MRSA in Dermatology Inpatients With a Vesiculobullous Disorder

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PRACTICE **POINTS**

- Methicillin-resistant *Staphylococcus aureus* (MRSA) infection in vesiculobullous disorders such as pemphigus vulgaris and toxic epidermal necrolysis is known to contribute to an increase in disease-related mortality.
- Methicillin-resistant *S aureus* is becoming the prominent pathogen in nosocomial infections, especially in bedridden patients.
- The prevalence of MRSA in vesiculobullous disorders is high; pemphigus vulgaris is the most common vesiculobullous disorder complicated by MRSA.
- Early diagnosis of MRSA helps reduce morbidity and mortality and improves the patient's prognosis.

Methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged worldwide as a major nosocomial pathogen that causes notable morbidity and mortality, especially in vesiculobullous disorders. To study the prevalence of MRSA among patients with autoimmune bullous and drug-induced vesiculobullous disorders and elucidate its predisposing factors and associated mortality, we conducted a prospective, descriptive, 1-year study of all vesiculobullous patients admitted to a tertiary-care center. The prevalence of MRSA in this study was high (32.6%); MRSA constituted 55.8% of all bacterial isolates. All MRSA isolates were resistant to cloxacillin, oxacillin, and cefoxitin; all isolates (100%) were sensitive to vancomycin and linezolid; and 79.1% of isolates (34 patients) were sensitive to amikacin, an inexpensive and readily available antibiotic.

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Methicillin, cloxacillin, flucloxacillin, and cefoxitin are stable, penicillinase-producing β-lactam antibiotics; *Staphylococcus aureus* strains resistant to these agents are designated as methicillin-resistant *S aureus* (MRSA). Based on genotypic and phenotypic differences there are 2 strains of MRSA: hospital acquired and community acquired.

The potential for nosocomial transmission and the limited number of antibiotics available to treat MRSA are problematic. Moreover, MRSA has emerged worldwide as a major nosocomial pathogen that contributes to morbidity and mortality. Methicillin-resistant *S aureus* infection in vesiculobullous disorders such as pemphigus vulgaris (PV) and toxic epidermal necrolysis (TEN) is known to contribute to mortality.[1]

The reported prevalence of MRSA in India ranges from 12% to 38.44%.[2-4] We frequently encounter MRSA in dermatology inpatients, especially those with a vesiculobullous disorder. The primary objective of this study was to determine the prevalence of MRSA in dermatology inpatients with a vesiculobullous disorder; the secondary objective was to determine if MRSA contributes to mortality.

Materials and Methods

A 1-year prospective, cross-sectional, descriptive study was conducted in a tertiary-care center. The study population included all dermatology inpatients with a vesiculobullous disorder. Patients with a vesiculobullous disorder secondary to a primary viral or bacterial disorder were excluded. Permission to conduct the study was granted by the institution's Human Ethics Committee.

All patients underwent a detailed history and clinical examination. Routine hematology testing, urinalysis, measurement of the blood glucose level, and other investigations relevant to the vesiculobullous disorder were performed. Special investigations were Gram staining, culture, and susceptibility testing of material from a nasal swab and a swab of a representative skin lesion.

Detection of MRSA—Skin lesions were thoroughly cleaned with sterile normal saline. Specimens of pus were drawn with a sterile swab for Gram staining, culture, and susceptibility testing and were analyzed in the institution's microbiology department. A direct colony suspension

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(equivalent to McFarland Standard No. 0.5) was inoculated on a Mueller-Hinton agar plate, incorporating cefoxitin, linezolid, vancomycin, amikacin, and rifampicin supplemented with sodium chloride 2% and incubated at 37°C for 24 hours. *Staphylococcus aureus* colonies were identified by their smooth, convex, shiny, and opaque appearance with a golden yellow pigment, as well as by coagulase positivity, mannitol fermentation, and production of phosphatase.

Methicillin-resistant *S aureus* was defined as an isolate having a minimum inhibitory concentration of more than 2 µg/mL of cefoxitin; a methicillin-sensitive *S aureus* isolate was defined as having a minimum inhibitory concentration of less than or equal to 2 µg/mL of cefoxitin. Specimens showing moderate to heavy growth of MRSA were included in the study. For specimens showing mild growth, testing was repeated; if no growth was seen on repeat testing, results were interpreted as negative.

Data were collected and analyzed for frequency and percentage; $P<.05$ was considered significant.

Results

The number of patients analyzed in the study period was 43. Table 1 shows their salient demographic characteristics, clinical features, and findings of the investigation. The youngest patient was aged 13 years; the oldest was aged 80 years. The male to female ratio was 0.65 to 1. The most common primary lesion was a combined vesicle and bulla (34 patients [79.1%]); the most common secondary lesion was a combination of erosion with crusting (22 patients [51.2%]).

Table 2 lists the types of vesiculobullous disorders seen in this study. Pemphigus vulgaris was the most common (21 patients [48.8%])(Figure 1). Drug-induced vesiculobullous disorders (eg, TEN) were noted in 11 patients (25.6%)(Figure 2).

Table 2 also lists pathogens cultured in the study group. There were 24 bacterial isolates, of which *S aureus* accounted for 22 (91.7%). Methicillin-resistant *S aureus* was cultured in 14 patients (32.6%); culture was sterile in 19 patients (44.2%).

Among the 22 cultured staphylococcal species, MRSA accounted for 14 (63.6%) and constituted 58.3% (14/24) of all bacterial isolates. The nasal swab for MRSA was positive in 4 PV patients (9.3%), 2 TEN patients (4.6%), and 1 bullous pemphigoid patient (2.3%). Methicillin-resistant

TABLE 1. Salient Demographic Characteristics of Study Patients, Clinical Features, and Investigations (N=43)

Characteristics and Features	Frequency
Most common age group (51–60 y), n (%)	13 (30.2)
Sex	
Male, n (%)	17 (39.5)
Female, n (%)	26 (60.5)
Most common duration of illness (<1 y), n (%)	33 (76.7)
Diabetes mellitus, n (%)	15 (34.9)
History of antibiotic therapy, n (%)	11 (25.6)
Mucosal involvement, n (%)	11 (25.6)
Anemia, n (%)	15 (34.9)
Leukocytosis, n (%)	18 (41.9)
Gram-positive cocci, n (%)	18 (41.9)
Nasal swab positive for MRSA, n (%)	7 (16.3)
Total MRSA isolates, n (%)	14 (32.6)
MRSA in pemphigus vulgaris, n (%)	8 (57.1)
MRSA in TEN, n (%)	3 (21.4)
MRSA in bullous pemphigoid, n (%)	2 (14.2)
MRSA in epidermolysis bullosa acquisita, n (%)	1 (7.1)
Death, n (%)	4 (9.3)

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; TEN, toxic epidermal necrolysis.

TABLE 2. Vesiculobullous Disorders, Pathogens Isolated, and Frequency of Pathogens (N=43)

Disorder	Patients, n (%)	Pathogens Cultured, n (%)
Pemphigus vulgaris	21 (48.8)	MRSA, 8 (38.1); MSSA, 3 (14.3); *Acinetobacter*, 1 (4.8); *Pseudomonas*, 1 (4.8); none, 8 (38.1)
Bullous pemphigoid	10 (23.2)	MRSA, 2 (20); MSSA, 2 (20); none, 6 (60)
Toxic epidermal necrolysis	9 (20.9)	MRSA, 3 (33.3); MSSA, 2 (22.2); none, 4 (44.4)
Stevens-Johnson syndrome–toxic epidermal necrolysis overlap	2 (4.6)	MSSA, 1 (50); none, 1 (50)
Epidermolysis bullosa acquisita	1 (2.3)	MRSA, 1 (100)

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *S aureus*.

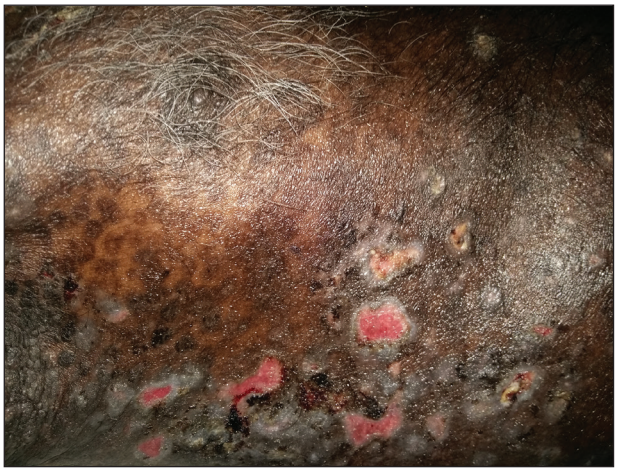

FIGURE 1. Multiple erosions and crusts in a patient with pemphigus vulgaris from which methicillin-resistant *Staphylococcus aureus* was isolated.

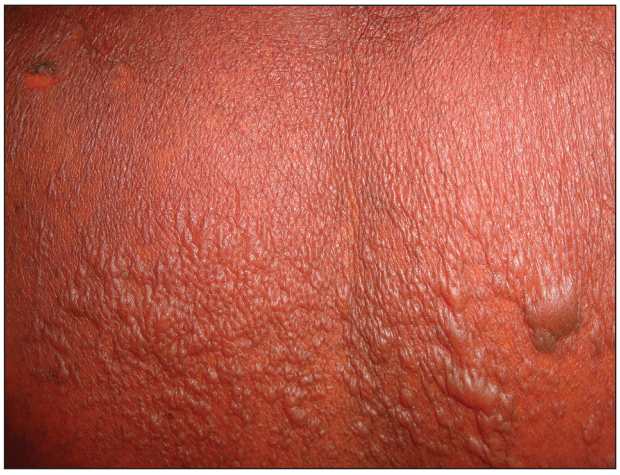

FIGURE 2. Fluid-filled blisters and denuded skin in toxic epidermal necrolysis from which methicillin-resistant *Staphylococcus aureus* was isolated.

S aureus was most commonly cultured in PV patients (8/14 [57.1%]).

All MRSA strains (100%) were sensitive to vancomycin and linezolid; 34 (79.1%) were sensitive to amikacin. Additionally, 100% of MRSA strains were resistant to oxacillin, cloxacillin, and cefoxitin.

Three patients with PV (7.0%) and 1 patient with TEN (2.3%) died during the course of the study; only 1 death (2.3%) occurred in a patient who had a positive MRSA culture.

Comment

In this 1-year study, we tested and followed 43 patients with autoimmune and drug-induced vesiculobullous disorders. Vesiculobullous disorders in dermatology inpatients are a cause of great concern. When lesions rupture, they leave behind a large area of erosion that forms a nidus of bacterial colonization; often, these bacteria cause severe infection, including septicemia, and result in death.[5] Moreover, autoimmune bullous disorders usually require a prolonged hospital stay and powerful immunosuppressive drugs, which contributes to bacterial infection, especially MRSA.[6]

The age of patients in this study ranged from 13 to 80 years; most patients were in the 6th decade, a pattern seen in studies worldwide.[5] In a study by Kanwar and De,[7] however, most cases were aged 20 to 40 years.[7] In our study, there was a female preponderance (male to female ratio of 0.65 to 1).

Studies have shown that the duration of illness in vesiculobullous disorder is directly associated with MRSA infection. However, in our study with MRSA detected in 14 patients, most patients had a duration of illness less than 1 year (statistically insignificant [$P>.05$]), a finding similar to Shafi et al.[8]

The symptomatic nature of these diseases, their unsightly appearance, and mucous-membrane involvement of vesiculobullous disorders prompts these patients to present to the hospital early. However, a prolonged hospital stay by patients with an autoimmune vesiculobullous disorders sets the stage for MRSA colonization.

In this study, diabetes mellitus (DM) was seen in 15 patients (34.9%); 5 of them had MRSA infection (statistically insignificant [$P>.05$]). Diabetes mellitus contributing to sepsis and MRSA infection, which in turn contributes to morbidity and mortality, has been well-documented.[2,4,9]

Methicillin-resistant *S aureus* in this study was isolated most often from blisters and erosions. Vesiculobullous disorders and drug reactions (eg, Stevens-Johnson syndrome, TEN) are characterized by blisters that rupture to form erosions and crusting, which form fissures in the epidermal barrier function that are nidi for colonization by microbes, especially *S aureus* and MRSA in particular; later, these bacteria can enter dermal vessels and then the bloodstream, leading to septicemia.[10]

The prevalence of MRSA in this study was 32.6% (14/43), which is high compared to other studies.[2-4] Pemphigus vulgaris was the most common disorder infected by MRSA in this study (57.1% [8/14] of MRSA isolates)(Table 1), a finding that reveals that the incidence of MRSA is high among staphylococcal isolates in vesiculobullous disorders. However, the high incidence of MRSA in this study could be a reflection of the number of patients with a severe and chronic vesiculobullous disorder, such as PV, and serious drug reactions such as TEN referred to our tertiary-care center, where we get a large number of patients affected by autoimmune and drug-induced vesiculobullous disorders. Similar findings have been reported by Stryjewski et al.[11]

A high prevalence of MRSA in a dermatology unit has grave consequences, contributing to morbidity and mortality in particular among patients with a vesiculobullous disorder. Immunosuppressive therapy and comorbidities

such as DM contribute to MRSA colonization in vesiculobullous disorders.[12] Overcrowding and poor sterilization techniques in public hospitals in India may contribute to the high prevalence of MRSA seen in hospital units.

Patients with a vesiculobullous disorder who are chronic nasal carriers of MRSA are at risk for cutaneous MRSA infection, which in turn can lead to MRSA septicemia and an elevated risk of death. In this study, however, a nasal swab was positive for MRSA in only 7 patients. One patient with MRSA colonization died, which was statistically insignificant ($P=1$).

In this study, all MRSA strains (100%) were resistant to first-line antibiotics, such as oxacillin, cloxacillin, and cefoxitin; all strains were susceptible to vancomycin and linezolid. This finding is similar to prior studies.[13,14] A distinctive finding in this study is that 34 (79.1%) of MRSA isolates were susceptible to amikacin. This finding has practical significance. Amikacin, an inexpensive antibiotic that is readily available in most units, can be used to treat MRSA infection in resource-poor settings where vancomycin and linezolid are unavailable.

Conclusion

Our study shows that MRSA is becoming the prominent pathogen in nosocomial infections, especially in bedridden patients, which has grave implications. The use of a prophylactic *S aureus* conjugate vaccine in patients with a chronic vesiculobullous disorder might be justified in the future.[15] We found a high prevalence (32.6%) of MRSA in vesiculobullous disorders, no relationship between DM and MRSA colonization, PV was the most common disorder complicated by MRSA, no relationship between nasal colonization and MRSA infection, no relationship between death during the study period and MRSA infection, 100% of MRSA strains were susceptible to vancomycin and linezolid, and 79.1% of MRSA strains were susceptible to amikacin.

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