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Risk factors associated with neonatal infectious and respiratory morbidity following preterm premature rupture of membranes

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ABSTRACT

Objectives: Preterm premature rupture of membranes (pPROM) is associated with the increased risk of chorioamnionitis, foetal exposure to inflammation, and respiratory complications in preterm neonates. The aim of the study was to identify patients at highest risk of developing neonatal infectious and respiratory morbidity following pPROM and preterm birth.

Material and methods: It was a retrospective cohort study including 299 consecutive patients in singleton pregnancies complicated by preterm premature rupture of membranes and giving birth between 22nd and 36th gestational week. Analysed factors included maternal characteristics, obstetric history, gestational age at pPROM and at delivery, latency and management. Multivariate logistic regression models were applied in order to identify risk factors for severe infectious and respiratory neonatal complications.

Results: Earlier gestational age at pPROM is associated with increased probability of developing early-onset neonatal sepsis and pulmonary hypertension. Earlier gestational age at birth and lower birth weight were independent factors associated with neonatal respiratory distress syndrome. Positive cervical culture was identified as a risk factor for acute neonatal respiratory failure.

Conclusions: Gestational age at pPROM, gestational age at birth and birth weight were the leading factors influencing the risk of developing neonatal infectious and respiratory morbidity following preterm premature rupture of membranes.

Key words: bronchopulmonary dysplasia; neonatal sepsis; pprom; premature birth; respiratory distress syndrome; respiratory insufficiency; transient tachypnea of the newborn

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INTRODUCTION

Preterm premature rupture of membranes (pPROM) is associated with the increased risk of chorioamnionitis and foetal exposure to inflammation [1]. Available data shows that inflammatory intrauterine environment could have long-term effects including impact on the incidence of respiratory morbidity and cardiovascular system condition through impaired endothelial function [2–6].

There is an association between infectious and respiratory complications in preterm neonates. Neonatal infection is a documented risk factor for developing long-term respiratory morbidity including bronchopulmonary dysplasia [7–9].

At the same time, premature birth remains the most common independent risk factor for neonatal mortality and morbidity worldwide [10, 11]. Therefore, during the

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management of patients with pPROM, efforts must be made in order to balance between the risk of prematurity complications and the risk of developing intrauterine infection.

Objectives

The aim of the study was to identify subgroups of patients at highest risk of developing neonatal infectious and respiratory complications following preterm premature rupture of membranes and preterm birth in singleton pregnancies.

MATERIAL AND METHODS

It was a retrospective cohort study performed in a tertiary obstetric referral centre. Study group included consecutive patients in pregnancies complicated by preterm premature rupture of membranes between 12th and 36th gestational weeks giving birth between 22nd and 36th gestational weeks in the time period between October 2016 and December 2018. Exclusion criteria were multiple pregnancy (n = 49), chromosomal and structural foetal abnormalities (n = 23) diagnosed antenatally or after birth, with the majority of structural heart defects and seven cases of fatal defects. During the study period there were 7198 births in our centre, including 755 singleton preterm births, out of which 322 were complicated by preterm premature rupture of membranes. A total of 299 women were enrolled in this analysis.

Preterm premature rupture of membranes was diagnosed based on the speculum examination, assessment of the pH level and the presence of insulin-like growth factor-binding protein 1 in the vaginal discharge. Bacterial culture from cervical canal was collected on admission from every woman. Patients were managed expectantly with strict monitoring of maternal and foetal wellbeing, antenatal corticosteroid therapy, prophylactic empirical antibiotic therapy, and regular assessment of inflammatory markers. Two doses of 12 mg betamethasone were administered after pPROM diagnosis with 24 h interval between completed 23rd and 36th gestational week. In case of latency exceeding 14 days, third dose of 12 mg betamethasone was administered after two weeks. Patients with pregestational diabetes mellitus received four doses of 6 mg betamethasone with 12 h intervals. The prophylactic antimicrobial treatment was established based on local epidemiological data and consisted of intravenous cefuroxime for 10 days. Therapy was adjusted in case of drug allergy or antimicrobial resistance detected in cervical specimen collected on admission. Analysed factors included: maternal characteristics, obstetric history, gestational age at pPROM, results of the cervical bacterial culture, latency, administered antenatal corticosteroid dose and its timing, introduction of tocolysis, delivery mode, gestational age at birth, birth weight, neonatal complications and management. Study endpoints included early-onset neonatal sepsis, pulmonary hypertension, bronchopulmonary dysplasia, acute neonatal respiratory failure, respiratory distress syndrome (RDS), and transient tachypnoea of the newborn.

Latency was counted as time between the rupture of membranes and delivery. Early-onset neonatal sepsis was diagnosed within the first 72 hours after birth based on both clinical symptoms (i.e., bradycardia, apnoea, cyanosis, lethargy) and laboratory findings — white blood cell and absolute neutrophil counts lower and upper normal limits, C-reactive protein with the cut-off value at 10 mg/L [12–14]. Positive neonatal blood culture was not required for the diagnosis as this study included in the analysis all cases of positive-culture sepsis and negative-culture clinical sepsis. Bronchopulmonary dysplasia was diagnosed in neonates requiring oxygen therapy for at least four weeks [15]. Acute neonatal respiratory failure was defined by laboratory criteria with two results from the following: $PaCO2 > 60$ mmHg, $PaO2 < 50$ mmHg or O2 saturation < 80% with an FiO2 of 1.0 and pH < 7.25 in infants requiring assisted ventilation due to acute clinical respiratory insufficiency [16, 17]. The diagnosis of respiratory distress syndrome was based on the clinical presentation of tachypnoea, retractions, expiratory grunting and cyanosis together with typical radiographic bronchogram findings [18]. Transient tachypnoea of the newborn was diagnosed based on presented symptoms, radiographic findings and exclusion of other respiratory morbidities [19]. Pulmonary hypertension was diagnosed during the hospitalization in the neonatal intensive care unit based on echocardiograms showing elevated right ventricle pressure with the estimated pulmonary pressures greater than 50% of the systemic pressure [20].

Statistical analysis was performed with the use of multivariate logistic regression models. Analysed variables included gestational age at birth, gestational age at PROM, latency, use of betamethasone, intravenous tocolysis, positive cervical culture, mode of delivery, sex of the neonate, birth weight, neonatal hypotrophy diagnosed at birth, and 1st minute Apgar score. Gestational age (at birth) stratification was performed by dividing neonates into four analysed subgroups: born before completed 28th gestational week, born between 28th and 31st gestational week, born between 32nd and 33rd gestational week, and born between 34th and 36th gestational week. In case of more than two analysed groups, the Kruskall-Wallis ANOVA analysis was performed as required. Two-tailed $p < 0.05$ was considered significant. SAS software, version 9.4 (SAS Institute, Cary, NC) was used.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the Medical University of Warsaw (protocol code AKBE/16/2018, date of approval 6th February 2018).

RESULTS

Study group included 299 singleton patients with preterm premature rupture of membranes. Maternal characteristics, obstetric history, gestational age at PROM, latency, mode of delivery, gestational age at delivery, birth weight, 1st minute Apgar score and neonatal hospitalization duration are presented in Table 1.

Mean gestational age at birth in the subgroup with latency under 48 hours was 34 weeks and 4 days. In the subgroup with latency between 48 hours and seven days mean gestational age was 32 weeks. Mean gestational age in patients with latency exceeding 7 days was 30 weeks and 5 days. In a post hoc analysis (least square difference test) it was observed that differences in mean gestational age at birth between all three subgroups were significant (Tab. 2).

One hundred and thirty-two (44%) analysed women were primiparous. Bacterial culture from cervical swab was positive in 130 (44%) patients. Identified pathogens were: *E. coli* (n = 43), *S. agalactiae* (n = 39), *C. albicans* (n = 31), *P. bivia* (n = 19), *E. faecalis* (n = 17), *G. vaginalis* (n = 7), *K. pneumoniae* (n = 5), *E. cloacae* (n = 3), *Ureaplasma* (n = 3), *P. melan*ogenica (n = 2), *S. pyogenes* (n = 2), *B fragilis* (n = 1), *B. ovatus* (n = 1), *C crusei* (n = 1), *C glabrata* (n = 1), *C. lusitaniae* (n = 1), *C. freundii* (n = 1), *C. krosei* (n = 1), *H. influenzae* (n = 1), *P. mirabilis* (n = 1). In 200 (67%) patients latency duration was below 48 hours. Intravenous tocolysis was administered

Table 1. Study group characteristics, n = 299

Feature	Mean	SD	Ranges
Maternal age [years]	32.57	5.4	17–47
Feature	Median	Lower and upper quartile	Ranges
Gestational age at PROM [weeks]	35	31; 36	12–36
Latency [h]	17.5	7; 96	0.5–3192
Gestational age at delivery [weeks]	35	32; 36	22–36
Neonatal hospitalization [days]	10	7; 27	1–120
Birth weight [g]	2520	1950; 2880	460–4820
Feature	**n**		**%**
Primigravid	132		44
Cesarean section	145		45
Emergency cesarean section	41		14
Gestational diabetes mellitus	71		24
Pregestational diabetes mellitus	20		7
Pregnancy-induced hypertension	9		3
Pregestational hypertension	15		5
Intrahepatic cholestasis of pregnancy	9		3
Pathological cervical microbiome	130		44
1st min Apgar score 8–10	225		75
1st min Apgar score 4–7	56		19
1st min Apgar score 0–3	10		3

SD — standard deviation; PROM — premature rupture of membranes

Table 2. Mean gestational age at birth in latency subgroups ($p < 0.001$)

Analyzed subgroup	n	Latency duration	Median latency duration [hours]	Lower and upper quartile [hours]	Latency ranges [hours]	Mean gestational age at birth [weeks + days]
I	200 (67%)	Under 48 hours	9	5; 17.75	0.5–48	34 + 4*
II	47 (16%)	Between 48 hours and 7 days	96	72; 144	50–168	32*
III	52 (17%)	Over 7 days	456	288; 768	192–3192	30 + 5*

*Post hoc analysis results for subgroups: significant differences between gestational ages in subgroup I and II $p < 0.001$, I and III $p < 0.001$, and II and III $p < 0.02$

Table 3. Factors associated with neonatal morbidity — results of the multivariate logistic regression

Parameter	Wald Chi-Square	p	OR	CI 95%
Early-onset neonatal sepsis: n = 23; Chi-Square = 24.09; p < 0.0001*				
Gestational age at PROM [weeks]	12.54	**0.0004**	0.85	(0.78; 0.93)
Caesarean delivery	8.35	0.009	5.62	(1.54; 20.43)
Acute respiratory failure: n = 77; Chi-Square = 111.55; p < 0.0001*				
Gestational age at birth 22nd–27th weeks	34.56	< 0.0001	46.35	(12.9; 166.5)
Gestational age at birth 28th–31st weeks	26.7	< 0.0001	10.97	(4.42; 27.2)
Gestational age at birth 32nd –33th weeks	15.41	< 0.0001	6.26	(2.5; 15.63)
Intravenous tocolysis	9.45	0.002	3.12	(1.51; 6.44)
Positive cervical culture	5.86	0.01	2.37	(1.78; 4.75)
Male sex of the neonate	5.86	0.01	2.58	(1.2; 5.54)
Transient tachypnoea: n = 72; Chi-Square = 30.59; p < 0.0001*				
Gestational age at birth 22nd–27th weeks	0.47	0.49	0.63	(0.17; 2.35)
Gestational age at birth 28th–31st weeks	1.32	0.25	1.62	(0.71; 3.7)
Gestational age at birth 32nd –33rd weeks	7.48	0.006	3.16	(1.39; 7.2)
Intravenous tocolysis	8.1	0.004	2.48	(1.33; 4.64)
Male sex of the neonate	4.86	0.03	2.02	(1.08; 3.78)
Respiratory distress syndrome: n = 38; Chi-Square = 102.73; p < 0.0001*				
Gestational age at birth 22nd–33rd weeks	7.74	0.005	11.3	(2.05; 62.39)
Latency between 48 h and 7 days	2.02	0.15	0.37	(0.097; 1.45)
Latency over 7 days	2.84	0.09	2.46	(0.86; 6.99)
Birth weight	9.77	**0.002**	0.999	(0.998; 0.999)
Hypotrophy	4.2	0.04	9.87	(1.1; 88)
Bronchopulmonary dysplasia: n = 20; Chi-Square = 57.75; p < 0.0001*				
Birth weight	24.7	< 0.0001	0.996	(0.995; 0.998)
Use of intravenous tocolysis	6.57	0.01	7.69	(1.62; 36.52)
Pulmonary hypertension: n = 12; Chi-Square = 46.49; p < 0.0001*				
Gestational age at PROM [weeks]	20.55	**< 0.0001**	0.74	(0.69; 0.84)

*Results of the model; OR — odds ratio; CI — confidence interval; PROM — premature rupture of membranes

in 105 (35%) women. One hundred and fifty-six (52%) received two doses of antenatal corticosteroids. Thirty-eight (13%) patients received incomplete antenatal corticosteroids dose because of labour progress. One hundred and thirty-five (45%) women delivered via caesarean section and 41 (14%) had emergency caesarean section. Twenty-four (8%) women were antenatally diagnosed with the onset of intrauterine infection. Sixteen of them (67%) delivered via caesarean section. In this subgroup of patients early-onset neonatal sepsis was more prevalent in children born by a c-section than vaginal birth — 7 (44%) vs 1 (12.5%). This result, however, was not statistically significant because of subgroup size.

Early-onset neonatal sepsis was diagnosed in 23 (7.7%) children. Acute respiratory failure was present in 77 (25.8%) neonates. Thirty-eight (12.7%) newborns were diagnosed with respiratory distress syndrome. Transient tachypnoea of the neonate was present in 72 (24.2%) neonates. Bronchopulmonary dysplasia was detected in 20 (6.7%) infants. Pulmonary hypertension was diagnosed in 12 (4%) children.

Table 3 shows the results of multivariate logistic regression. Earlier gestational age at PROM was associated with increased probability of developing early-onset neonatal sepsis and pulmonary hypertension. Earlier gestational age at birth, lower birth weight and hypotrophy were independent factors associated with the risk of neonatal respiratory distress syndrome. Infants of patients requiring intravenous tocolysis and male neonates were at higher risk of developing acute respiratory failure and transient tachypnoea. Positive cervical culture was identified as a risk factor for acute neonatal respiratory failure.

Table 4 presents differences in the incidence of neonatal mortality and morbidity in different gestational age groups at birth. The highest incidence of acute respiratory failure, respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary hypertension and neonatal mortality was

Table 4. Differences in the incidence of neonatal morbidity and mortality depending on the gestational age at birth: extremely preterm under 28th gestational week, very early preterm between 28th and 31st gestational week, early preterm between 32nd and 33rd gestational week, and late preterm between 34th and 36th gestational week

	Under 28th gestational week (n = 25)	28th–31st gestational week (n = 39)	32nd–33rd gestational week (n = 34)	34th–36th gestational week (n = 201)	p
Early-onset sepsis	4 (16%)	11 (28%)	2 (6%)	6 (3%)	< 0.001
Acute respiratory failure	18 (72%)	25 (64%)	17 (50%)	17 (8%)	< 0.001
Transient tachypnoea	3 (12%)	14 (36%)	18 (53%)	37 (18%)	< 0.001
Respiratory distress syndrome	15 (60%)	15 (38%)	6 (18%)	2 (1%)	< 0.001
Bronchopulmonary dysplasia	12 (48%)	8 (21%)	0	0	< 0.02
Pulmonary hypertension	5 (20%)	6 (15%)	0	1 (0.5%)	< 0.001
Neonatal mortality	5 (20%)	1 (3%)	0	0	< 0.03

observed in the extremely preterm gestational age group, born before completed 28th gestational week.

Mean median latency in the subgroup of neonates born between 22nd and 31st gestational week lasted significantly longer in case of children who developed pulmonary hypertension (n = 11) than in those who did not (n = 51) (552 hours vs 144 hours, p = 0.004). No significant differences in median latency durations were identified regarding the incidence of bronchopulmonary dysplasia, neonatal mortality, use of continuous positive airway pressure, nor use of synchronized intermittent mandatory ventilation in infants born before completed 32nd gestational week.

DISCUSSION

Main findings of our study show that birth weight and gestational age — both during the rupture of membranes and during delivery — are the leading factors associated with the risk of developing neonatal complications in pPROM population. Gestational week at PROM is a non-modifiable factor during patients' admission to the hospital. However, it could be a valuable source of information for the neonatology team about the prognosis and possible required management.

Intrauterine exposure to leakage of the amniotic fluid caused by membranes rupture is not only linked with short-term complications but also increases the risk of respiratory morbidity in later childhood. In a population-based cohort study by Imterat et al. [21] authors analysed whether pPROM was related to the number of hospitalizations for respiratory reasons. During 23 years of observation, it was found that the study group (n = 641) was burdened with higher number of respiratory hospitalizations in comparison to the control group of early preterm deliveries with intact membranes (n = 1954).

One of the partly modifiable characteristics of pPROM patients' management is the duration of amniotic fluid leakage. In the multivariate analysis we have not observed statistically significant association between latency and neonatal morbidity. Mean gestational ages were significantly different in the latency subgroups from our study (Tab. 2) — more than seven days of latency was observed in less advanced pregnancies with mean gestational age at birth of 30 weeks and 5 days. Therefore, gestational age at birth might be the leading factor influencing neonatal respiratory distress syndrome risk in this subgroup.

In a cohort study by Manuck et al. [22] the perinatal outcome of 360 patients with pPROM delivering at median of 31.4 gestational week were examined. The authors hypothesized that the incidence of severe perinatal morbidity would increase with latency duration. However, results of their multivariate models did not show any association between perinatal complications and latency. Higher incidence of severe neonatal morbidity was linked with lower gestational age and congenital sepsis. In a retrospective cohort study examining the outcome of 128 pregnancies with previable preterm premature rupture of membranes, longer latency duration, together with higher birth weight and more advanced gestational age at birth were associated with significantly lower postnatal mortality [23]. In a study by Yan et al. [24] analysing the outcome of 850 patients with pPROM, longer latency duration was a favourable factor for newborns delivered between 28th and 31st gestational week, but it was not beneficial beyond 32 weeks.

In another study examining neonatal outcome in pPROM depending on the latency duration only patients with latency exceeding 48 hours were included in the analysis (n = 206) [25]. The mean latency period in this study was 15.1 days. Authors observed that longer latency period did not contribute to higher neonatal morbidity. Conversely, in the subgroup with pPROM between completed 29th and 32nd gestational week, latency lasting more than 14 days was associated with lower incidence of neonatal complications compared to shorter latency periods (p = 0.001). After completed 32nd gestational week there was no difference

in neonatal complications incidence in latency duration subgroups: 3–7 days, 8–13 days, and 14 or more days. No statistically significant differences in the incidence of neonatal sepsis between the subgroups were identified. Similarly, to our study, latency period decreased with more advanced gestational age. However, in our analysis of the subgroup of neonates born before 32nd gestational week, longer median latency duration was observed in the subgroup of infants who developed pulmonary hypertension. This result was not confirmed in the multivariate analysis.

In a retrospective study on 159 pPROM cases by Jahromi et al. [26] authors presented the association between latency and neonatal respiratory distress syndrome incidence. There was a reverse linear relationship between latency and respiratory distress syndrome during the first 48 hours following the rupture of membranes — a gradual decrease in morbidity from 43% to 19% was observed. After 48 hours of latency the incidence of RDS increased again and reached 40%. Authors link this observation with pulmonary maturation due to antenatal corticosteroid therapy introduced shortly after PROM. However, the optimum time interval between PROM and delivery was not suggested because of big differences in leakage duration exceeding 48 hours. In another retrospective study Niesłuchowska-Hoxha et al. [27] analysed the occurrence of respiratory distress syndrome in 175 singleton pregnancies complicated by pPROM with median latency duration of 19 hours and 48 minutes. In a multivariate logistic regression authors reported association between RDS incidence and gestational age at birth, neonatal haemoglobin level, and neonatal platelet count.

We have observed association between caesarean delivery mode and the incidence of early-onset neonatal sepsis. This could be the consequence of qualifying patients with rapidly increasing inflammatory markers levels and foetal tachycardia for caesarean delivery. Results from our previous study showed that pPROM is associated with higher incidence of vaginal deliveries in comparison to preterm births with intact membranes (55% versus 35%, $p < 0.001$) [28]. It is also reported in the literature that spontaneous preterm labour is associated with higher risk of neonatal sepsis (22.9%) in comparison to patients with prolonged preterm amniotic fluid leakage without developing contractions directly afterwards (15.2%) [1]. However, in the study by Kachikis et al. [1] did not specify which type — early or late-onset sepsis — was analysed [1]. Regarding the association between caesarean delivery and neonatal sepsis, reported results vary and depend on the analysed population. In a retrospective study by Al-Lawama et al. [29] authors analysed sepsis risk factors among patients with rupture of membranes after completed 34th gestational week. Mode of delivery in the 176 analysed patients was not significant: 16 (50%) of newborns with sepsis and 65 (45%) controls were delivered via c-section, $p = 0.62$. Results of a prospective national population-based study by Lorthe et al. [30] examining the outcome of singleton pregnancies with pPROM between 24th and 32nd gestational week showed that 13 (52%) neonates with early-onset neonatal sepsis were delivered by caesarean section before labour onset compared to 253 (36%) neonates without early-onset sepsis with the same delivery mode (OR 1.9, 95% CI 0.6–6.5). In a prospective cohort study of 15926 deliveries by Zhuang et al. [31] multiple logistic models were performed in order to examine factors predisposing to the incidence of neonatal infectious diseases. Caesarean section was associated with increased risk of early-onset pneumonia in the group of term deliveries with intact membranes (OR = 1.45, 95% CI 1.05–2.02, $p = 0.03$) and term deliveries with PROM (OR = 1.83, 95% CI 1.07–3.13, $p = 0.03$). However, in this study mode of delivery was not significant in the subgroups of preterm deliveries. In a study by Polcwiartek et al. [32] analysing risk factors for early-onset sepsis in a cohort of 142,410 term infants, caesarean delivery was associated with decreased risk (OR 0.66, 95% CI 0.57–0.76, $p < 0.001$).

Our multivariate analysis did not show any association between use of intravenous tocolysis and the risk of developing neonatal infection. Similar results are presented in the literature. In a study by Lorthe et al. [30] tocolysis was used in 18 (64%) patients from the early-onset sepsis group and in 482 (73%) controls (OR 0.7, 95% CI 0.2–2.1). In a retrospective cohort study of 46968 deliveries following pPROM by Chackowicz et al. [33] it was examined whether use of tocolysis could affect the risk of neonatal septic death. Tocolysis was administered to 6264 (13.3%) patients, and it was not significantly associated with neonatal septic death at 7 days (OR 0.66, 95% CI 0.39–1.13) nor at 28 days (OR 0.85, 95% CI 0.60–1.19). However, in our study the subgroup of patients requiring intravenous tocolysis was at higher risk of developing neonatal respiratory morbidity: acute respiratory failure, transient tachypnoea of the newborn and bronchopulmonary dysplasia.

Our study identified earlier gestational age at PROM as another risk factor for neonatal morbidity**.** In a prospective cohort study by Winn et al. [34] with the incidence of pulmonary hypoplasia of 12.9% of the studied group, authors also pointed that gestational age at the rupture of membranes is the risk factors for neonatal complications. Other identified risk factors included latency duration, initial and average amniotic fluid index. According to Weiner et al. [35] increased incidence of severe neonatal respiratory morbidity following pPROM occurs in case of oligohydramnios, earlier gestational age at PROM, shorter latency, and caesarean section.

Our study showed that one of the identified independent risk factors for acute respiratory failure in neonates

was positive cervical culture. Association between vaginal dysbiosis in pPROM patients and early onset neonatal sepsis is well documented in the literature [36]. Together with the promising results of prophylactic antibiotic treatment resulting in decrease in neonatal mortality, chronic lung disease and reduced need for supplemental oxygen [37], these are the arguments standing for routine cervical culture screening and adjusted treatment based on antibiogram results in women with preterm premature rupture of membranes.

Limitations of this study include relatively high proportion of late preterm neonates and a single centre character, which determines the number of enrolled patients. This could be the reason why the gestational age at birth has not been identified as an independent risk factor for bronchopulmonary dysplasia in the presented multivariate analysis results. In a case-control study by Hernandez-Ronquillo et al. [38] identified risk factors for development of bronchopulmonary dysplasia were younger gestational age at birth, lower birth weight and neonatal infectious complications. In our study factors associated with bronchopulmonary dysplasia were lower birth weight and need for intravenous tocolysis.

CONCLUSIONS

Birth weight and gestational age at PROM and at birth are the leading factors influencing the risk of neonatal infectious and respiratory morbidity following preterm premature rupture of membranes. Another identified risk factor for neonatal morbidity was positive cervical culture, therefore collection of cervical specimen and analysis of aerobic, anaerobic, fungal, and atypical pathogens cultures results could lead to individualized and more effective management of patients resulting in fewer neonatal complications.

Conflict of interest

All authors declare no conflict of interest.

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