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Co, KJA, Ong-Lim, ALT. Prevalence of Rectal Carbapenem-Resistant Organism Colonization Among Neonates Admitted in the Neonatal Intensive Care Unit of the Philippine General Hospital
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ORIGINAL ARTICLE

PREVALENCE OF RECTAL CARBAPENEM-RESISTANT ORGANISM COLONIZATION AMONG NEONATES ADMITTED IN THE NEONATAL INTENSIVE CARE UNIT OF THE PHILIPPINE GENERAL HOSPITAL

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ABSTRACT

Objective: To determine the prevalence of rectal colonization with carbapenem-resistant organisms (CRO) among PGH neonatal intensive care unit (NICU) patients.

Methodology: A prospective single-center observational study conducted over a 1-month period included all NICU 3 and cohort area patients admitted on April 24, 2024. Rectal swabs were collected for multidrug-resistant organism (MDRO) screening and repeated weekly for 1 month while admitted. Swabs were inoculated on chromogenic media, and isolates were identified and tested for antimicrobial sensitivity by disk diffusion. Clinical characteristics and outcomes were collected for 30 days from initial MDRO screening. Descriptive statistics were used to summarize the data.

Results: The point prevalence of CRO colonization was 37% (14 of 38) at initial screening. There were 14 incident colonizations, hence the 4-week period prevalence of CRO colonization was 72.5% (29 of 40). The patients were mostly very preterm, very low birth weight neonates, majority were tested within the first 2 weeks of life, and half were exposed to meropenem at initial screening. Nosocomial infection developed in 29% and 64%, and 30-day mortality rate was 8% and 21% among initially non-CRO-colonized and CRO-colonized patients respectively. Despite high CRO colonization, no culture-proven CRO infection was observed. Surveillance screening documented persistent CRO colonization in 37%, but no decolonization. *Escherichia coli*, *Klebsiella* spp. and *Serratia* spp. were the most common colonizers.

Conclusion: The high prevalence of rectal CRO colonization in the NICU emphasizes the burden of antimicrobial resistance, but despite the high CRO colonization, no CRO infection was documented from the limited sample and study period.

KEYWORDS: *Newborn, Carbapenem-Resistant Enterobacteriaceae, Multidrug Resistance*

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The authors declare that the data presented are original material and have not been previously published, accepted or considered for publication elsewhere; that the manuscript has been approved by all authors, and that the authors have met the requirements for authorship.

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INTRODUCTION

In 2023, the Philippine General Hospital (PGH) neonatal intensive care unit (NICU) reported a healthcare associated infection (HAI) rate of 17.9 infections per 1000 patient-days, increasing in trend from 9.9 infections per 1000 patient-days documented between 2011 to 2014.[1] The current rate is higher than the international NICU HAI rate per 1000 patient-days of 3.2 in Italy (2013-2017)[2], 15.6 in Turkey (2014)[3], 7.3 in China (2015-2018)[4], and 8.1 in India (2022)[5]. Furthermore, in 2023, 58% of the PGH NICU culture-proven infections were due to multidrug-resistant organisms (MDRO). The unit also has a high rate of carbapenem use, since meropenem is the empiric antibiotic recommended for nosocomial infections. In addition, due to the increasing burden of MDRO infection, empiric combination regimens using polymyxin B are also used in high-risk patients to target extensively drug-resistant organisms.

MDRO colonization has been explored as a risk factor for MDRO infections, hence identification of MDRO colonized patients and cohorting are included in the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) guidance for infection prevention and control.[6,7] To mitigate the rise in MDRO infection, several studies are exploring interventions to effect decolonization using oral antimicrobials, probiotics and fecal microbiota transplant. Decolonization strategies aim to prevent eventual development and spread of MDRO infections.

Determining MDRO colonization can facilitate cohorting of colonized neonates, identify possible risk factors for developing MDR infections and to identify novel measures to improve infection control measures. In the context of a NICU with high burden of nosocomial infections and high rates of carbapenem use, this study aims to determine the prevalence of rectal colonization with carbapenem-resistant organisms (CRO) among NICU patients in a tertiary government hospital in the Philippines.

MATERIALS AND METHODS

This was a prospective single-center observational study conducted from April to May 2024 at a NICU catering to inborn neonates in a tertiary government hospital in Manila, Philippines. The PGH NICU has three main areas: 1) NICU 3 for ill newborns requiring close monitoring, 2) NICU 2 for stable newborns requiring specialized nursing care and as a stepdown area for patients transferred from the NICU 3, and 3) NICU cohort area for isolation of patients with culture-proven nosocomial infections or clinically diagnosed drug-resistant infections. Purposive sampling was done, and the study included all neonates who were admitted at the NICU 3 and cohort areas on April 24, 2024. Patients with congenital anomalies of the rectum or anus were excluded. The protocol was approved by the University of the Philippines Manila Research Ethics Board. Institutional infection prevention and control protocols were followed during the conduct of the study.

Demographic, clinical and outcome data of each patient were collected from the medical charts. The clinical characteristics included age, gestational age, birthweight, maternal infection and hospitalization, comorbidities, antibiotic use, central line use, respiratory support, and feeding status; outcome data included incidence of nosocomial infection, type of infection and culture results, and 30-day mortality. Rectal swabs for culture were collected from all patients admitted at the NICU 3 and cohort areas on April 24, 2024, and this population was swabbed weekly for 1 month while admitted at the NICU. The colonization surveillance sought to identify new MDRO colonization (positive rectal swab after a negative initial rectal swab), persistent MDRO colonization (two or more consecutive positive rectal swab) and decolonization (three consecutive negative rectal swabs after a positive rectal swab). Short-term clinical outcomes were observed for 30 days from the first rectal swab collection, or until discharge from the NICU, whichever was earlier.

Rectal MDRO screening

Rectal MDRO screening for CRO was performed by collecting stool samples using rectal swabs, which were transported in nutrient broth tubes. Samples were sent to the laboratory (Department of Microbiology, University of the Philippines College of Public Health) for culture. Rectal swabs for rectal MDRO screening were directly inoculated on the surface of a chromogenic media (CHROMagar™ mSuperCARBA™) to detect CRO. Plates were incubated at 37 degrees Celsius for 24 hours. After 24 hours, if no colonies were detected, incubation was continued until 48 hours. If no growth was further observed, the screening was reported as negative. A positive screening was reported if colonies were isolated.

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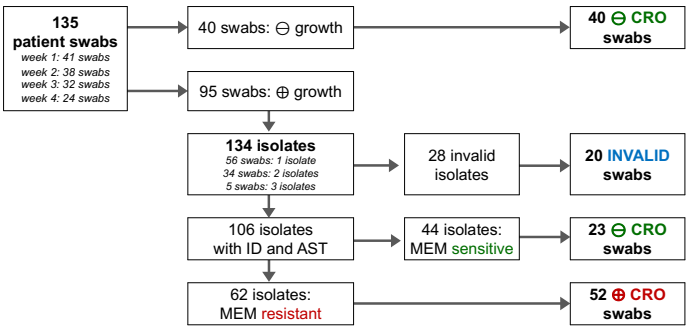
Each unique colony was subcultured to perform identification (ID) testing and antibiotic sensitivity testing (AST) via disk diffusion. Clinical and Laboratory Standards Institute (CLSI) breakpoints were used.

Data Analysis

Prevalence of rectal CRO colonization was computed by dividing the patients with positive rectal swab by the total number of patients tested. The patient's demographic, clinical and outcome data were summarized using descriptive statistics and reported as frequencies and proportions using Microsoft Excel. The microbial isolates were tabulated to reflect their antibiotic susceptibility pattern.

RESULTS

On April 24, 2024, rectal swab for initial MDRO screening were collected from 41 patients, and weekly surveillance swabs were taken from the remaining 38, 32 and 24 patients on weeks two to four. Among the 135 rectal swabs, 95 had growths on the chromogenic media with 134 isolates. Figure 1 summarizes the results from the rectal MDRO screening. Subculture did not grow for 28 isolates; hence, 20 (15%) swabs were interpreted as invalid swabs since AST could not be performed (Figure 1). Three invalid swabs were the initial MDRO screening at week 1, leaving 38 patients with valid initial MDRO screening.



Acronyms: ID: Identification, **AST:** Antibiotic susceptibility testing, **MEM:** Meropenem

Figure 1. Summary of rectal MDRO screening results over four weeks

Among the 38 neonates with valid screening on week 1, the median age was 14 days, where the majority were very preterm with a mean birthweight of 1357g. All patients had medical comorbidities, 11 patients had congenital anomalies, and seven patients were part of twin gestations, with two pairs of twins, one pair of conjoined twins, and one patient whose twin died prior to study initiation (Table 1). Four (11%) patients had surgical history, one underwent exploratory laparotomy for gastric rupture, and the rest underwent surgical repair for their congenital anomalies: congenital diaphragmatic hernia, patent omphalomesenteric duct and patent ductus arteriosus. At week 1, majority had a history of nosocomial infection. Among the 26 patients receiving antibiotics, eleven were given broad-spectrum antibiotics, either a carbapenem, quinolone or a polymyxin-based combination therapy (Table 2).

The point prevalence of rectal CRO colonization on initial MDRO screening among patients admitted at the NICU 3 and cohort areas was 37%. Tables 1 and 2 show the baseline and clinical characteristics of the 24 non-CRO-colonized (nCRO-C) and 14 CRO-colonized (CRO-C) patients on week 1.

Table 1. Baseline characteristics among colonized and non-colonized neonates at week 1

	All Patients (N=38)	MDRO screening on week 1	
		Non-colonized (N=24)	Colonized (N=14)
Median age/ length of NICU stay at enrollment (day, range)	**14 (0 – 121)**	**5 (1-87)**	**21 (0-121)**
Median gestational age (weeks, range)	**31 (27 – 41)**	**31 (27-39)**	**31 (27-41)**
Term (≥ 37 weeks)	2 (5%)	1 (4%)	1 (7%)
Late preterm (34 to ≤36 weeks)	2 (5%)	2 (8%)	0 (0%)
Early preterm (32 to <34 weeks)	9 (24%)	5 (21%)	4 (29%)
Very preterm (28 to <32 weeks)	21 (55%)	14 (58%)	7 (50%)
Extremely preterm (<28 weeks)	4 (11%)	2 (8%)	2 (14%)
Mean birthweight (grams, range)	**1357 (480-3080)**	**1400 (530-3080)**	**1353 (480-2970)**
≥ 2500	2 (5%)	1 (4%)	1 (7%)
1500 - 2499	11 (29%)	6 (25%)	5 (36%)
1000 - 1499	14 (37%)	12 (50%)	2 (14%)
<1000g	11 (29%)	5 (21%)	6 (43%)
Manner of delivery			
Vaginal delivery	7 (18%)	4 (17%)	3 (21%)
Caesarian section	31 (82%)	20 (83%)	11 (79%)
Maternal Infection	**31 (82%)**	**19 (79%)**	**12 (86%)**
Prolonged maternal hospitalization (≥ 48 hours)	**12 (32%)**	**7 (29%)**	**5 (36%)**
COMORBIDITIES AT BIRTH			
Medical conditions at birth	**38 (100%)**	27 (100%)	14 (100%)
Respiratory distress syndrome	*25 (66%)*	16 (67%)	9 (64%)
Neonatal pneumonia	*11 (29%)*	8 (33%)	3 (21%)
Transient tachypnea of the newborn	*7 (18%)*	5 (21%)	2 (14%)
Early onset neonatal sepsis	*5 (13%)*	3 (13%)	2 (14%)
Congenital anomalies	**11 (29%)**	**7 (29%)**	**4 (29%)**
Multiple congenital anomalies	*5 (13%)*	3 (13%)	2 (14%)
Congenital GI tract anomalies	*3 (8%)*	3 (13%)	0 (0%)
Isolated congenital heart disease	*3 (8%)*	2 (8%)	1 (7%)
Other congenital anomalies	*3 (8%)*	2 (8%)	1 (7%)
Twin gestation	**7 (18%)**	**4 (17%)**	**3 (21%)**

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Table 2. Clinical characteristics among colonized and non-colonized neonates at week 1

	All Patients (N=38)	MDRO screening on week 1	
		Non-colonized (N=24)	Colonized (N=14)
History of surgery	**4 (11%)**	**4 (17%)**	**0 (0%)**
Central line	**17 (45%)**	**11 (46%)**	**6 (43%)**
Umbilical/ Intrajugular	*9 (24%)*	*8 (33%)*	*1 (7%)*
PICC	*8 (21%)*	*3 (13%)*	*5 (36%)*
Respiratory support			
Room air	21 (55%)	12 (50%)	9 (64%)
Non-invasive ventilation	9 (24%)	6 (25%)	3 (21%)
Intubated	8 (21%)	6 (25%)	2 (14%)
Feeding			
NPO	16 (42%)	11 (46%)	5 (36%)
Trophic feeding (≤30% TFI)	6 (16%)	4 (17%)	2 (14%)
Feeding (>30%TFI)	6 (16%)	5 (21%)	1 (7%)
Full feeding (≥100% TFI)	10 (26%)	4 (17%)	6 (43%)
History of nosocomial infection	**19 (50%)**	**9 (38%)**	**10 (71%)**
1 bout of CN infection	*11 (29%)*	*6 (25%)*	*5 (36%)*
≥ 2 bouts of infections, at least 1 CP	*4 (11%)*	*2 (8%)*	*2 (14%)*
≥ 2 bouts of CN infections	*3 (8%)*	*1 (4%)*	*2 (14%)*
1 bout of CP infection	*1 (3%)*	*0 (0%)*	*1 (7%)*
ANTIBIOTIC EXPOSURE			
Ongoing antibiotic therapy	**26 (68%)**	**16 (59%)**	**10 (71%)**
Ampicillin	*9 (24%)*	*8 (33%)*	*1 (7%)*
Cefotaxime/Ceftazidime	*6 (16%)*	*4 (17%)*	*2 (14%)*
Meropenem	*8 (21%)*	*3 (13%)*	*5 (36%)*
Ciprofloxacin/Levofloxacin	*1 (3%)*	*0 (0%)*	*1 (7%)*
Polymixin-based therapy	*2 (5%)*	*1 (4%)*	*1 (7%)*
Recent antibiotic exposure*	**7 (18%)**	**6 (25%)**	**1 (7%)**
No antibiotics in the past 2 weeks	**5 (13%)**	**2 (8%)**	**3 (21%)**
History of carbapenem use	**19 (50%)**	**9 (38%)**	**10 (71%)**

PICC: Peripherally Inserted central catheter; **TFI**: total fluid intake, **CP**: Culture positive, **CN**: Culture negative
*antibiotic exposure within 2 weeks

The median age for nCRO-C is 5 days, while for CRO-C it is 21. For the twin gestations, two pairs were both nCRO-C, while one pair was CRO-C. The three patients with congenital GI tract anomalies and four with surgical history were all nCRO-C at initial screening. The most common ongoing antibiotic was ampicillin (33%) for nCRO-C, and meropenem (36%) for CRO-C. History of nosocomial infection and meropenem use were 38% for nCRO-C, and 71% for CRO-C. A patient was being treated for persistent meropenem-sensitive *Klebsiella pneumoniae* central line related bloodstream infection (CRBSI) with polymyxin and ciprofloxacin for clinically progressing infection. The central line could not be removed, and bacteremia persisted on the second week of antibiotics, hence regimen was shifted to polymyxin, meropenem and amikacin. The patient eventually died, and the initial MDRO screening revealed colonization with meropenem-resistant *K. pneumoniae* and *Escherichia coli.*

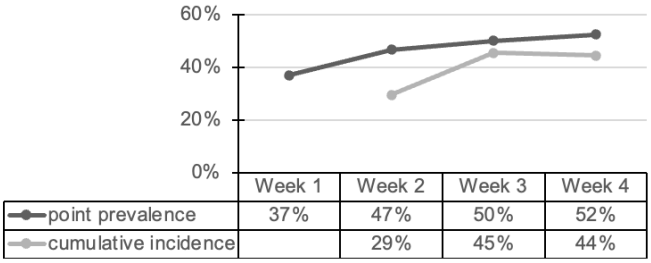

Figure 2. Point prevalence and cumulative incidence of MDRO colonization

Weekly surveillance rectal MDRO screening was valid for 30, 26, and 21 patients admitted on weeks two to four. Point prevalence for CRO-C increased to 47%, 50% and 52% on weeks two to four respectively (Figure 2). At the end of the study period, 14 patients had incident colonization during MDRO surveillance. CRO colonization was not detected in 8 patients with at least two MDRO screenings, three of which had negative MDRO screening on all four weeks. Persistent colonization was seen in 14, while decolonization was not observed (Table 3). Among the three patients with invalid initial MDRO screening, two patients had valid MDRO surveillance, where one patient was CRO-C. Among the 40 patients with at least one valid MDRO screening done during the 4-week study period, 29 had confirmed MDRO colonization giving a 4-week period prevalence of 72.5%.

Table 3. Rectal MDRO colonization surveillance

	MDRO screening on week 1		All Patients (N=38)
	Non-colonized	Colonized	
≥1 repeat MDRO screening (patients)	22	14	**36 (95%)**
Repeat MDRO screening (rectal swabs)	46	28	**74**
COLONIZATION SURVEILLANCE (week 2 to 4)			
New MDRO colonization	14	----	**14 (37%)**
Persistent MDRO colonization			
2 consecutive weeks	4	5	**9 (24%)**
≥3 consecutive weeks	2	3	**5 (13%)**
Decolonization *3 consecutive negative screening*	----	0	**0 (0%)**
Not colonized	8	----	**8 (21%)**

There were 62 CRO isolates from 52 positive swabs identified. The most common CROs were *E. coli* (28) followed by *Klebsiella* spp. (7) and *Serratia* spp. (6). All isolates showed multidrug resistance (Table 4).

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Table 4. Top 5 MDRO colonizers and antibiotic non-susceptibility rate

	Organism	n	Non-susceptibility rate by disk diffusion							
			Ampicillin-sulbactam	Ceftriaxone	Piperacillin-Tazobactam	Meropenem	Ciprofloxacin	Levofloxacin	Amikacin	Gentamicin
1	***Escherichia coli***	**28**	93%	96%	100%	75%	36%	89%	100%	93%
2	***Klebsiella* spp.** *Klebsiella* spp.(5), *K. ozanae*(1), *K. pneumoniae*(1)	**7**	100%	100%	100%	71%	29%	71%	86%	86%
3	***Serratia* spp.** *S. marcescens*(3), *Serratia* spp.(3)	**6**	100%	100%	100%	83%	17%	83%	100%	83%
4	***Proteus mirabilis***	**5**	100%	100%	100%	40%	0%	80%	100%	100%
5	***Providencia spp.***	**5**	100%	100%	100%	60%	0%	60%	100%	100%
	Other isolates*	**11**	100%	91%	100%	82%	64%	91%	88%	75%
		62	**97%**	**97%**	**100%**	**73%**	**32%**	**84%**	**97%**	**90%**

**Acinetobacter* spp. (3), *Pseudomonas fragi* (2), *Pseudomonas* sp. (1), *Citrobacter freundii* (1), *Citrobacter* sp. (1), *Enterobacter aerogenes* (1), *Enterobacter agglomerans* (1), *Hafnia alvei* (1)

During the 30-day period from initial MDRO screening, 16 patients acquired nosocomial infections, eight developing more than one event. Among the 25 events, 76% were culture-negative infections. Among these, four patients were empirically started on polymyxin-based combination therapy. There were two culture-proven gram-negative infections, which were both drug-sensitive *K. pneumoniae* central line-associated bloodstream infection (CLABSI); one patient was colonized with CRO *E. coli* while the other had CRO *Proteus mirabilis*. The rest of the culture-proven infections were gram-positive and fungal isolates. Among the colonized, there was no concordant infection observed. Nosocomial infections were acquired in 29% of nCRO-C and 64% of CRO-C, and the 30-day mortality rate was 8% in nCRO-C, and 21% among CRO-C (Table 5).

Table 5. Nosocomial infections and outcomes during 30-day period from initial MDRO screening

	All Patients (N=38)	MDRO screening on week 1	
		Non-colonized (N=24)	Colonized (N=14)
Nosocomial Infection (patients)	**16 (42%)**	**7 (29%)**	**9 (64%)**
Types of infections (events)			
Culture negative sepsis	11	5	6
Nosocomial pneumonia	5	3	2
Clinical fungal sepsis	3	1	2
Culture proven infection			
Methicillin-resistant *Staphylococcus epidermidis* sepsis	2	2	0
non-MDR *Klebsiella pneumoniae* CLABSI	2	1	1
Meyerozyma guilliermondii pneumonia	1	0	1
Candida parapsilosis CLABSI	1	0	1
Outcomes			
Discharged	17 (45%)	12 (50%)	5 (36%)
Still admitted	16 (38%)	10 (42%)	6 (43%)
30-day mortality	5 (13%)	2 (8%)	3 (21%)

CLABSI: central line-associated blood stream infection

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DISCUSSION

This study prospectively determined the prevalence of rectal colonization with carbapenem-resistant organism (CRO) in the NICU of a tertiary hospital in the Philippines. Point prevalence of CRO colonization was 37% at initial screening. The patients underwent weekly MDRO screening for four weeks, where 14 incident colonizations were identified. The 4-week period prevalence was high at 72.5%. The most common colonizers identified were *E. coli, Klebsiella* spp and *Serratia* spp. Surveillance screening documented persistent colonization, but decolonization was not observed. The study population was composed of very preterm infants with very low birth weight and different comorbidities. Majority were initially screened within the first two weeks of life. Hospitalization was complicated by prolonged placement of central lines, respiratory support and nosocomial infections, and half of the patients were exposed to meropenem at initial screening. During the 30-day observation, multiple culture-negative infections were acquired, some requiring antibiotic escalation to polymyxin-based combination therapy. Despite this setting of high CRO colonization, no culture-proven carbapenem-resistant infection was documented.

The prevalence of CRO colonization in the study was higher than previous reports. Earlier studies revealed a CRO colonization rate of 1.7% in New York (2009-2012)[8] and up to 27% among 4 to 28 days old in China (2013-2018).[9] More recent data on neonatal MDRO surveillance shows that CRO colonization was not observed in a study in Italy (2019-2020)[10] while CRO prevalence was 22% among preterm neonates in Morocco (2019-2022)[11]. Locally, this is the first report on CRO colonization among neonates. In 2003-2004, a study conducted at the PGH NICU documented that 40.6% were colonized with gram-negative bacteria resistant to ceftazidime and gentamicin.[12] After more than 20 years, this study demonstrated a significant increase in colonization with drug-resistant organisms underscoring the challenge of antimicrobial resistance.

Risk factors for neonatal CRO colonization identified in literature include duration of hospitalization, nasogastric tube feeding, lack of breastfeeding, invasive procedures (ventilation, central line), and antibiotic exposure,[13,14] specifically meropenem treatment for 10 or more days.[8] These previously reported risk factors for colonization were not always evident in our study.

In this study, the median age at initial screening among nCRO-C was 5 days old, compared to 21 days old among CRO-C, similar to a study in China which showed higher colonization among neonates 4-28 days old (27%) compared to the first 3 days of life (15%).[9] Likewise, in this study, central lines which remained in place for a longer period, such as peripherally inserted central catheters (PICC), tended to be associated with CRO-C, in comparison to short-term umbilical catheters among nCRO-C patients. However, in contrast to reports in the literature, a higher proportion of the nCRO-C patients (25%) were intubated, versus the 14% among CRO-C. Although feeding (particularly with breastmilk) has been cited as protective against colonization with resistant organisms,[13] in this study an almost equal number of patients belonged to each group: 46% of nCRO-C were on NPO, while 43% of CRO-C were fully feeding.

These findings may have been confounded by age. Younger neonates are likely to still be ventilated, with an umbilical catheter in place and still on NPO, whereas older patients are more likely weaned off ventilation and tolerated feeding progression. Hospital policy limits visitors and prohibits milk formula, hence direct breastfeeding among NICU patients was limited. All patients received expressed or pasteurized breastmilk.

At birth, infections are commonly suspected among preterm neonates, which leads to early antibiotic exposure that can alter microbial flora. A study among preterms below 32 weeks old found that antibiotic exposure in the first week of life did not increase the risk of MDRO colonization.[15] However, another study revealed that meropenem treatment (10 days or more) was associated with CRO colonization,[13] which may suggest that later exposure to broad spectrum antibiotics is contributory to colonization. Meropenem is the empiric treatment for the initial nosocomial infections in the unit. Accordingly, the proportion of patients with history of nosocomial infection and meropenem exposure was 38% for nCRO-C and 71% for CRO-C. Use of broad-spectrum antibiotics selects for drug-resistant organisms and alters gut microbiome, overcoming colonization resistance that facilitates colonization with drug-resistant pathogens.[16]

Interestingly, all patients with GI tract anomalies (two patients with omphalocele, one with omphalomesenteric duct) and surgical history were not colonized at initial screening. Among the three patients with GI tract anomalies, two were not colonized on

surveillance screening, while the third was only colonized after treatment of nosocomial pneumonia with polymyxin, ciprofloxacin and metronidazole. This contrasts with findings in the literature, indicating that invasive procedures were associated with MDRO colonization, likely because GI tract surgeries may cause inflammation, ileus, and possibly intestinal dysbiosis.[17,18] Congenital GI tract anomalies may also affect GI function and stool passage. The interplay between GI surgeries, congenital GI anomalies and MDRO colonization warrants more investigation.

Although the causal relationship between colonization and infection has not been established, several studies show concordant culture-proven infections among MDRO colonized patients.[19] In literature, risk factors for progression of MDRO colonization to infection include history of carbapenem use, neutropenia, and surgery.[20] A study by Migliorini *et al.* likewise showed that quantitative polymerase chain reaction (PCR) demonstrated that higher intestinal loads of carbapenem-resistant *Enterobacterales* (CRE) increased the risk for concordant *K. pneumoniae* infection.[21] This is supported by molecular typing studies that showed clonal relatedness of the gut colonizer and blood isolate in 50% of concordant infections.[22,23] However, despite the high prevalence of CRO colonization, no acquired CRO infection was observed from the patients during the study period. The two patients who developed drug-sensitive *K. pneumoniae* sepsis were colonized by different CROs. During the study period between April to May 2024, there was only one carbapenem-resistant *Acinetobacter baumannii* sepsis among the 12 culture-proven nosocomial infections recorded in the NICU nosocomial infection surveillance. Concordant endogenous infection among the CRO-colonized was not observed in this study, suggesting the need to focus on preventing exogenously-acquired infections.

The most common colonizers identified were *E. coli, Klebsiella* spp and *Serratia* spp; among these, *E. coli* and *Klebsiella* spp. are consistent with previous studies on neonatal colonization.[24,25] This contrasts with the 2003 PGH NICU study where *Klebsiella* spp., *Enterobacter* spp. and *Pseudomonas aeruginosa* were the most common neonatal MDRO colonizers.[12] The nosocomial infection report of the PGH NICU in 2023 revealed that 45% of culture-proven infections were extensively drug-resistant (XDR) or pandrug-resistant (PDR) gram-negative infections, and the most common isolates were *K. pneumoniae, A. baumannii* and *Serratia marcescens*. This may contribute to the inclusion of *Serratia* spp. as a common colonizer in the study. Studies have shown that CRO colonization may serve as a reservoir for MDRO, and homology analysis from whole genome sequencing among CRE isolates in concordant infections supports possible horizontal transmission among patients.[26] A meta-analysis showed that exposure to prior bed occupants with MDRO infection or colonization increases a patient's risk for MDRO colonization.[27] However, more studies on CRO transmission are needed.

The study reported 14 cases (37%) of persistent colonization; this is similar to data from hospital programs with surveillance MDRO screening.[28] In a study by Darda *et al*., the median duration of CRO colonization in children was 97 days, where 91% of neonates were spontaneously decolonized by 6 months old. Factors associated with late decolonization include use of carbapenems, immunosuppression, use of protein pump inhibitors, readmission, and urinary catheter placements.[29,30] Defining the parameters for decolonization is not yet established due to occurrence of recolonization, although some studies define decolonization as at least three consecutive negative MDRO screenings done at least one week apart.[30] By this definition, no case of decolonization was documented, likely limited by the duration of the study.

As a government hospital, all laboratory tests done for charity patients in the hospital are fully subsidized. The available stool culture in the hospital was designed to evaluate for enteric pathogens causing diarrhea; per protocol when more than one non-diarrheagenic bacteria is isolated, the result will be reported as "*no enteric pathogens seen*". This laboratory method is neither sensitive nor specifically designed for MDRO screening, hence this study adopted an MDRO screening method using chromogenic media to determine the prevalence of MDRO colonization. A limitation of the study was the inability for CRO confirmation for the 20 (15%) invalid swabs. Furthermore, AST was only based on disk diffusion and minimum inhibitory concentration (MIC) was not determined. Neither carbapenemase production nor carriage of carbapenemase genes were confirmed. A study conducted in Vietnam on MDRO colonization screening methods used the same chromogenic media and found that resistance to

meropenem was the best predictor of carbapenemase production (sensitivity 85.6%, specificity 100%); however, meropenem resistance alone was a poor predictor of OXA-48-like carbapenemase producers.[31] Given this limitation, the reported prevalence for this study was a conservative CRO colonization rate. If all swabs with growth on the chromogenic media were included, a higher estimate of CRO colonization would be reported: 63% (26 of 41) at week 1, with the 4-week period prevalence at 87% (36 of 41).

The limited sample and study period also precluded analysis of trends and correlation of colonization to infection. Colonized patients on week 1 were observed for 30 days, but the 14 patients with incident colonization were monitored for less than 30 days from initial detection of colonization. Some studies on MDRO colonization monitor patients during their entire hospitalization, but similar to this study, a meta-analysis on concordant infection among MDR carriers in adults had a median follow-up of 30 days.[32] In addition, a study among pediatric and neonatal ICU patients in Turkey demonstrated that concordant infection occurred after a mean of 10.6 ±1.9 days (median: 7 days, range: 2-38 days) after detection of CRO colonization.[20] In this study, four patients were observed for only 9 days from detection of colonization, and the rest were observed for at least 2 weeks.

CONCLUSION

The high prevalence of rectal colonization with carbapenem-resistant organisms in the NICU at 37% emphasizes the burden of antimicrobial resistance in an ICU setting. Despite a high colonization rate, no case of carbapenem-resistant infection was documented. However, the study is limited by the small sample size and the 30-day observation period.

RECOMMENDATIONS

As NICUs become more equipped to care for the very preterm and low birthweight neonates, infection prevention must be emphasized to improve their outcomes. Since colonization may serve as a reservoir for infection, there is a need to detect the MDRO-colonized infants and institute infection prevention measures to prevent transmission of drug-resistant pathogens. Expanding the population and extending the duration of surveillance screening and outcomes observation can establish trends. Patients should be screened upon admission and serially screened to identify incident colonization. Unit specific factors such as nurse-patient ratio, personal protective equipment (PPE) availability, hand hygiene compliance, and waste disposal practices may be incorporated into the observed variables to identify areas for intervention.

To improve the detection of CRO, isolates from the chromogenic media should be further tested using automated ID and AST methods such as VITEK®, carbapenemase production confirmed with the modified carbapenem inactivation method (mCIM), and PCR testing done to identify carbapenemase genes. Furthermore, genome sequencing for clonal homology can confirm MDRO transmission, or evaluate for correlation to infection.

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CONFLICT OF INTEREST

None declared.

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