Preterm meconium staining of the amniotic fluid: associated findings and risk of adverse clinical outcome

A T Tybulewicz, S K Clegg, G J Fonfé, B J Stenson

Background: The incidence of preterm meconium staining of the amniotic fluid (MSAF) is uncertain. It may be an indicator of possible listeriosis. It is unclear how great this risk is or whether preterm MSAF is a risk factor for adverse neonatal outcome.

Objective: To investigate the incidence of preterm MSAF, the incidence of associated maternal and neonatal infection, and the outcomes of the infants at discharge.

Design: Retrospective case-control study.

Methods: Infants < 33 weeks gestation with preterm MSAF born in the Simpson Memorial Maternity Pavilion, Edinburgh between 1 January 1994 and 2 January 2001 were matched with the next infant of the same sex and gestation with clear liquor. Maternal and infant characteristics, culture results, placental histology, and clinical outcomes were compared.

Results: Preterm MSAF was observed in 45/1054 (4.3%) infants below 33 weeks gestation. No maternal or infant listeriosis was identified in cases or controls. There was no significant difference in birth weight, Apgar score, or first pH between cases and controls. Preterm MSAF was associated with prolonged rupture of the membranes (odds ratio (OR) 3.34, 95% confidence interval (CI) 1.07 to 10.49), but not maternal hypertension, sepsis, or chorioamnionitis. Severe (grade 3/4) intraventricular haemorrhage was significantly more common in infants with preterm MSAF (OR 2.03, 95% CI 1.62 to 2.53). There was no significant difference in mortality. Early onset sepsis was observed in two cases and three controls.

Conclusions: Preterm meconium staining of the amniotic fluid may be associated with increased risk of intraventricular haemorrhage. It does not appear to be a useful indicator of listeriosis.
delivery, to be smokers, and to have concerns expressed in their delivery records about the cardiotocographic traces. Histological chorioamnionitis was equally common in cases and controls. There was no significant difference in the proportion of case and control mothers given antibiotics or steroids before delivery.

Table 3 shows the characteristics of the infants. Gestational age and sex were matched. There were no significant or clinically important differences in birth weight, Apgar scores, or first pH after birth between infants with preterm MSAF and controls. More case infants were intubated and more controls received surfactant, but these differences were not significant. Significantly more case infants were treated with antibiotics for more than 48 hours after birth than controls.

Table 4 shows the outcomes of the infants. Severe intraventricular haemorrhage (grade 3/4) was identified more often in infants with preterm MSAF than in controls (odds ratio 2.03, 95% confidence intervals 1.62 to 2.53). Six infants in each group had grade 1/2 intraventricular haemorrhage.

There was no difference in the proportions of infants with periventricular leucomalacia. More infants with preterm MSAF died or developed chronic lung disease than controls, but the differences were not significant. Of the seven infants born of multiple pregnancies, none died or developed severe intraventricular haemorrhage and one twin developed chronic lung disease.

Early onset sepsis was diagnosed in two case infants and three control infants: none of these infants died. None of the infants in each group had grade 1/2 intraventricular haemorrhage.

DISCUSSION

We observed preterm MSAF in 4.3% of 1054 infants born at less than 33 weeks gestation. None of our 45 cases had Listeria infection. Although MSAF has been described in preterm infants with Listeria infection, they are generally ill in other ways at birth. Meconium stained liquor alone does not appear to be a useful indicator of Listeria infection. The three cases of Listeria infection observed in our institution during the study period had clear liquor. Other series of infants with preterm MSAF have not reported this outcome.

Mazor et al. observed MSAF in 5.7% of 4872 infants delivered at 24–37 weeks gestation. As in our study, this did not appear to be gestation related, as 5.6% of infants of 32–37 weeks gestation had MSAF. In a smaller study, Scott et al. observed MSAF in 4.8% of infants delivered before 37 weeks. We chose to focus on more immature infants to enable us to study a population at greater risk of adverse perinatal outcome.

MSAF is a clinical diagnosis with no practicable confirmatory test. It is possible that in some cases in which MSAF was diagnosed, there may have been an alternative explanation for the discoloured liquor. None of the infants in our series had anatomical or functional intestinal obstruction diagnosed after birth. Some observers describe meconium as old, new, thick, thin, or particulate. These cannot be reliably defined and were not consistently recorded in this retrospective study. All MSAF was considered equivalent.

More of the mothers with MSAF in our study had prolonged rupture of the membranes. This was not associated with more histological chorioamnionitis or more positive cultures from the mothers. Mazor et al. also noted more premature rupture of the membranes in their series. In an earlier series where amniocentesis was performed on mothers in preterm labour, Mazor et al. obtained more positive cultures from MSAF than from clear amniotic fluid. More of the infants with MSAF in our study received antibiotics for longer than 48 hours, but there were no more positive blood cultures. The cultures were performed on admission to the neonatal unit before the infants were started on antibiotics. The increased antibiotic use in the babies may reflect anxiety about the possibility of Listeria infection. The lack of positive

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Incidence of preterm meconium staining of the amniotic fluid (MSAF) by gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation (weeks)</td>
<td>No of births</td>
</tr>
<tr>
<td>23</td>
<td>28</td>
</tr>
<tr>
<td>24</td>
<td>56</td>
</tr>
<tr>
<td>25</td>
<td>43</td>
</tr>
<tr>
<td>26</td>
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<td>30</td>
<td>147</td>
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<tr>
<td>31</td>
<td>186</td>
</tr>
<tr>
<td>32</td>
<td>244</td>
</tr>
<tr>
<td>All</td>
<td>1054</td>
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<table>
<thead>
<tr>
<th>Table 2</th>
<th>Maternal characteristics</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
<td>41</td>
</tr>
<tr>
<td>Age</td>
<td>28 (7)</td>
</tr>
<tr>
<td>PROM</td>
<td>24 (59)</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>10 (24)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>18 (44)</td>
</tr>
<tr>
<td>CTG concern</td>
<td>20 (49)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Steroids</td>
<td>37 (90)</td>
</tr>
<tr>
<td>Smoker</td>
<td>13 (32)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Infant characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>45</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>28.7 (4.6)</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>1249 (429)</td>
</tr>
<tr>
<td>Apgar at 5 min</td>
<td>8 (5–10)</td>
</tr>
<tr>
<td>First pH</td>
<td>7.32 (0.09)</td>
</tr>
<tr>
<td>Intubated</td>
<td>40 (89%)</td>
</tr>
<tr>
<td>Surfactant</td>
<td>18 (40%)</td>
</tr>
<tr>
<td>Antibiotics &gt; 48 hours</td>
<td>29 (64%)</td>
</tr>
</tbody>
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<thead>
<tr>
<th>Table 4</th>
<th>Adverse neonatal outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>45</td>
</tr>
<tr>
<td>Death</td>
<td>10 (22)</td>
</tr>
<tr>
<td>CLD (36 weeks)</td>
<td>8 (18)</td>
</tr>
<tr>
<td>PVL</td>
<td>1 (2)</td>
</tr>
<tr>
<td>VHI grade 3/4</td>
<td>5 (11)</td>
</tr>
</tbody>
</table>

Data are mean (SD), number (%), or median (interquartile range).
cultures may be attributable, in part, to the maternal antibiotic exposure before delivery.

Concerns about the cardiotocographic traces were more common in mothers with MSAF in our study and in that of Mazor et al. Because of the difficulty of defining cardiotocographic abnormality in preterm infants and relating this to clinical outcome, we did not attempt to analyse this further. It is possible that the presence of meconium in the liquor made clinicians more likely to be concerned about the cardiotocographic traces. The infants with preterm MSAF were not more depressed at birth or more acidic than controls in our study. Scott et al also found no significant difference in cord pH between infants with preterm MSAF and controls. We found no difference in first pH after birth.

More of our case infants were intubated at birth than controls. This difference was not significant and may be explained by our policy to suction directly the trachea in all infants with MSAF who are not vigorous at birth. No infant was diagnosed as having meconium aspiration syndrome. Although more infants with MSAF were intubated at birth, more control infants were treated with surfactant (p = 0.09). We used rescue surfactant treatment in intubated infants with clinical respiratory distress syndrome until 1999. From then on, prophylactic treatment was given to infants less than 29 weeks gestation and rescue treatment to more mature infants.

Although the affected infants were not in a worse condition at birth, preterm MSAF may reflect an earlier stressful event or illness, as some clinical outcomes appear to be worse. We observed significantly more severe intraventricular haemorrhages in infants with preterm MSAF than in controls. More infants died or developed chronic lung disease, although these differences were not significant. Because of the low incidence of preterm MSAF, a very large study, gathering data from several centres, would be required to obtain statistical confidence on mortality data. Spinillo et al observed proportionately more cerebral palsy at 2 years of age among 17 preterm infants with MSAF than among 345 preterm infants with clear liquor.

In conclusion, preterm MSAF is observed in about 5% of preterm deliveries regardless of gestation. It is not a useful marker of intrapartum hypoxia or *Listeria* infection. However, it may identify a population of infants who will develop severe intraventricular haemorrhage or other adverse neurological outcome.

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REFERENCES
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Arch Dis Child Fetal Neonatal Ed 2004 89: F328-F330
doi: 10.1136/adc.2002.021949

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