

MICROBIOLOGY OF CULTURE-POSITIVE SKIN AND SKIN STRUCTURE INFECTION AMONG HOSPITALIZED PATIENTS IN THE U.S., 2015-2017

G. S. TILLOTSON¹, S. K. CAMMARATA², M. ZILBERBERG³, J. MURRAY⁴; V. GUPTA⁴

¹GST MICRO LLC, Durham, NC, ²Melinta Therapeutics, Inc., Lincolnshire, IL, ³EviMed Res. Group, LLC, Goshen, MA, ⁴Becton, Dickinson & Company, Franklin Lakes, NJ

ABSTRACT

Background: Hospitalizations for treatment of acute skin and skin structure infections (SSSI) account for nearly 2%, hospitalizations in the US. In the past, Gram-negative (GN) organisms were thought to be an infrequent cause of SSSI. However, because of evolving microbiological shifts, this may have changed. We explored the current bacterial etiology of SSSIs.

Material/methods: We analyzed the first positive bacterial skin/wound isolates from consecutive patients treated with empiric antibiotic therapy and discharged with a primary or secondary ICD10 code for SSSI from 68 US acute care hospitals, 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, Gram-positive (GP) or mixed GN/GP bacterial pathogens.

Results: Among the 9,953 admissions who met the inclusion criteria, multiple infection types (47.5%), cellulitis (17.7%), chronic ulcer (15.3%), and abscess (8.4%) represented 88.9% of all SSSIs. Of the 4,731 episodes of multiple infections, 83.4% were cellulitis, 56.1% chronic ulcer, and 50.3% were abscess. Overall, 59.2% were GP only, 11.9% GN only and 27.9% mixed GN/GP bacterial pathogens. GN bacteria were most common in chronic ulcer (59.3%) and wound (52.7%) infections.

Conclusion: GN pathogens occur in almost 40% of patients hospitalized with SSSI. Along with resistant GP species, the risk for these organisms needs to be factored into decisions about empiric regimens for SSSI.

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.

INTRODUCTION

Acute bacterial skin infections account for >12 million infections annually in the US. The cause of acute 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 *Staphylococcus 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 prevalence of Gram negative species has increased with Enterobacteriaceae accounting for most of these Gram-negative isolates, although *Pseudomonas aeruginosa* is encountered in around 12% of episodes. 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 monomicrobial infections (6). We investigated a large national multicenter database to ascertain the pathogen distribution across several types of SSSI and source of causative pathogen.

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 2015-2017 in the BD Insights Research Database (Franklin Lakes, NJ).
- We categorized SSSIs as abscess, cellulitis, chronic ulcer, wound, other or multiple infection (ICD10 code for more than one infection type) types, and each was stratified into GN, GP or mixed GN/GP bacterial pathogens in patients treated with empiric antimicrobial therapy.
- Empiric antimicrobial therapy was defined as the receipt of any antimicrobial agent with a duration ≥ 24 hours within 5 days prior to final culture result.
- 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.

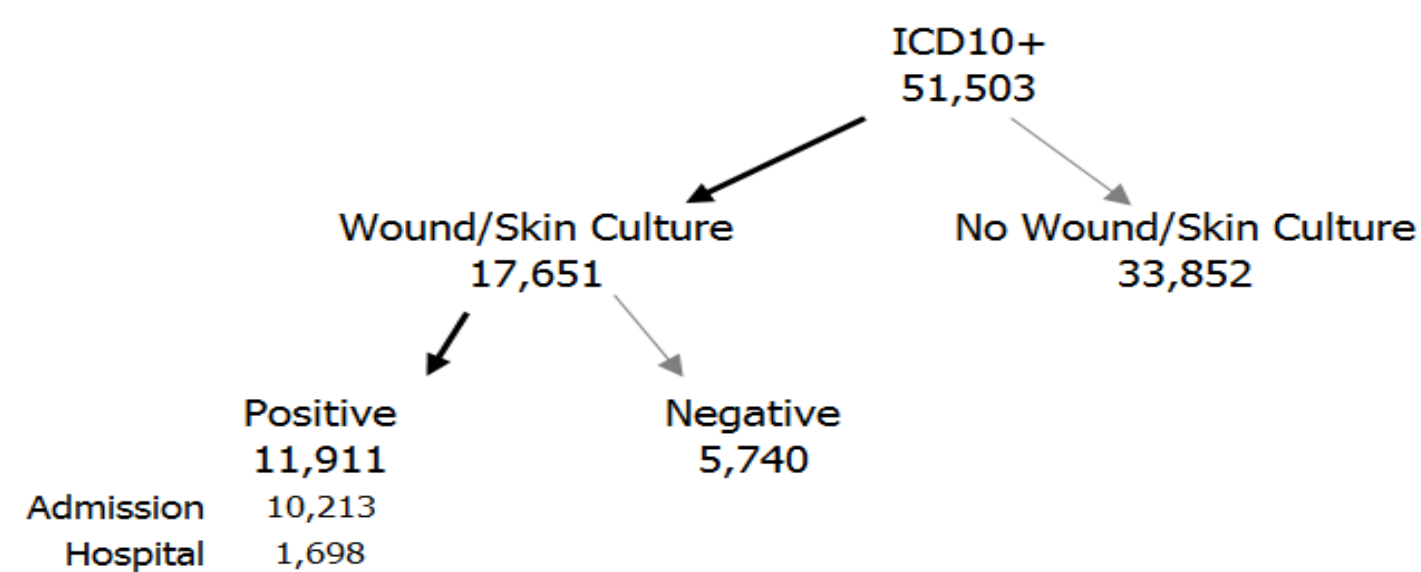


TABLE 2. CULTURE DISTRIBUTION BY PATHOGEN CATEGORY AND SSSI CATEGORY FOR THOSE TREATED WITH EMPIRIC ANTIBIOTIC THERAPY.

Pathogen Category	Abscess (n=831), N (%)	Cellulitis (n=1,763), N (%)	Chronic Ulcer (n=1,524), N (%)	Wound (n=774), N (%)	Other (n=330), N (%)	Multiple Categories (n=4,731), N (%)	All (n=9,953), N (%)
Monomicrobial GP	492 (59.2%)	838 (47.5%)	320 (21.0%)	268 (34.6%)	148 (44.8%)	1,937 (40.9%)	4,003 (40.2%)
Mixed GN and GP	136 (16.4%)	386 (21.9%)	667 (43.8%)	239 (30.9%)	78 (23.6%)	1,272 (26.9%)	2,778 (27.9%)
Polymicrobial GP	125 (15.0%)	364 (20.6%)	275 (18.0%)	86 (11.1%)	40 (12.1%)	998 (21.1%)	1,888 (19.0%)
Monomicrobial GN	60 (7.2%)	121 (6.9%)	161 (10.6%)	117 (15.1%)	46 (13.9%)	340 (7.2%)	845 (8.5%)
Polymicrobial GN	16 (1.9%)	43 (2.4%)	75 (4.9%)	52 (6.7%)	11 (3.3%)	142 (3.0%)	339 (3.4%)
3+ Organisms	2 (0.2%)	11 (0.6%)	26 (1.7%)	12 (1.6%)	7 (2.1%)	42 (0.9%)	100 (1.0%)

TABLE 3. CULTURE DISTRIBUTION BY PATHOGEN 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

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.
- 83.6% (n=9,953) of 11,911 culture positive admissions were started on empiric antimicrobial therapy.
- Among the 9,953 admissions who met the inclusion criteria, multiple infection types (47.5%), cellulitis (17.7%), chronic ulcer (15.3%), and abscess (8.3%) represented 88.8% of all SSSIs.
- Of the 4,731 episodes of multiple infections, 83.4% were cellulitis, 56.1% chronic ulcer, and 50.3% were abscess. Overall, 59.2% were GP only, 11.9% GN only and 27.9% mixed GN/GP bacterial pathogens.
- Among the 9,953 admissions who met the inclusion criteria, a substantial proportion (40.8%) involved a GN organism either as monomicrobial GN (8.5%), polymicrobial GN (3.4%) or mixed GN/GP (27.9%).
- GN bacteria were most common in chronic ulcer (59.3%) and wound (52.7%) infections.

CONCLUSION

- GN pathogens occur almost 40% of patients hospitalized with SSSI.
- Enterobacteriaceae species account >25% of infections, either alone or in mixed populations.
- Along with resistant GP species, the risk of these organisms needs to be factored into decisions about empiric regimens for SSSI.

REFERENCES

- Stevens DL et al IDSA 2014. Clin Infect Dis. 2014 Jul;59(2):e10-52.
- Zilberberg M 2012. SurgInfect (Larchmt). 2012 Dec;13 (6):377-82..
- Ray G 2013 BMC Infect Dis. 2013 May 30;13:252.
- Lipsky B2014. Diagn Microbiol Infect Dis. 2014 Jun;79(2):273-9.
- McGinnis E 2016. ISPOR 2016 PS 441.
- Zilberberg M 2009. Infect Control Hosp Epidemiol. 2009 Dec;30(12):1203-10.

Acknowledgments: This study was funded by a grant from Melinta Therapeutics, INC., New Haven, CT, USA.