A Retrospective Review of Treatment Appropriateness and Outcomes of Enterobacteriaceae (with Inducible ampC β-lactamase) Bacteremias at a Large Academic Medical Centre: Opportunities and Implications for Antimicrobial Stewardship

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BACKGROUND

- Timely administration of appropriate empiric antimicrobial therapy is associated with reduced mortality
- Certain *Enterobacteriaceae* have chromosomal ampC β-lactamase genes (may be induced upon exposure to β-lactams and lead to clinical treatment failure)
- Avoiding unnecessary broad-spectrum antibiotics is an important component of antimicrobial stewardship
- There is a lack of published clinical data supporting use of non-carbapenems to treat serious infections due to *Enterobacteriaceae* with inducible ampC β-lactamases

OBJECTIVE

Describe current practice:

- Provide clinical characteristics and outcomes of patients with bacteremia caused by selected *Enterobacteriaceae* with inducible ampC β-lactamase genes at a large, tertiary academic hospital
- Assess appropriateness of empiric and definitive antibiotic regimens chosen to treat these bacteremias

METHODS

- Included all patients with bacteremia caused by *Enterobacteriaceae* with inducible ampC beta-lactamase genes over a 2 year period (2013-2014) at St. Michael's Hospital
  - One organism per patient per admission was included (multiple isolates of the same organism were included if collected on separate admissions)
- Patient characteristics and treatment details included: patient demographics, comorbidities, allergies, laboratory and blood culture and sensitivity results, empiric and definitive antimicrobial therapy against gram negative bacilli (GNB) and clinical outcomes (Table 1)
- Appropriateness of empiric and definitive therapy was assessed by 2 independent reviewers (JY, EL)
  - Antimicrobial therapy was considered appropriate if the organism was reported as susceptible to the chosen agent

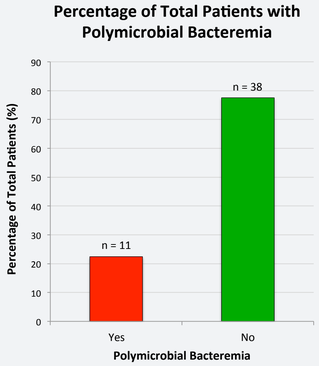
RESULTS

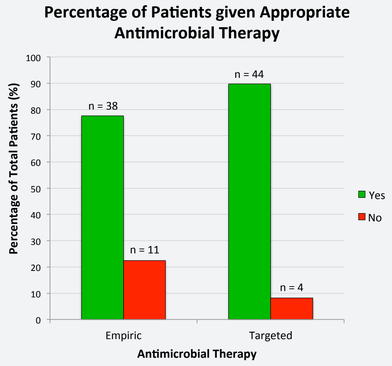
Table 1. Patient Characteristics.

Characteristic	Total patients (n = 49)
Clinical Characteristics	
Male sex, n (%)	39 (80)
Average age (min,max)	60 (18,96)
ICU on day of bacteremia, n (%)	12 (22)
Comorbid medical conditions, n (%)	
Liver disease	11 (22)
Renal disease	12 (24)
Structural lung disease	5 (10)
Neurologic disease	8 (16)
Cardiovascular disease	28 (57)
Immunocompromised	10 (20)
Malignancy	12 (24)
Diabetes mellitus	10 (20)
Laboratory Results, mean (SD)	
WBC count	11.57 (7.90)
Creatinine clearance	79.47 (54.75)
Pathogens Isolated, n (%)	
Enterobacter cloacae	32 (65)
Enterobacter aerogenes	7 (14)
Serratia marcescens	8 (16)
Citrobacter koseri	1 (2)
Citrobacter freundii	1 (2)
Microbiology results, n (%)	
AmpC producing	6 (12)
Also ESBL	3 (6)
Clinical Outcomes	
Survived during hospitalization, n (%)	42 (86)
Hospital length of stay, n (%)	
<20 days	21 (43)
20-40 days	18 (37)
>40 days	10 (20)
Mean hospital length of stay in days, mean (SD)	36.86 (50.53)

GNB Combination (n):	GNB + GP Combination (n):
P/T + CTX (1)	P/T + vancomycin (5)
P/T + CIP (1)	CTX + vancomycin (2)
P/T + LEV (1)	carbapenem + vancomycin (1)
P/T + TOB (1)	P/T + DAP (1)
carbapenem + CIP (1)	CTX + AMP (1)
CTX + AZI (1)	

Legend of Abbreviations:
ampicillin (AMP), azithromycin (AZI), ceftriaxone (CTX), ciprofloxacin (CIP), daptomycin (DAP), fluoroquinolone (FQN), gram negative bacilli (GNB), gram positive (GP), levofloxacin (LEV), piperacillin-tazobactam (P/T), sulfamethoxazole-trimethoprim (SMX-TMP), tobramycin (TOB)

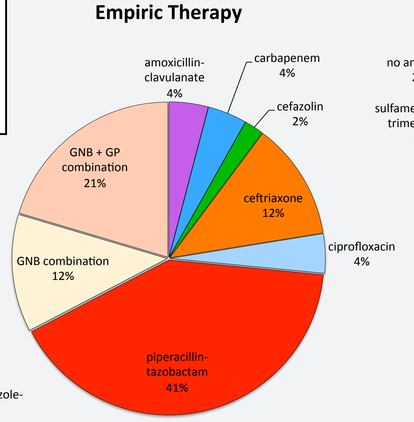


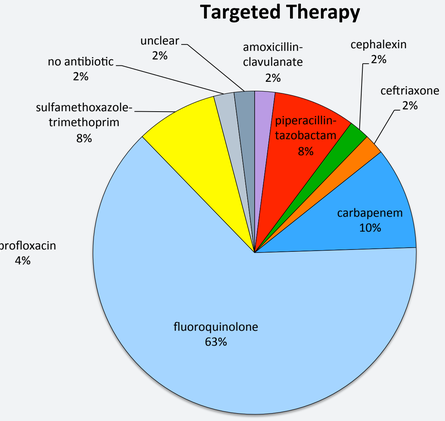


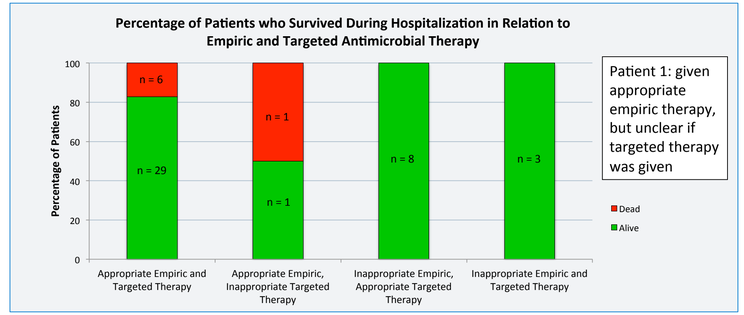
*Targeted Therapy sum does not add to 100%: unclear if targeted therapy was given for Patient 1 (i.e. outpatient prescription)

Table 2. Microbiological Outcomes.

Outcome	Total patients (n = 49)
No cultures from other sources positive, n (%)	41 (84)
Received repeat blood cultures during hospitalization, n (%)	30 (61)
If repeat cultures collected, positive for the same organism, n (%)	5 (10)







Patient 1: given appropriate empiric therapy, but unclear if targeted therapy was given

2013 Antibiogram Data

	Organism	cefotaxime	piperacillin/ tazobactam	imipenem	ciprofloxacin	SMX/TMP
Non-ICU	*Enterobacter cloacae*	77	77	96	95	82
	Enterobacter aerogenes	83	83	100	96	100
	Serratia marcescens	100	100	100	100	100
	Citrobacter freundii	83*	60	92	80	80
	Citrobacter koseri	100	100	100	100	100
MSICU	*Enterobacter cloacae*	71	71	90	95	100
TNICU	*Enterobacter cloacae*	91	94	100	100	94

2014 Antibiogram Data

	Organism	ceftazidime	piperacillin/ tazobactam	imipenem	ciprofloxacin	SMX/TMP
Non-ICU	*Enterobacter cloacae*	71	71	95	87	88
	Enterobacter aerogenes	82	82	94	100	100
	Serratia marcescens	100	100	100	96	100
	Citrobacter freundii	67	67	95	95	67
	Citrobacter koseri	94	94	100	100	100
MSICU	*Enterobacter cloacae*	63	63	95	95	95
TNICU	*Enterobacter cloacae*	63	63	95	95	95
	Enterobacter aerogenes	63	63	95	95	95

NB: cefotaxime susceptibility predicts ceftriaxone susceptibility; in 2013, only ceftazidime susceptibility was reported. * ceftazidime susceptibility = 60%

DISCUSSION AND CONCLUSIONS

- The majority of patients received appropriate empiric and definitive antimicrobial therapy
- Some patients received definitive therapy with a carbapenem, but many received a non-carbapenem agent with similar outcomes
- Non-β-lactams (i.e. sulfamethoxazole-trimethoprim, ciprofloxacin) should be considered as carbapenem-sparing treatment options for these *Enterobacteriaceae* infections
- Limitation: retrospective study with limited sample size
- Future work: ongoing data collection to monitor trends over time

References:
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