

# Mother-infant colonization and neonatal sepsis in prelabor rupture of membranes

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## ABSTRACT

**Objective:** This study aims to determine the incidence of prelabor rupture of membranes (PROM) in a tertiary care institution, the bacterial pathogens involved in maternal and neonatal colonization, and the major bacterial pathogens of neonatal sepsis in PROM.

**Methods:** This prospective study was conducted over 2 years from March 1999 to February 2001 in Abha Maternity Hospital, Abha, Kingdom of Saudi Arabia. Consecutive admissions of infant-and-mother pairs with PROM constitute the subjects of this survey. Every mother had endocervical swab taken before delivery, and their infants had surface swabs and sepsis screening before starting antibiotic therapy.

**Results:** The incidence of PROM was 12.6 per 1000 live births. Premature delivery rate was 54.6% while, the overall prematurity rate was 7.2%. The major microorganisms involved in genital colonization of the mothers were *coagulase negative Staphylococcus* (CONS)

(24%), *Klebsiella pneumoniae* (13%), *Pseudomonas aeruginosa* (11.3%) and *Enterococcus species* (11.3%). The infants were colonized largely with CONS (31%), *Klebsiella pneumoniae* (18%) and *Escherichia coli* (*E.coli*) (17%). Fourteen percent of the infants were infected but in only 6% was septicemia documented (*Staphylococcus aureus*, 3 cases and 1 case each with CONS, group B *Streptococci* (GBS) and *E.coli*). In contrast to Western experience, the incidence of GBS was uncommon in both mothers and infants. The bacterial pattern suggests vancomycin and cefotaxime or aminoglycoside combination as empirical antibiotic therapy for both infected infants and selected contaminated mothers with PROM.

**Conclusion:** Generally, it appears wasteful to routinely admit, screen and empirically treat all infants born after PROM; only ill infants, febrile mothers, or either, with associated chorioamnionitis deserve antibiotic treatment.

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Prelabor rupture of membranes (PROM) was defined as rupture of the amniotic membranes, or draining of liquor amnii for more than 24 hours before the onset of established labor irrespective of the gestational age. Though the pathogenesis of PROM remains uncertain, infection has since been recognized as its complication for both mother and infant, due to the ascent of cervicovaginal flora through the cervix.<sup>1</sup> Other well-known hazards of PROM are prolapsed cord, premature delivery, chorioamnionitis and asphyxia neonatorum and pulmonary hypoplasia. Rupture of the chorioamniotic membranes occurring 24-48 hours

before delivery is associated with increased incidence of neonatal infection.<sup>2-6</sup> The bacterial pathogens affecting infants with PROM tend to be those which colonize the anogenital tracts of the mothers. In the United States of America (USA),<sup>7</sup> Europe<sup>8</sup> and Australia,<sup>9</sup> group B *Streptococci* (GBS), *Listeria monocytogenes* and *Escherichia coli* (*E.coli*) are the major microorganisms that colonize the birth canal of pregnant women. In these countries, these are equally the most prevalent pathogens of neonatal sepsis including those born after PROM.<sup>7-9</sup>

The current practice in our neonatal unit is to admit, screen for sepsis and routinely treat with

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antibiotics all infants born after PROM. Inappropriate use of antimicrobial chemotherapy is financially wasteful and may increase the development of drug resistance. To our knowledge, the pattern of bacterial organisms involving women and infants with PROM has not been documented in our environment. This study therefore aims to determine the incidence of PROM in the institution, the bacterial pathogens involved in maternal and neonatal colonization and the bacterial isolates of neonatal sepsis in PROM. This knowledge is a prerequisite in determining the management strategy of mothers and infants with PROM.

Sepsis was established in the infants when the blood or cerebrospinal fluid yielded a positive microbial growth. Chorioamnionitis is the presence of turbid foul smelling liquor amnii with or without maternal fever. A premature infant is one born before 37 completed weeks of gestational age. The placenta specimens were not subjected to histopathological study. The hospital ethical committee approved this study.

**Methods.** This prospective study was conducted over 2 years, from March 1999 to February 2001, in Abha Maternity Hospital (AMH), Abha, Kingdom of Saudi Arabia. As a policy, all neonates born in the hospital with a history of PROM were admitted into the nursery. Consecutive admissions of infant-and-mother pairs with PROM constitute the subjects of this survey. Every mother with PROM had endocervical swab taken for culture and susceptibility on admission before antibiotic therapy was started. After delivery, swabs were taken from the infants' axilla and umbilical stump; blood was obtained from the peripheral vein for culture after the puncture site was thoroughly sterilized with the use of iodine solution. Other investigations included chest radiograph, complete blood count and blood glucose. Lumbar puncture was undertaken only if the infant looked septic at birth or at any other time. These have been the routine investigations on all cases of PROM, hence this survey did not create any additional financial burden on the institution and no extra stress on our patient population. Other biodata on the mother and baby included duration of leakage of liquor, date of birth, mode of delivery, maternal fever, nature of the liquor and maternal antibiotic medication before delivery. Other relevant information included the condition of the infant and signs of sepsis, if any. Fetal heart rate monitoring was routinely carried out in all cases but was not included in the study protocol.

All samples were cultured aerobically using blood agar (Difco Lab. Detroit Cat. No. 0690-17) and MacConkey's agar (BBL Cat. No.11387). Bacterial isolates were characterized and identified by the conventional procedures described by Lennette et al.<sup>10</sup> Antibiotic susceptibility testing was performed

using the disc diffusion method described by Bauer et al.<sup>11</sup> The standard reference strains, *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853, were tested regularly for monitoring the accuracy and precision of the disc diffusion test. The medium used was Mueller-Hinton agar (Difco, Cat. No.02520/4).

Mothers with PROM received amoxicillin or amoxicillin-clavulanic acid empirically while awaiting swab culture report. Mothers admitted with infected liquor amnii were started on intravenous cephalosporin and metronidazole. Women with ruptured membranes for >24 hours had induction of labor if the pregnancy period was up to 34 weeks and above. This induction was medical with the use of prostaglandin E2 for unfavorable cervix and syntocinon for favorable cervix. Cesarean section was not carried out unless there was a strong indication.

As a unit policy, every infant with PROM received antibiotics (ampicillin and gentamicin combination) from birth after sepsis work-up. The medication was discontinued after 3 days if the blood cultures were reported as negative and the infant was asymptomatic. If the infant's blood or spinal fluid yielded a positive growth, antimicrobial therapy of appropriate susceptibility was instituted for a total duration of 7-10 days.

**Results.** During the study period, there was 7713 live births in AMH of which 97 (44 term and 53 preterm) were associated with PROM. Thus, the incidence of PROM in the hospital was 12.6 per 1000 live births. The incidence of prematurity among PROM infants was 54.6% (53 of 97) while the overall incidence of premature delivery in the hospital during the period was 7.2% (556 of 7713). Twenty-nine (30%) of the 97 infants were of gestational age <34 weeks while 68 (70%) were 34 weeks and above. Eighteen of the 97 mothers were admitted in the 2nd stage of labor hence endocervical swabs could not be taken before delivery. Twenty (25.3%) of the 79 who were swabbed yielded no growth. From the remaining 59 mothers, 62 isolates were obtained (**Table 1**). The predominant microbial agents isolated *coagulase negative Staphylococcus* (*CONS*), 15 cases (24.2%); *Klebsiella pneumoniae*, 8 cases (12.9%) and *Pseudomonas* and *Enterococcus species*, 7 cases each (11.3%). There were 6 cases of chorioamnionitis. Only 14 (14.4%) of the 97 mothers had fever on admission while others were healthy; 3 of the febrile mothers had chorioamnionitis.

Surface swabs taken from 29 (30%) of the 97 infants were sterile; from the remaining 68 (70%) infants, 87 isolates were obtained (**Table 2**). The dominant organisms were *CONS*, 27 cases (31%); *Klebsiella pneumoniae*, 16 cases (18.4%) and *E.coli*, 15 cases (17.2%). Fourteen (14.4%) of the 97 infants

**Table 1** - Types of microorganisms isolated from mothers with PROM.

Type of microorganism	n (%)
<i>CONS</i>	15 (24.2)
<i>Klebsiella pneumoniae</i>	8 (12.9)
<i>Pseudomonas aeruginosa</i>	7 (11.3)
<i>Enterococcus species</i>	7 (11.3)
<i>E.coli</i>	5 (8)
<i>Staphylococcus aureus</i>	5 (8)
<i>Serratia species</i>	4 (6.5)
<i>Candida albicans</i>	4 (6.5)
Miscellaneous	7 (11.3)
<b>Total</b>	<b>62*(100)</b>
Miscellaneous includes: <i>Enterobacter</i> (3), group <i>B Streptococcus</i> , <i>Acinetobacter species</i> , <i>Chryseomonas luteola</i> and <i>Streptococcus faecalis</i> (1) each. * Swabs were not taken from 18 mothers, specimens from 20 mothers were sterile, specimens from the remaining 59 mothers yielded 62 isolates. <i>CONS</i> - coagulase negative <i>Staphylococcus</i> , <i>E.coli</i> - <i>Escherichia coli</i> , n - number, PROM - prelabor rupture of membranes	

**Table 2** - Types of microorganisms colonizing infants with PROM at birth.

Type of microorganism	n (%)
<i>CONS</i>	27 (31)
<i>Klebsiella pneumoniae</i>	16 (18.4)
<i>E.coli</i>	15 (17.2)
<i>Staphylococcus aureus</i>	7 (8.1)
<i>Enterococcus species</i>	5 (5.8)
<i>Pseudomonas aeruginosa</i>	4 (4.6)
<i>Candida albicans</i>	4 (4.6)
Miscellaneous	9 (10.3)
<b>Total</b>	<b>87* (100)</b>
Miscellaneous includes: group <i>B Streptococcus</i> and <i>Serratia species</i> (3) each; <i>Enterococcus species</i> and <i>Acinetobacter</i> (1) each. * Surface swabs in 29 infants were sterile, 87 isolates were derived from the remaining 68 infants. <i>CONS</i> - coagulase negative <i>Staphylococcus</i> , <i>E.coli</i> - <i>Escherichia coli</i> , n - number, PROM - prelabor rupture of membranes	

were ill and septic-looking, 8 with negative and 6 with positive blood culture. Five of the 8 infants with negative blood culture presented with clinical and radiological evidence of pneumonia. The organisms isolated from the 6 infants were *Staphylococcus aureus*, 3 cases (2 MRSA); *CONS*, *GBS* and *E.coli* (one case each). No infant had a positive growth from the cerebrospinal fluid. In 3 (50%) of the 6 infants, the PROM was complicated with chorioamnionitis while in the other 3 the liquor appeared normal. Chorioamnionitis was involved in only 3 (3.3%) of the other 91 infants who had no proven sepsis.

**Antepartum prophylactic antibiotic use.** Eighteen of the 97 mothers received no prophylactic antibiotics before delivery as they reported in the 2nd stage of labor. Surface swabs of 13 (72.2%) infants of the 18 mothers who received no antibiotics were colonized at birth; 5 (27.8%) were sterile. Surface swabs from 53 (67.1%) infants of the 79 mothers who were treated with prophylactic antibiotics were colonized while 26 (32.9%) were sterile at birth. All the mothers of the 14 infants with sepsis, except the one with *CONS* bacteremia, received antibiotics antepartum.

**Discussion.** In this study, the incidence of prelabor rupture of membrane was 12.6 per 1000 live births. A majority (54.6%) of these infants were preterm which is in consonance with global observations.<sup>1,12,13</sup> The frequency of different pathogens involved in PROM varies between geographical areas and should be defined in each setting.<sup>1,7-9,12,14</sup> In this study population, the pathogens derived from the genital tract of the women with PROM were predominantly *CONS* and *Klebsiella pneumoniae* and their infants were colonized predominantly with *CONS*, *Klebsiella pneumoniae*, and *E.coli*. This bacterial pattern involving the mother-infant pair is therefore at variance with the experience in the Western world where *GBS* constitutes 70–80% of the isolates of the maternal genital tract and the colonization/sepsis of infants born after PROM.<sup>7-9</sup> Maternal rectal swabbing was not carried out as part of the present study; perhaps this could have increased the yield of maternal *GBS*. Nevertheless, the paucity of *GBS* in this survey is in agreement with other researchers who have also observed a low incidence of *GBS* in the Saudi maternal and neonatal populations.<sup>15-19</sup>

In PROM, most of the babies are colonized without becoming infected.<sup>1</sup> In the present series, of the 68 infants who were colonized, only 14 (14%) were infected, and the overall incidence of culture-proven bacteremia in infants in this series was only 6%. The 14% incidence of neonatal sepsis in the present series is in consonance with figures from Nigeria (15.5%),<sup>12</sup> and Riyadh (15%)<sup>13</sup> but lower than reported in the USA (8.2%).<sup>3</sup> Various host factors or pathogenicity of the organisms influence tissue invasion and therefore systemic sepsis in the fetus. Newborn infants have poor immunity and less effective cutaneous and mucosal barriers. The heavier the colonization the greater the risk of invasion and sepsis.<sup>20</sup> Numerous studies have shown that the results of surface cultures are of limited value in diagnosis.<sup>21-23</sup> High vaginal or endocervical swab highlights possible exposure to pathogens and not infection. However, the results may help to decide the need to continue empirical antibiotic therapy and the choice thereof, as the specimen may well grow the responsible organism.<sup>1</sup>

Endocervical and surface specimens from some of the mothers and infants yielded multiple organisms. It is difficult to totally rule out contamination from the vaginal passage in these cases. These possible contaminants, most probably, remain relevant as they also have the potential of subsequently penetrating the fetal/newborn skin or mucosa to cause systemic infection.

The frequency of chorioamnionitis was 50% among the infants with proven sepsis but only 3.3% among infants with no proven sepsis. This difference underlines the relevance of chorioamnionitis as a predisposing factor for sepsis in infants born after PROM.<sup>1,2,12,13</sup>

The study has shown that 13 (72%) infants of the 18 mothers who received no antibiotics were colonized at birth and only 5 (28%) were sterile; 53 (67%) infants of the 79 mothers who were treated with prophylactic antibiotics were colonized while 26 (33%) were sterile at birth. Also, the mothers of 13 (93%) of the 14 infants who were septic at birth received antibiotics antepartum. This observation casts doubt on the benefit derived from the routine maternal antibiotic prophylaxis as currently practiced in our institution. A more serious problem is the danger that antepartum prophylactic antibiotics will alter the vaginal flora to a more resistant variety, thus making treatment more difficult. Individual studies<sup>24,25</sup> have, nevertheless, shown significant benefits of intrapartum antibiotic prophylaxis in reducing neonatal colonization and infection although this finding has not been universal.<sup>26</sup> However, antibiotics might be useful if there is evidence of chorioamnionitis and if the membranes have been ruptured for more than 24 hours after onset of labor. The American Academy of Pediatrics (AAP) recommends intrapartum antibiotics to all women with PROM >18 hours prior to delivery, and intrapartum fever.<sup>27</sup> Though this (AAP) policy refers to women with group B *Streptococcus*, the same could also be applied to women in other environments, provided the prevalent bacterial agents and their antibiotic susceptibility are taken into consideration.

In the present study the number of infants with culture-proven septicemia is too small to permit a reasonable and valid conclusion regarding the choice of empirical antibiotic therapy for infants with suspected systemic infection. Moreover, there was no significant correlation between the bacteria causing the blood infection (largely *Staphylococcus aureus*) and those that involved mother-infant colonization (largely *CONS* and *Klebsiella pneumoniae*). Most likely, had the number of infants with bacteremia been greater, a better correlation could have emerged; hence, these surface and endocervical organisms cannot be ignored in the determination of empirical antibiotics.

There is a tendency to regard the *CONS* isolated from the mothers and infants in this study as either normal flora/contaminants or non-pathogenic. In a study of neonatal septicemia in a referral neonatal unit in Assir Region, *CONS* was second to *Klebsiella pneumoniae* as the leading causative agent of both early and late-onset sepsis.<sup>28</sup> In our setting, *CONS* should therefore be regarded as an important cause of perinatal infection.

Previous isolated studies on mothers and newborns in our institution have each identified vancomycin as the drug of choice for staphylococcal organisms and cefotaxime followed by aminoglycosides (amikacin and gentamicin) for gram negative isolates including *Klebsiella species*.<sup>19,28,29</sup> Therefore, for our environment, we may suggest vancomycin and cefotaxime (or aminoglycosides) combination for empirical treatment of infants who appear septic following PROM. This is recommended for mothers with fever and chorioamnionitis. Mothers with PROM of less than 24 hours in the absence of chorioamnionitis do not need routine antibiotics. Neonatologists should, however, be mindful of the fact that superfluous use of vancomycin and cephalosporin can result in bacterial resistance very quickly. There is an increasing problem of vancomycin-resistant enterococci.

Most centers in Assir region combine ampicillin with aminoglycoside as first line empirical regimen for newborn sepsis. Surveys on neonatal septicemia in referral centers in this region have demonstrated that less than 5% of the prevalent bacterial organisms were susceptible to ampicillin,<sup>28,29</sup> hence it may not be wise to recommend ampicillin for neonatal sepsis in our environment.

In conclusion, the outcome of this study is at par with that of other centers in that a large majority of the infants born after PROM escape infection and hence are unnecessarily admitted, wastefully screened and treated with antibiotics. Only infants with chorioamnionitis and those who are clinically ill should be admitted into the Neonatal Intensive Care Unit for screening and empirical antibiotic therapy. It would be wise to apply this management schedule also to the asymptomatic preterm infants and their mothers with PROM, as the risk of infection is relatively high in this type of delivery. The asymptomatic term infant delivered after PROM with no additional risk factors for sepsis should be kept under observation and this can be safely carried out while the infant is with the mother in the rooming-in ward. Such a policy has been proven to be safe and cost-effective.<sup>13</sup>

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