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Research Article

Incidence of Gram-Negative Carbapenemase-Producing Bacteria from a Tertiary-Level Private Hospital

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ABSTRACT

Background and Objectives: This is a report of Gram-negative carbapenemase-producing bacteria (CPBs) in a tertiary-level private hospital in Davao City, Philippines. CPBs are placed in a high hazard level by the Centers of Diseases and Control (CDC) due to its capability of developing resistance to carbapenem antibiotics which are considered one of the last resort for many bacterial infections. Existence of such organisms will severely affect nosocomial infections and treatment modalities. This report shows the antibiotic-resistance profiles of Acinetobacter baumannii, Pseudomonas aeruginosa and Klebsiella pneumoniae.

Materials and Method: Collection of samples from different specimens were cultured and VITEK 2 System was used which optimizes a fluorogenic methodology for organism identification and a turbidimetric met**hod for susceptibility testing.**

Results: Around 827 CPB were isolated. Among the specimen gathered, ETA displayed the highest number of isolates with A. baumannii showing the greatest predilection. For P. aeruginosa, 466 samples were identified with majority also obtained from ETA. Samples for K. pneumoniae reflected around 52 isolates with diverse sources. P. aeruginosa exhibited the highest rate of resistance among carbapenem drugs, ertapenem, imipenem, and meropenem. K. pneumoniae has the least resistance to ertapenem, imipenem, and meropenem.

Conclusion: A significant number of CPBs were collected. This indicates a steady increase of antimicrobial resistance, and carbapenem-resistance has become a threat . Moreover, there exists significant species-only variance in antibiotic resistance, requiring more nuanced precautionary measures and control when handling patients who are positive for CPBs.

INTRODUCTION

Gram-negative carbapenemase-producing bacteria (CPB) are organisms that are resistant to carbapenem antimicrobials through the production of carbapenemase. As carbapenems are included in the last line of defense for antibiotics, CPB are one of the reasons that make bacterial infections hard to treat (2). In this paper, the CPBs of focus are Acinetobacter baumannii, Pseudomonas aeruginosa and Klebsiella pneumoniae.

K. pneumoniae was one of the first to emerge and spread globally and has become endemic to a number of countries worldwide. K. pneumoniae is a major cause of nosocomial infections, primarily among immunocompromised patients. The emergence of strains resistant to carbapenems has left few treatment options, making infection containment critical. Two [2] strains, NDM-producing Enterobacteriaceae and OXA-48-producing K. pneumoniae appears to have originated from South Asia and Northern Africa, respectively. These strains were believed to be resistant to all β-lactams including carbapenems and many other classes of antimicrobials. Overall, mortality rates due to CPBs is slowly rising and currently reaching up to 40% globally.

In the Philippines, studies have been performed on various species of Enterobacteriaceae and related carbapenemase-producers with confirmed reports of the microorganisms

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harboring bla genes that confer resistance to carbapenems with genes like NDM-1 and 7, IMP, KPC, and VIM. The Philippines was listed as one of the countries where NDM is commonly identified. 37.5% of the cases included in the study were defined to harbor IMP.

CPB is slowly rising leading to limitations of treatment options [10]. As the antibiotic pipeline offers little in the short term, our most important tools against the spread of antibiotic resistant organisms are intensified infection control, surveillance, and antimicrobial stewardship. A study was done by Public Health Ontario that initiated a voluntary surveillance program to assess the epidemiology of CPBs in Ontario, Canada. It stated the importance of surveillance in understanding the burden and transmission of these antibiotic resistant organisms especially in hospitals and local health integration networks.

In dealing with such infections, CDC has four core actions. These include preventing infections and spread of resistance, tracking, improving the use of current antibiotics and promoting development of new drugs and new tests for resistant bacteria (6).

METHODS

Data is taken from a tertiary level private hospital in Davao City, from a determined 5-year time period from 2012 to 2017. Samples are collected via standard procedures, cultured with the use of appropriate media, and identification is performed through VITEK® 2 automated system. Results are exported, and tabulated via Microsoft Excel for further data processing.

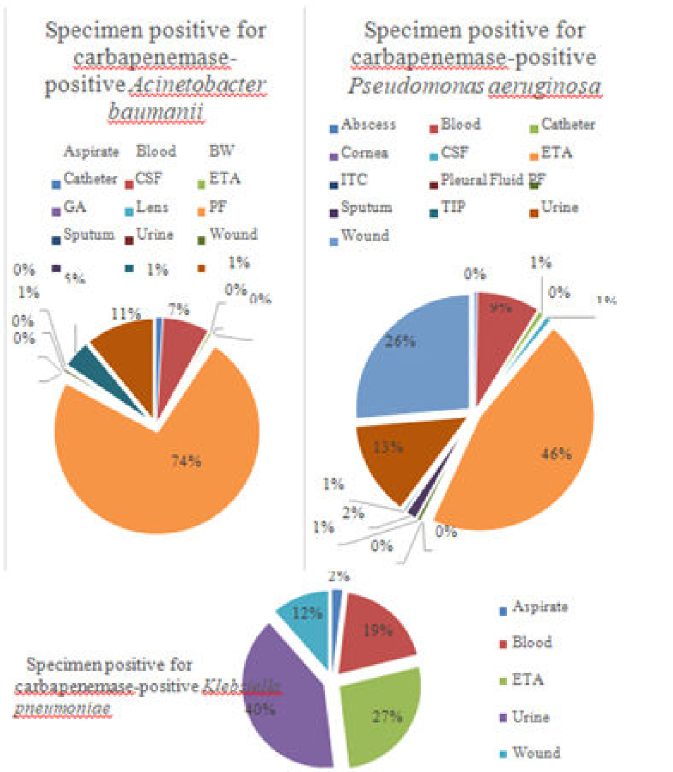
Antimicrobial Susceptibility: All breakpoints and interpretations of antibacterial susceptibility follow Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines of 2017.

RESULTS

Table 1: CPBs and the number of positive isolates taken from a particular source/site/sample.

		BACTERIA			
		Acinetobacter baumanii	Klebsiella pneumoniae	Pseudomonas aeruginosa	TOTAL
SPECIMEN	Abscess		0	1	1
	Aspirate	3	1		4
	Blood	22	10	36	68
	BW	2			2
	Catheter	1	0	4	5
	Cornea			1	1
	CSF	1		4	5
	ETA	227	14	191	432
	GA	1			1
	Gastric		0		0
	ITC			1	1
	Lens	1			1
	Pleural Fluid			1	1
	PF	2	0	3	5
	Sputum	1	0	7	8
	TIP			2	2
	Urine	14	21	55	90
	Wound	34	6	160	200
TOTAL ISOLATES		309	52	466	827

Figure 1: CPB proportion pie chart of each species and the sources in which they were isolated.



Sample Sourcing: Pseudomonas aeruginosa There are 466 samples of P. aeruginosa, the most common CPB isolated in this institution when compared to other CPBs such as K. pneumoniae (n = 52) and A. baumannii (n = 309). Majority of P.

aeruginosa isolates are obtained and isolated from ETAs (n = 191, 41%), followed by wound sites (n = 160, 34%) and blood (n = 36, 7%). Isolates were also identified in samples such as CSF (n = 4, 0.8%), the cornea (n = 1, 0.2%) and abscesses (n = 1, 0.2%).

Organisms of interest are carbapenemase producers A. baumanii, K.pneumoniae and P.aeruginosa; all of which are taken from a tertiary-level private hospital in Davao City. A total of 827 CPB isolates were collected, comprising 22.5% of total overall bacterial isolates (n = 3671) in this five-year period.

ETA is the major site from which these CPBs were isolated, with A. baumanii having the highest number. Other significant sites include urine, wound, and blood. Less common are sources such as pleural fluids, sputum, CSFs and catheters.

Acinetobacter baumannii A. baumanii was found in 309 isolates, and are mostly taken from ETA samples (n = 227, 73%). Wound, blood, and urine are also significant sources for this organism. Notably, this microbe was also isolated from the lens (n = 1, 0.3%), gastric acid (n = 1, 0.3%), and CSF (n = 1, 0.3%).

Klebsiella pneumoniae

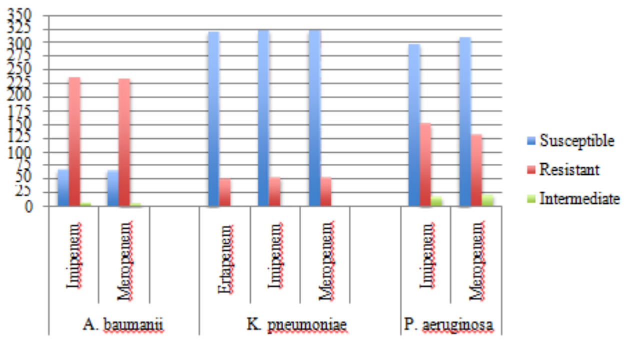
374 bacterial samples were positive for K. pneumonia, 13.9% (n = 52) of which were carbapenemase producers. Unlike P. aeruginosa and A. baumannii, sources for the organism are more widespread and are less localized to any single particular source. ETA (n = 135, 36%), urine (n = 85, 23%), wound (n = 86, 23%) and blood (n = 36, 13%) are the major sources of this organism with relatively greater distributions. An unusual isolate of K. pneumonia (n = 1, 0.3%) is taken from a gastric source. Other uncommon sites include aspirates (n = 1, 0.3%), catheters (n = 5, 1.6%) and pleural fluid (n = 1, 0.1%).

DRUG RESISTANCES

Table 2: CPBs and the number of isolates that manifest a particular susceptibility against common carbapenem-class drugs. Presence of resistance indicate positive carbapenemase capability.

		Susceptible	Resistant	Intermediate	Total
Ertapenem	Klebsiella pneumoniae	321	52	0	373
				Subtotal	373
Imipenem	Pseudomonas aeruginosa	297	152	17	466
	Acinetobacter baumannii	67	237	5	309
	Klebsiella pneumoniae	322	52	0	374
				Subtotal	1149
Meropenem	Pseudomonas aeruginosa	311	133	22	466
	Acinetobacter baumannii	67	235	7	309
	Klebsiella pneumoniae	322	52	0	374
				Subtotal	1149

Figure 2: Comparison of the number of A. baumannii, K. pneumoniae and P. aeruginosa isolates that showed susceptibility and resistance against a set of carbapenem drugs.



About the species in question, resistance against ertapenem, imipenem and meropenem are present (n = 827, 71.9%). These drugs serve as indicators that these isolates, should they exhibit resistance, have mechanisms intrinsically present that grant them carbapenem resistance, and are effectively considered CPBs. A small set of isolates are noted to have intermediate resistance (n = 51), but for practical reasons these are to be treated as if they are completely resistant.

Pseudomonas aeruginosa: Resistance can be noted against imipenem (n = 152, 32.6%) and meropenem (n = 133, 28.5%). Fortunately, more isolates remained susceptible to imipenem (n = 297, 63.7%) and meropenem (n = 311, 66.7%). These species are intrinsically resistant to ertapenem.

Acinetobacter baumannii: A. baumannii has a resistance profile across imipenem (n = 237, 76.6%), and meropenem (n = 235, 76%). These species are intrinsically resistant to ertapenem.

Klebsiella pneumonia: Among the CPBs, K. pneumoniae has the most carbapenem susceptibility especially noting the relatively smaller amounts of resistant isolates to Ertapenem (n = 52, 13.9%), Imipenem (n = 52, 13.9%) and Meropenem (n =52, 13.9%) overall.

Table 3: Percentage of resistance to carbapenems 2012-2017.

Gram Negative Bacteria	2013	2014	2015	2016	2017

Acinetobacter baumannii	19%	22%	28%	33%	38%
Pseudomonas aeruginosa	23%	27%	29%	29%	33%
Klabesiella pneumoniae	10%	11%	16%	16%	21%

(Table 3) shows yearly percentages of species-specific resistance. The highest percentage of carbapenemase-positive organisms was in year 2017, yielding a 5%-increase in carbapenem-resistant Acinetobacter baumannii.

Analysis and Discussion

This study focuses on 3 carbapenemase-producing gram negative bacteria namely, K. pneumonia, P. aeruginosa and A. baumannii. The total number of isolates collected were 1,149. As shown in Table 1, the number of isolates per bacteria varies depending on what specimen it was collected from. For example, there were isolates of K. pneumonia and P. aeruginosa collected from an abscess while there was none of the A. baumannii. Among bronchial wash specimens, the only isolate collected were that of A. baumannii and none of those from K. pneumonia and P. aeruginosa. Hence, different bacteria can manifest variance in where these can be obtained. Some of which are present in a single specimen while others have their own unique specimen for which they can grow on. Of the three (3) bacteria mentioned, the highest number of isolate collected were that of

A. baumanii, and the specimen that yielded the highest isolate of A. baumanii is that of from ETAs. These isolates identified are commonly found in immunocompromised patients and those who are hooked on to ventilators, which might have contributed to a larger number of isolates found in ETA.

In (Figure 2), susceptibility testing showed Acinetobacter baumanii as the CPB that had the highest resistant profile to the carbapenems used, while Klebsiella pneumoniae had the highest susceptibility to the same drugs. Pseudomonas aeruginosa, on the other hand, showed susceptibility to both

imipenem and meropenem. This aspect is important in the treatment of common illnesses because carbepanem antibiotics is considered a last-line of defense against highly infectious resistant bacteria (14).

In relation to the specimen that was used to obtain these isolates and their resistance to the carbepenems mentioned above, it is important to understand the common scenario that are greatly affected in the data that was gathered. Endotracheal aspirate (ETA) are specimens collected from endotracheal tubes and these are most commonly used by ventilator-associated pneumonia. Ventilator associated pneumonia is the most common healthcare-associated infection in the intensive care unit particularly in adults (3). Aside from the ETA, wound specimen also contained a number of isolates. Wound infections are also common in surgical operations that is important when dealing with post-operative patients (8). A large number of isolates were also collected from both urine and blood specimens. Urine specimens are commonly used in urinalysis testing for urinary tract infections. Urinary tract infection is one of the most common cause of nosocomial infection in the hospital (18). Infection that are found in the blood is an alarming case because these are usually associated with sepsis which is considered a medical emergency and is one of the leading cause of death in hospitals (10).

In treating carbapenemase-resistant bacteria, it is important to take note of the site of infections because based on the data given, the site of infection of different CPB varies and the susceptibility of each CPB also depends on the type of carbapenem used and the organism isolated, A. baumanii, K. pneumoniae or P. aeruginosa.

CONCLUSION

A significant number of CPBs are being collected in a particular institution in Davao City, indicating that resistant bacteria are already numerous, and that the presence of carbapenem resistance already poses a threat. In addition, there exists significant species-only variance in antibiotic resistances, warranting more nuanced approaches when handling patients that possess a particular CPB infection. Furthermore, this calls for heightened awareness amongst institutions in mounting greater infectious control efforts in response to this threat.

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