

THE IMPACT OF PRETERM PREMATURE RUPTURE OF MEMBRANES ON NEONATAL OUTCOME

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Abstract

Preterm premature rupture of membranes eventuate when the amniotic sac breaks at least 4 weeks before a pregnancy has reached full term. The motive of this study was to evaluate the effect of preterm premature rupture of membranes on neonatal outcome and to establish correlations between mother's infection and gestational age, weight as well as hospitalization days of the newborn. A retrospective study was conducted over a period of 1 year in Bega Clinic of Obstetrics-Gynecology and Neonatology Timisoara. The study included 36 premature newborns admitted to Neonatal Intensive Care Unit, who meet the inclusion criteria. Confirming the diagnosis of neonatal sepsis includes the history of the neonate, clinical signs, symptoms and paraclinical investigations. The present work focuses on the history of mothers with PPRM over 16 hours, with or without infection, which indicates the need to look up for a possible neonatal infection. For laboratory tests: complete blood count, C-reactive protein, blood and vernix cultures were taken. Further research will analyze new markers of infection. Corroborating new findings with the data taken so far, helps us developing a novel clinical protocol and to improve the therapeutic management of these cases.

Keywords: preterm premature rupture of the membranes, premature infants, infection

Introduction

Premature labor often ends with an early birth. The labor is considered to be premature if it starts more than three weeks before the predicted birth date [1]. Preterm birth is a high risk for perinatal mortality and long-term morbidity as well as the health consequences outcomes. Preterm birth is among the top causes of death in infants worldwide [2]. One of the conditions that lead to premature birth is the rupture of the membranes. Premature rupture of the membranes (PRM) was defined as leakage of amniotic fluid that precedes the onset of uterine contractions and cervical changes. PRM is considered prolonged when it occurs more

than 18 [3] or 24 [4] hours before labor. Preterm premature rupture of membranes (PPRM) is characterized as the tear of the amniotic sac during pregnancy before 37 weeks of gestation. It occurs in 3 percent of pregnancies and is the cause of approximately one third of preterm deliveries [5]. Before term, PPRM is frequently due to a uterus infection. Other factors that may be linked to PRM embrace the following: sexually transmitted infections like chlamydia and gonorrhea, low socioeconomic conditions, previous preterm birth, smoking during pregnancy. PPRM often conduct to significant perinatal morbidity, including neonatal sepsis, respiratory distress syndrome, and fetal death. Therefore, this study focuses on finding correlations between the PPRM and its direct consequences on the neonatal outcome.

Purpose

The purpose of the following study was to evaluate the impact of preterm premature rupture of membranes on neonatal outcome and to establish new correlation between mother's infection, and gestational age, weight and hospitalization days of the newborn.

Materials and methods

A retrospective study was conducted over a period of 1 year (January 2013 – January 2014) in the Neonatal Intensive Care Unit (NICU), Clinic of Obstetrics-Gynecology and Neonatology of the Emergency County Hospital Timisoara. There were selected 36 premature newborns admitted to NICU. One of the most important lot inclusion criteria was preterm labor due to preterm premature membrane rupture. Also, another eligible condition was that the membrane rupture occurs more than 16 hours before labor in all selected cases. All the parturient had a good follow up of the pregnancy and gynecological controls were performed regularly. Statistical analysis was performed using Microsoft Excel 2007 software.

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Results and Discussions

Confirming the diagnosis of neonatal sepsis includes the history of the neonate, clinical signs and symptoms (which can be early or late offset, so, in this study it was not taking them into consideration), laboratory investigations and imagistic investigations. The present work focuses on the history of mothers with PPRM over 16 hours, with or without infection, which indicates the need to look up for a possible neonatal infection. For laboratory

investigations: complete blood count (CBC), C-reactive protein (CRP), blood and vernix cultures were taken.

Leukocytopenia, also known as leukopenia, illustrates a decrease in the number of white blood cells (leukocytes), which places the neonates at high risk of infection [6]. In the present study, 25 newborns from all 36 cases had abnormal leukocytes count, with an absolute frequency of 69.44% (Tab.1).

Table 1. Relative and absolute frequency of the leukocytes values.

Leukocytes (values)	Relative frequency	Absolute frequency (%)
Normal	11	30.56
Decreased	22	61.11
Increased	3	8.33
Abnormal leukocytes count	25	69.44%

Thrombocytopenia develops in up to 50% of the newborns admitted to NICU and who require intensive care [7]. Newborn thrombocytopenia discovered at birth result from transplacental passage of maternal platelet alloantibodies and autoantibodies nearly always in babies

who are very affected, particularly associated with infection [8]. The data below reveals a noticeable thrombocytopenia in a majority of 27 cases (75%) from a total of 36 premature newborns included in the study (Tab. 2).

Table 2. Relative and absolute frequency of the thrombocytes values.

Thrombocytes (values)	Relative frequency	Absolute frequency (%)
Normal	4	11.11
Decreased	27	75.0
Increased	5	13.89

Almost all newborns experience a mild decrease in hemoglobin concentration after birth. Anemia of prematurity represents a form of anemia affecting preterm infants with decreased hemoglobin values. Associating the sepsis with the physiological destruction of the erythrocytes their number drops and the capacity of oxygen transport will be

low because of the disturbances in the iron metabolism. The study presented in this paper discloses low levels of hemoglobin in 41.67% of all cases (Tab. 3). Along with leukocytopenia and thrombocytopenia, anemia is a sign of neonatal infection.

Table 3. Relative and absolute frequency of the hemoglobin values.

Hemoglobin (values)	Relative frequency	Absolute frequency (%)
Normal	11	30.56
Decreased	15	41.67
Increased	10	27.78

C-reactive protein (CRP) is a ring-shaped pentameric protein found in the blood plasma and it is used mainly as a marker of inflammation [9]. CRP is the first specific investigation used when neonatal infection is assumed. In this work, there were 11 neonates representing 31.25% with positive CRP from a total of 36 premature newborns included in the study.

The second and also the most specific and sensitive laboratory investigation to determine the neonatal sepsis is the blood culture. Various studies are carried out in developed countries show that Gram positive bacteria such as Group B, and coagulase negative staphylococci (CONS) are usual isolates [10]. Klebsiella species is noted to be the commonest organism along with *E. coli*, *Staph. aureus*,

Staph. epidermidis, Group B Streptococci, *Enterobacter* sp., *Enterococcus faecalis*, *Pseudomonas* sp., *Proteus* sp., are seen in developing countries [11]. In the present study, the most common Gram-negative pathogens have been *Klebsiella pneumoniae* equalize 25.00%. Other important pathogens have been found to be *Pseudomonas aeruginosa* and *Candida albicans* (12.50%) found in blood culture. The most common Gram-positive isolate has been found to be *Staphylococcus aureus*, representing 37.50% of the cases with positive culture. *Flavimonas oryzihabitans*, also known as *Pseudomonas oryzihabitans*, is a nonfermenting yellow-pigmented, gram-negative bacterium that can cause septicemia. Interestingly, this type of microorganism was

isolated from the vernix caseosa and was associated with mother infection and PRM of more than 24 hours.

From all cases included in the study, 8 blood cultures came out positive. One of the 8 was also positive on the vernix culture.

As shown in table 4 from a total of 11 mothers with PPRM and infection, only 3 premature newborns were diagnosed with neonatal sepsis, while another 5 premature newborns with sepsis belongs to the group of mothers with PPRM and without infection. Consequently the study concluded that there is no direct correlation between the presence of infection at a mother with PPRM and the neonatal sepsis.

Table 4. Correlation between maternal and newborn's infection.

Infection		Neonatal	
		+	-
Maternal		8	28
+	11	3	8
		27.3%	72.7%
-	25	5	20
		20.0%	80.0%

The gestational age average of the newborns is 30.19 weeks, with a standard deviation of 2.9 weeks. Gestational age was established according to the first-trimester ultrasound. One of the most important causes of preterm birth might be the preterm premature rupture of the amniotic sac. This condition encourages high risk of the newborn sepsis. This is the reason why this study focused on PRM as a precursor of preterm birth and neonatal infection.

An inverse relationship exists between gestational age of the infant resulted by mothers with infections, which is significantly decreased, versus newborns resulted from mothers without infections (T-Test for independent variables, $p=0.046$, $\alpha=0.05$) (Tab. 5). Although the PRM is

the cause of preterm birth in all cases, not all parturient had an infection clinically manifested. The longer the period between PRM and delivery, the higher the risk for infection is.

According to birth weight classification (Tab. 6) the infants included into the study were classified as very low birth weight with an average of 1502.78 grams and with a standard deviation of 518.83 g.

Weights of the infants resulted by mothers with infections are significantly decreased versus newborns resulted from mothers without infections (T-Test for independent variables, $p=0.029$, $\alpha=0.05$) (Tab. 7).

Table 5. Comparison between mother's infection and newborn gestational age.

Maternal infection	No. of cases	Gestational age average	Std. deviation	Average std. error
Yes	11	28.82	2.442	0.736
No	25	30.80	2.915	0.583

Table 6. Birth weight classification (WHO Statistical Information Systems (WHOSIS). 2011).

Premature babies may be classified by weight independent of gestational age:		
Low birth weight	LBW	<2,500 g
Very low birth weight	VLBW	<1,500 g
Extremely low birth weight	ELBW	<1,000 g
Infants may also be classified by weight for a specific gestational age:		
Small for gestational age	SGA	Weight <10th percentile
Appropriate for gestational age	AGA	Weight 10-90th percentile
Large for gestational age	LGA	Weight >90th percentile

Table 7. Comparison between mother's infection and infant's birth weight.

Maternal infection	No. of cases	Weight average	Std. deviation	Average std. error
yes	11	1222.73	512.798	154.614
no	25	1626.00	480.867	96.173

Hospitalization is significantly raised in the case of newborns with infection (T-Test for independent variables $p=0.011$, $\alpha=0.05$) (Tab. 8). One of the most important consequences of prolonged hospitalization is the risk for

nosocomial infections overlapped an existing disease. Another concern for a long time admission is poor developmental outcome and augmented medical costs.

Table 8. Hospitalization days of cases with/without infection.

Infection	No. of cases	Hospitalization days average	Std. deviation	Average std. error
yes	8	33.25	29.149	10.306
no	28	11.69	16.835	3.182

Conclusions

The unfavorably outcome of the newborns resulted by mothers with infection and PPRM as a consequence, is given by prematurity and low weight at birth. Maternal infection and PPRM determines a premature birth in all analyzed cases. Considering the laboratory investigations taken above, it was concluded that only 8 (22.22%) from a total of 36 prematures newborns were diagnosed with neonatal sepsis although 31.25% revealed a positive CRP, 41.66% anemia, 69.44% abnormal leucocyte count and 75%

trombocytopenia. Although there is unquestionable clinical information that suggests connections among mother and neonatal infection status, this study could not establish a certain statistical correlation between parturients infection and positive cultures of the newborns. Further research in this field will analyze procalcitonin and interleukin 6 levels for the diagnosis of early-onset infection of the neonates. The data gathered so far, enhanced with new markers of infection will help us developing a new clinical protocol and to improve the therapeutic management of this cases.

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