A retrospective review of group B streptococcal infection in the Metro East area of the Western Cape province: 2010 to 2011

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Effective strategies to prevent infant death rely on knowledge of prevalent pathogens. Recent publications have drawn attention to limited data on the contribution of group B streptococcal infection to neonatal and infant mortality in resource-restricted settings. The aim was to describe all cases of group B streptococcal infection isolated from the blood culture of infants up to 90 days of age in two South African hospitals over a two-year period. A retrospective record review took place of infants in whom group B streptococcus was isolated from blood culture or cerebrospinal fluid from January 2010 and December 2011. The maternal records of infants were also reviewed. Data were analysed using Stata® version 1.1. Forty-one cases of group B streptococcal infection were identified, for which 33 records were available for analysis. There was early-onset disease in 14 (42.4%) and late-onset disease in 19 (57.6%) of the infants. Eight (24%) infants were human immunodeficiency virus (HIV)-exposed. There was a confirmed positive HIV PCR test for one infant only. Six infants had pneumonia, 11 meningitis and two died. Serotyping was not performed. All isolates were sensitive to penicillin. The crude incidence rate was calculated as 0.67/1 000 live births. The incidence rate of group B streptococcal disease was less than that in other African studies. Further data are needed for relevant prevention strategies to be established.

Introduction

The majority of neonatal deaths occur in middle- to low-income countries, where infection is responsible for more than a quarter of all neonatal mortality.1 Group B streptococcal infection or Streptococcus agalactiae is a leading cause of neonatal sepsis,2 causing severe morbidity and high mortality.3,4 Data on the incidence of group B streptococcus in these countries is limited. The mean global incidence is reported as 0.5 per 1 000 live births.5

Early-onset disease is defined as invasive group B streptococcus disease within days 0-6 after birth, while late-onset disease occurs from days 7-89 after birth. Early-onset disease is the result of maternal colonisation with group B streptococcus, resulting in vertical transmission. Early-onset disease often has a fulminant course, and double the case fatality ratio (12.1%) of late-onset disease.5

With the introduction of screening and/or intrapartum antibiotic prophylaxis, a reduction in the incidence of early-onset, but not late-onset, disease, was documented.6 Despite intrapartum antibiotic prophylaxis, preterm and black infants still have a higher risk of invasive group B streptococcus.7 Screening policies for group B streptococcus have not been established in developing countries, and intrapartum antibiotic prophylaxis is often either not possible or inconsistently practised. Maternal vaccination holds the highest promise in decreasing the incidence of group B streptococcus, but in order to proceed with this strategy, there is an urgent need to quantify the burden of group B streptococcus in these countries.

Infants born to human immunodeficiency virus (HIV)-infected mothers in resource-rich settings had a fourfold higher incidence of late-onset disease,8 but data from resource-limited settings suggest that there was no difference in group
B streptococcal carriage by HIV status. However, HIV-infected women with higher CD4 counts had increased carriage."

Thus, the aim of this study was to describe all cases of group B streptococcus isolated from the blood culture of infants up to 90 days of age in a high HIV prevalence setting.

**Method**

**Study site and population**

The records of children younger than 90 days of age were retrospectively reviewed where group B streptococcus was isolated from blood culture, and/or cerebrospinal fluid (CSF). Children were included from two linked hospitals in Cape Town; namely Karl Bremer Hospital, a primary level facility, and Tygerberg Academic Hospital, a tertiary level facility, between January 2010 and December 2011. These two hospitals serve the surrounding primary level midwife-obstetric units in the area referred to as Metro East. The number of infants born in Metro East was derived from routine data collected by Tygerberg Academic Hospital’s Obstetrics Department.

Cases were identified through the database of the National Health Laboratory Services at Tygerberg Academic Hospital. This department of microbiology serves both these hospitals and all peripheral clinics in Metro East. The identification of blood isolates was performed using the commercial automated BD BACTEC™ 9240 Blood Culture System (Becton Dickinson Diagnostic Instrument Systems, Sparks, USA), where samples were incubated for at least five days. Cultures were processed according to the standard operating procedures of the laboratory in accordance with standard microbiological methods.

There was no routine maternal screening for group B streptococcus during the reviewed period. Intrapartum antibiotic prophylaxis was routinely administered to women with intrapartum fever, prolonged rupture of membranes, preterm labour and signs of chorioamnionitis. Standard diagnostic protocols existed for the investigation of neonatal sepsis, and included a full blood count, blood culture, a lumbar puncture, an X-ray and C- reactive protein.

Older infants who were discharged, and who then presented in an outpatient setting with any signs of neonatal sepsis, received the same investigations, including urine culture according to standard protocols implemented in the review period.

**Definitions**

Early-onset disease was defined as the isolation of group B streptococcus from blood culture within six days of the birth. Late-onset disease was between seven and 90 days of age. Disease was classified as follows: Group B streptococcal meningitis was diagnosed when S. agalactiae was isolated from CSF. Probable meningitis was diagnosed when group B streptococcus was not cultured from CSF, but group B streptococcus was isolated from the blood, and when the CSF findings were consistent with meningitis. Infants were classified as premature if their gestational age was younger than 37 weeks. Low birthweight was defined as a weight of < 2.500 g.

**Statistical method**

A crude incidence rate was calculated for children born in Metro East using the formula: (number of group B streptococci cases/total number of live births in Metro East for that year) x 1 000 live births.

The study was approved and registered by the Health Research Ethics Committee of Stellenbosch University.

**Results**

The total birth cohort for the Metro East area of the Western Cape province was 24 025 in 2010, and 25 005 in 2011. From January 2010 to December 2011, 41 infants were identified with group B streptococcus. Records for 8 (19.5%) children were inadequate or unavailable for inclusion in the study. These included one case of early-onset disease, three of late-onset disease, and the remainder of indeterminate timing.

**Maternal features**

Complete maternal records were available for 27/33 (81.8%) of the mothers. None had a documented prior history of infection with group B streptococcus. Eight mothers were diagnosed with HIV. Antenatal CD4 was available for five mothers, of whom three had a count below 500, and two a count below 350 cells/ml. One woman in the late-onset disease group experienced a preterm rupture of membranes, and one woman in each group intrapartum fever. These women received intrapartum antibiotic prophylaxis. One woman in the early-onset disease group had a group B streptococcal urinary tract infection. Also, one case in each group was treated for a confirmed non-group B streptococcal urinary tract infection after delivery.

**Infant features**

Thirty-three infants presented with group B streptococcus at a median age of 10 days. Fourteen (42.4%) infants had early-onset disease, and 19 (57.6%) late-onset disease.

Eight (24.2%) infants were born at peripheral hospitals or clinics, and 25 (75.8%) at Tygerberg Academic Hospital or Karl Bremer Hospital. Twenty-one (63.3%) of the infants were female (63.6%). The mean birthweight for the entire group was 2.164 g (95% confidence interval: 1.771-2.559). The median gestational age was 36 (interquartile range 28-40) weeks.

Eleven (65%) early-onset disease cases occurred within 48 hours of birth. Fourteen (100%) occurred within 72 hours
of birth. Five (35.7%) of these infants had sepsicaemia and meningitis.

The age for late-onset disease was between eight and 52 days. Six (31.6%) infants presented with sepsicaemia and meningitis.

There were eleven (33.3%) children with confirmed meningitis and six (18.2%) with pneumonia. One case of meningitis was not included in this review (group B streptococcus on CSF culture, but not on blood culture). All isolates were sensitive to penicillin. Serotyping was not performed.

Eight (24%) children were HIV-exposed. Of these children, one was HIV-infected, four uninfected (as determined by a qualitative HIV DNA PCR), and three had no definitive result. The infant characteristics are depicted in Table I.

Discussion

The current global incidence of group B streptococcus in infants aged 0-89 days is reported as 0.53 per 1 000 live births. However, this incidence rate is based on a systematic review in which only five low-income countries were represented.\(^5\) The incidence of group B streptococcus in developing countries ranged between 0-3.1 per 1 000 live births in a recent study that reported on the incidence in hospital settings.\(^6\) Previous studies from South Africa have reported a higher incidence of 2.06 (early-onset disease)/per 1 000 live births, and 1 (late-onset disease)/1 000 live births.\(^11\)

The crude incidence rate in our study was 0.46/1 000 live births in 2010, and 0.88/1 000 live births in 2011. This was calculated for infants in the Metro East district of the Western Cape province. This is less than the 1.8/1 000 incidence rate that Gray et al found in Malawi in 2007.\(^12\) The majority (81%) of 2010 cases were early-onset disease compared to only 22% such cases in 2011, despite there being more cases. We would have expected higher rates of early-onset disease as there is no routine screening and prophylaxis. However, it is routine practice at Tygerberg Academic Hospital and Karl Bremer Hospital to give intrapartum antibiotics to women with preterm labour, prolonged rupture of the membranes, or any clinical signs of chorioamnionitis. This could have prevented some early-onset disease cases. There was no relationship between the place of birth and the time of onset of disease.

A study from Malawi showed that group B streptococcal carriage did not differ between HIV-negative and -infected women, but was higher in HIV-infected women with higher CD4 counts.\(^6\) Although this study was not designed to measure carriage rates in women, eight infants were HIV-exposed (8/33, 24.4%), which is what would be expected given that the antenatal HIV prevalence of women delivering in the Metro East area was 19.8% in 2011.\(^13\) Numbers were too small to make a meaningful comparison between risk factors for early-onset disease versus those for late-onset disease. Overall mortality was 6%, which is lower than that previously documented (19.8% for early-onset disease, and 13.6% for late-onset disease).\(^5\) This could be because of advances in neonatal and infant health care, and improved intensive care facilities, as previously documented morbidity and mortality occurred between 1997 and 1999, more than 10 years ago. Decreased mortality could also be owing to records that were unavailable for inclusion in our study. These were records of children who had died, and therefore mortality may have been underestimated. The findings may not be generalisable to other provinces in South Africa. The neonatal mortality rate was between 9.1 and 15 per 1 000 live births in the Metro East region over the study period, lower than the 20 per 1 000 live births for the same period for South Africa in total. It is possible that a higher

### Table I: A comparison of early-onset disease and late-onset disease: predisposing factors and clinical presentation

<table>
<thead>
<tr>
<th>Factors</th>
<th>Total, n = 33 (%)</th>
<th>Early-onset disease n = 14 (%)</th>
<th>Late-onset disease n = 19 (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>12 (36.4)</td>
<td>3 (21.4)</td>
<td>9 (47.4)</td>
<td>0.16</td>
</tr>
<tr>
<td>Preterm</td>
<td>18 (54.5)</td>
<td>3 (21.4)</td>
<td>15 (78.9)</td>
<td>0.01</td>
</tr>
<tr>
<td>HIV-exposed, uninfected</td>
<td>4 (12.1)</td>
<td>1 (7.1)</td>
<td>3 (15.8)</td>
<td>1.00</td>
</tr>
<tr>
<td>HIV-infected</td>
<td>1 (3)</td>
<td>0</td>
<td>1 (5.3)</td>
<td></td>
</tr>
<tr>
<td>Low birthweight</td>
<td>18 (54.5)</td>
<td>4 (28.6)</td>
<td>14 (73.7)</td>
<td>0.02</td>
</tr>
<tr>
<td>Apgar score or bradycardia at presentation</td>
<td>22 (66.7)</td>
<td>9 (64.3)</td>
<td>13 (68.4)</td>
<td>1.00</td>
</tr>
<tr>
<td>Seizure or irritability at presentation</td>
<td>10 (30.3)</td>
<td>5 (35.7)</td>
<td>5 (26.3)</td>
<td>0.71</td>
</tr>
<tr>
<td>White cell count &lt;5 000</td>
<td>12 (36.4)</td>
<td>4 (28.6)</td>
<td>8 (42.1)</td>
<td>0.69</td>
</tr>
<tr>
<td>C-reactive protein &gt;20</td>
<td>22 (66.7)</td>
<td>10 (71.4)</td>
<td>12 (63.2)</td>
<td>0.21</td>
</tr>
<tr>
<td>Meningitis</td>
<td>9 (27.3)</td>
<td>4 (28.6)</td>
<td>5 (26.3)</td>
<td>0.70</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>6 (18.2)</td>
<td>3 (21.4)</td>
<td>3 (15.8)</td>
<td>1.00</td>
</tr>
<tr>
<td>Meningitis plus pneumonia</td>
<td>2 (6.1)</td>
<td>1 (7.1)</td>
<td>1 (5.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Unspecified</td>
<td>16 (48.5)</td>
<td>6 (42.9)</td>
<td>10 (52.6)</td>
<td>0.55</td>
</tr>
<tr>
<td>Died</td>
<td>2 (6.1)</td>
<td>2 (14.3)</td>
<td>0</td>
<td>0.17</td>
</tr>
</tbody>
</table>

HIV: human immunodeficiency virus
incidence of group B streptococcus could be found in other regions of South Africa.

This study has several weaknesses as it was a retrospective review. Some of the records could not be reviewed and some were incomplete. Therefore, the data could have underestimated the incidence and severity of invasive group B streptococcal infection.

This method of estimating group B streptococcal incidence would not be able to identify infants who died at home or outside these healthcare facilities. Infants over seven days of age would have had blood culture tests performed at the discretion of the attending doctor, so there would not be blood culture results for all of the infants. Another limitation was the lack of serotyping of group B streptococcal isolates. However, this study describes infants born in tertiary hospitals, as well as in district and community care facilities. Data on group B streptococcus in these settings is scarce. Only one study in a review of 20 reported on neonatal group B streptococcal cases outside of the hospital setting.  

**Conclusion**

The incidence of group B streptococcus in this study was lower than that previously documented in other South African studies, but higher than that reported in other African countries. We hope that this data will add to the growing data that informs on best prevention strategies against group B streptococcus.

**References**