Clinical Outcomes and Safety of **Polymyxin-B-Based Combination Therapy** in the Treatment of Multidrug-Resistant Gram-Negative Infections in Children

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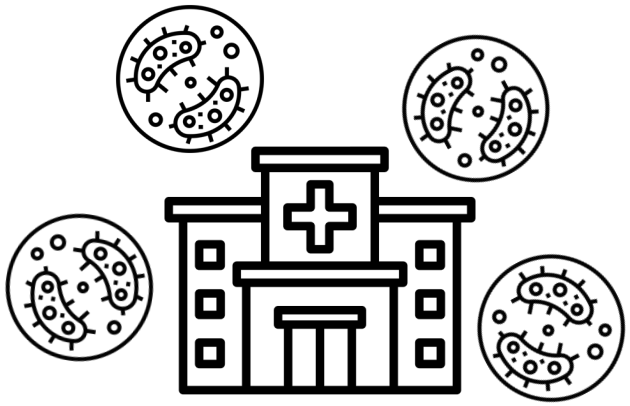
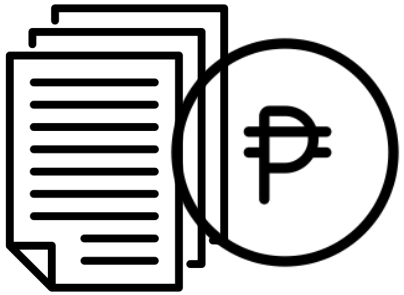
Why did we do this study and why is this significant?



MDR is not an emerging problem anymore.



Access to novel antibiotics is limited.

Data on the use of polymyxin B in children are also limited.

INTROP. Annual and Midyear Nosocomial Infection Rate Report 2022. Manila, Philippines. Division of Infectious and Tropical Diseases in Pediatrics, Department of Pediatrics, University of the Philippines – Philippine General Hospital

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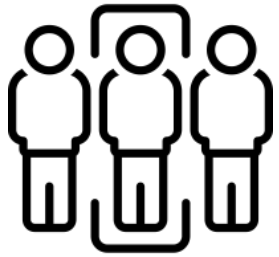
Thomas R, Velaphi S, Ellis S, et al. The use of polymyxins to treat carbapenem resistant infections in neonates and children. Expert Opin Pharmacother. 2019;20(4):415-422. doi:10.1080/14656566.2018.1559817

Jia X, Yin Z, Zhang W, Guo C, Du S, Zhang X. Effectiveness and nephrotoxicity of intravenous polymyxin B in carbapenem-resistant Gram-negative bacterial infections among Chinese children. Front Pharmacol. 2022;13:902054. Published 2022 May 27. doi:10.3389/fphar.2022.902054

Siddiqui NU, Qamar FN, Jurair H, Haque A. Multi-drug resistant gram negative infections and use of intravenous polymyxin B in critically ill children of developing country: retrospective cohort study. BMC Infect Dis. 2014;14:626. Published 2014 Nov 28. doi:10.1186/s12879-014-0626-9

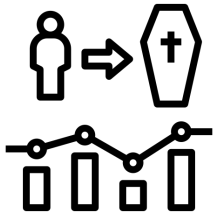
The objectives of this study are:



To describe the **demographic profiles** in terms of age, sex, and area of admission

To describe the **clinical profiles** in terms of comorbidities, types and sites of infection, pathogens, clinical manifestations, and laboratory markers

To describe the **outcomes**... and **adverse events**



14-day mortality

Bacteriologic cure

Clinical response

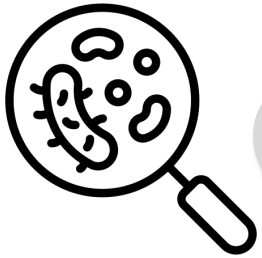
Adverse events

Pathogen isolated, level of resistance, and antibiotic regimen

This is a 31-month (Dec 2020 - Jun 2023) retrospective chart review of pediatric patients.

Inclusion Criteria

- Pediatric inpatient
- Diagnosed with infection
- Lab-confirmed GN bacterial isolate
- MDR
- PmB+Abx ≥48h



Excluded

4 culture-negative
- 1 rectal swab culture-positive
- 1 BioFire-positive

33 non-MDR GN isolates

28 polymyxin B <48 hours (0-3 doses)

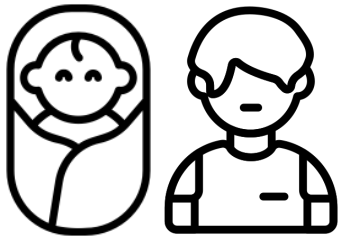
Included

172 episodes in 136 patients

Based on the demographic and clinical profiles…

Range: **2d – 18y**
Mean: **3y**
Median: **1 mo** (IQR 3y)

N = 136
Preterm neonates = **44** (32.3%)
Male = **72** (52.9%)
NICU = **70** (51.5%)
Cardiovascular = **40** (29.4%)
Recent surgery = **23** (16.9%)



N = 172
Tachycardia = **126** (73.2%)
Shock = **58** (33.7%)
Fever = **94** (54.7%)
Tachypnea = **84** (48.8%)
Desaturations = **69** (40.1%)
Abdominal distension = **34** (19.8%)
Pallor = **25** (14.5%)

Abnormal PLT count = **111/168** (66.1%)
Abnormal WBC count = **86** (50%)
Elevated CRP = **96/109** (88.1%)
Elevated Procal = **117/165** (70.9%)
Hypoglycemia = **42/129** (32.6%)

The most prevalent infection is of the **bloodstream**, with ***Klebsiella pneumoniae*** as the most common etiologic agent.

	NCLABSI	CLABSI	PNA	UTI	SSI	SSTI	IAI	CNSI	Total
ENTERO	29	33	20	4	4	1	2	4	97 (56.4)
K.pneu	19	25	18	2	2		1	3	70
K.oxy	5	5							10
E.coli	4		1	2	1		1	1	10
E.cloa		3	1		1				5
C.freu						1			1
C.werk	1								1
ACINETOB	14	15	25			5		5	64 (37.2)
A.bau	13	14	24			4		5	60
A.john			1						1
A.nos						1			1
A.pittii		1							1
A.ursu	1								1
PSEUDOM	1	5	4			1			11 (6.4)
TOTAL	44 (25.6)	53 (30.8)	49 (28.5)	4 (2.3)	4 (2.3)	7 (4.1)	2 (1.2)	9 (5.2)	172

Outcomes

14-day mortality

45 deaths out of 172

26%

Bacteriologic cure failure rate

17 failed out of 112

15%

Clinical response failure rate

32 failed out of 172

19%

PmB Regimens per Bacterial Group

Meropenem (MEM)- vs. Fluoroquinolone (FQ)-containing

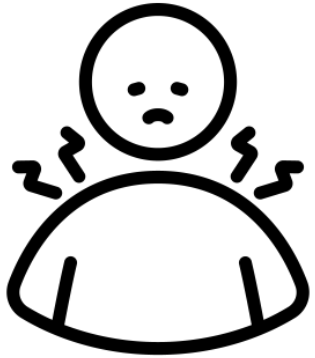
Enterobacterales	MEM		**FQ**
***Acinetobacter* spp.**	**MEM**		FQ
P. aeruginosa	MEM		FQ

Numerically, FQ had more favorable outcomes in Enterobacterales vs. MEM for *Acinetobacter* spp. *P. aeruginosa* had conflicting data on which regimen is better overall. *However, there are no statistically significant differences in outcomes between the regimens in all bacterial groups.*

There were only 8 documented cases of diagnosed adverse drug events.

Tubulopathy
5 cases

Anaphylaxis
2 cases



Neurotoxicity
1 case

Discussion, Conclusion, and Recommendations

Profiles = risk factors, consistent with literature

Management needs to be multifaceted to be optimal.

N=172 is the largest so far, yet still small; still an underestimation;
Recom: Larger size in future studies

Polymyxin B is a **safe and effective** option in our setting.

Outcomes are comparable with or more favorable than in other studies

MEM and FQ are good partner antibiotics; one may be numerically favored over the other, depending on isolate.

Aguilera-Alonso D, Escosa-García L, Saavedra-Lozano J, Cercenado E, Baquero-Artigao F. Carbapenem-Resistant Gram-Negative Bacterial Infections in Children. Antimicrob Agents Chemother. 2020;64(3):e02183-19. Published 2020 Feb 21. doi:10.1128/AAC.02183-19

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