The changing epidemiology of antimicrobial resistance in Fiji: a descriptive analysis of antimicrobial susceptibility and trends of endemic and emerging pathogens, 2019–2022

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Summary

Background There is a paucity of data on antimicrobial resistance in Fiji. The aim of this study was to determine the antimicrobial susceptibility profile of bacterial isolates from clinical samples at Colonial War Memorial Hospital in Fiji.

Methods This retrospective study reviewed four-year of data from January 1, 2019, through December 31, 2022. Laboratory testing was carried out using locally approved protocols. Selective antimicrobial susceptibility testing was performed whereby only isolates resistant to first line antimicrobials were tested against second line antimicrobials. Only the first isolate of a given species per patient in a single year were included in the analysis. WHONET software and Microsoft Excel were used for analysis.

Findings A total of 29,222 bacterial isolates were included, 62% (n = 18,084) were Gram-negative bacteria. *K. pneumoniae* was the most common (n = 5363), followed by *E. coli* (n = 4321). Extended spectrum beta lactamase (ESBL) production increased from 30% in 2019 to 43% in 2022 amongst *K. pneumoniae*, and 10%–23% *in E coli*. There were 733 carbapenem-resistant isolates identified from clinical samples, 61% (n = 445) were *A. baumannii*, 15% (n = 110) *E. coli* and 14% (n = 101) *P. aeruginosa*. Amongst the *E. coli* isolates tested, susceptibility to meropenem declined from 99% (272/274) in 2019 to 79% (255/325) in 2022. The rate of methicillin resistance amongst *Staphylococcus aureus* was steady, remaining between 11% and 13%.

Interpretation This study demonstrated a high rate of MDR amongst Gram-negative bacteria, especially ESBL producing *K. pneumoniae and E. coli* and carbapenem-resistant *A. baumannii*. The emergence and rapid spread of carbapenemase producing *E. coli* in Fiji's largest hospital is of particular concern. There is an urgent need to allocate resources to improve existing capacity and to develop effective multimodal strategies to detect, manage and control the spread of MDR organisms.

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Keywords: Antimicrobial resistance; Epidemiology; Fiji; Gram-negative organisms; Multidrug resistance

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Research in context

Evidence before this study

Antimicrobial resistance (AMR) is a growing public health threat globally. In Fiji, the burden of AMR has not been fully investigated. Available data from outbreak investigations showed high rates of healthcare associated infections from multidrug resistant (MDR) organisms. There is a need to better understand the antimicrobial susceptibility profile of common bacterial pathogens and describe the type and rates of MDR bacterial pathogens in Fiji.

Added value of this study

In this retrospective study, we used four years (2019–2022) of microbiology laboratory data to comprehensively describe the burden of AMR in Colonial War Memorial hospital (CWMH), the largest hospital in Fiji. We included only the first isolate of a given species per patient in a single year. Our study reported increasing isolation of extended spectrum beta lactamase (ESBL) producing strains amongst *Klebsiella pneumoniae* (30% in 2019–43% in 2022) and *Escherichia coli* (10% in 2019–23% in 2022). Carbapenem resistance was prevalent in *Acinetobacter baumannii* and an emerging problem in *E. coli K pneumonia* and *Pseudomonas aeruginosa*. The majority (>80%) of the carbapenem resistant *E. coli* and *K. pneumoniae* isolates were carbapenemase producing. The rate of methicillin resistant *Staphylococcus aureus* was stable, ranging from 11% to 13%.

Implications of all the available evidence

Our study demonstrated high rate of ESBL producing *K. pneumoniae and E coli,* endemic MDR and carbapenem-resistant *A. baumannii,* and the emergence and rapid dissemination of other carbapenemase producing Gram negative pathogens in CWMH. Our findings highlight the potential need to ensure access to appropriate antimicrobials for optimal treatment of MDR pathogens, possible updating of the hospital treatment guidelines and further development of antimicrobial stewardship policy and monitoring programs to promote the rational use of antimicrobials in both public and private sectors. Further support is required to improve the microbiology laboratory capabilities to accurately detect AMR and address shortages of laboratory consumables. Future studies, when possible with predefined sample collection criteria and additional clinical data, from all the three divisional hospitals could improve our understanding of the AMR burden in the country and provide a framework for the nationwide AMR prevention and mitigation interventions.

Introduction

The emergence and rapid spread of antimicrobial resistant organisms poses a significant threat to the management and control of infectious diseases globally.[1] The World Health Organization (WHO) recognises antimicrobial resistance (AMR) as a top priority for action at a national and global level.[2] The global burden of AMR review estimated that in 2019 almost 5 million deaths were directly associated with bacterial AMR.[3] The prevalence of AMR varies geographically but the resistant organisms associated with the highest mortality are *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, Streptococcus pneumoniae, Acinetobacter baumannii,* and *Pseudomonas aeruginosa*.[3]

The burden of AMR is likely to be significantly underestimated in low- and middle-income countries where there may be limited capacity for clinical sampling, laboratory detection or systematic surveillance.[3–6] One review that included some Pacific Island Countries (PIC) suggested a high burden of multidrug resistant (MDR) Gram-negative organisms which were often implicated in healthcare associated infections (HAI).[7] Gram-positive organisms such as *Staphylococcus aureus*, frequently related to skin and soft tissue infections and commonly causing bacteraemia and sepsis are a major clinical concern in some PICs.[7] MDR organisms are an emerging problem globally,[8] and with increased globalisation and movement of people between countries, it is possible that bacterial epidemiology may be changing.[6,9,10] The WHO has highlighted the need for national surveillance systems to monitor AMR in the Western Pacific Region.[11]

Fiji is an island nation in the South Pacific Ocean with a population of around 900,000.[12] Health services are provided by the Ministry of Health and Medical Services (MoHMS) and the country is divided into four geographical locations: the central, eastern, northern and western divisions for health services delivery.[13,14] Each division is further divided into subdivisions, medical areas, and zones. There are three main (divisional level) hospitals; Colonial War Memorial Hospital (CWMH) located in the capital, Suva, serves the central and eastern divisions, Lautoka hospital the western division and Labasa hospital the northern division. AMR is a priority health issue in Fiji and the first national AMR action plan was developed 2015 to provide a response framework.[15] There is a paucity of data on AMR in Fiji. Presently, Fiji does not have a national AMR surveillance system and is not enrolled into the WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS). The best available data regarding MDR bacterial isolates is documented in reports following outbreaks of HAIs in Intensive Care Units (ICU) at the CWMH.[16–20] Outbreaks involved carbapenem-resistant *A. baumannii* in the neonatal ICU (NICU)[17] and adult ICU[20] between 2016 and 2019.

Subsequently, there has been concern about a need to better understand the nature and extent of AMR more broadly in Fiji. The aim of this study is to determine the antimicrobial susceptibility profile of bacterial isolates and to specifically describe the type and rates of MDR organisms in CWMH, which is Fiji's national referral hospital.

Methods

Study design and settings

This retrospective study reviewed four year of data (January 1, 2019, through December 31, 2022) from the microbiology laboratory at CWMH which is the largest hospital in Fiji having over 500 beds.[21] CWMH is the main reference hospital for the central and eastern divisions which represents 47% of the total population.[12] The CWMH microbiological laboratory processes samples from all departments of the hospital and also from other health facilities in the two divisions of Fiji which includes seven subdivisional level hospitals, two specialised hospitals (dedicated to tuberculosis and mental health), 15 health centres and other private health facilities. On average, the laboratory processes 4500 samples per month for culture and when isolates require it, antimicrobial susceptibility testing (AST).

Inclusion and exclusion criteria

Samples were taken from patients according to clinical need as determined by the treating healthcare professional. Bacterial isolates from these clinical samples (both sterile and non-sterile sites) were included in the analysis. Reports of 'no growth', 'no bacterial growth', 'normal flora', 'mixed bacteria', organisms with no AST results, no definitive organism identification and specific known skin contaminants e.g., *Bacillus subtilis, Bacillus* species, *Corynebacterium* species, plus any fungal or parasitic isolates were excluded. Bacteria isolates from non-clinical samples such as environmental or surveillance samples and isolates from other hospitals or healthcare facilities were also excluded from analysis. Repeat isolates of the same species from the same patient irrespective of the sample type were excluded so that only first isolates per patient with AST results in a single year were included in the analysis.

It is acknowledged that the COVID-19 pandemic likely had impact on health care access and sample collection for microbiological investigation at CWMH over the study period. The community outbreak was declared in Fiji in April 2021[22] and community members were encouraged to seek healthcare close to home from local health centres rather than travel to CWMH for outpatient services.[23] In June 2021, CWMH was the designated hospital for inpatient care of patients affected by COVID-19[22] and all non-COVID-19 inpatient care was delivered from a Field Hospital established by the Fiji Emergency Medical Assistance Team.[22] Microbiological samples were still processed by the CWMH laboratory.

Laboratory methods

All laboratory tests were carried out as per the locally approved standard operating procedures. Detailed laboratory methods are described in Supplementary Methods. Briefly, for microbiological cultures primary isolates were obtained by aseptically inoculating clinical samples onto solid agar plates. Bacterial identification (ID) and AST were performed using conventional methods (including colony morphology, and biochemical testing) with disc diffusion or an automated bacterial ID system (Vitek 2 compact, Biomerieux, France) according to manufacturer's instructions. The 2019 Clinical and Laboratory Standards Institute (CLSI) breakpoints were used to determine susceptibility or resistance. AST was performed in step wise manner whereby all samples were tested with a first round antimicrobial panel and progressed to a second round panel if isolates were resistant to a pre-determined selection of antimicrobials (Supplementary Table S1). All culture, ID and AST results were entered into the laboratory information management system (LIMS). Testing for detection of carbapenemase production was performed using the modified carbapenem inactivation method (mCIM) as per the CLSI guidelines[23] (Supplementary Methods). Systematic mCIM testing commenced in 2021 for *Enterobacterales* and *P. aeruginosa*. While routine mCIM testing of *A. baumannii* isolates started in November 2022.

Data analysis

Data were sourced from the LIMS which included patient demographics (age and sex), health facility (name of health facility, ward, department), and laboratory data (laboratory number, specimen type, date of culture confirmation, organism isolated and antimicrobials susceptibility results). Data were uploaded into WHONET software (version 5.6),[24] and the following parameters were used to generate cumulative antibiograms: percentage susceptibility, first isolates with antimicrobial susceptibility results and all organisms. Susceptibility results for <30 isolates were indexed in the respective antibiograms. In addition, WHONET outputs for resistance profile (include both intermediate and resistant) were used to determine MDR profile and organism-drug resistance combinations. MDR was defined as resistance to three or more classes of antimicrobials that the species would usually be expected to be susceptible to in the hospital.[25] The WHONET outputs were exported into Microsoft Excel (version 16.79.2) for further descriptive data analyses. Chi-squared trend analysis was performed to determine any difference in percentage of susceptibility over the four-year study period. A P-value <0.05 was considered as statistically significant.

Ethics

The study received ethics approval from Fiji National Health Research Ethics Review Committee (ID number: 27/2022) and the human research ethics committee of the University of Melbourne (ID number: 2022-25025-33185-3).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Results

Patients, samples, and isolates characteristics

During the four-year study period, a total of 29,222 positive cultures were included from CWMH. The largest number (77%, n = 22,536) of bacterial isolates were identified from clinical samples of adult patients (Table 1). While 21% (n = 6122) were from children under 15 years of age (which includes 8% n = 2278 from newborns, up to 28 days old). Most, 56% (n = 16,257) of the positive cultures were from females. Regarding the location of patients at the time of sample collection, half of the positive cultures were from inpatient wards (n = 14,602). Throughout the study period, Gram-negative organisms were predominant (62%, n = 18,084). *K. pneumoniae* was the most common organism accounting for 18% of the total (n = 5363), followed by *E. coli* (15%, n = 4321), coagulase negative *Staphylococcus* spp. (14%, n = 4119) and *S. aureus* (10%, n = 3041) (Table 2, Supplementary Figure S1). Overall, the main sources of isolates were blood cultures (24%, n = 6950) or pus/wound swabs (24%, n = 6925). However, specific bacteria were more prevalent from specific sites, for example A. *baumannii* (24%) and *K. pneumoniae* (22%) were frequently cultured from respiratory samples (Fig. 1), *E. coli* isolates grew mostly from urine samples (34%) while *P. aeruginosa* (41%) and *S. aureus* (59%) were most often from pus/wound swabs. The majority of coagulase negative *Staphylococcus* spp. (85%) were isolated from blood culture (these may have represented contaminated samples).

Characteristics	2019	2020	2021	2022	Total
	CWMH n (%)	CWMH n (%)	CWMH n (%)	CWMH n (%)	CWMH n (%)
Sex					
Female	5355 (60)	4348 (54)	3179 (54)	3375 (50)	16,257 (56)
Male	3454 (39)	3397 (44)	2593 (44)	3276 (49)	12,720 (44)
Unknown	84 (1)	35 (0.4)	91 (2)	35 (1)	245 (1)
Age group					
<15 years	1651 (19)	1857 (24)	1174 (20)	1440 (22)	6122 (21)
≥15 years	7113 (80)	5875 (76)	4328 (74)	5220 (78)	22,536 (77)
Unknown	129 (1)	48 (1)	361 (6)	26 (0.4)	564 (2)
Patient Location[a]					
A & E	1845 (21)	1474 (19)	1118 (19)	1343 (20)	5780 (20)
ICU[b]	1232 (14)	1544 (20)	1028 (18)	927 (14)	4731 (16)
Inpatient	4420 (50)	3794 (49)	2989 (51)	3399 (51)	14,602 (50)
Outpatient	1396 (16)	967 (12)	724 (12)	1016 (15)	4103 (14)
Unknown	0	1 (0.01)	4 (0.1)	1 (0.01)	6 (0.02)
Sample type					
Blood	2031 (23)	1649 (21)	1537 (26)	1733 (26)	6950 (24)
Genital Swab	1642 (18)	979 (13)	585 (10)	514 (8)	3720 (13)
Other[c]	911 (10)	1174 (15)	943 (16)	1049 (16)	4077 (14)
Pus/wound swab	1890 (21)	1927 (25)	1460 (25)	1648 (25)	6925 (24)
Respiratory[d]	1065 (12)	1069 (14)	653 (11)	1020 (15)	3807 (13)
Urine	1354 (15)	982 (13)	685 (12)	722 (11)	3743 (13)
Organism group					
Gram negative	5514 (62)	4904 (63)	3578 (61)	4088 (61)	18,084 (62)
Gram positive	3379 (38)	2876 (37)	2285 (39)	2598 (39)	11,138 (38)

[a]Patient location at the time of sample collection. [b]Include adult, paediatrics, and maternity ICUs. [c]Includes body fluid, CSF, aspirates, tips etc. [d]Includes nasopharyngeal, throat and sputum samples.
A & E, Accident and Emergency; CWMH, Colonial War Memorial Hospital; ICU, Intensive Care Unit.

Table 1: **Patient characteristics, sample, and organism types, 2019–2022.**

Antimicrobial susceptibility profile

K. pneumoniae and E. coli were the most common *Enterobacterales* isolated at CWMH. Overall, fewer than 70% of the isolates were susceptible to at least one of the first line antimicrobials (Table 2, Supplementary Table S2a). Time trend analysis showed a steady decline in susceptibility to cefalotin (60% susceptible in 2019 to 46% in 2022, $P \leq 0.0001$), chloramphenicol (74%–59%, $P \leq 0.0001$), and trimethoprim-sulfamethoxazole (66%–64%, $P = 0.02$) among *K. pneumoniae*, and trends in reduced susceptibility to gentamicin (79%–65%, $P < 0.0001$) and chloramphenicol (86%–71%, $P < 0.0001$) among *E. coli* isolates (Fig. 2, Supplementary Table S3). Among antimicrobials tested in urine isolates, susceptibility to cefaclor, trimethoprim and nitrofurantoin decreased over the four-year study period. Due to selective AST practices, only a subset of isolates (38%–46% of *K. pneumoniae and* 28–44% of *E. coli)* were tested against second line antimicrobials each year. More than 97% of *K. pneumoniae*, isolates were susceptible to meropenem and amikacin throughout the study period. Similarly, over 97% of *E. coli* isolates were susceptible to amikacin. However, susceptibility to meropenem amongst *E coli* declined from 99% (272/274) in 2019 to 79% (255/325) in 2022 ($P < 0.0001$), for both organisms, susceptibility to ciprofloxacin and ceftriaxone also declined (Fig. 2, Supplementary Table S3). *Enterobacter cloacae* and *Proteus mirabilis* had low susceptibility (<70%) to first line antimicrobials but remained highly susceptible to meropenem and amikacin (Table 2, Supplementary Table S2a). For *Salmonella* Typhi over 98% of isolates were susceptible to all tested antimicrobials throughout the study period.

P. aeruginosa isolates had variable susceptibility (82%–92%) to first line antimicrobials including gentamicin, ceftazidime, piperacillin-tazobactam and

Organism	Number of patients	% of isolate		First round antimicrobials												Second round antimicrobials¶ (Only selected isolates tested)							
				AMP	CEC §	CEP	CHL‡	CLO	DOX	ERY	GEN	NAL †	NIT †	PEN	SXT‡	TMP†	AMK	CAZ§	CIP§	CRO	MEM	RIF	TZP§	VAN
Klebsiella pneumoniae	5363	18	%S	0	37	55	70	-	-	-	59	73	64	-	67	39	99	-	66	17	99	-	-	-
			n	*5016*	*916*	*3940*	*3725*				*5032*	*911*	*1014*		*4365*	*999*	*2018*		*2248*	*2489*	*1990*			
Escherichia coli	4321	15	%S	18	69	40	81	-	-	-	73	66	88	-	58	43	98	-	63	51	91	-	-	-
			n	*4048*	*1343*	*2547*	*2485*				*4018*	*1332*	*1479*		*2855*	*1466*	*1245*		*1728*	*1895*	*1231*			
Coagulase negative *Staphylococcus*	4119	14	%S	-	64	-	64	63	80	56	-	-	-	12	49	-	-	-	59	-	-	81	-	99
			n		*3928*		*758*	*3873*	*3928*	*3661*		-	-	*4116*	*1147*				*1329*			*1426*		*597*
Staphylococcus aureus	3041	10	%S	-	87	-	94	87	98	90	-	-	-	4	98	-	-	-	93	-	-	98	-	100
			n		*2989*		*224*	*2991*	*2888*	*2565*				*3030*	*366*				*345*			*385*		*237*
Pseudomonas aeruginosa	2128	7	%S	-	-	-	-	-	-	-	82	-	-	-	-	-	-	92	86	-	34	-	91	-
			n								*1987*							*1580*	*1824*		*152*		*1703*	
Acinetobacter baumannii	1826	6	%S	-	-	-	-	-	-	-	56	-	-	-	56	-	39	31	59	15	49	-	40	-
			n								*1741*				*1756*		*741*	*354*	*1046*	*1128*	*864*		*506*	
Beta-haemolytic, *Streptococcus* spp.	1767	6	%S	-	-	-	100	-	57	96	-	-	-	99	-	-	-	-	-	-	-	-	-	-
			n				*1545*		*1675*	*1512*				*1766*										
Enterococcus spp.	1054	4	%S	85	-	-	71	-	-	-	-	-	92	-	-	-	-	-	62	-	-	-	-	96
			n	*991*			*869*						*1052*						*525*					*458*
Enterobacter cloacae	621	2	%S	0	27	0	69	-	-	-	68	65	63	-	73	39	99	-	60	30	100	-	-	-
			n	*560*	*101*	*444*	*417*				*583*	*98*	*117*		*507*	*115*	*199*		*248*	*268*	*196*			
Proteus mirabilis	584	2	%S	20	58	50	58	-	-	-	59	65	0	-	73	47	95	-	66	56	100	-	-	-
			n	*538*	*87*	*420*	*408*				*554*	*85*	*101*		*483*	*99*	*208*		*295*	*321*	*206*			
Pseudomonas fluorescens	463	2	%S	-	-	-	-	-	-	-	77	-	-	-	-	-	-	95	93	-	-	-	93	-
			n								*232*							*229*	*385*				*276*	
Klebsiella oxytoca	407	1	%S	0	46	55	70	-	-	-	62	79	69	-	65	38	98	-	56	18	98	-	-	-
			n	*368*	*98*	*277*	*264*				*380*	*98*	*101*		*305*	*102*	*139*		*161*	*175*	*133*			
Acinetobacter lwoffii	299	1	%S	-	-	-	-	-	-	-	75	-	-	-	80	-	80	79*	87	55	72	-	88	-
			n								*274*				*287*		*79*	*28*	*148*	*157*	*78*		*48*	
Serratia marcescens	269	1	%S	0	6	0	50	-	-	-	48	85	0	-	55	30	92	-	72	27	100	-	-	-
			n	*243*	*33*	*195*	*181*				*259*	*34*	*38*		*232*	*37*	*134*		*172*	*177*	*132*			
Enterococcus faecalis	237	1	%S	95	-	-	64	-	-	-		-	98	-	-	-	-	-	68	-	-	-	-	98
			n	*230*			*96*						*237*						*196*					*126*

¶Tested in isolates resistant to first round antimicrobials § Among *Enterobacterales* CEC is tested on urine isolates only. †for urine isolates only. ‡second-round antimicrobial for *Staphylococcus* spp. ¥first -round antimicrobials for *Pseudomonas* spp. AMP, Ampicillin; CEC, Cefaclor; CEP, Cefoalotin; CHL, Chloramphenicol; CLO, Cloxacillin; DOX, Doxycycline; ERY, Erythromycin; GEN, Gentamicin; NAL, Nalidixic acid; NIT, Nitrofurantoin; PEN, Penicillin; SXT, Trimethoprim-Sulfamethoxazole; TMP, Trimethoprim; AMK, Amikacin; CAZ, Ceftazidime; CIP, Ciprofloxacin; CRO, Ceftriaxone; MEM, Meropenem; RIF, Rifampicin; TZP, Piperacillin-Tazobactam; VAN, Vancomycin; spp., species; %S, percent susceptibl; n, number of isolates tested. Green ≥90% of isolates susceptible, Amber 70–89% of isolates susceptible, Red ≤70% of isolates susceptible, Grey* <30 isolates tested, - not routinely tested for the specific isolates.

Table 2: **Antimicrobial susceptibility profile of common bacterial isolates from colonial war memorial hospital, 2019–2022.**

ciprofloxacin in each study year (Table 2). However, trend analysis showed declining susceptibility over time to ceftazidime and piperacillin-tazobactam (Fig. 2, Supplementary Table S3). Overall, 7% of *P. aeruginosa* isolates (fewer than 30 isolates in 2019 and 2021) were tested against meropenem and only 34% of these were susceptible. *A. baumannii* isolates had generally low (<70%) susceptibility to the first line drugs including gentamicin and trimethoprim-sulfamethoxazole. Overall, 41% of *A. baumannii* isolates were tested against amikacin, 47% were tested against meropenem, and 57% were tested against ciprofloxacin. Testing for ceftazidime and piperacillin-tazobactam started in 2020 and 25% and 46% of isolates were tested respectively.

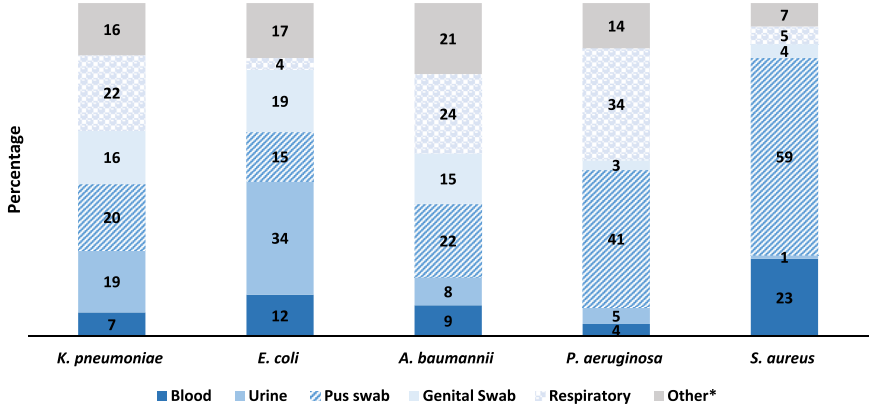

Fig. 1: **Common bacterial species isolated by sample type in colonial war memorial hospital, 2019–2022**. *Includes body fluid, CSF, aspirates, tips etc.

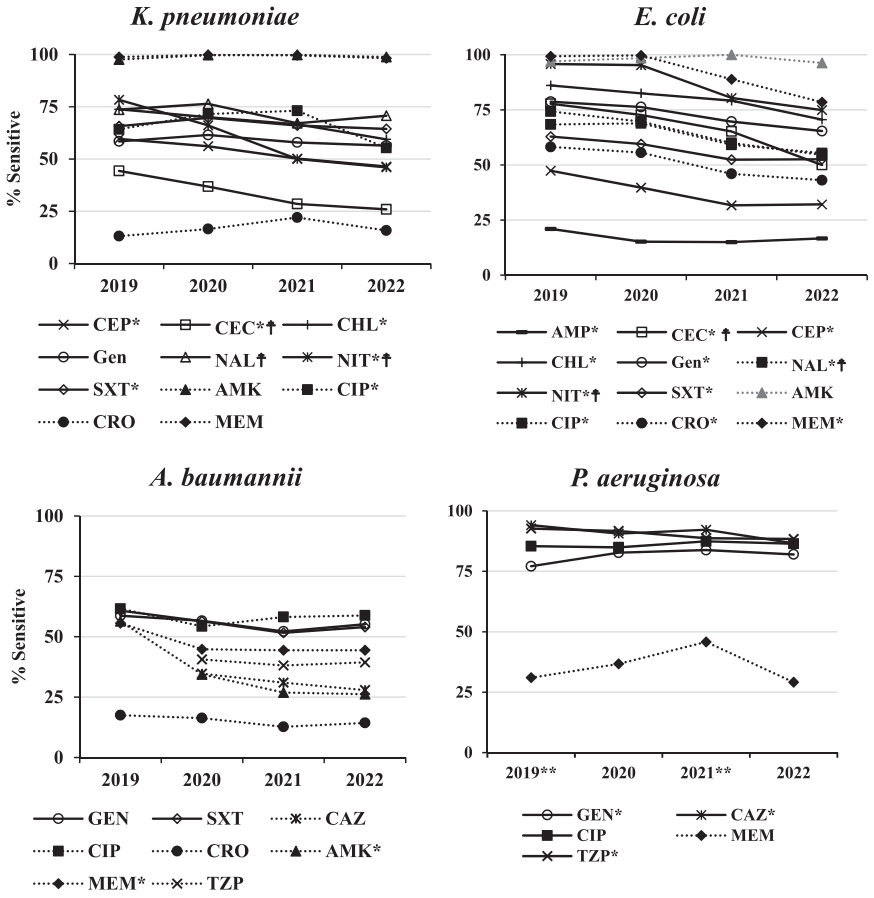

Fig. 2: **Trends in antimicrobial susceptibility profiles among common gram-negative organisms in colonial war memorial hospital, 2019–2022**. †Tested in urine isolates *P < 0.05, ** <30 isolates tested for meropenem. AMP, Ampicillin; CEC, Cefaclor; CEP, Cefalotin; CHL, Chloramphenicol; GEN, Gentamicin; NAL, Nalidixic acid; NIT, Nitrofurantoin; SXT, Trimethoprim-Sulfamethoxazole; AMK, Amikacin; CAZ, Ceftazidime; CIP, Ciprofloxacin; CRO, Ceftriaxone; MEM, Meropenem; RIF, Rifampicin; TZP, Piperacillin-Tazobactam.

A. baumannii isolate susceptibility to amikacin declined from 56% in 2019 to 26% in 2022, P < 0.0001, while there was no statistically significant change in ciprofloxacin, meropenem, ceftazidime, or piperacillin-tazobactam susceptibilities over time in the subsets of isolates tested (Fig. 2, Supplementary Table S3).

S. aureus accounted for 10% of all isolates identified, and more than 85% were methicillin susceptible throughout the study period while susceptibility to penicillin was <5% (Table 2, Supplementary Table S2b). Only 7–13% of *S. aureus* isolates were tested against vancomycin, but all were susceptible. Overall, 12% (n = 366) of *S. aureus* isolates were methicillin resistant (MRSA) which remained in the range of 11%–13% over the four years. The antimicrobial susceptibilities of coagulase negative *Staphylococcus spp.* are shown in Table 2 and Supplementary Table S2b. CWMH did not have procedures to differentiate if these isolates were likely to be skin contaminants or to modify reports issued accordingly during the study period.

The majority of enterococcal isolates were reported as undifferentiated *Enterococcus* spp. (Table 2) during the study period. A total of 1415 enterococcal isolates were reported from CWMH, of these 153 (11%) were from sterile sites (blood and cerebrospinal fluid). There were 41 vancomycin resistant enterococci (VRE), of these, 49% (n = 20) were *Enterococcus. faecium* and 44% (n = 18) were undifferentiated *Enterococcus* spp. The majority of VRE were cultured either from urine (34%, n = 14) or blood culture (27%, n = 11) samples.

Extended spectrum beta-lactamase (ESBL) producing *Enterobacterales*

Overall, 24%, (3107/12,853) of the *Enterobacterales* isolates from CWMH were ESBL producing. Of these, 64% (n = 2003) were *K. pneumoniae*, 25% (n = 781) *E. coli*, 4% (n = 138) *K. oxytoca* and 4% (n = 138) *Proteus mirabilis*. Around one third (29%) of the ESBL producing *Enterobacterales* were cultured from urine and 12% from blood. Among *K. pneumoniae*, the proportion of reported

ESBL producing isolates increased from 30% in 2019 to 43% in 2022. While in *E. coli*, the proportion of ESBL producing increased from 10% in 2019 to 23% in 2022.

Carbapenem-resistant organisms (CRO)

A total of 733 carbapenem resistant organisms (CRO) were reported from the CWMH. Over 90% of CROs were from inpatients in CWMH with 53%, (n = 389) from hospital wards, (mainly acute medical and surgical wards) and 37%, (n = 268) from the ICUs (Supplementary Figure S2, Supplementary Table S4). Carbapenem resistant *A. baumannii* and *P. aeruginosa* were reported from almost all wards at CWMH throughout the study period (Fig. 3, Supplementary Figure S2). *A. baumannii* was the most common CRO at CWMH overall, comprising 61% (n = 445) of CRO isolates followed by *E. coli* 15% (n = 110) and *P. aeruginosa* 14% (n = 101). Carbapenem resistant *A. baumannii* was the most common CRO reported in the adult ICU (80%, n = 148) (Supplementary Figure S2). *E. coli* strains resistant to carbapenem were uncommon in 2019 and 2020 where only three sporadic cases were reported (Fig. 3). However, from the beginning of 2021, the number steadily increased with the highest number reported between December 2021 and February 2022. Most (46%, n = 51) of the carbapenem resistant *E. coli* were from acute medical and surgical wards (Supplementary Figure S2). Carbapenem resistant *K. pneumoniae* were reported sporadically during the study period (Fig. 3).

Testing for carbapenemase production was able to be conducted for *Enterobacterales* and *P. aeruginosa* from 2021 to 2022, while testing of *A. baumannii* isolates started in November 2022. Overall, 83% of the carbapenem resistant *E. coli* tested were shown to producing carbapenemases (n = 91), 81% of the *K. pneumoniae* tested (n = 13) and 55% of the *P. aeruginosa* tested (n = 56) produced carbapenemases. This data will be reported elsewhere. The CROs identified were resistant to the majority of other antimicrobials tested except amikacin, where susceptibility was 92% among *E. coli* isolates, 56% in *K. pneumoniae* and 9% in *A. baumannii*. Colistin susceptibility data was available for eleven CROs, all except one *K. pneumoniae* isolate were susceptible.

Discussion

In this study, we used four years of systematically collected microbiology laboratory data to comprehensively describe the situation of AMR in CWMH, Fiji. Overall, Gram-negative organisms commonly had high rates of resistance to first line antimicrobials. The increasing rate of ESBL production (and third generation cephalosporin resistance) among *K. pneumoniae* and *E. coli* isolates is especially concerning, as ceftriaxone is widely used for treatment of severe infections in CWMH, so this changing epidemiology will have important clinical impact. The data from this study contrasts with data from other Pacific Island countries such as Vanuatu, Samoa, Tonga, Kiribati, and Cook Islands showing higher susceptibility of *K. pneumoniae* and *E. coli* isolates to ceftriaxone.[26,27]

Carbapenem-resistant *Enterobacterales* (CRE) have emerged as important pathogens globally.[28] Historical data indicates that carbapenem-resistant *K. pneumoniae* and other CROs were previously very uncommon in Fiji. According to the 2014 WHO report, carbapenem-resistance among *K. pneumoniae* isolates was <1%.[5] Similarly, in 2016, out of the 127 *E. coli* isolates tested against meropenem, only one was resistant (unpublished CWMH laboratory antibiogram). Our data revealed the emergence and rapid spread of carbapenemase producing *E. coli* in CWMH which were

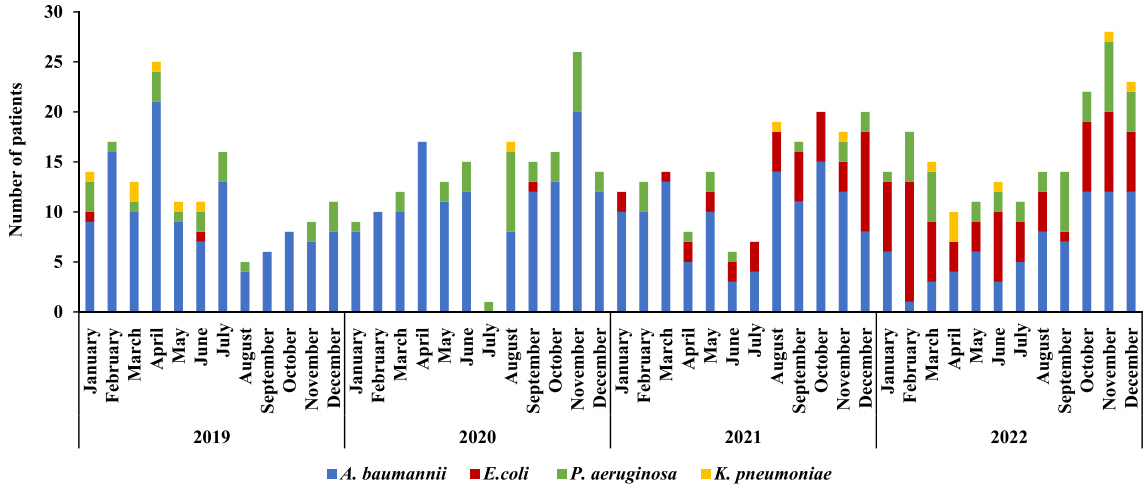

Fig. 3: **Number of carbapenem-resistant organisms reported in colonial war memorial hospital, 2019–2022.**

susceptible only to amikacin and colistin. This presents an important emerging clinical challenge and suggests that further studies are required to investigate this. Exploration of means to access newer antimicrobials is likely to be urgently required as infections due to CROs are likely to have major health and economic consequences.

A. baumannii is one of the common causes of HAI in the ICU at CWMH[16] and outbreaks with high mortality rates have previously been reported.[17,20] In this study, *A. baumannii* were reported from wards where nearly half of the isolates were resistant to carbapenems. A recent study by Baleivanualala et al.,[20] reported *A. baumannii* isolates from the adult ICU in 2019 to be genetically highly related to the 2016 NICU outbreak. This could indicate persistence of the isolates in environmental reservoirs in the hospital and more work is being done to understand this issue. HAIs caused by other MDR Gram-negative organisms have also been previously reported in CWMH. In 2007, ESBL producing *Enterobacter aerogenes* (presently known as *Klebsiella aerogenes*)[29] caused an outbreak of blood stream infections (BSI) in NICU.[18] ESBL-producing K. *pneumoniae* were also found to be the main cause of HAIs in the adult ICU in 2011 and 2012.[16] These outbreaks can be associated with significant patient morbidity and mortality.

There is some suggestion that the MRSA rate in the CWMH may have increased given a previous report of 5% in 2005[30] compared to 12% in our study, although this spans a prolonged period. The current MRSA rate in Fiji is higher than what has been reported from Vanuatu (3%)[26] but it is lower than the reported rate in Kiribati (26%), Samoa (43%), Tonga (43%) and Papua New Guinea (48%).[7,27] Consistent with previous studies in Fiji, all *S. aureus* isolates were vancomycin susceptible.[31] Of note, coagulase negative *Staphylococcus* spp. were prevalent and 85% were isolated from blood culture. It is not possible to determine if these isolates were associated with infection or were contaminants, but the high frequency does make contamination seem very likely. Poor blood sample collection techniques and frequent shortage of resources such as skin disinfectants could be associated with a high blood culture contamination rate. If in fact true, this may also have cost implication as the laboratory is utilising limited resources for isolates without clinical significance. Presently there is no publicly available data on enterococci in Fiji. Consistent with other studies, *E. faecium* exhibited a higher level of AMR including resistance to ampicillin and vancomycin.[32,33] Further studies are needed to better understand the burden of infection and colonisation in order to guide appropriate surveillance, screening, treatment, and control measures.

The causes of the emergence of MDR organisms and increasing numbers at CWMH are likely multifactorial. Overuse and misuse of antimicrobials may contribute to this observed increase. Fiji has national antibiotic guidelines to support clinical decisions regarding antimicrobial prescriptions.[34] CWMH also has an approval system for the use of restricted antimicrobials, however, there is no established system for monitoring the rational use of antimicrobials. Frequent and prolonged stockouts of antimicrobials further poses a significant challenge for the hospital. Overcrowding in the wards is a major issue in CWMH.[17,18] Workforce shortages[35,36] mean that nursing and cleaning staff may find it difficult to adhere to IPC practices (e.g., low hand hygiene compliance and inadequate cleaning) which could have facilitated cross-transmission and spread of MDR infections in the hospital. Equipment and infrastructure maintenance is a challenge, and access to consumables to support IPC can be problematic at the hospital.[17,18] Population movement is also one of the drivers for importation of MDR organisms.[9] Fiji uses overseas medical referral systems to countries[37] with high AMR rates.[38] This means that patients requiring complex care are often repatriated to CWMH after prolonged international hospitalisations and they may bring MDR isolates with them. This is worthy of further investigation to determine any evidence of epidemiologic links to international travel in patients affected by the MDR organisms.

Understanding the evolving AMR epidemiology is important for several reasons. Improving laboratory capabilities to accurately identify AMR patterns, (including addressing shortages of laboratory consumables) and the use of rapid diagnostic tests (such as PCR) where relevant can facilitate rapid identification of organisms and resistance patterns to guide clinical care, help recognize outbreaks early and inform IPC activities. Updating empiric treatment guidelines, and the essential drug list may also be required.

There are several limitations to our research. Clinical sample collection was determined by treating healthcare professionals. While no changes to clinicians usual sampling practices were anecdotally reported, the study period does span the COVID-19 pandemic which may have influenced hospital casemix. It is possible that patients were referred later from other healthcare settings after receiving more prolonged empirical antibiotics. However, patients with MDR infections would eventually have reached CWMH historically, as it is the national referral hospital. Our study uses data from a clinical microbiology laboratory, so the information obtained depends on the AST and reporting protocols. The 2019 CLSI guidelines were used throughout the study period, so breakpoints for some isolates might not have been updated which could have impacted classification of their susceptibility profiles.

The laboratory uses selective antimicrobial testing procedure whereby only organisms resistant to first line antimicrobials are tested against second line antimicrobials namely, ciprofloxacin, ceftriaxone, ceftazidime, piperacillin-tazobactam and vancomycin, this is likely to

have overestimated resistance rates among second line antimicrobials. Importantly CWMH has frequent shortages of antimicrobial discs required for AST, including those used for determination of ESBL production, which could have led to an underestimation of the rates of ESBLs. Additional antimicrobial discs including meropenem were procured in September 2022, this might have improved the detection of carbapenem resistant organism in the last quarter of 2022. Our study included first isolates of a given species with AST results per patient per year. As a result, we may have missed second or repeat infections by the same organism with altered susceptibility patterns. Due to the absence of clinical information, it was not possible to determine if isolates represented infection or colonisation, nor if isolates were healthcare or community associated.

CWMH is the largest national referral hospital which serves 47% of the Fijian population. Our study findings reflect the current AMR situation in the hospital but may not be representative of all other hospitals in Fiji. Similar studies need to be conducted in the remaining two divisional hospitals to better understand the national AMR profile.

In conclusion, our study provided new findings worthy of further examination. We demonstrated high rates of ESBL producing *K. pneumoniae,* endemic MDR and carbapenem-resistant *A. baumannii,* and the emergence and rapid dissemination of carbapenemase producing *E. coli* in Fiji's largest hospital. In recognition to the growing burden of AMR, there is a need to allocate more resources to improve existing capacity and to develop effective and multimodal strategies to control the spread of infections, mitigate the threat of AMR in the island nation.

Contributors

AGS, KB BPH, VP, and RN, conceived the study and designed the study protocol. AGS, PP, CRL, RJ, and VP analysed and interpreted data. RN, TYS, MR, DC, BPH provided clinical microbiology and infection prevention and control perspectives and expertise to study design and analysis. PP, SA, RP, and VP, managed sample testing and reporting. AGS, VP and PP prepared the manuscript which was edited by BPH and KB. AGS, PP, CRL, RN, SA, TYS, MR, AS, DC, RJ, RP, KB, BH and VP read and approved the final manuscript.

Data sharing statement

Data used in the analysis and interpretation of this work is available in the Supplementary tables.

Declaration of interests

All authors declare no competing interests and confirm that authors or their institutions have not received any payments or services in the past 36 months from a third party that could be perceived to influence, or give the appearance of potentially influencing, the submitted work.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2024.101036.

References

1 World Health Organization. *The evolving threat of antimicrobial resistance options for action*. Geneva, Switzerland: WHO; 2012.
2 *Guidelines on core components of infection prevention and control programmes*; 2018. [cited 5 August 2023]. Available from: https://iris.who.int/bitstream/handle/10665/251730/9789241549929-eng.pdf?sequence=1.
3 Antimicrobial Resistance C. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022;399(10325):629–655.
4 Dunachie SJ, Day NP, Dolecek C. The challenges of estimating the human global burden of disease of antimicrobial resistant bacteria. *Curr Opin Microbiol*. 2020;57:95–101.
5 World Health Organization. *Antimicrobial resistance: global report on surveillance 2014*. Geneva, Switzerland: WHO; 2014.
6 Loftus M, Stewardson A, Naidu R, et al. Antimicrobial resistance in the Pacific Island countries and territories. *BMJ Glob Health*. 2020;5(4):e002418.
7 Foxlee ND, Townell N, McIver L, Lau CL. Antibiotic resistance in pacific island countries and territories: a systematic scoping review. *Antibiotics (Basel)*. 2019;8(1):29.
8 *Prioritization of pathogens to guide discovery research and development of new antibiotics for drug-resistant bacterial infections including tuberculosis*. 2017 [cited 8 August 2023].
9 Frost I, Van Boeckel TP, Pires J, Craig J, Laxminarayan R. Global geographic trends in antimicrobial resistance: the role of international travel. *J Travel Med*. 2019;26(8):taz036.
10 World Health Organisation. In: Knobler S, Mahmoud A, Lemon S, Pray L, eds. *The impact of globalization on infectious disease emergence and control: exploring the consequences and opportunities: workshop summary*. Washington (DC): The National Academies Collection: Reports funded by National Institutes of Health; 2006.
11 World Health Organization. *Antimicrobial resistance in the Western Pacific Region: a review of surveillance and health systems response*. Geneva, Switzerland: WHO; 2014.
12 FBoS. *Population and housing census 2017*. Suva: Fiji Bureau of Statistics; 2018.
13 Roberts GI W, Tuiketei T, Nadakuitavuki R, Otealagi S, Singh S, Pellny M, Fong M, Mohammed J, Chang O. *The Fiji islands health system review*. Geneva: World Health Organization; 2011:1–150.
14 MoHMS. *Fiji ministry of health and medical services*. Suva Fiji: Annual report 2016; 2017.
15 MoHMS. *Fiji national antimicrobial resistance action plan*. Suva: Services MoHaM; 2015.
16 Naidu K, Nabose I, Ram S, Viney K, Graham SM, Bissell K. A descriptive study of nosocomial infections in an adult intensive care unit in Fiji: 2011-12. *J Trop Med*. 2014;2014:545160.
17 Zimmerman PA, Lyman M, Andersson P. Acinetobacter baumannii *outbreak in NICU at the Colonial war memorial hospital Suva, Fiji*. Technical report; 2017.
18 Narayan SA, Kool JL, Vakololoma M, et al. Investigation and control of an outbreak of Enterobacter aerogenes bloodstream infection in a neonatal intensive care unit in Fiji. *Infect Control Hosp Epidemiol*. 2009;30(8):797–800.
19 Kumar S, Graham SM, Varman S, Kado J, Viney K. Resistance of bacterial isolates from neonates with suspected sepsis to recommended first-line antibiotics in Fiji. *Pediatr Infect Dis J*. 2015;34(8):915–916.
20 Baleivanualala SC, Isaia L, Devi SV, et al. Molecular and clinical epidemiology of carbapenem resistant Acinetobacter baumannii ST2 in Oceania: a multicountry cohort study. *Lancet Reg Health West Pac*. 2023;40:100896.
21 MoHMS. *Fiji ministry of health and medical services*. Suva, Fiji: Annual report 2015; 2016.
22 *FEMAT field hospital, Fiji ministry of health and medical services*. 2021. [press release].
23 Clinical and Laboratory Standards Institute. *Test for carbapenemases in enterobacteriaceae and Pseudomonas aeruginosa*. 28th ed. CLSI supplement M100; 2018.

24 *WHONET version 5.6*; 2023. [cited 20 March 2023]. Available from: https://whonet.org/software.html.
25 Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect*. 2012;18(3):268–281.
26 Foxlee ND, Townell N, Tosul MAL, McIver L, Lau CL. Bacteriology and antimicrobial resistance in Vanuatu: January 2017 to December 2019. *Antibiotics (Basel)*. 2020;9(4):151.
27 Loftus MJ, Everts RJ, Cheng AC, et al. Antimicrobial susceptibility of bacterial isolates from clinical specimens in four Pacific Island countries, 2017-2021. *Lancet Reg Health West Pac*. 2023;32:100677.
28 World Health Organization. *Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae Acinetobacter baumannii and Pseudomonas aeruginosa in health care facilities*. 2017.
29 Tindall BJ, Sutton G, Garrity GM. Enterobacter aerogenes Hormaeche and Edwards 1960 (Approved Lists 1980) and Klebsiella mobilis Bascomb et al. 1971 (Approved Lists 1980) share the same nomenclatural type (ATCC 13048) on the Approved Lists and are homotypic synonyms, with consequences for the name Klebsiella mobilis Bascomb et al. 1971 (Approved Lists 1980). *Int J Syst Evol Microbiol*. 2017;67(2):502–504.
30 Jenney A, Holt D, Ritika R, et al. The clinical and molecular epidemiology of Staphylococcus aureus infections in Fiji. *BMC Infect Dis*. 2014;14:160.
31 Loftus MJ, Young-Sharma T, Wati S, et al. Epidemiology, antimicrobial resistance and outcomes of Staphylococcus aureus bacteraemia in a tertiary hospital in Fiji: a prospective cohort study. *Lancet Reg Health West Pac*. 2022;22:100438.
32 Zhou X, Willems RJL, Friedrich AW, Rossen JWA, Bathoorn E. Enterococcus faecium: from microbiological insights to practical recommendations for infection control and diagnostics. *Antimicrob Resist Infect Control*. 2020;9(1):130.
33 Coombs GW, Daley DA, Yee NWT, Shoby P, Mowlaboccus S. Australian group on antimicrobial resistance (AGAR) Australian enterococcal sepsis outcome programme (AESOP) annual report 2020. *Commun Dis Intell (2018)*. 2022;46.
34 Fiji Antibiotic Guidelines. *Ministry of health and medical services* [cited 5 August 2023]. 2019. Available from: https://www.health.gov.fj/wp-content/uploads/2020/12/Fiji-Antibiotic-Guidelines.pdf.
35 Shaw W. *Ministry still facing a shortage of nurses*. The Fiji times; 2023.
36 Mateboto P. *Fiji's health services in crisis as nurses migrate*. IND-IN-DepthNews; 2023.
37 Boudville AI W, Motofaga S, Gilbert K, Annear P. *Overseas medical referral: the health system challenges for Pacific Island Countries*. New Delhi: World Health Organization Regional Office for South-East Asia; 2020.
38 Dixit A, Kumar N, Kumar S, Trigun V. Antimicrobial resistance: progress in the decade since emergence of New Delhi metallo-beta-lactamase in India. *Indian J Community Med*. 2019;44(1):4–8.