Should we be afraid of methicillin-resistant Staphylococcus aureus in obstetrics?

MAJA KUFELNICKA-BABOUT¹, JAROSŁAW KALINKA²

Abstract

The emergence of community-acquired MRSA colonization represents a new, unrecognized reservoir of MRSA within hospitals, potentially increasing the risk for horizontal transmission. Taking into consideration the fact that this type of methicillin-resistant Staphylococcus aureus is usually recognized in young, healthy subjects without risk factors, obstetricians should be aware of the hazardous outbreak and detection of CA MRSA dependent infection. Although MRSA is not frequent in pregnant women, vaginal colonization can be detected in routine streptococci B screening. This article summarize the management in colonized and infected woman.

Key words: MRSA, pregnancy, vaginal colonisation

Introduction

As we have observed recently more frequent detection of methicillin-resistant Staphylococcus aureus (MRSA) in vaginal swab among our pregnant patients, the question arise whether routine screening is justified and how we should manage such a clinical situation.

Following a recent European report, the BURDEN study, which found that MRSA bacteraemia doubled the 30-day mortality compared with MSSA bacteremia [1], our fear for the MRSA patient’s outcome seems to be justified.

Methods

The published studies of MRSA in pregnant women (detection, frequency, outcome in mother and child, management in pregnancy) were identified from Medline database. The data concerning MRSA screening were collected essentially in the USA where vaginal and rectal swabs are routinely collected to test for colonization with group B streptococci.

Frequency of MRSA in pregnant women population

Staphylococcus aureus, Gram positive cocci colonizing the skin, anterior nares, genital tissue and oropharynx are commonly widespread in healthy population. Out of 20% of the persistent carriers of S. aureus, only in 10% (2% of global population) it is commenced by MRSA strains. Even 60% of population can be intermittent carriers of S. aureus [2]. Almost 50% of medical staff, considered as one of the most important sources of the infection can be colonized with S. aureus.

MRSA is not widespread in obstetrics. The prevalence of MRSA among mothers was evaluated mainly in US and UK studies. According to different publications among hospitalized pregnant women its presence varies from 0.1 to 10% and is on the level of global population.

The epidemiology of MRSA in the USA, where community-associated MRSA strains are frequently observed, is different from that in Europe. The most detailed data concerning MRSA detection in pregnant woman have been collected in the United Kingdom.

Gray et al. investigated nose swabs taken from 5548 of 21,770 (25.5%) women who delivered at Birmingham Women’s Hospital. Only 29 (0.5%) were MRSA positive. MRSA infections occurred later in three cases. MRSA infections occurred in further 13 mother-infant pairs, including six cases where mothers were MRSA screen negative. Seventeen mothers had risk factors for MRSA [3]. Chen et al. [3] screened rectal swabs from 2963 mothers and found only 14 (0.4%) cases of colonization by MRSA, 13 of these being CA MRSA (community acquired MRSA) [4]. Another study from the USA revealed the prevalence of 3.5% of MRSA in pregnant women [5]. Patel et al. investigated nasopharyngeal carriage of MRSA in 1046 pregnant women [6]. The incidence of MRSA in this group was similar to that estimated by Andrews et al. [5]. However some recent studies suggest that the level of MRSA isolates in pregnant women is much higher [7]. This study, however is not as statistically relevant as other studies presented in Table 1.

¹ Department of Perinatology, M. Pirogow Regional Specialist Hospital in Lodz, Poland
² Department of Perinatology, 1st Chair of Gynecology and Obstetrics, Medical University of Lodz, Poland
The data collected in our hospital in 2758 pregnant women during the last two years are significantly different from those presented by Anglo-Saxon authors (Table 1). *Staphylococcus aureus* vaginal colonization was present in 19 women (0.7%), and only one patient was colonized with MRSA (recto-vaginal colonization).

**Table 1. The extent of *Staphylococcus aureus* (MRSA) vaginal-rectal/nasal* colonization among pregnant women and their children. Nd – no data available**

<table>
<thead>
<tr>
<th>Population</th>
<th>Country</th>
<th>Mothers/infants</th>
<th>MRSA in mother (n)</th>
<th>MRSA in mother (%)</th>
<th>MRSA in infants (n)</th>
<th>MRSA in infants (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creech 2010</td>
<td>USA</td>
<td>250</td>
<td>Nd</td>
<td>10.4</td>
<td>Nd</td>
<td>Nd</td>
</tr>
<tr>
<td>Top 2010</td>
<td>USA</td>
<td>2921</td>
<td>17</td>
<td>0.6</td>
<td>Nd</td>
<td>Nd</td>
</tr>
<tr>
<td>Reusch 2008</td>
<td>USA</td>
<td>288</td>
<td>Nd</td>
<td>2.1</td>
<td>Nd</td>
<td>0.7</td>
</tr>
<tr>
<td>Andrews 2008</td>
<td>UK</td>
<td>5732/5804</td>
<td>Nd</td>
<td>3.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chen 2006</td>
<td>USA</td>
<td>2963</td>
<td>14</td>
<td>0.47</td>
<td>Nd</td>
<td>Nd</td>
</tr>
<tr>
<td>Ghanim 2011</td>
<td>USA</td>
<td>6626</td>
<td>7</td>
<td>0.1</td>
<td>Nd</td>
<td>Nd</td>
</tr>
<tr>
<td>Patel 2011</td>
<td>USA</td>
<td>1046</td>
<td>31</td>
<td>2.9</td>
<td>Nd</td>
<td>Nd</td>
</tr>
<tr>
<td>Tomlinson 2011</td>
<td>USA</td>
<td>1488</td>
<td>Nd</td>
<td>1.7</td>
<td>Nd</td>
<td>Nd</td>
</tr>
<tr>
<td>Gray 2013</td>
<td>UK</td>
<td>5548*</td>
<td>29</td>
<td>0.5</td>
<td>Nd</td>
<td>Nd</td>
</tr>
</tbody>
</table>

The emergence of CA-MRSA colonization represents a new, unrecognized reservoir of MRSA within hospitals, potentially increasing the risk for horizontal transmission. Taking into consideration the fact that this type of methicillin-resistant *Staphylococcus aureus* is usually recognized in young, healthy subjects without risk factors, obstetrical medical staff should be aware of the hazardous outbreak and detection of CA MRSA dependent infection. CA-MRSA are responsible, similarly to HA-MRSA (hospital acquired), for different types of infection, mostly concerning skin and soft tissues infection. The CDC defines hospital-acquired MRSA (HA-MRSA) in those who have had frequent or recent contact with hospitals or healthcare facilities (such as nursing homes or dialysis centers) within the previous year, have recently undergone an invasive medical procedure, organ transplantation, as well as hospitalized in intensive care unit, scalded or immunocompromised patients. The common sources of infection are colonized medical staff, specimens from patients, infected drainage, intubation tubes or catheters, infected medical equipment, open bottles of disinfectants, open garbage baskets. One of the most important sources of infection are also children in neonatal and pediatric units.

Although HA-MRSA and CA-MRSA have distinct clinical differences, both are transmitted in the same fashion—most frequently through direct skin-to-skin contact or contact with shared items or surfaces not properly disinfected (such as towels, bandages, door handles, phones, computer keyboards) that have come into contact with someone else’s colonized or infected skin. Currently, MRSA originates more frequently outside the hospital, implying it is brought into the hospital upon admission as either the CA-MRSA or HA-MRSA genotype [8].

**Significance for mother**

The three most common procedures associated with MRSA infections are surgical treatment of skin/subcutaneous infection, the débridement of wound infection, and bone excision [9]. Next to death, surgical site infection (SSI) remains the most unwanted postoperative complication, and yet it accounts for approximately one third of all hospital-acquired infections.

More than 29 percent of SSIs are MRSA-positive. Primary skin infection may be confused with spider bites and ignored. The most common sites of abscesses were extremities, gluteal and perirectal areas [10]. Necrotic pneumonia with bacteriemia caused by CA-MRSA is usually influenza virus complication [3].

MRSA is associated with several diseases unique to the pregnant and postpartum patient. SSTIs (skin and soft tissue infections) remain the most common localisa-
Should we be afraid of methicillin-resistant Staphylococcus aureus in obstetrics?

Should we be afraid of methicillin-resistant Staphylococcus aureus in obstetrics? Mastitis, which is found in up to 3% of breast-feeding mothers and often caused by *S. aureus*, has been detected in about 25% of MRSA cases, disrupting pregnancy. The association of MRSA with postpartum mastitis and breast abscess has also been revealed [11, 12]. Other infections in the puerperium concern vulvar abscesses [13], chorioamnionitis [14, 15], episiotomy site infections, and wound infections after cesarean delivery. Although MRSA is increasing as a cause of infectious morbidity in the obstetric population, a recent analysis concluded that universal screening and decolonization are currently not cost-effective [2].

**Significance for infants**

The rise in CA-MRSA infections in the pregnant population follows a similar increase of MRSA infections in the neonatal intensive care units [16]. Well known ways of MRSA transmission from mother or health care worker are skin infections, maternal mastitis, and expressed breast milk [17]. Another potential mode of transmission is vertical spread. Fortunately, this is a rare occurrence. Among 5732 pregnant women in Alabama in 2003 to 2006, the vaginal colonization rate was 3.5% with no documented neonatal MRSA infections [5]. Tomlinson et al. collected 1488 rectovaginal cultures and the rate of MRSA colonization was 1.7% [18]. In the period of ten years only 4 positive *S. aureus* cultures were obtained within 10 000 delivered neonates, who did not suffer from early onset neonatal sepsis. Despite the detection of MRSA in a newborn, the risk of vertical transmission is not sure. Reusch et al. presented the analysis of MRSA colonization in 288 mother-infant pairs (Table 1) and did not observe any case of intrapartum transmission [19].

The benefits for the infant from maternal screening are unknown.

**Management in colonized woman**

Once MRSA is identified, we should first determine the origin of MRSA strain – whether it is of its own colonization or a hospital acquired strain.

The next step should include the examination of MRSA carriage in other patients and medical staff. It is not sure if it should be recommended to isolate the colonized patient or health care member and if such preventive steps are effective [20].

Historically, multiple attempts to eradicate MRSA colonisation have been undertaken including the use of framycetine, gramicidin, oxacillin, meticillin, soframycin, neobactrin, neomycin, gentamicin, neosporin, rifampicin with bacitracin, 2% soap with hexachlorophene, chlorhexidine or lisostaphin ointment 1%.

Nowadays the use of abovementioned antibiotics in the purpose of decolonisation is no more justified [21]. Oral antimicrobial therapy is not routinely recommended for decolonization [22].

The appropriate management in case of colonized patient include hand hygiene (frequent soap and water washing and use of alcohol-based disinfectants) and preventing skin-to-skin contact or personal items sharing with infected patients. Increased environmental hygiene rules should be introduced in households or hospitals (high-touch surfaces cleaning with appropriate cleaners or detergents, frequent garbage voiding) [22].

In women with the history of MRSA, The Infectious Diseases Society of America (IDSA) recommends a single dose of vancomycin added to standard β-lactam prophylactic pre-caesarean dose.

**Management in infected woman**

Empiric treatment in case of invasive disease (pneumonia, bacteriemia, osteomyelitis or endocarditis, purulent cellulitis) usually includes vancomycin or clindamycin [10]. The final choice of an antibiotic depends on the antibiogram and resistance/sensitivity profile of the MRSA strains. General approach to treatment should be based on general population guidelines, taking account of the safety characteristics of the antibiotic in pregnant women.

Clindamycin, frequently used for the management of bacterial vaginosis during pregnancy, is FDA category B antibiotic. Despite resistance to clindamycine, clinicians should be aware of the occurrence of fulminant, severe Clostridium-difficile-related colitis arising in low-risk persons, including pregnant women, and monitor patients carefully for diarrhea.

In case of resistance to clindamycin: vancomycin or linezolid (both FDA category C) could be taken into consideration as the drugs of choice. FDA category D agents, including: doxycycline, minocycline, tetracycline are strictly contraindicated during pregnancy.

A TMP-SMZ (also TMP-SMX or TMP-Sulfa) disk is a combination of trimethoprim and sulfamethoxazole that acts synergistically in bactericidal action. TMP-SMX is not recommended in the 3rd trimester of pregnancy. Well tolerated drug Daptomicin with proven efficacy in SSTI is accessible in Poland.

Rifampicin is a bactericidal antibiotic, teratogenic in animals. In humans this old antibiotic is typically used to treat mycobacterium infections, including tuberculosis.
Table 2. The antibiotics commonly used in MRSA infections during pregnancy

<table>
<thead>
<tr>
<th>International name</th>
<th>Commercial name</th>
<th>FDA</th>
<th>Administration</th>
<th>Dose</th>
<th>per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycine</td>
<td>Clindamycin</td>
<td>B</td>
<td>p.o./i.v.</td>
<td>300-600 mg</td>
<td>3 × day</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>Vancomycin</td>
<td>C</td>
<td>i.v.</td>
<td>15-20 mg/kg</td>
<td>2-3 × day</td>
</tr>
<tr>
<td>Linezolid</td>
<td>Zyvoxid</td>
<td>C</td>
<td>i.v.</td>
<td>600 mg</td>
<td>2 × day</td>
</tr>
<tr>
<td>Daptomycine</td>
<td>Cubicin</td>
<td>B</td>
<td>i.v.</td>
<td>4-6 mg/kg</td>
<td>1 × day</td>
</tr>
<tr>
<td>TMP-SMX (Rifampicin)</td>
<td>Biseptol</td>
<td>C</td>
<td>p.o.</td>
<td>960</td>
<td>2 × day</td>
</tr>
</tbody>
</table>

and Hansen’s disease. Rifampicin should be used only in combination with other antibiotics due to the rapid onset of resistance in monotherapy. Rifampin can be considered in the combined treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) including difficult to treat infections such as osteomyelitis. Table 2 shows antibiotics most commonly used in MRSA infections and their dosage during pregnancy.

Skin and soft tissue infections should be treated with antibiotics only in severe, complicated cases, after bacterial culture sampling.

In the case of perineal abscess surgical decompression is highly recommended. For episiotomy or caesarean wound infection an appropriate surgical debridement should follow.

**Discussion**

**MRSA as a clinical problem in obstetrics**

Methicillin-resistant *Staphylococcus aureus* remains one of the most challenging medical problems causing health care-associated infections and more and more frequent community-associated infections. Bacteraemias caused by methicillin-resistant *S. aureus* increased until 2005 (7.6% per year; 95% CI 6.1-9.1%), and then decreased (~4.8% per year; 95% CI –6.1 to –3.5%), whereas the number attributable to methicillin-sensitive *S. aureus* increased continuously (3.4% per year; 95% CI 3.0-3.7) [23].

Young, healthy woman as a patient in obstetrical ward can potentially be a source of CA-MRSA. Nasal or rectovaginal swabs could be considered as a screening test. Sampling procedures performed on hospital admission have been recommended to identify patients colonized with methicillin-resistant *Staphylococcus aureus* (MRSA). General population screening could be based on nasal cultures. Nares have been identified as a main colonization site, however in obstetrical wards vaginal-rectal swabs are usually collected. It seems that routine screening of MRSA in pregnant women should not be recommended. Young and healthy women even hospitalized are considered as low risk population. It is not sure whether standard screening and decolonization treatment (which excludes vaginorectal sites) is appropriate [24]. Only few authors described a long term screening program in pregnant women[3-6]. In the most recent study concerning patients of obstetrical wards Gray et al. found that the large-scaled screening of nasal swabs is of limited value in preventing MRSA-related morbidity in this population [3].

Although rectovaginal swab is not considered harmful or dangerous, it should be accepted by patients. In Poland vaginal and rectal swabs are routinely collected to test for colonization with group B streptococci after 35 weeks of pregnancy. As mentioned above, there is no reason to introduce the test for colonization with MRSA as routine admission procedure in every pregnant woman.

**Decolonization**

The routine decolonization is actually not recommended [2].

Only Mupirocine, an antibiotic of the monoxycarbolic acid class, have been approved for its efficacy in decolonization of MRSA. The use of mupirocin ointment was used with success for postoperative infection with *Staphylococcus aureus* in patients undergoing upper gastrointestinal or cardiac surgery [25, 26]. Konvalinka et al. presented confusing data reporting that prophylactic intranasal mupirocin administered to *S. aureus* carriers did not reduce the rates of overall surgical site infections by *Staphylococcus aureus*, and only showed a tendency towards decreased incidence of nosocomial *S. aureus* infections [9]. IDSA guidelines allows decolonization in cases of recurrent SSTI or in the situation of familial contamination in ongoing transmission [22].

Hence, the use of this antibiotic is contraindicated in pregnancy. Moreover it seems that decolonization treatment for rectovaginal localization is not justified [27]. In UK, decolonization is followed with the use of nasal mupirocin and chlorhexidine washes for 5 days, despite the fact that decolonization procedures remains questionable [3].
Cost-effectiveness

Methicillin-resistant *S. aureus* is an important emerging pathogen responsible for a modest burden of perinatal infections and associated costs.

After three years screening program study followed in The Newcastle upon Tyne Hospitals (UK) with 168,073 results collected from nose, throat and perineum, it was shown that a screening strategy based upon clinical risk is more pragmatic and more cost-effective than the universal programme currently required in England [28]. Universal screening and decolonization efforts do not currently seem to be cost-effective [29, 30].

Conclusions

MRSA is not widespread in obstetrics, and large-scale screening is of limited value in preventing MRSA-related morbidity in this population. Although traditional attempts limiting the spread of MRSA such as decolonization or isolation seems not to be justified, many obstetrical centers continue the old schemas.

The treatment of invasive disease is usually efficient and should be adopted to pregnancy safety profile.

References


Jarosław Kalinka
Department of Perinatology
Medical University of Lodz
94-029 Łódź, Wileńska 37
j.kalinka@csk.am.lodz.pl