Clinical Profile and Susceptibility Patterns of Infections by Elizabethkingia Species in a Tertiary Care Hospital, Bhubaneswar, Odisha

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ABSTRACT

BACKGROUND

Elizabethkingia meningoseptica is an emerging pathogen causing meningitis, pneumonia, endocarditis, bacteremia, sepsis, wound & soft tissue infections, abdominal, respiratory and ocular infections, dialysis associated peritonitis and prosthesis associated septic arthritis, especially in immunodeficient hosts of various age groups. The prevalence of nosocomial infection by *E. meningoseptica* has increased, predominantly in patients with invasive procedures, prior use of broad-spectrum antimicrobial and co-morbid conditions. We wanted to determine the prevalence of *Elizabethkingia meningoseptica* among the clinical samples processed in our laboratory and their antimicrobial susceptibility pattern.

METHODS

This observational study was conducted in patients admitted to a tertiary care hospital, from October 2017 to October 2020. The study subjects were selected on positive bacterial culture reports after excluding patients of less than 18 years of age and their demographic and clinical features were obtained from their medical records. Blood samples were processed by BacT/Alert. VITEK-2 system was used to identify the bacteria and their antimicrobial susceptibility pattern.

RESULTS

Among the 3532 clinical samples processed, 16 (0.45 %) bacterial isolates were *Elizabethkingia meningoseptica*. Out of them, 5 (31.25 %) were from blood and 11 (68.75 %) were from endotracheal tubes. More number of cases 6 (38 %) were seen in the age group of 61 - 70 years. Most of the patients were on mechanical ventilation with common co-morbid condition associated was cardiovascular diseases 11 (68 %). *E. meningoseptica* was most often sensitive to nalidixic acid and ciprofloxacin (50 %), tigecycline 4 (30 %), minocycline 3 (18 %), cotrimoxazole 2 (15 %), piperacillin-tazobactam 1 (13 %) and minocyclin (18.75 %).

CONCLUSIONS

Infection with *E. meningoseptica* is clinically important as the organism causes nosocomial infection and is intrinsically resistant to multiple antibiotics, such as β-lactams, aminoglycosides, tetracycline, tigecycline, colistin, chloramphenicol and carbapenems. Early diagnosis and prompt treatment is required to prevent the morbidity and mortality.

KEYWORDS

Elizabethkingia Meningoseptica, Antimicrobial Susceptibility, Clinical Profile

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BACKGROUND

Elizabethkingia meningoseptica, is among the emerging pathogen causing infection especially in individuals with associated co-morbidities such as diabetes, hypertension etc. If they are left untreated it may lead to serious life-threatening conditions.

Elizabethkingia meningoseptica, was formerly known as *Flavobacterium meningosepticum* and *Chryseobacterium meningosepticum*. It was discovered in 1959 by an American bacteriologist, Elizabeth O. King, and was later identified as the cause of neonatal septicaemia.[1] It is a non-motile, non-fermenter, oxidase and catalase positive, gram-negative bacilli. It leads to a wide range of infections in both neonates and adults. In newborns, as they are in vulnerable group for acquiring infection, it is known to cause meningitis, pneumonia, bacteremia and sepsis in them.[2] It is pathogenic to immunocompetant as well as in immunocompromised individual but primarily in immunocompromised patients it causes pneumonia, endocarditis, bacteremia, meningitis and even skin and soft tissue infections.[3,4] No clinical signs and symptoms are seen in an individual who are susceptible to infection when the organism colonizes (e.g., in the respiratory tract), but this person has the potential to infect others unless and until necessary precautions are taken immediately. Under normal circumstances these individuals are not given any antibmicrobial therapy. However, if there is presence of clinical infection alongwith signs and symptoms of infection or the colonized individual infects another susceptible individual and causes infection, then "the infection" should be treated with appropriate antimicrobial therapy.[5]

These microorganisms are usually sensitive to minocycline, but are resistant to most antibiotics such as β-lactams, β-lactam/β-lactam inhibitors, carbapenems and aminoglycosides. They usually show different sensitivity pattern to piperacillin, piperacillin-tazobactam, fluoroquinolone and trimethoprim-sulfamethoxazole. Recently, these bacteria have emerged as a major cause of life-threatening infections in different countries.[6] The SENTRY antibacterial drug monitoring program conducted from 1997 to 2001 showed that quinolone, rifampicin, trimethoprim-sulfamethoxazole and piperacillin -tazobactam are the most effective drugs against *E. meningoseptica*.[7]

Currently, only a few studies are there on this rare opportunistic pathogen and their antimicrobial susceptibility pattern. Hence, this pathogen should be given utmost importance among the rare opportunistic organism causing nosocomial infection and morbidity in developing country like India where co-morbid conditions are rising day by day due to unhealthy living conditions.

Since it is a rare opportunistic pathogen, the samples with this pathogen were also very less, therefore, we did the study for a period of three years, with an objective to determine the prevalence, clinical profile, and the antimicrobial susceptibility pattern of infection with *E. meningoseptica*, so that proper treatment can be given at right time.

METHODS

This is an observational study carried out for a period of three years from May 2017 to May 2020 in our hospital.

Inclusion Criteria

During this three-year study period, all the clinical samples which were positive for *Elizabethkingia meningoseptica* were included. Patients were also categorized according to their various clinical and co-morbid condition.

Exclusion Criteria

After excluding patients younger than eighteen years old, the study subjects were selected from the bacterial culture report, and their demographic and clinical characteristics were obtained from the medical records department.

Sample Processing

The samples which were processed in our study were blood and endotracheal tube aspirates. These samples were aseptically collected from patients and sent to the microbiology laboratory for culture and identification as well as for antimicrobial susceptibility testing of the pathogen. Respiratory samples were first cultured on MacConkey agar and sheep blood agar and incubated at 37°C overnight aerobically.

After overnight incubation, round, yellowish non-hemolytic colonies were observed on blood agar, but no growth on MacConkey agar plates. Colonies were picked up from blood agar plate. Once confirmed as oxidase positive, gram-negative bacilli, further identification and susceptibility testing was carried out by VITEK - 2.

Blood cultures were processed with the help of automated blood culture systems (Bact / Alert, France) and subculture was done on sheep blood agar and MacConkey agar plates after the bottle was flagged positive by this machine and incubated for 18 - 24 h at 35 - 37°C. The bacterial isolates were first identified using the routine grams' staining as oxidase positive, gram-negative bacilli. Then the identity of bacteria was tested by the automated methods, with a Vitek - 2 GN card system (bioMérieux), an automated identification and susceptibility testing system.

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was done by the Kirby–Bauer disc diffusion method on Müller–Hinton agar and by Vitek-2 (bioMérieux) system.[8] The minimum inhibitory concentration (MICs) of the antibiotics tested by Kirby–Bauer disc diffusion method were explained using the clinical and laboratory standards institute (CLSI) guidelines for other non-enterobacteriaceae because there are no clear guidelines to explain the sensitivity of Elizabethkingia isolates.[9]

The antibiotic disc used for antimicrobial susceptibility testing by Kirby-Bauer disc diffusion method are ciprofloxacin, trimethoprim-sulfamethoxazole, piperacillin-

tazobactam, tigecycline, tetracycline, nalidixic acid, levofloxacin, minocyclin and colistin.

Statistical Analysis

Data analysis was done using statistical package for social sciences (SPSS) IBM software and percentage was calculated.

RESULTS

Over a period of three years, a total 3532 clinical samples were processed which was sent to our laboratory from different departments. A total of 16 (0.45%) samples were positive for *Elizabethkingia meningoseptica*. More number of cases 6 (38%) were seen in the age group of 61 - 70 years followed by 5 (32%) cases in the age group of more than 70 years (Fig. 1). Most isolates were positive from endotracheal tube aspirates 11 (69 %) followed by blood 5 (32 %) (Fig. 2).

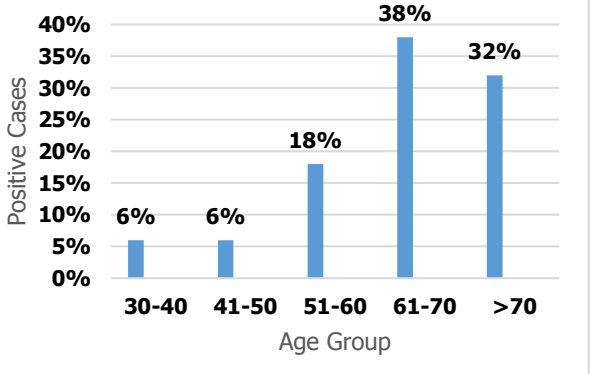

Figure 1. Age Wise Distribution of Positive Cases (N=16)

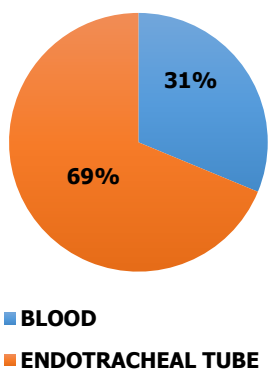

Figure 2. Isolation from Clinical Samples (N = 16)

Common Cause of Admission in ICU	Percentage (%)
ARDS	43
Urosepsis	25
Liver cirrhosis	6
Dengue	12
Coronary artery bypass grafting	6
Chronic kidney disease	6

Table 1. Common Cause of Admission in ICU (N = 16)

All the isolates were from patients admitted in intensive care unit (ICU). Subsequently, the causes of admissions were identified as acute respiratory distress syndrome (ARDS) 7 (43 %), urosepsis 4 (25 %), liver cirrhosis 1 (6 %), dengue 2 (12 %), coronary artery bypass grafting 1 (6 %) and chronic kidney disease 1 (6 %) (Table 1).

Most of the patients were on mechanical ventilation and/ or various types of catheterization. Most common associated risk factor in our study for colonisation or infection by *E. meningoseptica* was found to be mechanical ventilation, arterial line, central line 16 (100 %) alongwith other interventions such as endoscopy 13 (80 %), urinary catheter 12 (75 %) and dialysis 1 (7 %) (Table 2).

Interventions	Percentage
ICU admission	100
Mechanical ventilation	100
Urinary catheter	75
Central line	100
Arterial line	100
Naso-gastric tube	100
Endoscopy	87
Dialysis	7

Table 2. Frequency of Possible Risk Factors in the Study Population (N=16)

Co-morbidities were associated with all 16 cases of Elizabethkingia infection. The most common co-morbid condition associated were cardiovascular diseases 11 (68 %) followed by other diseased conditions requiring steroid treatment 7 (43 %), diabetes 2 (13 %) and immuno-suppressant 1(6 %) (Table 3).

Co-Morbid Condition	No. of Cases (%)
Diabetes	13
Steroid	43
Immunosuppression	6
Cardiovascular disease	68

Table 3. Associated Comorbid Conditions in the Study Population (N = 16)

Elizabethkingia meningoseptica was most sensitive to nalidixic acid and ciprofloxacin 8 (50 %), followed by tigecycline 4 (30 %), minocycline 3 (18 %), cotrimoxazole 2 (15 %), piperacillin-tazobactam 1 (13 %) (Table 4).

Antibiotics	MIC	No. of Isolates (%)
CIP	≤ 0.25	15
COT	40	50
PIT	16	13
TGC	2	30
TET	8	12
NA	8	50
LEV	≤ 0.25	18
MIN	2	18
CL	≤ 8	12

Table 4. Antimicrobial Susceptibility for E. Meningoseptica

* CIP- Ciprofloxacin, †COT - trimethoprim-sulfamethoxazole, ‡ PIT Piperacillin-tazobactam, §TGC- Tigecycline,‖TET- tetracycline, ** NA- Nalidixic acid, ††LEV-Levofloxacin, ‡‡MIN Minocyclin, §§CL- Colistin

DISCUSSION

Now a days, we are commonly observing patients infected with various emerging pathogens which were previously been under-reported or sometimes never reported. But in present era due to unhealthy lifestyle leading to various co-

morbid conditions such as diabetes, hypertension, cardiovascular diseases and other ailments which hampers our immune system as a result of which there is rapid rise in infection associated with these rare organisms which were previously been ignored. So, there is constant need for awareness among the people regarding healthy lifestyle and infection associated with the organisms affecting the individuals with various co-morbid conditions.

Elizabethkingia meningoseptica is a rare organism that causes meningitis in adults with weakened immune system. The first case of infection by this organism in India was reported way back in 1988-89 as a pathogen causing neonatal meningitis. Subsequently, various studies were conducted in India and reported that this rare pathogen can cause neonatal and adult meningitis, sepsis and endocarditis in patients admitted to the hospital for various medical reasons.[6]This bacterium grows in the hospital environment, on moist surfaces like sink, water tanks, ventilator tubing, saline solution for flushing devices, etc., thus making it an emerging hospital-acquired pathogen.[10]

Elizabethkingia meningoseptica is said to survive in municipal water systems which are treated with chlorine, so it often multiplies in sinks and taps in hospital environments. They act as reservoirs within the hospital environment and colonize patients through contaminated medical equipment that involves fluids (such as respirators, cannula, mist tent and humidifiers). More detailed research and work have further clarified this point and speculated that the contaminated hospital environment (such as infected catheters, intravenous fluids, and fluids) acts as a reservoir for such type of infections.[11] There are very limited studies regarding this new emerging infection. In different parts of the world, infections caused by the Elizabethkingia species are on the rise. This is indicated by a recent report in Taiwan, which reported multiple cases of *E. meningoseptica*.[3] We also have a large number of patients infected with *E. meningoseptica*. In our study, *Elizabethkingia meningoseptica* was isolated from a total of 16 individuals of various age groups ranging from 30 to 85 years which is supported by other studies done in Romania and Chicago regarding the prevalence of infection in different age groups.[12,13] Most cultures that were positive for Elizabethkingia isolates in our study were from endotracheal tube samples (69 %), followed by blood sample (32 %).

This finding indicates a certain correlation with similar research which was conducted by AIIMS in New Delhi, where the author recorded the highest positive rate of broncho alveolar lavage (BAL) samples (70%), followed by blood and cerebro spinal fluid (CSF).[14] But most of the study has got maximum positivity in blood sample which is in contrast to our study.[11] So, our study can be seen as one of the few studies where instead of positive blood sample we reported positive infection from endotracheal tube. In our case, the patients were on various invasive medical devices (risk factor) due to theier co-morbid condition for which they were required to stay in hospital for longer period which can be compared with other studies with similar data.[7,15,12,16,17] The common cause of admission in ICU was acute respiratory disease syndrome which is at par with other studies.[15,12,16,17]

In our study, all 16 patients required mechanical ventilation after their clinical symptoms worsened, and 12 patients required central or peripheral line. As reported in a study, it has got the ability to contaminate medical devices and the positive response of blood cultures to patients, patients may develop catheter-related bacteremia for *E. meningoseptica* through the hemodialysis catheter.[18] Infection by Elizabethkingia species is related with the presence of a central venous line infection, improper use of antibiotics, extended hospital stay, or a prolonged course of chemotherapy.[17,14] The infection with this pathogen becomes more severe if it is associated with some co-morbid condition as seen in our study which is cardiovascular diseases, diabetes, immunosuppression therapy which can be correlated with other studies.[12,16]

Various studies have shown the sensitivity of Elizabethkingia to cotrimoxazole, fluoroquinolone, minocycline, ticarcillin-clavulanate, piperacillin and piperacillin-tazobactam.[15,12,19] The extensive resistance to various β-lactams is due to the production of metalo-β-lactamase encoded by the BlaB and Bla (GOB) genes, which confers the ability to degrade most β-lactam antibiotics.[19,20] *Elizabethkingia meningoseptica* was sensitive to ciprofloxacin, nalidixic acid, tigecycline, levofloxacin and minocycline as seen in different studies.[7,15,12,16,17]

E. Meningoseptica infections are clinically important because the organism has inherent resistance to a variety of antibiotics, such as β - lactams, aminoglycosides, tetracyclines, tigecycline, colistin, cloramphenicol and carbapenems.[3,4,13,19,18] The mortality rate was nil in our study which must be due to the prompt identification of pathogen and proper treatment with antibiotics to the patients. *Elizabethkingia meningoseptica* infection rates in our hospital can be compared with other studies (Table 5).

	Our Study	Weaver et al. (2010)	Ratnamani et al. 2013	Pereir et al. 2013	Hyu et al. (2015)	Pen Lin Yun et al. (2010)
Study period	3 years	3 months	6 months	2 years	7 years	4 years
Age (yrs)	30 - 85	35 - 80	-	1 - 80	19 - 91	> 65
Positive samples	16	19	8	9	30	40
Time between admission & infection (days)	> 25	23	23	>30	>23	>2weeks
Co-morbid condition	CVD	-	-	CHD, PH	CVD	-
Risk factor	MV, Cath	MV	MV	MV, CVC	MV	Idwelling cath.
Common cause of admission in ICU	ARDS	Respiratory failure	Bacteremia, LRTI	Bacteremia, shock	Pneumonia	Pneumonia
AST pattern:	CIP (8, 50%) COT (2, 15%) PIT (1, 13%) LEV (3, 18%) MIN (3, 18%)	CTR 1 PI 3 PIT 12 COT 6	VAN 100% RIF 100% CIP 87.5% COT 75% PIT 75% TET 25%	CIP 100% VAN RIF	MIN (27, 90%) LEV (20, 66%) CIP (18, 60%)	CIP (11, 62%) PIT (4, 90%) COT (1)

Table 5. Comparison of Different Studies

*MV - Mechanical ventilation, † CVC - Central Venous catheter, ‡ CATH- Catheter, § IVD - Intravenous device,‖PH- Pulmonary Hypertension, **CHD - Congenital Heart Disease, †† CTR- Ceftriaxone, ‡‡PI - Piperacillin, §§VAN - Vancomycin,‖RIF- Rifampicin

CONCLUSIONS

E. meningoseptica is an emerging pathogen and is found everywhere in hospital environments. The prevalence of nosocomial infection by *E. meningoseptica* has increased, specially in patients with invasive procedures, prior use of broad-spectrum antimicrobial therapy and various co-morbid conditions. Therefore, precautionary measures should be taken to control its spread in the hospital environment. This organism is very rarely reported in the hospital setting. So, keeping in mind it's opportunistic potential and also emerging pathogen that can cause serious infection if not detected on time, we should be vigilant about this type of organism. When *E. meningoseptica* is isolated from clinical specimens, its pathogenic potential associated with clinical significance should be carefully evaluated and clinically correlated. Isolation of this organism in sink and water have been reported from hospital setting which can cause outbreak of the infection in hospitals. It can survive in water treated with chlorine. Hence, filtered water should be used for washing the hand and the sink should be disinfected from time to time. These steps can also help us prevent infections with this type of organism. Emphasis has to be given on the best infection control practices in the hospital. Training of the nurses and the related staff on their role in controlling and preventing these kinds of opportunistic and nosocomial infection for betterment and safety of the patients must be encouraged.

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