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AN OUTBREAK OF SERRATIA MARCESCENS AT A NEONATAL INTENSIVE CARE UNIT IN A TERTIARY CARE HOSPITAL OF BANGLADESH

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ABSTRACT

Background: Serratia marcescens represents an important pathogen involved in hospital acquired infections. Outbreaks are frequently reported and are difficult to eradicate. The aim of this study is to describe an outbreak of Serratia marcescens in a neonatal intensive care unit during early 2022. **Methods:** Following an abrupt increase in the isolation of Serratia marcescens from blood culture sample of NICU patients. extensive environmental sample, various clinical consumables and hand swab of the staff were screen for contamination of Serratia marcescens. Antimicrobial susceptibility of isolates were carried out by VITEK® 2 automated culture system. Effective hand hygiene measures were implemented. Infected babies were insulated. **Results:** A total of 17 newborns from NICU were studied. Blood culture and sensitivity were performed in all cases. Five Serratia marcescens isolates were collected from blood sample. Environmental and hand sampling resulted negative. All isolates were resistant to colistin. In our study, the average weight was 2434 g and forty percent population required artificial ventilation. The outcome was fatal in 40.0% cases. **Conclusions:** S. marcescens outbreak represents a serious challenge in NICU. Frequently, reservoirs of infection were not identified. However, extensive surveillance procedures are essential to control the outbreak in a neonatal intensive care unit.

KEYWORDS: Serratia marcescens, Outbreak, Neonatal intensive care unit, Colistin.

INTRODUCTION

The genus Serratia is a gram-negative rod pertains to the Enterobacteriaceae family. *Serratia marcescens* is the primary pathogenic species of Serratia most commonly isolated from human infections.[1] *S. marcescens* was considered a nonpathogenic saprophytic organism until late 20th century. Pathogenicity of this bacteria in human was first noted in 1913 and the first known outbreak of nosocomial *S. marcescens* infection was recorded in 1951.[2,3] Though *S. marcescens* show relatively low virulence, it causes hospital-acquired infections in severely immunocompromised or critically ill patients, particularly in settings such as intensive care units (ICUs), especially neonatal units (NICUs).[4,5] In newborn *S. marcescens* gives rise to a wide range of clinical manifestations as such asymptomatic colonization to keratitis, conjunctivitis, urinary tract infections, pneumonia, surgical wound infections, sepsis, bloodstream infection and meningitis.[6,7] Blood stream is the most frequent site of infection followed by the respiratory apparatus and the gastrointestinal tract by this organism.[8]

Management of infection by *S marcescens* is troublesome. As the fact that many strains of the bacterium manifest resistance to multiple antibiotics, including β-lactams, aminoglycosides, and quinolones.[1,9] The aim of the study was to illustrate an investigation and intervention conducted to terminate an increase in the number of cases of *S marcescens* which was observed in our NICU with a view to intercept further cases.

METHODS

Surveillance and environmental investigations

The study was carried out in the neonatal intensive care unit (NICU) of Bangabandhu Sheikh Mujib Medical University (BSMMU), a tertiary care hospital in Bangladesh. The NICU has 31 beds admitting critically ill neonates. The NICU admits between 600 to 700 patients annually. The study was commenced when a female infant was found to have *S marcescens* sepsis on 2nd February 2022. She (gestational week 38) was delivered by caesarian operation in our hospital, BSMMU. After birth the neonate was transferred immediately to our NICU because of ventricular septal defect for further management. On the 4th day of

admission, child developed septicemia and *S marcescens* was isolated from blood culture. Within a week, blood culture yielded *S marcescens* from four more neonates in the NICU. All neonates infected with *S marcescens* were treated with antibiotic regimens, including meropenem and amikacin.

During a *S. marcescens* outbreak in the NICU, extensive environmental sampling and screening of the staff from NICU and microbiology laboratory of BSMMU were performed. Cultures were obtained from other sites, as appropriate, in symptomatic patients. Ethical approval was not required because all swabs were carried out for managing the outbreak, according to criteria of good clinical practice.

Bacterial culturing and identification

All samples were inoculated onto bacteriological culture media, then incubated at 37°C for 24 hours. *S. marcescens* strains were identified using Vitek-2 (bioMérieux, Marcy L'Etoile, France) GN cards.

Antimicrobial susceptibility testing

The isolates were tested by Vitek-2 (Vitek 2, bioMérieux, Marcy L'Etoile, France), using VITEK® 2 Gram-Negative identification card (GN) card and VITEK® 2 Gram Negative Susceptibility Card VITEK® 2 AST-N280. Antimicrobial susceptibility results were interpreted according to the breakpoints established by the Clinical and Laboratory Standards Institute.[10] The antimicrobial agents included were amoxicillin, ampicillin, aztreonam, cefotaxime, ceftazidime, ciprofloxacin, amikacin, gentamicin, meropenem, colistin and piperacillin. The isolates were stored at -70^{0}C for further studies.

RESULTS

In the second week of February 2022, Microbiology & Immunology department of BSMMU became concerned about the frequent isolation of *S. marcescens* in blood samples from NICU. The first, second, third fourth and fifth blood culture positive *S. marcescens* were reported on 2nd, 3rd, 8th and 9th February in five neonates. A thorough investigation in the microbiology laboratory was conducted to determine if there was a source of contamination in the laboratory. Multiple Swabs from all laboratory equipment (incubators, suction tube, platinum wire loop, Vitek-2, class II safety cabinet, centrifuges, and fridges) and consumable reagents such as distilled water, peptone water, normal saline, and prepared bacterial culture media were inoculated on MacConkey and blood agar media. The result of the investigation of the laboratory sources gave out an absence of *S. marcescens*.

Infection control committee of the microbiology department planned an infection control meeting with NICU doctor and staff to establish infection control measures. Expanded environmental sampling, including sinks, soap and chlorhexidine dispensers, intravenous and topical solutions, CPAP machine, cots, ventilators, suction tube, balances, stethoscopes and hand plates of staff of NICU were all negative for *S. marcescens.*

Fifteen suspected NICU patients were sampled obtaining blood culture from each patient. Five out of 17 patients tested positive for S. marcescens during the study period. The epidemic set in motion in a term baby with 38.0 gestational age admitted for ventricular septal defect, which showed after 3 days of his hospitalization signs of sepsis with isolation of *S. marcescens* in the blood culture, and other four cases were diagnosed subsequently within seven to ten days. The mean gestational age of our patients was 35.82 weeks, with extremes ranging from 31.5 to 38.0 weeks. Newborns was premature in 40% of cases. The sex ratio (boy to girl) was 3:2. The weight ranged from 900 grams to 3015 grams with an average weight of 2434 grams. Neonatal pulmonary infection was the most diagnosis of hospitalization in 80% of cases (Table 1). On admission, all patients were treated with ampicillin and gentamicin antibiotics, and 40% of cases were artificially ventilated. The diagnosis of nosocomial infection was made over an average of 7 days of hospitalization, with extremes ranging from 4 days to 10 days. The diagnosis was made in the presence of clinical signs and/or biological abnormalities on the hemogram or high C-reactive protein with *S. marcescens*-positive blood cultures. Isolated *S. marcescens* strains were susceptible in 80% of cases to 3rd generation cephalosporins and all susceptible to meropenem, ciprofloxacin and amikacin. Gentamicin was susceptible in 80% of cases, but all were resistant to colistin (Table 2). All patients were treated with meropenem and amikacin after diagnosis of *S. marcescens* infection. The consequence was enthusiastic in 60% of the cases, and the death was reported in two cases. The average hospital stay was 20.50 days, with extremes ranging from 12 days to 34 days.

By reinforcing standard infection control procedures, including hand washing, isolating infected neonates, and disinfecting environmental surfaces the outbreak was stopped in the NICU.

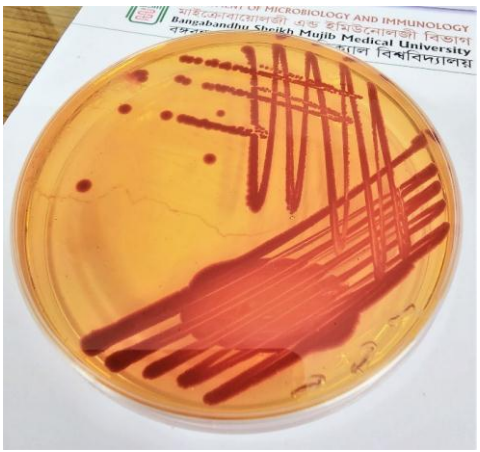

Figure: MacConkey agar media showing red colour colony.

Table 1: ***Patients' demographic data.***

Patients No	Diagnosis	Gestational age (weeks)	Weight (grams)	Method of delivery	Antibiotic prescription	Mechanical ventilation	Day of infection with *S marcescens*	Outcome
1	Ventricular septal defect	38 weeks	2960	Caesarean	Yes	Yes	3	Death
2	Neonatal pulmonary infection	37+3 weeks	2295	Caesarean	Yes	No	7	Favorable
3	Neonatal pulmonary infection	35+2 weeks	3000	Caesarean	Yes	No	5	Favorable
4	Neonatal pulmonary infection	37+1 weeks	3015	Caesarean	Yes	No	9	Favorable
5	Respiratory distress Syndrome with DIC	31+5 weeks	900	Caesarean	Yes	Yes	5	Death

Table 2: ***Susceptibility to antibiotics of Serratia marcescens.***

Antibiotic	Sensitivity	Resistance
Amoxicillin	None	100%
Ampicillin	None	100%
Aztreonam	60%	40%
Piperacillin	60%	40%
Cefotaxime	80%	20%
Ceftazidime	80%	20%
Meropenem	100%	None
Ciprofloxacin	100%	None
Gentamicin	80%	20%
Amikacin	100%	None
Colistin	None	100%

DISCUSSION

Serratia marcescens is a notable causative agent of hospital infections and can be the source of epidemic outbreak in NICU.[11] There have been several reports of S marcescens outbreaks in NICUs.[11,12,13-17] S. marcescens has emerged as a currently recognized pathogen for nosocomial infection in neonates, especially in epidemic form[18], which has also been reported in our study. We have identified five cases of *S. marcescens* bacteremia within 20 days. A similar report was published in 2010 by Bayramoglu et al., comprising 9 cases, in neonatal intensive care unit over a period of 36 days.[19] Daoudi et all found 8 cases of S. marcescens bacteremia in neonatal intensive care unit within 2 months.[20]

In *S. marcescens* outbreaks, sources of contamination were different: catheters, heparin solution, dialysis machine, propofol, liquid soap.[21–26] The invasive medical devices, environmental surfaces, intravenous and topical solutions, or soap may seem to be the pathogen's source[14,27,28], whereas the hands of HCWs can serve as an important source of infection.[1] In our study, environmental cultures from NICU were all negative for *S marcescens*. Our intensive efforts failed to determine the source of the outbreak.

According to Al Jarousha and coworkers the statistically significant risk factors of infection to Serratia were low birth weight less than 1500 g, gestational age greater than 37 weeks, and mechanical ventilation.[18] Other common risk factors of infection to Serratia are long hospital stay, antibiotic prescription, and the use of invasive methods: umbilical catheter, intubation, bladder catheterization, and parenteral nutrition.[29] However, our population was 40% premature and 40% artificially ventilated. The average weight recovered was 2434 g. Only one newborn had an umbilical vein catheter.

In our study, we isolated Serratia in blood culture. This isolate could be responsible for septicemia, pneumonia, conjunctivitis, urinary tract infections, and even gastroenteritis in newborns. In a study by Morillo et al., the clinical manifestations found in the ascending order were pneumonia, conjunctivitis, septicemia, and finally urinary tract infection.[30] Cerebromeningeal complications have recently been reported to be more frequent with *Serratia marcescens*, namely, meningitis, brain abscess, and empyema.[31] In our study we have found early onset sepsis, late onset sepsis, septic shock, DIC and one case of meningitis.

Concerning to the resistance of *S. marcescens* to antibiotics, high resistance to cephalosporins is often reported which can reach up to 100%.[30, 32] In our study, the cephalosporin resistance rate was lower and all strains were sensitive to meropenem, amikacin and ciprofloxacin, which is consistent with the results reported by Al Jarousha who reported a sensitivity of 90% to imipenem and 76% to ciprofloxacin.[18] As for colistin, all isolated strains were resistant concordant with the results of Buffet-Battailon et al.[33] and those of Adjide et al.[32] Outbreaks of *S. marcescens* have been reported to spread very rapidly with significant morbidity and mortality.[11,14,16] Furthermore to the resistance of ´ Serratia to antibiotics, its severity is clear in light of the high mortality rates reported, which varies from 14.3% to 62.5% of cases.[18, 19, 31, 32,34,35] In our study, we have a mortality rate was 40.0% (Table 1).

To cope with these epidemics, a number of measures were taken as soon as the first case is diagnosed, mainly the dissemination of knowledge to medical and paramedical staff on the importance of hand hygiene, the

use of double protection by gloves, the technical and geographical isolation of the infected patients, and the use of appropriate disinfection for any surface or equipment likely to be contaminated. We achieved all these measures, which allowed a control of the epidemic within a very short time.

Furthermore, more accurate molecular investigations concerning genetic determinants of resistance of antimicrobial agents are needed.

CONCLUSION

S. marcescens can cause rapidly spreading outbreaks of severe and potentially fatal infections in neonatal units. Extended and laborious epidemiologic investigations, as well as implementation of multiple appropriate infection-control measures, may be needed to contain such outbreaks. Genotyping can be proved to be a very useful tool for identification, tracing, and detailed analysis of consecutive outbreaks with distinct clones of the same bacterial species.

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ETHICAL MATTERS

Ethical approval was not required to carry out this work as the bacterial isolates were collected as part of routine patient care investigation in the hospital.

CONFLICT OF INTEREST

This article contents no conflict of interest.

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