2280. Bloodstream *Klebsiella pneumonia* Infection and Carbapenem Combination Treatment Regimen in High-Dose Vasopressor-Dependent Septic Shock

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Background. The clinical effectiveness of the double-carbapenem combination therapy in mechanically ventilated patients with carbapenemase-producing carbapenem-resistant *Enterobacteriaceae* bloodstream septic shock infection is not well studied.

Methods. Over a 4-year period (2013–2017), critically ill with high-dose vasopressor-dependent septic shock patients due to infections from *Enterobacteriaceae* were included in a single-center retrospective study. The clinical presentation of septic shock was defined in accordance with the international guidelines. Clinical characteristics and the presence of clinical success by the 3rd-day of treatment and 28-day outcome were evaluated. Clinical success was defined as the complete elimination of the vasopressors along with the absence of bacteria regrowth in blood cultures of Enterobacteriaceae. The combination therapy consisted of 1-hour ertapenem (1 g/day) infusion followed immediately by meropenem (6 g/day) in a prolonged 3-hour infusion. The therapeutic regimen was also included gentamicin (7 mg/kg) once daily for 3 total days because of the severity of shock.

Results. A total of 16 ICU patients with bloodstream infection causing septic shock included in the study. The bacterial strain of *Enterobacteriaceae* was exclusive of *Klebsiella pneumonia* isolated after the second week of ICU admission. Antibiotic resistance profile was carbapenem 16/16 (100%), colistin 16/16 (100%), tigecycline 14/16 (87%) aminoglycosides 10/16 (62.5%). Patients were comparable in terms of age, comorbidities, APACHE II score, and presence of concomitant ventilator-associated pneumonia. *Klebsiella pneumonia* bloodstream infection was catheter-related in 5/16 (31%), and the source was not identified in 11/16 (69%). Overall, complete microbiological eradication of *Klebsiella pneumonia* regrowth in blood cultures performed 72 h after therapy was observed in 14/16 (87%) patients, and complete shock resolution in 12/16 (75%). Death at day 28 occurred in 5/16 (31%) patients attributable to multiple organ failure.

Conclusion. The double-carbapenem regimen in critically ill patients suffering high-dose vasopressor-dependent septic shock due to bloodstream infections from *Klebsiella pneumonia* is an effective therapeutic option.

Disclosures. **All authors:** No reported disclosures.

2281. Ceftolozane–tazobactam (C/T) Treatment Outcomes in Immunocompromised (IC) Patients with Multidrug-Resistant (MDR) *Pseudomonas aeruginosa* (PA) Infections

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Background. Evaluations of clinical use and real-world outcomes following C/T treatment exist; however, data assessing outcomes in IC patients are limited. This study evaluated treatment patterns and clinical outcomes of IC patients treated with C/T for MDR PA across 15 US hospitals.

Methods. Adult IC inpatients treated for ≥ 24 hours with C/T admitted between 12/14–5/18 for MDR PA infections were included in this retrospective multicenter cohort study. IC was defined as patients with previous solid-organ transplant (SOT), diseases that suppress resistance to infection (HIV/AIDS, leukemia, lymphoma), or receipt of immunosuppressants, chemotherapy, radiation, long-term low-dose (≥ 1 month) or recent high-dose steroids (> 5 days). Clinical and microbiologic data were extracted from electronic records. The primary outcomes were all-cause 30-day mortality and clinical cure, defined as no escalation/additional therapy and improved signs and symptoms from baseline to end of therapy. PA isolates were characterized as MDR if non-susceptible to ≥ 3 classes of antipseudomonal agents. Classification and regression tree (CART) analysis was used to identify the 30-day mortality split in APACHE II scores.

Results. Seventy patients were included; 58 (83%) had received immunosuppressive agents, 47 (67%) had history of SOT, and 19 (27%) had diseases suppressing resistance to infection. Mean patient age was 57 ± 14 years, median (interquartile range) patient APACHE II and Charlson Comorbidity Index scores were 18 (12.5) and 5 (3.75), respectively, with 33 (47%) receiving ICU care at C/T initiation. The most frequent infection sources were respiratory (56%), wound (11%), intraabdominal (10%), and blood and urine (9% each), with 36% having a polymicrobial culture. All-cause 30-day mortality was 19% (n = 13) with clinical cure achieved in 48 (69%) patients. CART analysis identified the 30-day mortality split at APACHE II score > 25 (76% vs. 24%; P = 0.002).

Conclusion. Of 70 IC patients treated with C/T for MDR PA, clinical cure was achieved in 69% and mortality was 19%, consistent with other evaluations reporting on a cross section of patient populations. C/T represents a promising agent for treatment of PA resistant to many traditional antipseudomonal agents in this high-risk population.

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2282. Empiric Antimicrobial Therapy and Clinical Outcomes of Infections due to ESBL-producing *Klebsiella pneumoniae*

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Background. Currently, carbapenems are the treatment of choice for invasive infection due to extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-E). However, clinical data supporting this practice are generated largely from cases caused by ESBL-producing *Escherichia coli*. We aimed to describe the empiric treatments and clinical outcomes of patients infected with ESBL-producing *Klebsiella pneumoniae* (ESBL-Kp) at UPMC Presbyterian Hospital in Pittsburgh, PA.

Methods. This retrospective study included all adult patients from inpatient admissions at UPMC Presbyterian Hospital who were diagnosed with ESBL-Kp infections. Carbapenem-resistant cases were excluded. Types of cultures included blood, respiratory, urine, and wound. Only one type of culture per patient was included. Demographic and clinical data were collected from the electronic medical records. The study was approved by the University of Pittsburgh IRB.

Results. One-hundred sixty-four patients had ESBL-Kp infection between September 2016 and August 2018. Excluded were those who were considered colonized by the organism and therefore not treated (n = 15); treated with non-carbapenems as definitive therapy (n = 29); or were discharged before final susceptibilities (n = 14). In total, 70 patients met inclusion criteria. Eighteen had bacteremia, 24 had pneumonia, 13 had UTI, and 12 had wound infections. Most common sources of bacteremia included catheter-associated, intra-abdominal infection, and pneumonia. Median age of patients was 62 years. Mean Charleston Comorbidity Index was 4.6. Empiric treatment was divided between three classes: BL-BLI (n = 27, 38.6%), cephalosporins (n = 21, 30%) and carbapenems (n = 18, 25.7%). Twelve patients (17.1%) died during hospitalization. Average hospital length-of-stay was 33.2 days.

Conclusion. Although infections with ESBL-Kp are relatively uncommon, patients have high mortality and prolonged hospitalizations. Treatment practices, including which infections are considered colonization vs. true infection, as well as choice of empirical therapy, vary widely at our institution. Data are still needed to assess mortality outcomes in patients treated empirically with carbapenems vs. non-carbapenems, particularly in high-inoculum infection sites such as pneumonia.

Table 1. Demographics

Variable	N (%)
Sex	39 (55.7%) female
Mean age	57.5 years
Medical comorbidities	
Diabetes mellitus	24 (34.3%)
Liver disease	15 (21.4%)
Malignancy	9 (12.9%)
Chronic kidney disease	20 (28.6%)
Congestive heart failure	17 (24.3%)
COPD	20 (29.0%)
Average Charlson Comorbidity Index	4.6
History of solid organ transplant	17 (24.3%)
On immunosuppression	18 (25.7%)
Hospitalized in past 90 days	37 (52.9%)

Table 2. In-house and 90-day mortality of patients with ESBL *K. pneumoniae* infections

Empiric antibiotic choice	In-house mortality	90-day mortality
Carbapenems (n=18)	**2 (11.1%)**	**4 (22.2%)**
All non-carbapenems (n=54)	**11 (20.4%)**	**11 (20.4%)**
Beta-lactam/beta-lactamase inhibitors (n=27)	7 (25.9%)	7 (25.9%)
Cephalosporins (n=21)	3 (14.3%)	3 (14.3%)
Fluoroquinolones (n=2)	0	0
Other (n=4)	1 (25.0%)	1 (25.0%)

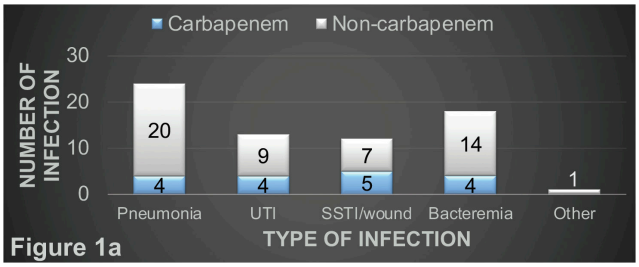

Figure 1a

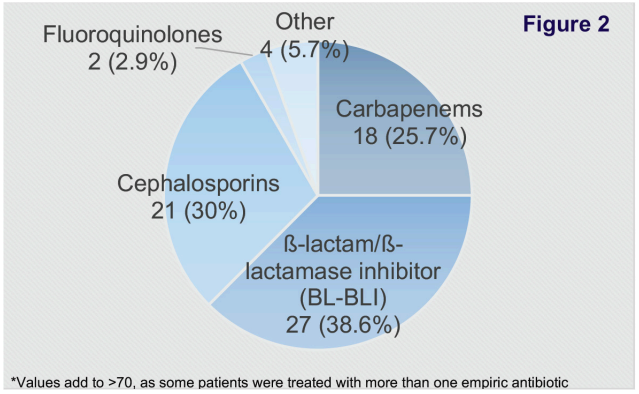

Figure 2

Disclosures. **All authors:** No reported disclosures.

2283. The Incidence and Risk Factors for Neurotoxicity in Patients on Ertapenem Therapy: a Retrospective Case- Control Study

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Background. Numerous reports have emerged about the neurotoxic effects of ertapenem. A recent study supports carbapenem use for the treatment of extended spectrum β-lactamase (ESBL)- producing Gram-negative bacteremia. This will likely bolster the use of ertapenem as it is a convenient choice to complete antibiotic treatment in an outpatient setting. This study aims to review the incidence of neurotoxicity with ertapenem and the risk factors associated with it.

Methods. A retrospective nested cohort study was conducted in Changi General Hospital in Singapore from January 2015 to Decemeber 2016. All patients who received at least 24 hours of ertapenem were identified. Those who exhibited ertapenem-associated neurotoxic effects were selected as cases while those who did not were included in the pool of controls and randomly selected at a 1:3 ratio.

Results. A total of 544 patients were treated with ertapenem in our hospital during this 2-year period. Twenty-five patients (incidence 4.6%) developed neurotoxic manifestations and 75 patients were included as controls. Acute confusion was the commonest reaction (n = 19, 76%) followed by hallucinations (n = 8, 32%) and seizures (n = 5, 20%). Baseline characteristics were similar in both groups; the median age of the cases was 79 years (IQR 71–83 years) and 14 (56%) were males. The median duration of ertapenem use before neurotoxicity occurred was 7 days (IQR 5–11days). The median Naranjo ADR probability score for cases was 7 (range 5 to 7) which suggests a probable relationship. Univariate analysis showed that renal impairment (with CrCl< 60 mL/minute) (OR 3.31, 95% CI 1.03–10.64), a history of a vulnerable brain (including stroke and epilepsy etc)(OR 2.61 95% CI 1.03–6.61) increased the risk of neurotoxicity. Neurotoxicity was also significantly associated with longer hospitalization (median 21 days, p = 0.03).

Conclusion. Our study suggests that renal impairment or a history of vulnerable brain may increase the risk for ertapenem-associated neurotoxicity. Hence, caution should be exercised when ertapenem is used to treat these individuals. Future prospective studies to further evaluate risk and to derive a prediction scoring system may help to reduce the incidence of neurotoxic adverse events with ertapenem use.

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2284. Treatment and Clinical Outcomes Among Infected Patients with Colistin-resistant *Klebsiella pneumoniae* Bacteremia.

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Background. In recent years, the emergence of carbapenem-resistant Klebsiella pneumoniae (CRKP) and colistin-resistant Klebsiella pneumoniae (CoRKP) is one of the leading causes of nosocomial infection worldwide. It has become a public health concern and high mortality, which the few treatment options are available. Salvage treatment caused by CoRKP is still unknown. Here, we explored the 14-day and in hospital mortality to understand the threat to clinical and public health. In addition, we determined the treatment regimen for salvage therapy due to CoRKP bacteremia.

Methods. This was a single-center retrospective cohort study conducted from 2016 to 2018. A total of 96 patients with bacteremia were included; they were classified into three groups according to the infected pathogens with non-carbapenem-resistant Klebsiella pneumoniae (non-CRKP); CRKP and CoRKP. Treatment regimen, 14-day mortality and in hospital mortality were reviewed and compared.

Results. Fifty-eight, 10 and 28 patients infected with non-CRKP, CRKP and CoRKP, respectively. The 14-day mortality rate of patients infected with non-CRKP, CRKP and CoRKP was 12.07%, 40% and 60.71%. In hospital mortality was 24.41%, 70% and 82.14%, respectively. All of mortality outcomes had statistically significant different between both of the CoRKP and CRKP group compare to non-CRKP group ($P < 0.05$). The treatment regimen associated with a favorable outcome on 14-day survival rate in patients with bacteremia due to CoRKP was the antibiotic combination therapy included aminoglycoside (gentamicin or amikacin) with fosfomycin with or without tigecycline. In addition, combination therapy should be avoided prescribing of colistin which supported by lowest survival rate.

Conclusion. Patients infected with CoRKP bacteremia was the highest 14-day and in hospital mortality. However, the new salvage regimen consisting of aminoglycoside with fosfomycin with or without tigecycline combination was associated with favorable the 14-day survival rate.

Table 1. Baseline characteristics of patients infected with *Klebsiella pneumoniae*

Characteristic	non-CR*KP* (n=58)	CR*KP* (n=10)	Co*RKP* (n=28)
Age, median (IQR), y	65 (57-81)	62 (52-76)	66 (61-79)
Male	40 (68.97)	4 (40.00)	18 (64.29)
Source of bacteremia			
Urinary tract	4 (6.90)	1 (10)	0 (0)
Intra-abdominal	9 (15.52)	0 (0)	2 (7.14)
Vascular catheter-related infection	8 (13.79)	1 (10)	9 (32.14)
Pneumonia	7 (12.07)	0 (0)	4 (14.29)
Skin and soft tissue	3 (5.17)	0 (0)	1 (3.57)
Unknown	26 (44.83)	8 (80)	12 (42.86)
Other	1 (1.72)	0 (0)	0 (0)
Surgery within past 7 d	0 (0)	1 (10)	2 (7.14)
ICU admission	17 (29.31)	5 (50)	19 (67.86)
Charlson Comorbidity Index score, median (IQR)	2 (1-4)	2.5 (1.8-4)	3 (1.3-4)
Pitt score, median (IQR)	1 (0-5)	3.5 (1.8-5)	5 (4.25-6.75)
Neutropenia	5 (8.62)	1 (10)	4 (14.29)
Septic shock	24 (41.38)	5 (50)	22 (78.57)
Appropriate empirical antibiotic	48 (82.76)	5 (50)	5 (17.86)
Prior antibiotic use			
Fluoroquinolone	1 (1.72)	1 (10)	5 (17.86)
Cephalosporin	14 (24.14)	3 (30)	18 (64.29)
Carbapenem	2 (3.45)	6 (60)	26 (92.82)
Colistin	1 (1.72)	1 (10)	15 (53.57)
Antibiotic regimen			
colistin-including therapy	3 (5.17)	9 (90)	11 (39.29)
colistin-excluding therapy	-	-	17 (60.71)
Fluoroquinolone-based	2 (3.45)	-	1 (3.57)
cephalosporin-based	34 (58.62)	-	-
β-lactam/β-lactamse inhibitor-based	3 (5.17)	-	-
carbapenem-based	16 (27.59)	-	-
aminoglycoside-based			
AG + FOF	-	1 (10)	8 (28.57)
AG + TGC	-	-	3 (10.71)
AG + FOF + TGC	-	-	3 (10.71)
AG + other *	-	-	2 (7.14)
Treatment duration, median (IQR), d	14 (8-17)	11 (7-14)	11 (4-16)

Abbreviation: AG, aminoglycoside; FOF, fosfomycin; TGC, tigecycline Note: * sulbactam + ciprofloxacin, or imipenem