

Bacteremia Caused by Rare NFGNB in the ICU: A Single-center Experience

Parikshit S Prayag¹, Prasad Rajhans², Nilesh Mahale³, Sampada A Patwardhan⁴, Pruthi N Dhekane⁵, Rajeev N Soman⁶, Deepak Sethia⁷, Mousami Dalvi⁸, Surabhi Dhupad⁹, Surabhi Tyagi¹⁰, Rasika S Joshi¹¹, Abhishek Deshmukh¹², Madhavi Wavhal¹³, Priyamvada Sharma¹⁴, Amrita P Prayag¹⁵

Received on: 05 February 2025; Accepted on: 18 March 2025; Published on: 31 March 2025

ABSTRACT

Introduction: Amongst the non-fermenting gram-negative bacteria (NFGNB), *Pseudomonas* (P.) and *Acinetobacter* species predominate the landscape. However, less common NFGNB such as *Burkholderia*, *Stenotrophomonas*, *Achromobacter*, *Ralstonia* and *Elizabethkingia* species, amongst others, are assuming increasing importance. We describe a single-center experience of bacteremia caused by rare NFGNBs in an Indian intensive care unit (ICU).

Materials and methods: A retrospective study of adult patients with bacteremia caused by rare NFGNB in the ICU.

Results: Of the total 205 cases, *Burkholderia* (B.) species (43.4%, $n = 89$) were the commonest, followed by *Stenotrophomonas* species (20.4%, $n = 42$). The bacteremia was related to an indwelling catheter in 42.9 % of the patients. The median duration of hospitalization preceding the bacteremia was 16 days. Except for *B. Achromobacter* and *Aeromonas* species, meropenem showed high rates of resistance. Overall, cotrimoxazole, levofloxacin and minocycline were the most effective antibiotics active *in vitro*; with some differences noted specific to different organisms. The overall day 28 mortality was 34.1%. On multivariate analysis, the presence of shock ($p = 0.008$, CI: 1.188–5.052) and receipt of steroids ($p = 0.015$, CI: 1.032–3.891) were significantly associated with mortality.

Conclusions: This is one of the largest studies from India, describing the landscape of NFGNB causing bacteremia in the ICU. Our study shows that these infections are acquired late during the course of hospitalization, have limited therapeutic options, and can be associated with significant mortality. Implementation of stringent infection control practices is needed to reduce this threat.

Keywords: Bacteremia, *Burkholderia*, Gram-negative bacteria, Non-fermenters.

Indian Journal of Critical Care Medicine (2025): 10.5005/jp-journals-10071-24940

HIGHLIGHTS

- One of the largest studies, describing the landscape of non-fermenting gram-negative bacteria (NFGNB) causing bacteremia in the intensive care unit (ICU).
- These infections are acquired late during the course of hospitalization, they have limited therapeutic options and can be associated with significant mortality.
- Implementation of stringent infection control practices is needed to reduce this threat.

INTRODUCTION

Gram-negative infections pose major diagnostic and therapeutic challenges in the ICUs in India. Nearly half of the infections in ICUs in Tertiary Care Centers in the country can be attributed too difficult to treat gram-negative infections.¹ The annual report of the Indian Council of Medical Research (ICMR) for the year 2023 stated that the most prevalent gram-negative organisms isolated from various samples across the country were *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Escherichia coli*, and *Pseudomonas* (P.) *aeruginosa*.² These 4 organisms do indeed form the bulk of this problem, which is compounded by high resistance rates, lack of uniformly available diagnostic infrastructure and the significant cost of management of such infections. Non-fermenting gram-negative bacteria either do not utilize glucose as a source of energy or utilize it oxidatively. Amongst the non-fermenting bacteria, P. and *Acinetobacter* species predominate the Indian landscape. However,

^{1,5,9–11}Department of Infectious Diseases, Deenanath Mangeshkar Hospital, Pune, Maharashtra, India

^{2,3,7,12–14}Department of Critical Care Medicine, Deenanath Mangeshkar Hospital, Pune, Maharashtra, India

^{4,8}Department of Microbiology, Deenanath Mangeshkar Hospital, Pune, Maharashtra, India

⁶Department of Infectious Diseases, Jupiter Hospital, Pune, Maharashtra, India

¹⁵Department of In-house Research, Deenanath Mangeshkar Hospital, Pune, Maharashtra, India

Corresponding Author: Parikshit S Prayag, Department of Infectious Diseases, Deenanath Mangeshkar Hospital, Pune, Maharashtra, India, Phone: +91 7420079058, e-mail: pprayag100@gmail.com

How to cite this article: Prayag PS, Rajhans P, Mahale N, Patwardhan SA, Dhekane PN, Soman RN, et al. Bacteremia Caused by Rare NFGNB in the ICU: A Single-center Experience. Indian J Crit Care Med 2025;29(4):345–351.

Source of support: Nil

Conflict of interest: Dr Amrita P Prayag is associated as Associate Editor of this journal and this manuscript was subjected to this journal's standard review procedures, with this peer review handled independently of the Associate Editor and her research group.

there are other less common non-fermenting bacteria which are assuming increasing importance in our healthcare settings. These include organisms such as *Stenotrophomonas* spp., *Burkholderia*

(*B.*) spp., *Achromobacter* spp., *Ralstonia* spp., *Elizabethkingia* spp., amongst others. These are found universally in nature, and are also common in hospital environments, where they may contaminate drug and fluid solutions, hospital equipment, may colonize the surfaces of healthcare workers and are known to form biofilms.

The data on the epidemiology and susceptibility patterns of NFGNB beyond *P.* and *Acinetobacter* species in India is very limited. In the annual report published by the ICMR for the year 2023, NFGNB formed 25% of the total isolates.² However, a majority of these were *Acinetobacter baumannii* and *P. aeruginosa*, followed by *Stenotrophomonas (S.) maltophilia* and *B. cepacia*.² Nearly 97% of the NFGNB included in this report were isolates of either *A. baumannii* or *P. aeruginosa*. Trimethoprim sulfamethoxazole, minocycline and levofloxacin remained the most susceptible antibiotics for *S. maltophilia*; while meropenem, ceftazidime and trimethoprim sulfamethoxazole displayed the highest susceptibility for *B. cepacia*.² There is very limited data beyond these pathogens in India with respect to the non fermenters. A case series of 8 patients reported invasive infections caused by *Elizabethkingia meningoseptica* from a Tertiary Care Center in South India.³ Another retrospective experience of rare NFGNB was reported in 2020.⁴ The analysis of survivor's vs non-survivors showed a statistically significant difference in the duration of antimicrobial therapy prior to bacteremia caused by NFGNB as well as an increased length of stay in the ICU (29.5 and 34 days) among non-survivors.⁴ There is a need to generate more elaborate data about these rare non-fermenters, including their risk factors, prevalence in the Indian ICUs, susceptibility patterns and outcomes. This will not only be useful for the management of patients infected by these organisms, but will also help infection control practices. We describe a single center experience of bacteremia caused by rare NFGNBs in the ICU from a Tertiary Care Center in Western India, including the epidemiology, resistance rates, outcomes and factors associated with mortality in patients with these infections.

MATERIALS AND METHODS

We conducted a retrospective study analysis at a Tertiary Care Center in the Western part of India. The study commenced after an approval from the Institutional Ethics Committee (IEC). A waiver of consent was obtained from the IEC due to the retrospective study design.

Patient Selection

Adult patients with bacteremia caused by rare NFGNB from January 2019 to June 2024 were included in the study. Patients were excluded if they were outside the ICU on the day of onset of bacteremia. Patients included in the final analysis were treated for at least 72 hours with an appropriate antimicrobial agent.

Microbiological Methods

Blood culture was performed on an automated blood culture system, BD Bactec Fx (BD Diagnostics, Sparks, MD, USA) with at least one blood culture set. Bacterial growth on solid media was identified up to species level by matrix-assisted laser desorption ionization-time of flight-mass spectrometry (MALDI-TOF-MS) technology using the Bruker Biotyper® Sirius Platform (Bruker Daltonics Bremen, Germany). Antibiotic susceptibility testing was performed by commercial broth microdilution method, BD Phoenix™ M50 using the BD CPO NMIC 500 and NMIC 404 antibiotic

susceptibility panels. Interpretation of MICs into categories as "sensitive (S)", "intermediate (I)" or "resistant (R)" was done using clinical breakpoints set by Clinical Laboratory Standard Institute (CLSI) M 100 performance standard for antimicrobial susceptibility testing (Clinical Laboratory Standard Institute, Wayne, PA, USA). Susceptibility to NFGNB excluding *B. cepacia* and *S. maltophilia* was interpreted with reference to CLSI breakpoints for "other non-enterobacterales". Susceptibility to *Aeromonas* spp. was interpreted as per CLSI M45 guidelines. Colistin susceptibility was interpreted using breakpoints for *P. aeruginosa*. For *S. maltophilia*, breakpoints for minocycline were lowered in 2023, and the new recommendations were followed since the update.

Statistical Analysis

The inter-group statistical comparison of distribution of categorical variables was done using Chi-square test or Fisher's exact probability test. Multivariate logistic regression analysis with backward stepwise procedure was used to obtain the statistically significant and independent determinants of incidence of mortality. The entire data was statistically analyzed using Statistical Package for Social Sciences (SPSS version 24.0, IBM Corporation, USA) for MS Windows.

Definitions used in the Study

Clinical cure was defined as cessation of all antimicrobials and survival for at least 72 hours without the need to restart antibiotics. Microbiological cure was defined as repeat blood cultures being negative (sent after at least 72 hours of definitive therapy).

Central related bloodstream infection (CRBSI) was diagnosed on the basis of a positive differential time to positivity (DTP) with a central line draw becoming positive ≥ 2 hours earlier compared to the peripheral sample within a simultaneously collected blood culture set.

RESULTS

The total number of positive blood cultures during the study period were 2824. Thus, rare NFGNB were 205. Thus, rare NFGNB contributed to 7.3% of the total positive blood cultures.

A total of 205 cases were included in the final analysis. Table 1 shows the etiological agent of the episodes of bacteremia and the yearly episodes. As seen in Table 1, *B.* species (other than *B. pseudomallei*) (43.4%, $n = 89$) predominate the landscape of rare NFGNBs in our center, followed by *Stenotrophomonas* species (20.4%, $n = 42$).

Table 2 shows the demographic characteristics and comorbidities of the patients included in the study. Central related bloodstream infection was found in 42.9% of the patients; the line was removed in a majority of these patients.

Table 3 shows the resistance rates for the commonly tested antimicrobial agents against the rare NFGNBs included in our study. Overall, except for *B.* species and *Aeromonas* species, meropenem showed high rates of resistance.

Table 4 shows the percentage of cases for which microbiological and clinical cure was obtained, as well as the 14 and 28-day mortality in patients with bacteremia caused by rare NFGNBs. As shown in the table, the 28-day mortality was 34.1%.

Table 5 shows the factors associated with 28-day mortality on univariate analysis. As shown in Table 5, receipt of steroids in the preceding 14 days, hematopoietic stem cell transplantation,

Table 1: Yearly episodes of bacteremia caused by various uncommon NFGNBs

Microorganism	2019	2020	2021	2022	2023	2024	Total
<i>Achromobacter</i> spp.	0	1	3	2	1	3	10
<i>Aeromonas</i> spp.	0	1	2	3	3	4	13
<i>Burkholderia</i> spp. (other than <i>Burkholderia pseudomallei</i>)	6	12	14	14	16	27	89
<i>Chryseobacterium</i> spp.	1	3	4	2	1	0	11
<i>Elizabethkingia</i> spp.	4	1	6	3	3	3	20
<i>Ralstonia</i> spp.	0	3	1	5	7	2	18
<i>Sphingomonas</i> spp.	0	1	1	0	0	0	2
<i>Stenotrophomonas</i> spp.	2	7	12	10	3	8	42
Total	13	29	43	39	34	47	205

Table 2: Demographic characteristics and comorbidities of patients included in the study

Demographic characteristics/ comorbidities	No. of cases (N = 205)	% of cases
Age (years)		
Median (min–max)	57 (15–89)	
Gender		
Male	139	67.8
Female	66	32.2
Presence of catheter		
CVC	121	59.0
HD catheter	48	23.4
CRBSI	88	42.9
Line removed	79	38.5
Comorbidities/Clinical conditions		
Malignancy	59	28.8
Type 2 diabetes mellitus	79	38.5
Chronic kidney disease	35	17.1
Autoimmune disease	9	4.4
COVID-19 (in the preceding 2 weeks)	25	12.2
Neutropenic sepsis	27	13.2
On steroids (in the preceding 2 weeks)	62	30.2
On immunosuppression (in the preceding 2 weeks)	42	20.5
Length of hospital stay: Median (range)	16 (1–99)	
SOFA score: Median (range)	6 (0–19)	
CCI: Median (range)	3 (0–11)	

CCI, Charlson comorbidity index; CRBSI, catheter-related bloodstream infection; CVC, central venous catheter; HD, hemodialysis; SOFA, sequential organ failure assessment

COVID-19 infection in the preceding 14 days, mechanical ventilation, presence of shock, central line associated bloodstream infections and high SOFA scores were associated with mortality on the univariate analysis.

Table 6 shows the factors associated with 28 day mortality on multivariate analysis. As shown in Table 6, receipt of corticosteroids in the preceding 14 days and presence of shock were associated with mortality on the multivariate analysis.

DISCUSSION

Infections caused by non-fermenting gram-negative bacteria is an important problem in ICUs. In India, the available data largely focuses on *P.* and *Acinetobacter* species. However, rare NFGNBs can also pose a considerable challenge, given the high rates of resistance in India. We describe a retrospective experience of bacteremias caused by rare NFGNBs in the ICU. As shown in Table 1, *B. species* (other than *pseudomallei*) were the commonest cause of bacteremia due to rare NFGNB. *Stenotrophomonas maltophilia* was the second-commonest species in our study; while *Elizabethkingia* and *Ralstonia* species ranked third and fourth respectively.

A variety of sources have been described for these rare NFGNBs including hospital environments, tap water faucets, sinks, contaminated solutions, medical equipment, catheters, and skin surfaces of healthcare workers.^{5–7} Table 2 shows the baseline characteristics and comorbidities of the included patients. As shown in Table 2, the bacteremia was related to an indwelling catheter in 42.9 % of the patients, highlighting the fact that central catheters are an important source of these rare infections. Also in our study, the median duration of hospitalization on the day of onset of bacteremia was 16 days, showing that these were acquired fairly late into the course of hospitalization. This highlights the importance of stringent infection control measures to prevent these infections. More than half of the patients were either on steroids or on immunosuppressive therapy in the 14 days prior to the onset of bacteremia. Previous studies have found that the risk for infections due to NFGNB is higher in immunocompromised patients.^{8,9} Hence, these organisms must be included in the differentials in the relevant clinical settings.

Table 3 shows the resistance rates for the commonly tested antibiotics for the organisms included in the study. *Burkholderia cepacia* complex (BCC) remains the most important atypical NFGNB in our settings. These organisms are intrinsically resistant to polymyxins and aminoglycosides. The presence of Ambler class A beta-lactamases is an important mechanism of resistance in these organisms.¹⁰ Pen B is a Class A penicillinase with broad spectrum carbapenemase character, while *B. multivorans* contains a Pen A enzyme that is related to Pen B.¹⁰ The presence of efflux pumps and porin mutations may further compound the problem of resistance. The meropenem susceptibility in our center for BCC was comparable to the national data (82.1 vs 86.7%).² Trimethoprim sulfamethoxazole (TMP-SMX) was the most effective antimicrobial *in vitro*, which again is consistent with the national data.² However, susceptibility rates

Table 3: Resistance rates (percentage) for commonly tested antibiotics for included atypical NFGNBs

Antibiotic	<i>Achromobacter</i> (n = 10)	<i>Aeromonas</i> (n = 13)	<i>Burkholderia</i> (n = 89)	<i>Chryseobacterium</i> (n = 11)	<i>Elizabethkingia</i> (n = 20)	<i>Ralstonia</i> (n = 18)	<i>Sphingomonas</i> (n = 2)	<i>Stenotrophomonas</i> (n = 42)
Amikacin	100.0	15.4	100.0	100.0	100.0	61.1	100.0	100.0
Tobramycin	100.0	0.0	100.0	100.0	100.0	76.9	100.0	100.0
Meropenem	0.0	0.0	17.9	100.0	100.0	94.4	100.0	100.0
Ceftazidime	30.0	15.4	28.4	100.0	100.0	94.4	100.0	65.0
Cefepime	30.0	15.4	NA	100.0	100.0	94.4	100.0	NA
Piperacillin - Tazobactam	30.0	7.7	100.0	100.0	100.0	94.4	100.0	100.0
Colistin	20.0	0.0	100.0	100.0	100.0	100	100.0	100.0
Cotrimoxazole	30.0	7.7	6.7	9.1	0.0	5.5	0.0	9.5
Chloramphenicol	30.0	0.0	30.3	33.3	100.0	92.8	100.0	6.2
Ciprofloxacin	40.0	7.7	100.0	72.7	70.0	22.2	0.0	NA
Levofloxacin	10.0	0.0	12.6	60.0	55.0	0.0	0.0	7.1
Minocycline	30.0	0.0	12.8	0.0	5.0	37.5	0.0	0.0

NA, not applicable due to absence of clinical breakpoints

Table 4: Distribution of outcome measures

Outcome measure	Number of cases	Percentage
Microbiological cure		
No	53	25.8
Yes	50	24.4
Follow-up cultures not done	102	49.8
Clinical cure		
No	71	34.6
Yes	134	65.4
14-day mortality		
Death	68	33.2
Survived	137	66.8
28-day mortality		
Death	70	34.1
Survived	135	65.9

for minocycline and levofloxacin were higher in our study than what has been reported nationally.² *Stenotrophomonas maltophilia* is inherently resistant to a number of antibiotics. It encodes the inducible beta lactamases L1 and L2.¹¹ Besides, multidrug efflux pumps and the presence of aminoglycoside modifying enzymes further compound the problem of antimicrobial resistance. Trimethoprim sulfamethoxazole, minocycline, levofloxacin and chloramphenicol were the most effective drugs *in vitro* in our study, similar to previously published reports from India.¹² For *Elizabethkingia* and *Chryseobacterium* species, levofloxacin showed considerable resistance in our study; TMP-SMX and minocycline showed much better susceptibility rates. For *Elizabethkingia* species, there is some data regarding drugs such as vancomycin, and rifampicin, which can even have a synergistic effect, however these options were not explored in our study.¹³ For *Ralstonia* species, TMP-SMX and levofloxacin were more effective *in vitro* compared to minocycline. As shown in Table 3, *Aeromonas* species displayed relatively higher susceptibility rates compared to other atypical NFGNB, presenting more options for therapy. For *Achromobacter* species, TMP-SMX displayed higher resistance rates than for other

atypical NFGNB. Variable susceptibility has been reported for this drug with respect to *Achromobacter* species.¹⁴ There were only two isolates of *Sphingomonas* species, and hence, it was difficult to draw meaningful conclusions.

Table 4 shows the outcomes of these episodes caused by NFGNB. Microbiological cure was reported only in approximately 50% of the patients in whom repeat blood cultures were sent. This shows that blood cultures may take some time to turn negative and persistence of organisms in blood cultures is not uncommon, even when the right antimicrobial is administered. It is also important to consider sending follow-up blood cultures in these patients, given the fact that these organisms may be difficult to clear. It is important to address the possible sources of infection in these patients, including indwelling catheters. There is some, although sparse, literature regarding the use of combination therapy for these infections in critically ill patients or when there is refractory bacteremia. A combination of beta-lactam antibiotics and TMP-SMX has been proposed for BCC.¹⁵ The Infectious Diseases Society of America guidance on the treatment of antimicrobial resistant gram-negative infections which was published in 2024 recommends combining two drugs from minocycline, TMP-SMX, cefiderocol and levofloxacin.¹⁶ Cefiderocol is not available in India; *aztreonam-avibactam* is a promising option on the horizon. As shown in Table 4, there was considerable mortality in patients with bacteremia caused by rare NFGNB. This re-emphasizes the need for strict infection control practices, given the mortality associated with these infections. Table 5 shows the factors associated with mortality in these patients, on univariate analysis, while Table 6 shows the factors associated with mortality on multivariate analysis. The presence of shock and receipt of steroids were factors which were associated with increased mortality in these patients.

Overall, this study describes one of the largest experiences of rare NFGNB published from an ICU in India. It shows that BCC dominates the landscape of rare NFGNB, followed by *S. maltophilia*. Our study shows that these infections are acquired fairly late into the course of hospitalization, and central indwelling catheters are important sources of these infections. Overall TMP-SMX, levofloxacin and minocycline remain potent drugs, while carbapenems remain an effective choice for BCC. However, it is important to have access to local data. These infections are associated with considerable

Table 5: Univariate statistical analysis showing the incidence of day 28 mortality according to different demographic and clinical characteristics of cases studied

Demographic characteristics/ comorbidities	Death (n = 70)		Survived (n = 135)		Total (n = 205)		p-value
	n	%	n	%	n	%	
Age-group							
≤50 years	23	28.4	58	71.6	81	100.0	0.160 ^{NS}
>50 years	47	37.9	77	62.1	124	100.0	
Gender							
Male	22	33.3	44	66.7	66	100.0	0.865 ^{NS}
Female	48	34.5	91	65.5	139	100.0	
Neutropenic sepsis							
No	58	32.6	120	67.4	178	100.0	0.225 ^{NS}
Yes	12	44.4	15	55.6	27	100.0	
On steroids (in the preceding 2 weeks)							
No	35	24.5	108	75.5	143	100.0	0.001 ^{***}
Yes	35	56.5	27	43.5	62	100.0	
On immunosuppression (in the preceding 2 weeks)							
No	53	32.5	110	67.5	163	100.0	0.331 ^{NS}
Yes	17	40.5	25	59.5	42	100.0	
Malignancy							
No	52	35.6	94	64.4	146	100.0	0.485 ^{NS}
Yes	18	30.5	41	69.5	59	100.0	
SOT recipients							
No	68	33.8	133	66.2	201	100.0	0.607 ^{NS}
Yes	2	50.0	2	50.0	4	100.0	
HSCT recipients							
No	66	33.0	134	67.0	200	100.0	0.047 [*]
Yes	4	80.0	1	20.0	5	100.0	
Type 2 DM							
No	46	36.5	80	63.5	126	100.0	0.368 ^{NS}
Yes	24	30.4	55	69.6	79	100.0	
CKD							
No	62	36.5	108	63.5	170	100.0	0.122 ^{NS}
Yes	8	22.9	27	77.1	35	100.0	
CLD							
No	63	32.8	129	67.2	192	100.0	0.138 ^{NS}
Yes	7	53.8	6	46.2	13	100.0	
Autoimmune disease							
No	66	33.7	130	66.3	196	100.0	0.494 ^{NS}
Yes	4	44.4	5	55.6	9	100.0	
COVID-19 (in the preceding 2 weeks)							
No	52	28.9	128	71.1	180	100.0	0.001 ^{***}
Yes	18	72.0	7	28.0	25	100.0	
Major surgery (in the preceding 2 weeks)							
No	58	35.6	105	64.4	163	100.0	0.392 ^{NS}
Yes	12	28.6	30	71.4	42	100.0	
Mechanical ventilation							
No	4	4.0	96	96.0	100	100.0	0.001 ^{***}
Yes	66	62.9	39	37.1	105	100.0	

(Contd...)

Table 5: (Contd...)

Demographic characteristics/ comorbidities	Death (n = 70)		Survived (n = 135)		Total (n = 205)		p-value
	n	%	n	%	n	%	
RRT							
No	51	32.3	107	67.7	158	100.0	0.301 ^{NS}
Yes	19	40.4	28	59.6	47	100.0	
Shock							
No	6	5.8	98	94.2	104	100.0	0.001 ^{***}
Yes	64	63.4	37	36.6	101	100.0	
CRBSI							
No	33	28.2	84	71.8	117	100.0	0.038 [*]
Yes	37	42.0	51	58.0	88	100.0	
Line removal							
No	46	36.5	80	63.5	126	100.0	0.367 ^{NS}
Yes	24	30.4	55	69.6	79	100.0	
SOFA score							
0–6	16	13.3	104	86.7	120	100.0	0.001 ^{***}
7–9	12	36.4	21	63.6	33	100.0	
10–12	24	70.6	10	29.4	34	100.0	
>12	18	100.0	0	0.0	18	100.0	
CCI							
0 (none)	12	44.4	15	55.6	27	100.0	0.577 ^{NS}
1–2 (mild)	18	29.5	43	70.5	61	100.0	
3–4 (moderate)	19	35.8	34	64.2	53	100.0	
≥5 (severe)	21	32.8	43	67.2	64	100.0	

p-value by Chi-square test; p-value < 0.05 is considered to be statistically significant; *p-value < 0.05; ***p-value < 0.001; CCI, Charlson comorbidity index; CLABSI, catheter-related bloodstream infection; CLD, chronic liver disease; COVID-19, coronavirus disease; CKD, chronic kidney disease; DM, diabetes mellitus; HSCT, hematopoietic stem cell transplantation; NS, statistically non-significant; RRT, renal replacement therapy; SOFA, sequential organ failure assessment; SOT, solid organ transplantation

Table 6: Multivariate logistic regression analysis for finding the independent predictors of 28-days mortality incidence (Backward stepwise procedure)

Risk factors (variables in the model)	Odds ratio (OR)	95% CI for odds ratio	p-value
On steroids (in the preceding 2 weeks)			
No	1.00	–	–
Yes	1.825	1.032–3.891	0.015*
Shock			
No	1.00	–	–
Yes	3.196	1.188–5.052	0.008**

Odds ratio (OR) = 1: Reference category; dependent variable: Mortality–Binary coded (0: Survived, 1: Death); *p-value < 0.05; **p-value < 0.01; NS, statistically non-significant. Other variables in the model: Age, gender, HSCT recipient, COVID-19 (last 2 weeks), mechanical ventilation, CLABSI, and SOFA score

mortality and high rates of microbiological failure. Further large scale studies are needed to explore the role of combination therapy. Stringent infection control measures must be deployed to reduce the burden of these infections.

Limitations

For certain organisms, the number of episodes were relatively smaller; though this is one of the largest studies from India describing these infections. Also, this was a retrospective experience and was not designed to compare the efficacies of various regimens used for treating these infections and measuring the outcomes. Also the usage of prior antibiotics needs to be studied in greater detail to look at specific risk factors for these infections. Patients with central nervous system shunts, and other devices beyond central venous catheters, were not well represented in our study.

CONCLUSIONS

To the best of our knowledge, this is one of the largest studies from India, describing the landscape of NFGNB causing *bacteremia* in the ICU. Our study shows that these infections are important and can be acquired late during the course of hospitalization. Accurate identification of these organisms is important in the microbiology lab in order to initiate the optimal therapy. The usage of MALDI-TOF-MS technology can enhance the accuracy of identification. These infections can be associated with significant morbidity and mortality, despite appropriate antimicrobial therapy. Our study shows that these organisms can be resistant to a number of commonly used antimicrobials in the ICU and hence knowledge of

the resistance patterns is important to plan therapy. The patterns of susceptibility may vary across different institutes, cities and regions and hence it is important to generate local data. Further, larger studies need to focus on the relative efficacies of the commonly used drugs for treating these infections. Stringent infection control practices are needed to reduce the burden of rare NFGNB in our ICUs.

ORCID

Parikshit S Prayag  <https://orcid.org/0000-0003-2102-7627>
 Prasad Rajhans  <https://orcid.org/0000-0002-0111-6123>
 Nilesh Mahale  <https://orcid.org/0000-0002-7952-8259>
 Sampada A Patwardhan  <https://orcid.org/0000-0003-0998-5742>
 Pruthi N Dhekane  <https://orcid.org/0009-0005-5673-5430>
 Rajeev N Soman  <https://orcid.org/0000-0003-1578-9932>
 Deepak Sethia  <https://orcid.org/0000-0001-9230-4009>
 Mousami Dalvi  <https://orcid.org/0009-0004-7017-1195>
 Surabhi Dhupad  <https://orcid.org/0000-0003-4251-6411>
 Surbhi Tyagi  <https://orcid.org/0009-0005-0548-8935>
 Rasika S Joshi  <https://orcid.org/0009-0005-1551-0390>
 Abhishek Deshmukh  <https://orcid.org/0009-0005-3033-2270>
 Madhavi Wavhal  <https://orcid.org/0009-0003-8459-1548>
 Priyamvada Sharma  <https://orcid.org/0000-0002-5485-3477>
 Amrita P Prayag  <https://orcid.org/0000-0002-2498-9576>

REFERENCES

- Bannore N, Kapadia F, Hegde A. Difficult to treat gram-negative bacteria—the Indian scenario. *Curr Infect Dis Rep* 2024;26(2):69–77. DOI: 10.1007/s11908-024-00834-y.
- Indian Council of Medical Research (ICMR). Annual report (January 2023 to December 2023) of the Antimicrobial Resistance Research & Surveillance Network (AMRSN). Division of epidemiology and communicable diseases. 2023. [online] Available from: https://www.icmr.gov.in/icmrobject/uploads/Documents/1725536060_annual_report_2023.pdf. [Last accessed March, 2025].
- Ganesan V, Sundaramurthy R. *Elizabethkingia* meningoseptica Infections: A case series from a tertiary hospital in South Tamil Nadu. *Indian J Crit Care Med* 2022;26(8):958–960. DOI: 10.5005/jp-journals-10071-24292.
- Saran S, Gurjar M, Garg A, Sahu C, Bhaskar B, Mishra P, et al. Uncommon non-fermenting Gram-negative bacillary bacteraemia in ICU patients. *Infectious Diseases* 2020;52(5):372–375. DOI: 10.1080/23744235.2020.1716991.
- Geiger AM, Hogardt M, Heesemann J. *Burkholderia/Stenotrophomonas*. *Contrib Microbiol* 2001;8:20–34. DOI: 10.1159/000060400.
- Weber DJ, Rutala WA, Blanchet CN, Jordan M, Gergen MF. Faucet aerators: A source of patient colonization with *Stenotrophomonas maltophilia*. *Am J Infect Control* 1999;27(1):59–63. DOI: 10.1016/s0196-6553(99)70077-5.
- Looney WJ. Role of *Stenotrophomonas maltophilia* in hospital-acquired infection. *Br J Biomed Sci*. 2005;62(3):145–154; quiz 1 p following 154. DOI: 10.1080/09674845.2005.11732702.
- Wang N, Tang C, Wang L. Risk Factors for acquired *stenotrophomonas maltophilia* pneumonia in intensive care unit: A systematic review and meta-analysis. *Front Med (Lausanne)* 2022;12;8:808391. DOI: 10.3389/fmed.2021.808391.
- Xu C, Lin Q, Zhao Y, Zhu G, Jiang E, Li S, et al. Clinical characteristics and risk factors of *Aeromonas* bloodstream infections in patients with hematological diseases. *BMC Infect Dis* 2022;22(1):303. DOI: 10.1186/s12879-022-07277-7.
- Rhodes KA, Schweizer HP. Antibiotic resistance in *Burkholderia* species. *Drug Resist Updat* 2016;28:82–90. DOI: 10.1016/j.drug.2016.07.003.
- Wang Y, He T, Shen Z, Wu C. Antimicrobial resistance in *stenotrophomonas* spp. *Microbiol Spectr*. 2018;6(1). DOI: 10.1128/microbiolspec.ARBA-0005-2017.
- Varshini MK, Ganesan V, Sundaramurthy R, Rajendran T. Risk factors and clinical outcomes of *stenotrophomonas maltophilia* infections: Scenario in a Tertiary Care Center from South India. *Indian J Crit Care Med* 2022;26(8):935–937. DOI: 10.5005/jp-journals-10071-24288.
- Lin IF, Lai CH, Lin SY, Lee CC, Lee NY, Liu PY, et al. *In vitro* and *in vivo* antimicrobial activities of vancomycin and rifampin against *elizabethkingia anophelis*. *Int J Mol Sci* 2023;24(23):17012. DOI: 10.3390/ijms242317012.
- Isler B, Kidd TJ, Stewart AG, Harris P, Paterson DL. *Achromobacter* Infections and Treatment Options. *Antimicrob Agents Chemother*. 2020;64(11):e01025–e010220. DOI: 10.1128/AAC.01025-20.
- Huang CH, Jang TN, Liu CY, Fung CP, Yu KW, Wong WW. Characteristics of patients with *Burkholderia cepacia* bacteremia. *J Microbiol Immunol Infect* 2001;34(3):215–219. PMID: 11605815.
- Tamma PD, Heil EL, Justo JA, Mathers AJ, Satlin MJ, Bonomo RA. Infectious Diseases Society of America 2024 guidance on the treatment of antimicrobial-resistant gram-negative infections. *Clin Infect Dis* 2024;ciae403. DOI: 10.1093/cid/ciae403.