Late preterm neonates – a significant neonatal problem?

Czy „późne wcześniaki" to znaczący problem neonatologiczny?

Tołłoczko Justyna, Kornacka Maria K., Sonczyk Anna, Zapała Łukasz

Neonatal and Intensive Care Department, Medical University of Warsaw

Abstract

Background: *The survival rate and quality of life of extremely low birthweight infants remain to be one of the main challenges of modern neonatology. Therefore, pre-term children born after 32 weeks of gestation with more normal birthweight, have become a relatively minor medical problem in comparison.*

Objectives: *The aim of the following work was to compare the frequency of complications occurring in neonatal period in groups of late preterms and full-term neonates.*

Methods: *A group of 725 late pre-term babies, born between 34-36 6/7 GA, constituted the study group and has been analyzed retrospectively. 5040 neonates born at term comprised the control group. The results were analyzed statistically using chi-square test.*

Results: *Respiratory disturbances were diagnosed in 178 neonates in the study group (24.55%), while in the control group in 138 cases (2.74%), p=0.0000. Intrauterine infections were present in 92 neonates in the study group (12.69%) and in 327 infants in the control group (6.49%), p=0.0000. Hiperbilirubinemia developed in 520 neonates in the study group (71.72%), and in 1895 babies in the control group (37.60%), p=0.0000.*

Conclusions:

1. *Respiratory disturbances, hiperbilirubinemia and intrauterine infections are more frequently observed in late preterms.*
2. *Increased morbidity in late preterm neonates prolongs the time of hospitalization.*

Key words: **neonatology** / **newborns** / **premature infants** / **complications** /

Corresponding author:
Maria K. Kornacka
Neonatal and Intensive Care Department, Medical University of Warsaw
Karowa 2, 00-315 Warsaw
tel. (22) 59 66 155
tel./fax. (22) 59 66 484
e-mail: mariak@szpitalkarowa.pl

Otrzymano: **15.07.2010**
Zaakceptowano do druku: **01.09.2010**

Ginekol Pol. 2010, 81, 693-698

Streszczenie

Wstęp: *Wielkim wyzwaniem dla współczesnej neonatologii jest zwiększenie przeżywalności oraz poprawa jakości życia noworodków urodzonych z ekstremalnie małą masą ciała. Dlatego też stan zdrowia dzieci urodzonych po 32 tygodniu ciąży wydaje się mniejszym problemem medycznym.*

Cel: *Celem pracy było porównanie występowania powikłań w okresie adaptacyjnym w grupie późnych wcześniaków i noworodków donoszonych.*

Metoda: *Retrospektywnie przeanalizowano grupę 725 późnych wcześniaków urodzonych między 34-36 t c. 6/7 GA. Grupę kontrolną stanowiło 5040 noworodków urodzonych w terminie. Wyniki opracowano statystycznie przy użyciu testu chi².*

Wyniki: *Zaburzenia oddychania były zdiagnozowane u 178 noworodków w grupie badanej (24,55%) a w grupie kontrolnej u 138 (2,74%) p=0,0000. Zakażenie wewnątrzmaciczne rozpoznano u 92 (12,69%) późnych wcześniaków i u 432 (6,49%) noworodków urodzonych w terminie p=0,0000. Żółtaczka wystąpiła u 520 (71,72%) noworodków w grupie badanej i u 1895 (37,60%) w grupie kontrolnej p=0,0000.*

Wnioski:

1. *W grupie późnych wcześniaków obserwujemy częściej zaburzenia oddychania, zakażenia wewnątrzmaciczne i żółtaczki*
2. *Wyższa zachorowalność w grupie późnych wcześniaków wydłuża czas hospitalizacji.*

Słowa kluczowe: **neonatologia** / **noworodki** / **wcześniaki** / **powikłania** /

Introduction

The survival rate and quality of life of extremely low birthweight infants remain to be one of the main challenges of modern neonatology. Therefore, pre-term children born after 32 weeks of gestation with more normal birthweight, have become a relatively minor medical problem in comparison. However, the existence and issues of the subgroup consisting of more mature pre-term babies, born after 35 but before 37 GA, i.e. near-term infants [1], has become increasingly present in worldwide literature.

Other authors include in that group children born after 34 GA and characterize them as late pre-term infants. Those neonates comprise a population that is at higher risk of complications, both in perinatal and in the subsequent development. Quite often the birth weight and length of late pre-term and full-term neonates are similar. However, despite the fact that the infants are in fact immature in terms of physiology and metabolism, there is a noticeable tendency to treat them as full-term babies, both by parents ad medical staff. Nevertheless, the risk of morbidity and mortality in that group remains to be considerably higher in comparison with the group of neonates born at term [2, 3, 4].

Aim of the study

The aim of the study was to compare the frequency of the complications occurring in neonatal period in groups of late pre-term and full-term neonates.

Material and methods

6375 neonates, born at the 2nd Department of Obstetrics and Gynecology Medical University of Warsaw, were hospitalized in the, Neonatal and Intensive Care Department Medical University of Warsaw between 2008-2009. The study group consisted of 725 late pre-term babies, i.e. neonates born between 34-36 6/7 weeks gestation.

The control group included 5040 neonates born at term. The following factors have been analyzed retrospectively: completion of pregnancy, general condition of neonates assessed according to the Apgar score at 1 minute, birth weight and length, presence of respiratory disturbances (respiratory distress syndrome, adaptation respiratory disorders), hiperbilirubinemia, intrauterine infections, intrauterine growth restrictions (IUGR) (birth weight <10 centile), intraventricular hemorrhages and duration of hospitalization.

The results were analyzed statistically using chi-square test with Yates modification in Statistica 9.0 software (StatSoft®). P-value below 0.05 was considered as statistically significant.

Results

6375 neonates were hospitalized in the Neonatal and Intensive Care Department Medical University of Warsaw between 2008 and 2009.725 (11,37%) late pre-term neonates, born after the completion of 34 but before 37 GA, were included into the study group. 5040 (79.06%) neonates, born after 37 GA, comprised the control group. (Figure 1).

The remaining 610 (9,5%) children were neonates born before 34 GA and they were excluded from the study). Median gestational age in the study group was 36 GA, while in the control group it was 39 GA. 350 children (48.28%) from the study group and 1416 neonates (28.10%) from the control group were born by cesarean section, p=0.0000. (Figure 2).

In the study group 614 children (84.69%) were born in good overall condition (8-10 points in the Apgar score), 95 (13.1%) were born in moderate condition (4-7 points in the Apgar score) and 13 (1.79%) were born in severe condition (0-3 Apgar score). In the control group the statistics were: 4805 (95.34%), 183 (3.63%) and 41 (0.81%) respectively. (Figure 3).

Median birth weight and length were 2550g and 50cm in the study group and 3430g and 55cm in the control group, respectively. (Figure 4, 5)

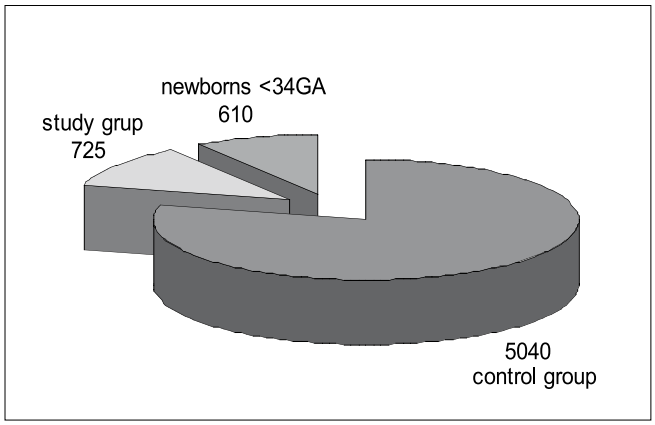

Figure 1. Number of children in the study and control groups. The remaining (610) children are neonates born <34 GA.

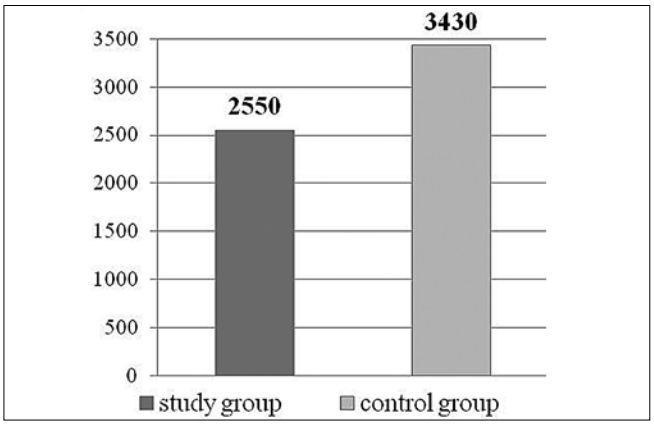

Figure 4. Median birth weight in the study and control group.

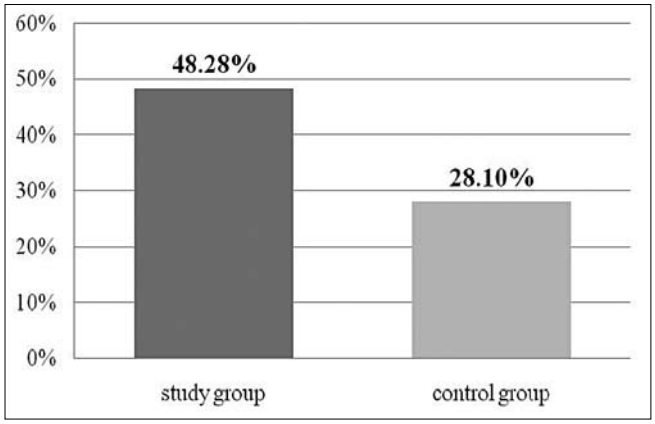

Figure 2. Percentage of cesarean sections in the study and control group.

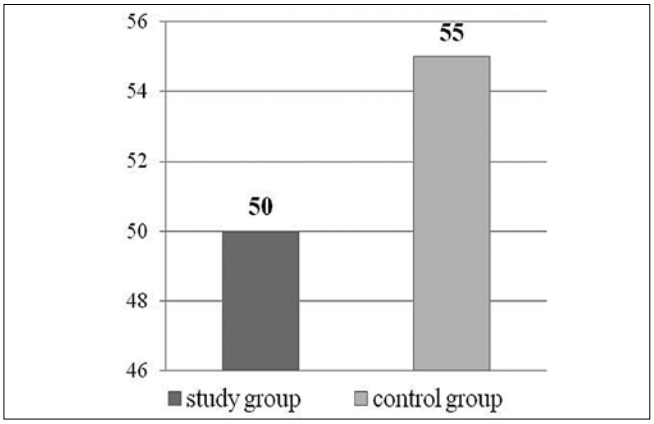

Figure 5. Median birth length in the study and control group.

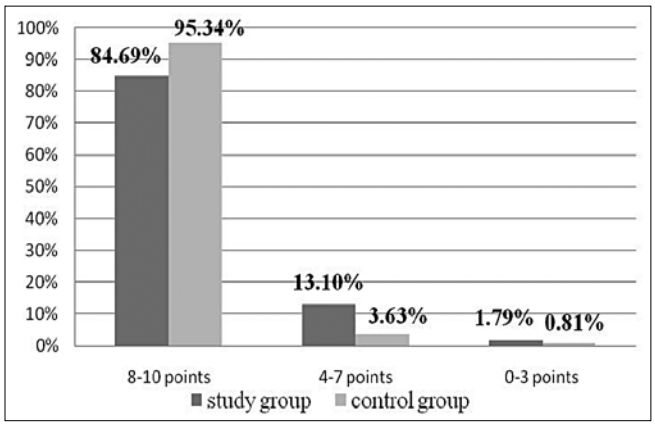

Figure 3. Apgar score result in 1 minute: the study group vs. the control group.

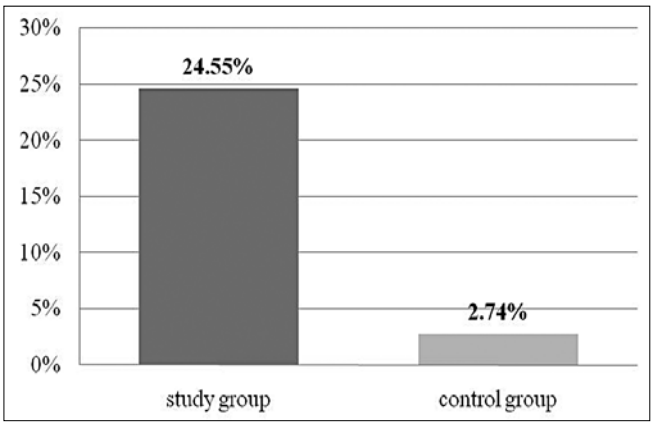

Figure 6. Respiratory disturbances incidence in the study and control group.

Respiratory disturbances in the adaptation period were diagnosed in 178 neonates (24.55%) in the study group and in 138 infants (2.74%) in the control group. (Figure 6). It was a statistically significant result, p=0.0000.

Intrauterine infections were present in 92 (12.69%) neonates in the study group and in 327 babies (6.49%) in the control group. (Figure 7). It was a statistically significant result, p=0.0000.

520 (71.72%) neonates from the study group and 1895 (37.60%) from the control group developed hiperbilirubinemia (Figure 8). It was a statistically significant result, p=0.0000.

Intraventricular hemorrhages were diagnosed in 65 (8.97%) neonates in the study group and in 64 (1.27%) in the control group. (Figure 9). It was a statistically significant result, p=0.0000.

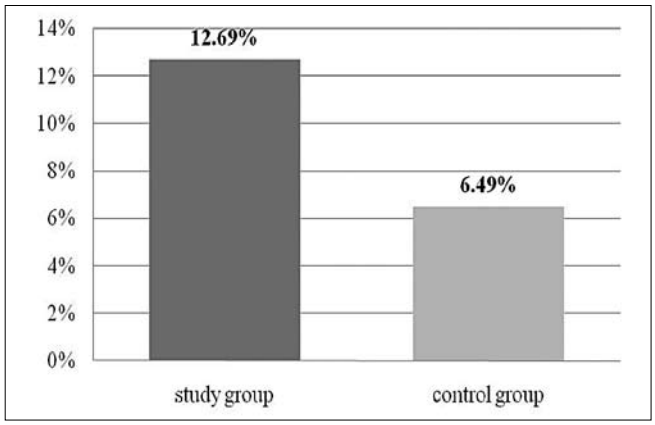

Figure 7. Intrauterine infections incidence in the study and control group.

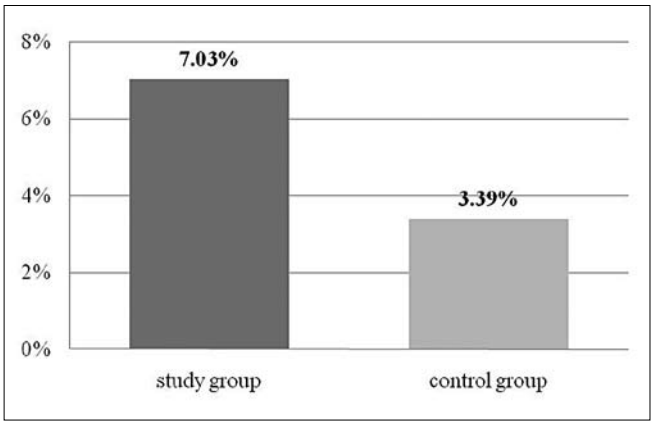

Figure 10. Hypotrophy incidence in the study and control group.

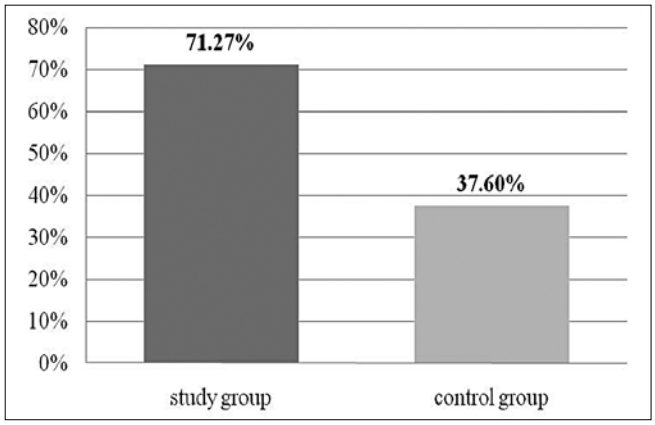

Figure 8. Hiperbilirubinemia incidence in the study and control group.

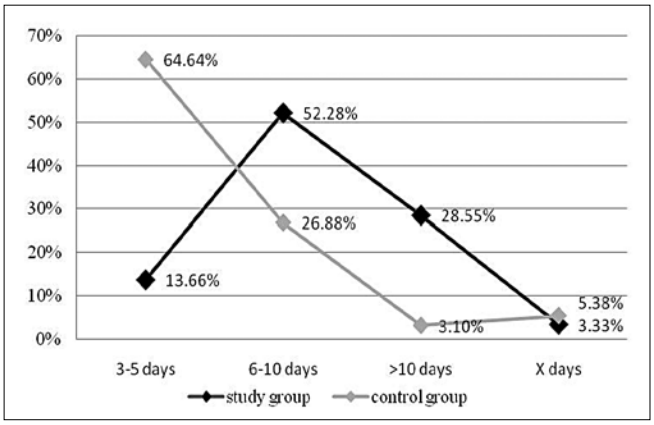

Figure 11. Length of hospitalization in the study and control group.

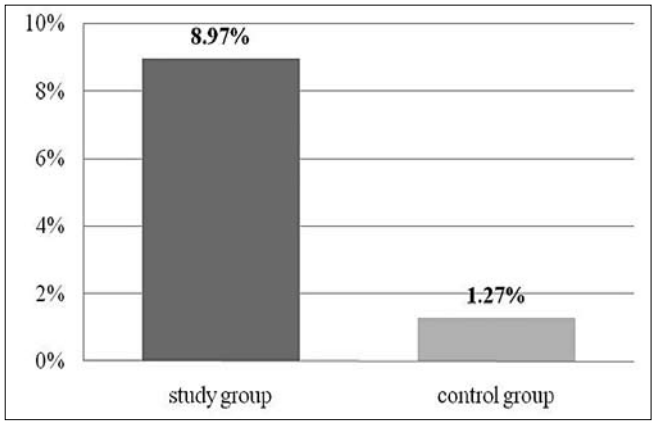

Figure 9. Intraventricular hemorrhages incidence in the study and control group.

IUGR was diagnosed in 51 (7.03%) neonates in the study group and in 171 (3.39%) in the control group. (Figure 10). It was a statistically significant result, p=0.0000.

Length of hospitalization was divided into four time intervals as follows: I – from 3 to 5 days, II – from 6 to 10 days, and III > 10 days. IV group comprised neonates that had to be referred to other specialist departments in order to continue the treatment (X days). The results have been presented in Figure 11.

Discussion

In recent years the percentage of late pre-term neonates in the population of live-born children has been steadily increasing [2, 3]. In 1990 in the USA that group amounted to 7.3%. In the presented material from Clinic of Neonatology and Neonatal Intensive Care the percentage reached 11.37% in years 2008-2009. Several hypotheses need to be taken into consideration to explain the origin of that phenomenon. First of them is connected with the use of more and more advanced methods of assisted conception, which dramatically increases the frequency of multiple pregnancies, predominantly finished before 37 GA. Another hypothesis assumes that development of obstetric care resulted in the increase of the number of induced labor and cesarean sections in the last decade [2, 5, 6].

Analysis of changes in the time of pregnancy completion over the period of 10 years (1992-2002) in the USA revealed a decrease in gestational age at birth from 40 to 39 GA. It is believed to be dependent on race, ethnical conditions and to affect especially white, non-Latin American women [7].

Elective cesarean sections performed between 38 and 40 GA are connected with lower risk of morbidity in neonatal period. [5, 6] Regardless of the fact whether cesarean section was planned or spontaneous, it is always connected with an increase of the frequency of complications.

According to the American College of Obstetricians and Gynecologists, the decision to complete a pregnancy before 39 weeks gestation should be made due to medical reasons (occurrence of complications) or after lung maturity of the fetus has been documented [9]. Prospective studies of De Luca et al. on the group of 56549 neonates revealed that elective caesarean section should not be performed before term [8]. Reddy et al. analyzed 348496 labors between 34 and 41 GA in the USA in 2001 and concluded that the lowest incidence of perinatal complications was observed in the group of children born at 39 0/7 and 39 6/7 GA.

In our study 48.28% of late pre-term neonates and 28,15% of babies in the control group were born by cesarean section, which was a statistically significant difference. Median gestational age was 36 weeks in the study group and 39 weeks in the control group. General condition of neonates from both groups assessed in 1 minute in the Apgar scale did not differ significantly. Nevertheless, a slightly smaller percentage of children in the study group (85%) born in good overall condition in comparison with the full-term babies (95%) ought not to go unnoticed. Noticeably fewer children were born in moderate condition in the group of late pre-term neonates (13%) in comparison with the control group (4%). The percentage of children born in severe condition was similar (1 and 2%, respectively).

In the first days of life in the group of near-term neonates the following have been observed more frequently: respiratory failure, greater weight loss, dehydratation, hiperbilirubinemia. Those children develop disturbances in sucking and swallowing coordination and breathing. They are more often admitted to hospital in their first week of life in comparison with full-term babies [10].

Hiperbilirubinemia of the neonatal period is more intense in case of late pre-term neonates. The peak of bilirubin concentration is observed later than in full-term children, that is on 4-6 day of life according to some authors, or even on 5-7 day of life according to others [11, 12]. The correlation between the gestational age and intensity of jaundice in perinatal period is particularly emphasized in the literature [12, 13]. The bilirubin concentration assessment should be performed within the first 24 hours of life. It is necessary to determine precisely when a child may be discharged from hospital, depending on the intensity of jaundice, gestational age, body weight and number of days of life – not earlier than after 52 hours of life. The use of nomograms, recommended by American Academy of Pediatrics, decreases the risk of repeated hospitalization and complications of hiperbilirubinemia [10, 14, 15].

In the study group, hiperbilirubinemia was observed twice as often (in 71.27%) as in the control group, and the difference was statistically significant. Similar results were reported by Wang, but the difference between the study and the control group was not so obvious. In the group of late-term neonates, jaundice was diagnosed in 54%, whereas in the full-term children group in 37.9% [1].

In our study the percentage of neonatal jaundice reached 37.6%, as well. The difference in percentages observed in the study group may be the consequence of the fact that Wang enrolled in the group of the late preterm babies neonates born after 35 GA, while in our study the study group consisted of children born after 34 GA

Respiratory disturbances in the form of respiratory distress syndrome (RDS) and adaptation respiratory disorders occur more frequently in the group of neonates born near term [10, 11, 15, 16]. Yoder et al. [17] during a 10-year follow-up concluded that the decrease of mean gestational age of children born from 40 to 39 GA, results in the increase of the number of late pre-term neonates and greater morbidity (RDS, MAS, pneumonia) [10]. Thus, a 24-hour observation in order to estimate the risk of potential respiratory disturbances is recommended.

In the presented analysis the respiratory disturbances incidence (RDS or pulmonary adaptation disturbances) reached 24.55% in the study group and only 2.74% in the control group. The difference is statistically significant. Wang et al. observed similar percentage of respiratory disturbances in the study group (30%) [1]. The observed children proved to be in need of additional oxygen in the first hours of their life more often, as well. Vital signs should be controlled every 4 hours in the first day of life, and in children in stable condition every 8 hours. Other serious conditions such as apnea, bradycardia, periodical breathing may occur as well. In that group of neonates sudden infant death syndrome (SIDS) is observed twofold more frequently than in full-term babies. Thus, in such case supine position is recommended during the sleep. American Academy of Pediatrics also recommends pulsoxymetry monitoring in order to detect any potential episodes of desaturation [10].

Wang et al. reported that sepsis incidence in the group of late pre-term neonates is even threefold more frequent than in the group of full-term children [1]. In the presented analysis performed in our department, intrauterine infections were observed statistically significantly more frequently in the study than in the control group.

Minimal recommended length of hospitalization after birth for neonates born between 34 and 35 GA. is 72 hours, and between 35 and 36 GA. – 48 hours [8]. In our department, majority of children from the study group (52.8%) was hospitalized from 6-10 days. In the control group 64.64% neonates remained in the hospital for 3 to 5 days.

Prior to being discharged from the hospital, late pre-term children should meet the following criteria: stabilized, increasing body weight and stabilized concentration of bilirubin. It is also absolutely essential that the mothers are educated and informed accordingly so that they fully realize their children are in the group of high risk of morbidity and mortality in comparison with full-term babies. A control visit within 24-48 hours since a neonate was discharged home is necessary, with special attention being paid to nutrition, body weight increase and neonatal jaundice [10].

Conclusions

1. In the group of late preterm neonates respiratory disturbances, hiperbilirubinemia and intrauterine infections are observed more frequently than in full-term children.
2. Increased morbidity in the group of late preterm neonates increases the time of hospitalization.

References

1. Wang M, Dorer D, Fleming M, [et al.]. Clinical Outcomes of Near-Term Infants. *Pediatrics.* 2004, 114, 372-376.
2. Engle W, Tomashek K, Wallman C, [et al.]. Late-preterm infants: a population at risk. *Pediatrics.* 2007, 120, 1390-1401.
3. Pulver L, Guest-Warnick G, Stoddard G, [et al.]. Weight for gestational age affects the mortality of late preterm infants. *Pediatrics.* 2009, 123, 1072-1077.
4. Escobar G, Clark R, Greene J. Short – term outcomes of infants born at 35 and 36 weeks gestation: we need to ask more questions. *Semin Perinatol.* 2006, 60, 775-778.
5. Rekomendacje Polskiego Towarzystwa Ginekologicznego: cięcie cesarskie. *Ginekol Pol.* 2008, 79, 378-384.
6. Troszyński M, Niemiec T, Wilczyńska A. Ocena funkcjonowania selektywnej trójstopniowej opieki perinatalnej na podstawie analizy umieralności okołoporodowej wczesnej i cięć cesarskich w 2008 roku. *Ginekol Pol.* 2009, 80, 670-677.
7. Davidoff M, Dias T, Damus K, [et al.]. Changes in the gestational age distribution among U.S. singleton births : impact on rates of late preterm birth, 1992-2002. Semin. *Perinatol.* 2006, 30, 8-15.
8. De Luca R, Boulvain M, Irion O, [et al.]. Incidence of early neonatal mortality and morbidity after late-preterm and term cesarean delivery. *Pediatrics.* 2009, 123, 1064-1071.
9. Reddy U, Ko C, Royin T, [et al.]. Delivery indications at late-preterm gestations and infant mortality rates in the United States. *Pediatrics.* 2009, 124, 234-240.
10. Raju T, Higgins R, Stark A, [et al.]. 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.* 2006, 118, 1207-1214.
11. Santos I, Matijasevich A, Silveira M, [et al.]. Associated factors and consequences of late preterm births: results from the 2004 Pelotas birth cohort. *Paediatr Perinat Epidemiol.* 2008, 22, 350-359.
12. Sarici S, Serdar M, Korkmaz A, [et al.]. Incidence, Course and Prediction of Hyperbilirubinemia in Near – Term and Term Newborns. *Pediatrics.* 2004, 113, 775-780.
13. Keren R, Luan X, Friedman S, [et al.]. A comparison of alternative risk – assessment strategies for predicting significant neonatal hyperbilirubinemia in term and near – term infants. *Pediatrics*. 2008, 121, 170-179.
14. Barclay L. Predischarge bilirubin, gestational age may predict risk of hyperbilirubinemia. *Medscape Medical News.* 2009, Jan,17.
15. Bhutani V, Maisels J, Stark A, [et al.]. Management of jaundice and prevention of severe neonatal hyperbilirubinemia in infants. 35 Weeks Gestation. *Neonatology.* 2008, 94, 63-67.
16. Mc Intire D, Leveno K. Neonatal mortality and morbidity rates in late preterm births compared with births at term. *Obstet Gynecol.* 2008, 111, 35-41.
17. Yoder B, Gordon M, Barth W Jr. Late-preterm birth: does the changing obstetric paradigm alter the epidemiology of respiratory complications? *Obstet Gynecol.* 2008, 111, 814-822.

KOMUNIKAT

Informuję, iż podczas
Konferencji Naukowej Sekcji Genetyki Klinicznej
Polskiego Towarzystwa Ginekologicznego

odbywającej się

w Karpaczu w dniach 01-03.10.2010 roku,

dnia 03.10.2010 r. o godz. 9.00
przeprowadzone będzie

zebranie sprawozdawczo-wyborcze Sekcji Endokrynologii Ginekologicznej PTG

Prezes Sekcji Endokrynologii
Ginekologicznej PTG
Prof.zw. dr. hab. n. med. Piotr Skałba

Sekretarz Sekcji Endokrynologii
Ginekologicznej PTG
dr n. med. Paweł Madej