Isolation Pattern and Clinical Outcome of Genital Mycoplasma in Neonates from a Tertiary Care Neonatal Unit

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Summary
The role of genital mycoplasma in perinatal mortality and morbidity has been debated. This study was undertaken to determine the frequency of isolation of genital mycoplasma and evaluate its association with clinical outcome. Sixty-six cerebrospinal fluid (CSF) and 49 tracheal aspirates taken from 100 low birthweight infants who had suspected meningitis and/or respiratory distress respectively were cultured for genital mycoplasma. Ureaplasma urealyticum was isolated from 9 per cent of CSF and 14 per cent of tracheal aspirates. Mycoplasma hominis was isolated from CSF in one case and none at the tracheal aspirates. Three out of seven mycoplasma-infected CNS cases showed CSF pleocytosis while three out of seven patients whose tracheal aspirates grew mycoplasma had congenital pneumonia. None of the patients were treated with antimycoplasmal therapy and none developed chronic lung disease.

Introduction
Mycoplasma frequently colonizes the genital tract and may be transmitted to the fetus in utero or at the time of delivery.1–3 Genital mycoplasma have been associated with chorioamnionitis, spontaneous abortion, stillbirth, prematurity, low birthweight (LBW) congenital pneumonia, chronic lung disease (CLD), and meningitis.3–6 Ureaplasma urealyticum is the single most common organism isolated from the lower respiratory tract and central nervous system (CNS) of preterm neonates according to some studies.5,6 While others have failed to isolate it from CSF, U. urealyticum is implicated as a cause for pneumonia and CLD.5,8–10 Its isolation from endotracheal aspirate in the absence of other respiratory pathogens is significantly associated with radiographic evidence of pneumonia, increased numbers of circulating white blood cells, and increased numbers of neutrophils in tracheal aspirate.5–10 Moreover, babies of less than 34 weeks’ gestation who had U. urealyticum in their tracheal aspirate showed significantly higher incidence of hyaline membrane disease (HMD), need for ventilation, and severe respiratory insufficiency.11 Meningeal invasion by mycoplasma may not be associated with CSF pleocytosis because of a poor inflammatory response.12 Moreover, poor or absent mycoplasmal growth on bacteriological media, minimal or absent neurological signs and symptoms suggest the possibility that the majority of mycoplasmal CNS infections in neonates are never diagnosed.12

The current study was undertaken to determine the frequency of isolation of U. urealyticum and Mycoplasma hominis from tracheal aspirates and CSF specimens from neonates in a tertiary care unit and to evaluate the association of genital mycoplasmas with clinical outcome.

Patients and Methods
One hundred and fifteen samples of CSF and tracheal aspirate were taken from 100 LBW infants less than 1 month old admitted to the Neonatal Intensive Care Unit (NICU), PGIMER, during a period of 1 year (March 1995–March 1996).

These samples were cultured for isolation of genital mycoplasma. While CSF was collected from infants undergoing lumbar puncture for suspected meningitis, tracheal aspirate was collected from babies with respiratory distress who underwent endotracheal intubation.

Clinical details of these babies were recorded with regard to birthweight, sex, delivery route, maternal chorioamnionitis/PROM, age at the time of sampling, and final outcome.

CSF and/or tracheal aspirate (0.2 ml each) was collected in 1 ml of Pleuropneumonia-like organism (PPLO) broth and transported to the mycoplasma laboratory within 1 h. The organisms were identified by standard methods.13 The study was approved by the Institute’s Ethical Committee. Student’s t-test and chi-squared tests were used for statistical analysis.

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Results

Sixty-six samples of CSF and 49 samples of tracheal aspirate were taken from 100 LBW neonates. *U. urealyticum* was isolated from CSF in six cases (9 per cent) and from tracheal aspirate in seven cases (14.2 per cent). *M. hominis* was isolated in only one case from CSF (1.5%) and from none of the tracheal aspirates. In one neonate, *U. urealyticum* was isolated from both CSF and tracheal aspirate.

Table 1 details the demographic characteristics of patients where CSF and tracheal aspirate cultured positive or negative for genital mycoplasma.

The two groups were not statistically different with regard to gestation, sex, mode of delivery, birthweight, age at the time of sampling, and maternal amnionitis/PROM > 24 h.

Three cases out of seven showed CSF pleocytosis (10–100 cells/mm³) and polymorphs ranging from 60 to 100 per cent. These three patients were treated with third generation cephalosporins and amikacin for 14 days. None of the neonates received specific antimycoplasma therapy.

None of the 49 cases from whom tracheal aspirate was taken developed CLD. Outcome variables of cases positive or negative for *U. urealyticum* in tracheal aspirate are described in Table 2.

Three out of seven positive cases were found to have congenital pneumonia. The remaining four had hyaline membrane disease (HMD) (Table 2). None of the seven had grown any other microorganisms which included *Klebsiella pneumoniae* (5), *Acinetobacter anitratus* (8), *Streptococcus viridans* (1), and coagulase-negative *Staphylococcus* (2).

Out of 11 pneumonia cases in the *U. urealyticum*-negative group, eight had grown microorganisms other than mycoplasma in the tracheal aspirate.

Discussion

Mycoplasma are opportunistic organisms causing systemic disease in patients with underlying immune defects, which is why preterm are more likely to get infected than term babies. 2,6

*U. urealyticum* isolated from CSF in six infants (9 per cent) in the current study is similar to the finding of 8 per cent by Waites et al.,6 but Heggi et al., on screening the CSF of 920 infants, isolated *U. urealyticum* in only two

Table 2

Outcome variables in babies with tracheal aspirate culture positive or negative for *Ureaplasma urealyticum*

<table>
<thead>
<tr>
<th>Outcome variables</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of infants</td>
<td>7 (43%)</td>
<td>11 (26%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>3 (43%)</td>
<td>11 (26%)</td>
</tr>
<tr>
<td>HMD</td>
<td>4 (57%)</td>
<td>20 (47%)</td>
</tr>
<tr>
<td>Transient tachypnea of newborn</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Asphyxial lung disease</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>1 (14%)</td>
<td>4 (10%)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (14%)</td>
<td>4 (10%)</td>
</tr>
</tbody>
</table>

HMD = hyaline membrane disease.
cases (0.2 per cent).\textsuperscript{14} \textit{M. hominis} was isolated in only one case in CSF (1.5 per cent) compared to 5 per cent by Waites \textit{et al.}\textsuperscript{2} but Heggie \textit{et al.} did not isolate it from any case.\textsuperscript{14} Follow-up sampling was not done in mycoplasma-positive cases, but the persistence of organisms in CSF for weeks to months has been documented in premature babies by several studies.\textsuperscript{3,6}

Three infants from whom genital mycoplasma were isolated from CSF were born by vaginal route and four by Caesarean section. Vaginally delivered babies must have acquired mycoplasma through a colonized birth canal while Caesarean section delivered ones must have acquired it \textit{in utero} either by an ascending route, secondary to a colonized maternal genital tract, or transplacentally from maternal blood.\textsuperscript{1,3} Three out of four neonates delivered by Caesarean section had clinical chorioamnionitis or PROM suggestive of an ascending route of infection, though mycoplasma are also known to cause silent chorioamnionitis.\textsuperscript{15}

Meningitis implies CSF inflammation and strictly speaking only three cases out seven can thus be classified. These findings are consistent with the study by Waites \textit{et al.}\textsuperscript{6} in which CSF pleocytosis was minimal. Inflammatory reaction in CSF may be minimal or absent with mycoplasma.\textsuperscript{6,14} due to their lack of a cell wall.

No specific treatment was given to any neonate and they responded to routine antibiotics. However, spontaneous eradication of genital mycoplasma has been well documented.\textsuperscript{16}

That mycoplasma are the commonest microorganism infecting the CNS in premature babies necessitates further studies to understand its clinical implications.

\textit{U. urealyticum} isolation from 14 per cent of tracheal aspirate specimens is similar to the 17 per cent seen by Cassell \textit{et al.}\textsuperscript{5} and the 18 per cent seen by Payne \textit{et al.}\textsuperscript{10} Three out of seven cases with tracheal aspirate positive for mycoplasma had congenital pneumonia. Two out of these three had evidence of maternal chorioamnionitis. As tracheal aspirate or blood in these cases did not grow any other microorganism, it is likely that this organism was the cause of the congenital pneumonia. Several studies have reported an association between \textit{U urealyticum} and congenital pneumonia.\textsuperscript{1,17,18} Whether treating mycoplasma-infected patients with specific antimycoplasmal therapy would have altered the clinical course of these neonates needs further blinded studies. None of the 100 infants from whom tracheal aspirate or CSF samples were taken developed chronic lung disease.

\section*{References}