



## Review Article

# The primary microbial pathogens associated with premature rupture of the membranes in China: A systematic review



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## ABSTRACT

To describe the spectrum of pathogens isolated from Chinese women experiencing premature rupture of the membranes (PROM) and those of their neonates, in order to provide effective management of PROM. We searched Ovid Medline, Chinese Biomedical Literature Database, China National Knowledge Infrastructure, and VIP Database for Chinese Technical Periodicals up to April 2012. The quality of studies was assessed utilizing the Strengthening the Reporting of Observational Studies in Epidemiology Statement. Among the included 36 studies, 11 (30.55%) were deemed to be at Level A, 12 (33.33%) at Level B, three (8.33%) at Level C, and 10 (27.78%) at Level D. *Staphylococcus* and *Escherichia coli* were the two primary microorganisms isolated from women with PROM and their infants. Subgroup analysis showed the distribution of microorganisms from the six regions of China varied. *Staphylococcus* bacteria were resistant to penicillins, except oxacillin, but more sensitive to first- and second-generation cephalosporins. *Escherichia* were sensitive to first- and second-generation cephalosporins and were more sensitive to aztreonam than cephalosporins. The main pathogens derived from women with PROM and their newborns were *Staphylococcus* and *E. coli*, which differs from the pathogens in Western countries. Hence, one might infer that the pathogens involved in PROM should be defined in each region to maximize antibiotic effectiveness. In addition, randomized controlled studies are needed to compare prophylactic use of antibiotics versus use of antibiotics after a positive culture for newborn infants with a history of PROM.

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## Introduction

The definition of premature rupture of the membranes (PROM) is rupture of membranes prior to the onset of labor [1]. Membrane rupture that occurs before 37 weeks of gestation is referred to as preterm premature rupture of membranes (PPROM) [1]. PROM occurs in about 8% of pregnant women worldwide [2–4]. A report from Mainland China found that the incidence of PROM was significantly higher at 19.5% [5]. PROM presents in 30–40% of

preterm births, and is the most common cause of deliveries occurring between 20 weeks and 37 weeks of gestation [6]. In addition, prematurity and low birth weight are leading causes of neonatal death (31%) in the world [7]. Determining the most efficacious method to manage PROM in order to minimize its adverse impact on newborns is necessary and paramount to a positive outcome.

Infection can be associated with PROM as either a cause or a consequence [8]. Current literature has identified a broad range of organisms present in amniotic fluid specimens after PROM [9–11]. In the USA and Canada, Group B Streptococci (GBS) appears to be the microorganism that colonizes the majority of pregnant women with PROM [12,13]. It is also the primary causative agent associated with PPRM [14–16]. Guidelines issued by these two countries

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have suggested administering prophylactic ampicillin to women with PROM.

However, the distribution of microorganisms associated with PROM in pregnant women and neonates in China is still uncertain. Although there are studies investigating microorganisms in Chinese women with PROM and their neonates, all of them were carried out in single hospitals with limited sample sizes. The purpose of this study is to describe the spectrum of pathogens in this group of Chinese mothers and neonates by a systematic review. The results may aid in choosing the most appropriate antibiotic in the management of PROM in China.

## Materials and methods

### Search strategy

We searched Ovid Medline, Chinese Biomedical Literature Database (1989–2012), China National Knowledge Infrastructure (1979–2012), and VIP Database for Chinese Technical Periodicals (1989–2012) using the keywords: *premature rupture of membranes*, *microbiological*, *pathogenesis*, and *etiology*, without limitation of language. The references of eligible studies were also searched.

### Criteria for considering studies for this review

Types of participants: pregnant women diagnosed with PROM and their newborns.

Types of specimens: mothers: cervical secretions, vaginal discharge, amniotic fluid, placenta or blood sample; neonates: mouth and throat swabs or blood sample.

Types of outcomes: categories and antimicrobial susceptibility of microorganisms isolated from mothers with PROM and/or their infants.

Study designs: prospective or retrospective studies.

### Quality assessment and data collection

Two authors (L.-I.Z., L.-I. Gu) independently performed quality assessments. Seven items were used to assess the quality of studies based on the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) Statement [17,18]. These seven items were: (1) whether the study reported study period; (2) source of participants; (3) inclusion and exclusion criteria; (4) type of specimens (e.g., cervical secretions) and the method of collection; (5) method of pathogen detection; (6) whether the study performed antimicrobial susceptibility testing and reported its method of antimicrobial susceptibility testing; and (7) completeness of outcome data. A study received one point for each item. The total potential score is 7 for each study. Therefore, Level A scored 6–7, Level B scored 5–6, Level C scored 4–5, and Level D scored <4. Dissension was resolved by discussion with a third person (L.-I.Z.).

Two authors (L.-n. Zeng, L.-I. Gu) independently extracted the following data from the included studies: study period, institution, region of institution, sample size, type of specimens, characteristics of patients (gestational age in weeks, length of PROM, whether or not prophylactic antibiotics were administered), categories and number of microorganisms, and the antimicrobial susceptibility of microorganisms. We classified microorganisms according to Bergey's *Manual of Systematic Bacteriology* [19].

### Data analysis

To determine the predominant microbial pathogens in pregnant women with PROM and their infants in China, descriptive data

reported as continuous variables were expressed as ranges or medians with interquartile ranges. Data reported as categorical variables are expressed as a number or percentage.

## Results

### Characteristics of included studies

We included a total of 36 studies (Fig. 1; Table 1) [20–56]. Of these, 31 took specimens from mothers and six from neonates. Studies were from south China (27.77%, 10/36), north China (22.22%, 8/36), and central China and east China (16.67%, 6/36, respectively); one was from northwest China (2.77%). The sample sizes varied from 5 to 3432 (median: 53, interquartile: 32–100). Most studies collected cervical secretions (44.44%, 16/36) or vaginal secretions (27.77%, 10/36) to detect colonized microorganisms. The pathogen positive rates varied among studies (9.55–100% in mothers and 7.60–72.77% in neonates). The positive rates of aerobes were 10.53–62.5%, while that of anaerobes and mycoplasma were 12.5–91.7% and 5.26–45.16% respectively.

### Quality assessment of included studies

Quality assessments were as follows: 11 studies (30.55%) scored at Level A, 12 (33.33%) studies scored at Level B, three (8.33%) studies scored at Level C and 10 (27.78%) studies scored at Level D (Table 2). Two significant problems that emerged were: lack of antimicrobial susceptibility testing and incomplete outcomes data. Only three (8.33%) studies performed both antimicrobial susceptibility testing and reported the methods.

### The predominant microbial agents in PROM

#### Microorganisms isolated from mothers with PROM in China (1980–2012)

From 3782 mothers, 1706 isolates were obtained. Gram-positive bacteria were the predominant microbial organisms (54%), while Gram-negative bacteria made up 23% (Fig. 2). The top six bacteria isolated were *Staphylococcus* ( $n = 643$ ), *Escherichia* ( $n = 204$ ), *Enterococcus* ( $n = 88$ ), *Lactobacillus* ( $n = 78$ ), *Enterobacter* ( $n = 61$ ), and *Streptococcus* ( $n = 60$ ). Among Gram-positive bacteria, *Staphylococcus* was the most frequently isolated organism ( $n = 643$ , 70%), followed by *Enterococcus* ( $n = 88$ , 10%) and *Lactobacillus* ( $n = 78$ , 8%; Fig. 3). The primary Gram-negative bacteria isolated were *Escherichia* ( $n = 204$ , 53%), *Enterobacter* ( $n = 31$ , 8%), and *Gardnerella* ( $n = 20$ , 5%; Fig. 4). The fungal isolates were primarily *Candida* (86%; Fig. 5). The main anaerobe was *Bacteroides* (37%; Fig. 6).

Eleven studies of intrauterine cultures (amniotic fluid or placenta) were sub-analyzed and the results were consistent with data from the full analysis set: the predominant Gram-positive organism was *Staphylococcus* ( $n = 77$ , 48%), while the predominant Gram-negative organisms were *Enterobacter* ( $n = 29$ , 34%) and *Escherichia* ( $n = 18$ , 21%).

#### Microorganisms isolated from neonates with PROM in China (1980–2012)

Six studies cultured specimens from neonates born to mothers with PROM. Three of them reported categories of all microorganisms [43,46,47] (Table 3) and showed that *Staphylococcus* was the main pathogen in affected neonates. The others did not report all categories of microorganisms, but showed that *Staphylococcus aureus* and *E. coli* were the main pathogens.

Among these three studies, a study of 47 of central cultures (blood samples) with a large sample size ( $n = 3432$ ) showed the overall positive rate of blood culture was 7.6% in newborns with PROM.

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