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Managing Infection Prevention and Control for Multidrug-Resistant Organism Patients in Ebeye Hospital

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Abstract

Ebeye Hospital is a 60-bed acute care and district hospital in the Republic of the Marshall Islands (RMI). In October 2022, the hospital's Infection Prevention and Control (IPC) Program initiated health care-associated infection and antimicrobial resistance surveillance, along with efforts to promote appropriate antimicrobial use. New National IPC Guidelines call for the institution of appropriate infection control measures (based on the organism identified and site of infection) and adjustment, when needed, of patients' antibiotic regimen within 24 hours of release of multidrug-resistant organism culture results. A descriptive cohort study was conducted on hospital inpatients who tested positive for multidrug-resistant organisms, using program data from October 25, 2022, to December 31, 2023. Each case (n=58) was reviewed to assess: a) the timeliness of initiating infection control measures, and b) the timeliness and appropriateness of antibiotic selection, as guided by the RMI National Antimicrobial Guidelines. Multidrug-resistant organism cases involved a variety of organisms and occurred across all clinical wards. Of these, 35 cases (60%) met IPC standards. The primary reasons for not meeting IPC standards were lack of isolation rooms (n=10, 44%) and failure to meet the IPC initiation criterion per the working definition (n=13, 56%). Only 8 cases (14%) adhered to antibiotic usage guidelines. The most common reasons for non-adherence were prolonged antibiotic duration (n=19, 38%) and shorter-than-recommended duration (n=16, 32%). Management of a substantial proportion of multidrug-resistant cases at Ebeye Hospital failed to meet IPC standards. These findings highlight several areas for improvement.

Abbreviations and Acronyms

CDC = US Centers for Disease Control & Prevention
COVID-19 = Coronavirus disease 2019
CRAB = carbapenem-resistant Acinetobacter baumannii
ESBL = extended-spectrum beta-lactamase-producing *Enterobacteriaceae*
HAI = hospital-acquired infection
HAI/AR = health care-associated infections/antimicrobial resistance
IPC = infection prevention and control
KPN = Klebsiella pneumoniae
MDRO = multidrug-resistant organism
MRSA = Methicillin-resistant Staphylococcus aureus
PPE = personal protective equipment
VRE = Vancomycin-resistant enterococcus
WHO = World Health Organization

Introduction

Multidrug-resistant organisms (MDROs) are bacteria resistant to 1 or more classes of antimicrobial agents.[1] Although certain MDROs are named after resistance to only 1 agent (eg, Methicillin-resistant Staphylococcus aureus [MRSA] or Vancomycin-resistant enterococcus [VRE]), these pathogens are often resistant to most available antimicrobial agents. The prevalence of MDROs varies over time, by location, and by health care setting.[1] MDRO infections lead to prolonged hospital stays, increased morbidity and mortality, and result in significant economic burdens.[2] The United Nations General Assembly (UNGA) issued a call to action in September 2022 to combat antimicrobial resistance.[2] Infection prevention and control (IPC) interventions can significantly reduce health care-associated infection rates by 35-70%, regardless of a country's income level. However, only 15% of all countries worldwide meet the minimum IPC requirements.[3]

Ebeye Hospital is a district hospital and acute care facility in the Republic of the Marshall Islands (RMI) with a capacity of 60 beds. Located in the Kwajalein Atoll, Ebeye is the central point of the Ralik Chain of atolls and is home to approximately 9789 people. The Ministry of Health & Human Services (MOHHS) in the RMI implemented the IPC Program in response to the emergence of novel COVID-19. The ministry collaborated with The Pacific Community to provide technical support for the RMI National IPC team, resulting in the development and launch of the National Infection Prevention and Control Guidelines in October 2022.[4] The Pacific Community is the premier regional scientific and technical organization in the Pacific region, and an international development organization owned and governed by its 27 countries and 22 territory members.[5]

The RMI IPC Program work plan is aligned with the World Health Organization (WHO) Core Components for IPC.[6] The WHO has identified a set of core components for IPC programs,[6] which are essential to improving patient safety, reducing health care-associated infections (HAIs), and combating antimicrobial resistance.[7] These compo-

nents serve as a framework for countries and health care facilities to build or strengthen their IPC strategies. According to WHO, HAIs "also referred to as 'nosocomial' or 'hospital' infection, is an infection occurring in a patient during the process of care in a hospital or other health care facility which was not present or incubating at the time of admission".[8] One of the program's key focuses is the proper treatment and prevention of the spread of MDROs. The RMI Antimicrobial Guidelines 2018[9] provide guidance on adjusting antimicrobial therapy based on culture results for MDROs.

Ebeye Hospital's IPC Program, under WHO Core Component Six for IPC,[6] aims to enhance standards within the inpatient setting to combat healthcare-associated infections, antimicrobial resistance, and outbreak prevention and response. The IPC program guidelines require the implementation of standard measures within 24 hours of receiving culture results from the hospital microbiology lab. These measures include isolating the patient in an isolation room or cohorting with another patient with the same organism, displaying standard and transmission-based precaution signage outside room doors, providing personal protective equipment (PPE) carts, hand hygiene supplies, waste management supplies, educating the patient and their attendant, informing housekeeping staff, and enforcing visitation policies for the target population.

In October 2022, the Ebeye IPC Program initiated HAI/AR surveillance in conjunction with IPC and the National RMI Antimicrobial Guidelines 2018.[9] The antimicrobial guidelines were instituted in January 2018. This document serves as a guide for use with the intent of aligning practices on appropriate selection, dosage, frequency, and duration of antibiotics according to diagnosis, using a microbiology-guided methodology to avoid erroneous antibiotic prescription, and optimizing antibiotic prescribing. The guidelines cover the management of recommended antibiotic coverage for some MDROs (MRSA, ESBL – E.coli & Klebsiella, Carbapenemase-producing Enterobacterales – E.coli & Klebsiella) based on the drug listing of the national drug formulary. This surveillance fosters the collaboration between IPC, antibiotic stewardship, and clinicians to develop and implement comprehensive strategies to combat antimicrobial resistance.

This study aims to examine laboratory-confirmed MDRO cases among inpatients since the program's inception. It will evaluate whether IPC standard measures were promptly applied to each case, and whether antibiotic regimens were changed promptly based on culture sensitivity reports following the National RMI Antimicrobial Guidelines 2018.[9]

Methods

This is a descriptive cohort study of patients who were admitted to inpatient wards (Pediatric, Medical, Surgical, Maternity, and Intensive Care Unit) who had laboratory-confirmed cultures for any MDROs listed under the RMI Reportable Conditions, Class 2 (report within 48 hours) from October 25, 2022, to December 31, 2023.

Data was obtained from the Health care-Associated Infections/Antimicrobial Resistance (HAI/AR) database, maintained by the Ebeye Hospital IPC nurse, which includes all microbiology test results for inpatients during the study period. In addition, an MDRO Surveillance Form was completed for each identified case.

Each case was evaluated and classified as followed:

- Whether it met standards for initiating IPC measures (ie, initiated within 1 day of the culture result release date).
- Whether an adjustment to the antibiotic regimen was needed, based on the RMI Antimicrobial Guidelines 2018 (**Figure 1**).
- For cases requiring adjustment, whether the correct antibiotic type, dose, and duration were applied promptly (within 1 day of the culture result release date).

For cases that did not meet IPC initiation or antibiotic selection standards, the reasons for noncompliance were documented.

Ethics Approval

Ethics approval was obtained from the Ministry of Health and Human Services ethics board.

Results

Table 1 presents the culture isolates, sex, age, and inpatient ward distribution of the 58 MDRO cases identified during the study period. Cases were reported across all clinical wards, with the surgical ward accounting for most cases (n=32, 55%). The age group with the most confirmed MDROs was 45 – 65 years, representing 29 cases (50%). The majority of cases were male (n=33, 60%). MRSA was the most commonly identified organism (9 cases), while CRAB was the least common (4 cases) (**Table 1**). Based on the program's IPC definitions, 38 were classified as community-acquired infections, and 20 were health care-associated infections.

Of the 58 cases identified, 35 (60%) met IPC standards (**Table 2**). Among the 23 cases that did not meet these standards, the primary reasons were failure to isolate due to lack of isolation rooms (n=10, 44%) and failure to meet the IPC initiation criterion based on the working definition (n=13, 56%). A total of 50 cases did not meet antibiotic usage guidelines, while 8 cases (14%) complied with the standards for proper antibiotic selection, dose, and duration (**Table 2**). The major reasons for not meeting antibiotic usage standards include: prolonged antibiotic duration (n=19, 38%), shortened duration due to medication stockouts or early discharge (n=16, 32%), and frequent changes in antibiotics based on clinician preference rather than guideline recommendations (n=2, 4%). The 13 cases (56%) that did not meet IPC initiation criteria highlight an area for further investigation in future studies.

Sepsis Antibiotic Recommendations for Adults and Children TWO blood cultures should be taken before administering antibiotics. Give antibiotics as early as possible and always within one hour of presentation				
SOURCE of sepsis	ANTIBIOTIC		PENICILLIN ALLERGY	
SOURCE OF SEPSIS NOT KNOWN	Give 1st: Give 2nd:	ceftriaxone lg (child 40kg 25mg/kg) q12h PLUS flucloxacillin 2g (child < 40kg 25mg/kg) IV q6h If MRSA suspected, add clindamycin 600mg (child < 40kg 15mg/kg/dose) IV q8h	Give 1st: Give 2nd:	ciprofloxacin 400mg (child < 40 years 10mg/kg dose) IV q8h PLUS clindamycin 600mg (child <40kg 15mg/kg/dose) V q8h
INTRABDOMINAL	Give 1st: Give 2nd:	ceftriaxone lg (child < 40kg 25mg/kg/dose) q12h PLUS metronidazole 500 mg (child 12.5mg/kg/dose) qi2h	Give 1st: Give 2nd:	ciprofloxacin 500mg (child •z 40 years 12.5mg/kg/does) PO/IV q8h PLUS clindamycin 600mg (child <40kg 15mg/kg/dose) V q8h
	If patient is known or high risk to be colonized with an ESBL producer, instead of above regimen use meropenem Ig (child < 40kg 25mg/kg/dose) q8h pending culture results			
URINARY TRACT SOURCE	Give 1st: Give 2nd:	gentamicin 7mg/kg (ideal body weight) IV OD— maximum 3 days of therapy. PLUS ampicillin 2g (25mg mg/kg/dose) IV qid	gentamicin 7mg/kg (ideal body weight) IV OD— maximum 3 days of therapy.	
	In patients where gentamicin toxicity is a concern (known renal impairment, diabetic with known complications, history of gentamicin adverse event) use ceftriaxone Ig bd			
	If patient is known or high risk to be colonized with an ESBL producer, instead of above regimen use meropenem lg (child < 40kg 25mg/kg/dose) q8h pending culture results			
SKIN SOURCE	Excluding ischemic or diabetic foot ulcers, water related infections, necrotizing fasciitis — see relevant section in skin and soft tissue infection			
	Give 1st: Give 2nd:	flucloxacillin 2 g (child <40kg 50mg/kg/dose) IV q6h PLUS clindamycin 600mg (child < 40 kg 15mg/kg/dose) IV q8h	If penicillin non-immediate allergy — instead of flucloxacillin, give cefazolin 2g (child <40kg 50mg/kg/dose) IV q6h If immediate penicillin allergy — only give clindamycin 600mg (child < 40kg 15mg/kg/dose) IV q8h	
INTRAVASCULAR DEVICES	Give 1st: Give 2nd:	ceftriaxone lg (child < 40kg 25mg/kg/dose) qi2h PLUS vancomycin 30 mg/kg (actual body weight) up to a maximum of 3 g initial dose -> 15mg/kg bd. (children<40kg 15mg/kg/dose qid)	Give 1st: Give 2nd:	ciprofloxacin 500mg (child < 40kg 12.5mg/kg/dose) PO/IV q8h PLUS vancomycin 30 mg/kg (actual body weight) up to a maximum of 3 g initial dose -> 15mg/kg bd. (children <40kg 15mg/kg/dose qid)
Review therapy and modify based on pathogen and susceptibility results ESBL = extended-spectrum beta-lactamase-producing Enterobacteriaceae, MRSA = Methicillin-resistant Staphylococcus aureus				

Figure 1. Sepsis Antibiotic Recommendations for Adults and Children.[9]

Discussion

This is the first study in the Pacific region to assess compliance with IPC standard measures and antibiotic usage guidelines for MDRO cases. The study also evaluated Ebeye Hospital's capacity to institute and sustain IPC practices in alignment with the WHO Core components. The findings suggest potential areas for improvement, including strengthening monitoring and feedback systems, promoting adherence to IPC guidelines, enhancing health care worker training, and ensuring the availability of essential supplies such as hand hygiene at points of care. Addressing these gaps through in-service training for nurses and doctors, improving procurement and inventory systems, and resolving staffing shortages across key departments could improve IPC compliance and impact future outcomes.

Several factors may explain the gaps observed in both the initiation of IPC standard measures and adherence to antibiotic usage guidelines during the study period. Isolation rooms in the clinical wards were designated predominantly for infectious diseases when the building was built, and the practice of isolating MDRO cases is relatively new to the facility. One potential solution is to designate non-isolation rooms for cohorting patients with MDRO. Barri-

Table 1. Characteristics of Multidrug-Resistant Organism (MDRO) Cases in Ebeye Hospital, October 25, 2022, to December 31, 2023 (N=58)

	MRSA	CRAB	ESBL	PAE	KPN	Total (%)
MDRO Isolates	19	4	6	13	16	58 (100%)
Age Group in No.						
≤ 14	4	0	0	0	0	4 (7%)
14 - 44	9	0	0	4	3	16 (27%)
45 - 64	2	3	5	7	12	29 (50%)
≥ 65	4	1	1	2	1	9 (16%)
Sex						
Female	7	1	4	8	5	25 (40%)
Male	12	3	2	5	11	33 (60%)
Wards						
• Maternity	1	0	0	0	0	1 (2%)
• Medical	3	1	1	2	3	10 (17%)
• Surgical	10	2	4	6	10	32 (55%)
• Pediatric	4	0	0	0	0	4 (7%)
• Intensive Care Unit (ICU)	1	1	1	5	3	11 (19%)

MRSA = Methicillin Resistant Staphylococcus Aureus; CRAB = Carbapenem-Resistant Acinetobacter Baumannii; ESBL = Extended-Spectrum Beta-Lactamase; PAE = Pseudomonas aeruginosa; KPN = Klebsiella Pneumonia

Table 2. Compliance with IPC Standard Measures and Antibiotic Usage Guidelines and Reasons for Non-Compliance Among MDRO Cases in Ebeye Hospital, October 25, 2022, to September 20, 2023 (N=58)

IPC Standard Measures	Meets Standards	35 (60%)
	Does not meet standards	23 (40%)
	Reasons for Failure:[a] • No isolation rooms were available. • Does not meet IPC initiation criterion	10 (44%) 13 (56%)
Antibiotic Usage Guidelines	Meet Standards	8 (14%)
	Does not meet standards	50 (86%)

	Reasons for Failure:[b]
	• Unavailability of antimicrobials/shortage
	• Patients discharged before the results
	• Antibiotic duration:
	  ◦ Too long
	  ◦ Too short
	• Frequent changes in antibiotics
		7 (14%)
		6 (12%)
		19 (38%)
		16 (32%)
		2 (4%)

IPC = Infection prevention and control, MDRO = multidrug-resistant organism
[a]Percentages are calculated based on 23 cases that did not meet IPC Standard Measures
[b]Percentages are calculated based on 50 cases that did not meet Antibiotic Usage Guidelines.

ers to antibiotic usage guidelines include the unavailability and shortage of key antimicrobials, largely due to gaps in stock auditing and inventory management. This highlights the importance of balancing improved access to proper antibiotics and avoiding excess use of restricted antibiotics. In 2 cases, non-compliance resulted from the absence of recommended medications in the hospital drug formulary, an issue that should be addressed by the national therapeutics committee. It is also recommended that the national drug formulary and the National Antimicrobial Guidelines 2018 be reviewed to add new medications and reassess the current restricted drug list. As a country, RMI must prioritize the development of a robust inventory management system and a comprehensive antibiotic approval and stewardship protocol to mitigate ongoing shortages and ensure appropriate usage.

Birgand G, et al in "Overcoming the obstacles of implementing infection prevention and control guidelines",[10] concluded that multidisciplinary approaches are essential for success and that the mere existence of guidelines is insufficient for effective IPC. Ebeye Hospital's IPC committee is a multidisciplinary team. However, the IPC committee has not consistently enforced standards or ensured that staff fully understand and apply those standards. These is-

sues could be addressed through regular department meetings and IPC refresher training. Additionally, the hospital could benefit from appointing a qualified quality assurance and quality improvement (QA/QI) officer to oversee adherence to standards and reinforce IPC practices as part of a broader patient safety strategy.

One of the study's strengths was the existence of a robust system – the HAI/AR database - which systematically logs all microbiology specimen results for inpatients across all clinical wards. This database is regularly updated, allowing for consistent, ongoing data collection and dissemination. Furthermore, PPE was readily available throughout the study period, supported by a dedicated, pre-staged cart for efficient access.

This study has several limitations. One major limitation is the relatively small cohort size (N = 58), which limits generalizability. The database was limited to culture result release times, IPC control measure initiation, and antibiotic adjustment times and details. The facility still relies on paper-based medical records, so documentation was often unclear on antibiotic change dates, especially for longer-staying patients, and discharge dates were occasionally missing. The facility is planning to implement an electronic health records system to resolve many of these issues. In the interim, periodic audits are necessary to assess staff competency and give constructive feedback. Additionally, due to limitations in laboratory reagents and technology, some MDROs, such as *Clostridioides difficile*, *Candida auris*, and VRE, cannot be detected. Thus, laboratory capacity should be improved to sustain testing needs and insights into our local MDRO strains. This requires qualified microbiologists.

In December of 2023, Ebeye Hospital lost its only microbiologist, who was an expatriate on contract. Since that time, there have been no cultures performed at the hospital, and it is no longer able to identify MDROs. This highlights the vulnerability of hospitals in the region to the loss of key staff members and the importance of building the skills of Indigenous staff.

The design and consistent updating of the MDRO surveillance forms ensured accurate classification of cases, allowing for prompt initiation of IPC measures. However, in the absence of direct observation, there is no guarantee that all of the recommended IPC measures were applied in each case. This is an area for further study and monitoring if any strategies in antibiotic usage and IPC standard measures are to be sustained. Innovative and combination strategies could be effective, but the key is strong ongoing support from senior clinicians and senior leadership. Adherence to IPC evidence-based standards and robust antimicrobial stewardship are essential in the fight against MDROs. In summary, the study identified shortcomings in both the initiation of IPC measures and adherence to antibiotic usage guidelines based on culture results. These findings point to actionable interventions that could improve infection control and antibiotic management, ultimately improving patient outcomes.

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Conflict of Interest

None of the authors identify a conflict of interest.

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