neonatal period and for longer time than their term counterparts. Neonatal complications of LPN include: temperature instability, serum glucose level instability, circulatory and respiratory problems, dysfunction of digestive and immunological systems, jaundice and neurological problems. All of them are the reasons for prolonged and multiple hospitalizations in these patients. In conclusion it is very important for future to continue three-level obstetric and neonatal care in Poland to decrease the rates of preterm delivery and to enhance maturity of late-preterm newborns.

Key words: prematurity, late-preterm infants, outcome, morbidity, mortality

Preterm delivery is one of the most important problems of present neonatology and obstetrics. It is the determinant factor of neonatal morbidity and mortality. In spite that only 6-14% pregnancies are terminated before 37 weeks' gestation, as many as 70-80% of all newborns deaths concerns preterm newborns [1-3]. Most searches are focused on extremely preterm neonates. However among preterm deliveries which number is still increasing in the last 20 years, the late-preterm newborns are dominant [4-7]. Neonatologists and obstetricians think that there is a need to pay more attention to late-preterm newborns still treated as functionally mature newborns. Late-preterm newborns are at higher risk of morbidity and mortality during neonatal period and later. The risk of death among late-preterm neonates is much lower than among neonates delivered before 32 weeks' gestation but because the number of late-preterm deliveries is increasing they have a big impact on total neonatal mortality [5, 6]. According to Pulvera et al. [8], if preterm neonate delivered before 34 weeks' gestation with features of intrauterine growth restriction (IUGR) the risk of mortality of these babies in the first year of life is 22 times higher than among neonates in the same weeks' gestation but without IUGR.

In United States in 1981-2003 the number of premature deliveries has increased for about 31%. Three quarter from these newborns constitute the late-preterm (called sometimes "near term") newborns [4, 6, 9, 10]. In Denmark in 1995-2004 the number of LPN has increased for about 22% [11]. The crucial point in newborns care was to consider the late-preterm newborns as the group of higher risk of mortality and morbidity than term newborns [4, 10].

In 2005 in United States The National Institute of Child Health and Human Development set the experts' group to search the problems of late-preterm newborns [4]. This group suggests to give a name to the newborns born between 34^{0/7}-36^{6/7} weeks' gestation (between 239-259 days' gestation) „late preterm”, instead of „near term” or „almost term” neonates, to prevent a lack of attention to problems connected with this group of neonates [4]. At the beginning the late-preterm newborns can behave as normal newborns but they are not functionally mature and always we should remember that they are at higher risk of morbidity, prolonged hospitalization and mortality compared to term newborns [4, 9, 12-15].

Maternal medical complications of pregnancy such as hypertensive disorders of pregnancy (HDP), asthma,

¹ Division of Neonatology, Department of Perinatology, Ist Chair of Obstetrics and Gynecology, Medical University of Łódź, Poland

² Medical and Environmental Pregnancy Health Hazards Unit, Department of Perinatology, Ist Chair of Obstetrics and Gynecology, Medical University of Łódź, Poland

³ Members of PREBIC (Preterm Birth International Collaborative), USA

intrauterine growth restriction (IUGR), congenital infections, congenital anomalies, multiple pregnancy, premature rupture of membranes (PROM) and increased maternal age constitute the risk factors for delivery of late-preterm newborns [10, 11]. In such conditions the decision of induction of preterm delivery has to be balanced – the morbidity and/or mortality of newborn associated with prematurity against maternal consequences associated with continuation of pregnancy [7].

Late-preterm newborns delivered before 37 weeks’ gestations differs from term ones. There are many diffe-

rences in the post-delivery course of adaptation of many organs and the most important systems between late-preterm newborns and term newborns [16]. Neonatal complications of late-preterm newborns include: temperature instability, serum glucose level instability, circulatory and respiratory systems problems, dysfunction of digestive and immunological systems, jaundice and neurological problems. Late-preterm newborns are more likely to have late sepsis and prolonged birth hospitalization and/or re-hospitalization [4, 6, 7, 11, 14, 15, 17, 18] (Table 1).

Table 1. Neonatal complications of late-preterm newborns according to National Institute of Child Health and Human Development [6]

Diseases	Late-preterm newborns	Term newborns
Respiratory distress syndrome	12%-33-34 weeks’ gestation 2%-35-36 weeks’ gestation	0.11%
Transient tachypnoe of neonates	11.6%-33-34 weeks’ gestation 5%-35-36 weeks’ gestation	0.7%
Apnea	4-5%	–
Temperature instability	10%-35-36 weeks’ gestation	–
Hypoglycemia	18%-35-36 weeks’ gestation	4%
Jaundice as the reason or prolonged hospitalization	16.3%-35-36 weeks’ gestation	0.03%
Kernicterus	higher risk	–
Feeding problems	7.19	
Re-hospitalization	5.3%-9.6% -33-37 weeks’ gestation	3.6-4,4%
Long-term growing complications	higher risk	
Mortality	higher risk	

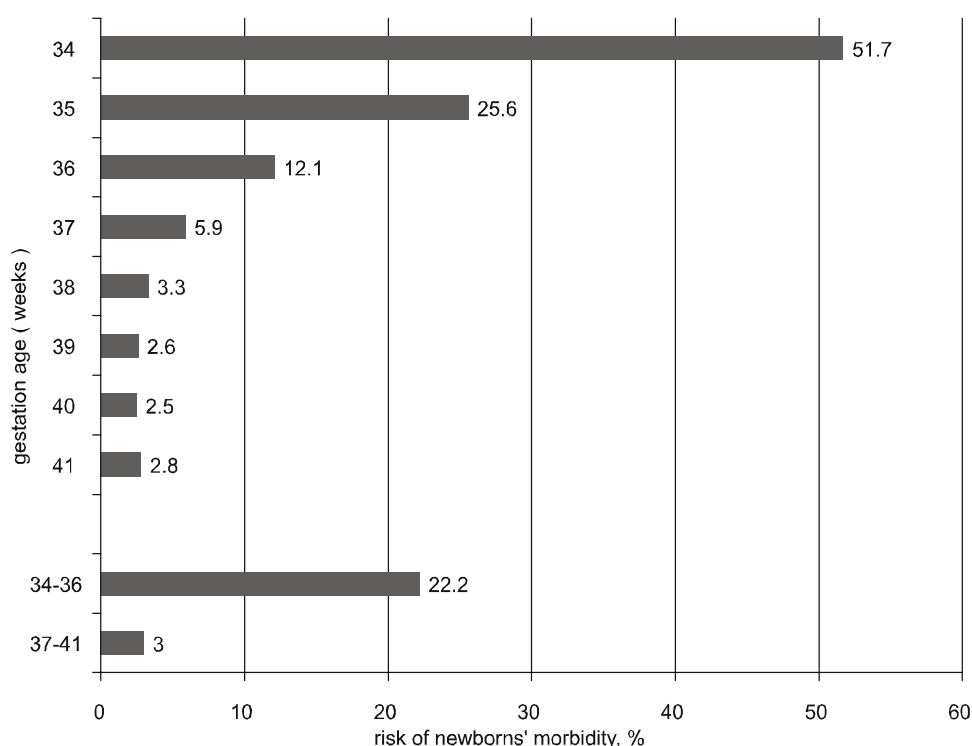


Fig. 1. Risk of newborns' morbidity depending on gestation age [11]

Bastek et al. concluded that the risk of neonatal complications in late-preterm newborns is higher than in term newborns and is decreasing about 23% every week of gestation over 32 or 34 weeks' gestation [19].

Demestre Guasch et al. searched the large group of preterm newborns born between 34(0/7) and 36(6/7) weeks' gestation ($n = 2003$) and term neonates ($n = 3215$), and they concluded that mortality and morbidity of late-preterm newborns are statistically significant higher than in term newborns [20]. Late-preterm newborns had statistically significant higher risk of Neonatal Intensive Care Unit admission ($p < 0.0001$), elective cesarean section delivery, assisted and/or mechanical ventilation, need to treat jaundice and hypoglycemia than term ones. Mortality of late-preterm newborns was estimated for about 5.0 ‰ in contrast to 1.1 ‰ in term neonates [20]. Demestre Guasch et al. stated that decision of late-preterm delivery should be always weighted against probable expected neonatal complications and future neonatal and maternal consequences of pregnancy continuation [20].

Elective cesarean section delivery compared with vaginal delivery contributes to iatrogenic prematurity, increased frequency of Transient Tachypnea of Newborn (TTN), Respiratory Distress Syndrome (RDS) and morbidity in late-preterm newborns [21-23].

Late-preterm newborns are at higher risk for hypothermia, early hypoglycemia and adaptation period disturbances in the first 12 hours of life as the results of prematurity. They can provoke developing of Respiratory Distress Syndrome [3, 4, 9].

Transient Tachypnea of Newborn (TTN) and Respiratory Distress Syndrome (RDS) are more common in preterm newborns born between 34^{0/7} and 36^{6/7} weeks' gestation than in term newborns. This situation results from delayed lung fluid clearance, relative deficiency of surfactant, the smooth progression of labor and lack of proper hormonal stimulation [4, 17, 18].

Jain [18] study found that pregnant women in 33 weeks' gestation are qualified for tocolysis and antenatal steroids, but when their pregnancy lasted a few days more and crossed over to the "magic limit" of 34 weeks' gestation, they are not routinely considered for this treatment. But we should remember that approximately 50% of these late-preterm newborns will require intensive care. This publication suggests that the inaccuracies in the estimation of pregnancy duration could result in incorrect decision about the delivery date. This could be one of the main reasons of several-fold higher risk of mortality and morbidity observed in the group of late-pre-

term newborns as compare to the term ones. Jain suggests that there is need to work out the strategies to enhance maturity of late-preterm newborns by more wide use of antenatal steroids. [18]. From the other side McIntire [10] noticed that there are no documented benefits from antenatal steroids after 34 weeks' gestation [10].

Late-preterm newborns are more likely to have apnea. The risk of sudden infant death syndrome (SIDS) is twice higher than in term newborns. (1.4 case/1000 in 33-36 weeks' gestation vs. 0.7 case /1000 in neonates born after 37 weeks' gestation) [4].

Late-preterm newborns relatively quickly adept to enteral feeding but their gastrointestinal tract are still functionally immature compared with term neonates. Some complications in enteral feeding are observed in this group of neonates such as problems in coordination of suckling and swallowing, problems in breast feeding and putting on weight. Some changes in microbiologic environment of intestines of late-preterm newborns can result in future diseases such allergy or diabetes [4].

The prolonged jaundice and the risk of its damaging effects on central nervous system are very important problem connecting with late prematurity [4, 9, 12]. In late-preterm newborns the immaturity of the blood-brain barrier, infections and hypoxia are the additional factors which can damage the endothelium increasing the risk of kernicterus. In late-preterm newborns the jaundice can prolong to 4-6-12 weeks after delivery and this is the reason why these babies should not be discharged from hospital with bilirubin level exceeding 15 mg/dl [16].

The late-preterm newborns because of functional immaturity of their liver and kidney are at higher risk of incorrect drug dosing and cholestasis during parenteral nutrition [4].

Late-preterm newborns are more susceptible to infections than term newborns. Prolonged afterbirth hospitalization, most common hospitalization in Neonatal Intensive Care Units and less matured immune system are the additional risk factors of infections [4, 14]. Wang et al. suggest that the risk for infections among preterm infants of 34^{0/7} and 36^{6/7} weeks' gestation is five-fold higher than in term newborns [11], and Tomashek et al. emphasized higher risk for re-hospitalization in this group as compared to term infants. (3.5% vs. 2%) [11]. According to Shapiro-Mendoza et al. [7] morbidity rates of newborns born in 34, 35 and 36 weeks' gestation are 20, 10 and 5 times higher as compared to term newborns (Fig. 1).

Early after birth hospital discharge of late-preterm newborns, often during first 2 days of life, is one of the

reasons of common re-hospitalization and increased costs of their treatment [4]. In 2003 in the United States approximately 10 billions dollars were spend on medical care of newborns and about 12% of this money were spend on preterm neonates (3/4 of them are the newborns born between 34^{0/7} and 36^{6/7} weeks' gestation) [13].

The brain of late-preterm newborns is less matured than in term ones and the intensity of cerebral development during the late fetal phase is the reason of the higher risk of brain injury. The neurodevelopmental impairments of late-preterm newborns will be described in the second part of this paper.

It is important to promote three-degree mother and newborn perinatal health care system in Poland and to put into practice prematurity prophylactic program (primeval or derivative prophylactic program) [24].

Primeval prophylactic program such as free perinatal health care, early recognition and better treatment of women with chronic and/or pregnancy-related diseases, discovering the high risk pregnancy, future-mother education is the most effective and important [5, 24].

Derivative prophylactic program is unfortunately less effective [24]. According to Kramer [5] obstetricians and pediatricians should inform pregnant women about long-term consequences for babies delivering between 34^{0/7}-36^{6/7} postconceptional weeks and decision about late-preterm delivery should be weighed against the risk of neonatal and maternal risk.

Conclusions

Concluding that newborns born between 34^{0/7}-36^{6/7} postconceptional weeks – called late-preterm newborns – are at higher risk of morbidity and mortality during neonatal period and later. Despite the improved medical techniques the late-preterm newborns are at three-fold higher risk for developing neurodeveloping impairments, cerebral palsy and psychomotor delay than term infants. Greater awareness of consequences of late-prematurity, better mother and newborns health care and working out the standards of care for late-preterm newborns and their mothers are needed.

References

- [1] Sikora J., Bakon I., Kellas S. et al. (2004) *Poród przedwczesny w materiale ośrodka referencyjnego*. Klin. Perinat. Ginekol. 40, 3: 51-53.
- [2] Kmita G. (2003) *Rozwój psychiczny dzieci urodzonych przedwcześnie* [In:] K.M. Kornacka. *Noworodek przedwcześnie urodzony – pierwsze lata*. PZWL Warszawa.
- [3] Garg M., Devaskar S.U. (2006) *Glucose metabolism in the late preterm infant*. Clin.Perinatol. 33(4): 853-70.
- [4] Raju T.N., Higgins R.D., Stark A.R., Leveno K.J. (2006) *Optimizing care and outcome for late-preterm (near-term) infants: a summary of the workshop sponsored by National Institute of Child Health and Human Development*. Pediatrics 118 (3): 1207-14.
- [5] Kramer M.S. (2009) *Late preterm birth: appreciable risks, rising incidence*. J. Pediatr. 154(2): 159-160.
- [6] Melamed N., Klinger G., Tenenbaum-Gavish K. et al. (2009) *Short-term neonatal outcome in low-risk, spontaneous, singleton, late preterm deliveries*. Obstet. Gynecol. 114(2 PT 1): 253-260.
- [7] Shapiro-Mendoza C.K., Tomashek K.M., Kotelchuck M. et al. (2008) *Effect of late-preterm birth and medical condition on newborn morbidity risk*. Pediatrics 121(2): 223-32.
- [8] Pulver L.S., Guest-Warnick G., Stoddard G.J. et al. (2009) *Weight for gestational age affects the mortality of late preterm infants*. Pediatrics 123(6): 1072-7.
- [9] Adamkin D.H. (2009) *Late preterm infants: severe hyperbilirubinemia and postnatal glucose homeostasis*. J. Perinatol. 29 (suppl. 2): 12-17.
- [10] McIntire D.D., Leveno K.J. (2008) *Neonatal mortality and morbidity rates in late preterm births compared with births at term*. Obstet.Gynecol. 111(1): 35-41.
- [11] Khashu M., Narayanan M., Bhargava S., Osiovič H. (2009) *Perinatal outcomes associated with preterm birth at 33 to 36 weeks' gestation: a population-based cohort study*. Pediatrics 123(1): 109-13.
- [12] Buthani V.K., Johanson L. (2006) *Kernicterus in late preterm infants cared for as term healthy infants*. Semin. Perinatol. 30(2): 89-97.
- [13] Cuevas K.D., Silver D.R., Brooten D. et al. (2005) *The cost prematurity: hospital charges at birth and frequency of rehospitalizations and acute care visits over the first year of life: a comparison by gestational age and birth weight*. Am. J. Nurs. 105(7): 56-64
- [14] Benjamin D.K., Stoll B.J. (2006) *Infection in late preterm infants*. Clin. Perinatol. 33(4): 871-82.
- [15] Engle W.A., Tomashek K.M., Wallman C., Committee on Fetus and Newborn, American Academy of Pediatrics (2007) *„Late-preterm” infants: a population at risk*. Pediatrics 120(6): 1390-401.
- [16] Kornacka K.M. (2003) *Opieka specjalistyczna nad dzieckiem urodzonym przedwcześnie*. [In:] K.M. Kornacka. *Noworodek przedwcześnie urodzony – pierwsze lata*. PZWL Warszawa.
- [17] Jain L. (2008) *School outcome in late preterm infants: a cause for concern*. J. Pediatr. 153(10): 25-31.
- [18] Jain L. (2007) *Morbidity and mortality in late-preterm infants: more than just transient tachypnea!* J. Pediatr. 151(5): 445-6.
- [19] Bastek J.A., Sammel M.D., Pare E. et al. (2008) *Adverse neonatal outcome: examining the risks between preterm, late preterm and term*. Am. J. Obstet. Gynecol. 199(4): 329-31.
- [20] Demestre Guasch X., Raspall Torrent F., Martinez-Nadal S. et al. (2009) *Late preterm infants: A population at underestimated risk*. An. Pediatr. (Barc.) 71(4): 291-8.
- [21] De Luca R., Boulvain M., Irion O. et al. (2009) *Incidence of early neonatal mortality and morbidity after late-preterm and term cesarean delivery*. Pediatrics 123: 1064-71.

- [22] Fuchs K., Wapner R. (2006) *Elective cesarean section and induction and their impact on late preterm births*. Clin.Perinatol. 33(4): 793-801.
- [23] Malloy M.H. (2009) *Impact of cesarean section on intermediate and late preterm births: United States, 2000-2003*. Birth. 36(1): 26-33.
- [24] Gadzinowski J. (2003) *Problem wcześniactwa w Polsce*. Med.Wieku Rozwojowego (3 suppl. 1): 31-34.



Anita Chudzik

Division of Neonatology, Department of Perinatology
Ist Chair of Obstetrics and Gynecology
Medical University of Łódź
37 Wileńska Street, 94-016 Łódź, Poland
e-mail: anita-chudzik@wp.pl