ORIGINAL ARTICLE

Management of multidrug-resistant *Serratia marcescens* outbreak in a tertiary cardiac care center's pediatric ward: A comprehensive analysis

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ABSTRACT

Background: *S. marcescens* is the one most commonly associated with human infections, known for causing serious hospital acquired infections, particularly in those who are immunocompromised, critically ill patients, mainly in settings such as intensive care units (ICUs), especially neonatal units (NICUs). Outbreaks of *Serratia marcescens* are often linked to poor environmental disinfection.The primary objective of this study was the identification of the source of infection and management of this outbreak.

Material and Methods:A prospective cross-sectional study was carried out from September to November 2022 to investigate the increase in Carbapenem-resistant *Serratia marcescens* bloodstream infections. (BSIs)

Results:A total of 21 patients meeting the case definitionof Carbapenem-resistant *Serratia marcescens* bloodstream infections were identified during the outbreak period. Three main groups of observations were identified through detailed rounds and audits that could have contributed to this outbreak: overcrowding, antibiotic use and limitations in implementation of satisfactory infection prevention and control practices especially poor hand hygiene.Environmental Cultures findings showed isolation of *Pseudomonas species*, MRSA and *Burkholderia cepacia* however *Serratia marcescens* was not detected.

Conclusion: A concerted effort involving healthcare facilities, healthcare workers, patients, and public health agencies is essential for the effective prevention of *Serratia* outbreaks, requiring continuous vigilance, education, and adherence to infection control measures.

Keywords: Intensive care units, Neonatal intensive care units, Bloodstream infections, *Multidrug resistant*

BACKGROUND

Serratia marcescens, a gram-negative rod that iscommonly found in the environment and was initially thought to be a non-pathogenic organism came to be recognized as an opportunistic human pathogen in 1931.[1] The prevalence of *S. marcescens* infections in humans was not fully understood for many years. However, the first known outbreak of *S. marcescens* infection in a hospital in 1951 helped to raise awareness of this organism's ability to cause disease. Since then, infections caused by *S. marcescens* have been reported more and more often. The genus *Serratia* comprises at least 14 species and two subspecies.[2] Of these species, *S. marcescens* is the one most commonly associated with human infections, known for causing serious hospital acquired infections, particularly in those who are immunocompromised, critically ill patients, mainly in settings such as intensive care units (ICUs), especially neonatal units (NICUs).[5] Outbreaks of *Serratia marcescens* are often linked to poor environmental disinfection. This can occur in hospitals, nursing homes, and other healthcare settings where there is a high concentration of bacteria which can spread through contaminated surfaces, equipment, and fluids. Disruptions in infection prevention practices can also contribute to *Serratia marcescens* outbreaks. Because of their undeveloped immune systems and the extensive medical interventions and long hospital stays, newborns admitted to a NICU have a high risk of contracting nosocomial infections.[3]Nosocomial infections, such as keratitis, conjunctivitis, urinary tract infections, pneumonia, surgical wound infections, sepsis, bloodstream infection and meningitis have been linked

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to high morbidity and mortality.[3] In pediatric populations, outbreaks are often associated with the use of indwelling medical devices, such as central lines and urinary catheters which provide a direct route for the bacteria to enter the body and cause infection.[4] Furthermore, low birth weight, preterm, duration of stay, mechanical ventilation, and antibiotic use are also important risk factors for *S. marcescens* infections.[4]

As many infected neonates seem to retain colonization for extended periods of time despite antibiotic therapy.Hence preventing these outbreaks of MDR organisms' infections depends in large part on the early identification of colonized or infected patients, isolation of such patients and the rapid adoption of infection control measures including thorough cleaning and disinfecting environmental surfaces and equipment, sustaining hand hygiene etc.[6,7]

The National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan's largest tertiary cardiac center, serves 2.3 million patients annually, providing free, life-saving care. This high patient volume, coupled with a strict no-deferral policy, often overwhelms the pediatric ward and can lead to circumvention of infection prevention and control protocols. In September 2022, prospective laboratory surveillance reported a surge in carbapenem-resistant (CRE) *Serratia* bloodstream infections in pediatric patients, which signaled an outbreak. A multidisciplinary team, including infection prevention and control, microbiologists, pediatricians and infectious disease physicians was formalized to contain the outbreak. This study investigates the outbreak's origins using retrospective and prospective data.

MATERIAL AND METHODS

A prospective cross-sectional study was carried out from September to November 2022 after taking the institutional review board approval vide letter number IRB-50/2023 dated 04 September 2023 to investigate the increase in CRE BSIs. A case definition was finalized to define the inclusion criteria, according to which 'All patients, aged 0-18 years, both genders, admitted in pediatric ward from September to November 2022, with laboratory confirmed blood stream infection with CRE *Serratia marcescens* with similar sensitivity on antibiogram' were included in the study. A total of 21 patients meeting the case definition were identified during the outbreak period. Environmental cultures, regular ward rounds, audits, weekly meetings were done as a part of outbreak investigation. Environmental swabs were taken from various sites of wards and different devices used on patients.

Blood cultures were processed using the BACT/ALERT® system. Upon detection of growth, the culture bottles were removed and subjected to Gram staining. Subsequent sub culturing onto solid media agar was performed, followed by overnight incubation at an appropriate temperature for 24 hours to assess bacterial growth. Bacterial identification was performed by conventional biochemical tests including triple sugar iron, citrate utilization, urease detection and motility detection, using sulphide indole media. RapID system (Thermo Fisher) was used to confirm the results. Antimicrobial sensitivity has been performed by Broth micro dilution method and disc diffusion Kirby bauer method.

Data was collected using findings of daily infection control rounds and audits that had been conducted with infection preventionists to monitor the outbreak, observe the HCWs and staff adherence to infection control practices, hand hygiene compliance, proper PPE usage and environmental disinfection. Audit tool was formulated including various observations to determine the root cause of outbreak. Data was analyzed using Microsoft Excel. Study variables included number of cases, age, gender, outcome and the findings of environmental cultures of pediatric ward.

RESULTS

A total of 21 cases of Carbapenem-resistant *Serratia marcescens*bloodstream infections were identified during the study period. The patients ranged in age from 0 to 18 years, with a median age of 4 years (IQR 2-7.5). Majority of the patients were male (15/21). All of these infections were categorized as hospital acquired infections as per guidance of National Healthcare Safety Network (NHSN) and reported after 48 hours of admission. (CDC, Jan2024) The clinical outcome indicates complete resolution of infection in 19 cases while mortality was reported in 2 cases. The antimicrobial agents included in Disk diffusion method were amoxicillin/ clavulanate, ampicillin, cefotaxime, ciprofloxacin, levofloxacin, trimethoprim/ sulphamethoxazole, amikacin, gentamicin,

meropenem, imipenem, piperacillin/ tazobactam, and fosfomycin. Fosfomycin and cotrimoxazole was utilized for the treatment of all cases on the basis of antimicrobial susceptibility result performed by disc diffusion Kirby bauer method and broth microdilution respectively as shown in antibiogram in Figure-I.

Environmental cultures were done as a part of outbreak investigation as shown in Table-I. Though *Serratia* species were not recovered from any of the environmental cultures, identification of other pathogenic bacteria from environment as shown in the Table-I represents poor environmental disinfection and environment serving as a major reservoir of microorganisms especially *Burkholderia cepacia* which is repeatedly identified in pediatric patients causing sepsis.

Table-I: Environmental cultures findings show isolation of various gram negative and positive organisms from pediatric ward during outbreak investigation.

S. No	Codes	Themes
1.	- Attitude - Lack of Commitment - Denial - Acceptance	Unprofessional behavior/ Self autonomy
2.	- Leadership - Role model - Leadership commitment	Leadership
3	- Lack of handwashing facilities - Lack of isolation facilities - Poor infrastructure - Lack of PPEs - Lack of sterilized dressings - Under staffing	Resources
4	- Lack of training - Lack of education - Awareness from gross root level	Training and education
5	- Multifactorial responsibility like doctors, system, nurse and S/W - System improvement - No team buildup as people rotate - Fear of punishment	System driven problems

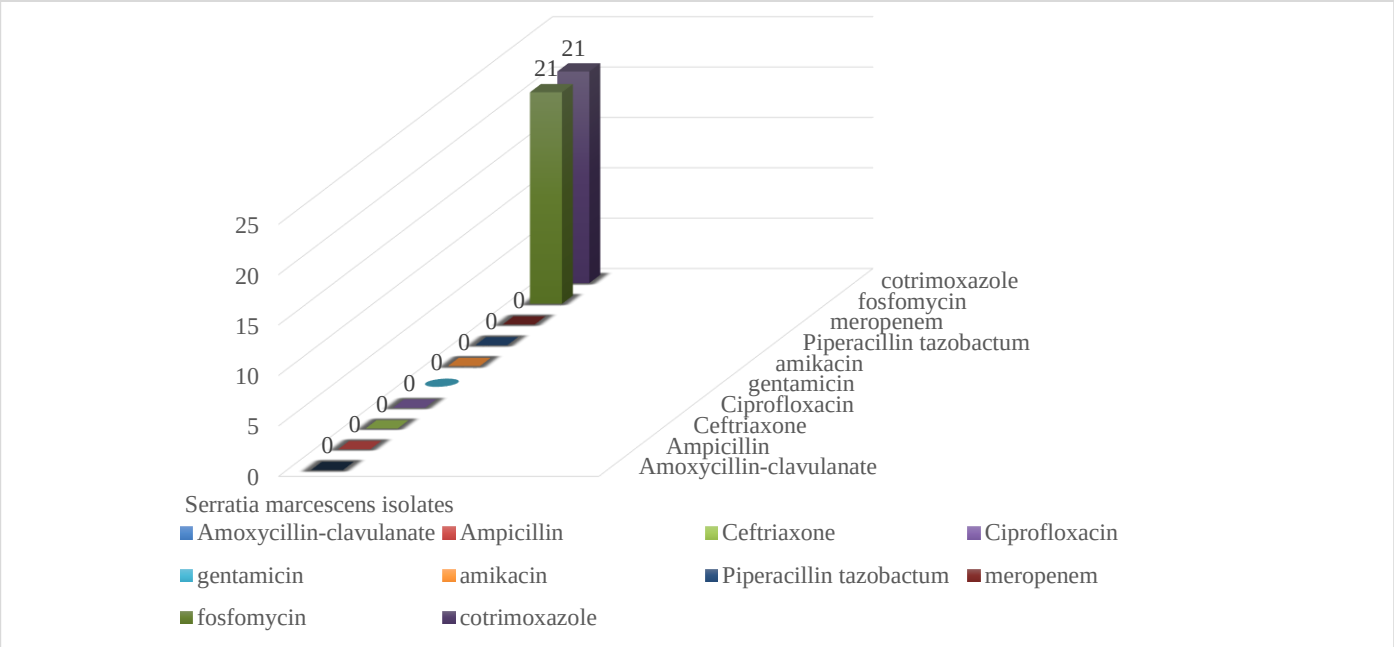

Figure-I:The above figure shows the antimicrobial sensitivity pattern of all 21 isolates of *Serratia marcescens* isolated from Blood sample of patients admitted to paeds ward during September 2022 to November 2022.The antibiogram shows the 100 percent susceptibility to fosfomycin and cotrimoxazole in all isolates.

DISCUSSION

This study set out with the aim of highlighting the importance of surveillance and proper infection control measures in pediatric patients admitted at cardiovascular institute. Early identification and intervention are essential to prevent the spread of CRE and improve patient outcomes. During comprehensive rounds along with audits, three primary observation groups were found in our study that may have attributed to this outbreak: inadequate adherence to hand hygiene, overcrowding, and restrictions in the use of adequate infection prevention and control measures. Prolong antibiotic therapy usage also has been observed in some patients. However poor hand hygiene compliance was the foremost of all the observations responsible for the outbreak.

A multidisciplinary team comprising of Infectious disease consultant, Microbiologists, Paeds cardiologist and infection control practitioner implemented targeted interventions to control the *Serratia marcescens* outbreak. Dedicated patient bays, a day care room for same-day discharges, and strict visitor controls reduced transmission risk of CRE *Serratia* cases. Overcrowding was addressed through early discharge and outpatient antibiotic therapy and IPC-led training, audits, and environmental upgrades, including flooring replacement and bathroom repairs, further reinforced infection control practices. Consistent supply of hand hygiene agents by the administration department further supported containment of the outbreak. By November, the incidence of cases had significantly declined, and no new cases were reported throughout December, demonstrating the effectiveness of the implemented control measures in successfully containing the outbreak.

This study provided a notable and prolonged outbreak of *Serratia marcescens* within the pediatric unit of a tertiary care cardiac hospital. This situation highlights several critical issues. Firstly, the neonatology unit, due to its focus on the care of vulnerable newborns and the frequent medical interventions required, represents an environment particularly susceptible to outbreaks caused by pathogens such as *Serratia marcescens*.[9]Secondly patients were admitted for cardiac issues needing surgical interventions and frequent device insertions making them susceptible to various nosocomial infections.

The primary mode of pathogen transmission in this outbreak appears to be through the contaminated hands of healthcare workers as stated in other studies.[8,9] The movement of healthcare workers between different hospital wards further compounds the risk of dissemination. Therefore, the implementation of stringent hand hygiene protocols and robust infection control measures is imperative.[10,11] The most important reason for poor compliance for hand hygiene was improper technique, lack of time and limitations in supplies of hand cleaning and disinfecting agents. Patients and their families also play a pivotal role in propagating the infection, primarily through contact with contaminated surfaces and objects within the ward. Effective education and awareness initiatives targeting families and visitors are indispensable in preventing further spread.[12]

Inadequate cleaning and maintenance practices within the paeds unit have been identified, including the neglect of air conditioner ducts, fans, lighting fixtures, and humidifiers. Such shortcomings create potential reservoirs for bacterial growth, underscoring the necessity for the implementation of stringent cleaning and disinfection protocols.[16] The identification of Pseudomonas aeruginosa in close proximity to humidifiers also signifies the likelihood of other bacterial reservoirs within the NICU. This underscores the necessity for a comprehensive approach to infection control. Environmental cleanliness is another vital component of prevention. Whether environmental reservoirs play a major role in nosocomial infections is still under debate, but new evidence suggests it may be significant.[15]Temperature and humidity influences environmental contamination and in countries with excessive dust or damp, the environment is difficult to keep clean.[14]Healthcare facilities should have well-established and meticulously executed cleaning and disinfection protocols, with particular attention to frequently-touched surfaces like bedrails, doorknobs, and medical equipment. Effective disinfectants known to combat *Serratia* species should be employed, and cleaning practices should be consistently and thoroughly executed.[17]

Moreover, a crucial element in preventing *Serratia* outbreaks is antibiotic stewardship. Overuse or misuse of antibiotics can contribute to the development of antibiotic-resistant strains. Therefore, healthcare

facilities should implement strict antibiotic stewardship programs to ensure that antibiotics are prescribed judiciously.[18]Another notable observation in this study was significant overuse and extended usage of antibiotics in the unit. Numerous broad-spectrum medications, particularly aminoglycosides and carbapenems, were being used empirically; nevertheless, they were regularly switched when patients failed to respond to treatment. Healthcare providers should adhere to established guidelines for appropriate antibiotic use, and monitoring of antibiotic usage within healthcare settings should be routine. Emphasis should be placed on accurate diagnosis and the judicious utilization of antibiotics to mitigate the proliferation of resistance as evidenced by some studies.[13]

Surveillance of infections plays a pivotal role in outbreak prevention. Robust surveillance systems should be established to closely monitor healthcare-associated infections, including those caused by *Serratia.*[19]Regular reviews and analyses of infection data can help identify outbreaks early, facilitating prompt intervention. Continuous education and training are also essential for healthcare workers, ensuring they remain well-informed about infection control practices, especially in the context of preventing *Serratia* outbreaks.

Since every child had a parent with them, overcrowding was one of the variables associated with this outbreak. Multiple family members were noticed in the unit at various times as families couldn't afford a place to stay after traveling from remote areas to the hospital. As a result, the administrative policies pertaining to patient attendants had not been implemented properly. Patients and their families should also be educated on the importance of infection prevention measures and encouraged to actively participate in their own care, including practicing good hand hygiene and following isolation precautions when necessary. In high-risk healthcare units, well-defined outbreak response plans should be established, encompassing protocols for identifying, isolating, and treating infected patients, as well as strategies for communication and coordination among healthcare facilities and public health agencies.[19]Lastly, research and innovation should be ongoing endeavors. Investing in research to better understand *Serratia* species and their transmission patterns can lead to the development of new prevention strategies and improved diagnostics, ultimately enhancing our ability to safeguard public health from *Serratia* outbreaks.[20]

CONCLUSION:

In conclusion, multiple strategies need to be taken to combat the *Serratia marcescens* outbreak in the cardiology institute's pediatric department. This encompasses enhancements in hand hygiene practices among healthcare professionals, comprehensive education efforts targeting patients and their families, prudent antibiotic use, surveillance of BSI and the stringent implementation of infection control measures, notably including thorough environmental cleaning and disinfection. One of the limitations of this study was inability to perform the bacterial typing due to resource constraints, however our antibiogram profile was precise. The long-term management of such outbreaks still depends extensively on maintaining the effectiveness of antibiotics and preventing the spread of antibiotic resistance. Hence, a concerted effort involving healthcare facilities, healthcare workers, patients, pharmacists and public health agencies is essential for the effective prevention of *Serratia marcescens* outbreaks.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Tazeen Fatima: Idealized and conceptualized the study, manuscript writing, final approval, agreement to be accountable for all aspects of the work

Faiza Rezwan: Subsequently critically reviewed and revised, final approval, agreement to be accountable for all aspects of the work

Muhammad Amaan Nadeem: Statistical analysis, final approval, agreement to be accountable for all aspects of the work

Farheen Ali: Criticalrevisions, final approval, agreement to be accountable for all aspects of the work

Shobha Luxmi Aisha Jamal: Subsequently critically reviewed, final approval, agreement to be accountable for all aspects of the work

Aneera Ahmed: Data collection, proofread, final approval, agreement to be accountable for all aspects of the work

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