

Clinical Features and Outcomes of Patients with Elizabethkingia Meningoseptica Infection: An Emerging Pathogen

Abdullah Umair

Aga Khan University Medical College Pakistan

Nosheen Nasir (✉ nosheen.nasir@aku.edu)

Aga Khan University <https://orcid.org/0000-0003-1610-8748>

Research article

Keywords: Elizabethkingia, meningoseptica, Chryseobacterium, clinical features, outcomes

Posted Date: October 1st, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-74236/v1>

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Abstract

Background:

Elizabethkingia meningoseptica, formerly known as *Chryseobacterium meningosepticum*, is a non-motile, non-fastidious, catalase and oxidase-positive, aerobic, glucose-non-fermentative Gram-negative bacillus first defined by Elizabeth O. King in 1959. It has recently emerged as an opportunistic pathogen infecting people in the extremes of age and the immunocompromised, especially in nosocomial settings. There has been an increased interest in this pathogen due to its rising occurrence around the world, its ubiquity in nature, and inherent capacity for antimicrobial resistance.

Methods:

We describe a retrospective case series at the Aga Khan University Hospital in Karachi, Pakistan on patients admitted from January 2013 to December 2018 with *Elizabethkingia meningoseptica* infections. All patients identified to have any clinical culture specimen positive for *Elizabethkingia meningoseptica* were included. Data was collected on a structured proforma from the Hospital Information Management Systems (HIMS).

Results:

Sixteen patients with *E. meningoseptica* were identified. The mean Charlson's co-morbidity index was 3.25. Nine patients had bacteremia with *E. meningosepticum*. Three of the isolates were extensively drug resistant with sensitivity only to minocycline. Nine out of 16 patients required intubation and mechanical ventilation. The median length of hospital stay was 13 days and four out of 16 patients died during hospital stay,

Conclusion:

This is the first case series from Pakistan reporting *Elizabethkingia meningoseptica* infections.

Background

Elizabethkingia meningoseptica, formerly known as *Chryseobacterium meningosepticum*, is a non-motile, non-fastidious, catalase and oxidase-positive, aerobic, glucose-non-fermentative Gram-negative bacillus first defined by Elizabeth O. King in 1959. Formerly the most pathological member of the *Chryseobacterium* genus, it was reclassified into the genus *Elizabethkingia* in 2005. [1] *Elizabethkingia* genus has been noted for its genes that grant it great degree of genetic variability and subsequent antimicrobial resistance. This fact combined with lack of literature, wide distribution in nature, and lack proper treatment regimens have led to high mortality rates in hospital-settings, particularly in Intensive Care Units since 2004. [2] This has led to increased interest in *E. meningoseptica* as an emerging pathogen in the past decade.

E. meningoseptica are most frequently isolated from soil, saltwater and freshwater and from dry and moist clinical environmental and equipment surfaces, intravenous lipid solutions, and municipal water supplies including those which have been adequately chlorinated. [3] Although nearly ubiquitous in nature, it is an uncommon human pathogen. *E. meningoseptica* predominately causes outbreaks of meningitis in immunocompromised patients, particularly in premature newborns and infants in neonatal intensive care units of developing countries. [4] The bacterium is a rare cause of nosocomial pneumonia, endocarditis, and meningitis in

immunocompromised adults. Recently in the past few years, it has been found to cause soft tissue infection and sepsis in immunocompetent adults. [5]

In a study from Wisconsin, 48 cases of *Elizabethkingia* were reported during an outbreak, which resulted in 17 deaths in a 5-month period beginning in November 2015. [9] Most data on *E. meningoseptica* related septicemia is derived from Taiwan. A large case series showed that yearly incidence of *E. meningoseptica* bacteraemia increased substantially from 2002 (from 6.8–13.1 to 26.6–39.9 per 100,000 admissions; $P = 0.006$). [10] A recent review of literature suggests that almost all cases of septicemia from *E. meningoseptica* occur in a nosocomial setting. [3]

Moreover, *Elizabethkingia*, alongside its genetic relative *Chryseobacterium* spp., are inherently extensively drug resistant. They are resistant to broad spectrum of antibiotic classes, including marcolides, tetracyclines, linezolid, polymyxin group, chloramphenicol, aminoglycosides, and beta-lactam drugs. [11] Vancomycin, rifampicin, new fluoroquinolones, piperacillin-tazobactam, and minocycline the current preferred empirical choices for *E. meningoseptica* infections. [3] Tigecycline as the preferred drug of choice for infections is currently being studied. [3]

Elizabethkingia meningoseptica is an important emerging opportunistic bacterium that primarily occurs in nosocomial settings. Given its ubiquitous nature, arsenal of multidrug resistant genes, and affinity to infect primarily the immunocompromised; it is paramount that more resources be devoted to study this emerging pathogen. It is also unclear as to which treatment regimen is most effective and what are the factors associated with adverse outcomes. The aim of this study is to describe the clinical features and outcomes of *Elizabethkingia meningoseptica* infections in a tertiary care center at Karachi, Pakistan. Furthermore, a systematic review of literature regarding this pathogen is also presented in this study.

Methods

This was a retrospective case series of patients admitted between January 2013 and December 2018 with *Elizabethkingia meningoseptica* infections at the Aga Khan University (AKU) Hospital in Karachi, Pakistan. All patients identified to have any clinical culture specimen positive for *Elizabethkingia meningoseptica* were included. Data was collected on a structured proforma from the Hospital Information Management Systems (HIMS). Identification and susceptibility of *Elizabethkingia meningoseptica* isolated from cultures is performed by automated systems in accordance with Clinical Laboratory Standards Institute (CLSI) recommendations at Aga Khan University Hospital. All patients who were found to be colonized but not infected were excluded. Data was analyzed using SPSS ver 19. Descriptive analysis was performed for demographic features with median and IQR reported for quantitative variables such as age and lengths of hospital stay and frequencies (percentage) for qualitative variables such as gender, co-morbid conditions, mortality and complications etc. All p value ≤ 0.05 will be taken as significant. Ethical exemption was taken for the study by the Ethics Review Committee (ERC) of Aga Khan University (AKU) (ERC #2019-1786-4439). Data was kept confidential and no personal identifiers were used.

Results

Sixteen patients with *E. meningoseptica* were identified. The median age was 35 years with 44% males and 56% females, from the ages of 4 days to 83 years. The most common co-morbid conditions were diabetes (31%) and hypertension (37.5%). The average Charlson's co-morbidity index was found to be 3.25. Three patients had some

form of pre-existing malignancy, and five patients had a history of repeated hospitalizations. Fifty six percent (n = 9) had bacteremia with *E. meningosepticum*. Among other sites of infection, three had urinary tract infection, n = 3 had meningitis and one had pneumonia. 61% (n = 8) had monomicrobial growth whereas 38% had polymicrobial growth in culture. 43% of patients required a Foley's catheter. 56% (n = 9) required intubation and mechanical ventilation. *E. meningosepticum* was sensitive to beta lactam and quinolones in 68% (n = 11). These patients were treated with levofloxacin. Three of the *E. meningosepticum* isolates were extensively drug resistant (XDR) with sensitivity only to minocycline, which was the drug used for definitive treatment.

Only one out of the four patients infected by the XDR strain expired. This case presented with a history of left middle cerebral artery infarction and septic shock. Four out of 16 patients died, and median length of hospital stay was 13 days. The most common co-infection was with *Trichosporon beigelii* (n = 2) and multi-drug resistant *Acinetobacter* (n = 2). Both co-infections in case of *Trichosporon beigelii* were found in urine cultures. In one case, the urine culture yielded a three: *Candida tropicalis*, *Trichosporon beigelii*, and *E. meningoseptica*. This patient had a history of colon carcinoma and colostomy and he expired.

All four patients who died had a history of repeated hospitalizations and significant comorbidities. All of them had been mechanically ventilated and underwent invasive catheterization. *E. meningoseptica* was isolated in blood of three and tracheal aspirate in one patient who had undergone esophagectomy, thoracotomy, and tracheostomy.

There were four confirmed samples collected from outpatient services. Three of these cases were women. Two were isolated from urine, both were women, and two from blood. One patient was of 12-year girl with a known history of neurogenic bladder with recurrent urinary tract infections, seizure disorder and had a polymicrobial infection with *E. coli*.

There were three neonates with *E. meningoseptica* infections identified in the neonatal intensive care unit (NICU). One of these presented with meningitis and CSF culture confirmed growth of *E. meningoseptica*. The other neonate presented with congenital abnormalities of the web of the larynx and in severe respiratory distress. Confirmed cultures were blood were shown nine days after admission. This was likely a hospital acquired infection. The third case was of a 33-week preterm who had been born with bilateral intraventricular hemorrhages and showed signs of respiratory distress. Blood cultures were confirmed *E. meningoseptica* growth on the 3rd day of life. Both of the cases which had both positive blood cultures and respiratory distress were intubated in the NICU, likely pointing towards hospital acquired infection.

Discussion

A review of literature was conducted to identify clinical case series reporting infections with *Elizabethkingia meningoseptica* and their outcomes (Table 1). While many isolated case reports and series were found [12–17], only one [18] looked at *Elizabethkingia* cases that were more than four in number. Much of the literature covered one or two cases in any given hospital or area, and none of the articles searched yielded a case series of more than 4 cases. There were no case series or reports on *Elizabethkingia* cases from Pakistan. Our study identified 16 patients in the last 6 years with *Elizabethkingia meningosepticum* infections. Unlike other case series with predominantly neonatal age group [18]; our patients had a median age of 35 years. Similar to case reports published, the sites of infection were urinary tract infection and meningitis [15, 16]. The outcomes have been variable with significant mortality among neonates [18]. However, those patients whose isolates had susceptibility

to quinolones and were treated with Ciprofloxacin had better survival [13]. This is similar to patients who were treated with a quinolone in our study.

Table 1
Summary of studies reporting *Elizabethkingia* infections and their outcomes

#	Title	Year	Author	Type of Study	Diagnostic Criteria	Key Findings
1	Multiresistant <i>Elizabethkingia meningoseptica</i> infections in tertiary care	2015	Inam Danish Khan, Maj, Mahima Lall, Lt Col, Sourav Sen, Col, S.M. Ninawe, Maj, and P. Chandola, Surg Lt Cdr [17]	Case Series	Culture	4 cases studied. 1 Case died due to post-operative complications 3 successfully treated.
2	Emerging Infection with <i>Elizabethkingia Meningoseptica</i> in Neonate. A Case Report	2018	Manuela Arbune, Silvia Fotea, Aurel Nechita, and Victorita Stefanescu [15]	Case Study	Culture	33 week premature female infant case of meningitis in NICU. Patient recovered with Pip-tazo, Rifampicin combo.
3	Colonization and infection with a rare microorganism in a neonatal intensive care unit: three preterm infants with <i>Elizabethkingia meningoseptica</i>	2019	Kiyemet Celika, Demet Tereka, Ozgur Olukmana, Gamze Gulfidanb, Sebnem Calkavura, Ilker Devrimc, Sertac Arslanoglua [13]	Case Series	Culture	2 cases. Case 1 managed on cefoperazone-sulbactam. Case 2 intubated and managed on cipro.
4	Epidemiological analysis of <i>Elizabethkingia meningoseptica</i> infection cluster among mechanically ventilated pediatric intensive care patients	2018	Wafaa Seddik Hamza, Samar Saeed Morsi, Ebtehal Saleh Al Roomi, Vincent Olubunmi Rotimi [14]	Case Series	Culture	Four patients were colonized/infected, mean age 22 months. All patients were mechanically ventilated.
5	<i>Elizabethkingia Meningoseptica</i> : An Emerging Nosocomial Pathogen Causing Septicemia in Critically Ill Patients.	2019	Sahu K, Balasubramaniam U, C B, Singh SP, Talwar S [12]	Case Report	Culture	Sepsis in 22 month old after cardiac surgery and intubation in NICU.

#	Title	Year	Author	Type of Study	Diagnostic Criteria	Key Findings
6	Elizabethkingia meningoseptica: emerging multidrug resistance in a nosocomial pathogen.	2017	Raghavan S, Thomas B, Shastry BA [16]	Case Report	Culture	46 CHF male patient presented with burning micturition for 2 days. UCS showed E.kingia sensitive to minocycline only.
7	Elizabethkingia in Children: A Comprehensive Review of Symptomatic Cases Reported From 1944 to 2017.	2018	Dziuban EJ, Franks JL, So M, Peacock G, Blaney DD [18]	Review	-	283 pediatric cases reviewed. Neonatal meningitis was the most common presentation. The majority of reported cases occurred as isolated cases, rather than within outbreaks. Mortality was high but has decreased in recent years.

E. meningosepticum is intrinsically resistant to most commonly used antimicrobial resistance; therefore, options of treating it are quite limited. Most studies have established that clinical isolates are always resistant to aminoglycosides and beta lactams, with the notable exception of piperacillin-tazobactam, and show sensitivities to fluoroquinolones and tetracyclines [11]. This fact stood to reason in this study as well. All cases were resistant to aminoglycosides, colistin and carbapenems. All the cases showed sensitivity to either piperacillin-tazobactam, fluoroquinolones, or tetracyclines, minocycline in particular.

This study is a single center retrospective analysis and therefore is associated with several limitations. Four cases were outpatients and were lost to follow-up. However, this study is the first case series to date from Pakistan reporting the clinical features and treatment outcomes of *Elizabethkingia meningoseptica* infections. Moreover, it offers insight into the sensitivity pattern of this organism in our region.

Conclusion

E.meningosepticum is an emerging nosocomial infection and associated with good survival especially if isolates are susceptible to quinolones and can be treated with them.

Declarations

Ethics approval and consent to participate

The study was submitted for ethical approval to the AKUH ethical review committee and received exemption (ERC #2019-1786-4439).

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article

Competing interests

The authors declare that they have no competing interests

Funding

No funding was obtained for this study.

Authors' contributions

AU data acquisition and analysis, major contributor to manuscript

NN conceived idea, major contributor to manuscript, collected and analyzed data

All authors read and approved the manuscript

Acknowledgements

None

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