Multi-Drug Resistant and Extensively Drug-resistant Enterobacteriaceae: Prevalence, Treatments, and Outcomes

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Deanship of Scientific Research

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Introduction

- Antimicrobial resistance is an emerging problem that affects public health.[1]
- More than 70% of the bacteria that cause infections acquired in hospitals are resistant to ≥one of the drugs most commonly used to treat them.[2]
- There are 3 types of antimicrobial resistance: multi-drug resistance (MDR), extensive-drug resistance (XDR), and pan-drug resistance (PDR).[3]
- Limited data are available in the region regarding resistance rates, treatment approaches, and clinical outcomes for patients infected with resistant gram-negative bacteria.[1]
- Raising awareness of antimicrobial resistance is essential to limit inappropriate use of antibiotics in the hospital setting.

Objectives

- Describe the prevalence of MDR and XDR Enterobacteriaceae infections including: *Klebsiella pneumoniae*, *Escherichia coli*, and *Enterobacter* in intensive care unit (ICU) setting.
- List the common empirical therapies used and whether they were appropriate or not.
- Report the microbiological cure rate, ICU length of stay (LOS), and hospital mortality rates in subjects admitted to the ICU with these infections.

Methods

Study Design and Setting:

Retrospective cohort study conducted from 2015-2018 at the ICUs in King Saud University Medical City.

Population:

- Adults admitted to the ICUs
- Positive cultures for MDR or XDR *Enterobacteriaceae*: *Klebsiella pneumonia*, *Escherichia coli*, and *Enterobacter* regardless of site of infection

Data Collection:

Demographics, microbiological, medications, and mortality data were collected.

Methods

Definitions:

Multidrug-resistance (MDR):

Non-susceptibility to at least 1 agent in ≥3 antimicrobial categories.[3]

Extensive drug-resistance (XDR):

Bacterial isolates remain susceptible to only 1-2 categories.[3]

Appropriate empirical regimen:

If a patient received at ≥1 antimicrobial agent to which the causative microorganisms were susceptible within 24 hour of culture collection.[4]

Statistical Analysis:

- Descriptive analysis using mean ± standard deviation and frequencies were used when appropriate.
- Ethical approval was obtained.

Results

Prevalence of Resistance:

- 227 Enterobacteriaceae cultures.
- >60% were either MDR, or XDR bacteria

Figure 1: Prevalence of MDR, and XDR Infections

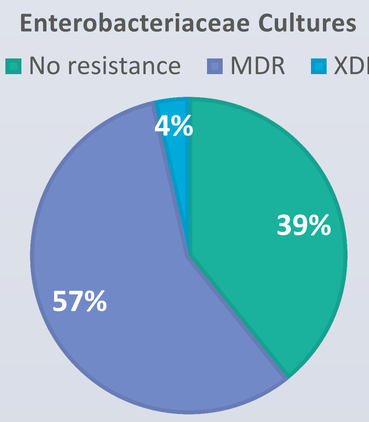

Table 1. Baseline Characteristics

		MDR (n=130)	XDR (n=8)
Gender	Male	58 (45%)	6 (75%)
Age (years)		60 ± 17	63 ± 16
Comorbidities	Diabetes	69 (53%)	6 (75%)
	Cancer	27 (21%)	0 (0%)
Bacteria	Escherichia Coli	71 (55%)	0 (0%)
	Klebsiella Pneumoniae	40 (31%)	5 (63%)
	Enterobacter species	19 (15%)	3 (38%)
Source	Urine	34 (26%)	0 (0%)
	Wound	16 (12%)	0 (0%)
	Blood	15 (12%)	0 (0%)
	Sputum	14 (11%)	0 (0%)
	Tracheal Aspirate	11 (8%)	1 (13%)
	Central line	10 (8%)	2 (25%)
	Urinary Catheter	7 (5%)	1 (13%)
	Peritoneal Fluid	6 (5%)	1 (13%)
	Tissue	5 (4%)	2 (25%)
	Other	12 (10%)	1 (13%)
Ventilation		79 (61%)	6 (75%)
ESRD		24 (18%)	2 (25%)
Prior 90 days Antibiotics use		102 (78%)	8(100%)
Prior 4 weeks Antibiotics use		92 (71%)	7 (88%)
Inotropes		71 (55%)	4 (50%)
ICU length stay ≥ 72 hours		55 (42%)	8 (100%)

Data presented as number and (percentage)
ESRD: End stage renal disease; ICU: Intensive care unit

Results

Use of Antibiotics:

Figure 2: Number of Antibiotics Used

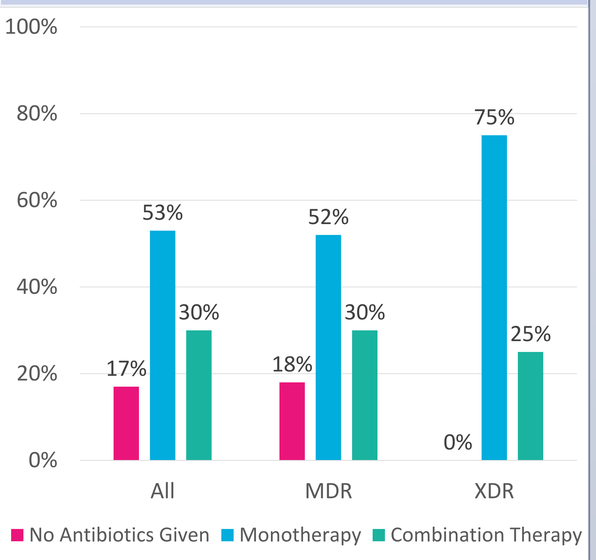

Figure 3: Percentage of Appropriate Antibiotics Prescribed

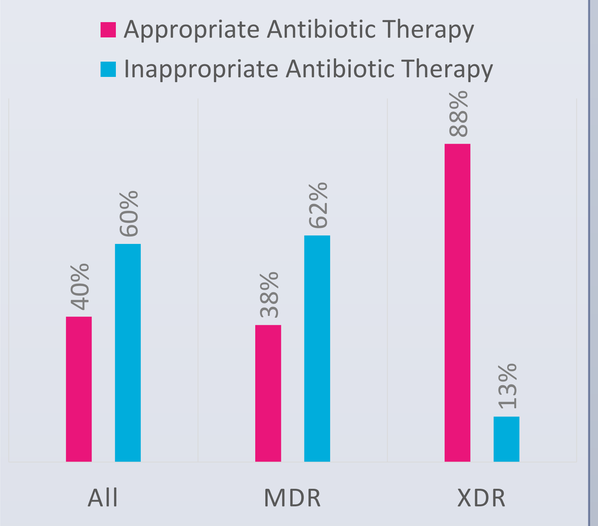

Table 2: Most Frequently Used Antibiotics

Type of Therapy	Antibiotic Used	MDR	XDR
Mono-Therapy	Piperacillin/ Tazobactam	31 (24%)	2 (25%)
	Carbapenem	22 (17%)	2 (25%)
	Colistin	1 (1%)	0 (0%)
Combination Therapy	Carbapenem + Aminoglycoside	7 (6%)	1 (1%)
	Fluoroquinolone + Piperacillin/ Tazobactam	7 (6%)	0 (0%)
	Carbapenem + Piperacillin/ Tazobactam	7 (6%)	0 (0%)
	Carbapenem + Fluoroquinolone	1 (1%)	1 (13%)

Outcomes:

Table 3: Patients Outcomes

	MDR (n=130)	XDR (n=8)
ICU LOS (days), median (IQR)	14 (28)	38.5 (20.3)
Microbiological cure, N (%)	52 (40%)	4 (50%)
Mortality, N (%)	108 (83%)	7 (79%)

ICU: Intensive care unit; IQR: Interquartile range; LOS: Length of stay; N= Number

Conclusions

- In an ICU setting there was high prevalence of resistant *Enterobacteriaceae* infections.
- Most infections were treated with piperacillin/tazobactam or carbapenems.
- Most patients with XDR infections received inappropriate therapy.
- Mortality rates in subjects with these infections were generally high.
- This study highlight the importance of appropriate antibiotic selection and have been shown to be effective at minimizing the negative clinical and economic consequences associated with antibiotic resistant organisms.

Acknowledgment

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References

1- Hasanin A, et al. Prevalence of extensively drug-resistant gram negative bacilli in surgical intensive care in Egypt. *Pan Afr Med J.* 2014;19:177.

2- Natarajan S, et al. Demographical Study of Extensive Drug-Resistant Gram-Negative Bacteria with Precise Attention on XDR Uropathogen E.coli. *Int.J.Curr.Microbiol.App.Sci.* (2015) 4(10 :(794-806 .

3- Magiorakos A, et al. Extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard):268-281. definitions for acquired resistance. *Clin Microbiol Infect.* 2012;18(3)

4- Kang, Cheol-In, et al. Bloodstream infections caused by antibiotic-resistant gram-negative bacilli: risk factors for mortality and impact of inappropriate initial antimicrobial therapy on outcome. *Antimicrob agents ch.* 49.2 (2005): 760-766.

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