ORIGINAL ARTICLE

Microbial Profile, Antimicrobial Susceptibility, and Prevalence of MDR/XDR Pathogens Causing Medical Device Associated Infections: A Single Center Study

Vaibhav R Suryawanshi[1], Atmaram Pawar[2], Bharat Purandare[3], Niveda Vijayvargiya[4], Sandesh Sancheti[5], Susan Philip[6], Prasad Nagare[7]

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Abstract

Background: There is a scarcity of studies evaluating the microbial profile, antimicrobial susceptibility, and prevalence of MDR/XDR pathogens causing medical device-associated infections (MDAIs). The present study was sought in this regard.

Materials and methods: An ambispective-observational, site-specific, surveillance-based study was performed for a period of 2 years in the intensive care unit (ICU) and high dependency unit (HDU) (medicine/surgery) of a Tertiary-care University Hospital. Three commonly encountered MDAIs including central-line-associated bloodstream infections (CLABSI), catheter-associated urinary tract infections (CAUTI), and ventilator-associated pneumonia (VAP), were targeted.

Results and conclusion: Of the total 90 patients, 46 (51.1%) were admitted to the ICU (medicine/surgery), and the remaining 44 (48.8%) were admitted to the HDU (medicine/surgery). The median (P_{25}–P_{75}) age of the total patients was 55 (43.1–62.3) years. Male 61 (67.8%) preponderance was observed. Sixty-two of 90 (68.9%) were immunocompromised. A total of 104 pathogens causing MDAIs were isolated. *Staphylococcus epidermidis (CoNS), and Staphylococcus capitis* were commonly isolated multi-drug resistant (MDR) gram-positive pathogens causing MDAIs. Similarly, carba-resistant *Klebsiella pneumoniae, Stenotrophomonas maltophilia, and* carba-resistant *Acinetobacter baumanni* were commonly isolated MDR gram-negative pathogens causing MDAIs. Five of 9 (55.5%) *K. pneumoniae* and three of 9 (33.3%) *S. maltophilia* isolates were found to be extensively drug resistant. Among *Candida*, *C. parapsilosis* was the most prevalent fungal pathogen causing CLABSI and CAUTI in patients admitted to ICU/HDU.

Keywords: Antimicrobial susceptibility, Medical device-associated infections, MDR/XDR, Microbial profile.

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Highlights

- Hospital-associated pathogens, including *E. coli*, *S. aureus*, coagulase-negative *Staphylococci*, *P. aeruginosa*, and *K. pneumoniae*, were frequently identified as the bacteria causative of medical device-associated infections (MDAIs).
- An emerging trend of gram-negative bacteria causing MDAIs, including *A. baumanni* and *S. maltophilia*, which were identified to be MDR and XDR.
- *K. pneumoniae*, *A. baumanii*, and *S. maltophilia* were the isolated NDM-1 (blaNDM-1 gene carrier) bacteria. The treatment strategies for the same include polymyxins, tigecycline, and ceftazidime-avibactam-aztreonam in combination.

Introduction

A disease condition acquired during a hospital stay without evidence that it was active or incubating at the time of admission is recognized as a nosocomial infection, often known as a "healthcare-associated infection".[1] The centers for disease control and prevention (CDC) broadly categorizes the types of nosocomial infection as central line-associated bloodstream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), ventilator-associated pneumonia (VAP), and surgical-site infection (SSI). Central venous catheters continue to be the inevitable access to facilitating care for the patients receiving intensive care, resulting in catheter-associated infections (CAIs), especially bloodstream infections, which became a critical threat to the lives of the patients. Based on the data from the CDC's National Nosocomial Infections Surveillance (NNIS) system, in all types of intensive care units (ICUs),

[1,4–7]Department of Pharmacy Practice, Bharati Vidyapeeth (Deemed to be University), Poona College of Pharmacy, BVDU Katraj Campus, Pune, Maharashtra, India

[2]Department of Pharmaceutics, Bharati Vidyapeeth (Deemed to be University), Poona College of Pharmacy, Pune, Maharashtra, India

[3]Department of Infectious Diseases, Bharati Vidyapeeth (Deemed to be University) Medical College, Pune, Maharashtra, India

Corresponding Author: Vaibhav R Suryawanshi, Department of Pharmacy Practice, Bharati Vidyapeeth (Deemed to be University), Poona College of Pharmacy, BVDU Katraj Campus, Pune, Maharashtra, India, Phone: +91 9552956860, e-mail: phdrvaibhav@gmail.com

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the median rate of CLABSI is around 25.6% and ranges from 1.8 to 5.2 per 1000 catheter days.[2] These rates can be expected to be significantly higher for developing countries such as India, but they are exceptionally variable. The reported incidence rate of CLABSI (then referred to as central venous catheter-associated bloodstream infection) in India in 2007 was 7.92 per 1000 catheter days.[3] Whereas, the other studies showed incidence rates of 27 and 16 per 1000 catheter days, respectively.[4,5] In a recent epidemiological study, the rate of VAP was 65.4%, followed by CLABSI, which was 22.2%, and CAUTI, which was 12.35%.[6]

Medical device-associated infection is a critical clinical issue that is constantly changing due to factors such as the population at risk, the range of pathogens that are available, the shifting microbial spectrum brought on by climate change, and the ongoing emergence of superbugs (multi-drug, extensively-drug, and pan-drug resistant). Multi-drug-resistant (MDR) pathogens are the isolates resistant to representatives of three or more classes of antimicrobial agents, while extensively-drug-resistant (XDR) pathogens are the isolates resistant to all the drugs of at least one or two classes of antimicrobial agents. Patients who develop CLABSIs require prolonged ICU hospitalization, and prolonged total length of hospitalization, and it also increases the cost of illness for an individual or bearing agencies. On the other hand, patients with CLABSIs may develop septicemia very quickly, which may result in septic shock, which eventually leads to mortality. The reported rates of septicemia in one study were around 4–14% and a mortality rate of 12–25%.[7] In addition, CLABSI increases the likelihood that patients will experience secondary complications, such as infections at the injection site, terminal infections like sepsis, end-organ infections like endocarditis, meningitis, septic thrombophlebitis, and encephalopathies, which can eventually result in multi-organ dysfunction and death. As a result, it is crucial to identify these infections as soon as they manifest, and confirmation should be made using robust culture identification and susceptibility analysis tools, such as the BD BACTEC-TM and VITEK-2® systems. Furthermore, it is essential to implement antimicrobial stewardship principles in the management of these infections based on susceptibility analysis and rational use of antimicrobials.

The development and implementation of hospital antibiograms are of critical importance to stop the emergence of superbugs. It is essential to distinguish between contamination and infection, yet clinical studies often fail to provide clarity in this regard. Recent research on MDAIs in Indian patients receiving long-term catheterization has been scant. Rarely have we come across a study that evaluated CLABSIs, CAUTIs, and VAP alongside the prevalence of MDR/XDR pathogens. Hence, the present study sought to characterize the microbiological pattern, antimicrobial resistance, and prevalence of MDR and XDR organisms in patients admitted to intensive care and high dependency units (HDUs) who developed MDAIs.

Materials and Methods

Study Design, Settings, Patients, and Ethics

The present research was performed in an urban tertiary-care university hospital situated in Pune, India. In this ambispective-observational, site-specific surveillance study, we have included the patients admitted to the various units (medical ICU, surgical ICU, medical HDU, and surgical HDU) of the hospital between July 2021 and June 2023. The retrospective data was collected from the medical records room. The patient's data (admitted between July 2021 and May 2022) was obtained from medical case files and concern medical records with permission from the 'Medical Records Department' of our hospital. The study was approved by an institutional ethics committee with a waiver for patient informed consent (Ref no. MC/IEC/222). The following three commonly encountered MDAI: CLABSI, CAUTI, and VAP, as per the definition of the CDC's NNIS system criteria, were targeted.[1,2] The patients who had catheterization (involving intermittent, indwelling, or suprapubic catheters, etc.) were reviewed for chart analysis. The study's methodology, purpose, and voluntary nature were all communicated to the patients and their family members, along with the confidentiality of the patient's data. Patients and family members of unconscious patients admitted to the ICU or HDU were asked for consent before sharing the information. Patient inclusion criteria required ICU or HDU admission for more than or equal to 48 hours and were exposed to intravenous catheters [central venous catheter (CVC) or peripherally inserted central catheter (PICC)], urinary catheters (indwelling or suprapubic), and endotracheal or tracheostomy tubes. Whereas, the patients who underwent Hickman's catheterization, peripheral venous catheterization, who were receiving cancer chemotherapy, admitted to chronic wards, and who underwent recent surgery were excluded. Pediatrics, pregnant women, and patients who were diagnosed with psychiatric diseases were also excluded from the study.

Patients and Data/Sample Collection

For data collection, sociodemographic profile and clinical profile sheets were prepared. The following data were collected from the medical case files of the patients: immune status (competent or compromised), co-morbid conditions, onset of sign-symptoms, presence of catheters, site of cannulation, no. of catheters (single or multiple), types of catheters, no. of catheter-days, routine laboratory reports, procalcitonin levels, type of sample sent for culture identification and susceptibility analysis (performed using BACTEC™ and VITEK-2® systems), prophylactic or empirical antimicrobials given, type of microbial species (one, many, or mixed), colony count, length of ICU hospitalization, total length of hospitalization, etc. The criteria developed by the CDC were used to decide whether the patients were immunocompetent or immunocompromised.[8]

Central-line Associated Bloodstream Infection (CLABSI)

When a patient with a central venous catheter reported fever or additional signs of undetermined sepsis, the diagnosis of CLABSI was made. Under these conditions, two aseptic blood samples were obtained: one from the catheter itself and the other from the arm across from it. At our institution, the CVCs used were 2–4 lumen polyurethane latex-free catheters. Hands were cleaned thoroughly and a fresh pair of sterile gloves was put on at the time of specimen collection. Terminating the tubing from the injection cap and fastening a Luer lock stopped any continuous infusion. The injection cap was scrubbed with 70% alcohol and left to dry for a duration of one to three minutes. After that, a 10 mL prefilled normal saline syringe was used to flush the catheter. The first 3–5 mL of blood were extracted and thrown away. The 50 mL BACTEC bottles were then injected with 5–10 mL blood samples in order to process it further in a BACTEC device. The Luer lock was taken off, and the catheter was unclamped in order to resume the infusion. We used 70% alcohol to clean the hub. The infusion was resumed once the administration set was fastened to the injection cap.

At the time of the replacement of the old central venous catheter with a new one, and at the physician's discretion, the catheter was removed. Hands were properly cleaned before the catheter was removed, and fresh pairs of sterile gloves were put on. The bandage was taken off. The catheter was gradually withdrawn while a dry 2 × 2 gauze pad was kept over the site of insertion. After 3–4 minutes of constant pressure, the puncture site was covered with a bandage. A sterile container containing the tip of the line and a 5 cm distal portion of the catheter was sent to the lab for microorganism culture along with the necessary investigation form. The catheter was rolled over a blood agar plate containing 5% sheep blood using the semiquantitative "Maki's roll" approach.[9] Following a 48 hour incubation period at 37°C, the plate was examined for the development of any microorganisms, and the number of colonies that have been identified was recorded. The catheter was processed using the semiquantitative approach outlined by Maki et al.[9] and the blood culture samples were handled in accordance with customary microbiological protocols only. A significant colony count was defined as >15 CFU/plate.[9] The same microorganism was isolated from the catheter and blood culture, as indicated by CLABSI.

Catheter Associated Urinary Tract Infection (CAUTI)

In the case of CAUTI, a urine sample was collected aseptically using a sterile syringe and needle from the sampling port of the indwelling urinary catheter. The urine sample was transferred on blood agar, Mac Conkey's agar, and Sabouraud dextrose agar (SDA) and incubated from 24 to 48 hours at 35°C. The diagnosis of a CAUTI was made when the patient exhibited one or more of the following symptoms: 38°C temperature, urgency, suprapubic tenderness, gram-stained smear derived from centrifuged urine featuring bacteria or yeast cells, and isolation of bacteria or yeast from urine as a pure growth with a colony count of >104 colony forming units (CFUs)/mL.[10] A colony count >105 CFU/mL was considered significant in cases of bacteriuria.

Ventilator Associated Pneumonia (VAP)

When a mechanically ventilated patient developed a new fever, cough, and purulent expectoration and there was radiological evidence of a developing or growing pulmonary infiltrate as well as leukocytosis, VAP was suspected.[1,2,5] These patients' tracheal aspirate and bronchoalveolar lavage (BAL) fluid were used to inoculate blood agar, MacConkey's agar, and SDA. The plates were incubated for 24–48 hours at 35°C. In the case of a tracheal aspirate, a colony counts of >105 CFU/mL and >103 CFU/mL, respectively, was deemed significant.

Clinical and Laboratory Standards Institute (CLSI) 2018 manual was used to assess the susceptibility of all isolates derived from the cases of CLABSI, CAUTI, and VAP to different antimicrobials using the Kirby-Bauer disk diffusion technique.[11] Bacterial isolates were identified as per the standard microbiological profile. Carbapenamase-producing carbapenem-resistant organism (CP-CRO) testing was performed in a limited number of patients, mainly the patients who were severely ill and immunocompromised. Carbapenem-resistant *Enterobacteriaceae* (CRE) was defined as *Enterobacteriaceae* resistant to imipenem, meropenem, or ertapenem. Similarly, glucose non-fermenting (NFCROs) are glucose NF gram-negative bacilli that are resistant to imipenem and/or meropenem. Candida isolates were identified up to the species level by assessing the formation of germ tubes, sugar assimilation, and colony color on Candida agar. A Candida identification kit supplemented the species identification.

Results

Of 261 suspected cases of MDAI, 126 (48.3%) were on a CVC, 55 (21.1%) were on a PICC, and 80 (30.6%) were on a urinary catheter. Among the 126 suspected cases of CVC, 48 (38.1%) were positive by differential time to positivity. Similarly, of the 55 suspected cases of PICC and 80 suspected cases of urinary catheters, 16 (29%) and 21 (26.2%) were positive by differential time to positivity, respectively. Of 58 suspected cases that required invasive mechanical ventilation, 19 (32.7%) were positive by differential time to positivity for VAP. Using Maki's roll plate procedure, 12 CVCs were removed in total at the physicians' choice, but no PICCs were removed. By using Maki's roll plate approach, a total of 5 (41%) CVCs were found to be culture-positive; 4 (33%) of them were also shown to be positive by differential time to positivity. Figure 1 represents patient identification and study flow.

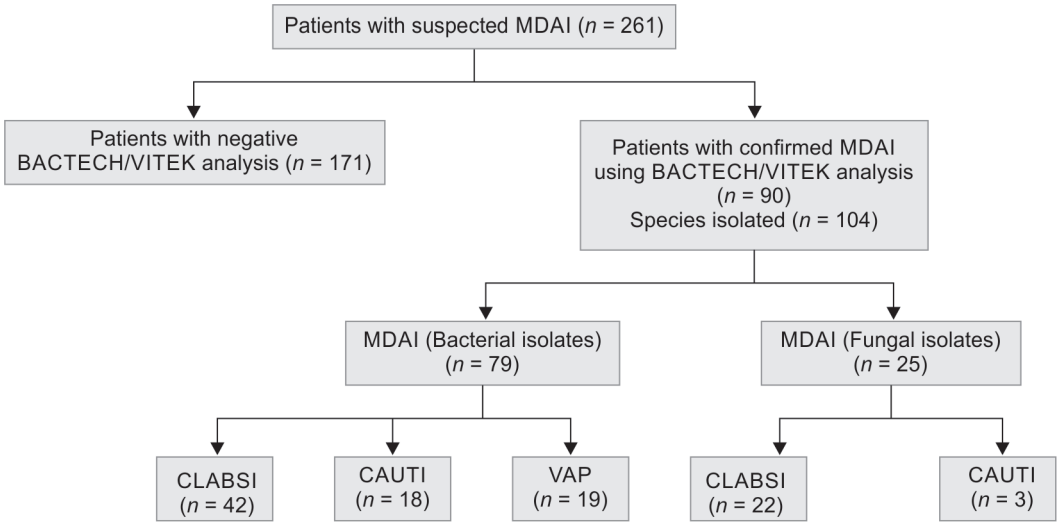

Fig. 1: Patient identification and study flow

CAUTI, catheter associated urinary tract infection; CLABSI, central line associated bloodstream infection; MDAI, medical device associated infection; VAP, ventilator associated pneumonia

Table 1: Demographics and clinical characteristics of ICU patients and HDU patients with MDAIs

Characteristics	*Total patients [N = 90, n (%)]*	*ICU patients with MDAIs [N = 46, n (%)]*	*HDU patients with MDAIs [N = 44, n (%)]*
Age (years)			
Mean (SD)	51.8 (13.2)	54.2 (12.5)	49.3 (13.7)
Median (P_{25}–P_{75})	55 (43.1–62.3)	56 (43.8–62.2)	51 (38.3–32.8)
Gender			
Male	61 (67.8)	32 (35.6)	29 (32.2)
Female	29 (32.2)	14 (15.6)	15 (16.7)
Comorbidities			
Chronic kidney disease	74 (82.2)	33 (36.6)	41 (45.5)
Hypertension	71 (78.9)	40 (44.4)	31 (34.4)
Uncontrolled diabetes mellitus	41 (45.6)	26 (28.9)	15 (16.7)
Ischemic heart disease	28 (31.1)	21 (23.3)	7 (7.8)
Neurological disease	10 (11.1)	7 (7.8)	3 (3.3)
Chronic liver disease	7 (7.8)	5 (5.6)	2 (2.2)
Asthma or COPD exacerbation	7 (7.8)	3 (3.3)	4 (4.4)
Immune status			
Immunocompromised	62 (68.9)	40 (86.9)	22 (50)
Immunocompetent	28 (31.1)	11 (23.9)	17 (38.6)
Types of MDAI (*N* = 104), *n* (%)			
CLABSI	64 (61.5)	25 (46.3)	39 (78)
CAUTI	21 (20.2)	10 (18.5)	11 (22)
VAP	19 (18.3)	19 (35.2)	–
Site of venous cannulation			
Femoral vein	37 (41.1)	18 (20)	19 (21.1)
Jugular vein	24 (26.6)	14 (15.5)	10 (11.1)
Basilic vein	20 (22.2)	09 (10)	11 (12.2)
Subclavian vein	09 (10.6)	05 (5.6)	04 (4.4)
Duration of catheterization (d)			
Median (P_{25}–P_{75})	10 (7–18)	10 (6–13)	9 (7–18)
≥12 days	40 (44.4)	22 (47.8)	18 (40.9)
<12 days	50 (55.6)	24 (52.2)	26 (59.1)
Length of ICU/HDU hospitalization (d)			
Median (P_{25}–P_{75})	7 (4–9)	7 (5–9)	6 (4–8)
ICU/HDU hospitalization			
≥7 days	57 (63.3)	34 (73.9)	23 (52.3)
Endotracheal intubation	–	12 (26.1)	–
Tracheostomy	–	7 (15.2)	–
Mortality rate			
Survived: Not survived	88:2	44:2	44:0

CLABSI, central-line associated bloodstream infection; CAUTI, catheter associated urinary tract infection; COPD, chronic obstructive pulmonary disease; HDU, high dependency unit; ICU, intensive care unit; VAP, ventilator associated pneumonia

During the 2 years of study duration, data from ambispectively followed 90 hospitalized (ICU plus HDU) patients were included in the analysis. Of these 90 patients, 46 (51.1%) were admitted to the ICU (medicine/surgery), and the remaining 44 (48.8%) were admitted to the HDU (medicine/surgery). The median (P_{25}–P_{75}) age of the total patients was 55 (43.1–62.3) years. Male 61 (67.8%) preponderance was observed. Chronic kidney disease 74 (82.2%), followed by hypertension 71 (78.9%), were the most common comorbidities among study participants. Sixty-two of 90 (68.9%) were immunocompromised. Femoral vein 43 (41.3%), followed by jugular vein 24 (23.1%), was the most common site of cannulation. The median (P_{25}–P_{75}) duration of catheterization was 10 (7–18) days. Whereas, 40 (44.4) patients had ≥12 days of catheterization. The median (P_{25}–P_{75}) total length of hospitalization was 9 (6–16) days, whereas the length of ICU/HDU hospitalization was 7 (4–9) days. Of 46 ICU patients, 34 (73.9%) had prolonged (≥7 days) ICU stays; this

Table 2A: Antimicrobial susceptibility and resistance pattern of gram-negative pathogens in ICU patients with MDAIs

ICU PATIENTS ($N = 26$)																
VAP ($n = 11$)						CAUTI ($n = 5$)			CLABSI ($n = 10$)							
Klebsiella pneumoniae (n=2)	*Acinetobacter baumanni Carba Resistant (n=1)*	*Acinetobacter baumanni (n=2)*	*Stenotrophomonas maltophilia (n=4)*	*Pseudomonas aeruginosa (n=2)*	*Pseudomonas aeruginosa (n=2)*	*Chryseobacterium indologenes (n=1)*	*Escherichia coli Carba Resistant (n=2)*	*Citrobacter koseri (n=1)*	*Acinetobacter lwoffi (n=2)*	*Elizabethkingia meningoseptica (n=1)*	*Klebsiella pneumoniae Carba Resistant (n=1)*	*Klebsiella pneumoniae (n=2)*	*Stenotrophomonas maltophilia (n=3)*	PATHOGENS / DRUGS		
				I	-	-	-	100	-	-	-	-	-	S	AMOXICILLIN	
50	-	-	-		100	100	50	-	-	-	100	100	-	R		
50	-	-	-	100	-	-	-	100	-	-	-	-	-	S	PIPERACILLIN	
50	100	-	-		100	100	50	-	-	100	100	100	100	R		
50	-	-	-		-	-	-	100	-	-	-	-	-	S	CEFUOROXIME	
50	-	-	-		-	-	100	-	-	-	100	100	100	R		
50	-	100	-	50	-	-	-	100		-	-	-	-	S	CEFTRIAXONE	
50	100	-	-	50	100	-	100	-	-	100	100	100	100	R		
50	-	100	-	-	-	I	-	100	100	-	-	-	-	S	CEFOPERAZONE	
50	100	-	-	-	-		100	-	-	100	100	100	100	R		
50	-	100	-	50	100	-	-	100	100	-	-	-	-	S	CEFEPIME	
50	100	-	-	50	-	100	100	-	-	100	100	100	-	R		
50	-	-	-	-	-	-	-	100	-	-	-	-	-	S	ERTAPENEM	
50	-	-	-	-	-	-	-	-	-	-	100	100	100	R		
50	-	-	75	-	100	-	-	100	-	-	-	-	-	S	IMIPENEM	
50	100	-	25	-	-	100	-	-	-	100	-	100	100	R		
50	-		-	-	-	-	-	100	-	-	-	-	-	S	MEROPENEM	
50	100	-	-	-	100	100	100	-	-	100	100	100	-	R		
50	-	100	-	100	100	-	100	100	100	-	I	I	66.6	S	AMIKACIN	
I	-	-	-	-	-	100	-	-	-	100			33.3	R		
50	-	100	50	-	100	-	100	100		-	-	-	100	S	GENTAMICIN	
50	100	-	50	-	-	100	-	-	-	100	100	100	-	R		
50	-	100	-	50	100	-	50	100	100		-	-	100	S	CIPROFLOXACIN	
50	100	-	-	50	-	100	50	-	-	I	100	100	-	R		
100	-	-	-	-	-	-	-	100	-	-	-	100	-	S	TIGECYCLINE	
-	-	-	-	-	-	-	-	-	-	-	-	-	-	R		
100	100	-	-	-	-	-	-	100	-	-	100	100	-	S	COLISTIN	
-	-	-	-	-	-	-	-	-	-	100	-	-	-	R		
50	100	-	75	-	-	-	-	100	-	-	-	-	100	S	TRIMETHOPRIM	
50	-	-	25	-	-	100	100	-	-	100	100	100	-	R		
-	-	100	75	-	-	I	-	100	100	-	-	-	100	S	LEVOFLOXACIN	
-	-	-	25	100	-		-	-	-	-	-	-	-	R		
-	-	-	-	-	-	-	-	100	-	-	-	-	-	S	DORIPENEM	
-	-	-	-	-	-	-	-	-	-	-	-	-	-	R		
-	-	-	25	-	-	-	-	100	-	-	-	-	100	S	MINOCYCLINE	
-	-	-	75	-	-	-	-	-	-	-	-	-	-	R		
-	-	-	-	-	-	-	-	100	-		-	-	-	S	AZTREONAM	
-	-	-	-	-	-	100	-	-	-	-	-	-	-	R		
-	-	-	75	50	I	-	-	100	-	-	-	-	-	S	CEFTAZIDIME	
-	-	-	25	50		100	-	-	-	-	-	-	100	R		

HDU PATIENTS (*N* = 17)											
CAUTI (*n* = 2)	CLABSI (*n* = 15)									PATHOGENS / DRUGS	
Klebsiella pneumoniae (n=2)	*Ochrobactrum anthropi (n=1)*	*Pseudomonas fluoroscens (n=1)*	*Klebsiella pneumoniae (n=2)*	*Escherichia coli (n=2)*	*Serratia marcescens (n=1)*	*Stenotrophomonas maltophilia (n=2)*	*Acinetobacter baumanni (n=2)*	*Enterobacter cloacae ESBL (n=1)*	*Enterobacter cloacae (n=3)*		
-	-	100	-	-	-	-	-	-	-	S	AMOXICILLIN
100	100	-	100	100	100	-	-	100	100	R	
-	-	-	-	100	-	-	-	100	100	S	PIPERACILLIN
100	100	-	100	-	100	-	-	-	-	R	
-	-	-	-	-	-	-	-		-	S	CEFUOROXIME
100	100	-	100	100	100	-	-	100	100	R	
-	-	-	-	I	-	-	100	100		S	CEFTRIAXONE
100	100	100	100		100	-	-	-	66.6	R	
-	-	-	-	100	-	-	100	100	100	S	CEFOPERAZONE
100	-	100	100	-	100	-	-	-	-	R	
-	-	I	-	100	-	-	100	100		S	CEFEPIME
-	100		100	-	100	-	-	-		R	
-	-	-	-	-	-	-	-	100		S	ERTAPENEM
-	-	-	100	-	100	-	-	-	-	R	
-	-	100	-	-	-	-	-	100	100	S	IMIPENEM
-	100	-	100	-	100	-	-	-	-	R	
-	100	100	-	-	-	-	-	100	100	S	MEROPENEM
100	-	-	100	-	100	-	-	-	-	R	
I	-	-	I	100	-	-	100	100	100	S	AMIKACIN
	-	-		-	100	-	-	-	-	R	
-	100	100	-	100	-	-	100	100	100	S	GENTAMICIN
100	-	-	100	-	100	-	-	-	-	R	
-	100	-	-	I	-	-	100	100		S	CIPROFLOXACIN
100	-	-	100		-	-	-	-	100	R	
-	-	-	100	-	-	-	-	-	66.6	S	TIGECYCLINE
-	-	-	-	-	-	-	-	-	33.3	R	
100	-	-	100	100	-	-	-	100	100	S	COLISTIN
-	-	-	-	-	-	-	-	-	-	R	
-	-	-	-	-	-	100	100	100	100	S	TRIMETHOPRIM
100	-	100	100	-	-	-	-	-	-	R	
-	-	100	-	-	100	-	-	-	-	S	LEVOFLOXACIN
-	-	-	-	-	-	-	-	-	-	R	
-	-	-	-	-	-	-	-	-	-	S	DORIPENEM
-	100	-	-	-	-	-	-	-	-	R	
-	-	-	-	-	-	-	-	-	-	S	AZTREONAM
-	100	100	-	-	-	-	-	-	-	R	
-	-	100	-	-	-	-	-	-	-	S	CEFTAZIDIME
-	-	-	-	-	-	-	-	-	-	R	

Table 2B: Antimicrobial susceptibility and resistance pattern of gram-negative pathogens in HDU patients with MDAIs

Table 3A: Antimicrobial susceptibility and resistance pattern of gram-positive pathogens in ICU patients with MDAIs

ICU PATIENTS ($N = 19$)													
VAP ($n = 8$)					CLABSI ($n = 6$)							PATHOGENS / DRUGS	
Staphylococcus epidermis (n=1)	*MRSA (n=1)*	*Staphylococcus aureus (n=2)*	*MSSA (n=2)*	*Staphylococcus capitis (n=2)*	*Enterococcus faecalis (n=2)*	*Staphylococcus capitis (n=1)*	*Staphylococcus aureus (n=1)*	*MSSA (n=1)*	*Staphylococcus capitis (n=1)*	*MRCoNS (n=2)*	*Staphylococcus epidermis (n=2)*		
POS	POS	NEG	NEG	POS		POS	NEG	NEG	POS	POS	POS	+	CEFOXITIN SCREEN
												-	
-	-	100	-	-	100	-	-	-	-	-	-	S	BENZYLPENICILLIN
100	100	-	100	100	-	100	100	100	100	100	100	R	
-	-	100	100	-		-	100	100	-	-	-	S	OXACILLIN
100	100	-	-	100		100	-	-	100	100	100	R	
-	I	100	100	-		-	100	100	-	100	-	S	GENTAMICIN
100		-	-	100		100	-	-	100	-	100	R	
100	-	-	100	-	100	-	-	-	-	-	-	S	CIPROFLOXACIN
-	100	100	-	100	-	100	100	100	100	100	100	R	
100	100	100	100	100	-	100	100	100	100	100	100	S	TETRACYCLINE
-	-	-	-	-	100	-	-	-	-	-	-	R	
100	100	100	100	-	-	-	-	100	-	100	-	S	TRIMETHOPRIM/ SULPHAMETHOAZOLE
-	-	-	-	100	-	100	100	-	100	-	100	R	
100	100	-	-	I	-	I	100		I	100	100	S	TEICOPLANIN
-	-	-	-		-		-			-	-	R	
100	-	-	100	-	-	-	100	100	-	100	100	S	TEIGYCYCLINE
-	-	-	-	-	-	-	-	-	-	-	-	R	
100	100	-	-	-	-	-	100		-	100	100	S	DAPTOMYCIN
	-	-	-	-	-	-	-		-	-	-	R	
NEG	NEG	NEG	POS	NEG	-	NEG	-	POS	NEG	NEG	-	+	ICR
												-	
100	-	-	-	-	-	-	100		-	-	-	S	LEVOFLAOXACIN
-	-	100	-	100	-	100	-		100	100	100	R	
-	100	100	-	-	-	-	-	-	-	50	-	S	ERYTHROMYCIN
100	-	-	100	100	100	100	-	100	100	50	100	R	
100	100	100	-	-	-	-	-	-	-	100	-	S	CLINDAMYCIN
-	-	-	100	100	-	100	-	100	100	-	100	R	
100	100	100	-	-	-	-	100	-	-	100	100	S	LINEZOLID
	-	-	-	-	-	-	-	-	-	-	-	R	
	-	-	-	-	-	-	100	-	-	100	100	S	VANCOMYCIN
	-	-	-	100	-	100	-	-	100	-	-	R	

Table 3B: Antimicrobial susceptibility and resistance pattern of gram-positive pathogens in HDU patients with MDAIs

HDU PATIENTS ($N = 17$)										
CAUTI ($n = 6$)			CLABSI ($n = 11$)							
Enterococcus faecalis (n=1)	*Staphylococcus epidermis* (n=3)	*Staphylococcus hominis* (n=2)	*Enterococcus faecalis* (n=2)	*Staphylococcus capitis* (n=1)	*Staphylococcus hominis* (n=2)	*MRSA (n=2)*	*Staphylococcus aureus* (n=2)	*Staphylococcus epidermis* (n=2)	PATHOGENS / DRUGS	
--	NEG	POS	-	POS	POS	POS	NEG	POS	+	CEFOXITIN SCREEN
									-	
100	-	-	100	-	-	-	50	-	S	BENZYLPENICILLIN
-	100	100	-	100	100	100	50	100	R	
-	-	-	-	-	-	-	100	-	S	OXACILLIN
-	100	100	-	100	100	100	-	100	R	
-	-	I	-	-	-	I	100	-	S	GENTAMICIN
-	100		-	100	100		-	100	R	
100	66.6	-	50	-	-	-		50	S	CIPROFLOXACIN
-	33.3	100	50	100	100	100	100	50	R	
-	33.3	100	-	100	-	100	100	100	S	TETRACYCLINE
100	66.6	-	100	-	-	-	-	-	R	
-	66.6	100	-	-	I	100	50	50	S	TRIMETHOPRIM/ SULPHAMETHOAZOLE
-	33.3	-	-	100		-	50	50	R	
-	100	100	100	I	100	100	100	100	S	TEICOPLANIN
-	-	-	-		-	-	-	-	R	
-	100	-	100	-	-	-	100	100	S	TEIGYCYCLINE
-	-	-	-	-	-	-	-	-	R	
-	100	-	100	-	100	100	100	100	S	DAPTOMYCIN
-	-	-	-	-	-	-	-	-	R	
-	NEG	-	-	NEG	NEG	NEG	NEG	NEG	+	ICR
									-	
-	66.6	-	50	-	-	-	-	50	S	LEVOFLAOXACIN
-	33.3	100	50	100	-	-	100	50	R	
-	-	-	I	-	-	100	100	-	S	ERYTHROMYCIN
100	100	100	50	100	100	-	-	100	R	
-	100	-	-	-	-	100	100	50	S	CLINDAMYCIN
-	-	-	--	100	100	-	-	50	R	
-	100	-	100	-	100	-	100	100	S	LINEZOLID
-	-	-	-	-	-	-	-	-	R	
-	100	100	100	100	100	100	100	100	S	VANCOMYCIN
-	-	-	-	-	-	-	-	-	R	
-	-	-	50	-	-	-	-		S	GENTAMYCIN
-	-	-	50	-	-	-	-		R	
-	-	-	-	-	-	-	100	50	S	RIFAMPICIN
-	-	-	-	100	-	-	-	50	R	

Table 4: Antimicrobial susceptibility and resistance pattern of fungal pathogens in ICU patients and HDU patients with MDAIs

ICU / HDU PATIENTS (*N* = 25)		DRUGS / PATHOGENS	FLUCONAZOLE		VORICONAZOLE		CASPOFUNGIN		MICAFUNGIN		AMPHOTERICIN-B	
			S	R	S	R	S	R	S	R	S	R
HDU PATIENTS (*N* = 16)	CLABSI (*n* = 13)	*Candida parapsilosis (n=9)*	77.7	22.2	-	-	100	-	100	-	77.7	22.2
		Candida glabrata (n=1)	-	-	-	-	100	-	100	-	-	-
		Candida albicans (n=3)	-	-	-	-	100	-	100	-	-	-
	CAUTI (*n* = 3)	*Candida parapsilosis (n=3)*	100	-	100	-	100	-	100	-	100	-
ICU PATIENTS (*N* = 9)	CLABSI (*n* = 9)	*Candida parapsilosis (n=9)*	88.8	11.1	-	-	100	-	100	-	88.8	11.1

Table 5: The prevalence of ESBL, CRE, MDR, and XDR pathogens isolated from ICU and HDU patients with MDAIs

Pathogen	*Total (N = 79)*	*ESBL (N = 22)*	*CRE (N = 18)*	*MDR (N = 54)*	*XDR (N = 11)*
Gram-positive pathogen (*n* = 36)					
Staphylococcus aureus (MSSA)	8/36 (22.2)	–	–	–	–
Staphylococcus epidermidis (CoNS)	8/36 (22.2)	–	–	6	–
Staphylococcus capitis	5/36 (13.8)	–	–	5	–
Enterococcus faecalis	5/36 (13.8)	–	–	4	–
Staphylococcus hominis	4/36 (11.1)	–	–	4	–
Staphylococcus aureus (MRSA)	3/36 (8.3)	–	–	3	–
Staphylococcus epidermidis (MRCoNS)	2/36 (5.5)	–	–	2	–
Kochuria rhizophila	1/36 (2.7)	–	–	–	–
Gram-negative pathogen (*n* = 43)					
Klebsiella pneumoniae	9/43 (20.9)	9	8	7	5
Stenotrophomonas maltophilia	9/43 (20.9)	–	4	7	3
Acinetobacter baumanni	5/43 (11.6)	5	1	3	–
Enterobacter cloacae	4/43 (9.3)	2	–	2	–
Escherichia coli	4/43 (9.3)	2	2	3	1
Pseudomonas aeruginosa	4/43 (9.3)	2	1	3	–
Acinetobacter iwoffii	2/43 (4.6)	–	–	–	–
Elizabethkingia meningoseptica	1/43 (2.3)	–	–	1	1
Serratia marcescens	1/43 (2.3)	1	1	1	1
Pseudomonas fluorescens	1/43 (2.3)	–	–	1	–
Orchobactrum anthropi	1/43 (2.3)	–	–	1	–
Chryseobacterium indologenes	1/43 (2.3)	–	1	1	–
Citrobacter koseri	1/43 (2.3)	1	–	–	–

CRE, carbapenem-resistant *Enterobacteriaceae*; ESBL, extended-spectrum beta-lactamases; MDR, multi-drug resistant; MRCoNS, methicillin-resistant coagulase negative *Staphylococci;* MRSA, methicillin-resistant *Staphylococcus aureus;* MSSA, methicillin-sensitive *Staphylococcus aureus;* XDR, extended-drug resistant

could be one of the important risk factors for ICU-acquired MDAI in the study patients. Endotracheal intubation and tracheostomy were performed in 12 (26.1%) and 7 (15.2%) patients, respectively. Two of 46 (4.3%) ICU patients [2/19 (10.5%) who had VAP] had mortality. Data on the demographics and clinical characteristics of ICU patients and HDU patients with MDAI are shown in Table 1.

Among gram-negative pathogens isolated from ICU/HDU patients with CLABSI, the most common were *Stenotrophomonas maltophilia* and *Enterobacter cloacae*. Similarly, *Escherichia coli* (carba-resistant), *Pseudomonas aeruginosa* (CP-CRO), and *Klebsiella pneumoniae* (CP-CRO) were the most commonly isolated organisms from ICU/HDU patients with CAUTI. In patients with VAP, the most commonly isolated pathogens were *S. maltophilia*, followed by *Acinetobacter baumanni* and *K. pneumoniae (CRE)*. Tables 2A and B demonstrate the antimicrobial susceptibility and resistance patterns of gram-negative pathogens isolated from ICU and HDU patients with MDAIs, respectively. Among gram-positive pathogens isolated from ICU/HDU patients with CLABSI, *Staphylococcus epidermis*, Methicillin-resistant *coagulase-negative staphylococci*, Methicillin-resistant *Staphylococcus aureus* and *Enterococcus faecalis* were the most common. Considering CAUTI, the most commonly isolated pathogens were *S. epidermis*, followed by *S. hominis*. In patients with VAP, the most common were *S. capitis* and *S. aureus*. Tables 3A and B demonstrate the antimicrobial susceptibility and resistance patterns of gram-positive pathogens isolated from ICU and HDU patients with MDAIs, respectively.

Of 64 CLABSI patients, 22 (34.4%) had central-line-associated candidemia, of which 13 (20.3%) were admitted to the ICU and 9 (14.1%) were in the HDU. CAUTI was observed in 3 patients who were admitted to HDU. *Candida parapsilosis* was the most prevalent in both CLABSI and CAUTI patients. Table 4 demonstrates the antimicrobial susceptibility and resistance pattern of fungal pathogens in ICU patients and HDU patients with MDAIs.

A total of 104 pathogens were isolated; 43 (41.3%) were gram-positive, 36 (34.6%) were gram-negative, and 25 (24%) were fungal. Of the total 79 pathogens isolated, 22 (27.8%) were extended-spectrum beta-lactamases (ESBL) producing, 18 (22.8%) were carbapenem-resistant *Enterobacteriaceae* (CRE), 54 (68.3%) were MDR, and 11 (13.9%) were XDR. Among the gram-positive pathogens, *S. epidermidis* (CoNS), followed by *S. capitis*, were the most commonly isolated pathogens, which were found to be MDR. Whereas, among gram-negative pathogens, *K. pneumoniae* (CRE) and *S. maltophilia* were the most commonly isolated pathogens, which were found to be MDR. Considering XDR, *K. pneumoniae (CRE)*, followed by *S. maltophilia*, were found to be the most prevalent gram-negative pathogens. No gram-positive organism isolated had XDR in this study. Table 5 demonstrates the prevalence of ESBL, CRE, MDR, and XDR pathogens isolated from the patients with MDAIs.

Discussion

In this ambispective-observational, site-specific surveillance-based study, we examined the microbial profile, antimicrobial susceptibility, and prevalence of MDR/XDR pathogens causing MDAIs in a tertiary-care university hospital. Previous literature supports the evidence for nosocomial infections as a leading cause of in-hospital mortality. These infections create an extra burden of healthcare expenditures on both patients and their caregivers, as well as on hospitals. Using the surveillance forms developed by the 'International Nosocomial Infection Control Consortium' (INICC, founded in 1998 with Latin American hospitals) for data collection of patients with and without nosocomial infections, infection control experts are able to assess clinical features, increase in length of hospital stay, increment in healthcare costs, mortality rates, and identify key nosocomial infection risk factors.[12] Mehta et al.,[3] described these nosocomial infections in a surveillance-based study in seven Indian cities as CLABSI (61.3%), VAP (29%), and CAUTI (9%). However, comparing this data with INICC worldwide data, VAP represented 41% of all nosocomial infections, followed by CLABSI (30%) and CAUTI (29%).[12] In our analyses, this distribution was recorded as CLABSI (61.5%), CAUTI (20.2%), and VAP (18.3%), which was in line with findings reported by Mehta et al.[3]

Intravenous catheters are often used for the administration of parenteral nutrition, antibiotics, blood products, and chemotherapy drugs; nevertheless, they can serve as "double-edged swords" and cause major infections. The study performed in England between 1997 and 2001 determined that central lines were the most prevalent source of CLABSI, accounting for 43.3–52.4% of total nosocomial bloodstream infections.[13] These numbers are evidently higher in developing countries, where there may not be enough monitoring to estimate the actual rates of infection. These percentages may vary, ranging from 4.4 to 88.8%, in accordance with particular studies.[12,14,15] There are only a few studies available on the prevalence of CLABSI in India.[3–7,16,17] In a recent study, the prevalence of CLABSI caused by CVC was found to be 39.2%, whereas in other studies it was 27–56%.[4–7,16,17] In our study, it was found to be 38.1%, which was in close accord with previously published Indian studies.[4–7,16,17]

In the present analysis, with a frequency of 29%, PICC was revealed to have a decreased risk of developing CLABSI. Several studies have revealed that the PICC carries a lower risk of CLABSI than the CVC, with some studies predicting the risk of CLABSI to be 64 times higher with the CVC than the PICC.[18,19] Our findings also showed similarities with these findings. On the other hand, some studies have observed no significant changes in the likelihood of CLABSI when comparing CVC with PICC.[20] Numerous studies have compared the semiquantitative roll plate approach and the differential time to positivity approach for CLABSI diagnosis. These research findings were extremely diverse, but the majority of them came to the conclusion that the roll plate only depicts extraluminal pathogens or catheter colonization, whereas differential time to positivity indicates the intraluminal source of infection and, thus, true CLABSI in the patients.[21,22] The reported range of semiquantitative roll plate method positivity in several studies was 6–57.5%.[23,24] Pandit et al.[16] reported positivity rates of 22.58%, whereas in our study it was found to be 36.3%.

The overall MDAI rates reported in previous Indian studies ranged from 2.1 to 47.3 per 1000 device days.[4–7,17,25] The category of hospital and healthcare facility undergoing surveillance influences the rates of MDAI. The relentless efforts of the Hospital Acquired Infection Control Committee (HAICC) team and the stringent hygienic upkeep of the hospital and wards/units can reduce these rates. For healthcare professionals of all cadres, frequent sensitization sessions regarding hand hygiene, universal standard precautions, and hospital infection control practices are adopted and well implemented in our facility. The overall rate, taking into account the CLABSI, reported in the INCC study by Mehta et al. was 7.9 per 1000 CVC catheter days, whereas it was higher than the rate reported by Deorukhkar and Saini (0.8 per 1000 catheter days).[3,25] This variation may be the outcome of the fact that Deorukhkar and Saini performed a monocentric

evaluation, whereas the INICC's ICU-acquired CLABSI study was performed in seven Indian cities.[3,25]

Candida species are the fourth most prevalent cause of BSI in the United States, while they are rather uncommon in Europe.[26] Though the true incidence of nosocomial Candida BSI in India is unknown.[27] In our analyses, a total of 22/64 (34.4%) different Candida species were identified; 18 of those 22 (81.8%) isolates were *C. parapsilosis*, followed by *C. albicans* 3/22 (13.6%) and *C. glabrata* 1/22 (4.5%). According to previous reports, *C. parapsilosis* is the second- or third-most prevalent Candida species causing nosocomial BSI in Europe, Canada, Asia, and Latin America.[26,28–30] But this species was evidently the most prevalent of all Candida in our surveillance. Six of the 18 (33.3%) *C. parapsilosis* isolates in our evaluation were fluconazole and amphotericin-B resistant, whereas all of them were sensitive to echinocandins. *C. parapsilosis* may grow selectively in hyperalimentation solution, can develop a biofilm on intravascular and prosthetic devices, and can colonize human hands, all of which are favorable to its survival and dissemination in hospital environment.[31]

We identified *Klebsiella pneumoniae* as an MDR/XDR superbug causing CAUTI in our evaluation of 2 (9.5%) patients. In one patient, *Chryseobacterium indologenes* was isolated, which was found to be XDR, and it was susceptible to nitrofurantoin only; hence, it was treated with the same. Among Candida, *C. parapsilosis* was the only isolated pathogen causing CAUTI. The recent data identifies *C. parapsilosis* as an emerging Candida pathogen causing CAUTI in recent times.[32] Studies have reported other candida species-induced CAUTI as well, but this was not evident in our setting.

Despite the advances in antimicrobial therapy, VAP continues to be an important driver of morbidity and mortality. The reported VAP rate by Mehta et al. was 10.4 per 1000 MV-days.[3] Whereas, the NNIS global rate and INCC global rate were 5.1 and 24.1 per 1000 MV-days, respectively.[12,33] Ventilator-associated pneumonia complicates the course of illness in 8–28% of the patients who are on mechanical ventilation. Two (10.5%) patients in the current analysis had VAP-associated mortality, mainly due to acute respiratory distress syndrome. The causative pathogens isolated were carba-resistant *A. baumanni* in one patient and *K. pneumoniae* in another patient. Both pathogens have been recognized as VAP-causing MDR/XDR superbugs in previous studies.[34] To combat the rates across the world, better supportive care modalities should be used, and the application of a wide variety of preventive measures is needed.

In our study, we have found *K. pneumoniae*, *A. baumanii*, and *S. maltophilia* among NDM bacteria (bla_{NDM-1} gene carrier). The treatment approaches for the same were Polymyxins (mainly colistin), Tigecycline, and a combination of Ceftazidime-avibactam-aztreonam. Similar findings were also reported by Larcher et al., where the authors concluded that in real-life scenarios, using beta-lactam antibiotics as a last resort was a safe and effective treatment option for fatal infections caused by gram-negative bacteria with difficult-to-treat resistance.[35] Some researchers have also identified high rates of colistin resistance among patients with carbapenem-resistant *K. pneumoniae* infection which accounts for an excess of mortality in individuals.[36] Fortunately, in our analysis, we did not find colistin resistance in *K. pneumoniae* isolates. The patients who received the above treatment options responded well to the therapy and had better outcomes.

Conclusion

The potential risk of MDAI cannot be totally eradicated, even though many healthcare facilities have infection-control measures and the hospital personnel make every effort to avoid infection. Therefore, it is crucial to monitor MDAI in order to comprehend the scope of the issue and start more intensive preventative efforts for better patient care. With regard to the three most significant forms of MDAI (CLABSI, CAUTI, and VAP), the current surveillance helped us in the methodical compilation of institutional data. The healthcare practitioner ended up with few therapeutic alternatives because most of the patient isolates were found to be multidrug resistant. For the early detection and better treatment of MDAIs, the study highlights the importance of regular surveillance programs, strict adherence to antiseptic procedures (during device insertion and care), an efficient infection control program, and the use of a restricted and pragmatic antimicrobial policy.

One of the shortcomings of this study is the inability to semiquantitatively culture all the catheters from suspected cases of CLABSI. This is because they were only removed at the physician's discretion and, in this case, recurrent access was not a problem. Another limitation was the inability to determine the exact incidence rate of MDAI at our facility due to discrepancies in the collected data, which was not easily accessible to us. Also, we were unable to isolate a few invasive fungal pathogens like *Candia auris* due to a lack of equipment and other concerns about laboratory limitations.

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Authors Contributions

VRS and BP conceived the idea. NV, SS, SP, PN, and VRS were involved in data acquisition, and interpretation/analysis. VRS, NV, SS, and SP performed a review of the literature and drafted the manuscript. VRS, BP, and AP supervised the study, reviewed the manuscript, and improved for intellectual content. All authors contributed in writing and approved the final version.

Data Availability

All data relevant to the study are included in the article.

Orcid

Vaibhav R Suryawanshi https://orcid.org/0000-0001-8334-4025
Atmaram Pawar https://orcid.org/0000-0003-0280-2499
Bharat Purandare https://orcid.org/0009-0000-9597-4606
Niveda Vijayvargiya https://orcid.org/0009-0008-0867-3310
Sandesh Sancheti https://orcid.org/0009-0002-7397-9646
Susan Philip https://orcid.org/0009-0003-9929-6269
Prasad Nagare https://orcid.org/0009-0007-4578-7491

References

1. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. American journal of infection control 1988;16(3):128–140. DOI: https://doi.org/10.1016/0196-6553(88)90053-3.
2. Magill SS, Edwards JR, Bamberg W, Beldavs ZG, Dumyati G, Kainer MA, et al. Multistate point-prevalence survey of health care–associated infections. N Engl J Med 2014;370(13):1198–1208. DOI: https://doi.org/10.1056/NEJMoa1306801.
3. Mehta A, Rosenthal VD, Mehta Y, Chakravarthy M, Todi SK, Sen N, et al. Device-associated nosocomial infection rates in intensive care units of seven Indian cities. Findings of the International Nosocomial Infection Control Consortium (INICC). Journal of Hospital Infection 2007;67(2):168–174. DOI: https://doi.org/10.1016/j.jhin.2007.07.008.
4. Chopdekar K, Chande C, Chavan S, Veer P, Wabale V, Vishwakarma K, et al. Central venous catheter-related blood stream infection rate in critical care units in a tertiary care, teaching hospital in Mumbai. Indian J Med Microbiol 2011;29(2):169–171. DOI: https://doi.org/10.4103/0255-0857.81796.
5. Singh S, Pandya Y, Patel R, Paliwal M, Wilson A, Trivedi S. Surveillance of device-associated infections at a teaching hospital in rural Gujarat-India. Indian Journal of Medical Microbiology 2010;28(4):342–347. DOI: https://doi.org/10.4103/0255-0857.71830.
6. Kumar A, Chaudhry D, Goel N, Tanwar S. Epidemiology of intensive care unit-acquired infections in a tertiary care hospital of North India. Indian J Crit Care Med 2021;25(12):1427–1433. DOI: https://doi.org/10.5005/jp-journals-10071-24058.
7. Patil HV, Patil VC, Ramteerthkar MN, Kulkarni RD. Central venous catheter-related bloodstream infections in the intensive care unit. Indian J Crit Care Med 2011;15(4):213–223. DOI: https://doi.org/10.4103/0972-5229.92074.
8. Centres for Disease Control and Prevention. Altered Immunocompetence Guidelines for Immunizations-CDC;2018. Available from: http://www.cdc.gov/hcp/generalrecs/immunocompetence.
9. Maki DG, Weise CE, Sarafin HW. A semiquantitative culture method for identifying intravenous-catheter-related infection. N Engl J Med 1977;296(23):1305–1309. DOI: https://doi.org/10.1056/NEJM197706092962301.
10. Jain M, Dogra V, Mishra B, Thakur A, Loomba PS, Bhargava A. Candiduria in catheterized intensive care unit patients: Emerging microbiological trends. Indian J Pathol Microbiol 2011;54(3):552–555. DOI: https://doi.org/10.4103/0377-4929.85091.
11. CLSI. Performance Standards for Antimicrobial Susceptibility Testing. CLSI supplement M100. 28th edition. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.
12. Rosenthal VD, Maki DG, Salomao R, Moreno CA, Mehta Y, Higuera F, et al. Device-associated nosocomial infections in 55 intensive care units of 8 developing countries. Ann Intern Med 2006;145(8):582–591. DOI: https://doi.org/10.7326/0003-4819-145-8-200610170-00007.
13. Jo Johnston B, Conly J. What do central venous catheter-associated bloodstream infections have to do with bundles? Can J Infect Dis Med Microbiol 2005;16(4):215–218. DOI: https://doi.org/10.1155/2005/582156.
14. Singhi S, Nallaswamy K. Catheter related blood stream infection in Indian PICUs: Several unanswered issues! Indian J Crit Care Med 2013;17(3):127–128. DOI: https://doi.org/10.4103/0972-5229.117035.
15. Ulu-Kilic A, Ahmed S, Alp E, Doğanay M. Challenge of intensive care unit-acquired infections and Acinetobacter baumannii in developing countries. OA Critical Care 2013;1(1):2. DOI: 10.13172/2052-9309-1-1-382.
16. Pandit P, Sahni AK, Grover N, Dudhat V, Das NK, Biswas AK. Catheter-related blood stream infections: prevalence, risk factors and antimicrobial resistance pattern. Med J Armed Forces India 2021;77(1):38–45. DOI: https://doi.org/10.1016/j.mjafi.2019.07.002.
17. Singh S, Chaturvedi R, Garg SM, Datta R, Kumar A. Incidence of healthcare associated infection in the surgical ICU of a tertiary care hospital. Med J Armed Forces India 2013;69(2):124–129. DOI: https://doi.org/10.1016/j.mjafi.2012.08.028.
18. Cicalini S, Palmieri F, Petrosillo N. Clinical review: New technologies for prevention of intravascular catheter-related infections. Crit Care 2004;8(3):157–162. DOI: https://doi.org/10.1186/cc2380.
19. Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: A systematic review of 200 published prospective studies. Mayo Clin Proc 2006;81(9):1159–1171. DOI: https://doi.org/10.4065/81.9.1159.
20. Safdar N, Maki DG. Risk of catheter-related bloodstream infection with peripherally inserted central venous catheters used in hospitalized patients. Chest 2005;128(2):489–495. DOI: https://doi.org/10.1378/chest.128.2.489.
21. Goldmann DA, Pier GB. Pathogenesis of infections related to intravascular catheterization. Clin Microbiol Rev 1993;6(2):176–192. DOI: https://doi.org/10.1128/CMR.6.2.176.
22. Wassil SK, Crill CM, Phelps SJ. Antimicrobial impregnated catheters in the prevention of catheter-related bloodstream infection in hospitalized patients. J Pediatr Pharmacol Ther 2007;12(2):77–90. DOI: https://doi.org/10.5863/1551-6776-12.2.77.
23. Bouza E, Alvarado N, Alcalá L, Pérez MJ, Rincón C, Muñoz P. A randomized and prospective study of 3 procedures for the diagnosis of catheter-related bloodstream infection without catheter withdrawal. Clin Infect Dis 2007;44(6):820–826. DOI: https://doi.org/10.1086/511865.
24. Sherertz RJ, Raad II, Belani A, Koo LC, Rand KH, Pickett D, et al. Three-year experience with sonicated vascular catheter cultures in a clinical microbiology laboratory. J Clin Microbiol 1990;28(1):76–82. DOI: https://doi.org/10.1128/jcm.28.1.76-82.1990.
25. Deorukhkar SC, Saini S. Medical device-associated candida infections in a rural tertiary care teaching hospital of India. Interdiscip Perspect Infect Dis 2016;2016:1854673. DOI: https://doi.org/10.1155/2016/1854673.
26. Méan M, Marchetti O, Calandra T. Bench-to-bedside review: Candida infections in the intensive care unit. Crit Care 2008;12(1):204. DOI: https://doi.org/10.1186/cc6212.
27. Chakrabarti A, Sood P, Rudramurthy SM, Chen S, Kaur H, Capoor M, et al. Incidence, characteristics and outcome of ICU-acquired candidemia in India. Intensive Care Med 2015;41(2):285–295. DOI: https://doi.org/10.1007/s00134-014-3603-2.
28. Bagshaw SM, Laupland KB. Epidemiology of intensive care unit-acquired urinary tract infections. Curr Opin Infect Dis 2006;19(1):67–71. DOI: https://doi.org/10.1097/01.qco.0000200292.37909.e0.
29. Tay ST, Na SL, Chong J. Molecular differentiation and antifungal susceptibilities of Candida parapsilosis isolated from patients with bloodstream infections. J Med Microbiol 2009;58(Pt 2):185–191. DOI: https://doi.org/10.1099/jmm.0.004242-0.
30. Nucci M, Thompson-Moya L, Guzman-Blanco M, Tiraboschi IN, Cortes JA, Echevarría J, et al. Recommendations for the management of candidemia in adults in Latin America. Latin America Invasive Mycosis Network. Rev Iberoam Micol 2013;30(3):179–188. DOI: https://doi.org/10.1016/j.riam.2013.05.007.
31. Silva S, Negri M, Henriques M, Oliveira R, Williams DW, Azeredo J. Candida glabrata, Candida parapsilosis and Candida tropicalis: biology, epidemiology, pathogenicity and antifungal resistance. FEMS Microbiol Rev 2012;36(2):288–305. DOI: https://doi.org/10.1111/j.1574-6976.2011.00278.x.
32. Mishra M, Agrawal S, Raut S, Kurhade AM, Powar RM. Profile of yeasts isolated from urinary tracts of catheterized patients. J Clin Diagn Res 2014;8(2):44–46. DOI: https://doi.org/10.7860/JCDR/2014/6614.4003.
33. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control 2004; 32(8):470–485. DOI: 10.1016/S0196655304005425.
34. Lalwani S, Mathur P, Tak V, Janani S, Kumar SI, Bagala R, et al. Diagnosis of ventilator-associated pneumonia: Comparison between ante-

mortem and post-mortem cultures in trauma patients. Indian J Med Microbiol 2014;32(3):294–300. DOI: https://doi.org/10.4103/0255-0857.136572.
35. Larcher R, Laffont-Lozes P, Roger C, Doncesco R, Groul-Viaud C, Martin A, et al. Last resort beta-lactam antibiotics for treatment of New-Delhi Metallo-Beta-Lactamase producing Enterobacterales and other difficult-to-treat resistance in Gram-negative bacteria: A real-life study. Frontiers in Cellular and Infection Microbiology 2022;12:1048633. DOI: https://doi.org/10.3389/fcimb.2022.1048633.
36. Capone A, Giannella M, Fortini D, Giordano A, Meledandri M, Ballardini M, et al. High rate of colistin resistance among patients with carbapenem-resistant Klebsiella pneumoniae infection accounts for an excess of mortality. Clinical Microbiology and Infection 2013;19(1):E23–E30. DOI: https://doi.org/10.1111/1469-0691.12070.