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Citation	Branch-Elliman, Westyn, Grace M. Lee, Toni H. Golen, Howard S. Gold, Linda M. Baldini, and Sharon B. Wright. 2013. "Health and Economic Burden of Post-Partum Staphylococcus aureus Breast Abscess." PLoS ONE 8 (9): e73155. doi:10.1371/journal.pone.0073155. http://dx.doi.org/10.1371/journal.pone.0073155.
Published Version	doi:10.1371/journal.pone.0073155
Accessed	April 17, 2018 4:39:25 PM EDT
Citable Link	http://nrs.harvard.edu/urn-3:HUL.InstRepos:11877018
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Health and Economic Burden of Post-Partum *Staphylococcus aureus* Breast Abscess

Westyn Branch-Elliman^{1,2}*, Grace M. Lee^{3,4}, Toni H. Golen⁵, Howard S. Gold^{1,2}, Linda M. Baldini², Sharon B. Wright^{1,2}

1 Division of Infectious Diseases, Beth Israel Deaconess Medical Center, Boston, Massachusetts, United States of America, 2 Division of Infection Control/Hospital Epidemiology. Silverman Institute for Health Care Quality and Safety, Beth Israel Deaconess Medical Center, Boston, Massachusetts, United States of America, 3 Department of Population Medicine, Center for Child Health Care Studies, Harvard Pilgrim Institute and Harvard Medical School, Boston, Massachusetts, United States of America, 4 Division of Pediatric Infectious Disease and Department of Laboratory Medicine, Boston Children's Hospital, Boston, Massachusetts, United States of America, 5 Department of Obstetrics and Gynecology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, United States of America,

Abstract

Objectives: To determine the health and economic burdens of post-partum Staphylococcus aureus breast abscess.

Study design: We conducted a matched cohort study (N = 216) in a population of pregnant women (N = 32,770) who delivered at our center during the study period from 10/1/03 - 9/30/10. Data were extracted from hospital databases, or via chart review if unavailable electronically. We compared cases of *S. aureus* breast abscess to controls matched by delivery date to compare health services utilization and mean attributable medical costs in 2012 United States dollars using Medicare and hospital-based estimates. We also evaluated whether resource utilization and health care costs differed between cases with methicillin-resistant and -susceptible *S. aureus* isolates.

Results: Fifty-four cases of culture-confirmed post-partum *S. aureus* breast abscess were identified. Breastfeeding cessation (41%), milk fistula (11.1%) and hospital readmission (50%) occurred frequently among case patients. Breast abscess case patients had high rates of health services utilization compared to controls, including high rates of imaging and drainage procedures. The mean attributable cost of post-partum *S. aureus* breast abscess ranged from \$2,340–\$4,012, depending on the methods and data sources used. Mean attributable costs were not significantly higher among methicillin-resistant vs. – susceptible *S. aureus* cases.

Conclusions: Post-partum *S. aureus* breast abscess is associated with worse health and economic outcomes for women and their infants, including high rates of breastfeeding cessation. Future study is needed to determine the optimal treatment and prevention of these infections.

Citation: Branch-Elliman W, Lee GM, Golen TH, Gold HS, Baldini LM, et al. (2013) Health and Economic Burden of Post-Partum Staphylococcus aureus Breast Abscess. PLoS ONE 8(9): e73155. doi:10.1371/journal.pone.0073155

Editor: Vishnu Chaturvedi, California Department of Public Health, United States of America

Received March 14, 2013; Accepted July 17, 2013; Published September 5, 2013

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Funding: This work was conducted with support from Harvard Catalyst | The Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award #UL1 RR 025758 and financial contributions from Harvard University and its affiliated academic health care centers). The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic health care centers, or the National Institutes of Health. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have the following interests: Howard Gold, one of the study's authors, has a sibling who is employed as an executive at Merck, but does not work with antimicrobial drugs. This does not alter the authors' adherence to all the PLOS ONE policies on sharing data and materials.

* E-mail: wbranche@bidmc.harvard.edu

Introduction

Mastitis, most often caused by *Staphylococcus aureus* [1,2,3], occurs in approximately 20% of breastfeeding mothers and may be a precursor to the development of breast abscess [4,5,6,7]. *S. aureus* is also the predominant pathogen in post-partum breast abscess [8,9,10], and rates of methicillin-resistant *S. aureus* (MRSA) have increased in the pregnant and post-partum population [10,11,12].

Although breast abscess is a serious, uncommon complication of mastitis with high morbidity [13,14], health services utilized by patients with these infections have been poorly characterized. Neither the clinical outcomes, such as milk fistula formation and rates of breastfeeding cessation, nor the attributable medical costs of these infections are known. Further, it is unknown if the

emergence of MRSA has worsened outcomes and increased health services utilization and medical cost.

The aims of this study were to: (1) characterize the health and economic outcomes of patients with post-partum *S. aureus* breast abscess, such as breastfeeding cessation, development of milk fistulae, rates of adverse reactions to antibiotics, rates of health service utilization and medical costs and (2) explore whether costs are higher for MRSA vs. methicillin-susceptible *S. aureus* (MSSA) infections.

Methods

Setting

We conducted a population-based matched cohort study among post-partum women who delivered at Beth Israel Deaconess Medical Center (BIDMC), an academic tertiary care center with approximately 4,750 deliveries per year, between 10/1/2003–8/31/2010. From 10/2008–3/2010, a cluster of pulse-field type USA300–0114 MRSA infections in post-partum women and their infants who delivered at our center were identified; the majority of infections in mothers were mastitis and breast abscesses [10,15,16]. Cluster cases were defined as onset of MRSA post-partum breast abscess within one year after delivery.

Case and Control Selection

Cases were defined as any woman with a culture-confirmed *S. aureus* breast abscess within one year after delivery identified via needle drainage, incision and drainage, operative intervention, or spontaneous drainage. Women with uncomplicated infectious mastitis as well as a prior history of any *S. aureus* infection were excluded from the case definition.

We selected population-based controls of pregnant women who delivered at our center (N = 32,770). Exclusion criteria for control selection included pre-partum breast abscess, neonatal demise within 24 hours of delivery, stillbirth, and culture-confirmed *S. aureus* infection at another body site. Controls were matched to cases in a 3:1 fashion by delivery date to minimize potential bias due to secular trends in diagnosis or management of breast abscesses. Controls with a history of any prior *S. aureus* infection were excluded from the case-control analysis.

Data Collection

Hospital databases (Infection Control, Microbiology, Obstetrics, Admission Discharge Transfer, Fiscal databases) were used to extract data for the full population-based cohort, including inpatient admissions, laboratory tests, and radiologic studies. If hospital cost data were not available, we estimated components of medical costs using the Medicare Fee schedule [17,18].

Additional variables not available electronically were abstracted via medical record review for matched cohort study patients for up to one year after delivery or at the first visit for a subsequent pregnancy, whichever came first. Information was collected on follow-up outpatient visits to obstetrics and gynecology, internal medicine, dermatology, infectious diseases and allergy. Additional information was also collected about relevant radiographic studies (breast ultrasounds, mammograms, and breast magnetic resonance imaging), laboratory testing (complete blood counts (CBC), chemistries, wound and blood cultures), pathology (breast biopsy), central venous catheter placement, and antibiotic use and type, including use of outpatient intravenous antibiotics.

Overall hospital readmission rates were collected for the entire birth cohort. Associated adverse outcomes were extracted via chart review for matched cohort study patients only (breastfeeding cessation, milk fistula formation, and adverse effects of antibiotic use (rash, allergy)).

Data Analysis

Health outcomes, health services utilization, and medical costs were evaluated for both the full cohort and the matched cohort. Descriptive analyses were performed using proportions, means, and medians. We compared rates of outcomes, health service utilization and costs using Wilcoxon rank-sum or Chi-squared tests as appropriate.

To maximize accuracy and generalizability, the attributable medical cost of post-partum *S. aureus* breast abscess was estimated in three ways (Table 1). First, total direct medical costs for cases and non-cases in the overall cohort were estimated from hospital fiscal databases with attributable medical costs calculated as the difference between cases and non-cases and averaged across the

entire cohort. A second approach was based on estimating the difference in direct medical costs, based on hospital fiscal databases, only for those services potentially associated with *S. aureus* breast abscess (i.e., readmission, outpatient visits, laboratory testing, and radiology) for cases and non-cases in the overall cohort. Indirect medical costs, such as facility costs including overhead costs and equipment costs, were not available for analysis.

Finally, a third approach to estimating attributable total medical costs in the matched cohort study used national estimates of costs for each unit of health service utilization. The attributable costs were then calculated using the difference in the costs for cases versus controls, averaged across the matched cohort population. More specifically, each unit of service (e.g., hospitalization, procedures, laboratory and radiographic testing, outpatient visits) was multiplied by the cost of the unit of service based on the Medicare Fee Schedule and the Physician Fee Schedule [17,18]. Laboratory costs were based on maximum Centers for Medicare and Medicaid Services reimbursement rates. Medication costs were estimated using the average wholesale price from the pharmacy Red Book [19] multiplied by the number of pills required to complete a standard antibiotic course.

Medical costs were adjusted to 2012 dollars using the medical aspect of the gross domestic product deflator, available from the United States Bureau of Labor Statistics [20]. Attributable cost was calculated by determining the mean medical cost of cases and subtracting the mean medical cost of control patients.

Pre-specified sub-analysis. We compared health services utilization and medical costs in case patients with MSSA to case patients with MRSA using descriptive statistics, as outlined above. A p-value of <0.05 was considered statistically significant. Data were analyzed using SAS version 9.3 (SAS Institute, Cary NC).

Ethical Considerations

Institutional Review Board approval from BIDMC was obtained prior to data collection and analysis. Due to the retrospective study design, and acquisition of data through medical record review, waiver of informed consent was granted.

Results

Study Population

A total of 32,770 women delivered at our center during the study period. The mean maternal age among all women delivering at our center was 32.4 years, and 48.1% were primiparous. Baseline demographic description of the entire cohort including the 54 cases and 162 matched controls as well as the epidemic curve were previously published [10]. The cases included were 30 patients with MRSA abscess and 24 with MSSA breast abscess. The median time to diagnosis of *S. aureus* breast abscess after postpartum discharge was 34 days (Interquartile range (IQR), 24–49 days). There was no effect of MRSA or cluster period on time to clinical diagnosis.

During the cluster period (10/2008–3/2010), a total of 31 patients were diagnosed with culture-confirmed *S. aureus* breast abscess; 6 with MSSA infection and 25 with MRSA infection. The predominant MRSA strain found during the cluster period was pulsed-field type USA 300–0114 (data not shown) [15,16].

Of the full cohort of 32,770 deliveries, 98.2% (32,188/32,770) returned to our center for any type of care during the one-year period following delivery. Among patients enrolled in the matched cohort study, 98.6% (213/216) patients received care at our facility during the one-year period after delivery.

Table 1. Cost Estimate Methodologies.

	Total Hospital Direct Cost	Partial Hospital Direct Cost	Medicare Cost Estimate
Time period	One year	One year	One year
Basis for estimate	Hospital fiscal database	Hospital fiscal database	HSU x Cost per service ¹
Inpatient direct medical costs included ²	All	Potentially relevant	Disease-attributable
Inpatient indirect medical costs included ³	No	No	Yes
Outpatient costs included ⁴	All	Potentially relevant	Disease-attributable
Outpatient indirect medical costs included	No	No	Yes
Medication costs included	Some	Some	All

¹HSU = Health services utilization. Cost per service based on Medicare Fee Schedules.

²Direct medical costs include those directly related to services provided, such as inpatient stay, outpatient office visits, laboratory and radiographic testing.

³Indirect medical costs include facility operating costs, such as building costs, electricity costs, and costs of equipment.

⁴"All" indicates that all direct medical costs, including those that may not be related to a diagnosis of post-partum breast abscess were included in the estimate of cost. "Potentially relevant" indicates that only direct medical costs related to potentially relevant services (such as visits to internal medicine, obstetrics, infectious diseases, and radiology) were included in the estimate of cost. "Disease-attributable" indicates that only services attributable to the diagnosis of post-partum breast abscess were included in the estimate of cost.

doi:10.1371/journal.pone.0073155.t001

Outcomes

Matched cohort study. The readmission rate among case patients was 50%, compared to less than 2% among control patients (Table 2). The overall rate of breastfeeding cessation among breast abscess cases was 41%, and did not differ between MRSA and MSSA infections (Table 3). Data regarding breast-feeding cessation was unavailable for control patients.

Among all breast abscess cases, six patients developed milk fistulae. The rate of breastfeeding cessation among milk fistula cases was high (66.7%) but not significantly different from all other breast abscess cases.

Health Services Utilization

Full cohort. The overall rate of readmission among patients in the full cohort who returned to our center (N = 32,188) was 3.2%, and in cases (N = 54), 50% (p<0.0001).

Matched cohort study. Cases in the matched cohort study had significantly higher rates of physician visits, radiology utilization and antibiotic utilization than controls without postpartum breast abscess (Table 2). Across all cases, the median number of ultrasounds per patient was 3.5, range 0–17. Forty-one percent of cases (22/54) had greater than or equal to five breast ultrasounds. For controls, the median number of breast ultrasounds was zero. The rate of mammography was similar in case and control patients. No patients in the matched cohort study received breast magnetic resonance imaging.

The majority (75.9%) of the 54 breast abscess cases were treated with needle-guided drainage [21,22,23]. The median number of drainage procedures was two (interquartile range, 1.0–4.0), with a maximum of 15 drainage procedures in one patient. Thirteen (24%) required greater than or equal to five drainage procedures. Six (11%) had surgical incision and drainage; one occurred in the operating room. 14.8% of case patients (8/54) had spontaneous abscess drainage.

Antibiotic utilization was available for 92.5% (50/54) case patients. Ninety-eight percent (49/50) of case patients received antimicrobial therapy. In total, 16 different types of antibiotics were prescribed, including two (doxycycline, linezolid) that have

 Table 2. Health Services Utilization and Clinical Outcomes Among Women During the Year After Post-Partum Discharge: Matched

 Cohort Study Results.

	Breast Abscess Cases (N = 54)	<i>Controls (N = 162)</i>	P-value ¹
Outcomes			
Readmission Rate	50%	1.9%	< 0.0001
Resource Utilization			
Total Number of Drainage Procedures (Median, IQR)	2 (1–4)	0 (0–0)	< 0.0001
Antibiotic Utilization ²	86.0%	5.6%	< 0.0001
Breast Surgery Consultation	53.7%	0.6%	< 0.0001
Infectious Diseases Consultation	35.2%	0.6%	< 0.0001
Readmission Length of Stay (Median, IQR)	1 (0–5.5)	0 (0–0)	< 0.0001
Number of Breast Ultrasounds (Median, IQR)	3.5 (2–6)	0 (0–0)	< 0.0001
Outpatient Office Visits ³ (Median, IQR)	5 (2–7)	0 (0–0)	< 0.0001

¹Wilcoxon rank-sum test, Fisher's exact test or Chi square test used as appropriate.

²During the one-year period following post-partum discharge. Includes oral and intravenous antibiotics.

³Includes relevant office visits to obstetrics and gynecology (excluding routine post-partum care, preventive care, and visits for contraception), infectious diseases, breast surgery, internal medicine, and dermatology. No patients in the matched cohort study had allergy/immunology outpatient visits.

doi:10.1371/iournal.pone.0073155.t002

unsafe or unknown safety profiles in breastfeeding women [24,25]. Trimethoprim-sulfamethoxazole was prescribed frequently during the cluster period with a high rate of MRSA infections. 79.5% (39/49) patients were initially treated with a beta-lactam antibiotic, including 60% (18/30) patients ultimately diagnosed with MRSA infection.

Among the six patients who developed milk fistulae, there was a significantly higher rate of breast surgery consultations (6/6, 100% versus 23/48, 47.9%, p = 0.025), number of outpatient physician visits [median 8.5 (IQR, 6.0–15.0) versus median 4.0 (IQR, 2.0–7.0), p = 0.016], and outpatient parenteral antibiotic utilization (2/6, 33.3% versus 1/48, 2.1%, p = 0.030). There was a trend toward increased rates of surgical incision and drainage procedures (33% versus 9.3%, p = 0.089), number of breast ultrasounds [median 4.5 (IQR, 3.0–7.0) versus 3.0 (IQR, 1.5–6.0), p = 0.29], and number of antibiotics prescribed (3.2 versus 2.4, p = 0.080) among case patients who developed milk fistulae and those who did not.

Costs

For the entire cohort, the mean attributable cost based on total direct medical cost was \$2,414 (95% CI, \$1,458–\$3,370) and \$2,340 (95% CI, \$2027–\$2610) based on only including potentially relevant services (Table 4).

In the matched cohort study, the attributable cost estimate for the matched cohort study ranged from a minimum in the partial direct facility costs of \$2386 (95% CI, \$2,027–\$2,745) to a maximum estimate based on Medicare cost of \$4,012 (95% CI, \$3,443–\$4,581) (Table 4).

MRSA vs. MSSA Cases

Outcomes. Approximately 11% (6/54) of post-partum breast abscess cases developed milk fistulae; five patients with MRSA (17%) and one patient with MSSA (4%). In total, 5/54 patients (9.3%) of patients had allergic reactions to antibiotic therapy. All allergic reactions occurred in patients with MRSA infection (5/30, 16.7%) versus MSSA infection (0/24, 0%), however, this difference did not reach statistical significance (p = 0.06) (Table 3). Allergic reactions to antibiotic therapy were primarily due to the use of trimethoprim-sulfamethoxazole and vancomycin in patients with MRSA.

Health services utilization. Health services utilization was similar among case patients with MRSA and MSSA breast abscesses (Table 3); however, MRSA cases had significantly more outpatient visits (median 6.0 versus 3.0) and a higher proportion of infectious diseases consultations (57% versus 8.3%, p<0.0001). There were no significant differences in readmission rates or duration of readmissions between MRSA and MSSA cases. Among MRSA cases, there was a trend toward a higher rate of outpatient parenteral antibiotic therapy (10% versus 0%) and number of different antibiotics prescribed (2.6 versus 2.1); however, these differences were not statistically significant.

Costs. Despite an increase in both physician visits and antimicrobial usage, there was no significant cost difference between patients with MRSA infection and those with MSSA infection, or between patients who had milk fistulae compared to those who did not (Table 5). Attributable costs were similar regardless of methodology used.

Discussion

Our study is the first to comprehensively evaluate the outcomes and health and economic burdens of post-partum *S. aureus* breast abscess. In general, we found that the consequences of this infection in a generally healthy population are substantial. According to ambulatory medical records, many women who developed post-partum breast abscess chose to stop breastfeeding due to their infection (41%). In addition, a high proportion of patients with post-partum *S. aureus* breast abscess required inpatient readmission (50%) and treatment with intravenous antibiotics. Patients with MRSA breast abscess showed a trend towards increased allergic reactions to antibiotic therapy due to the prevalent use in this group of trimethoprim-sulfamethoxazole and vancomycin, drugs that have been associated with among the highest estimated number of emergency department visits per 10,000 outpatient prescriptions [26]. Notably, in the same study sulfonamide use was associated with a significantly higher rate of moderate-to-severe allergic reactions, compared with all other antibiotic classes combined (4.3% [95% CI, 2.9%–5.8%] vs. 1.9% [95% CI, 1.5%–2.3%]) [26].

In the BIDMC cohort, the majority of patients received ultrasound-guided drainage for definitive management of their infection rather than open drainage. Multiple previous studies have demonstrated the safety and efficacy of ultrasound-guided needle drainage in the management of breast abscess [21,22,27,28,29], and that MRSA infections can be successfully treated with needle drainage [14]. Few patients (6/45) in our study required surgical incision and drainage for management, and only one required incision and drainage in the operating room, which is similar to rates in previous studies [23,30]. A significant proportion of patients in our study required five or more drainage procedures, and some up to 17 prior to resolution, which is higher than has been found in other studies [23,30,31]. There was no association between MRSA infection and requirement for additional drainage procedures, which is consistent with findings in other investigations [14].

We found no association between surgical incision and milk fistula formation. In fact, five of the six patients who developed milk fistulae underwent ultrasound-guided needle aspiration of their abscesses only; prior work has demonstrated that milk fistulae occur rarely in this setting [29,32,33].

The attributable medical cost of post-partum *S. aureus* breast abscess was high, and in the same range as other post-partum infections, including surgical site infection after Cesarean delivery (\$3761, 95% CI, \$3309–\$4275) and post-partum endometritis (\$4216, 95% CI, \$3710–\$4792). Medical costs were also similar to surgical site infections following breast surgery (\$4967, 95% CI, \$3447–\$6719), all adjusted to 2012 dollars [34,35].

To estimate medical cost, we utilized multiple methods, including an evaluation of total hospital direct cost, partial hospital direct cost, and a Medicare-based cost estimation to improve the accuracy and generalizability of our findings; all methods yielded similar results. The hospital-based estimates of cost may have been lower than the Medicare cost estimate because indirect hospital costs were not available for inclusion in the analysis (Table 1).

Interestingly, despite the fact that MRSA cases had significantly more outpatient visits and a higher proportion of infectious diseases consultations, as well as trends toward a higher rate of outpatient parenteral antibiotic therapy and allergic reactions to antibiotic treatment, we found no increase in cost associated with MRSA breast abscess when compared to MSSA infection, perhaps due to limited power to detect a difference between the two groups. Alternatively, outpatient management of these infections may have averted more costly readmissions or procedures [36]. MRSA patients and MSSA patients did not differ significantly in rates of readmission and readmission length of stay. Our results should be viewed in the context of published data on other types of *S. aureus* infections that have yielded inconsistent results as to the **Table 3.** Health Services Utilization and Clinical Outcomes: Comparing MRSA to MSSA Cases of Post-partum Staphylococcus aureus

 Breast Abscess During the Year after Post-Partum Discharge.

	MRSA (N = 30)	MSSA (N = 24)	P-value ¹
Outcomes			
Readmission Rate	46.7%	54.2%	0.78
Milk Fistula Formation	16.7%	4.2%	0.21
Breastfeeding Cessation ²	50%	29.2%	0.25
Allergic Reaction to Antibiotic ³	16.7%	0%	0.059
Resource Utilization			
Total Number of Drainage Procedures (Median, IQR)	2.0 (1.0–4.0)	1.0 (1.0–5.0)	0.87
Antibiotics Prescribed (Mean, 95% CI)	2.64 (2.20-3.08)	2.09 (1.71–2.48)	0.064
Breast Surgery Consultation	60%	45.8%	0.41
Infectious Diseases Consultation	56.7%	8.33%	<0.0001
Readmission Length of Stay, Days (Median, IQR)	0.0 (0.0–6.5)	2.5 (0.0-4.0)	0.49
Number of Breast Ultrasounds (Median, IQR)	4.5 (2.0–6.0)	3 (2.0–5.5)	0.35
Outpatient Office Visits (Median, IQR) ⁴	6.0 (4.0-8.5)	3.0 (1.0-6.0)	0.0019

¹Wilcoxon rank-sum test, Chi-square, or Fisher's Exact Test used as appropriate.

²Data missing for 5/54 patients.

³Includes only severe adverse allergic reactions, including hives and severe skin rash. Minor complications excluded.

⁴Includes relevant office visits to obstetrics and gynecology (excluding routine post-partum care, preventive care, and visits for contraception), infectious diseases, breast surgery, internal medicine, and dermatology. No patients in the matched cohort study received allergy and immunology outpatient visits.

doi:10.1371/journal.pone.0073155.t003

importance of methicillin-resistance in changing economic costs [37,38,39]; [40].

Limitations

All data were collected from a single large birth cohort at a tertiary academic referral center and thus included patients with the most severe complications of post-partum breast abscess, such as milk fistulae. Thus, our experiences and cost analysis may not be generalizable to all practices or settings. To improve the generalizability of our findings, we used multiple methods to estimate attributable medical costs, including an evaluation of total and partial direct hospital costs, as well as an analysis using Medicare estimates. Medicare costs are not directly applicable to a post-partum population; however, Medicare reimbursement has been used in many analyses of healthcare costs [17,18]. Although practices may have changed during the study period, all cases were matched to contemporary controls, which should control for changes in hospital practice.

The patients included in our study were all women of childbearing age, a traditionally young and healthy population. Our prior work demonstrated that the effect of maternal age on risk of post-partum breast abscess in the BIDMC cohort was very

Table 4. Healthcare Costs of Post-partum Staphylococcus aureus Breast Abscess Compared to Non-infected Controls.

	Cases	Controls	Difference	P-value
Total Hospital Direct Costs ¹ (Mean, 95% Cl)	\$2809 (2148–3470)	\$240 (150–330)	\$2569 (2162–2,976)	<0.0001
Partial Hospital Direct Costs ² (Mean, 95% CI)	\$2515 (1908–3122)	\$129 (73–185)	\$2,386 (2,027–2,745)	< 0.0001
Costs based on health service utilization ³ (Mean, 95% CI)	\$4073 (3097–5049)	\$61 (21–142)	\$4,012 (3,443–4,581)	<0.0001
Total Cohort (N = 32,188)				
	Cases	Controls	Difference	P-value
Total Hospital Direct Costs ¹ (Mean, 95% CI)	\$2809 (2148–3470)	\$395 (356–434)	\$2414 (1458–3370)	< 0.0001
Partial Hospital Direct Costs ² (Mean, 95% CI)	\$2515 (1908–3122)	\$175 (164–186)	\$2,340 (2,070–2,610)	<0.0001

¹Includes all direct healthcare costs based on hospital fiscal databases during the one-year period following post-partum discharge.

²Includes only potentially relevant healthcare costs based on hospital fiscal databases, such as inpatient readmission, relevant outpatient office visits, radiology, and laboratory costs.

³Estimated by multiplying the number of units of each relevant healthcare service by Medicare reimbursement for each service. doi:10.1371/journal.pone.0073155.t004

Table 5. Attributable Healthcare Costs of MRSA Cases Compared to MSSA Cases.

	MRSA (N = 30) v. MSSA (N = 24)	P-value
Total Hospital Direct Costs ¹ (Mean, 95% CI)	\$507 (-818, 1842)	0.45
Partial Hospital Direct Costs ² (Mean, 95% CI)	\$ 806 (-408, 2020)	0.19
Medicare Estimate of Costs ³ (Mean, 95% Cl)	\$-148 (-212, 1812)	0.88

¹Includes all direct healthcare costs during the one-year period following post-partum discharge.

²Includes only potentially relevant healthcare costs, such as inpatient readmission, relevant outpatient office visits, radiology, and laboratory costs.

³Estimated by multiplying the number of units of each relevant healthcare service by the Medicare reimbursement level for that service.

doi:10.1371/journal.pone.0073155.t005

small (OR 1.08 per year), therefore, we did not control for age as a potential confounder in medical cost in this generally young and healthy population [10].

During our study period, there was a large cluster of healthcareassociated, community-onset infections with MRSA USA300-0114. As there was no significant difference in overall health services utilization or medical cost between MRSA and MSSA cases, this likely did not affect our overall findings. However, our results may not be reflective of all MRSA infections, but USA300-0114 MRSA infections in particular.

Additionally, although 98.2% of the patients evaluated in our study followed up at our center, we did not have complete follow up data on the entire cohort. It is therefore possible that some health services utilization and costs were not included. Further, in our evaluation of total and partial direct costs, we only included patients with follow up at our center.

Conclusions

Post-partum S. aureus breast abscess frequently led to breastfeeding cessation and was associated with additional poor patient

References

- Cardoso Del Monte MC, Pinto Neto AM (2010) Postdischarge surveillance following cesarean section: the incidence of surgical site infection and associated factors. Am J Infect Control 38: 467–472.
- Maraqa NF, Aigbivbalu L, Masnita-Iusan C, Wludyka P, Shareef Z, et al. (2011) Prevalence of and risk factors for methicillin-resistant *Staphylococcus aureus* colonization and infection among infants at a level III neonatal intensive care unit. Am J Infect Control 39: 35–41.
- Moir-Bussy BR, Hutton RM, Thompson JR (1984) Wound infection after caesarean section. J Hosp Infect 5: 359–370.
- Amir LH, Forster DA, Lumley J, McLachlan H (2007) A descriptive study of mastitis in Australian breastfeeding women: incidence and determinants. BMC Public Health 7: 62.
- Scott JA, Robertson M, Fitzpatrick J, Knight C, Mulholland S (2008) Occurrence of lactational mastitis and medical management: a prospective cohort study in Glasgow. Int Breastfeed J 3: 21.
- Kinlay JR, O'Connell DL, Kinlay S (1998) Incidence of mastitis in breastfeeding women during the six months after delivery: a prospective cohort study. Med J Aust 169: 310–312.
- Vogel A, Hutchison BL, Mitchell EA (1999) Mastitis in the first year postpartum. Birth 26: 218–225.
- Moazzez A, Kelso RL, Towfigh S, Sohn H, Berne TV, et al. (2007) Breast abscess bacteriologic features in the era of community-acquired methicillinresistant *Staphylococcus aureus* epidemics. Arch Surg 142: 881–884.
- Stafford I, Hernandez J, Laibl V, Sheffield J, Roberts S, et al. (2008) Community-acquired methicillin-resistant *Staphylococcus aureus* among patients with puerperal mastitis requiring hospitalization. Obstet Gynecol 112: 533–537.
- Branch-Elliman W, Golen TH, Gold HS, Yassa DS, Baldini LM, et al. (2012) Risk factors for *Staphylococcus aureus* postpartum breast abscess. Clin Infect Dis 54: 71–77.
- Reddy P, Qi C, Zembower T, Noskin GA, Bolon M (2007) Postpartum mastitis and community-acquired methicillin-resistant *Staphylococcus aureus*. Emerg Infect Dis 13: 298–301.
- Berens P, Swaim L, Peterson B (2010) Incidence of methicillin-resistant Staphylococcus aureus in postpartum breast abscesses. Breastfeed Med 5: 113–115.

outcomes, high health services utilization, and significant attributable medical costs; the economic burden was similar for MRSA and MSSA infections.

Prevention efforts should be focused on prevention of all types of *S. aureus* breast abscess – not just MRSA. Further investigation is warranted to determine the optimal means of preventing *S. aureus* breast infections during the post-partum period.

Acknowledgments

We would like to thank Jane J. Kim, PhD at the Harvard School of Public Health and Eli Perencevich, MD, MS from the University of Iowa for the expert guidance they provided in designing the economic costing portion of our analysis. We would also like to thank Elizabeth Wood and George Silva, both from the Division of Decision Support at Beth Israel Deaconess Medical Center for their assistance in obtaining cost data.

Author Contributions

Conceived and designed the experiments: WBE GML THG HSG LMB SBW. Analyzed the data: WBE GML SBW. Wrote the paper: WBE GML THG HSG LMB SBW.

- Chuwa EW, Wong CM, Tan YY, Hong GS (2009) MRSA breast abscesses in postpartum women. Asian J Surg 32: 55–58.
- Chen CY, Anderson BO, Lo SS, Lin CH, Chen HM (2010) Methicillin-resistant Staphylococcus aureus infections may not impede the success of ultrasound-guided drainage of puerperal breast abscesses. J Am Coll Surg 210: 148–154.
- Yassa D, Pillai S, Gold HS, Venkataraman L, Golen TH, et al. (2010) Mupriocin-Resistant Methicillin-Resistant *Staphylococcus aureus* in Mothers and Newborns; 2010 March 20, 2010.
- Wise ME, Lamb M, Marston H, Yassa D, Baldini L, et al. (2010) Outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) USA300 skin and soft tissue infections among well newborns and post-partum women; 2010 March 20, 2010.
- (2011) Medicare and Medicaid programs: hospital outpatient prospective payment; ambulatory surgical center payment; hospital value-based purchasing program; physician self-referral; and patient notification requirements in provider agreements. Final rule with comment period. Fed Regist 76: 74122– 74584.
- (2011) Medicare program; hospital inpatient prospective payment systems for acute care hospitals and the long-term care hospital prospective payment system and FY 2012 rates; hospitals' FTE resident caps for graduate medical education payment. Final rules. Fed Regist 76: 51476–51846.
- Thomson Healthcare (Firm) (2004) Red book. Montvale, NJ: Thomson PDR. pp. v.
- Statistics USDoL (2012). US Department of Labor Statistics Consumer Price Index.
- Karstrup S, Solvig J, Nolsoe CP, Nilsson P, Khattar S, et al. (1993) Acute puerperal breast abscesses: US-guided drainage. Radiology 188: 807–809.
- Schwarz RJ, Shrestha R (2001) Needle aspiration of breast abscesses. Am J Surg 182: 117–119.
- Eryilmaz R, Sahin M, Hakan Tekelioglu M, Daldal E (2005) Management of lactational breast abscesses. Breast 14: 375–379.
- Mitrano JA, Spooner LM, Belliveau P (2009) Excretion of antimicrobials used to treat methicillin-resistant *Staphylococcus aureus* infections during lactation: safety in breastfeeding infants. Pharmacotherapy 29: 1103–1109.

- Nahum GG, Uhl K, Kennedy DL (2006) Antibiotic use in pregnancy and lactation: what is and is not known about teratogenic and toxic risks. Obstet Gynecol 107: 1120–1138.
- Shehab N, Patel PR, Srinivasan A, Budnitz DS (2008) Emergency department visits for antibiotic-associated adverse events. Clin Infect Dis 47: 735–743.
- Christensen AF, Al-Suliman N, Nielsen KR, Vejborg I, Severinsen N, et al. (2005) Ultrasound-guided drainage of breast abscesses: results in 151 patients. Br J Radiol 78: 186–188.
- Berna-Serna JD, Madrigal M (2004) Percutaneous management of breast abscesses. An experience of 39 cases. Ultrasound Med Biol 30: 1–6.
- Ozseker B, Ozcan UA, Rasa K, Cizmeli OM (2008) Treatment of breast abscesses with ultrasound-guided aspiration and irrigation in the emergency setting. Emerg Radiol 15: 105–108.
- Elagili F, Abdullah N, Fong L, Pei T (2007) Aspiration of breast abscess under ultrasound guidance: outcome obtained and factors affecting success. Asian J Surg 30: 40–44.
- Leborgne F (2003) Treatment of breast abscesses with sonographically guided aspiration, irrigation, and instillation of antibiotics. AJR Am J Roentgenol 181: 1089–1091.
- Barker P (1988) Milk fistula: an unusual complication of breast biopsy. J R Coll Surg Edinb 33: 106.
- Schackmuth EM, Harlow CL, Norton LW (1993) Milk fistula: a complication after core breast biopsy. AJR Am J Roentgenol 161: 961–962.

- Olsen MA, Butler AM, Willers DM, Gross GA, Fraser VJ (2010) Comparison of costs of surgical site infection and endometritis after cesarean delivery using claims and medical record data. Infect Control Hosp Epidemiol 31: 872–875.
- Olsen MA, Chu-Ongsakul S, Brandt KE, Dietz JR, Mayfield J, et al. (2008) Hospital-associated costs due to surgical site infection after breast surgery. Arch Surg 143: 53–60; discussion 61.
- Eisenberg JM, Kitz DS (1986) Savings from outpatient antibiotic therapy for osteomyelitis. Economic analysis of a therapeutic strategy. JAMA 255: 1584– 1588.
- Abramson MA, Sexton DJ (1999) Nosocomial methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* primary bacteremia: at what costs? Infect Control Hosp Epidemiol 20: 408–411.
- Anderson DJ, Kaye KS, Chen LF, Schmader KE, Choi Y, et al. (2009) Clinical and financial outcomes due to methicillin resistant *Staphylococcus aureus* surgical site infection: a multi-center matched outcomes study. PLoS One 4: e8305.
- Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, et al. (2005) The impact of methicillin resistance in *Staphylococcus aureus* bacteremia on patient outcomes: mortality, length of stay, and hospital charges. Infect Control Hosp Epidemiol 26: 166–174.
- 40. Ben-David D, Novikov I, Mermel LA (2009) Are there differences in hospital cost between patients with nosocomial methicillin-resistant *Staphylococcus aureus* bloodstream infection and those with methicillin-susceptible *S. aureus* bloodstream infection? Infect Control Hosp Epidemiol 30: 453–460.