Premature Rupture of Membranes is a Provoking Factor in the Birth of Premature Newborns

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Abstract: The authors of the work conducted a study to study the provoking factors of preterm birth and their consequences in the neonatal period of adaptation. The main clinical manifestations of complications of premature rupture of the membranes are considered: RDS, early and late neonatal sepsis, neurological disorders. The possibility of predicting the outcomes of PRFM in preterm birth by determining cytokines in the serum and urine of preterm infants has been established.

Keywords: Premature rupture of membranes, preterm labor, cytokines, fetus, gestation.

Relevance

Amniotic fluid is a biologically active environment surrounding the fetus, intermediate between it and the mother's body, is a complex structure that performs diverse functions throughout pregnancy and childbirth. Amniotic fluid has antimicrobial activity due to the production of interferon by the fetal membranes, contains lysozyme, antibodies to certain types of bacteria and viruses, and immunoglobulins [4].

Premature rupture of the fetal membranes (PRFM), provoking premature birth, is an urgent problem in the field of obstetrics and neonatology and accounts for 38 to 51% of all premature births [2,8], in fact, every tenth child is born prematurely, almost a third of them die, and the percentage of disability among survivors is high (43.8%). In about 36% of cases, PRFM is accompanied by an intrauterine infection, most often without clinical manifestations, the significance of infection in preterm labor decreases with increasing gestation: in 22-27 weeks of pregnancy, the infectious factor and congenital pathology – infectious fetopathies are in the lead, in 28-33 weeks, infection is detected in 50% of cases, from 34 weeks of premature birth may be due to a lot of reasons unrelated to infection. PRFM often leads to the manifestation of infection with the development of chorioamnionitis, septicemia, endometritis or neonatal sepsis, pulmonary hypoplasia, fetal respiratory distress syndrome, contractures and deformities [3,6].

Deeply premature infants, especially those with extremely low body weight, are often on the threshold of viability, with survival are subject to an increase in morbidity, there is a high probability of cardiorespiratory problems, mental retardation, cerebral palsy, visual and hearing impairment, compared with infants born on time, which creates a significant medical, financial and psychosocial burden [1].

PRFM risk factors

Maternal factors:

- PRFM – during the previous pregnancy premature to term (risk 16-32%).
- Uterine bleeding during this pregnancy.

- Long-term therapy with glucocorticoids.
- Systemic connective tissue diseases.

Uteroplacental factors:

- Placental abruption (10-15% of cases of PRFM).
- Abnormalities of uterine development.
- Chorioamnionitis. The shorter the gestation period, the higher the risk.
- Multiple pregnancies (7-10% of twin pregnancies).

Consequences of PRFM

The most common complication of preterm labor in premature pregnancy is premature birth and associated conditions: malnutrition, sepsis, hypoplasia of the lungs. Stillbirth is observed 8-13 times more often in premature births than in timely ones. A [9].PRFM in premature pregnancy (up to 36 weeks 6 days) increases perinatal mortality by 4 times, and neonatal morbidity by 3 times. The most frequent complications include respiratory distress syndrome of 10-40% (40-70% neonatal mortality), intraamnial infection of 15-30% (3-20% mortality), as well as intraventricular hemorrhages, necrotizing enter colitis, retinopathy, persistent ductusarteriosus, neurological disorders [7,10].

In this regard, it is extremely urgent to search for markers of IUI, which allow assessing the degree of risk and making an informed decision on the tactics of management of premature infants with PRFM at up to 37 weeks of gestation.

The aim of the study is to develop effective prognostic criteria for assessing the severity of maladaptation of a premature newborn with premature rupture of fetal membranes to reduce perinatal morbidity and mortality.

Materials and methods. A retrospective analysis of 1182 birth histories of pregnant women hospitalized in the Bukhara Regional Perinatal Center (BOPC) from 2018 to 2020 for premature birth was carried out. Risk factors for preterm labor were determined by calculating the Odds ratio - Odds Ratio (OR) based on the results of a survey of 80 women giving birth in the BOPC. The study of the causal relationship of risk factors with the occurrence of premature birth was carried out using the analytical study "case–control". The distribution of groups was as follows: 1-group consisted of 20 women with preterm labor, with preterm labor, 2- group consisted of 20 women with preterm labor, without preterm labor, 3- group of 20 women with physiological pregnancy and urgent labor with preterm labor, and 4-group of 20 women with physiological pregnancy and urgent labor without PRFM. The age of the mother was determined as <18, 18-34 and ≥35 years. The mother's employment was determined by the categories of working/studying and not working. Marital status was classified as registered marriage and single (including widows and women with an officially dissolved marriage). The mother's education was defined as higher, full secondary and incomplete secondary. By parity, the first- and second-born were distinguished. The maternal body mass index was divided into the categories of insufficient (<18.5 kg/m2), normal (18.5–24.9 kg/m2) and overweight and obese (≥25.0 kg/m2) recommended by the World Health Organization. The assessment of the condition of newborns was carried out on the Apgar scale and NACS (registration of the neuropsychiatric status of newborns).

The clinical assessment of the degree of respiratory insufficiency was carried out according to the Silverman scale, on the basis of which a conclusion was made about the presence and dynamics of respiratory distress syndrome (RDS) and the necessary amount of respiratory care

Results and their discussion. The results of the study showed that the highest incidence of PRFM was observed in 2018, which was 83 (43.9%), in 2019 – 74 (39.1%) and the lowest figure was in 2020 – 35 (18.5%), in just 3 years 189 cases. Among all premature babies born in the BOPC in 2018-2020, children from rural areas prevailed – 968 (81.9%). This is probably due to the living and working conditions of women, the lack of qualified medical care, which lead to premature birth.

In the distribution by gestation period of preterm labor, 35 (3.0%) extremely low birth weight newborns were born at 22-27 weeks, the highest frequency of preterm labor occurred at 28-34 weeks - 590 (49.9%) and at 35-37 weeks – 557 (47.1%) births, respectively (Fig.1).

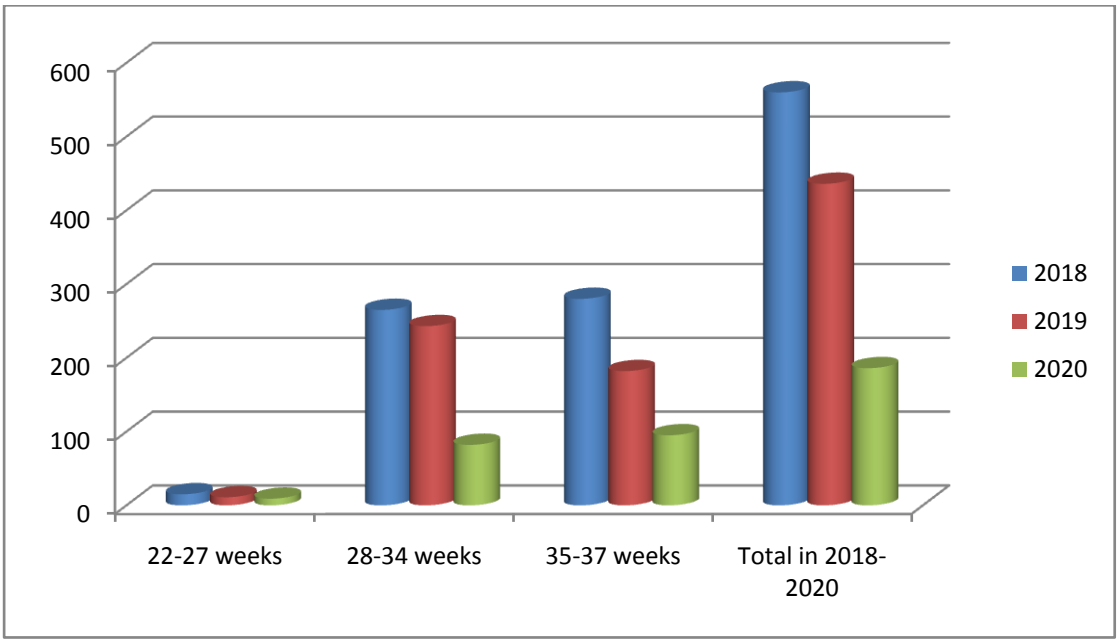
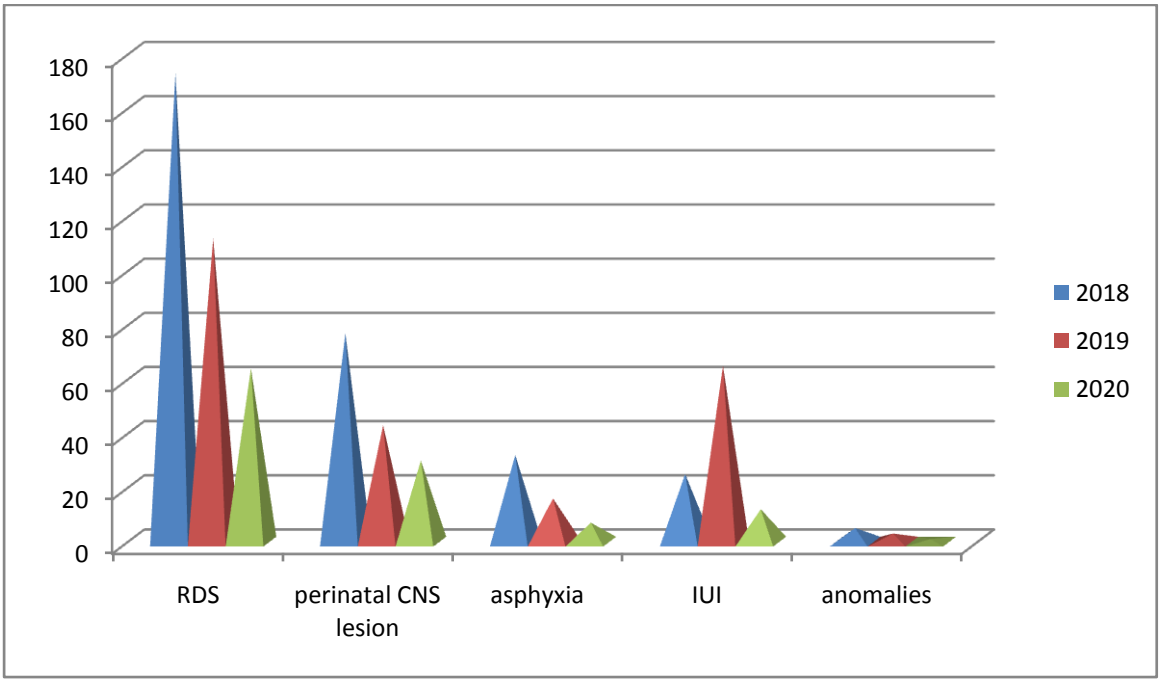


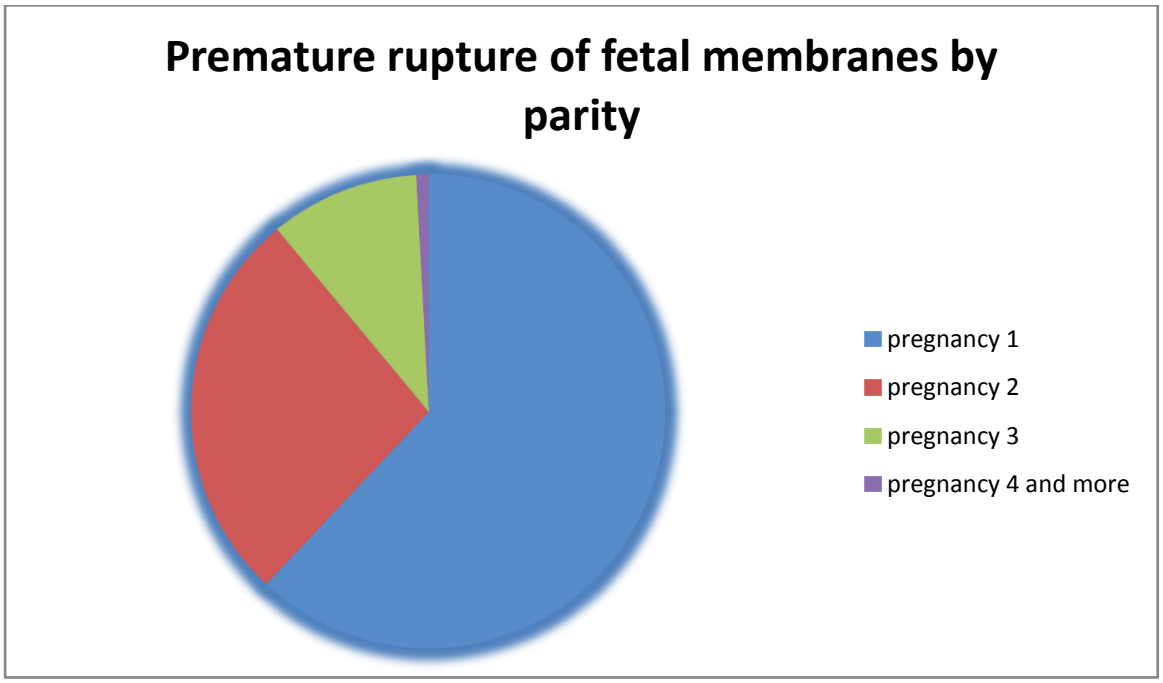
Figure 1. Distribution of premature births by gestation period

According to the structure of morbidity in premature infants, the most common were: RDS syndrome-349 cases, perinatal CNS lesion-123, IUI-102,anomalies-2



In case of premature discharge of amniotic fluid with a gestation period of up to 34 weeks, all pregnant women underwent prevention of RDS syndrome.

According to the parity, PRFM was often found in 1 pregnancy, which was 62%, in 2 pregnancies 27%, in 3 pregnancies-11% (Fig.2)



All newborns underwent general clinical examination methods and determined cytokines IL-6 and IL-8 in umbilical cord blood (Table.1). Newborn children were included in the study after receiving the written informed consent of the mother.

Determination of the level of IL-6 in newborns is necessary to confirm bacterial sepsis, because this cytokine has a high sensitivity and specificity. It was found that IL-8 causes chemotaxis and activation of neutrophils, which contributes to the further production of cytokines and increases the contractility of the uterus. There is a correlation between the increased concentration of IL-8 in amniotic fluid and leukocyte infiltration of amniotic membranes during premature and urgent labor [16].

Table 1. The level of cytokines in the blood serum of newborns in the period of early neonatal adaptation

№	Cytokinestatusofnewborns	Group 1 (urgent delivery without complications) n=30	Group 2 (preterm labor with PRPO from a mother with PE) n=30	Group 3 (premature birth without PR from a mother with PE) n=30
1	IL-6 (pg/ml)	22,17±3,83	57,07±12,22**	29,05±1,57**
2	IL-8 (pg/ml)	33,62±4,77	75,21±13,4**	62,89±3,19**

Note: * - differences relative to the control group data are significant (* - P<0.05, ** - P<0.01, *** - P<0.001)

The study showed that the level of IL-6 in the umbilical cord blood of premature newborns with PRFM from mothers with preeclampsia was 3-fold increased 57.07±12.22 pg/ml, and in the group of premature infants without PRPO from mothers with PE increased by 1.3 times 29.05±1.57pg/ml in relation to the control 22.19±3.83pg/ml, which indicates the presence of a systemic inflammatory response syndrome and a high risk of developing sepsis in premature infants.

It is known that IL-8 as a pro-inflammatory cytokine stimulates the secretion of histamine by basophils and is one of the stimulators of angiogenesis [4]. A natural stimulus to angiogenesis in physiological and pathological conditions is a lack of oxygen (hypoxia or ischemia), both in the embryonic and postnatal period of the body's development [2].

Conclusion

In the course of our study, we noted that in newborns born prematurely with PRFM, there is a predominant anti-inflammatory orientation of the immune response. The most pronounced differences in the level of cytokine production were found in premature infants born prematurely with premature rupture of the membranes compared with children born prematurely without premature rupture of the membranes. A significant increase in the content of IL-8 (75.21 pg/ml) and IL-6 (57.07pg/ml) was demonstrated in the group of premature infants with PRFM. The data obtained in the course of this study on the features of the cytokine profile of premature newborns of various gestational ages with PRFM can be used both for the rapid diagnosis of sepsis and for the differential diagnosis of pathological conditions of the early neonatal period.

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