Review of the bacteriology of puerperal sepsis in resource-poor settings

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Key messages

- Severe infection (sepsis) is estimated to be the third most important cause of maternal deaths in resource-poor settings. ‘Puerperal sepsis’ refers to infection in the genital tract that occurs during the period from the onset of labour to the first six weeks after childbirth.
- Bacterial causes of puerperal sepsis have not been well studied in any setting, especially resource-poor settings where they are likely to be more prevalent.
- The limited evidence available indicates that polymicrobial infection (concurrent infection with multiple microorganisms) is common in puerperal sepsis.
- Operational research is urgently needed to provide better guidance on antibiotic regimens, including regimens that could be provided at a community level.

Background

Estimates of the contribution of sepsis to maternal mortality vary from 8 to 16%. A 2006 systematic review, with more than 35,000 women included in the analysis, provided a robust estimate of the distribution of causes of maternal deaths. Maternal sepsis was the third most important cause after haemorrhage and hypertensive disorders, responsible for 11.6% of maternal deaths in Asia, 9.7% in Africa and 7.7% in Latin America and Caribbean.

However, in countries with high numbers of maternal deaths, such as Papua New Guinea (PNG), which has an estimated maternal mortality rate (MMR) of 230/100,000, sepsis may cause an even larger proportion of maternal deaths in some settings. Data relating to causes of death in community settings is very limited. However facility-based data from a provincial hospital in PNG revealed that puerperal sepsis and sepsis after unsafe abortion accounted for 48% of total maternal deaths.

While sepsis is a common cause of maternal deaths, there are significant gaps in knowledge of the infective organisms that cause puerperal sepsis in resource-poor settings and the antibiotic management needed to treat it.

Definitions

Maternal sepsis is most commonly understood to mean any infection occurring in a woman between the onset of labour or rupture of membranes to 42 days postpartum. Changes in the immune system during pregnancy to avoid rejection of the foetus increase maternal susceptibility to particular infections. During this period, a number of infections not related to pregnancy can occur, including pneumonia, urinary tract infection, malaria, HIV, TB, endocarditis and meningitis.

Maternal sepsis related to pregnancy includes puerperal sepsis, post-abortion infection and wound infections after caesarean section or instrumental delivery.

In this review we will focus on puerperal sepsis, defined by WHO as genital tract infection occurring from time of onset of labour or rupture of membranes to 42 days postpartum. ‘Puerperal fever’ or ‘puerperal pyrexia’ are other commonly used terms, though they refer to any cause of fever occurring in the puerperium, not specifically genital tract infection. Clinical diagnostic criteria for puerperal sepsis include fever and one or more of pelvic pain, abnormal vaginal discharge, abnormal odour of discharge and delay in the rate in reduction of the size of the uterus. The most common site for infection is the endometrium (endometritis). Organisms that cause puerperal sepsis are from the environment, gastrointestinal tract or genital tract.

The contribution of puerperal sepsis to all maternal sepsis is significant. However, estimates are difficult to obtain, partly due to variation in definitions between studies. The Confidential Enquiries into Maternal Mortality, a reporting method used by individual countries to document maternal deaths and monitor outcomes on a long-term basis, are a useful source of data. In the South African 2005-2007 Confidential Enquiry, a total of 3959 maternal deaths were included, with 223 deaths (5.6%) attributed to pregnancy related sepsis (presumed to be analogous to puerperal sepsis). Abortion, most commonly complicated by infection or haemorrhage, caused 136 deaths (3.4%) and was reported separately from pregnancy-related sepsis. Acute infections not related to pregnancy, including pneumonia, UTI, malaria and meningitis, accounted for a total of 585 deaths (14.8%). Thus although the exact proportion is not clear, puerperal sepsis contributes significantly to total maternal infective deaths.

Given the large burden of disease, puerperal sepsis is a maternal health issue that needs to be addressed through both improved preventive strategies and treatment. Emphasis has been placed on detection and treatment of sexually transmitted infections during pregnancy as well as preventive strategies such as clean delivery kits and education about hygiene practices at the time of delivery. There have been several studies, including randomised controlled trials, suggesting that chlorhexidine vaginal washes during labour can reduce rates of puerperal and neonatal sepsis. In developed countries antibiotic regimens have been recommended for women identified to be at risk, for example because of prolonged rupture of membranes. Where institutional deliveries have been scaled up in resource-poor settings, concerns are already being raised about the increased risk of maternal and neonatal morbidity and mortality associated with greater use of interventions during deliveries. However, we have confined our review to puerperal sepsis following vaginal delivery without intervention because our aim is to provide guidance about the most appropriate antibiotic regimens for use in settings where most women deliver at home. WHO and UNICEF recommend postnatal home visits in high mortality settings, with the first within 24 hours of a home-birth, providing an opportunity for delivery of treatment during the high risk early postpartum period.

There is little published research from either high- or low-income countries documenting the spectrum of bacterial causes of puerperal sepsis. We have reviewed the primary literature on puerperal sepsis and documented current knowledge of the causal bacteria to help guide choice of appropriate antibiotic regimens for community-based care.
Method

We reviewed current knowledge regarding the bacteriology of puerperal sepsis from peer-reviewed published primary research articles. We identified studies that included culture results from the genital tract of women taken during the intrapartum or postpartum period in resource-poor settings through searching PubMed and references from relevant articles. The search terms used were: ‘maternal sepsis’, ‘puerperal sepsis’, ‘bacteriology’, ‘vaginal swabs’ and ‘developing countries’. Search terms were combined using both MeSH and non MeSH search engines. Only articles published in English since 1980 were included, as articles published prior to this time were likely to have used different laboratory techniques and may have shown a spectrum of organisms less relevant to those seen today.

Using the broadest PubMed search term ‘puerperal sepsis’ 556 articles were identified. Manually searching the titles and abstracts identified 94 articles with a focus on puerperal infections in women from developing countries. Abstracts and/or full text from these were extracted; eight articles included primary data with bacterial swab results from women in the intrapartum or postpartum period. Three further articles with bacterial swab results were later identified using a combination of the other search terms outlined above. A total of 11 articles were included in our final analysis; seven from women with diagnosed puerperal sepsis, and four from asymptomatic women either in labour or in the postpartum period.

Results

The studies identified included those in which swabs for microbiology were taken during labour or postpartum from either asymptomatic women or those diagnosed with puerperal sepsis.

Organisms were grouped into categories: sexually transmitted organisms, maternal genital tract normal flora, maternal gastrointestinal tract flora, group B streptococcus, environmental pathogens and ‘other’. Some organisms, for example Streptococci, were included in more than one category.

Table 1 part A shows the results of seven studies with swabs taken from women diagnosed with puerperal sepsis. Six of the papers are from sub-Saharan Africa;36-33 one is from Bangladesh.34 All swabs were of the genital tract except for Perine’s Ethiopian study, which included cultures of blood, pus or abscesses from 46 women with pelvic inflammatory disease in the postpartum period.33

Table 1 part B shows the results of studies with swab results from asymptomatic women in labour or postpartum.35-37 A wide variety of organisms were cultured from swabs from the women with a diagnosis of puerperal sepsis. Sexually transmitted organisms were identified in five of seven studies, and maternal gut flora was also identified in five different studies. However, four of the studies found organisms across three or more categories, making generalisation difficult. It is also important to note that in Dare’s study of women with clinical puerperal sepsis, 37% had negative genital swabs.28

Swabs from asymptomatic women also showed a wide variety of bacterial growth patterns. This shows that positive growth from a vaginal tract swab does not necessarily correlate with clinical disease. In particular, the presence of vaginal normal flora is difficult to interpret, as growth on a swab does not differentiate between its role as commensal or invasive organism.

Thus in both groups of symptomatic and asymptomatic women, a variety of organisms were identified, with interpretation difficult due to the possibility of false negative (i.e. no growth but clinical disease apparent) and false positive (i.e. positive swab without clinical disease) results.
### Table 1: Organisms from vaginal swabs of intrapartum/postpartum women in resource poor settings

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<td><strong>N. gonorrhoea</strong></td>
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<td><strong>C. trachomatis</strong></td>
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<td><strong>T. pallidum</strong></td>
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<td><strong>T. vaginalis</strong></td>
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<td><strong>G. vaginalis</strong></td>
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<td><strong>P. melaninogenica</strong></td>
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<td><strong>E. coli</strong></td>
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<td><strong>Peptostreptococci</strong></td>
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<td><strong>Bacteroides</strong></td>
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<td><strong>C. perfringens</strong></td>
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<td><strong>E. faecalis</strong></td>
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<td><strong>Group B Streptococcus</strong></td>
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<td><strong>Streptococci</strong></td>
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<td><strong>S. pyogenes</strong></td>
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<td><strong>Protozoa</strong></td>
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<td><strong>Yeast (Candida species)</strong></td>
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**Organisms from vaginal swabs of intrapartum/postpartum women with clinical symptoms**

**Environmental pathogens**

- **S. aureus**
- **Klebsiella spp**
- **Pseudomonas spp**
- **C. perfringens**
- **Streptococci**
- **C. pyogenes**

**Maternal gut flora**

- **E. coli**
- **Peptostreptococci**
- **Bacteroides**
- **C. perfringens**
- **E. faecalis**
- **"Anaerobes"**
- **"Enterobacteria"**

**Maternal normal flora**

- **S. pyogenes**
- **"Anaerobes"**
- **"Enterobacteria"**
- **"Anaerobes"**

**STI organisms**

- **C. trachomatis**
- **N. gonorrhoea**
- **T. pallidum**
- **T. vaginalis**
- **"Enterococci"**
- **"Enterobacteria"**
- **"Pus cells"**
- **"Anaerobes"**
- **"Enterobacteria"**
- **"Anaerobes"**
- **S. pyogenes**

**No growth**
Discussion

Our literature review found a limited number of research papers documenting the spectrum of bacterial causes of puerperal sepsis in developing countries. There is also limited data from high-income countries. The lack of data is likely due to recognition that definitive results are often not available and interpretation of genital tract swab results is difficult and unreliable. The polymicrobial nature of maternal genital tract infections, as well as the high rates of false positive and false negative results from swabs, also means that further research into this area is unlikely to provide more accurate data.

Our results correlate with recent literature from high income settings; these confirm that organism identification and patterns of disease are difficult to define, even without resource limitations.1,11 Maharaj states that the majority of cases of endometritis are polymicrobial, and include a mixture of aerobes and anaerobes.11 Key organisms identified as important in puerperal sepsis include group B Streptococci, Neisseria gonorrhoea, Chlamydia trachomatis, Herpes simplex, genital Mycoplasma and bacterial vaginosis. Van Dillen concurs that causative organisms in severe maternal sepsis are generally polymicrobial.1

The WHO midwifery guidelines for management of puerperal sepsis similarly recognise that more than one type of bacteria may be involved when a woman develops puerperal sepsis.38 These guidelines identify streptococci, staphylococci, Escherichia coli, Clostridium tetani, Clostridium welchii, Chlamydia trachomatis and Neisseria gonorrhoea as important organisms.

Aside from the polymicrobial nature of puerperal infection affecting an individual patient, the techniques used to identify infection also affect results. The sophistication of laboratory techniques affects the spectrum of organisms able to be identified – a laboratory with more capacity will identify more organisms. This makes interpretation across the studies identified in our literature review difficult – specific laboratory techniques were not well defined within the research methods of the majority of papers, which affects our ability to draw comparisons between results.

The culture results of a specific group of organisms, sexually transmitted infections, must be interpreted with particular caution. Positive culture results do not necessarily correlate with clinical disease. Specifically, identification of Treponema pallidum in the vaginal tract cannot be interpreted as active disease; serology is the definitive test for active syphilis.39

A further limitation of our findings relates to the populations studied. While the group we are interested in is women who access community-based care, the populations in the studies we reviewed were all able to access hospital-based care for antenatal visits or delivery. This affects the generalisability of results. It might be expected that hospital-acquired infections would be more common in the women included in these research studies, while community acquired pathogens may have a more important role in women from more remote settings.

As discussed, the polymicrobial nature of the discharge associated with puerperal sepsis includes a combination of organisms, which can include anaerobic organisms. For this reason women with clinical signs of puerperal sepsis always need broad-spectrum cover. A standard protocol should be used rather than relying on bacteriology results for an individual patient, given the difficulties in interpretation of laboratory results as outlined.

Conclusion

There is limited primary research available to provide data on the organisms that cause puerperal sepsis in resource-poor settings. The research available suggests that a variety of organisms can cause infection, and that for a single patient infection may be polymicrobial; this is consistent with findings from high-income countries. Preventative strategies remain important in reducing the incidence of puerperal sepsis. The outcome of our paper supports the need for broad-spectrum antibiotics in women with clinical signs of puerperal sepsis. In resource poor settings, local health workers in the community are likely to be those responsible for early recognition of illness and initiation of treatment in the majority of cases. Operational research is urgently needed to provide better guidance on antibiotic regimens, including regimens that could be provided at a community level.
<table>
<thead>
<tr>
<th>Study</th>
<th>Study population; swab types</th>
<th>Other</th>
<th>Environmental pathogens (community and nosocomial)</th>
<th>Maternal normal vaginal flora (&gt;\text{ovaginosis})</th>
<th>Maternal gut flora</th>
<th>Group B strep</th>
<th>Sexually transmitted organisms</th>
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<tbody>
<tr>
<td><strong>Ahmed</strong> Bangladesh 2010</td>
<td>50 women with puerperal sepsis; endocervical swabs/secretions sent for anaerobic culture</td>
<td><strong>Prevotella melaninogenica</strong></td>
<td><strong>Peptostreptococcus</strong>, <strong>Bacteroides fragilis</strong>, <strong>Clostridium perfringens</strong></td>
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<td><strong>Dare</strong> Nigeria 1998</td>
<td>8428 deliveries 1.7% diagnosed with puerperal sepsis (clinically +/- by swab); genital tract swabs</td>
<td><strong>E. coli</strong></td>
<td><strong>Staph aureus</strong>, <strong>Klebsiella species</strong>, <strong>Pseudomonas</strong></td>
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<td><strong>Kampikaho</strong> Uganda 1993</td>
<td>737 postpartum women; vaginal swabs</td>
<td><strong>Neisseria gonorrhoea</strong>, <strong>Enterobacteria</strong></td>
<td><strong>Streptococci</strong>, <strong>Staphylococci</strong>, <strong>Streptococci</strong></td>
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<td><strong>Mason</strong> Zimbabwe 1989</td>
<td>Swabs from 95 postpartum women with clinical sepsis compared with 111 controls; prevalence of 3 organisms higher in sepsis versus control group</td>
<td><strong>Neisseria gonorrhoea</strong>, <strong>Chlamydia trachomatis</strong></td>
<td><strong>Anaerobes</strong></td>
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<td><strong>Temmerman</strong> Kenya 1988</td>
<td>35 women with endometritis compared to 30 controls; vaginal swabs</td>
<td><strong>Neisseria gonorrhoea</strong>, <strong>Chlamydia trachomatis</strong></td>
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<tr>
<td><strong>Plummer</strong> Kenya 1987</td>
<td>1013 pregnant women enrolled during labour; genital swabs</td>
<td><strong>Neisseria gonorrhoea</strong>, <strong>Chlamydia trachomatis</strong></td>
<td><strong>Streptococci</strong></td>
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<td><strong>Perine</strong> Ethiopia 1980</td>
<td>300 postpartum women enrolled from hospitals for any reason; vaginal swabs</td>
<td><strong>Neisseria gonorrhoea</strong>, <strong>Enterobacteria</strong>, <strong>Anaerobes</strong></td>
<td><strong>Streptococci</strong></td>
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<td><strong>Dechen</strong> India 2010</td>
<td>524 pregnant women; 3 high vaginal swabs taken at time of admission (term &amp; preterm)</td>
<td><strong>Enterococcus species</strong></td>
<td><strong>Group B streptococci</strong></td>
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<tr>
<td><strong>Aboye</strong> Nigeria 2003</td>
<td>230 asymptomatic pregnant women; vaginal swabs</td>
<td><strong>Trichomonas vaginalis</strong>, <strong>Syphilis</strong>, <strong>Neisseria gonorrhoea</strong></td>
<td><strong>Gardnerella vaginalis</strong></td>
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<td><strong>Lagro</strong> Zambia 2003</td>
<td>630 postpartum women presenting to hospital for any reason; vaginal swabs</td>
<td><strong>Trichomonas vaginalis</strong>, <strong>Gm –ve cocci</strong> (suggestive of Neisseria gonorrhoea)</td>
<td><strong>Pus cells (suggestive of bacterial vaginosis)</strong></td>
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<td><strong>Vacca</strong> PNG 1980</td>
<td>Endocervical cultures obtained from 103 ante-partum and 50 afebrile postpartum women</td>
<td><strong>Peptostreptococcus</strong>, <strong>Bacteroides</strong></td>
<td><strong>Streptococcus pyogenes</strong></td>
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References


