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Inadequate research on methicillin-resistant *Staphylococcus aureus* (MRSA) risk among postpartum women

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Abstract

Methicillin-resistant *Staphylococcus aureus* (MRSA) has become an increasingly important pathogen in obstetrics. MRSA infections can result in morbidity for both mothers and their infants. Over the past decade, MRSA infection has increased in pregnant women and neonates [1]. Indeed, there is increasing evidence that horizontal transmission from MRSA colonized mothers to their neonates plays a role in increasing neonatal MRSA colonization and, sometimes, infection [2]. Additionally, obstetric patients are frequently exposed to antibiotics, a known risk factor for infection by drug resistant organisms including MRSA.[3] Infection in the postpartum period is still common, even in developed countries [4]. Nonetheless, there is inadequate information in the published literature about the epidemiology of MRSA infections in postpartum women and no consensus on how to reduce the burden and consequences of such infections. This is worrisome given the urgency of the double threat of (multi-)drug resistance and stagnating antibiotic development.

Keywords

methicillin-resistant *Staphylococcus aureus*, puerperal infection; obstetrics; anti-bacterial agents; bacterial colonization

Burden of MRSA Colonization and Infection

Asymptomatic colonization with MRSA is a communicable condition and a risk factor for invasive infections.[5,6] Several studies have investigated the prevalence of asymptomatic

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MRSA colonization in US and UK women in late pregnancy and women who are laboring. Prevalences range from 0.5% in Birmingham, UK; to 16.6% in Memphis and Nashville, Tennessee [2,7–12]. Studies varied in terms of timing of culture collection (late pregnancy versus labor/delivery) and sites cultured (rectovaginal versus nasal). Studies which examine only rectovaginal cultures likely underestimate true colonization rates, as nasal carriage appears to be more common than rectovaginal carriage [2,11]. A positive association between Black ethnicity and MRSA colonization was seen in two studies [8,11]. There may be an association between MRSA carriage and Group B Streptococcus (GBS) colonization [2,8].

The overall burden and risk of MRSA in obstetric populations is unknown. Using a Monte-Carlo simulation model, Beigi and colleagues estimated that MRSA causes approximately 8,900 cases of postpartum mastitis and 5,400 Cesarean wound infections per year in the United States [13]. Using administrative data from the Nationwide Inpatient Sample weighted to represent the population of US inpatients, a recent study estimated that there were approximately 2,600 cases of MRSA infection in pregnant and postpartum inpatients each year [14]. However, the sensitivity of administrative data for identifying MRSA infections appears to be very low and the majority of postpartum infections are diagnosed in outpatient settings, so this figure likely dramatically underestimates the true burden of obstetric MRSA infections [4,15].

We could find no estimates of the burden of postpartum MRSA infections outside the United States.

MRSA Breast Infections

Staphylococcus aureus is the most commonly isolated organism in infectious postpartum mastitis.[16] Mastitis, breast abscesses, and other breast infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) are probably the best characterized antibiotic resistant infections among postpartum women. A number of studies have sought to characterize the epidemiology of MRSA breast infections. Recent hospital based studies in Dallas and Houston found MRSA in the majority of cultures from breast abscesses [17,18].

Nonetheless, there is much more potential for studying the epidemiology of MRSA breast infections. Studies have generally been small, limited to one or two hospitals in the United States, and primarily involved inpatients. Laboratory cultures, which are needed for diagnosis of MRSA infection, may not be performed routinely, leading to selection bias. It is still unclear what proportion of mastitis and breast abscesses are caused by MRSA, what the risk factors and geographical variations are, and whether prenatal or intrapartum antibiotic treatment and prophylaxis predispose a woman towards these infections.

Other MRSA Infections

While most studies of postpartum MRSA infection focus on breast abscesses, there are other documented presentations of postpartum MRSA, including cellulitis, pelvic thrombophlebitis, pneumonia, septicemia, Cesarean wound infections, episiotomy infections, and urinary tract infections. In our previous investigation of MRSA infections in

obstetric inpatients using US hospital discharge data, we found that a majority of infections were of sites other than the breast, although site of infection was not clear in many cases. In women diagnosed before discharge for delivery, the most common infection sites were skin (31%), urinary tract (6%), other genitourinary sites (5%), wound infections, (3%), and blood (septicemia) (2%); approximately half of the infections had no identifiable site.[19] In women admitted for postpartum conditions, only 27% of infections were in the breast, while 41% were wound infections, and 21% had an unidentifiable site [14].

Antibiotic Use in Labor and Delivery

It is generally accepted that women undergoing Cesarean section should receive prophylactic antibiotics to decrease the risk of postsurgical infections. Cefazolin and ampicillin are recommended agents [20]. Cesarean section is a common procedure; for 2008, Cesarean sections rates were 30.3% for the United States, 22.0% for the United Kingdom, 26.3% for Canada, and in excess of 15% for the majority of countries [21].

In addition, many laboring women are given prophylactic antibiotics to prevent group B streptococcal (GBS) infections of the neonate. Guidelines for GBS screening and prophylaxis vary between countries. The United States Centers for Disease Control and Prevention and other US agencies recommend universal screening for GBS colonization late in pregnancy and universal antibiotic prophylaxis in colonized women. In the United States, between 10 and 30% of women screen positive for GBS, and compliance with prophylaxis is high. The recommended agent in intravenous penicillin G, with cefazolin, erythromycin, or clindamycin recommended in women allergic to penicillin [22].

Other countries, including the United Kingdom have adopted neonatal GBS prevention guidelines that recommend targeting prophylaxis based on other pregnancy and intrapartum risk factors (notably, preterm delivery, prolonged rupture of the membranes, intrapartum fever, or a previous infant with GBS disease). In these countries, fewer women are expected to receive intrapartum antibiotic prophylaxis.[23]

Because the antibiotic regimens for Cesarean section and GBS prophylaxis are short (often consisting of a single dose), some believe that there is little risk for subsequent infection with resistant organisms [20]. However, changes in skin flora have been observed after prophylaxis for non-obstetric surgical procedures, and intrapartum antibiotics for GBS prophylaxis appears to be associated with increased resistance to penicillin and ampicillin in Enterobacteriaceae isolated from vaginal flora [24,25].

MRSA Screening

Targeted antenatal MRSA screening and decolonization of MRSA-carriage in women at high-risk for MRSA infections (such as pre-pregnancy diabetics [19]) could reduce MRSA infections. However, contrary to GBS where screening guidelines are well-established, MRSA screening remains controversial. There is a paucity of data on the acquisition or persistence of MRSA to direct the optimal gestational age for screening [26]. MRSA screening should ideally be undertaken within a time frame that allows MRSA-carriers to receive decolonization treatment prior to their estimated dates of delivery.

In the UK, certain categories of obstetric cases are screened for MRSA, including elective Caesarean sections and other cases where there is a high risk of complications in the mother and/or infant. A 3-year review of a single-center's program suggests that decolonization of women undergoing Caesarean section and who are nasal MRSA carriers can help to prevent surgical site infections with MRSA [27].

Standard MRSA decolonization therapy does not include treatment for rectovaginal colonization. There is a lack of data to show either the likelihood of successful decolonization in pregnant women, or whether decolonization treatment results in better clinical outcomes for mother and child [26].

Directions for Research

Better information on the prevalence and predictors of MRSA in postpartum women is needed to weigh the risks and benefits of intrapartum antibiotic use and guide treatment of MRSA infections. Additionally, multicenter studies are necessary to evaluate the effect of MRSA screening in obstetrics on the reduction of MRSA infections in mothers and their infants. Given the different pathogens involved and the evidence needed for targeted versus routine screening, it will be important to study MRSA acquired in different (healthcare and community) settings. Furthermore, we need more research into MRSA screening methods and techniques, such as the use of real-time Polymerase Chain Reaction (PCR) to detect MRSA within one hour [28,29]. Studies from outside the United States and the United Kingdom are also needed.

There are challenges in studying this topic. The majority of postpartum infections are diagnosed after discharge from the hospitalization for delivery, and most are diagnosed in ambulatory rather than inpatient settings [4]. Thus, hospital-based studies may not provide a complete picture of the epidemiology of these infections. Future research designs should integrate data from the delivery episode, and ideally, prenatal medical care, with follow-up after discharge from the delivery admission. Studies should be able to identify infections diagnosed in both inpatient and ambulatory care settings. We also need comparative effectiveness studies that show which interventions work best, for whom and under what settings with the aim of maximizing effectiveness (i.e. maternal and child outcomes) and efficiency (i.e. cost-effectiveness) while curbing the tide of drug resistance in hospitals and the community.

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