

PERINATAL COMPLICATIONS IN TWO COHORT GROUPS OF PRETERM NEWBORNS IN INTENSIVE CARE UNIT FOR CHILDREN'S DISEASES OF UNIVERSITY CLINICAL HOSPITAL MOSTAR

Vedran Bjelanović^{1,2}, Marjana Jerković Raguž^{1,3}, Matea Galić¹, Ana Čuljak¹,
Ivana Bjelanović¹ & Vajdana Tomić^{1,2}

¹University School of Medicine Mostar, Mostar, Bosnia and Herzegovina

²Clinic of Gynaecology and Obstetrics of the University Clinical Hospital Mostar, Mostar, Bosnia and Herzegovina

³Department of Neonatology and Intensive Care Unit, Clinic for Children's Diseases, University Clinical Hospital Mostar, Mostar, Bosnia and Herzegovina

received: 29.3.2017;

revised: 3.7.2017;

accepted: 28.9.2017

SUMMARY

Aim: To determine the frequency and type of complications in two cohort groups of preterm newborns.

Subjects and methods: The research involved 100 preterm newborns divided into two groups according to their gestational age: newborns from 24 to 33+6/7 weeks GA and newborns from 34 to 36+6/7 weeks GA. Parameters which were observed with mother were: age, number of births, course and complications in pregnancy. Parameters with infant: gestational age, weight, newborn small for gestational age (IUGR), asphyxia, respiratory distress syndrome, sepsis, hyperbilirubinemia, apnea, anemia, intracranial hemorrhage and metabolic disorder (hypoglycaemia, hypocalcaemia). Research criterion for exclusion was all preterm newborn infants with chromosome anomalies which cause death, fetal death during pregnancy (in utero) and newborns (born after full 37 weeks).

Results: After dividing exminees according to their gestational age into two groups, the group with higher gestational age (from 34 to 36+6/7 weeks GA) had 76% and the group with lower gestational age (from 24 to 33+6/7 weeks GA) had 24% of infants. The course of pregnancy was pathological in 68% of pregnancies and normal with 32% of pregnancies, the difference is statistically significant. 97% of pregnant woman had pathological course in the group of preterm newborns with lower GA. The most common perinatal complication was hyperbilirubinemia in 42% of cases, while sepsis was present in 1% of infants. The first group of infants (< 33 GA) had mostly combination of 3 or more complications in 46% of infants while the other group mostly had hyperbilirubinemia in 50% and combination of complications in 24% of infants.

Conclusion: Perinatal complication occurrence depends on premature birth and course of pregnancy. Larger number of complications and harder complications which may result with death are more common in patients with lower gestational age (24 to 33+6/7 weeks GA) than in patients with higher gestational age (34 to 36+6/7 weeks GA).

Key words: pregnancy - preterm newborns - gestational age

* * * * *

INTRODUCTION

Perinatal complications occur in 5 to 18% of births, that is in 12,9 million of births in a year there is one or more complications developed. For the last two decades the rate of those births has grown both in developed and non-developed countries (Elrath et al. 2002). Perinatal complications appear during the period from 22nd week of gestational age (GA) until the first 7 days after the birth and occur more with infants with lower GA. Those infants are exposed to complications during pregnancy because of their immature organs and organic systems, during the birth itself and to the complications which occur after birth and during adaption to the outside of uterus conditions (Goldenberg et al. 2008). Prospective twenty year research conducted in America shows decrease in mortality for preterm newborns with GA 23-24 weeks and decrease of perinatal complications with

preterm newborns 24-28 weeks GA (Stoll et al. 2015). Symptomatology of perinatal complications is different and depends on occurrence of certain complication (Heron et al. 2010). One of the most dramatic clinical diagnoses is perinatal asphyxia which leaves permanent consequences on neurological development of the infant (Rodin et al. 2014). However, for the last years severe consequences of asphyxia were reduced by implementing hypothermia of the newborns and late preterm newborns which is stated in a research conducted in 2015 (Silveira & Procionoy 2015). The research show significantly less occurrence of respiration distress syndrome in preterm newborns owing to antenatal intake of corticosteroid in pregnant women with the risk of premature birth (Boghossian et al. 2016). It is estimated that yearly 1.4 million newborns in the world have severe sepsis as a consequence of prematurity, mother factors and excessive intake of antibiotics in intensive neonatal

units (Shane & Stoll 2016). Number and length of apneic crisis in preterm newborns are increased with the decrease of GA and there is no significant correlation between apnea and severe intraventricular hemorrhage, retinopathy and lung dysplasia in premature newborns under 31 weeks GA which is shown by the research in 2016 (Fairchild et al. 2016). The research shows that the type of birth is a significantly higher risk factor in late premature cases for hyperbilirubinemia development in relation to other factors connected to pregnant women (Ozdemirci et al. 2016). Thanks to increase of health care and quality of high risk pregnancy care, morbidity and mortality of prematurely born infants is highly decreased (Stoll & Hansen 2003). Decrease of morbidity and mortality caused by premature birth can be primary, aimed at all women, secondary, aimed at elimination and reduction of present risks or tertiary that is improvement of health of prematurely born infants. The rate of survival of prematurely born infants who had developed severe complications and which have left permanent consequences on their development has increased during the years and raised more ethic problems and questions. There is a question of the best interest of the child, parents and society since those children can often have problems with physical and mental health. Considering the fact that perinatal complications can result with very severe outcome, I consider that it is necessary to pay more scientific attention and conduct more detailed research regarding this clinical and also public health topic.

Aim of this research was to determine frequency and type of perinatal complications in two cohort groups of prematurely born infants divided by gestational age.

SUBJECTS AND METHODS

The research was conducted in the Clinic for Gynaecology and Obstetrics of the University Clinical Hospital Mostar (SKB) and in the Department for Neonatology and Intensive Care Unit of the Clinic for Children's Diseases of the University Clinical Hospital Mostar during 2014. The research included 100 prematurely born infants from the gestational age of 24 weeks to 36+6/7 weeks who had developed perinatal complications. The data was collected and processed based on medical documentation of the Clinic for Gynaecology and Obstetrics of the University Clinical Hospital Mostar and in the Department for Neonatology and Intensive Care Unit of the Clinic for Children's Diseases of the University Clinical Hospital Mostar where the charts of the patients and infants who were hospitalised in this clinic during the 2014 were taken. Parameters which were considered were: mother's age, number of births, course of pregnancy, complications and type of pregnancy and infant's gestational age, weight, small for gestational age (IUGR), asphyxia, respiratory distress syndrome,

sepsis, hyperbilirubinemia, apnea, anemia, intracranial hemorrhage and metabolic disorder (hypoglycaemia, hypocalcaemia).

In order to show nominal variables frequency and percentage were used, and for continuous variables middle value and standard deviation were used. For analysis of nominal variables Chi-Square-Test was used. For testing differences between continuous variables Student's t-test was used. For statistical analysis of given data SPSS for Windows program system (version 17.0. SPSS Inc, Chicago, Illinois, USA) and Microsoft Excel (version Office 2007, Microsoft Corporation, Redmond, WA, USA) were used.

RESULTS

The research conducted during 2014 included 100 prematurely born infants. 76% of 100 examinees who were involved in this research were in the group of 34 to 36+6/7 weeks GA, and 24% belong to the group from 24 to 33+6/7 weeks GA. Most of the complications occurred with newborns in second births (41%), then with first births (39%) which are different from infants of multiple births where the number of complications was less represented. However, statistically significant difference between number of birth of mother and gestational age of examinee was not determined. Middle value of newborn birthweight in the group from 24 to 33+6/7 weeks GA was 1572.50 ± 374.076 grams, while the group from 34 to 36+6/7 weeks GA was 2442.70 ± 483.395 grams which using statistical analysis showed that birthweight depends on gestational age and is less when the gestational age is lower. The course of pregnancy of mothers with prematurely born infants was pathological in 68% of pregnancies, and normal in 32% of pregnancies which shows statistically significant difference in gestational age in relation to the course of pregnancy. Higher number of newborns with low gestational age, 97% of them was born from a pregnancy which had pathological course unlike newborns of higher gestational age, 60.5% of them.

Statistical analysis determined existence of statistically significant difference in gestational age depending on the course of the pregnancy. However, there was not a statistically significant difference in gestation age considering the type of pregnancy, as there was not statistically significant difference depending on pregnancy complications (Table 1).

Regarding complications which existed in prematurely born infants, most of them had hyperbilirubinemia, which is followed by combination of 3 or more complications. Other complications which reappear: IUGR (small for gestational age), sepsis, asphyxia, anemia, metabolic disorders and respiratory distress syndrome (RDS) (Figure 1).

Table 1. Review of examined parameters of mother considering gestational age

	GA Groups				χ^2	p
	24-33 + 6/7		34-36 + 6/7			
	N	%	N	%		
Pregnancy course					8.760	0.009
Normal	2	8.3	30	39.5		
Pathological	22	91.7	46	60.5		
Pregnancy type					2.132	0.144
Singletone	22	91.7	57	75.0		
Multiple	2	8.3	19	25.0		
Complications					3.493	0.174
None	5	20.8	31	40.8		
Hypertension	10	41.7	27	35.5		
PPI	9	37.5	18	23.7		

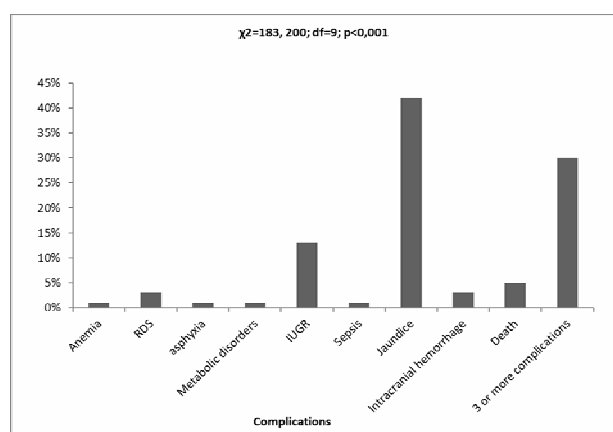


Figure 1. Review of perinatal complication with prematurely born infants according to gestational age.

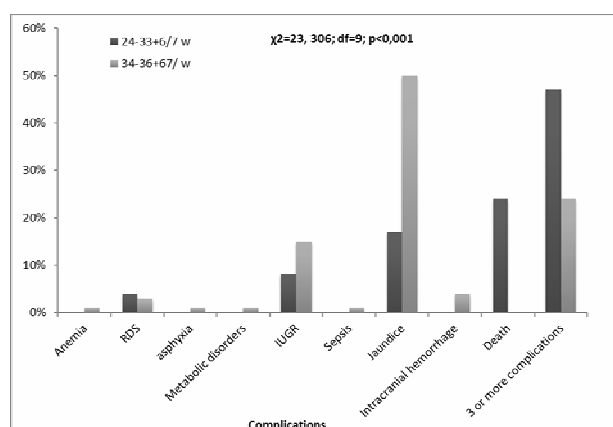


Figure 2. Review of occurrence of perinatal complications in prematurely born infants regarding gestational age

According to statistical analysis it is determined that a larger number of perinatal complications occurs with prematurely born infants in the age of 24 to 33+6/7 weeks GA, differently from prematurely born children of age 34 to 36+6/7 weeks GA. It is also determined that the deathly outcome occurs only with infants born between the age of 24 and 33+6/7 weeks GA (Figure 2).

DISCUSSION

With the insight into scientific works and researches conducted worldwide regarding similar topic we have perceived that perinatal complications more often occur with prematurely born infants. This research shows that the most common cause of appearance of those complications is premature birth and that its number, severity and deathly outcome mostly depend on gestational age of the newborn. The research conducted in several countries with low standards of living show that mortality of preterm newborns can be prevented with increase of prenatal care and prevention of infections. Use of corticosteroids in high-risk pregnancies is just one of measures which reduced frequency of respiratory distress syndrome (McClure et al. 2016). Furthermore, gender acts as a significant determiner in appearance of premature birth, therefore mortality and perinatal complications with male sex appear significantly more frequently (Peelen et al. 2016). Our research shows that there is no difference between frequency of gender towards gestational age. For the last years, researches show the recommendation for preventing premature birth and at the same time also the perinatal complications. Also, hypovitaminosis D of the pregnant women is considered to be a relevant high-risk factor for premature birth which need to be prevented (Qin et al. 2016). The research has shown that the occurrence of higher number of complications as well as deathly outcome is more frequent with prematurely born infants with the age of 24 to 33+6/7 weeks GA. This also contributes recent research which state that perinatal complications are more frequent and harder and that they mostly result with deathly outcome when the gestation age of the infant is lower (Stoll et al. 2015, Romero et al. 2014). Furthermore, in the second group of infants with higher gestational age (> 34 weeks GA) the most common complication is hyperbilirubinemia, with 50% of the examinees, while the deathly outcome is not even noted. Statistical analysis shows that the combination of 3 or more complications appears in 46% of examinees and deathly outcome with 24 % of examinees in the group of 24 to 33+6/7 weeks GA. The most recent studies show that frequency of one of the most severe perinatal complications such as sepsis can be reduced with rational use of antibiotics and more critical estimation of newborn sepsis development doubt (Herk et al. 2016). Our results show that sepsis is a rare complication with about 1% in each group of newborns. Statistical analysis showed a larger number of single fetus pregnancies, 79% of them in relation with multiple pregnancies of 21%. However, significant difference between type of pregnancy and GA was not determined, although many authors state how multiple pregnancies present more risk and are tend more to complications and premature births (Wieczorek & Krasomski 2015).

Also, the studies conducted in America show that there is a significantly higher risk for premature birth and low birthweight in pregnant women with assessed pregnancies but without influence of other mother risk factors (Dhalwani et al. 2016). The conclusion of this research is that insufficient prenatal care has its consequences not only for health of pregnant women but also newborn and it is a significant health factor for population and future generations. Prenatal complication are necessary to prevent and it can be done the best by reducing the frequency of premature births and using guidelines in treating newborns in units for intensive treatment.

Acknowledgements: None.

Conflict of interest : None to declare.

Contribution of individual authors:

Vedran Bjelanović and Marjana Jerković Raguž conception and design of the publication, writing the first draft participate in drafting the article, execution of tables, approval of the final version;

Matea Galić and Ana Čuljak, statistical analyses, participate in revising it critically for important intellectual content, approval of the final version;

Ivana Bjelanović and Vajdana Tomić, revising the manuscript, approval of the final version.

References

1. Boghossian NS, McDonald SA, Bell EF, Carlo WA, Brumbaugh JE. Association of Antenatal Corticosteroids With Mortality, Morbidity, and Neurodevelopmental Outcomes in Extremely Preterm Multiple Gestation Infants. *JAMA Pediatr*. 2016;18.
2. Mc Clure EM, Goldenberg RL, Jobe AH, Miodovnik M, Koso-Thomas M, Buekens P, et al. Reducing neonatal mortality associated with preterm birth: gaps in knowledge of the impact of antenatal corticosteroids on preterm birth outcomes in low-middle income countries. *Reprod Health* 2016; 13:61
3. Dhalwani NN, Boulet SL, Kissin DM, Zhang Y, McKane P, Bailey MA, Hood ME. Assisted reproductive technology and perinatal outcomes: conventional versus discordant-sibling design. *Fertil Steril* 2016; 61135-4.
4. Mc Elrath TF, Norwitz ER, Nour N, Robinson JN. Contemporary Trends in the Managements of Delivery at 23 weeks' Gestation. *Am J Perinatol*. 2002;19:9-15.
5. Fairchild K, Mohr M, Paget-Brown A, Tabacaru C, Lake D, Delos J, Moorman JR, Kattwinkel J. Clinical associations of immature breathing in preterm infants: part 1-central apnea. *Pediatr Res*. 2016.43.
6. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008; 371:75-84.
7. Heron M, Sutton PD, Xu J, Ventura SJ, Strobino DM, Guyer B. Annual summary of vital statistics: 2007. *Pediatrics*. 2010;125:4-15.
8. Herk W, Stocker M, van Rossum AM. Recognising early onset neonatal sepsis: An essential step in appropriate antimicrobial use. *J Infect*. 2016; (16)30053-6.
9. Ozdemirci S, Kut A, Salgur F. Late Preterm and Term Birth: Neonatal Hyperbilirubinemia and Birth Model. *Fetal Pediatr Pathol*. 2016; 26:1-7.
10. Peelen MJ, Kazemier BM, Ravelli AC, de Groot CJ, van der Post JA, Mol BW, Hajenius PJ, Kok M. Impact of fetal gender on the risk of preterm birth, a national cohort study. *Acta Obstet Gynecol Scand*. 2016. 24.
11. Romero R, Dey SK, Fisher SJ. Preterm labor: one syndrome, many causes. *Science*. 2014;345:760-5.
12. Rodin U, Filipović-Grčić B, Ćorić T, Juras J. Uzroci perinatalnih smrti u Hrvatskoj u 2013. godini. *Gynaecol Perinatol*. 2014;23:19-24.
13. Stoll BJ, Hansen NI, Bell EF, Walsh MC, Carlo WA, Shankaran S, et al. Trends in Care Practices, Morbidity, and Mortality of Extremely Preterm Neonates, 1993-2012. *JAMA*. 2015. 314:1039-51.
14. Silveira RC, Procianny RS. Hypothermia therapy for newborns with hypoxic ischemic encephalopathy. *J Pediatr (Rio J)*. 2015;91:S78-83.
15. Shane AL, Stoll BJ. Neonatal sepsis: progress towards improved outcomes. *J Infect*. 2014;68:S24-32.
16. Stoll BJ, Hansen N. Infections in VLBW infants: studies from the NICHD Neonatal Research Network. *Semin Perinatol* 2003; 4:293-301
17. Qin LL, Lu FG, Yang SH, Xu HL, Luo BA. Does Maternal Vitamin D Deficiency Increase the Risk of Preterm Birth: A Meta-Analysis of Observational Studies. *Nutrients* 2016; 20:8
18. Wieczorek AI, Krasomski G. Twin pregnancy as the risk factor for neonatal intraventricular hemorrhage. *Ginekol Pol*. 2015;86:137-42.

Correspondence:

Vedran Bjelanović, MD, PhD

Clinic of Gynecology and Obstetrics of the University Clinical Hospital Mostar

University Clinical Hospital Mostar

Bijeli Brijeg bb, 88000 Mostar, Bosnia and Herzegovina

E-mail: vedranbjelanovic@yahoo.com