ORIGINAL RESEARCH ARTICLE

Effect of timing of antibiotic use on premature rupture of membranes and its impact on reproductive tract infection and fetal membrane cell scorching indicators

DOI: 10.29063/ajrh2024/v28i12.15

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Abstract

The study was designed to appraise the effects of early antibiotic administration on reproductive tract infections and fetal membrane cell scorching in instances of premature rupture of membranes (PROM). A total of 107 pregnant women diagnosed with PROM between July 2020 and June 2022 were randomly assigned to two groups: the Intervention (n=54), where ampicillin were administered within 24 hours of PROM onset, and the control group (n=53), where ampicillin were given 24-48 hours after PROM. Maternal and neonatal outcomes, incidence of reproductive tract infections, and fetal membrane cell scorching indicators (Caspase-1, Caspase -3, Caspase-9 and IL-β) were compared. The intervention group had significantly fewer adverse maternal and neonatal outcomes ($p<0.05$). Post-treatment, rates of Chlamydia trachomatis, Mycoplasma solium, and genital tract infections decreased in both groups, with lower rates in the intervention group ($p<0.05$). Positive expression rates of Caspase-1, -3, -9, and IL-β in placental tissues were also lower in the intervention group ($p<0.05$). We conclude that administering antibiotics within 12 hours of PROM reduces reproductive tract infections, lowers fetal membrane cell scorching, and improves maternal and neonatal outcomes, supporting early antibiotic use in the management of PROM *(Afr J Reprod Health 2024; 28 [12]: 139-147)*

Keywords: Premature rupture of membranes; Antibiotics; Reproductive tract infection; Fetal membrane cell scorching

Résumé

L'étude a été conçue pour évaluer les effets de l'administration précoce d'antibiotiques sur les infections de l'appareil reproducteur et la brûlure des cellules membranaires fœtales en cas de rupture prématurée des membranes (PROM). Au total, 107 femmes enceintes diagnostiquées avec une PROM entre juillet 2020 et juin 2022 ont été réparties au hasard en deux groupes : l'intervention (n = 54), où l'ampicilline a été administrée dans les 24 heures suivant le début de la PROM, et le groupe témoin (n = 53). , où l'ampicilline a été administrée 24 à 48 heures après la PROM. Les résultats maternels et néonatals, l'incidence des infections de l'appareil reproducteur et les indicateurs de brûlure des cellules de la membrane fœtale (Caspase-1, Caspase -3, Caspase-9 et IL-β) ont été comparés. Le groupe d'intervention présentait significativement moins d'issues maternelles et néonatales indésirables ($p <0,05$). Après le traitement, les taux d'infections à Chlamydia trachomatis, à Mycoplasma solium et des voies génitales ont diminué dans les deux groupes, avec des taux plus faibles dans le groupe d'intervention ($p < 0,05$). Les taux d'expression positifs des caspases-1, -3, -9 et de l'IL-β dans les tissus placentaires étaient également plus faibles dans le groupe d'intervention ($p <0,05$). Nous concluons que l'administration d'antibiotiques dans les 12 heures suivant la PROM réduit les infections de l'appareil reproducteur, diminue la brûlure des cellules de la membrane fœtale et améliore les résultats maternels et néonatals, favorisant ainsi l'utilisation précoce d'antibiotiques dans la gestion de la PROM. *(Afr J Reprod Health 2024; 28 [12]: 139-147).*

Mots-clés: Rupture prématurée des membranes ; Antibiotiques ; Infection des voies génitales ; Brûlure des cellules de la membrane fœtale

Introduction

Premature rupture of membranes (PROM), occurring in the gestational period between 28 and 37 weeks, is a prominent cause of preterm labor and presents hazards to the health of both the pregnant woman and the fetus.[1-2] Untreated PROM, particularly at term, can lead to severe complications such as preterm labor, obstructed labour, perinatal mortality, and maternal and neonatal infections. Consequently, obstetric clinicians face the pressing challenge of devising

effective strategies to prevent and manage PROM, aiming to reduce maternal and neonatal complications and enhance perinatal outcomes.

The etiology of PROM is multifactorial, involving factors such as fetal membrane integrity, infection, increased intrauterine pressure, and cervical insufficiency. Infection, particularly with pathogenic bacteria in the maternal reproductive tract, is a significant contributor to PROM, preterm labor, and puerperal infections, highlighting the causal relationship between infection and PROM.[3-4]Antibiotics, known for their efficacy in controlling infections, have emerged as a therapeutic option for PROM, albeit with variations in efficacy depending on the timing of administration. However, limited research has explored the effectiveness of antibiotics at different stages of PROM.

Furthermore, studies suggest a correlation between cellular damage and the development of PROM. When fetal membranes encounter danger signals, they initiate cell death pathways, accelerating extracellular matrix metabolism and leading to membrane swelling and rupture. However, clinical research on the mechanisms underlying premature fetal membrane cell death remains limited.[5-6] Consequently, assessing fetal membrane cell damage provides a novel perspective for evaluating the effectiveness of PROM prevention and treatment programs.

Based on this, this study investigates the effects of timing of antibiotic administration in PROM on genital tract infection and indicators of fetal membrane cell damage. The findings aim to offer valuable insights for the effective clinical management of PROM, thereby improving maternal and neonatal outcomes.

Methods

One hundred and seven patients who underwent routine preconception screening in Changshu Hospital Affiliated to Nanjing University of Chinese Medicine throughout the period from July 2020 to June 2022 and were diagnosed as having PROM were selected for the study . By using the random number table method, they were randomly assigned to an intervention group (n=54, antibiotics within <24h of PROM) and a control group (n=53, antibiotics between 24 and 48h of PROM).

The inclusion criteria were: (1) those who met the diagnostic criteria for PROM in reference to the eighth edition of Obstetrics and Gynaecology, edited by Le Jie.[7] The pregnant woman had sudden vaginal discharge of clear fluid or fetal fat-like material and the pH of the effluent was determined to be ≥6.5; (2) the age range of the pregnant woman was 22-36 years; (3) reduced amniotic fluid volume was detected by ultrasound; (4) the patients all underwent caesarean section in our hospital and placental tissue was obtained for the detection of fetal membrane cell scorching; and (5) singleton, live births. The exclusion criteria were: (1) patients with combined fibroids or other tumours; (2) those who did not undertake antenatal examination in the hospital and have incomplete records; (3) patients with severe underlying diseases (myocardial infarction, renal failure, liver and kidney failure, heart valve disease, etc.); and (4) those with combined systemic infections and those who had taken drugs, alcohol, sedative drugs, etc. during pregnancy.

All patients received the identical antibiotic treatment protocol to prevent infection. Specifically, ampicillin was administered intravenously at a dose of 2g every 6 hours for a total of 48 hours. After the completion of 48 hours, azithromycin tablets (manufactured by Southwest Pharmaceutical Co., Ltd., with the approval number of Guomao Zizhi H20054767 and a specification of 0.25g) were given orally, with an initial dose of 0.5g per day and then 0.25g per day thereafter. For those patients who did not give birth within 1 week, the antibiotics were ceased at the conclusion of the treatment course. For patients who delivered within 1 week, the antibiotics were halted at the moment of fetal delivery, and the decision regarding the continuation of antibiotics was determined based on the maternal condition after delivery.

In the intervention group and control group, the types of antibiotics used and the overall treatment plan principles are the same, but there is a difference in the usage time. The intervention group starts using antibiotics within 24 hours after the onset of premature rupture of membranes (PROM), aiming to inhibit bacterial reproduction as soon as possible and reduce the risk of adverse maternal and infant outcomes and infection-related complications. The control group starts using

antibiotics between 24 and 48 hours after the onset of PROM. By comparing and studying the impact of different usage times on the efficacy of antibiotics, the optimal usage timing is determined to provide a basis for clinical practice.

Observed indicators

The adverse maternal and fetal outcomes identified in intervention and control groups included the following 1): the incidence of maternal chorioamnionitis (Confirmed by pathological examination), postpartum haemorrhage and puerperal infection and calculate the incidence. (2) Adverse neonatal outcomes: the incidence of neonatal respiratory distress syndrome, sepsis, intrauterine distress, asphyxia and hyperbilirubinemia, and the incidences were calculated in both groups. (3) Genital tract infections: sterile swabs were taken from secretions on the lateral wall of the vagina, and were examined for chlamydia trachomatis using the chlamydia rapid test reagent from Unipath Ltd. is used. The interpretation was as follows: no line in the result window was considered negative; one line in the control window and one in the result window were considered positive; while no line in the control window was considered invalid and needed to be repeated. Streptococcus B test: After 48 hours of incubation and smear, microscopic examination of Gram stain was performed. Microscopic gram-positive cocci in a chain-like pattern and negative by catalase test were considered positive for streptococci.

Fungal test: After being incubated at 37°C according to the instructions of the fungal test kit, the sample was observed under the microscope after 48 h. The presence of spores was considered positive and vice versa. (4) Fetal membrane cell scorching index: the fetal membrane tissue was tested by removing the exfoliated material from the surface, and then washing the surface blood with phosphate buffered saline three times. After treatment, the fetal membranes were fixed in 10% paraformaldehyde, after which paraffin sections were routinely prepared at a thickness of 4 μm. After routine hematoxylin-eosin staining, immunohistochemistry was performed. Caspase 3, 8, 9 and IL-β mouse anti-human monoclonal antibodies (MAIXIN-BIO) were prepared at a working concentration of 1:50 according to the instructions of the immunohistochemistry kit (Fuzhou MAIXIN product) and the antigen was repaired at high pressure. After adding the primary antibody, it was incubated at °C for 1h. and transferred to a 4°C shaker for overnight incubation. Immunohistochemical results were analysed using the HPIAS image analysis system. caspase-1, caspase-3, caspase-9 and IL-β positive were stained yellow, tan, brown and yellow in the fetal membrane tissue respectively.

Data analysis

SPSS 21.0 was employed to process the data, and statistical descriptions were completed using ($\bar{\chi} \pm$ s) for count data that conformed to a normal distribution. As for the above measurement data, the hypothesis test for comparison between groups was an independent samples t-test. The count data were represented by applying the number of cases (percentage), and the chi-square test was employed for comparative analysis between groups for these two data categories. P less than 0.05 implied that the statistical discrepancies were statistically meaningful.

Ethical consideration: The Medical Ethics Committee of Changshu Hospital Affiliated to Nanjing University of Chinese Medicine sanctioned this research, and all the individuals put their signatures on an informed consent form.

Results

Basic information

Table 1 presents the basic information of two groups involved in the research, comprising an intervention Group and a Control Group. As shown in Table 1, each group consisted of 54 and 53 participants, respectively. As shown in Table 1, there was no difference in the mean age between the intervention and control groups as well as the gestational ages in which they presented.

Table 1: Basic information

Group	N	Age (year)	Week of gestation (Week)
Intervention group	54	27.69±3.28	31.13±2.81
Control Group	53	27.73±3.24	30.79±2.85
χ^2 or t	-	0.064	0.621
P	-	0.950	0.536

Table 2: Adverse maternal outcomes in both groups [n (%)]

Group	n	Chorioamnionitis	Postnatal bleeding	Infeksi nifas	Total
Intervention group	54	3 (5.56)	2 (3.70)	1 (1.85)	6 (11.11)
Control Group	53	7 (13.21)	5 (9.43)	3 (5.56)	15 (28.30)
χ^2	-	-	-	-	5.011
P	-	-	-	-	0.025

Table 3: Incidence of adverse neonatal outcomes in both groups [n (%)]

Group	n	Sindrom gangguan pernapasan	Sepsis	Intrauterine distress	Asphyxiation	Hiperbilirubinemia	Total
Intervention group	54	1 (1.85)	1 (1.85)	1 (1.85)	1 (1.85)	1 (1.85)	5 (9.26)
Control Group	53	2 (3.77)	3 (5.66)	2 (3.77)	1 (1.89)	5 (9.43)	13 (24.53)
χ^2	-	-	-	-	-	-	4.457
P	-	-	-	-	-	-	0.035

Comparison of adverse maternal outcomes

The appearance of adverse maternal outcomes in the research and control groups is presented in Table 2. Statistical analysis using the χ^2 revealed a notable distinction between groups concerning adverse maternal outcomes, with a p-value of 0.025 (Table 2). This suggests that the intervention group displayed a lesser occurrence of adverse maternal outcomes as opposed to the control group ($p<0.05$, Table 2).

Comparison of adverse neonatal outcomes

Analysis using the χ^2 demonstrated a significant difference between the two groups regarding adverse neonatal outcomes, with a p-value of 0.035 (Table 3). This suggests that the intervention group (9.26%) exhibited a lower occurrence of adverse neonatal outcomes in relative to the control group (24.53%) ($p<0.05$, Table 3).

Comparison of reproductive tract infections

Prior to treatment, no statistically remarkable distinctions were identified in the rates of Chlamydia trachomatis positivity, Mycoplasma solium positivity, genital tract infection, genital tract fungal infection, Streptococcus B infection and human mycoplasma infection in the lower genital tract between groups ($P>0.05$, Table 4). Following treatment, the rates of Chlamydia trachomatis positivity, Mycoplasma solium positivity and genital tract infection in both groups lessened, with the intervention group being substantially lower.

Table 4: Genital tract infections in both groups [n (%)]

Group	n	Fungus				Streptococcus group B				Chlamydia trachomatis			
		Positive		Feminine		Positive		Feminine		Positive		Feminine	
		Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Intervention group	54	5 (9.26)	3 (5.56)	49 (90.74)	51 (94.44)	3 (5.56)	1 (1.85)	51 (94.44)	53 (98.15)	9 (16.67)	2 (3.70)	45 (83.33)	52 (96.30)
Control Group	53	5 (9.43)	3 (5.66)	48 (90.57)	50 (94.34)	4 (7.55)	1 (1.89)	49 (92.45)	52 (98.11)	9 (16.98)	8 (15.09)	44 (83.02)	45 (83.91)
χ^2	-	0.001	0.000	0.001	0.001	0.174	0.000	0.174	0.000	0.000	4.096	0.002	4.096
P	-	0.975	1.000	0.975	0.981	0.677	0.989	0.677	0.989	1.000	0.043	0.965	0.043

Continued Table 1: Genital tract infections in both groups [n (%)]

Group	n	Uroplasma lytica				Mycoplasma hominis				Reproductive tract infection			
		Positive		Feminine		Positive		Feminine		Positive		Feminine	
		Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
Intervention group	54	8 (14.81)	1 (1.85) (1.85)	46 (85.19)	53 (98.15)	4 (7.41)	1 (1.85)	50 (92.59)	53 (98.15)	24 (44.44)	16 (29.63)	30 (55.56)	38 (70.37)
Control Group	53	9 (16.98)	6 (11.32)	44 (83.02)	47 (88.68)	4 (7.55)	1 (1.89)	49 (92.45)	52 (98.11)	23 (43.40)	26 (49.06)	30 (56.60)	27 (50.94)
χ^2	-	0.094	3.922	0.094	3.922	0.001	0.000	0.001	0.000	0.012	5.490	0.012	5.490
P	-	0.759	0.048	0.759	0.048	0.978	0.989	0.978	0.989	0.913	0.019	0.913	0.019

Table 5: Indicators of fetal membrane cell scorch death in both groups [n (%)]

Group	n	Caspase-1		Caspase-3		Caspase-9		IL-β	
		Positive	Feminine	Positive	Feminine	Positive	Feminine	Positive	Feminine
Intervention group	54	31 (57.41)	23 (42.59)	20 (37.04)	34 (62.96)	19 (35.19)	35 (64.81)	33 (61.11)	21 (38.89)
Control Group	53	41 (77.36)	12 (22.64)	31 (58.49)	22 (41.51)	29 (54.72)	(45.28)	42 (79.25)	11 (20.75)
χ^2	-	4.837		4.935		4.125		4.169	
P	-	0.028		0.026		0.042		0.041	

Meanwhile, the rates of genital tract fungal infection, Streptococcus B infection, and human mycoplasma infection went down in both groups, but the comparison between groups was not statistically noteworthy (P>0.05, Table 4).

Comparison of indicators of fetal membrane cell scorch death

Analysis utilizing the chi-square test (c2) disclosed noteworthy differences between groups for all indicators, with p-values ranging from 0.026 to 0.042 (Table 5). This suggests a notable disparity in the incidence of fetal membrane cell scorch death indicators between the two groups, with higher proportions observed in the control group as opposed to the intervention group (P<0.05, Table 5)

Discussion

PROM means the spontaneous breaking of fetal membranes before labour begins. The incidence varies from one report to another and accounts for approximately 3%-16%[8] and is the most common perinatal complication. PROM is a precursor to labour and is the principal cause of preterm labour in about 70% of women who deliver within 72h of PROM. The data shows that about 40% of preterm deliveries are linked to intrauterine infections. Additionally, the incidence of intrauterine infection in women with preterm births due to PROM is 2.5 times higher than that of normal preterm births. Antibiotic treatment after rupture of membranes is therefore important in preventing intrauterine infections and preventing the upward transmission of pathogens from the vagina after rupture of membranes. The hazard of intrauterine infection depends on how long the membranes have been ruptured. The longer the period after rupture, the increased risk of infection and the greater the chance of unfavourable maternal and infant results.

However, the timing of antibiotic use has been controversial.[9] It is reported that prophylactic antibiotics within 12 h of PROM substantially reduced the incidence of intrauterine infection and optimised maternal and infant outcomes.[10] However, it has been reported that premature antibiotic use was not beneficial in improving pregnancy outcomes and neonatal outcomes. Reports indicate that in pregnant women with premature rupture of membranes who were not full-term, prophylactic use of antibiotics did not enhance maternal and infant outcomes for those with PROM. By contrast, extending prophylactic antibiotics to 12 hours after premature rupture of membranes remarkably decreased the rates of chorioamnionitis and endometritis by 51% and 88% respectively.[11] This shows that there is no uniform standard for the timing of antibiotic use in the management of PROM.

In order to investigate the timing of antibiotics use in the effective treatment of PROM, our study analysed the effect of different timing of antibiotics on reproductive tract infections in patients with PROM. The results showed that the rates of Chlamydia trachomatis positivity, Mycoplasma solium positivity and reproductive tract infections were fewer in the intervention group than the control group following treatment. This confirmed that the use of antibiotics within 12h of PROM can significantly reduce reproductive tract infections. Reproductive tract infections are the main cause of PROM. When pathogenic bacteria invade the genital tract, they indirectly lead to increased glial

fragility and a greater tendency for fetal membrane rupture, as well as affecting the immune activity of the genital tract.[12] Reports in the clinical literature[13] indicate that Mycoplasma solium and Chlamydia trachomatis are key pathogens in the pathogenesis of PROM. In contrast, the role of Streptococcus B and fungal infections is not significant.

The results of this investigation are analogous to those in the literature. Streptococcus B and fungal infections do not differ significantly, while Mycoplasma urealyticum and Chlamydia trachomatis infections may have a greater impact on premature rupture of membranes. When Chlamydia trachomatis is carried in the body in normal amounts, the immune system regulates its mechanisms, but when it increases to a certain number, the immune balance is disturbed, leading to reproductive tract infection and PROM or preterm birth[14-15]The use of antibiotics within 24 h of the onset of PROM is effective in reducing the rate of positive pathogens, reducing the extent of reproductive tract infection and mitigating the negative effects of reproductive tract infection on the mother and baby.

Our study further analyzed the efficacy of different timing of antibiotics in PROM from the perspective of fetal membrane cell scorching. The outcome revealed that the positive expression of Caspase-1, Caspase-3, Caspase-9 and IL-β in the placental tissues of the intervention group were less than those of the control group. This further validates the efficacy of antibiotics within 24h of the onset of PROM to reduce fetal membrane cell scorching. A decrease in extracellular matrix, including collagen and laminin, has been found to occur in normal labour and PROM, particularly in PROM.[16-17] In PROM, cell scorching accelerates fetal membrane degradation and causes rupture of the membranes.[18]Caspases-3 is present at higher levels in premature rupture of membranes than in normal pregnancy, and after labour initiation If there are changes in the endocrine process, activation of a large number of scorch death genes promotes rupture of the membranes. Caspases-9 expression also promotes Caspase-3 expression. Caspases-1, an initiator of the mitochondria-dependent pathway, is expressed at low levels under normal physiological conditions, and the mitochondria-dependent pathway is abnormal in fetal membrane tissues.[19-20] IL-1β may promote high expression of matrix metalloproteinases, which in turn accelerates the metabolism of extracellular matrix proteins in fetal membrane tissues, causing PROM.

In conclusion, abnormal expression of the above factors may contribute to the development of PROM and could offer a basis for preventing and treating PROM.[21] The outcomes of this study found that early application of antibiotics reduced the level of fetal membrane cell scorching in patients with PROM, which provides a basis for the early use of antibiotics to treat PROM from a completely new direction. However, due to limited conditions, the mechanism of early antibiotic administration on fetal membrane cell scorching in PROM has not been investigated in depth, and this is a direction we will focus on in the future.

The main effect of PROM on mother and baby is that it causes adverse maternal and neonatal outcomes. Our results indicated that the frequency of maternal and neonatal adverse outcomes was less in the intervention group as opposed to the control group. This means that the use of antibiotics within 24h was beneficial in lowering the incidence of maternal and neonatal adverse outcomes. It provides a valid basis for the effectiveness of early antibiotic therapy for PROM and verifies the substantial and realistic benefit of early antibiotic treatment of PROM.

The reasons considered are that PROM leads to massive loss of amniotic fluid, causing pressure on the umbilical cord and the fetus immediately adjacent to the uterine wall during contractions, and in severe cases, cord prolapse, which affects placental circulation and ultimately leads to acute and chronic hypoxia, asphyxia and even death of the intrauterine fetus.[22] After PROM, the natural barrier between the uterine cavity and the outside world disappears, and a variety of pathogenic microorganisms can be transmitted upstream to the uterus, causing intrauterine infection and chorioamnionitis in the mother and sepsis in the newborn.[23] Intrauterine infections that existed before or during labour can continue into the postpartum period and even worsen, eventually leading to puerperal infections and postpartum haemorrhage and worsening maternal and infant outcomes. The use of antibiotics within 12h of the onset of PROM can block the upstream pathway of

pathogenic microorganisms as early as possible, curb the continuation of intrauterine infections existing before or during labour into the postpartum period, reduce the adverse outcomes of the mother such as postpartum puerperal infections, and reduce the occurrence of adverse outcomes of the newborn such as postpartum sepsis, optimising maternal and infant outcomes.

Study strengths and limitations: This study has several limitations. Firstly, the relatively small sample size included might give rise to statistical fluctuations. Secondly, there is a deficiency in the exploration of the specific mechanism through which early antibiotic use reduces the scorching of fetal membrane cells in cases of PROM. Based on the above shortcomings, we will further expand the number of cases and investigate the mechanism of early antibiotics to reduce the scorching of PROM fetal membrane cells, so as to provide more feasible and reliable opinions for the effective clinical management of PROM.

This study found that using antibiotics within 24 hours of the onset of PROM has many benefits, which is of great significance for clinical practice. Clinicians should pay attention to administering antibiotics within 24 hours while also taking into account the individual conditions of patients. From a policy perspective, the research results can provide a reference for the formulation of guidelines and promote the strengthening of standardized management, such as training doctors and establishing a quality control system, in order to improve maternal and infant health and optimize the utilization of medical resources. More research is needed in the future to improve relevant strategies.

Conclusion

In pregnant women with PROM, early administration of antibiotics (<24 hours after PROM onset) led to improved maternal and neonatal outcomes compared to delayed antibiotic administration (24 to 48 hours after PROM onset). The intervention group exhibited lower incidences of adverse outcomes and reproductive tract infections, along with reduced fetal membrane cell scorching indicators. These findings suggest that timely antibiotic use in PROM may effectively mitigate reproductive tract infections and mitigate fetal membrane damage. Further studies are warranted to look into the long-term consequences of early antibiotic administration on maternal and neonatal health results in cases of PROM. Additionally, investigating the optimal timing and duration of antibiotic therapy, as well as potential antibiotic resistance implications, could provide valuable insights for clinical practice. Moreover, appraising the influence of early antibiotic use on other pregnancy-related complications and fetal development parameters would contribute to a comprehensive understanding of its benefits and risks.

Acknowledgments

We are deeply indebted to all the medical staff and departments who contributed to this research.

Author's contribution

Conceptualization, Y.Y.Q. and G.Y.Q.; Methodology, Y.Y.Q.; Software, HYN.; Validation, Y.Y.Q., G.Y.Q., and H.Y.N.; Formal Analysis, D.Y.Z.; Investigation, Y.Y.Q.; Resources, Y.Y.Q.; Data Curation, Y.Y.Q.; Writing – Original Draft Preparation, Y.Y.Q.; Writing – Review & Editing, Y.Y.Q.; Visualization, W.Q.G.; Supervision, X.M.C.; Project Administration, Y.Y.Q.; Funding Acquisition, X.M.C.

Conflicting interests

No competing interests.

References

1. D'Souza V P , Parvathi S and Appalaraju B . Microbiological and Molecular Profile of Preterm Premature Rupture of Membranes (Pprom), Preterm Labor (Ptl) and Neonatal Outcome[J]. *Indian Journal of Medical Microbiology*, 2021, 39(8):37-38.
2. Lee W L , Chang W H and Wang P H . Risk factors associated with preterm premature rupture of membranes (PPROM)[J]. *Taiwanese journal of obstetrics & gynecology*, 2021, 60(5):805-806.
3. Yan H, Zhang S and Lin QD. Research progress of miRNAs related to pre-eclampsia [J]. *International Journal of Obstetrics and Gynecology*, 2016(4):377-380.
4. Boyd HA, Hassaan T, Jan W, Sundaram R, Zhan M, Tong J

and Wylie BJ. Associations of personal and family preeclampsia history with the risk of early-, intermediate- and late-onset preeclampsia.[J]. *American Journal of Epidemiology*,2013,178(11):1611-161.

5. Ruth H, Janine Z, Jana P, Hans K, Maria S, Karl K and Sandra M. Placenta inflammation, vaginal microbiome and Early-Onset Neonatal Sepsis (EONS) after Preterm Premature Rupture of Membranes (PPROM)[J]. *Placenta*, 2021, 112(66):e66.
6. Rodriguez A M , Pastor A and Fox N S . The Association between Shirodkar Cerclage and Preterm Premature Rupture of Membranes in Singleton Pregnancies[J]. *American Journal of Perinatology*, 2021,38(1):e347-e350.
7. Han Y, Wang W, Wang X, Duan Y, Zhang Q, Zhao L and Hu H .Prenatal exposure to fine particles, premature rupture of membranes and gestational age: A prospective cohort study[J]. *Environment 54international*, 2020, 145(87):e106146.
8. Xie X.,= Gou W. L. Obstetrics and gynecology [M]. 8th ed. *Beijing: People's Health Press*,2014: 64.
9. Eleje GU, Adinma JI, Ghasi S, Ugwu EO, Ikechebelu JI and Ezeama CO. Antibiotic susceptibility pattern of genital tract bacteria in pregnant women with preterm premature rupture of membranes in a resource-limited setting[J]. *Int J Gynaecol Obstet*, 2014, 127(1):10-14.
10. Legros X, Volumenie JL, Janky E, Couillandre E and Magnin G .A case study regarding the use of antibiotic therapies for the treatment of preterm rupture of fetal membranes, and emergence of antibiotic resistant bacteria[J]. *J Gynecol Obstet Biol Reprod(Paris)*, 2015, 44(2):164-170.
11. Saccone G and Berghella V. Antibiotic prophylaxis for term or near-term premature rupture of membranes: metanalysis of randomized trials[J]. *Am J Obstet Gynecol*, 2015,212(5):627.e1-627.e9.
12. Helble JD, Gonzalez RJ, von Andrian UH and Starnbach MN .Gamma Interferon Is Required for Chlamydia Clearance but Is Dispensable for T Cell Homing to the Genital Tract[J]. *mBio*, 2020,11(2):e00191-e00200.
13. Nguyen QHV, Le HN, Nu VD, Nguyen ND and Le MT. Lower genital tract infections in preterm premature rupture of membranes and preterm labor: a case-control study from Vietnam.[J]. *The Journal of Infection in Developing Countries*, 2021, 15(6):805-811.
14. Yao Z and Xzla B. Updates in Prevention Policies of Early-Onset Group B streptococcal Infection in Newborns[J]. *Pediatrics & Neonatology*, 2021, 62(5):465-475.
15. Amirah Assabahi, Rita Driggers, Christopher A. Keeys, Alexa Mader and Paul Norris. Evaluation of appropriate vancomycin prescribing for the prevention of newborn group B streptococcal infections in a community hospital obstetrics service [J]. *J Perinat Med*,2022,332(7):e4443.
16. Feng C, Li R, Shamim AA, Ullah MB, Li M, Dev R, Wang Y, Zhao T, Liao J, Du Z, Ling Y, Lai Y and Hao Y. High-resolution mapping of reproductive tract infections among women of childbearing age in Bangladesh: a spatial-temporal analysis of the demographic and health survey[J]. *BMC Public Health*, 2021, 21(1):342-346.
17. Kacerovsky M, Pliskova L, Bolehovska R, Musilova I, Hornychova H, Stepanek P and Andrys C. Cervical Gardnerella vaginalis in women with preterm prelabor rupture of membranes[J]. *PLoS ONE*, 2021, 16(1):e0245937.
18. Nikel K, Ricci M, Majeau L, Baschat AA, Shambaugh V, Friedman A, Iams JD, Seitz E and Bukowski R. Examining the relationship between previable premature prelabour rupture of membranes and neurodevelopmental outcomes at 18–24 months of age[J]. *Ultrasound in Obstetrics and Gynecology*, 2020, 56(1):284-284.
19. Nery N, Ticona J, Gambrah C, Castillo-Salgado C, Passos VM, Aliaga G and Barreto ML. Social determinants associated with Zika virus infection in pregnant women[J]. *PLoS Neglected Tropical Diseases*, 2021, 15(7):e0009612.
20. Samantha W, Blair A, Michelle C, McCartney SA, Fairweather D, Rajagopalan S and Newburg DS. MicroRNA Signature of Epithelial-Mesenchymal Transition in Group B Streptococcal Infection of the Placental Chorioamniotic Membranes[J]. *The Journal of Infectious Diseases*, 2020,222(10):1713-1722.
21. Eleje GU, Ukah CO, Onyiaorah IV, Ezugwu EC, Ugwu EO, Ohayi SR, Eleje LI, Egeonu RO, Ezebialu IU, Obiora CC, Enebe JT, Ajah LO, Okafor CG, Okoro CC, Asogwa AO, Ogbuokiri DK, Ikechebelu JI and Eke AC. Diagnostic value of Chorioquick for detecting chorioamnionitis in women with premature rupture of membranes[J]. *International Journal of Gynecology & Obstetrics*, 2020, 149(1):98-105.
22. Cai N, Chen C, Tao M and Liao W. Study on the correlation between premature rupture of membranes combined with chorioamnionitis and respiratory distress syndrome in very preterm infants[J]. *Chinese Journal of Infection Control*,2022,21(09):905-910
23. Zhang H, Ding W M and Liu L. Analysis of the effect of latency time of premature rupture of membranes on pregnancy outcome at different gestational weeks[J]. *China Maternal and Child Health Care*,2019,34(08):1721-1724.