

Clinical and Microbiological Profile of *Elizabethkingia meningoseptica* Bacteraemia: A Cross-sectional Study from a Tertiary Care Centre in Northern India

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ABSTRACT

Introduction: *Elizabethkingia meningoseptica* (*E. meningoseptica*) is an emerging pathogen that causes bloodstream infections, especially among immunocompromised or critically ill patients. Due to its multidrug resistance, limited antibiotic treatments are available. Therefore, correct identification with a proper susceptibility report is compulsory to reduce mortality and morbidity caused by this rare pathogen.

Aim: To analyse the clinical features, underlying co-morbidity, outcomes, and antibiotic resistance potential of *E. meningoseptica* causing bacteraemia.

Materials and Methods: This cross-sectional study was conducted in Department of Microbiology, Rajshree Medical Research Institute (RMRI), Bareilly, Uttar Pradesh, India. The study spanned three years from August 2020 to July 2023. All patients with *E. meningoseptica* bacteraemia were identified from blood culture reports and included in the study. As it was a duration-based study, all consecutive patients identified with *E. meningoseptica* bacteraemia were enrolled. The total sample size was 43. Blood samples growing gram negative, non fermenting, non motile isolates that were positive for the oxidase reaction were further identified using the Vitek 2

compact system (Biomerieux, France). All relevant data regarding demographic and clinical characteristics, underlying diseases, and antibiotic treatments were collected from the hospital information system. Patient demographics were presented as mean±standard deviation. Clinical characteristics and co-morbid conditions were presented as frequency and percentages.

Results: The majority of patients were elderly males admitted to the Intensive Care Unit (ICU). The most common underlying co-morbidity was malignancy in 12 (27.9%), and pneumonia in 12 (48.8%) was the major diagnosis among these bacteraemic patients. A total of 10 (23.25%) infections were polymicrobial, with common concomitant pathogens being *Pseudomonas aeruginosa* and Methicillin-Resistant *Staphylococcus aureus* (MRSA). Co-trimoxazole, fluoroquinolones, and Piperacillin/Tazobactam were the most effective antibiotics. Thirty-nine (90.7%) patients recovered completely, while four patients (9.3%) died of complications.

Conclusion: Improper antimicrobial therapy increases resistance and mortality among patients with *E. meningoseptica* infections. It is imperative that clinicians remain vigilant about this rare pathogen and advise antimicrobial susceptibility testing for appropriate treatment, leading to favourable outcomes.

Keywords: Co-morbidity, Immunocompromised, Multidrug resistance

INTRODUCTION

Elizabethkingia meningoseptica, a Gram negative, non fermenting, and oxidase-positive bacillus, is an emerging pathogen causing bloodstream infections, especially among immunocompromised or critically ill patients [1]. It is a non fastidious, non spore-forming, slender, slightly curved, and non motile bacillus that is indole-positive [2]. Formerly known as *Flavobacterium meningoseptica*, it is widely recognised to cause meningitis in premature newborns and infants [3,4]. However, pneumonia, endocarditis, cellulitis, wound infections, ocular infections, sinusitis, epididymitis, and prosthesis-associated septic arthritis have also been reported [5]. Some of the known risk factors for acquiring such infections are immunosuppression, underlying co-morbidity, prolonged hospital stay, and the presence of invasive devices [6]. It is a multidrug-resistant bacterium as it produces two types of beta-lactamases: Extended-Spectrum Beta-Lactamases (ESBL) and Metallo-Beta-Lactamases (MBL) [7]. Hence, it exhibits resistance to beta-lactam antibiotics and carbapenems. It also shows resistance to aminoglycosides, tetracycline, and chloramphenicol, which usually provide Gram negative coverage. However, it shows susceptibility to clindamycin, erythromycin, cotrimoxazole, and quinolones, which are commonly used to treat infections due to Gram positive bacteria [8]. This leads to improper selection of

antimicrobials by clinicians, contributing to poor outcomes. Hence, correct identification with a proper susceptibility report is compulsory to reduce mortality and morbidity due to *E. meningoseptica* infections.

As limited information is found in the literature about this rare pathogen, the present study aims to enlighten clinicians about underlying co-morbidity, proper antibiotic therapy, and the prevention of these emerging human pathogens. It was also noted that *E. meningoseptica* bacteraemia was a nosocomial infection among elderly males admitted to the ICU and was found to be a multidrug-resistant pathogen.

In this study, all patients with *E. meningoseptica* bacteraemia admitted to RMRI hospital were prospectively analysed over a three-year period with the aim of analysing the clinical features, underlying co-morbidity, outcomes, and evaluating antibiotic resistance potential among these isolates.

MATERIALS AND METHODS

This cross-sectional study was conducted in Department of Microbiology, Rajshree Medical Research Institute (RMRI), a tertiary healthcare centre located in Bareilly, Uttar Pradesh, India. The hospital has a capacity of 1080 beds. The study was carried out over a period of three years, from August 2020 to July 2023. Approval

was obtained from the Institutional Ethical Committee (IEC) (Reference number: RMRI/IEC/58/2020) prior to conducting the study.

Inclusion criteria: All patients admitted to the hospital with *E. meningoseptica* bacteraemia were included in the study.

Exclusion criteria: Patients who had received previous antibiotic treatment were excluded from the study.

Sample size and justification: Since this was a duration-based study, all consecutive patients identified with *E. meningoseptica* bacteraemia during the study period were enrolled. The total sample size was 43.

Study tools: Relevant data regarding demographic and clinical characteristics, underlying co-morbid conditions, antibiotic treatment before and after blood culture results, and outcomes were collected from the hospital information system. Standard definitions were used to categorise community or healthcare-associated bacteraemia [9].

Definitions [9]: An episode of significant bacteraemia was defined as the presence of one or more blood cultures that were positive for *E. meningoseptica* and contributed to clinical sepsis. Nosocomial bacteraemia was defined as bacteraemia that developed at least 48 hours after hospital admission, according to the standard definition proposed by the Centers for Disease Control and Prevention.

Lab procedures: Sets of blood samples were collected before starting antibiotic therapy and cultured conventionally on blood agar, chocolate agar, and MacConkey agar. Both blood and chocolate agar demonstrated the growth of Gram negative bacilli that produced light yellow-coloured colonies measuring 1-2 mm in diameter. MacConkey agar showed no growth. The organism was non motile in the hanging drop preparation from the colonies. They were positive for oxidase and catalase tests. All isolates were subjected to the Vitek 2 compact system (Biomérieux, France) for identification and antimicrobial susceptibility testing. *E. meningoseptica* was confirmed when the probability given by Vitek was >99%. As standard guidelines regarding breakpoints for this emerging pathogen are not available, the Clinical and Laboratory Standards Institute (CLSI) criteria for Gram negative and Gram positive bacteria were used to determine antimicrobial sensitivity [10]. The Minimum Inhibitory Concentration (MIC) values were determined for the following antibiotics: amikacin, gentamicin, ceftazidime, ciprofloxacin, ceftriaxone, colistin, cefepime, imipenem, levofloxacin, meropenem, piperacillin, ampicillin/sulbactam, cefoperazone/sulbactam, cotrimoxazole, tetracycline, tigecycline, ticarcillin, tobramycin, piperacillin/tazobactam, aztreonam, and minocycline using the broth microdilution method with the Vitek 2 compact system. The disk diffusion test was not performed in the present study as it is not recommended by the CLSI guidelines [10]. Interpretative criteria for these antibiotics were derived from those described in the CLSI M100 guidelines [10]. In patients with *E. meningoseptica* bacteraemia, repeat blood cultures were performed to rule out contamination, and all of them were found to be positive again with the same organism.

STATISTICAL ANALYSIS

Patient demographics were presented as mean±standard deviation. Clinical characteristics and co-morbid conditions were presented as frequencies and percentages.

RESULTS

The demographic and clinical characteristics of the 43 infected patients are depicted in [Table/Fig-1,2].

Demographic findings: The mean±SD age of the patients was 66.65±13.44 years, with a range of 25-88 years. Among the 43 patients infected with *E. meningoseptica*, 67.4% (29/43) were male.

Clinical findings: Among the infected patients, 67.4% (29/43) had nosocomial infections, with the majority of these infections acquired in the ICU. The most common underlying co-morbidity

Character	n (%)
Age (years)	
20-30	1 (2.3)
31-50	6 (14)
51-70	15 (34.9)
71-90	21 (48.8)
Gender	
Male	29 (67.4)
Female	14 (32.6)
Location	
Medicine ICU	15 (34.9)
Surgery ICU	12 (27.9)
Oncology	11 (25.6)
Orthopaedics	5 (11.6)

[Table/Fig-1]: Demographic characteristics of 43 patients with *E.meningoseptica* bacteraemia.

ICU: Intensive care unit

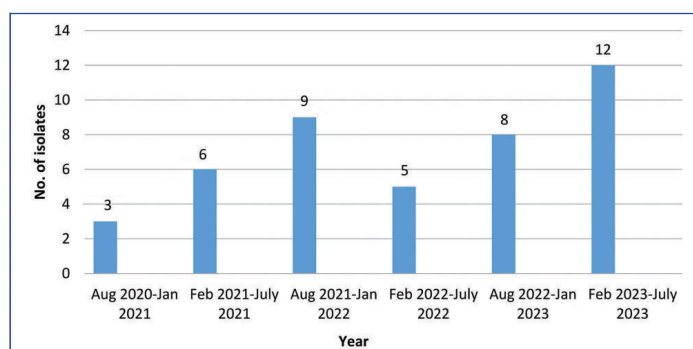
Character	n (%)
Infectious diagnosis	
Pneumonia	21 (48.8)
Cellulitis	7 (16.3)
Osteomyelitis	6 (14)
Catheter-related infection	4 (9.3)
Wound infection	2 (4.7)
Biliary tract infection	2 (4.7)
Intra-abdominal infection	1 (2.3)
Type of infection	
Mono-microbial	33 (76.74)
Poly-microbial <i>Pseudomonas spp.</i> (6) MRSA (3) <i>Acinetobacter spp.</i> (1)	10 (23.25)
Underlying co-morbidity	
Malignancy	12 (27.9)
DM	10 (23.3)
CHF	9 (20.9)
Chronic renal disease	5 (11.6)
Liver cirrhosis	3 (7)
COPD	2 (4.7)
Interstitial lung disease	1 (2.3)
SLE	1 (2.3)
Mode of infection	
Hospital-acquired	29 (67.4)
Community-acquired	14 (32.6)
Treatment	
Effective antibiotic therapy before culture	12 (27.9)
Effective antibiotic therapy after culture	31 (72)
Outcome	
Cured	39 (90.7)
Died	4 (9.3)

[Table/Fig-2]: Clinical characteristics of 43 patients with *E.meningoseptica* bacteraemia.

COPD: Chronic obstructive pulmonary disease; DM: Diabetes mellitus; CHF: Congestive heart failure; SLE: Systemic lupus erythematosus; MRSA: Methicillin-resistant staphylococcus aureus

was malignancy 12 (27.9%), followed by diabetes 10 (23.3%). Pneumonia 21 (48.8%) and cellulitis 7 (16.3%) were the major diagnosis among these bacteraemic patients. The majority 31 (72%) received appropriate treatment after obtaining the culture report. Four patients (9.3%) had a fatal outcome due to cardiopulmonary diseases.

[Table/Fig-3] reveals the trend in *E. meningoseptica* bacteraemia over a three-year period. There was a significant increasing trend in the prevalence rate of *E. meningoseptica* bacteraemia, from 7% in August 2020 to 21% in January 2022 and then again from 18.6% in August 2022 to 28% in February 2023.



[Table/Fig-3]: Trends in prevalence of *E. meningoseptica* bacteraemia during three years period.

Microbiological findings: *Pseudomonas aeruginosa* (n=6, 13.9%) and MRSA (n=3, 6.9%) followed by *Acinetobacter* spp. (n=1, 2.3%) were the predominant concomitant pathogens grown in blood cultures along with *E. meningoseptica*.

The antibiotic resistance patterns of *E. meningoseptica* isolates from blood samples against different antibiotics are shown in [Table/Fig-4]. Complete resistance was observed against amikacin, aztreonam, ceftazidime, colistin, imipenem, meropenem, piperacillin, ampicillin/sulbactam, tetracycline, ticarcillin, and tobramycin, with all isolates (n=43, 100%) showing resistance. Resistance to cefepime was observed in 42 (97.7%) isolates, while resistance to gentamicin was observed in 38 (88.4%) isolates, and resistance to minocycline was observed in 36 (83.7%) isolates. The major effective antibiotic showing more than 90.7% (n=39) sensitivity was co-trimoxazole.

Sensitivity rates ranging between 79% to 81% were seen for fluoroquinolones and piperacillin/tazobactam.

S. No.	Antimicrobial agent	Sensitive n (%)	Resistant n (%)
1	Amikacin	0	43 (100)
2	Aztreonam	0	43 (100)
3	Ceftazidime	0	43 (100)
4	Ciprofloxacin	34 (79.1)	9 (20.9)
5	Ceftriaxone	3 (7)	40 (93)
6	Colistin	0	43 (100)
7	Cefepime	1 (2.3)	42 (97.7)
8	Gentamicin	5 (11.6)	38 (88.4)
9	Imipenem	0	43 (100)
10	Levofloxacin	35 (81.4)	8 (18.6)
11	Meropenem	0	43 (100%)
12	Minocycline	7 (16.3)	36 (83.7)
13	Piperacillin	0	43 (100)
14	Ampicillin-Sulbactam	0	43 (100)
15	Cefoperazone-Sulbactam	21 (48.8)	22 (51.2)
16	Cotrimoxazole	39 (90.7)	4 (9.3)
17	Tetracycline	0	43 (100)
18	Tigecycline	22 (51.2)	21 (48.8)
19	Ticarcillin	0	43 (100)
20	Tobramycin	0	43 (100)
21	Piperacillin-Tazobactam	34 (79.1)	9 (20.9)

[Table/Fig-4]: Percentage of antibiotic resistance pattern of *E. meningoseptica* isolates.

DISCUSSION

E. meningoseptica is widespread in nature, and the first outbreak of neonatal meningitis due to this organism was described in 1958 [11]. Since then, several outbreaks of sepsis, pneumonia, and wound infections have been reported [12]. A literature search reveals that the majority of infections are healthcare-associated and reported in immunocompromised patients [13], which was consistent with the present study. Environmental studies on *E. meningoseptica* have shown that this organism can exist in chlorinated municipal water supplies, thus colonising sinks, basins, and taps. This explains the potential for this organism to serve as a reservoir of infection in the hospital environment [5]. *E. meningoseptica* infections have also been documented in immunocompetent individuals in the form of sepsis [8,13].

The present study recorded a male preponderance, and the mean age of the patients was 66.65 years, which has also been reported by Lin PY et al., and Chiu CH et al., [8,14]. It is well-documented that this rare pathogen has a strong predilection for extremes of age.

It was found that the majority of patients (67.4%) acquired *E. meningoseptica* bacteraemia in the ICU, which is also reported by Hsu MS et al., [15]. These patients were subjected to numerous modes of invasive monitoring and support, which may have predisposed them to healthcare-associated infections. The most common underlying co-morbidity noted was malignancy 12 (27.9%), followed by diabetes 10 (23.3%) among the bacteraemic patients, which was consistent with the study by Hsu MS et al., where the frequency of malignancy was 35.6% and diabetes was 25.4% [15]. However, Hung PP et al., reported cardiopulmonary disease (14/32, 43%) as the most common underlying disease [7]. Thus, the present study highlights the clinical significance of this emerging pathogen as a cause of bacteraemia, especially among immunocompromised patients.

This study reported pneumonia 12 (48.8%) as the predominant infectious diagnosis, followed by cellulitis 7 (16.3%). This was in line with the findings of Hung PP et al., who reported pneumonia in 18/32 (56.2%) cases and cellulitis in 6/32 (18.7%) cases [7]. Moore LS et al., also reported a high frequency of isolation of *E. meningoseptica* from hospital-acquired pneumonia cases [16]. In contrast, Hsu MS et al., reported primary bacteraemia in 78% of patients and pneumonia in 9% of patients [15].

Studies like Hsu MS et al., and Aldoghaim FS et al., reported polymicrobial bacteraemia in 38% and 25% of cases, respectively, which was consistent with the present study [15,17]. However, in the present study, *Pseudomonas aeruginosa* (13.9%) and MRSA (6.9%) followed by *Acinetobacter* spp. (2.3%) were the predominant concomitant pathogens grown, which does not correlate with Aldoghaim FS et al., who reported *Serratia marcescens* and *Enterococcus faecalis* as the predominant pathogens [17]. This indicates variation in the distribution of concomitant pathogens and suggests a need for changes in treatment patterns accordingly.

All the isolates showed 100% resistance to amikacin, aztreonam, ceftazidime, colistin, imipenem, meropenem, piperacillin, ampicillin/sulbactam, tetracycline, ticarcillin, and tobramycin, which was consistent with previous studies [5,7]. The most active antibiotics in the present study, with sensitivity rates of over 90%, were co-trimoxazole, followed by fluoroquinolones and piperacillin/tazobactam, which was similar to the findings of a previous study [18]. Waleed MS et al., reported rifampicin, along with fluoroquinolones and minocycline, to be the most effective drugs against this pathogen [19]. The mechanism of drug resistance in this pathogen is attributed to the production of ESBL and MBL [5]. Two types of MBL, namely BlaB and GOB, have been described in *E. meningoseptica* isolates, which are responsible for resistance to carbapenems [5]. The findings from this study suggest that antibiotic

sensitivity testing should be advised for all clinically significant strains, as ineffective empirical therapy may lead to poor outcomes.

The majority of patients 31 (72%) in the present study received appropriate treatment after obtaining the culture report. Appropriate antibiotic treatment was defined as a regimen to which *E. meningoseptica* was sensitive, if sensitivity results were available. If the sensitivity of the organism to any given antibiotic was unknown, treatment was considered inappropriate [20]. This fact correlated with a favourable outcome in the present study. The mortality rate was found to be 9.3%, which was lower than the mortality rates reported by Hsu MS et al., (23%) [15]. A study by Govindaswamy A et al., showed a very high mortality rate (75%) among septicemic critically ill patients due to the unusual resistance pattern of this pathogen, leading to improper antibiotic regimens [18].

The present study reported an increasing trend in *E. meningoseptica* bacteraemia, which was in accordance with the findings of Hsu MS et al., [15]. This increase is attributed to the rising prevalence of comorbidities and the emergence of drug resistance patterns.

This study provides clinicians with insights into the clinical and microbiological profile of this rare human pathogen, along with its antimicrobial susceptibility pattern, which will help reduce mortality and morbidity in the future.

Limitation(s)

The isolates in the present study were not subjected to molecular methods for confirmation, and the sample size was small.

CONCLUSION(S)

The current study sheds light on the clinical and microbiological profiles of *E. meningoseptica* causing bacteraemia, especially among immunocompromised patients. It is an emerging human pathogen that exhibits a significant antimicrobial resistance pattern. Improper antimicrobial therapy increases resistance and mortality rates among patients. It is imperative for clinicians to be vigilant about this rare pathogen, advise antimicrobial susceptibility testing, and treat accordingly to achieve favourable outcomes.

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