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ELIZABETHKINGIA MENINGOSEPTICUM: AN EMERGING PATHOGEN OF HOSPITAL INFECTIONS WITH HIGH MORTALITY RATE

Microbiology

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ABSTRACT

Context: *Elizabethkingia meningosepticum* is an emerging pathogen in hospital settings. It is an opportunistic pathogen with high mortality rate and outbreaks have occurred throughout the world.

Aim: We aimed here to find out *Elizabethkingia meningosepticum* infections in our hospital, its clinical spectrum significance and mortality rate.

Settings and Design: Retrospective one year study.

Materials and Methods: All patients who had a microbiological examination of various clinical samples and isolated *Elizabethkingia meningosepticum* organism were assessed. Pathogen identification and antibiotic susceptibility testing was done using VITEK 2 compact system. The data were collected from laboratory charts, laboratory and hospital information system in the study period of 1 year.

Results: Out of 15 patients of *Elizabethkingia meningosepticum*, majority were above 50 years age group (60%) followed by neonates (13.3%). Most of the *Elizabethkingia meningosepticum* organisms was isolated from respiratory specimens (56.2%) and blood (31.2%). Out of 15 patients, 4 (26.6%) were expired, within 4 days of diagnosis and all of them were associated with comorbidities and had frequent hospitalizations. Out of 16 isolates, 1 (6.2%) were sensitive to piperacillin-tazobactum, 6 (37.5%) sensitive to ceftazidime-sulbactum, 9 (56.2%) sensitive to ciprofloxacin, 11(68.7%) sensitive to cotrimoxazole, 12 (75%) sensitive to levofloxacin, 14 (87.5%) were sensitive to minocycline.

Conclusion: Early diagnosis and treatment with susceptible antibiotic improves patient outcome. Varied Antibiotic susceptibility pattern and high mortality rate, making us to focus more on early detection, rapid sensitivity testing approaches and surveillance.

KEYWORDS

Elizabethkingia meningosepticum, Mortality, Nosocomial infection.

INTRODUCTION

Elizabethkingia meningosepticum is a ubiquitous, gram negative rod shaped bacterium which is a non fermenting, non motile, catalase and oxidase positive bacilli grows on enriched media only. This pathogen is commonly detected in theenvironment particularly soil, plants, water, food and hospital water sources, including incubators, sink, faucets, tap water, saline solutions, medical devices like feeding tubes, respirators, hemodialysis systems, humidifiers, ice chests, syringes and other pharmaceutical solutions has become apotential reservoirs for infection in the hospital environment [1,2].

Although *Elizabethkingia meningosepticum* is not a part of human flora, can colonize respiratory tract of patients during hospitalization[3].*Elizabethkingia meningosepticum* has been identified as an emerging nosocomial pathogen following increase in incidence rates of *Elizabethkingia meningosepticum* infection at ICU's since 2004. Association with high mortality rate is because of lack of effective therapeutic regimens and antibiotic resistance towards commonly using empirical therapy drugs [4].

This bacterium typically grows on blood agar and chocolate agar with in 24 hours of incubation. Colonies can be either not pigmented or produce a pale yellow, smooth, circular, large, shiny with entire edge, non lactose fermenter and strains growing at 40^0C more often associated with invasive meningitis [5].

Elizabethkingia meningosepticum is an opportunistic pathogen has a strong predilection for extremes of age, usually affectsPremature infants, Neonates, Elderly people, Immuno compromised patients on prolonged hospitalization[6,7] and also responsible for hospital outbreaks [8].It can cause cellulitis, wound infection, sinusitis, abdominal infection, endocarditis, meningitis, pneumonia and subsequently results in bacteria depending on patients health [6,7,9].

*Elizabethkingia meningosepticum*usually express multidrug resistant to most of the beta lactam antibiotics[10]. The aim of this study to find out *Elizabethkingia meningosepticum* infections in our hospital, its clinical spectrum significance and mortality rate.

MATERIALS AND METHODS

A Retrospective analysis done during October 2016 to September 2017 (1 year) on *Elizabethkingia meningosepticum* clinically significant infections. All Patient data were unlinked anonymized and the institutional Ethical committee approved this study.

This Observational study retrospectively examined for all the clinically relevant *Elizabethkingia meningosepticum* infections.

All patients who had a microbiological examination of various clinical samples and isolated *Elizabethkingia meningosepticum* organism were assessed. *Elizabethkingia meningosepticum* infections which are clinically related were included in this study.

Based on clinical relevance a total of 15 patients diagnosed septicaemia, pneumonia and other infections triggered by *Elizabethkingia meningosepticum*, who were treated on the general wards, intensive care units of hospital.

Pathogen identification and antibiotic susceptibility testing was done using VITEK 2 compact system. Based on MIC break points, susceptible antibiotics to a particular *Elizabethkingia meningosepticum* strain was suggested to clinicians.

As *Elizabethkingia meningosepticum* ubiquitous organism, has been isolated from hospital and laboratory environments. As there are chances of contaminating clinical samples, significance of this pathogen should assess clinically after isolating it from culture. *Elizabethkingia meningospeticum* should be considered as an actual pathogen, only if it is clinically related. Clinical relevance was assessed by patients condition, comorbidities, immunosuppressive state, days of hospitalization and laboratory investigations.

The data were collected from laboratory charts, laboratory and hospital information system in the study period of 1 year. We observed for antibiotic resistance patterns of *Elizabethkingia meningosepticum* infections, clinical relevance and outcome. We routinely recorded the

patient's age, sex, type of sample, the susceptibility and resistance pattern of *Elizabethkingia meningosepticum* isolates, clinical diagnosis and outcome of patients.

All the data entered into spread excel sheet and analysed.

RESULTS

10 (66.6%) out of 15 patients reported with *Elizabethkingia meningosepticum* were males. Males were distributed in extremes of age group, whereas female patients were diagnosed with *Elizabethkingia meningosepticum* present in all the age groups. Out of 15 patients of *Elizabethkingia menigosepticum* isolates, majority were above 50 years age group (60%) followed by neonates (13.3%) (Table 1). 4 (26.6%) out of 15 patients were below 18 years of age, both neonates were term babies.

Most of the *Elizabethkingia meningosepticum* organisms was isolated from respiratory specimens (56.2%) and blood (31.2%). In the present study, 5 isolates from bacteremia cases, 7 were pneumonia, 2 were bronchitis, 1 peritonitis and 1 neonatal meningitis case (Table 2).

Polymicrobial was observed in 5 (31.2%) out of 16 isolates of *Elizabethkingia meningosepticum*. Out of 5 coinfections, 4 were respiratory specimens and 1 from Ascitic fluid (Table 3).

Out of 15 patients, 4 (26.6%) were expired, within 4 days of diagnosis and all of them were associated with comorbidities and had frequent hospitalizations. 3 patients out of 4 had respiratory pathology and one patient had septicaemia.

Out of 16 isolates, 100% resistant shown towards Amikacin, Gentamicin, Aztreonam, cefipime, ceftazidime, Tigecycline, Imipenem, colistin.

Out of 16 isolates, 1 (6.2%) were sensitive to piperacillin-tazobactum, 6 (37.5%) sensitive to ceftazidime-sulbactum, 9 (56.2%) sensitive to ciprofloxacin, 11(68.7%) sensitive to cotrimoxazole, 12 (75%) sensitive to levofloxacin, 14 (87.5%) were sensitive to minocycline (Chart .1).

DISCUSSION

Elizabethkingia meningosepticum is previously named as *Flavobacterium meningospeticum* by an American bacteriologist Elizabeth O king. She isolated from paediatric meningitis sample at CDC, Atlanta in 1959[11]. In 1994 Flavobacterium was renamed in the genus *Chryseobacterium* and again in 2005 as per 16s rRNA, renamed as *Elizabethkingia meningosepticum* named after the discoverer. *Elizabethkingia meningosepticum* is most common human pathogen among all species of *Elizabethkingia*. Among A to F serotypes of *E.meningosepticum*, most common epidemics reported by type C [12].

Pathogenicity of *Elizabethkingia meningosepticum* infection is unclear, limited information exists. Virulence of this pathogen can be due to encapsulated nature or express gelatinases and proteinases that destroy host cells and tissues[3]. *Elizabethkingia meningosepticum* gained attention originally as it caused neonatal meningitis. It can also cause meningitis or bacteremia in compromised adults.

In high risk patients, *Elizabethkingia meningospeticum* may colonize upper respiratory tract, usually precedes development of invasive infection. In outbreaks, respiratory colonization occurs more often than infections[2]. Infection may reveal when patient expose to contaminated medical devices or solutions, source is always not known [8,13]. Rarely reported there are chances of vertical infection[3].

Elizabethkingia meningosepticum can infect all age groups of immunocompromised population whether hospitalised or not. Infection caused by *E.meningosepticum* depends on type of exposure to source and site of infection. Infections including cellulitis, bronchitis, dialysis associated peritonitis, meningitis, peritonitis, pneumonia, bacteremia, endocarditis, intra abdominal abscess, sinusitis and produces postinfectious sequelae including brain abscess, hydorocephalus, deafness, developmental delay[14]. *E.meningosepticum* infections such as keratitis, cellulitis, septic arthritis, community acquired respiratory tract infection, bacteremia have been reported even without any underlying diseases[15].

In the present study of one year (Oct 2016 to Sep 2017), 5 isolates of *E.meningosepticum* from bacteremia associated patients, 7 pathogens isolated from pneumonia patients, 2 were bronchitis, 1 peritonitis and 1 neonatal meningitis case.

Di Pentima et al [16] reported a study done from 1982 to 1996 at Texas Children's hospital, 4 strains of *Chryseobacterium meningosepticum* (*Elizabethkingia meningosepticum*) from cerebrospinal fluid and Blood. Most of the studies reported outbreak of meningitis among neonates [7,17] and premature infants[18] in hospital nursery. George et al[19] documented neonatal ward outbreak of 14 meningitis cases and 30 asymptomatic nasophayrngeal carriers. Gungor et al [7] observed 4 cases of neonatal sepsis outbreak in NICU, 1 patient expired. All remaining three were survived with one complication (hydrocephalus).

Polymicrobial was observed in 5 (31.2%) out of 16 isolates of *Elizabethkingia meningosepticum* in this study. Hsu et al [20] reported 45 (38.1%) out of 118 patients had polymicrobial bacteremia. As per this study, 4 (26.6%) out of 15 patients were below 18 years of age, both neonates were not premature babies. In similar to our study, Hsu et al [20] studied from 1999 to 2006 observed lower percentage of children and none of the neonates were premature babies.

Ratnamani MS et al [21] did a study on *Elizabethkingia meningosepticum* isolated from patients were on mechanical ventilation undergoing bedside hemodialysis in ICU, 2 out of 7 patients were expired. All seven patients were on colistin for multidrug resistant bacteria isolates from bacteremia and lower respiratory tract infections.

Elizabethkingia meningosepticum express poor invitro susceptibility to antibiotics, usually resistant to most of the beta lactam antibiotics such as carbapenems, aztreonam, colistin, aminoglycosides, tetracycline, chloramphenicol [2,22,23]. Resistance patterns and mechanisms of *E.meningosepticum* are unusual, possess two types of β-lactamases such as Class A ESBLs and Class B MBLs. BlaB and GOB are two types of MBLs identified in *E.meningosepticum*, can possess both types simultaneously[24]. Intrinsic resistant to carbapenems expressed by chromosomal mediated MBLs[25]. Yum JH et al [26] from Korea reported that DNA sequence analysis suggested *C. meningosepticum* isolates possessed 7 types of blaB gene, including 5 novel variants (blaB-9 to blaB-13), and 11 types of blaGOB gene, including 10 novel variants (blaGOB-8 to blaGOB-17). The most common combination of MBLs was BlaB-12 plus GOB-17.

E.meningosepticum express sensitive to gram positive bacterial infections treating agents such as fluoroquinolones, clindamycin, erythromycin, linezolid, cotrimoxazole, vancomycin, rifampicin [1,7,22]. Few reports showed poor activity of vancomycin to *E.meningosepticum*[27]. As India is an endemic tuberculosis, rifampicin and fluoroquinolones are not supposed to use for empiric therapy.

In the present study, out of 16 *E.meningosepticum* isolates, 1 (6.2%) were sensitive to piperacillin-tazobactum, 6 (37.5%) sensitive to ceftazidime-sulbactum, 9 (56.2%) sensitive to ciprofloxacin, 11(68.7%) sensitive to cotrimoxazole, 12 (75%) sensitive to levofloxacin, 14 (87.5%) were sensitive to minocycline. Vancomycin was tested using Vitek2 compact system for only 2 multidrug resistant isolates, both were sensitive. Kirby et al [6] documented piperacillin-tazobactum susceptibility was 100% in North American and European isolates, while in Southeast Asia only 50% of isolates were susceptible. Hsu et al [20] reported Asia isolates more resistant to cephalosporins than North America and Europe isolates. This may be due to varied resistance mechanisms in strains. 28-day mortality of 41% reported in Health care associated *E.meningosepticum* infection, whereas 9.1% of mortality rate in community acquired infection [22].

In the present study, most of the isolates were from bacteremia and pneumonia cases, showing >50% susceptibility to ciprofloxacin, cotrimoxazole, levofloxacin and minocycline. All the patients were associated with one or more comorbidities such as Diabetes, Hypertension, Decompensated liver disease, Carcinoma, encephalitis, coronary heart disease etc. 26.6% was mortality rate.

CONCLUSION

Elizabethkingia meningosepticum is an emerging nosocomial pathogen with less antibiotic choice for empiric therapy. Early diagnosis and treatment with susceptible antibiotic improves patient outcome. Varied Antibiotic susceptibility pattern and high mortality

rate, making us to focus more on early detection, rapid sensitivity testing approaches and surveillance. Of course there is a need of close surveillance of *E.meningosepticum* clinical and susceptibility changes in future.

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Table 1. Age wise distribution of Elizabethkingia meningosepticum infections

Age Group	Male		Female		Total	
	No. of patients	Percentage	No. of patients	Percentage	No. of patients	Percentage
Neonates	1	6.6%	1	6.6%	2	13.3%
1-10 years	0	0	1	6.6%	1	6.6%
11-20 years	0	0	1	6.6%	1	6.6%
21-30 years	0	0	0	0	0	0
31-40 years	0	0	1	6.6%	1	6.6%
41-50 years	1	6.6%	0	0	1	6.6%
>50 years	8	53.3%	1	6.6%	9	60%
Total	10	66.6%	5	33.3%	15	100%

Table 2. Elizabethkingia meningosepticum distribution in relation to clinical samples.

Sample	No. of organisms isolated	Percentage (%)
Blood	5	31.2
Sputum	4	25
BAL	4	25
Pleural fluid	1	6.2
Ascitic fluid	1	6.2
CSF	1	6.2
Total	16	100%

Table 3. Organisms isolated from various clinical samples

Organsims	Sample
Elizabethkingia meningosepticum + Candida tropicalis	Ascitic fluid
Elizabethkingia meningosepticum + Klebsiella pneumoniae	Sputum
Elizabethkingia meningosepticum + Enterococcus faecalis	Pleural fluid
Elizabethkingia meningosepticum + Stenotrophomonas spp	Sputum
Elizabethkingia meningosepticum + Pseudomonas aeruginosa	Sputum

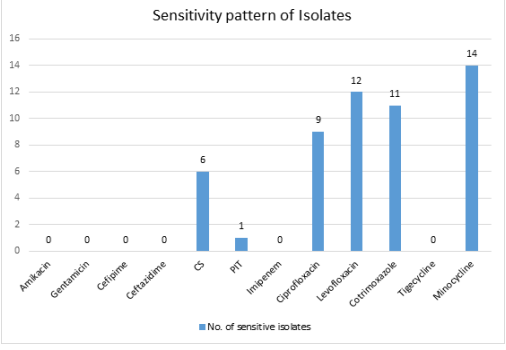

Chart 1. Sensitivity pattern of Elizabethkingia meningosepticum
CS - ceftazidime-sulbactum; PIT-Piperacillin-Tazobactum

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