Implant-based Breast Reconstruction Infections: The Importance of Recognizing Local Pathogens

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ABSTRACT **Background:** Implant-based breast reconstruction (IBR) is the most common method of reconstruction for breast cancer. Bacterial infection is a well-known risk with reported rates ranging from 1% to 43%. The most common pathogens of breast implant infection described in the literature are *Staphylococcus aureus, Staphylococcus epidermidis*, and coagulase-negative staphylococci. However, the prevalence of other pathogens and their antibiotic sensitivity profile differs profoundly in different parts of the world.

Objectives: To review the current literature and protocols with respect to our region and to determine a more accurate antibiotic protocol aimed at our specific local pathogens.

Methods: A retrospective review was conducted of all cases of clinically infected implant-based breast reconstruction in our institution from June 2013 to June 2019, as well as review of microbiologic data from around the world based on current literature.

Results: A total of 28 patients representing 28 clinically infected implant-based breast reconstruction were identified during the studied period. Thirteen patients (46.4%) had a positive bacterial culture growth, with *P. aeruginosa* being the most common microorganism identified (46.1%). Review of international microbiological data demonstrated significant variation at different places and time periods.

Conclusions: Microbiological data in cases of infected breast reconstructions should be collected and analyzed in every medical center and updated every few years due to the variations observed. These data will help to adjust the optimal empirical antibiotic regimens given to patients presenting with infections after breast reconstruction.

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Implant-based breast reconstruction (IBR) is the most common method of reconstruction for breast cancer. According to the American Society of Plastic Surgeons statistics, 101,657 breast reconstructions were performed in the United States in 2018, of which 69,921 involved using an expander or an implant [1].

Bacterial infection is a well-known and dreaded complication of implant-based breast reconstruction because it increases patient morbidity and readmissions, may delay oncologic treatment, and increases the risk of reconstructive failure [2]. Reported infection rates following IBR vary among studies, ranging from 1% to 43% [4,5]. The onset of infections can occur early in the postoperative period and as late as months or even years later, with variable clinical presentation [6]. Breast implant infection may present as a wound site purulent discharge, cellulitis, or an indolent isolated redness and swelling. Late infections can even be more subtle and present with vague breast pain or swelling.

The initial step in managing such infections is often starting empiric antibiotic therapy. The U.S. Centers for Disease Control and Prevention (CDC) recommends a first-generation cephalosporin for perioperative prophylaxis. However, no guidelines exist for the empiric treatment of established breast implant infections. The optimal duration of antibiotic prophylaxis is also debated [7].

The most commonly isolated pathogens of breast implant infection are *Staphylococcus aureus*, *Staphylococcus epidermidis*, and coagulase-negative staphylococci [6]. However, the prevalence of other pathogens and their antibiotic sensitivity profile differs profoundly in different parts of the world [8]. Moreover, new and resistant forms of bacteria are rising throughout different areas due to the vast and prolonged use of antibiotics. Early and accurate identification of bacteria is a critical requirement for prompt and appropriate antimicrobial treatment. In practice, microbiological data gathering might be prolonged and frequently yields negative results. In the absence of patient-specific culture data, antibiotic selection is generally directed toward broad-spectrum coverage based on historical data from different parts of the world. Management strategies vary widely across centers, particularly with regard to the choice and duration of antimicrobial treatment and, in the case of failure, the explantation of the implant.

We hypothesized that reviewing our institution's microbiological data from infected implant-based breast reconstructions would provide a rational basis for antibiotic selection in the future, both for prophylaxis and empiric treatment in cases of infection.

We examined the current literature and protocols around the world with respect to our region to determine a more accurate antibiotic protocol aimed to target our specific local pathogens.

PATIENTS AND METHODS

A retrospective review of all medical records of implant-based breast reconstruction performed in our institution from June 2013 to June 2019 identified all patients who developed breast implant-related infection by identifying the appropriate diagnosis. Included were all the patients who fulfilled the definition of a deep surgical site infections (SSIs) involving an implant, as determined by the CDC. According to this definition, patients met at least one of the following criteria: purulent discharge, wound dehiscence or surgically opened incision with positive cultures or evidence of abscess, or diagnosis by the surgeon of a deep infection occurring up to 1 year postoperatively.

We collected data regarding patient demographics including age, co-morbidities, and previous radiotherapy, chemotherapy, and lymphadenectomy. We also reviewed surgical characteristics (i.e., type of operation and implant), timing of infection onset, clinical signs, and microbiological results. We followed the treatment strategy used for each case while identifying swab and tissue cultures and evaluated the final outcomes.

This study was approved by the institutional research ethics board. Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 20 (SPSS, IBM Corp, Armonk, NY, USA).

RESULTS

A total of 28 patients representing 28 clinically infected breasts were included in the study. The mean age was 47.86 years (range 40–80 years). Ten patients (35.71%) had undergone sentinel lymph node dissection and nine patients (32.14%) had undergone axillary lymph node dissection. Four patients (14.29%) were treated with a combination of chemotherapy and radiation while nine patients (32.14%) were treated with radiotherapy alone. Four patients (14.29%) were active smokers [Table 1].

The most common reconstruction method among these patients was direct-to-implant (DTI) reconstruction with an implant placed under the pectoralis major muscle and a TIGR® Matrix Surgical Mesh (Novus Scientific, Uppsala, Sweden) to cover the lower pole (n=7; 25.0%). A breast expander with a TIGR® mesh was used in two cases (7.14%). In total, TIGR® mesh was used in nine patients (32.14%). AlloDerm (LifeCell Corp., Branchburg, NJ, USA) was used in six patients (21.4%). Breast infection after reconstruction with a latissimus dorsi muscle flap and an underlying breast implant was noted in four cases (14.29%). Altogether, silicone implants were used in 20 patients (71.5%) and tissue expanders filled with saline in eight (28.6%) [Table 1].

All patients received perioperative antibiotic therapy. Eighteen (64.3%) patients were treated with amoxicillin/clavulanic acid, eight (28.6%) with a combination of amoxicillin/clavulanic acid and ciprofloxacin, and two (7.1%) with cefalexin. Twenty-four patients were treated until drain removal, whereas four patients received antibiotic therapy for a period of one week regardless of the drain status.

Seventeen patients (60.7%) presented with early infection within 6 weeks of the reconstruction, while 11 patients (39.3%) had a late infection more than 6 weeks after the reconstruction. Fourteen patients (50.0%) presented with an open wound. A representative case is presented in Figure 1. Ten patients (71.4%) had a positive microbiological culture. Four wound samples (28.6%) did not exhibit any growth. Drain cultures were retrieved from six patients of which three had a positive culture (50%) and the other three did not demonstrate any growth. In total, 13 patients (46.4%) had a positive bacterial culture growth either from an open wound or a drain sample. Among these 13 bacterial isolates involved in breast implant infection, the most common microorganism identified was *Pseudomonas aeruginosa* (n=6; 46.1%). The second most common pathogen was *S. aureus* identified in three cases (23%) followed by two isolates (15.4%) of *S. epidermis*. *Acinetobacter spp.* and *Enterococcus spp.* were identified in only one case each (7.7%) [Table 2].

Table 1. Patients and reconstruction characteristics

Variable	Number (%)
Number	28
Age in years, mean (range)	47.86 (40–80)
Active smoker	4 (14.29%)
Sentinel lymph node biopsy	10 (35.71%)
Axillary lymph node dissection	9 (32.14%)
Radiotherapy	13 (46.43%)
Tissue expander	8 (28.6%)
Silicone implant	20 (71.5%)
Implant coverage	
TIGR®	9 (32.14%)
AlloDerm	6 (21.4%)
Latissmus dorsi muscle flap	4 (14.29%)
Perioperative antibiotics	
Amoxicillin/clavulanic acid	18 (64.3%)
Amoxicillin/clavulanic acid + ciprofloxaxin	8 (28.6%)
Cefalexin	2 (7.1%)

Figure 1. A female patient who underwent left mastectomy and sentinel lymph node biopsy and immediate direct to implant breast reconstruction using a 700 cc round silicone implant, placed beneath the pectoralis major muscle and TIGR® mesh. After 23 days, due to necrotic tissue around the mastectomy scar, the patient underwent debridement of the necrotic tissue and primary closure. Dehiscence and signs of infection appeared after 7 days, requiring explantation of the implant and TIGR® mesh. Intraoperative culture was positive for Staphylococcus epidermis.

On detection of signs and symptoms of infection, empiric antibiotic therapy was initiated immediately. The main antimicrobial treatment was amoxicillin-calvulonic acid in combination with ciprofloxacin. This treatment regimen was used in 21 cases (75%) followed by cephalexin in 3 cases (10.7%). A combination of vancomycin with ciprofloxacin was used in two cases (7.1%) and cefazolin was also used in two cases (7.1%).

Twenty-three patients (82.1%) had undergone surgery for explantation of the implant. The decision to remove the implant was based on the surgeon's clinical judgment. Most implants were explanted due to a significant infection without improvement with antibiotic therapy, purulent discharge from the implant's pocket and inability to close the wound due to large necrotic area, or poor tissue quality.

In three cases (10.7%), salvage was successful with antimicrobial therapy alone. One patient (3.6%) had undergone a successful wound debridement with primary closure along with antimicrobial therapy and did not need further implant explantation. One patient (3.6%) was lost to follow-up after receiving antibiotic treatment.

All four implants who were salvaged (14.3%) were treated with a combination of amoxicillin-calvulonic acid and ciprofloxacin on detection of signs of infection. The mean duration of treatment was 4 weeks.

Bacterial culture samples were obtained intra operatively in all 24 patients (85.7%) who underwent surgery. Eighteen samples (64.3%) demonstrated a positive culture growth. Two cultures

Table 2. Characteristics of infection

Variable	Number, (%)
Infection timing	
Early (< 6 weeks)	17 (60.7%)
Late (> 6 weeks)	11 (39.3%)
Clinical signs of infection	25 (89.3%)
Clinical open wound	14 (50%)
Fever > 38°C	6 (21.4%)
Leukocytosis, >10.5 × 109/L	19 (67.9%)
Positive bacterial culture	13 (46.4%)
Pathogen Identified	
Pseudomonas aeruginosa	6 (46.1%)
Staphylococcus aureus	3 (23%)
Staphylococcus epidermis	2 (15.4%)
Acinetobacter spp.	1 (7.7%)
Enterococcus spp.	1 (7.7%)

(7.1%) were polymicrobial. Ten microbial cultures (35.7%) were sterile and did not demonstrate any microorganism at all. *P. Aeruginosa* was identified in 10 isolates (55.5%) making it the most prevalent pathogen. *S. aureus* was identified in three isolates (16.6%) followed by *S. epidermidis* grown on two isolates (11.1%). *Escherichia coli*, *Enterobacter spp*, *Acinetobacter*, and *Klebsiella spp* were all identified in one isolate each (5.5%). When comparing these results to the ones obtained from wound discharge or drain fluid cultures, we found that a wound culture had a predictive value of more than 70% for positive intraoperative sample culture.

DISCUSSION

Infection rates following breast reconstruction have been reported in up to 40% of cases [3] and have continued to complicate implant-based reconstruction to the point of reconstructive failure accompanied with psychological, social, and financial burden. It is essential to optimize the empiric antimicrobial regimen to try and salvage the implant.

Due to the presence of prosthetic devices and drains and the relatively high infection rate with possibly poor and unwanted outcomes, prophylactic antibiotics are administered by many surgeons. When prescribed, they are usually given for an extended duration and the choice of which drug is usually based on personal experience rather than data [9].

We investigated 28 cases of breast implant infection following breast reconstruction, representing 8.6% of all implant-based breast reconstructions performed in our institution during the study period of 5 years. This study is the first at our institution, and to the best of our knowledge in the country (Israel), to identify the most common microorganisms involved in breast implant infection following breast reconstruction. We believe that

by identifying and specifically targeting the most frequent local pathogens, we can better tailor our empiric antibacterial therapy.

In the past, common microorganisms isolated in cases of breast implant infections were mostly limited to skin flora (e.g., staphylococci species) while fewer studies reported infections caused by gram-negative bacilli [10-12]. Positive culture results were documented in 64.3% of the cases, and no bacterial growth was reported in the remaining 35.7%.

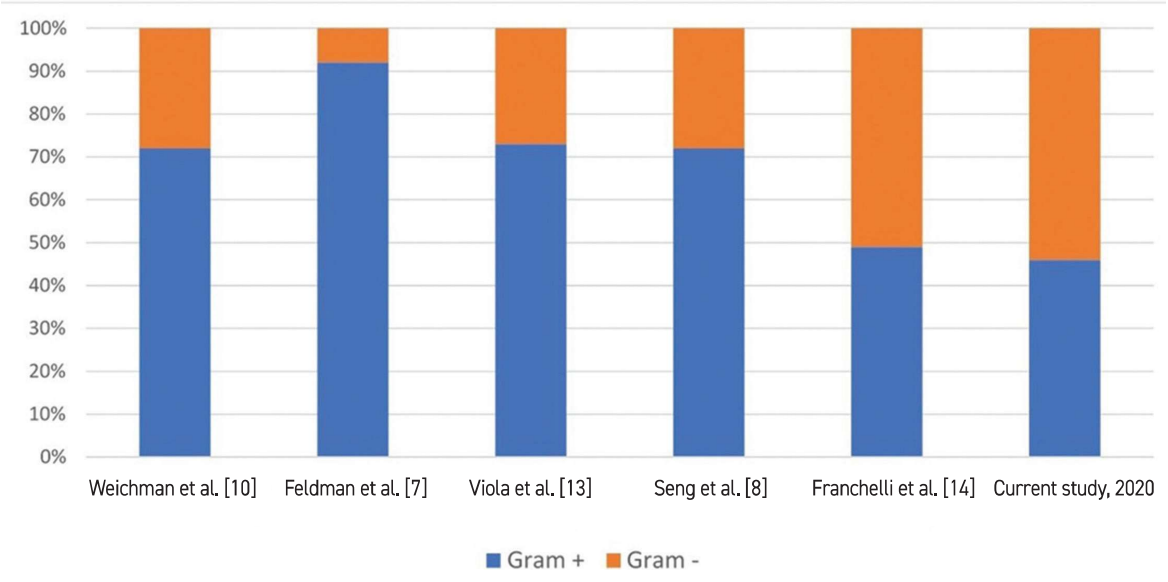
Among the culture positive cases, the most common pathogen isolated was *P. aeruginosa* (55.5%), which, much to our surprise, was more than three-fold the incidence of *S. aureus* isolation that came out as the second most frequent isolate followed by *S. epidermidis* and *E. coli* (another gram-negative bacteria). This finding contrasts many other studies where *S. aureus* was found to be the most frequent pathogen identified for breast implant infection with up to 67% rate and pseudomonas remains much far behind [7,8]. When reviewing similar research, we found that different geographic locations had their own distribution of different pathogens, which also shifted with time. For example, during the same period as our study, in a similar study from New York, gram-negative bacteria had represented 28% of breast implant infection cultures with pseudomonas representing only 9% [10]. In Houston, between 2001 and 2006, gram-negative isolates represented only 6% of all cultures while staphylococcal species represented 68% [7]. A few years later in Houston, there is a 280% increase in the rate of gram-negative cultures to 17% [13]. In Marseille, France, gram-negative isolates represented 28% of all cultures with pseudomonas isolated in 22%. Still, 63% of all positive cultures were staphylococcal species [8]. In Genova, another Mediterranean city gram-negative isolates led with 51% of all positive cultures. Pseudomonas represented in 25% while staphylococcal species represented in 49% [14] [Figure 2].

We think that any attempt at successful implant salvage requires broad spectrum gram-positive and gram-negative antibiotic coverage. Even for patients presenting with minor cellulitis, it is important to consider the likely possibility of gram-negative species serving as the causative organism. Failure to account for gram-negative species could have severe consequences for the patient and the reconstructive process; therefore, it is necessary to adapt an empiric antimicrobial treatment that includes the coverage of gram-negative bacteria, particularly pseudomonas, when signs and symptoms of breast infection arise.

In our review, cultures were negative in 35.7% of the cases. These findings are consistent with other studies reporting similar rates [12,15]. Reasons can be attributed to initiating antibiotics prior to obtaining cultures, presence of fastidious or slow-growing microorganism such as mycobacterium or mycoplasma, or the formation of biofilm on implant surface [16-19]. To minimize these sterile cultures and improve yield, some measures can be taken such as, early and multiple culture collecting, extended incubation time, and search for other rare pathogens like mycobacteria and fungi requiring different culture media [20].

Subgroup analysis showed that the use of synthetic TIGR® mesh was associated with higher infection rates as it accounted for about one-third of the cases (n=9, 32.14%). The use of matrices, such as biologic acellular dermal matrices, has gained popularity in implant-based breast reconstruction. They provide a better definition and coverage giving a more naturally shaped lower breast pole and diminish the need for extensive muscle

Figure 2. Worldwide microbiological data



dissection. They have been shown to decrease the risk of capsule contraction [21,22]. However, their drawback is a possible increased risk for complications, including infection and seroma formation in up to 30% of cases [23]. Little is known about the incidence of complications and results when synthetic matrices are used. One study found a seroma frequency of 3.1% and infection rate of 1.5% with TIGR® mesh, which states a good safety profile. Further investigation is needed. Nevertheless, surgeons must be aware that the use of matrices may cause higher infection rates.

Reported salvage rates following breast implant reconstruction vary tremendously in the literature and range from 20% to 83% [11,24,25]. One reason can be the lack of a precise definition of what constitutes a breast implant infection across different studies, while some can manifest as blurred superficial redness others may manifest as deep fulminant cellulitis with an open wound or even implant exposure. In our study, the salvage rate was 14.3%. This result can be attributed to most of the cases represented in this cohort being admitted to our department for thorough treatment following a serious infection, in which 50% of cases presented with an open wound, making them less amenable to antibiotic treatment alone.

Limitations

The scope of this study did not include a risk factor analysis, which could have revealed some associations between certain risk factors and specific pathogens. We also did not address the issue of arising resistance to antimicrobial therapy and the need to change empiric treatment accordingly. Further large-scale studies examining associations between institution-host-pathogen are necessary.

Conclusions

This review of the microbiological characteristics of breast implant infection following reconstruction demonstrates the prevalence of the different pathogens involved. It is apparent there are significant differences in the prevalence of specific pathogens isolated in different parts of the world, as are the changes in pathogen species isolated in one place over time. We recommend that surgeons and medical facilities review the causative organisms associated with these infections in their workplace and habitat and keep it updated every few years, to be able to administer the optimal empirical antibiotic regimens to patients perioperatively and those presenting with early signs infection postoperatively. A failure to broadly cover with antibiotics the most prevalent bacterial species, based on local microbiological data, may contribute to severe consequences for the patient and the reconstructive process.

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