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

A T Tybulewicz, S K Clegg, G J Fonfè, 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.

RESULTS

During the seven year study period, there were 39 043 live births in the hospital, of which 1054 infants were less than 33 weeks gestation. MSAF was observed in 45/1054 of these infants (4.3%). Table 1 gives the percentage of cases observed during each week of gestation. There were no cases at 23 or 24 weeks gestation. Other than this, there was no apparent effect of increasing gestational age on the incidence of MSAF in this population group.

Of the 45 case infants, seven were born of multiple pregnancies (one 28 week triplet pregnancy and two 30 week twin pregnancies). The 41 mothers of these case infants were matched to 41 control mothers with singleton pregnancies, yielding 41 case mothers, 41 control mothers, 45 case infants and 41 control infants.

Table 2 shows the maternal characteristics. Mothers of infants with preterm MSAF were more likely to have prolonged rupture of the membranes for > 24 hours before...
delivery, to be smokers, and to have concerns expressed in their
delivery records about the cardiotoigrahic 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
istereoids 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, Appgar 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
(dds 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 with preterm 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.

Table 2 Maternal characteristics

<table>
<thead>
<tr>
<th>Number</th>
<th>Cases</th>
<th>Controls</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>41</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>28 (7)</td>
<td>28 (6)</td>
<td>0.73</td>
</tr>
<tr>
<td>PROM</td>
<td>24 (59%)</td>
<td>12 (29%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>10 (24%)</td>
<td>10 (24%)</td>
<td>0.95</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>18 (44%)</td>
<td>13 (32%)</td>
<td>0.29</td>
</tr>
<tr>
<td>CTG concern</td>
<td>20 (49%)</td>
<td>10 (24%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (7%)</td>
<td>7 (17%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Steroids</td>
<td>37 (90%)</td>
<td>34 (83%)</td>
<td>0.78</td>
</tr>
<tr>
<td>Smoker</td>
<td>13 (32%)</td>
<td>5 (12%)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Data are mean (SD) or number (%).

Table 3 Infant characteristics

<table>
<thead>
<tr>
<th>Number</th>
<th>Cases</th>
<th>Controls</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age (weeks)</td>
<td>28.7 (4.6)</td>
<td>28.9 (2.2)</td>
<td>0.79</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>19:26</td>
<td>18:23</td>
<td></td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>1249 (429)</td>
<td>1241 (401)</td>
<td>0.93</td>
</tr>
<tr>
<td>Apgar at 5 min</td>
<td>8 (5-10)</td>
<td>9 (7-9)</td>
<td>0.79</td>
</tr>
<tr>
<td>First pH</td>
<td>7.32 (0.09)</td>
<td>7.3 (0.14)</td>
<td>0.88</td>
</tr>
<tr>
<td>Intubated</td>
<td>40 (89%)</td>
<td>32 (78%)</td>
<td>0.6</td>
</tr>
<tr>
<td>Surfactant</td>
<td>18 (40%)</td>
<td>24 (59%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Antibiotics &gt; 48 hours</td>
<td>29 (64%)</td>
<td>13 (32%)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Data are mean (SD), number (%), or median (interquartile range).

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 con-
firmatory 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 retro-
pective 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
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 acidoic 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.

Authors’ affiliations
A T Tybulewicz, Royal Hospital for Sick Children, Edinburgh, Scotland, UK
S K Clegg, B J Stenson, Neonatal Unit, Simpson Centre for Reproductive Health, Royal Infirmary, Little France, Edinburgh, Scotland, UK
G J Fonfeé, St James’s University Hospital, Leeds, UK

REFERENCES