

and anaerobes accounted for 73.3% of the microbial population. Gastroenterologists (94, 37.6%) and general surgeons (52, 20.8%) were the most common prescribers. Hepatobiliary (83, 33.2%), respiratory (58, 23.2%), and intra-abdominal infections (IAI; 34, 13.6%) were the major suspected diagnoses. Blood-culture collection was associated with the use of immunosuppressive agents (OR, 3.48; 95% CI, 1.49–8.99), intra-abdominal infection (OR, 0.28; 95% CI, 0.12–0.67), systemic inflammatory response syndrome criteria ≥ 2 (OR, 4.50; 95% CI, 2.25–9.42), and surgical specialty (OR, 0.33; 95% CI, 0.18–0.60). **Conclusions:** More than one-third of patients requiring hospitalization and empiric piperacillin-tazobactam did not undergo blood-culture collection. The finding that blood cultures were less likely to be obtained in patients with suspected IAI requiring hospitalization and by surgical specialties raises a concern regarding suboptimal evaluation. Further assessment of the appropriateness of blood-culture collection in the setting of broad-spectrum antibiotic prescription and tailored promotion of blood-culture collection to surgical specialties may be warranted.

Disclosures: S.K.: The author (during graduate school (PhD) was involved in antiviral research relevant to a neglected tropical disease and favipiravir. During this graduate school research, favipiravir was provided by FUJIFILM Toyama Chemical Co. Ltd

Antimicrobial Stewardship & Healthcare Epidemiology 2023;3(Suppl. S2):s30–s31
doi:10.1017/ash.2023.257

Presentation Type:

Poster Presentation - Poster Presentation

Subject Category: Antibiotic Stewardship

Risk Factors and outcomes associated with inappropriate empiric broad-spectrum antibiotic use in hospitalized patients with community-acquired pneumonia

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Background: Inappropriate broad-spectrum antibiotic use targeting methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* can result in increased adverse events, antibiotic resistance, and *Clostridioides difficile* infection. In 2019, revised ATS/IDSA community-acquired pneumonia (CAP) guidelines removed healthcare-associated pneumonia (HCAP) as a clinical entity and modified patient factors warranting empiric broad-spectrum antibiotic (BSA) use. As a result, most patients hospitalized with CAP should receive empiric antibiotics targeting standard CAP pathogens. Based on revised guidelines, we evaluated predictors and outcomes associated with inappropriate BSA use among hospitalized patients with CAP. **Methods:** Between November 2019 and July 2022, trained abstractors collected data on non-ICU adult medical patients admitted with CAP at 67 Michigan hospitals who received either an inappropriate empiric BSA on hospital day 1 or 2 or a standard CAP regimen. Inappropriate empiric BSA use was defined as use of an anti-MRSA or anti-pseudomonal antibiotic in a patient eligible for standard CAP coverage per IDSA guidelines. Patients with immune compromise, moderate or severe chronic obstructive pulmonary disease (COPD), pulmonary complication, or guideline-concordant treatment with BSA were excluded. Data collected included comorbidities, antibiotic use and hospitalizations in the preceding 90 days, cultures in the preceding year, signs or symptoms of pneumonia, hospital characteristics, and 30-day postdischarge patient outcomes. Data were collected through chart review and patient phone calls. Predictors of inappropriate empiric BSA were evaluated using logistic general estimating equation (GEE) models, accounting for hospital-level clustering. We assessed the effect of inappropriate empiric BSA (vs standard CAP therapy) on 30-day patient outcomes using logistic GEE models controlling for predictors associated with the outcome and probability of treatment. **Results:** Of 8,286 included patients with CAP, 2,215 (26.7%) were empirically treated with inappropriate BSA. The median BSA treatment was 3 days (IQR, 2.5). After adjustments, factors associated with inappropriate empiric BSA treatment

Figure 1. Multivariable model of Patient and Hospital-Level Factors Associated with Inappropriate Empiric Broad-Spectrum Antibiotic Treatment of Community-Acquired Pneumonia in Hospitalized Patients

Variable	CAP Coverage (N= 6071)	Inappropriate Empiric Broad-Spectrum Coverage (N=2215)	Adjusted Odds Ratio (95% CI)	P-Value
Hemodialysis in preceding 30 days	144 (2.4%)	168 (7.6%)	2.19 (1.68-2.85)	<.001
Hospitalization in preceding 90 days ^a	643 (10.6%)	801 (36.2%)	3.71 (3.22-4.27)	<.001
Received high-risk antibiotic in preceding 90 days ^b	597 (9.8%)	524 (23.7%)	1.82 (1.55-2.13)	<.001
Transfer from post-acute care facility ^c	286 (4.7%)	419 (18.9%)	3.37 (2.81-4.04)	<.001
Supplemental oxygen ^d				
Room air	2237 (37.0%)	685 (31.1%)	REF	REF
1-2L	1329 (22.0%)	467 (21.2%)	1.12 (0.96-1.30)	0.16
3-4L	1717 (28.4%)	658 (29.8%)	1.17 (1.02-1.35)	0.03
5+ L	768 (12.7%)	396 (17.9%)	1.50 (1.26-1.77)	<.001
Pneumonia Severity Index ^e (per 20-point increase)	96.6 (73.3-121.4)	109.2 (85.0-133.9)	1.10 (1.06-1.14)	<.001
Severe sepsis ^f	1578 (26.0%)	844 (38.1%)	1.50 (1.32-1.70)	<.001
Leukocytosis (>10,000 cells/uL) ^g	3959 (65.2%)	1537 (69.4%)	1.26 (1.12-1.42)	<.001
Academic hospital ^h	4842 (79.8%)	1665 (75.2%)	0.76 (0.56-1.02)	0.065

^a Does not include patients receiving empiric antibiotics targeting MRSA or *Pseudomonas aeruginosa* on hospital day 1 or day 2 with severe community-acquired pneumonia as defined by IDSA/ATS 2019 guidelines and were hospitalized in past 90 days and additionally received high-risk antibiotics in previous 90 days. These patients were considered to have received guideline concordant empiric broad-spectrum antibiotics and not included in the inappropriate empiric broad-spectrum treatment cohort.
^b Includes any intravenous antibiotic, any fluoroquinolone, or linezolid as these are associated with increased risk for multidrug-resistant organisms or are active against methicillin-resistant *Staphylococcus aureus* or *Pseudomonas* species.
^c Includes patients transferred from subacute rehabilitation center, skilled nursing home, acute rehabilitation center, assisted living facility or resided in these facilities in the preceding 30 days.
^d Highest level of oxygen support on either hospital day 1 or 2.
^e Highest pneumonia severity index (PSI) on hospital day 1 or 2. PSI includes age, sex, comorbidities, vital sign and laboratory abnormalities, and pleural effusion on imaging. Higher scores indicate more severe disease.
^f Present on hospital day 1 or 2.
^g Academic hospital status was obtained from the American Hospital Association's data hub. Odds ratios > 1 indicates factors associated with receiving inappropriate empiric broad-spectrum antibiotic treatment on hospital day 1 or day 2; P-value <0.05 is considered significant
 CI, confidence interval; OR, Odds ratio

Figure 2. Outcomes for Patients Hospitalized with CAP Receiving Standard Empiric CAP Treatment vs Inappropriate Empiric Broad-Spectrum Antibiotic Treatment N=8286

Outcome ^a	CAP Coverage (n=6071)	Inappropriate Empiric Broad-Spectrum Coverage (n=2215)	Unadjusted Odds Ratio (95% CI)	Unadjusted P-value	Adjusted Odds Ratio (95%CI)	Adjusted P-Value
In-Hospital and 30-d Postdischarge mortality ^b	183 (3.0%)	117 (5.3%)	1.80 (1.42-2.29)	<.001	1.02 (0.81-1.30)	0.85
30-d Postdischarge Re-admission ^b	626 ^c (10.4%)	344 ^c (15.8%)	1.63 (1.41-1.88)	<.001	1.18 (1.03-1.35)	0.02
30-d Postdischarge ED-Visit ^b	548 ^c (9.1%)	236 ^c (10.9%)	1.24 (1.05-1.46)	0.01	1.11 (0.95-1.29)	0.18
In-Hospital and 30-d Postdischarge <i>Clostridioides difficile</i> Infection ^d	15 (0.3%)	12 (0.5%)	2.20 (1.03-4.71)	0.04	1.88 (0.85-4.16)	0.12
In-Hospital and 30-d Postdischarge Antibiotic-Associated ADE ^e	139 (2.3%)	71 (3.2%)	1.46 (1.09-1.96)	0.01	1.73 (1.24-2.43)	0.001
Duration of Hospitalization, median (IQR) ^f	4 (3-6)	5 (4-7)	1.19 (1.16-1.21)	<.001	1.11 (1.09-1.13)	<.001
Transfer to ICU ^g	86 (1.4%)	60 (2.7%)	1.95 (1.39-2.75)	<.001	1.55 (1.10-2.19)	0.01

^a Outcomes were adjusted for patient variables found to be significant (P<.05) and associated with treatment in the multivariate analysis as well as baseline characteristics known to be associated with each individual outcome (see other footnotes).
^b Mortality, readmission, and return to ED are adjusted for age, length of stay (LOS), Charlson comorbidity index, prior hospitalization, transfer from post-acute care facility, discharge to a long-term acute care facility, subacute nursing facility, or rehabilitation facility, Medicaid insurance, Pneumonia Severity Index, chronic obstructive pulmonary disease (COPD) exacerbation, congestive heart failure (CHF) exacerbation.
^c *Clostridioides difficile* infection is adjusted for age, antibiotics in prior 90 days, hospitalization in prior 90 days, transfer from post-acute care facility, LOS, Charlson comorbidity index, and proton-pump inhibitor.
^d Antibiotic-associated ADE is adjusted for age, gender, and Charlson comorbidity index
^e Duration of hospitalization is adjusted for age, gender, Charlson comorbidity index, transfer from post-acute care facility, hospitalization in prior 90 days, and expected duration category.
^f Transfer to ICU is adjusted for age, Charlson comorbidity index, hospitalization in prior 90 days, transfer from post-acute care facility, Pneumonia severity index, and Medicaid insurance.
^g Cohort includes 6027 patients because patients who died in the hospital were excluded from this outcome
^h Cohort includes 2173 patients because patients who died in the hospital were excluded from this outcome
 CAP: Community-acquired pneumonia; ED: Emergency Department; ADE: adverse drug event; ICU: Intensive Care Unit.

included hospitalization or treatment with high-risk antibiotics in preceding 90 days, transfer from a postacute care facility, hemodialysis, support with ≥ 3 L supplemental oxygen, severe sepsis, leukocytosis, and higher pneumonia severity index (Fig. 1). After adjustments, patients with

inappropriate empiric BSA treatment had higher readmissions 30 days after discharge, more transfers to the intensive care unit, more antibiotic-associated adverse events, and longer hospitalizations (Fig. 2). **Conclusions:** Patients hospitalized with CAP often received inappropriate BSA as empiric coverage, and this inappropriate antibiotic selection was associated with worse patient outcomes. To improve patient outcomes, stewardship efforts should focus on reducing inappropriate BSA use in patients hospitalized for CAP with historic HCAP risk factors or severe CAP without other guideline-directed indications for BSA.

Financial support. H.M.S. initiative is underwritten by Blue Cross and Blue Shield of Michigan.

Disclosures: None

Antimicrobial Stewardship & Healthcare Epidemiology 2023;3(Suppl. S2):s31–s32

doi:10.1017/ash.2023.258

Presentation Type:

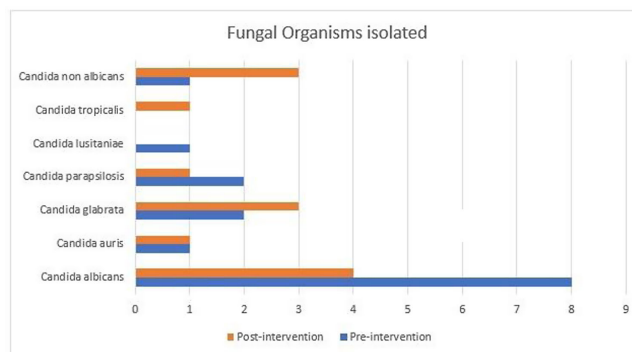
Poster Presentation - Poster Presentation

Subject Category: Antibiotic Stewardship

Effect of antifungal stewardship on micafungin prescribing practices in intensive care units at a tertiary-care hospital

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Background: Fungal diseases are associated with substantial global mortality and economic burden, especially in critically ill or immunocompromised patients. Antifungal resistance has emerged as a barrier to treating invasive fungal infections, but antifungal stewardship is still a developing effort due to limited data. Here, we describe the antifungal prescribing practices and the impact of antifungal stewardship on micafungin days of therapy (DOTs) in critical care units. **Methods:** This retrospective study included patients who



were admitted to the intensive care unit (ICU) at a tertiary-care hospital in Washington, DC. The preintervention group included baseline micafungin use data between January 1, 2021, and May 31, 2021. The postintervention group included prospective audits, feedback on micafungin orders by a clinical pharmacist, and education on the appropriateness of the antifungal agents. The postintervention group included patients admitted between June 1, 2021, and December 31, 2021. Approval was obtained from the institutional review board. **Results:** The overall average of micafungin days of therapy (DOT) per 1,000 patient days present in the preintervention group versus the postintervention group was 33 versus 24 days, respectively. Moreover, 121 patients were randomly selected for a more detailed retrospective review to define micafungin prescribing practices further. Of these, 73 patients (60.3%) were male; the median age was 63 years. The most common cause for prescribing micafungin in both groups was empiric anti-fungal coverage (62.8%), followed by fungemia (12.4%). The most common organism isolated was *Candida albicans*. For other sources of infection and organisms isolated, refer to Table 1. In-hospital mortality occurred in 63 (52.06%) patients in both groups. **Conclusions:** Antifungal stewardship through prospective audit and feedback and education by clinical pharmacists decreased micafungin DOTs in critical care units. Empiric prescribing of micafungin is highly prevalent in the ICU despite the low incidence of invasive fungal infections. Although periodic drug utilization reviews and pharmaceutical surveillance can help reduce the prolonged duration of micafungin therapy in the ICU, more robust and routine antifungal stewardship is key to the appropriate use of micafungin to avoid the emergence of antifungal resistance.

Disclosures: None

Antimicrobial Stewardship & Healthcare Epidemiology 2023;3(Suppl. S2):s32

doi:10.1017/ash.2023.259

Presentation Type:

Poster Presentation - Poster Presentation

Subject Category: Antibiotic Stewardship

Serotonergic agents and linezolid: Impact of exposure to more than one agent concomitantly on risk of adverse effects

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Background: The off-target effects linezolid have the potential to cause serotonin syndrome when given in conjunction with serotonergic agents. Despite package insert labeling as a contraindication, several postmarketing studies have demonstrated a low incidence of serotonin syndrome with the concomitant use of linezolid and other serotonergic agents. Linezolid provides a convenient oral option for gram-positive infections. However, due to concerns for serotonin syndrome, the use of linezolid is sometimes avoided. **Methods:** We performed a single-center, retrospective, medical record review of all adult inpatients from September 2021 to September 2022. Patients included had 1 administration of linezolid and 1 inpatient administration of a selective serotonin reuptake inhibitor (SSRI) or serotonin and norepinephrine reuptake inhibitor (SNRI) within 14 days. The primary outcome was the incidence of serotonin

	All patients	Pre-intervention	Post-intervention
Total no. of patients	121	58	63
Sex, n (%)			
Male	73(60.3)	37(63.7)	36(57.1)
Female	48(39.7)	21(36.3)	27(42.8)
Race, n (%)			
African American	88(72.7)	44(75.8)	44(69.8)
Caucasian	23(19)	11(18.9)	12(19)
Hispanic	4(3.3)	1(1.7)	3(4.7)
Other	6(4.9)	2(3.4)	4(6.3)
Age, Years, Median	63	62	63
Median BMI (kg/m²)	27.53	28.37	27.35
Comorbidities, n (%)			
Diabetes	39(32.2)	17(29.3)	22(34.9)
HIV	5(7.9)	3(5.1)	2(3.2)
Cancer			
Active Cancer	20(16.5)	10(17.2)	10(15.8)
H/o Cancer	4(3.3)	2(3.4)	2(3.2)
On Immunosuppression	20(16.5)	10(17.2)	10(15.8)
Trauma	6(4.9)	3(5.1)	3(4.8)
In house mortality, n (%)	63(52.1)	35(60.1)	28(44.4)
Infection Source, n (%)			
Empiric	76(62.8)	41(70.6)	35(55.5)
Fungemia	15(12.4)	8(13.8)	7(11.1)
Cardiac device	1(0.8)	0	1(1.6)
Abdominal	14(11.6)	4(6.9)	10(15.8)
SSTI	5(4.1)	1(1.7)	4(6.3)
IV catheter/vascular graft	13(10.7)	8(13.8)	5(7.9)
Endocarditis	0	0	0
Osteomyelitis	1(0.8)	1(1.7)	0
Other ^a	9(7.4)	3(5.1)	6(9.5)

a: Including head and neck infections, antifungal prophylaxis etc.

Table 1: Demographic and Microbiological data