

## INTRODUCTION

- Staphylococcus aureus* (SA) is considered one of the leading causes of many invasive infections such as bacteremia, skin and soft tissue infections, osteomyelitis, infective endocarditis, and pneumonia.
- SA infections compared to other infections lead to<sup>1</sup>:
  - 3-fold longer hospital stays
  - 3 times higher costs associated with hospitalization
  - 5-fold increase in mortality
- Methicillin resistant *S. aureus* (MRSA) are more difficult to treat than methicillin susceptible *S. aureus* (MSSA) infections<sup>2</sup>.
- Vancomycin is considered first line therapy for most MRSA infections
  - Therapeutic Drug Monitoring is recommended to optimize efficacy and minimize toxicity
- Vancomycin area under the curve (AUC) over minimum inhibitory concentration (MIC)  $\geq 400$  is considered to be the best predictor for efficacy of *Staph aureus* (SA) infections<sup>4,5</sup>.
- Vancomycin day 2 AUC<sub>24</sub> was identified to be the best estimate of vancomycin exposure near steady state conditions of initial vancomycin regimen<sup>6</sup>.
- Recent study by Lodise et al suggested that AUC<sub>24</sub> and not AUC<sub>24</sub>/MIC would be reasonable to target for vancomycin dosing<sup>6</sup>:
  - Range of Vancomycin MIC by BMD is between 0.5-1mg/L for most MRSA isolates
  - High degree of variability between MIC testing methods
  - MIC values available after 72 hr and cannot be incorporated into empiric dosing
  - However, this study only included patients with *S. aureus* bacteremia

## OBJECTIVES

- Evaluate whether achievement of vancomycin AUC<sub>24</sub> $\geq 400$  on day 2 improved patient outcomes of SA infections.

## STUDY METHODS

- This was a retrospective study of adult hospitalized patients with SA infections and received at least 2 days of vancomycin therapy between 2018-2019.

Inclusion Criteria	Exclusion Criteria
Age $\geq 18$	Unavailable medical chart
Inpatient admission	<48 hours of vancomycin therapy
Positive SA culture $\geq 1$	
Symptoms consistent with infection	

- Study outcomes: 90-day mortality, hospital length of stay (LOS), hospital readmission, nephrotoxicity
- Medical charts were reviewed for pertinent patient clinical data:
  - Demographics/ Medical history
  - Clinical presentation/ Clinical outcomes
  - Microbiological data/ Antimicrobial therapy/ Adverse drug reactions
- Vancomycin dose administrations and blood concentrations.
- Collected data was stored in RedCap.
- Daily vancomycin AUC was determined using BestDose software.
- Patients were grouped based on achieving AUC<sub>24</sub>  $\geq 400$  vs AUC<sub>24</sub>  $< 400$  on day 2 and compared for outcomes
- Statistical methods:
  - Categorical variables were analyzed using chi-square or Fisher's exact test
  - Continuous variables were analyzed using student t-test or Mann Whitney U-test
  - P<0.05 values denoted statistical significance
  - Statistical analysis performed with GraphPad Prism Software

## RESULTS

**Table 1: Baseline Demographics**

	Vancomycin Day 2 AUC <sub>24</sub> $\geq 400$ (N= 52)		Vancomycin Day2 AUC <sub>24</sub> $< 400$ (N= 47)		P-value
	N	%	N	%	
Age	46.00	(33.00, 60.50)	47.00	(39.00, 56.00)	0.6018
Age $\geq 65$	5	9.62	3	6.38	0.7179
BMI	25.85	(20.33, 31.60)	27.55	(23.68, 31.75)	0.2885
<b>Ethnicity</b>					
Hispanic	31	59.62	33	70.21	0.2990
African American	6	11.54	3	6.38	0.4923
Asian	3	5.56	0	0	0.2461
Non-Hispanic White	2	3.85	6	12.77	0.1452
Unknown/ Not reported	7	13.46	5	10.64	0.7635
<b>Gender</b>					
Female	9	17.31	8	17.02	>0.999
<b>Residence prior to admission</b>					
Home	34	65.38	26	55.32	0.4102
Homeless off Street	7	13.46	10	21.28	0.4244
Jail	5	9.62	3	6.38	0.7179
Homeless from Shelter	2	3.85	3	6.38	0.6660
LTC/SNF	2	3.85	2	4.26	>0.999
Other Hospital	1	1.92	2	4.26	0.6027
Rehabilitation Center	0	0	1	2.13	0.4747

**Table 3: Distribution of *S. aureus* infections**

	Vancomycin Day 2 AUC <sub>24</sub> $\geq 400$ (N= 52)		Vancomycin Day 2 AUC <sub>24</sub> $< 400$ (N= 47)		p-value
	N	%	N	%	
<b>Microbiology</b>					
MRSA Nares test positive	7	13.46	2	4.26	0.1645
MRSA infecting pathogen	25	48.08	19	40.43	0.5442
Community onset SA infection	35	67.31	39	82.98	0.1045
<b>Type of SA infection</b>					
Skin and soft tissue infections	26	50.00	31	65.96	0.1538
Pneumonia	15	28.85	6	12.77	0.0834
Osteoarticular	7	13.46	2	4.26	0.1645
Bacteremia	6	11.54	3	6.38	0.4923

**Table 5: Antibiotic Therapy**

	Vancomycin Day 2 AUC <sub>24</sub> $\geq 400$ (N= 52)		Vancomycin Day2 AUC <sub>24</sub> $< 400$ (N= 47)		p-value
	N	%	N	%	
<b>Definitive Antibiotic Therapy</b>					
Vancomycin monotherapy	20	38.46	16	34.04	0.6805
Beta-lactam	14	26.92	14	29.79	0.8248
Vancomycin/Beta-lactam	8	15.38	8	17.02	>0.999
TMP/SMX	3	5.77	5	10.64	0.4718
<b>Inpatient antibiotic duration (days)</b>					
	8.0	(5.00, 14.00)	7.0	(4.00, 12.00)	0.1942
<b>Discharged with antibiotics</b>	24	46.15	31	65.96	0.0681

**Table 2: Comorbidities**

	Vancomycin Day 2 AUC <sub>24</sub> $\geq 400$ (N= 52)		Vancomycin Day2 AUC <sub>24</sub> $< 400$ (N= 47)		p-value
	N	%	N	%	
Diabetes	24	46.15	21	44.68	>0.9999
Hypertension	20	38.46	17	36.17	0.8381
Hyperlipidemia	12	23.08	8	17.02	0.6170
<b>Immunosuppressed States</b>					
States	10	19.23	13	27.66	0.3498
Psychiatric Illness	8	15.38	10	21.28	0.6028
Heart Failure	6	11.54	2	4.26	0.2738
<b>Coronary Artery Disease</b>					
Disease	5	9.62	3	6.38	0.7179
Liver Disease	5	9.62	7	14.89	0.5415
<b>Past Myocardial Infarction</b>					
Infarction	4	7.69	1	2.13	0.3654
<b>COPD/Asthma</b>					
	3	5.77	1	2.13	0.6192
<b>Cirrhosis</b>					
	3	5.77	1	2.13	0.6192
<b>CKD not ESRD</b>					
	3	5.77	0	0	0.2443
<b>Others</b>					
	17	32.69	12	25.53	0.5099
<b><math>\geq 3</math> comorbidities</b>	25	48.08	19	40.43	0.5442

**Table4: Clinical Presentation**

	Vancomycin Day 2 AUC <sub>24</sub> $\geq 400$ (N= 52)		Vancomycin Day2 AUC <sub>24</sub> $< 400$ (N= 47)		p-value
	N	%	N	%	
qSOFA $\geq 2$	12	23.08	7	14.89	0.3217
SIRS $\geq 2$	28	53.85	19	40.43	0.2278
SOFA (median, IQR)*	6.00	(0,10)	1.00	(0,6)	0.0589
ICU admission upon infection onset	32	61.54	13	27.66	0.0011*

\*SOFA score calculated for patients admitted to ICU

**Table6: Clinical Outcomes**

	Vancomycin Day 2 AUC <sub>24</sub> $\geq 400$ (N= 52)		Vancomycin Day2 AUC <sub>24</sub> $< 400$ (N= 47)		p-value
	N	%	N	%	
Clinical Failure	5	9.62	2	4.26	0.440
Length of Stay	9.00	(5.00, 24.50)	7.00	(5.00, 13.00)	0.291
In-hospital mortality	5	9.62	1	2.13	0.208
90-day mortality	8	15.38	1	2.13	0.033*
<b>Re-Admission</b>					
30-day	18	34.62	7	14.89	0.036*
90-day	19	36.54	8	17.02	0.042*
ED visit w/in 1 year	20	38.46	21	44.68	0.547
Re-infection (SA)	9	17.31	7	14.89	0.791
Infection (other)	3	5.77	7	14.89	0.185
Non-infectious	7	13.46	6	12.77	>0.999
<b>ADR</b>					
Hematologic	15	28.85	16	34.04	0.6660
Acute Kidney Injury	10	19.23	1	2.13	0.009*
Liver Enzyme Abnormalities	8	15.38	8	17.02	>0.999
Others	4	7.69	3	6.38	>0.999

## DISCUSSION

- Most common indication for vancomycin was SA SSTI
  - Duration of vancomycin treatment was 1 day longer in AUC<sub>24</sub> $\geq 400$  group (p=0.0111)
- Clinical presentation of AUC<sub>24</sub> $\geq 400$  group was worse:
  - ICU admission at infection onset (AUC<sub>24</sub> $\geq 400$  62% vs AUC<sub>24</sub> $< 400$  28%, p=0.011)
- Outcomes of 90-day mortality (AUC<sub>24</sub> $\geq 400$  15% vs AUC<sub>24</sub> $< 400$  2%, p=0.033), 30-day readmission (AUC<sub>24</sub> $\geq 400$  35% vs AUC<sub>24</sub> $< 400$  15%, p=0.036) were worse in AUC<sub>24</sub> $\geq 400$  group
- Vancomycin associated nephrotoxicity (AUC<sub>24</sub> $\geq 400$  19% vs AUC<sub>24</sub> $< 400$  2%, p=0.0087) was significantly higher in the AUC<sub>24</sub> $\geq 400$  group

## CONCLUSION

- Achievement of vancomycin AUC<sub>24</sub> $\geq 400$  on day 2 was not associated with better clinical outcomes, however, was associated with higher incidence of nephrotoxicity.

## FUTURE DIRECTIONS

- Further evaluate risk factors for vancomycin associated nephrotoxicity
  - Match patients by initial severity of illness and risk factors and re-evaluate outcome of AKI
- Re-evaluate the AUC<sub>24</sub> threshold needed for better clinical outcomes in patients with SA SSTI
  - Currently AUC<sub>24</sub> thresholds are better established for invasive infections such as bacteremia and pneumonia

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