Does Antibiotic Resistance Really Contribute to Mortality among Patients with Gram-Negative Blood Stream Infections: A Real World Single Center Study

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Introduction

Antibiotic resistance is always considered an important contributor to mortality among patients with gram-negative blood stream infections (BSI), but host related factors like co-morbidity status, non-infection related factors and severity of sickness are also equally important.

We did this study with objective of determining the true contribution of clinically relevant antibiotic resistance (carbapenems in case of Enterobacterales; *E coli [CRE] & Klebsiella pneumoniae [*CRKP], carbapenems in case of *Acinetobacter baumannii* [CRAB], and resistance to carbapenems, β-lactams and fluoroquinolones in case of *Pseudomonas aeroginosa* [DTR-PA]) in patients with gram-negative BSI.

AMR may not be driving all the mortality among GNB infections.

Patients sickness and co-morbidity also contributes.

> **"We did not find carbapenem resistance as a major contributing factor for death among patients with BSI due to Enterobacterales (*E coli [CRE] & Klebsiella pneumoniae [*CRKP])"**

Methods

This prospective cohort study (June 2023- June 2024) was conducted in a tertiary care hospital in Delhi. All patients found to have mono-microbial gram-negative BSI were included in the study.

Data required to understand basic demographics, Charlson Co-morbidity Index (CCI), Sequential Organ Failure Assessment Score (SOFA), Pitts Bacteremia Score, source of infection, causative organism and its resistance pattern was collected along with crude mortality at day 30 of onset of BSI.

Data was analysed in MS Excel and intergroup analysis between patients alive and dead at day 30 was done. Attributable mortality to CRE, CRKP, CRAB and DTR-PA along with Relative Risk (RR) was also calculated.

Table: Variables of the study cohort

			Univariate Analysis		Multivariate Analysis
Variables	**Mortality (n=76)**	**Alive (n=218)**	**Odds Ratio (95% CI)**	**p-value**	**p-value**
Median Age in Years (Range)	51 (4-74)	53 (13-76)	-	0.232	
Females (%)	30 (38.9%)	102 (46.7%)	0.74 (0.43-1.26)	0.269	
Charlson Co-morbidity Index: Median (Range)	3 (2-11)	4 (0-9)	-	0.641	
SOFA Score: Median (Range)	8 (2-18)	5 (1-10)	-	<0.001	<0.001
Pitts Bacteraemia Score: Median (Range)	2 (0-8)	1 (0-4)	-	<0.001	
Source of BSI					
Intra-abdominal: n (%)	24 (31.5%)	64 (29.4%)	1.11 (0.63-1.95)	0.715	
Urine: n (%)	10 (13.1%)	44 (20.2%)	0.59 (0.28-1.24)	0.173	
Catheter: n (%)	12 (15.7%)	36 (16.5%)	0.93 (0.46-1.91)	0.883	
GI Translocation (Febrile Neutropenia): n (%)	20 (26.3%)	70 (32.1%)	0.74 (0.41-1.34)	0.345	
Hospital Acquired: n (%)	62 (81.6%)	174 (79.8%)	0.75 (0.41-1.37)	0.739	
Organism and Resistance Pattern					
E. coli: n (%)	26 (34.2%)	90 (41.3%)	0.73 (0.42-1.26)	0.277	
CR E. coli: n (%)	6 (23.1%)	22 (24.4%)	0.92 (0.33-2.60)	0.885	
Klebsiella pneumoniae: n (%)	28 (36.8%)	80 (36.7%)	0.99 (0.58-1.70)	0.982	
CR KP: n (%)	16 (57.1%)	40 (50.0%)	1.33 (0.56-3.17)	0.515	
Pseudomonas aeroginosa: n (%)	10 (13.1%)	26 (11.9%)	1.11 (0.51-2.42)	0.778	
DTR Pseudomonas: n (%)	6 (60.0%)	2 (7.6%)	18.0 (2.64-122.6)	<0.001	0.011
Acinetobacter baumannii: n (%)	8 (10.5%)	4 (1.8%)	6.23 (1.82-21.3)	<0.001	
CRAB: n (%)	8 (100%)	0 (0%)	-	<0.001	

	CRAB (n=8)	CR E. Coli (n=28)	CRKP (n=56)	DTR Pseudomonas (n=8)
Attributable Mortality to Carbapenem Resistance (Relative Risk)	100% (∞)	6.07% (0.94)	19.2% (1.2)	77.3% (5.35)

Results

- A total of 294 patients were identified (Median age: 52 years [Range: 4-76]; females (n=132)) during the study period.
- Most of the infections were hospital acquired (n= 236; 80%) and most common source of infection was GI translocation (n=90; 30.5%) followed by intra-abdominal (n= 88; 29.8%) and then by urinary (n= 54; 18.3%).
- Most common organism was *E coli (*n= 116; 43.7%) followed by *Klebsiella pneumoniae* (n= 108; 40.7%). Overall mortality at day 30 happened in 28.6% (n=76) patients.
- Univariate analysis [Table 1] between patients alive (n=218) and dead (n=76) at day 30 revealed that higher SOFA score (p <0.001) and higher Pitts Bacteremia score (p <0.001) predicted mortality and not resistance in Enterobacterales (CRE, p = 0.885; CRKP, p = 0.515), age (p=0.232) or CCI (p=0.641).
- On multivariate regression analysis, higher SOFA score (p< 0.001) and BSI due to DTR-PA (p = 0.011) were found to be independent predictors of mortality.
- Relative risk of dying due to CRE and CRKP was 0.94 and 1.2 respectively.

Conclusion

We did not find carbapenem resistance as a major contributing factor for death among patients with BSI due to Enterobacterales (*E coli [CRE] & Klebsiella pneumoniae [*CRKP*]*) in our study cohort with limitation that it is a single centre study and other important pathogens like DTP-PA and CRAB were not recruited in good numbers.