Risk Factors for \textit{Staphylococcus aureus} Postpartum Breast Abscess

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\textbf{Background.} \textit{Staphylococcus aureus} (SA) breast abscesses are a complication of the postpartum period. Risk factors for postpartum SA breast abscesses are poorly defined, and literature is conflicting. Whether risk factors for methicillin-resistant SA (MRSA) and methicillin-susceptible SA (MSSA) infections differ is unknown. We describe novel risk factors associated with postpartum breast abscesses and the changing epidemiology of this infection.

\textbf{Methods.} We conducted a cohort study with a nested case-control study \((n = 216)\) involving all patients with culture-confirmed SA breast abscess among >30 000 deliveries at our academic tertiary care center from 2003 through 2010. Data were collected from hospital databases and through abstraction from medical records. All SA cases were compared with both nested controls and full cohort controls. A subanalysis was completed to determine whether risk factors for MSSA and MRSA breast abscess differ. Univariate analysis was completed using Student’s \(t\) test, Wilcoxon rank-sum test, and analysis of variance, as appropriate. A multivariable stepwise logistic regression was used to determine final adjusted results for both the case-control and the cohort analyses.

\textbf{Results.} Fifty-four cases of culture-confirmed abscess were identified: 30 MRSA and 24 MSSA. Risk factors for postpartum SA breast abscess in multivariable analysis include in-hospital identification of a mother having difficulty breastfeeding (odds ratio, 5.00) and being a mother employed outside the home (odds ratio, 2.74). Risk factors did not differ between patients who developed MRSA and MSSA infections.

\textbf{Conclusions.} MRSA is an increasingly important pathogen in postpartum women; risk factors for postpartum SA breast abscess have not changed with the advent of community-associated MRSA.

Breast infections are a common complication of the postpartum period. Mastitis, both infectious and non-infectious, afflicts 9%-33% of all lactating women [1–5], and abscesses complicate mastitis up to 11% of the time [1, 6]. \textit{Staphylococcus aureus} (SA) is the predominant pathogen in postpartum breast abscess seen in up to 100% of culture-confirmed cases [7–9]. Several previous studies examined risk factors associated with the development of postpartum breast abscess and found that low parity is a consistent predictor of later infection [7, 9–11]. Other associations have been made inconsistently. Some studies found both young maternal age and obesity to be predictive of postpartum development of breast abscess, whereas others report that young maternal age and obesity are protective [7, 10–12]. Few studies have examined whether risk factors for breast abscess development have changed with the advent of community-associated methicillin-resistant \textit{S. aureus} (CA-MRSA).

Our study was divided into 2 periods. During the first period, from 1 October 2003 through 30 September 2008, there was a low incidence of MRSA infection. During the second period, from 1 October 2008 through 31 August 2010, there was a high rate of MRSA infection among mothers associated with a hospital cluster of CA-MRSA pulsed-field type USA300-0114. Infections in mothers during this period were predominantly breast abscess, and infections in infants were mainly diaper pustulosis [13, 14].
**METHODS**

**Setting**
We conducted a cohort study with a nested case-control design among all postpartum women who delivered at our academic tertiary care center with ~5500 deliveries per year from 1 October 2003 through 31 August 2010. The frequency of postpartum SA breast abscesses was examined over time using an epidemic curve. Data regarding methicillin resistance in SA breast abscesses over time were analyzed using the Cochran-Armitage test for trend. Routine antibiotic susceptibility testing was performed for each SA isolate at the Beth Israel Deaconess Medical Center Clinical Microbiology Laboratory.

**Case Definition and Selection**
Case patients were defined as any woman who developed a culture-confirmed SA breast abscess within 1 year after delivering at our center that required needle drainage, incision, and drainage; operative intervention; or spontaneous drainage. Cases were identified using the microbiology database; all cases of positive SA culture results within 1 year after delivery at our center were reviewed. Women with uncomplicated mastitis were excluded. Attempts to find additional breast abscess cases were made by searching relevant International Classification of Diseases, Ninth Revision (ICD-9), codes.

**Nested Study Control Selection**
Three controls were chosen for every abscess case; selection was based on the 3 closest delivery times to the case. Exclusion criteria for control selection included prepartum breast abscess, neonatal demise within 24 hours after delivery, stillbirth, and SA infection at another body site.

**Cohort Control Selection**
Any woman who was not a case patient during the study period was eligible to serve as a control subject in the case-cohort analysis.

**Potential Risk Factors for S. aureus Breast Abscess**
Potential risk factors for development of SA breast abscess were examined, including maternal and infant demographic characteristics and peripartum variables. Patient-specific data for the cohort analysis were extracted from hospital databases when available, including the standard Admission Discharge Transfer database, which contains admission and discharge information and baseline maternal demographic characteristics, including date of birth, race, marital status, employment status, and insurance status. Data were also used from the hospital birth database. Peripartum variables, including maternal body mass index, smoking status, group B streptococcus (GBS) colonization status, induction and/or augmentation of labor, delivery type, and number of gestations were collected. Infant variables, including gestational age, neonatal bilirubin at 24–48 hours of life, birthweight, and neonatal intensive care unit admission status, were obtained. The infection control database and the microbiology database were used to obtain culture data and sensitivities of SA isolates.

Several variables were not available in electronic hospital databases and, therefore, were only analyzed in the nested case-control study (n = 216). These variables were abstracted from the medical record, including maternal employment status, intrapartum variables (such as induction of labor, augmentation of labor, the use of oxytocin during delivery, and antibiotic administration during delivery), and all in-hospital postpartum variables (such as exclusive breastfeeding, the need for lactation consultation and lactation consult comment and suggestion, and in-hospital use of a breast pump). Validation of the accuracy of variables obtained from the electronic databases was performed by comparison with the same variables obtained through chart review among the subpopulation in the nested case-control study. Variables in the database determined to be <85% accurate were not included in the case-cohort analysis.

Potential risk factors were first compared in univariate analyses, using the Student t test, Wilcoxon rank-sum test, Fisher’s exact test, and analysis of variance, as appropriate. Collinearity testing was completed using Pearson and Spearman correlation coefficients. All risk factors significant at the P < .2 level were then entered into a stepwise logistic regression model, and variables significant to P < .05 were retained. The Hosmer-Lemeshow test was used for evaluation of model goodness-of-fit. The same statistical techniques were used for the cohort study, except that relative risk estimates were calculated when possible. All data were analyzed using SAS, version 9.1.3 (SAS Institute). Approval for the study was obtained from the medical center Institutional Review Board before data collection and analysis.

**RESULTS**
During the 7-year study period, there were 32 770 deliveries: 23 908 during the precluster period and 8862 during the cluster and postcluster period. Almost 50% of women delivering at our center during the entire study period were primiparous, and the mean maternal age was 32.4 years. Approximately 4% of women had >1 birth during the study period. (See Table 1 for description of full cohort.)

Fifty-four cases of culture-confirmed SA postpartum breast abscess were found after review of the microbiology database; ICD-9 code searching failed to identify additional breast abscess cases among women who delivered at our center, regardless of organism (Figure 1). Abscesses occurred at 10–342 days after delivery (mean, 51.3 days; median, 31 days).
During the first period, 3 cases of MRSA and 18 cases of MSSA postpartum breast abscess were identified. During the subsequent period, 27 MRSA cases and 6 MSSA cases were identified; MRSA cases during this period were predominantly due to USA 300-0114. Rates of MSSA infection remained constant during both periods; however, rates of MRSA infection increased over time. With cluster cases included, there was statistically significant increase in the proportion of MRSA abscesses over time ($P < .0001$); when cluster cases were excluded, a trend toward significance remained ($P = .07$). The epidemic curve is displayed in Figure 2.

All SA isolates tested were susceptible to trimethoprim-sulfamethoxazole, regardless of period (44 of 54 isolates were tested). More than half of all MSSA isolates were susceptible to erythromycin (15 of 24 susceptible, 1 of 24 intermediate, 7 of 24 resistant, and 1 of 24 not tested); however, no isolates of MRSA were susceptible (0 of 30). Clindamycin susceptibility testing was incomplete; however, all 15 MSSA isolates that were tested were susceptible by d-testing. Clindamycin susceptibility was also incomplete for MRSA infection; however, the majority of isolates tested were susceptible by d-testing (15 of 30 susceptible, 1 of 30 resistant, and 14 of 30 not tested).

### Potential Risk Factors for S. aureus Breast Abscess

#### Nested Case-Control Results

All case patients had 3 control subjects successfully selected. Four potential control subjects were excluded for mastitis (1 case), fetal demise within 24 hours after birth (1 case), and other SA infection (2 cases). In all, 54 patients and 162 control subjects had full data available for analysis.

#### Table 1. Baseline Characteristics of Staphylococcus aureus Postpartum Breast Abscess: Cases Versus Controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>All SA cases</th>
<th>Nested controls</th>
<th>$P$ value$^a$</th>
<th>Cohort</th>
<th>$P$ value$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maternal demographic variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal age (years)$^c$</td>
<td>34.2 (32.9–35.5)</td>
<td>32.5 (31.7–33.3)</td>
<td>.03</td>
<td>32.4 (32.4–32.5)</td>
<td>.014</td>
</tr>
<tr>
<td>Body mass index$^c$</td>
<td>29.4 (28.0–30.8)</td>
<td>29.6 (28.7–30.5)</td>
<td>.8</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Race (%)$^d$</td>
<td></td>
<td></td>
<td>.1930</td>
<td></td>
<td>.1232</td>
</tr>
<tr>
<td>Caucasian</td>
<td>68.5</td>
<td>63.4</td>
<td>63.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>3.7</td>
<td>8.7</td>
<td>13.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>18.6</td>
<td>11.2</td>
<td>11.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>9.3</td>
<td>16.8</td>
<td>10.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed outside the home (%)</td>
<td>88.7</td>
<td>70.7</td>
<td>.0095</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Married (%)</td>
<td>94.4</td>
<td>82.0</td>
<td>.041</td>
<td>83.0</td>
<td>.027</td>
</tr>
<tr>
<td>Smokers (%)</td>
<td>0</td>
<td>4.3</td>
<td>.20</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Private insurance (%)</td>
<td>88.9</td>
<td>81.4</td>
<td>.29</td>
<td>82.2</td>
<td>.28</td>
</tr>
<tr>
<td><strong>Peri-partum variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primiparous (%)</td>
<td>59.3</td>
<td>38.9</td>
<td>.011</td>
<td>48.1</td>
<td>.009</td>
</tr>
<tr>
<td>Group B streptococcus positive (%)$^e$</td>
<td>25</td>
<td>33.6</td>
<td>.34</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>C-section (%)</td>
<td>35.2</td>
<td>32</td>
<td>.62</td>
<td>38.2</td>
<td>.68</td>
</tr>
<tr>
<td>Augmentation of labor (%)</td>
<td>51.9</td>
<td>45.7</td>
<td>.44</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Multiple births (%)</td>
<td>5.5</td>
<td>1.8</td>
<td>.067</td>
<td>3.8</td>
<td>.65</td>
</tr>
<tr>
<td>Exclusive breastfeeding in hospital (%)</td>
<td>48.8</td>
<td>62.7</td>
<td>.084</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td><strong>Infant variables</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactation consultation (%)</td>
<td>59.3</td>
<td>38.9</td>
<td>.011</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Gestational age (weeks)$^c$</td>
<td>38.9 (38.5–39.4)</td>
<td>38.6 (38.1–39.2)</td>
<td>.55</td>
<td>38.3 (38.3–38.3)</td>
<td>.33</td>
</tr>
<tr>
<td>Neonatal bilirubin (mg/dl)$^f$</td>
<td>7.56 (6.72–8.39)</td>
<td>7.09 (6.62–7.55)</td>
<td>.32</td>
<td>7.57 (7.53–7.60)</td>
<td>.33</td>
</tr>
<tr>
<td>NICU admission (%)</td>
<td>16.7</td>
<td>24.7</td>
<td>.26</td>
<td>24.1</td>
<td>.15</td>
</tr>
</tbody>
</table>

Abbreviations: NICU, Neonatal Intensive Care Unit; SA, Staphylococcus aureus.

$^a$ $P$ value presented is the univariate $P$ value comparing all S. aureus cases to nested controls.

$^b$ $P$ value presented is the univariate $P$ value comparing all S. aureus cases to cohort controls.

$^c$ Mean and upper and lower limit of 95% confidence interval reported.

$^d$ Race is presented as a categorical variable, with a Chi-squared $P$ value.

$^e$ 16% of patients had unknown Group B Streptococcus status.

During the first period, 3 cases of MRSA and 18 cases of MSSA postpartum breast abscess were identified. During the subsequent period, 27 MRSA cases and 6 MSSA cases were identified; MRSA cases during this period were predominantly due to USA 300-0114. Rates of MSSA infection remained constant during both periods; however, rates of MRSA infection increased over time. With cluster cases included, there was statistically significant increase in the proportion of MRSA abscesses over time ($P < .0001$); when cluster cases were excluded, a trend toward significance remained ($P = .07$). The epidemic curve is displayed in Figure 2.

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a postpartum nurse (P < .001). Having sore or cracked nipples identified by a nurse or lactation consultant was also significant in univariate analysis. We found a trend toward a higher rate of smoking among control subjects (P = .2) and a trend toward a difference in the racial background between case patients and control subjects that did not reach statistical significance (P = .19).

We found no association between SA postpartum breast abscess and mode of delivery, augmentation of labor, or use of oxytocin. Obesity was unrelated to SA breast abscess development. Similarly, there was no association between the use of intrapartum antibiotics and postpartum breast abscesses, regardless of antibiotic type. This lack of association remained when antibiotics used for surgical prophylaxis were excluded from the analysis. We did not find an association between GBS colonization and development of abscess, although 16% of patients in the case-control analysis had unknown GBS status.

Multivariable analysis confirmed 2 novel risk factors for the development of postpartum breast abscess: being a mother employed outside the home (odds ratio [OR], 2.74) and identification of maternal breastfeeding difficulties by a lactation consultant or a postpartum nurse (OR, 5.00) (Table 2). The Hosmer-Lemeshow statistic for goodness of model fit was 0.32. In our nested case-control study, neither maternal age at delivery nor primiparity was significant in the multivariable model. However, primiparity, increasing maternal age, and being a mother employed outside the home were all collinear terms, which may have reduced our power to find an effect on all 4 variables in the model.

Cohort Analysis
The multivariable case-cohort analysis confirmed 2 previously described maternal risk factors for abscess development: increasing maternal age (per year) (OR, 1.08) and being a first-time mother (OR, 2.63) (Table 3). The Hosmer-Lemeshow test for goodness of fit of this case-cohort model was 0.90. Being married (relative risk, 3.06) was significant in univariate analysis but did not meet entry criteria for our final model. We did not detect an association between race and breast abscess development; however, we had limited power because of the demographic characteristics at our center. The 2 variables found to be significant in the aforementioned multivariable nested case-control model were unable to be examined for the entire cohort of patients because of their lack of availability.

Among mothers ≥30 years of age and primiparous (2 risk factors), the absolute risk of SA postpartum breast abscess was 31 cases per 10 000 deliveries. Among mothers with 1 risk factor (≥30 years of age or primiparous), the risk was 11 cases per 10 000 deliveries, and among mothers with no risk factors (<30 years of age and multiparous), the risk was 5.9 cases per 10 000 deliveries.

Methicillin-Resistant Staphylococcus aureus Versus Methicillin-Susceptible Staphylococcus aureus Postpartum Breast Abscess Sub-analysis
Subanalysis comparing all patients with MRSA infection with those with MSSA infection over the entire study period found no risk factor differences between the 2 groups and no difference in time to development of breast abscess between patients who developed MRSA infection and those who developed MSSA infection. To ensure that risk factors for acquiring infection and time to development of infection did not differ during the outbreak, cluster cases were compared with noncluster cases, and no differences were identified.
DISCUSSION

SA is the predominant pathogen in postpartum breast abscesses, accounting for 32%–100% of all culture-confirmed cases [7–9, 11]. In our center, we found SA to be the etiologic agent in all culture-confirmed cases over a 7-year period. In recent years, MRSA has emerged as a significant cause of breast abscess, both in postpartum mothers and in the general population [7, 8, 15], and several cases of hospital-associated MRSA transmission associated with maternal breast abscess have been described [9, 16]. The rate of MRSA postpartum breast abscess at our center increased during the cluster of CA-MRSA infections and then decreased to a lower rate of 0.24 breast abscess cases per 10,000 deliveries after the hospital-associated cluster ended, but this new baseline rate was higher than rates before the appearance of MRSA infection in this population in 2006. Throughout the study period, the rate of MSSA breast abscess was 6–9 cases per 10,000 deliveries.

MRSA colonization rates of up to 3.5% have been reported among pregnant women [17, 18]. Andrews et al screened pregnant women for SA colonization at the time of routine GBS screening and found that MRSA isolates comprised 25% of all SA isolates in the obstetric population [18]. During the cluster and postcluster period, we found that <1% of pregnant women were colonized by MRSA at the time of admission (unpublished hospital surveillance data).

Because of the emergence of MRSA as a causative agent of breast abscess in this population (possibly resulting from the increase in CA-MRSA), failure of empirical β-lactam therapy for mastitis or early breast abscess should prompt consideration of treatment with an agent active against MRSA. In our center, both clindamycin and trimethoprim-sulfamethoxazole were reliable and potentially useful oral antibiotic agents [19]. Susceptibility profiles for CA-MRSA often vary by region, highlighting the importance of performing cultures for antimicrobial susceptibility testing in this population.

Risk factors for SA postpartum breast abscesses in multivariable analysis of our nested case-control study included identification of breastfeeding difficulties in hospital by a lactation consultant or postpartum nurse and being a mother employed outside the home; neither has been previously reported. Of interest, our nested case-control study did not find an association between the development of breast abscess and GBS status, despite previous reports of positive and negative association between GBS colonization and SA colonization [17, 18].

Multivariable analysis of our case-cohort study found that advancing maternal age and low parity were predictive of development of postpartum SA breast abscess; these findings are in accordance with some previous studies [10]. Our cohort analysis was limited, because several variables, including those found to be significant in the nested case-control study, were not available for examination in the full cohort analysis. We did not find an association between race and postpartum breast abscess development; however, we had limited power to detect an association because of the demographic characteristics at our center.

We examined the receipt of any antibiotic during labor or delivery and the receipt of antibiotics for reasons other than...
surgical prophylaxis and found no effect on the development of SA postpartum breast abscess. Our study agreed with prior studies that did not find an association among mode of delivery, induction of labor, and oxytocin use during delivery [7, 10]. In addition to examining variables associated with the mother, we also examined variables associated with the infant, including birth weight, neonatal bilirubin level, and neonatal intensive care unit admission; none was associated with maternal SA breast abscess.

Our study is unique because of its comparison of risk factors for MRSA and MSSA postpartum breast abscesses. We did not find any significant risk factor differences between the 2 types of infection; analysis comparing cluster cases with noncluster cases also failed to reveal any maternal variables that differed between these 2 groups. Our ability to detect differences, however, was limited by the relatively small sample size available for the subanalysis.

Although we had a large number of deliveries at our center, many of the obstetricians who deliver in our hospital have offices where outpatient care is provided in a nonhospital setting. There is a theoretical concern that some patients with breast abscess may have been referred elsewhere for evaluation and treatment. This is largely offset by the fact that 100% of our obstetricians provide inpatient maternity care exclusively at our center, and virtually all cases of breast abscess require radiologic evaluation and intervention. These obstetricians use our center for such procedures and for breast surgery consultation; therefore, we are confident that our search found the majority, if not all, postpartum breast abscess cases among women who delivered at our center during the study period.

The majority of cases of MRSA breast abscess occurred during a hospital-associated cluster, which may have biased some of our findings. However, it was reassuring that our analysis of maternal variables associated with the development of breast abscess did not change, regardless of the time during the study period. Not all variables available in the nested case-control study were available for analysis in the cohort study, which may have limited our ability to control for confounding and collinear variables in the larger population.

Our study included hospital-based risk factors only; thus, we were unable to determine whether community factors, such as having an older child in daycare, was associated with breast abscess development. However, because the majority of women who developed breast abscess (59.3%) and almost half of the women in our cohort (48.1%) were primiparous, having an older child in daycare is unlikely to be a major contributing factor.

Several variables significant in the univariate analysis (being a working mother, increasing maternal age, primiparity, and being married) were collinear. It is difficult to disentangle these variables, but being a mother employed outside the home was an independent risk factor for postpartum SA breast abscess with use of a stepwise logistic regression model. Furthermore, because of the timing of infection development, this variable seemed to be a biologically plausible risk factor, because the majority of the infections occurred at a time when maternity leave generally ends and mothers are returning to work. After return to work, we postulate that women are less likely to breastfeed or pump on a regular schedule and are less likely to empty their breasts fully. Incomplete milk drainage related to these activities may predispose to breast engorgement, which, in turn, may predispose them to breast abscess development. Because of the limitations of our database, we were unable to determine breastfeeding duration or whether breastfeeding continued through the time of the abscess; however, another contributing factor to abscess development may be that mothers tend to wean at the time when they are returning to work.

Risk factors found in our case-control analysis for the development of postpartum SA breast abscess include being a mother employed outside the home and having in-hospital breastfeeding difficulties. Our cohort analysis identified increasing maternal age and being a first-time mother as risk factors for later development of this infection. Although the risk of developing a postpartum abscess is highest among older women having their first baby, the absolute risk is small and should not outweigh the well-recognized benefits of breastfeeding.

Note

Potential conflicts of interest. H. S. G. has received research grant support from Cubist, GlaxoSmithKline, Merck, and Pfizer and has been a paid consultant for Rlb-X, SR One (independent venture capital unit of GlaxoSmithKline), and Biogen Idec. S. B. W. has received research grant support from Cubist, GlaxoSmithKline, and Pfizer. All other authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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