

A MULTICENTER EVALUATION OF PATHOGEN DISTRIBUTION IN CULTURE POSITIVE PATIENTS ADMITTED WITH SKIN AND SKIN STRUCTURE INFECTION IN THE US



ABSTRACT

Background: Acute bacterial skin infections account for >12 million infections annually in the US. The demographics and underlying conditions are shifting and the etiology of these infections was previously considered to be Staphylococcal, this study sought to confirm this viewpoint.

Materials/methods: We analyzed the first positive bacterial skin/wound isolates for patients discharged with a primary or secondary ICD10 code for skin and skin structure infection (SSSI) from 68 US acute care hospitals from 2015-2017 (24 months?) in the BD Insights Research Database (Franklin Lakes, NJ). Gram-negative (GN) and Gram-positive (GP) bacterial pathogens were categorized as admission period (ADM) if collected within 3 days of admission and hospital-onset (HO) if collected ≥ 3 days from hospital admission.

Results: Skin infections were reported in 51,503 patients in whom 17,651 (34%) had a skin/wound culture taken of which 11,911 yielded a positive culture (68%) for GN and GP pathogens. Of 11,911 admissions with positive skin/wound cultures, 86% (10,213) were collected in the admission period. Overall, 79% (9,425), 36% (4,292), and 28% (3,390) were positive for GP, GN, and mixed GN/GP bacterial pathogens, respectively. Of mono/polymicrobial and mixed infections, *S aureus* (59% [6,982]), MRSA (30% [3,591]), Enterobacteriaceae (29% [3,487]), MSSA (28% [3,391]), *P aeruginosa* (12% [1,368]), and *S agalactiae* (Group B) (10% [1,243]) were the most common bacterial pathogens.

Culture Type	Onset		Overall	
	ADM	HO	N	%
Monomicrobial GP	4,190	649	4,839	41%
MRSA	3,126	465	3,591	30%
Mixed GN and GP	2,924	466	3,390	28%
Polymicrobial GP	1,894	243	2,137	18%
Monomicrobial GN	805	206	1,011	8%
Polymicrobial GN	325	80	405	3%
3+ Organisms	75	54	129	1%
Overall	10,213	1,698	11,911	

Conclusion: The epidemiology of acute skin infections is evolving with a higher incidence of gram-negative species being reported. This change in etiology should be considered when prescribing antibiotic therapy.

INTRODUCTION

Acute bacterial skin infections account for >12 million infections annually in the US. The cause of skin and skin structure infections (SSSI) has traditionally been considered to be *Staphylococcus species*, more frequently MRSA and Group B Streptococci. IDSA guidelines (1) based their empiric antibiotic therapy on the dominance of *S aureus*. Typically, methicillin-susceptible *Staphylococcus aureus* account 20.6% to 30.7%, MRSA 23.0-37.0% and B-Hemolytic Streptococci approximately 10% (2, 3, 4.). However, within some of these reports the recognition of Gram negative species has increased with Enterobacteriaceae accounting for most of these Gram-negative isolates, although *Pseudomonas aeruginosa* is encountered in around 12%. Notably several authors have also reported the occurrence of mixed infections, due to both gram-positive and gram-negative organisms (3, 4, 5, 6). The concept of healthcare or hospital acquired compared with community acquired infections has demonstrated the presence of mixed and gram-negative mono infections (6). We investigated a large national multicenter database to ascertain the pathogen distribution across several types of SSSI and source of causative pathogen.

TABLE 1. US HOSPITAL CHARACTERISTICS.

BD Sites: n=68	
Region	
Northeast	5 (7.4%)
South	32 (47.1%)
Midwest	26 (38.2%)
West	5 (7.4%)
Urban/Rural	
Urban	62 (91.2%)
Rural	6 (8.8%)
Medical School Affiliation	
Major	4 (5.9%)
Limited	12 (17.6%)
Graduate	2 (2.9%)
No Affiliation	50 (73.5%)
Bed size	
<100	12 (17.6%)
100-300	27 (39.7%)
>300	29 (42.6%)

Short-term acute hospitals: Acute & Critical Access, excludes Children's & Specialty sites.

METHODS

- We analyzed the first positive bacterial skin/wound isolates for patients discharged with a primary or secondary ICD10 code for skin and skin structure infection (SSSI, Figure 1) from 68 US acute care hospitals (Table 1.) from October 1, 2015-2017 in the BD Insights Research Database (Franklin Lakes, NJ).
- We categorized SSSIs as abscess, cellulitis, chronic ulcer, wound, other or multiple infection types, and each was stratified into GN, GP or mixed GN/GP bacterial pathogens.
- Bacterial pathogens were categorized as admission period (ADM) if collected within 3 days of admission and hospital-onset (HO) if collected ≥ 3 days from hospital admission.
- Healthcare associated episodes were defined as admitted from another acute care facility/SNF/LTACH/rehab/hospice, admission in prior 30 days, dialysis ICD10 code Z99.2 [Dependence on renal dialysis], or cancer comorbidity as identified in the AHRQ CCS comorbidity classification.

FIGURE 1. CASE TREE FOR ADMISSIONS WITH AN ICD10 CODE FOR SSSI.

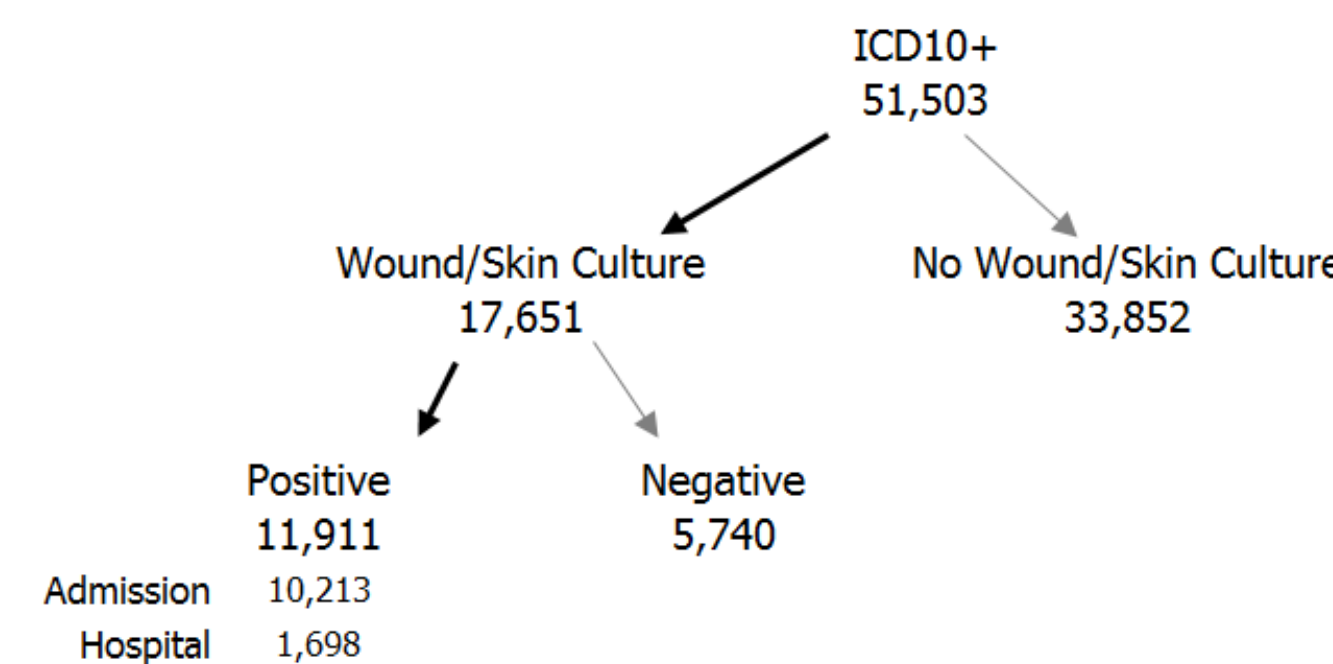


TABLE 2. CULTURE DISTRIBUTION BY PATHOGEN CATEGORY AND ADMISSION VS. HOSPITAL-ONSET (HO) TIME PERIODS (CULTURE TYPE CATEGORIES ARE NOT MUTUALLY EXCLUSIVE).

Culture Type	Onset, N (%)		Overall N (%)
	ADM	HO	
Monomicrobial GP	4,190 (41.0%)	649 (38.2%)	4,839 (40.6%)
MRSA	3,126 (30.6%)	465 (27.4%)	3,591 (30.1%)
Mixed GN and GP	2,924 (28.6%)	466 (27.4%)	3,390 (28.5%)
Polymicrobial GP	1,894 (18.6%)	243 (14.3%)	2,137 (17.9%)
Monomicrobial GN	805 (7.9%)	206 (12.1%)	1,011 (8.5%)
Polymicrobial GN	325 (3.2%)	80 (4.7%)	405 (3.4%)
<i>P. aeruginosa</i>	1,134 (11.1%)	234 (13.8%)	1,368 (11.5%)
3+ Organisms	75 (0.7%)	54 (3.2%)	129 (1.1%)
Overall	10,213 (85.7%)	1,698 (14.3%)	11,911

RESULTS

- Skin infections were reported in 51,503 patients in whom 17,651 (34%) had a skin/wound culture taken of which 11,911 yielded a positive culture (68%) for GN and GP pathogens and 86% (10,213) of cultures were collected in the admission period. See Figure 1.
- Overall, 79% (9,425) and 36% (4,292) were positive for GP, GN, respectively with 28% (3,390) of them being mixed GN/GP.
- Of all culture positive admissions, including polymicrobial (multiple GP or GN species) and mixed infections (GP + GN), *S aureus* (59% [6,982]) including MRSA (30% [3,591]), Enterobacteriaceae (29% [3,487]), MSSA (28% [3,391]), *Pseudomonas aeruginosa* (12% [1,368]), and *Streptococcus agalactiae* (Group B) (10% [1,243]) were the most common bacterial pathogens. See Table 2.
- Of culture positive episodes, 83.6% (9,953) were treated with empiric antibiotic therapy and also 25.7% (2,557) were healthcare-associated.
- The distribution by SSSI category for admissions with positive skin/wound cultures treated with empiric antimicrobial therapy (n=9,953) is as follows: abscess (8.3), cellulitis (17.7%), chronic ulcer (15.3%), wound (7.8%), other (3.3%) or multiple infection types (47.5%). See Table 3.

TABLE 3. CULTURE DISTRIBUTION BY PATHOGEN CATEGORY AND SSSI CATEGORY FOR THOSE TREATED WITH EMPIRIC ANTIBIOTIC THERAPY.

Pathogen	Abscess	Cellulitis	Chronic Ulcer	Multiple	Wound	Other	Grand Total
MRSA	300 (36.1%)	517 (29.3%)	438 (28.7%)	1,521 (32.2%)	165 (21.3%)	73 (22.1%)	3,014 (30.2%)
MSSA	231 (27.8%)	624 (35.4%)	311 (20.4%)	1,436 (30.4%)	189 (24.4%)	102 (30.9%)	2,893 (29.1%)
<i>Pseudomonas aeruginosa</i>	32 (3.9%)	167 (9.5%)	296 (19.4%)	505 (10.7%)	106 (13.7%)	29 (8.8%)	1,135 (11.4%)
<i>Streptococcus agalactiae</i>	69 (8.3%)	193 (11.0%)	139 (9.1%)	619 (13.1%)	39 (5.0%)	15 (4.5%)	1,074 (10.8%)
<i>Escherichia coli</i>	83 (10.0%)	106 (6.0%)	218 (14.3%)	367 (7.8%)	153 (19.8%)	66 (20.0%)	993 (10.0%)
<i>Enterococcus faecalis</i>	42 (5.1%)	116 (6.6%)	170 (11.2%)	372 (7.9%)	90 (11.6%)	20 (6.1%)	810 (8.1%)
<i>Proteus mirabilis</i>	24 (2.9%)	80 (4.5%)	204 (13.4%)	290 (6.1%)	41 (5.3%)	12 (3.6%)	651 (6.5%)
<i>Klebsiella pneumoniae</i>	33 (4.0%)	42 (2.4%)	83 (5.4%)	156 (3.3%)	54 (7.0%)	15 (4.5%)	383 (3.9%)
<i>Enterobacter cloacae</i>	16 (1.9%)	68 (3.9%)	49 (3.2%)	158 (3.3%)	35 (4.5%)	9 (2.7%)	335 (3.4%)
<i>Streptococcus pyogenes</i>	23 (2.8%)	99 (5.6%)	19 (1.3%)	144 (3.0%)	7 (0.9%)	6 (1.8%)	298 (3.0%)
Other	98 (11.8%)	234 (13.3%)	372 (24.4%)	625 (13.2%)	161 (20.8%)	46 (13.9%)	1,536 (15.4%)
Total	831 (8.4%)	1,763 (17.7%)	1,524 (15.3%)	4,731 (47.5%)	774 (7.8%)	330 (3.3%)	9,953

CONCLUSION

- The etiology of acute skin and skin structure infections is evolving with a higher incidence of gram-negative species being reported.
- Almost 40% of cultures yielded a gram-negative species in mono culture or mixed with gram positive species.
- The gram-negative species isolated encompass several Enterobacteriaceae species and *P aeruginosa*.
- MRSA was isolated as often as MSSA this observation highlights the continued need to account for MRSA.
- Streptococcus agalactiae* (Group B) was reported almost four times more frequently than *S pyogenes* (Group A).
- This changing etiology should be considered when prescribing empiric antibiotic therapy.

TABLE 4. PATHOGEN DISTRIBUTION BY NON-HCA VS. HCA STATUS FOR THOSE TREATED WITH EMPIRIC ANTIBIOTIC THERAPY.

Pathogen	Non-HCA N, (%)	HCA N (%)	Total N (%)
MRSA	2,312 (31.3%)	702 (27.5%)	3,014 (30.3%)
MSSA	2,231 (30.2%)	662 (25.9%)	2,893 (29.1%)
<i>Pseudomonas aeruginosa</i>	762 (10.3%)	373 (14.6%)	1,135 (11.4%)
<i>Streptococcus agalactiae</i>	878 (11.9%)	196 (7.7%)	1,074 (10.8%)
<i>Escherichia coli</i>	654 (8.8%)	339 (13.3%)	993 (10.0%)
<i>Enterococcus faecalis</i>	559 (7.6%)	251 (9.8%)	810 (8.1%)
<i>Proteus mirabilis</i>	468 (6.3%)	183 (7.2%)	651 (6.5%)
<i>Klebsiella pneumoniae</i>	244 (3.3%)	139 (5.4%)	383 (3.8%)
<i>Enterobacter cloacae</i>	242 (3.3%)	93 (3.6%)	335 (3.4%)
<i>Streptococcus pyogenes</i>	251 (3.4%)	47 (1.8%)	298 (3.0%)
Other	1049 (14.2%)	487 (19.0%)	1536 (15.4%)
Total	7,396 (74.3%)	2,557 (25.7%)	9953

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