POSTER # 569

PATHOGEN TYPE AND INAPPROPRIATE EMPIRIC THERAPY (IET) IN CULTURE-POSITIVE SKIN AND SOFT TISSUE INFECTION AMONG HOSPITALIZED PATIENTS IN THE U.S., 2015-2017

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ABSTRACT

Background: Hospitalizations for treatment of acute skin and skin structure infections (SSSI) account for nearly 2% of all hospitalizations in the US. Inappropriate empiric therapy (IET) is an important driver of hospital outcomes. As Gram-negative (GN) organisms gain in prevalence in SSSI, we hypothesized that the likelihood of empiric coverage to include GN infections lags behind that for Gram-positives (GP).

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, GP or mixed GN/GP bacterial pathogens. IET was present if the antibiotic did not cover the organism(s) or was not started within 5 days prior to final culture result. We relied on ICD 10 codes to classify SSSI as abscess, cellulitis, chronic ulcer, wound, other or multiple categories.

Results: Among the 9,953 admissions who met the inclusion criteria, a substantial proportion (40.8%) involved a GN organism. IET was administered to 1,284 (13.0%) admissions. Compared to those with a GP organism only, patients with a GN organism only (OR with 95% confidence interval (CI): 4.3 (3.6, 5.1), p < 0.0001) or those with mixed GN/GP pathogens (OR with 95% CI: 4.3 (3.7, 4.9), p < 0.0001) were more likely to receive IET. These differences persisted across all SSSI categories (all p < 0.01).

Conclusion: Compared to those with a GP SSSI, patients with GN or a mixed GN/GP infection, irrespective of the type, have some four times higher likelihood of being exposed to IET. To optimize empiric treatment, clinicians need to be cognizant of the increasing prevalence of GN SSSIs.

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 are a common infection in all healthcare settings in the US. It was found that both the total number and rate of SSSI-related visits to ambulatory physicians increased from 1997 to 2005. Total visits increased by 65% from 8.6 million (95% CI, 7.0 million to 10.2 million) in 1997 to 14.2 million (95% CI, 11.7 million to 16.8 million) in 2005, and the overall rate of ambulatory visits increased by 50% from 32.1 (95% CI, 26.1-38.1) visits/1000 population in 1997 to 48.1 (95% CI, 39.4-56.7) (P=.003 for trend) in 2005 [1]. Recently, in a large US-based multicenter retrospective cohort of ambulatory and inpatient encounters among nearly 50 million commercially insured individuals aged 0–64 years, Miller and coworkers reported that not only did 2.3 million cases of SSSI occur between the years 2005 and 2010, but also that during this time period, the incidence of SSSIs was far higher than that of either urinary tract infections or pneumonia. [2]. Kaye and colleagues noted that the absolute volume of SSSI hospitalizations rose from 641,863 in 2005 to 752,770 in 2011, as did the SSSI diagnoses as a proportion of all admissions, going from 1.6% to 2.0% [3]. Based on the available evidence, SSSI is a high-volume condition in both in-and outpatient settings and some studies show a rising incidence in recent history. Moreover, the concept of healthcare or hospital acquired compared with community acquired infections has demonstrated the presence of mixed and gram-negative mono infections [4]. We used a large national multicenter database to ascertain the demography several types of SSSI and the underlying comorbidities.

Objectives:

- To evaluate the incidence of GP. GN or mixed GN/GP in patients admitted with SSSI.
- To evaluate the feasibility of a single antibiotic regimen to cover such infections.

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 (Table 1) from 2015-2017 in the BD Insights Research Database (Franklin Lakes, NJ).
- We categorized SSSI as abscess, cellulitis, chronic ulcer, wound, other or multiple infection types, and each was stratified into GN, GP or mixed GN/GP bacterial pathogens. Inappropriate empiric antimicrobial therapy (IET) was present if the antibiotic that was started within 5 days prior to final culture result did not cover the organism(s) or was resistant.
- We relied on ICD 10 codes to classify SSSI as abscess, cellulitis, chronic ulcer, wound, and other or multiple categories.
- IET was defined as the receipt of any antimicrobial with a duration ≥ 24 hours within 5 days prior to final culture result where the regimen did not cover or was proven inactive against the cultured pathogen.
- We defined fluoroquinolone non-susceptibility (FQ NS) as any GN or GP isolate that as reported as either intermediate or resistant to ciprofloxacin, levofloxacin or moxifloxacin.
- Logistic regression method was used to assess significance and estimate odds ratios (OR).

RESULTS

- Among the 9,953 SSSI admissions who met the inclusion criteria, a substantial proportion (40.8%) involved a GN organism either as monomicrobial GN, polymicrobial GN or mixed GN/GP (Table 2.).
- Overall, IET was prescribed in 1,284 (13.0%) of SSSI admissions and in the following SSSI categories: abscess (10.7%), cellulitis (11.5%), chronic ulcer (19.3%), wound (14.3%), other (14.6%), and multiple SSSI categories (11.6%) [Tables 3, 4].
- Compared to those with a GP organism only, patients with a GN only (odds ratio (OR) with 95% CI: 4.3 (3.6, 5.1), p < 0.0001) or mixed GN/GP pathogens (OR with 95% CI: 4.3 (3.7, 4.9), p < 0.0001) were more likely to receive IET. These differences persisted across all SSSI categories.
- Vancomycin and piperacillin/tazobactam were the most common empiric antimicrobials prescribed in SSSI (Table 5).

CONCLUSION

- Compared to those with a GP SSSI, patients with GN or a mixed GN/GP infection, irrespective of the type, have some four times higher likelihood of being exposed to IET.
- Although gram-negative resistance to FQ may be common, only 10.8% of SSSI admissions had a GN that was FQ NS.
- To optimize empiric treatment, clinicians should consider agents which provide appropriate therapy to accommodate the increasing prevalence of GN SSSIs.

REFERENCES

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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%)
MRSA	300 (36.1%)	517 (29.3%)	438 (28.7%)	165 (21.3%)	73 (22.2%)	1,521 (32.1%)	3,014 (30.3%)
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%)
P. aeruginosa	32 (3.9%)	167 (9.6%)	296 (19.4%)	106 (13.7%)	29 (8.8%)	505 (10.7%)	1,135 (11.4%)
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. PATHOGEN DISTRIBUTION BY SSSI CATEGORY FOR ADMISSIONS 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%)**
Pseudomonas aeruginosa	32 (3.9%)	167 (9.5%)	296 (19.4%)	505 (10.7%)	106 (13.7%)	29 (8.8%)	**1,135 (11.4%)**
Streptococcus agalactiae	69 (8.3%)	193 (11.0%)	139 (9.1%)	619 (13.1%)	39 (5.0%)	15 (4.5%)	**1,074 (10.8%)**
Escherichia coli	83 (10.0%)	106 (6.0%)	218 (14.3%)	367 (7.8%)	153 (19.8%)	66 (20.0%)	**993 (10.0%)**
Enterococcus faecalis	42 (5.1%)	116 (6.6%)	170 (11/2%)	372 (7.9%)	90 (11.6%)	20 (6.1%)	**810 (8.1%)**
Proteus mirabilis	24 (2.9%)	80 (4.5%)	204 (13.4%)	290 (6.1%)	41 (5.3%)	12 (3.6%)	**651 (6.5%)**
Klebsiella pneumoniae	33 (4.0%)	42 (2.4%)	83 (5.4%)	156 (3.3%)	54 (7.0%)	15 (4.5%)	**383 (3.9%)**
Enterobacter cloacae	16 (1.9%)	68 (3.9%)	49 (3.2%)	158 (3.3%)	35 (4.5%)	9 (2.7%)	**335 (3.4%)**
Streptococcus pyogenes	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**

TABLE 4. INAPPROPRIATE EMPIRIC THERAPY (IET) BY PATHOGEN CATEGORY AND SSSI CATEGORY AND PATHOGEN CATEGORY.

Pathogen Category	Abscess, N (%)	Cellulitis N (%)	Chronic Ulcer N (%)	Wound N (%)	Other N (%)	Multiple Categories N (%)	All N (%)
GN Only IET*	19.7% (15/76)	26.8% (44/164)	21.6% (51/236)	21.3% (36/169)	24.6% (14/57)	22.8% (110/482)	22.8% (270/1184)
GP Only IET	6.8% (42/617)	5.7% (68/1202)	12.4% (74/595)	7.3% (26/354)	8.0% (15/188)	5.3% (156/2935)	6.5% (381/5891)
Mixed IET^	23.5% (32/136)	23.8% (92/386)	24.5% (164/667)	19.7% (47/239)	23.1% (18/78)	22.0% (280/1272)	22.8% (633/2778)
All†	**10.7% (89/829)**	**11.5% (204/1772)**	**19.3% (289/1498)**	**14.3% (109/762)**	**14.6% (47/323)**	**11.6% (546/4689)**	**13.0% (1284/9853)**

* p < .0012 GN only IET vs. GP only IET for all categories; ^ p <.0011 Mixed IET vs. GP only IET for all categories. † Admissions with "more than 3 stains" were excluded in this assessment.

TABLE 5. ANTIMICROBIAL USE BY PATHOGEN CATEGORY†

Antibiotic	GN Only		GP Only		Mixed GN/GP		Overall	
	IET	Total	IET	Total	IET	Total	IET	Total
Total Admissions	**270 (22.8%)**	**1,184**	**381 (6.5%)**	**5,891**	**633 (22.8%)**	**2,778**	**1,284 (13.0%)**	**9,853**
Vancomycin-IV	126 (46.7%)	126 (10.6%)	27 (7.0%)	4,166 (70.7%)	117 (18.5%)	1,333 (48.0%)	270 (21.0%)	5,624 (57.1%)
Piperacillin / Tazobactam-IV	42 (15.6%)	566 (47.8%)	112 (29.4%)	1,600 (27.2%)	47 (7.4%)	1,332 (47.9%)	201 (15.7%)	3,498 (35.5%)
Clindamycin-IV	30 (11.1%)	30 (2.5%)	41 (10.8%)	558 (9.5%)	41 (6.5%)	139 (5.0%)	112 (8.7%)	727 (7.4%)
Cefepime-IV	6 (2.2%)	134 (11.3%)	36 (9.4%)	264 (4.5%)	22 (3.5%)	264 (9.5%)	64 (5.0%)	662 (6.7%)
Ceftriaxone-IV	18 (6.7%)	107 (9.0%)	31 (8.1%)	346 (5.9%)	27 (4.3%)	188 (6.8%)	76 (5.9%)	641 (6.5%)
Meropenem-IV	9 (3.3%)	133 (11.2%)	25 (6.6%)	189 (3.2%)	8 (1.3%)	277 (10.0%)	42 (3.3%)	599 (6.1%)
Levofloxacin-IV	18 (6.7%)	66 (5.6%)	12 (3.1%)	286 (4.9%)	11 (1.7%)	190 (6.8%)	41 (3.2%)	542 (5.5%)
Cefazolin-IV	17 (6.3%)	35 (3.0%)	39 (10.2%)	347 (5.9%)	19 (3.0%)	109 (3.9%)	75 (5.8%)	491 (5.0%)
Ampicillin / Sulbactam-IV	16 (5.9%)	24 (2.0%)	14 (3.7%)	269 (4.6%)	12 (1.9%)	123 (4.4%)	42 (3.3%)	416 (4.2%)
Daptomycin-IV	7 (2.6%)	7 (0.6%)	1 (0.3%)	198 (3.4%)	4 (0.6%)	78 (2.8%)	12 (0.9%)	283 (2.9%)
Linezolid-IV	6 (2.2%)	6 (0.5%)		137 (2.3%)	5 (0.8%)	75 (2.7%)	11 (0.9%)	218 (2.2%)
Ciprofloxacin-IV	7 (2.6%)	35 (3.0%)	3 (0.8%)	90 (1.5%)	5 (0.8%)	80 (2.9%)	15 (1.2%)	205 (2.1%)
Ceftaroline-IV	6 (2.2%)	8 (0.7%)	2 (0.5%)	118 (2.0%)	3 (0.5%)	26 (0.9%)	11 (0.9%)	152 (1.5%)
Sulfamethoxazole / Trimethoprim-ORAL	1 (0.4%)	15 (1.3%)	2 (0.5%)	91 (1.5%)	7 (1.1%)	45 (1.6%)	10 (0.8%)	151 (1.5%)
Ertapenem-IV	1 (0.4%)	28 (2.4%)	10 (2.6%)	51 (0.9%)	5 (0.8%)	59 (2.1%)	16 (1.2%)	138 (1.4%)
Doxycycline-ORAL	4 (1.5%)	10 (0.8%)	1 (0.3%)	79 (1.3%)	4 (0.6%)	32 (1.2%)	9 (0.7%)	121 (1.2%)
Ciprofloxacin-ORAL	4 (1.5%)	21 (1.8%)	2 (0.5%)	40 (0.7%)	3 (0.5%)	52 (1.9%)	9 (0.7%)	113 (1.1%)
Metronidazole-IV	20 (7.4%)	20 (1.7%)	31 (8.1%)	31 (0.5%)	52 (8.2%)	52 (1.9%)	103 (8.0%)	103 (1.0%)
Levofloxacin-ORAL	4 (1.5%)	16 (1.4%)	3 (0.8%)	52 (0.9%)	1 (0.2%)	35 (1.3%)	8 (0.6%)	103 (1.0%)

† Admissions with "more than 3 stains" were excluded in this assessment.