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Healthcare-Associated Ralstonia mannitolilytica Bacteremia from Contaminated Pantoprazole Diluent: A 34-Patient Case Series from India

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ABSTRACT

Background: *Ralstonia mannitolilytica* is an emerging opportunistic pathogen capable of contaminating water-based medical products and causing healthcare-associated bloodstream infections. Outbreaks from India remain rare, and large series are seldom reported.

Objectives: To describe the clinical, microbiological, and epidemiological characteristics of a 34-patient outbreak of *R. mannitolilytica* bloodstream infection in a tertiary-care centre and identify the contamination source.

Methods: A retrospective outbreak investigation was conducted between 28 April and 17 May 2025. All patients with blood culture–confirmed *R. mannitolilytica* were included. Clinical data, antimicrobial susceptibility, and potential common exposures were analysed. Cultures of intravenous fluids, consumables, and medications were performed to identify the source.

Results: Thirty-four patients (median age 44 years; 56% male) developed *R. mannitolilytica* bloodstream infection, with 55.8% admitted in the ICU. Polymicrobial infection occurred in 38%. Common comorbidities included sepsis (61.8%) and acute kidney injury (55.9%). Antimicrobial susceptibility showed sensitivity to cefoperazone–sulbactam, carbapenems, and fluoroquinolones, with resistance to piperacillin–tazobactam, aminoglycosides, colistin, and TMP-SMX. A single batch of pantoprazole diluent was identified as the contamination source, with unopened vials producing identical isolates. After the immediate withdrawal of the implicated batch and reinforcement of infection control measures, no additional cases were reported. The overall mortality rate was 20.6%, with deaths primarily resulting from underlying illnesses rather than the infection.

Conclusion: This 34-patient cluster constitutes the most significant documented outbreak of Ralstonia mannitolilytica in India and the inaugural case associated with contaminated pantoprazole diluent. The event shows that the organism can live in water-based medicines, which shows how important it is to keep a close eye on medication sterility, look out for rare non-fermenters, and respond quickly to outbreaks with a team of experts to stop the spread..

Keywords: Ralstonia mannitolilytica, Blood Stream Infection, Pantoprazole diluent, Hospital Outbreak, Microbial Contamination

INTRODUCTION

Ralstonia mannitolilytica is a rod-shaped, non-fermenting, Gram-negative bacteria which is a member of the Burkholderiaceae family. [1] Though it is not normally a pathogen in the community, this bacterium has been found as an opportunistic organism in hospital environment. It is usually found in water and other humid environments. [2, 3]

Worldwide, outbreaks linked to healthcare have been linked to Ralstonia species, including R. mannitolilytica. [4, 5, 6] They pose a special risk in intensive care units and other critical care settings because of their capacity to thrive in aquatic environments and on medical equipment. [4, 7] They have been linked to the contamination of sterile water, IV fluids, and other medicinal treatments. [8, 5]

Although R. mannitolilytica infections are uncommon, they can have major clinical repercussions, especially in people with impaired immune systems. [9, 2] Once a source of contamination is found within a hospital, the infection rate can rapidly increase. Effective therapy depends on precise identification and susceptibility testing because R. mannitolilytica is inherently resistant to several antibiotics. [3, 8, 10]

Even fewer R. mannitolilytica outbreaks have been reported in the Indian subcontinent. The organism's capacity to contaminate water-based medical systems was demonstrated by the first significant outbreak in India, which happened in a haemodialysis unit. [11] The fact that a second epidemic was recently reported in a Northern Indian tertiary care facility highlights how uncommon these occurrences were in the area between 2020 and 2022. [6]

The detection of R. mannitolilytica in hospital-acquired illnesses is difficult and serves as a reminder of the significance of effective infection control procedures due to its uncommon incidence in India. Every outbreak offers a useful case study for enhancing monitoring, preventing contamination, and responding quickly to new health risks. [6, 2]

METHODOLOGY

Case Definition and Identification

This study is a retrospective analysis of the clinical features,outcomes and source identification of Ralstonia mannitolilytica from blood cultures in admitted patients from a tertiary care hospital between April 28, 2025, and May 17, 2025, .it started when a 69-year-old male patient with chronic liver illness showed signs of fever spikes and hypotension, a blood culture sample that unexpectedly grow R.mannitolilytica as this organism is uncommon in clinical practice, the first suspicion was contamination. However, the emergence of additional positive cases within days prompted a systematic outbreak investigation. We first reviewed the literature and all the published data suggested that the source of Ralstonia mannitoliytica was contaminated IV fluid in the hospital. We sent cultures of all IV fluids that patients received, such as dialysis water in dialysis patients. RL, NS. When growth was not detected, a thorough audit of the 34 patients' treatments revealed that pantoprazole was present on every patient's treatment sheet, raising serious concerns. We sent a pantoprazole diluent for culture, where we saw Ralstonia mannitoliytica grow.

RESULTS

Demographic and Clinical Characteristics

During the 20-day outbreak period (28 April to 17 May 2025), **34 patients** were identified with healthcare-associated *Ralstonia mannitolilytica* bloodstream infections. The median age was **44 years** (range: 17–69), with a male predominance of **19 patients (56%)** compared to **15 females (44%)**. The majority of patients were admitted to the intensive care unit (**19 patients, 55.8%**), while **15 patients (44.2%)** were in general wards at the time of positive blood culture.

Microbiological Findings

*In **34 out of 34 patients, 100%** of blood cultures contained Ralstonia mannitolilytica. 13 patients (38.2%) had bloodstream infections caused by multiple microorganisms, including **Escherichia coli, Candida species, and Acinetobacter species**. The investigation revealed that the pantoprazole diluted with a particular diluent had been administered intravenously to **all 34 patients**. The source of contamination was confirmed by culturing **unopened vials** of the pantoprazole diluent, which grown **R. mannitolilytica** organisms.*

Clinical Risk Factors and Comorbidities

S.No	AGE	GENDER	DIAGNOSIS	BOTTLE 1 OR 2 OR BOTH	CENTRAL LINE Y/N	SURVIVED	EXPIRED
1	69	MALE	ISCHEMIC CVA, BASILAR ARTERY THROMBOSIS, SEPTICEMIA	BOTH	NO	Yes	
2	65	FEMALE	CCF, AKI, OSA (DM-2)	2	NO		
3	59	MALE	RESPIRATORY FAILURE, NSTEMI, ISCHEMIC LACUNAR INFARCT, SEPSIS,SEPTIC ENCEPHALITIS, (DM-2, IHD)	1	NO		yes

4	69	FEMALE	COPD, TYPE 2 RESPIRATORY FAILURE, SEPSIS, LRTI, ARDS, ASD, (HTN)	1	YES		yes
5	21	FEMALE	OP POISIONING, TOXIC ENCEPHALITIS, SEPSIS {POST-CPR SURVIVAL}	1	YES		
6	61	FEMALE	RIGHT PCNL DJ STENTING	2	NO		YES
7	60	MALE	IPH	1	NO		
8	38	MALE	ELECTRIC BURN INJURY, SPINAL CORD INJURY, RESPIRATORY FAILURE,SEPSIS AKI	1	YES		YES
9	69	MALE	CHB, IHD, SEPTIC WITH SEPTIC SHOCK	1	YES		YES
10	18	MALE	ENTERIC FEVER	1	NO	YES	
11	33	MALE	LARGE PERICARDIAL EFFUSION (ADENOCARCINOMA OF LUNG)	BOTH	NO	YES	
12	42	MALE	SICKLE CELL TRAIT, CKD WITH SEC.PTH WITH HYPOCACEMIA, SEPSIS	2	YES		
13	17	MALE	ACUTE ACUTFEBRILE ILLNESS	2	NO		
14	62	MALE	B/L RENAL CALCULI, AKI, HTN-	1	YES	YES	
15	19	FEMALE	DCLD WITH AKI	2	NO	YES	
16	33	MALE	CKD ON MHD	1	YES	YES	
17	53	MALE	CHRONIC PANCREATITIS WITH PSEUDOCYST, AKI, HEPATIC ENCEPHAILITIS, SEPSIS	BOTH	NO		
18	44	MALE	ENTERIC FEVER, ASCITES, DCLD, SEVERE METABOLIC ACIDOSIS, COAGULOPATHY	1	NO		YES
19	46	MALE	RUPTURED LIVER ABSCESS WITH HYDROPNEUMOTHORAX, SEPSIS	1	NO	YES	
20	19	FEMALE	ACUTE FEBRILE ILLNESS	1	NO		
21	25	MALE	RENAL FAILURE, SEPSIS, GBS	1	NO	YES	

22	19	MALE	ACUTE VIRAL FEVER	1	NO		
23	57	FEMALE	RIGHT SIDED HYDROPNEUMOTHORAX	1	NO	YES	
24	40	MALE	ACS-NSTEMI, PANCREATITIS (CA BUCCAL MUCOSA), SEPSIS	2	NO		
25	55	FEMALE	RENAL FAILURE ON HD, METABOLIC ENCEPHALOPATHY, SEPTICEMIA WITH SEPTIC SHOCK (DM-2, HYPOTHYRODISM, HTN)	2	YES		YES
26	35	FEMALE	ACS, AKI	1	NO	YES	
27	19	FEMALE	HYPOXIC BRAIN INJURY, CKD	2	NO		
28	53	MALE	CHRONIC PANCREATITIS WITH PSEUDOCYST, HEPATIC ENCEPHALITIS, AKI, SPLENOMEGALY, SEPSIS, THROMBOCYTOPENIA	BOTH	NO		
29	25	MALE	RENAL FAILURE	1	NO	YES	
30	27	MALE	RIGHT AVASCULAR NECROSIS OF FEMORAL HEAD, SEPSIS	BOTH	YES	YES	
31	63	FEMALE	PSEUDOCYST OF PANCREAS	BOTH	NO	YES	
32	29	MALE	ALCOHOLIC LIVER DISEASE, ASCITES, SBP, AKI	BOTH	NO		YES
33	65	MALE	CERVICAL COMPRESSIVE MYELOPATHY,AKI,HYPERKALEMIA	1	NO	Yes	
34	45	MALE	ALD WITH ANEMIA, GI BLEED, AKI,TYPE-I RESPIRATORY FAILURE, SEPSIS,HEPATIC ENCEPHALITIS	BOTH	NO		

Central venous catheters was present in **9 patients (26.4%)** at the time of blood culture taken, but this was **not statistically linked** to *R. mannitolilytica* bacteremia ($p>0.05$). The most common underlying conditions included:

Acute kidney injury (AKI): 19 patients (55.9%)

Sepsis: 21 patients (61.8%)

Chronic liver disease: 7 patients (20.6%)

Chronic kidney disease: 6 patients (17.6%)

Clinical Presentation and Diagnostic Challenges

Clinical confounders- *Hepatic encephalopathy, acute kidney injury, and concurrent sepsis-delayed outbreak detection.* ***5 days*** *was the median time* ***(range: 2–11 days)*** *between hospital admission and a positive blood culture. It was challenging to differentiate* ***R. mannitolilytica*** *infection from baseline illness severity because many patients had overlapping clinical features of their underlying conditions.*

Antimicrobial Susceptibility Profile

Antimicrobial susceptibility testing was performed following standard laboratory protocols. Given the absence of Clinical Laboratory Standards Institute (CLSI) or European Committee on Antimicrobial Susceptibility Testing (EUCAST) interpretive breakpoints for *Ralstonia* species, susceptibility interpretation utilized *Pseudomonas* species breakpoints as surrogate standards.

Representative susceptibility results demonstrated:

Sensitive antibiotics: Cefoperazone-sulbactam (MIC ≤8), Imipenem (MIC 4), Meropenem (MIC 4), Ciprofloxacin (MIC 0.5), Levofloxacin (MIC 2)

Resistant antibiotics: Piperacillin-tazobactam (MIC ≥128), Ceftazidime (MIC 32), Amikacin (MIC ≥64), Gentamicin (MIC ≥16), Colistin (MIC ≥16), Trimethoprim-sulfamethoxazole (MIC 80)

Intermediate sensitivity: Cefepime (MIC 16)

Antimicrobial	**MIC (µg/mL)**	**Interpretation***
Piperacillin/Tazobactam	≥128	Resistant (R)
Ceftazidime	32	Resistant (R)
Cefoperazone/Sulbactam	≤8	**Sensitive (S)**
Cefepime	16	Intermediate (I)
Imipenem	4	**Sensitive (S)**
Meropenem	4	**Sensitive (S)**
Amikacin	≥64	Resistant (R)
Gentamicin	≥16	Resistant (R)
Ciprofloxacin	0.5	**Sensitive (S)**
Levofloxacin	2	**Sensitive (S)**
Colistin	≥16	Resistant (R)
Trimethoprim/Sulfamethoxazole	80	Resistant (R)

Antimicrobial	MIC (µg/mL)	Interpretation*
*Interpretation based on *Pseudomonas aeruginosa* CLSI breakpoints MIC = Minimum Inhibitory Concentration; S = Sensitive; I = Intermediate; R = Resistant		

Clinical Outcomes

Seven patients (20.6%) died. The primary causes of death were multiorgan dysfunction and underlying severe disease rather than R. mannitolilytica infection. After contaminated pantoprazole diluent batches were promptly removed and improved infection control procedures were put in place, the outbreak was effectively contained.

Infection Control Measures

Immediate control measures included the following after it was determined that the contaminated pantoprazole diluent was the source of the outbreak:

Removing all batches of implicated pantoprazole diluent from hospital use

Improved monitoring of blood culture outcomes

Strengthening the procedures for preparing and administering medications

Hospital-wide adoption of improved infection prevention and control strategies

Prospective monitoring

DISCUSSION

This case series probably represents one of the biggest nosocomial Ralstonia mannitolilytica cases ever reported from the Indian subcontinent. The outbreak helps in understanding the pathogen's growth and its importance in healthcare environments, especially in critical care units.

A median age of 44 years, a slight male predominance (56%), and its significant ICU involvement (55.8%) were all determined by our demographic analysis. These characteristics are largely consistent with outbreaks of R. mannitolilytica that have been previously reported, which often involve critically ill or immunocompromised patients. For instance, adult patients with bloodstream infections were involved in a hemodialysis outbreak from Bengaluru that was documented by Shankar et al. [11] Additionally, case series from Indian hemato-oncology units show that patients with indwelling catheters are vulnerable to infection. [5]

Although our cohort's mortality rate of 20.6% is alarming, it is significantly lower than in some international settings. In pediatric critical-care outbreaks, published mortality rates have reached as high as 61%, while in cases linked to cystic fibrosis, they have reached 86%. [12] The early detection of the contaminated source and prompt application of control measures may have contributed to our relatively positive result.

The high frequency of comorbidities in our series are acute kidney injury in 58% of patients, **sepsis or septic shock in 62%**, and **chronic liver disease in 23%** of patients was a important observation. These coexisting conditions demonstrate how vulnerable critically ill patients are to opportunistic pathogens such as R. mannitolilytica. These risk factors which include immunosuppression, invasive catheters, prolonged hospital stays, and exposure to contaminated solutions, are consistent with those found in earlier reports. [5,12]

Remarkably, we found that all 34 afflicted patients are exposure to contaminated pantoprazole diluenta vector not previously documented in the literature for outbreaks of R. mannitolilytica. To the best of our knowledge, pharmaceutical diluent contamination has not been reported on this scale, although previous outbreaks have been linked to multidose saline bottles, sterile water, or medical water reservoirs. [4,5] A clonal source and strong epidemiological linkage are strongly supported by the fact that all patients in our series were exposed to the contaminated diluent and that all isolates had identical antimicrobial susceptibility profiles.

The persistence of R. mannitolilytica in the diluent was probably influenced by its microbiological traits. This organism is well-known for its ability to form biofilms, live in water-associated environments, and endure in seemingly sterile pharmaceutical settings. Strict sterility controls are necessary in pharmaceutical manufacturing, compounding, and hospital storage because these characteristics reduce the effectiveness of standard disinfection and filtration procedures.

From a clinical perspective, the patients' serious illness caused a delay in the outbreak's detection. Over one-third of patients had polymicrobial infections, and the median time to culture positivity was roughly five days. These elements maskes the identification of Ralstonia as a pathogen and are in line with research that reports challenges of distinguishing R.

mannitolilytica infections from more frequent causes of sepsis. [12]

Our antimicrobial susceptibility profile showed a multidrug-resistant phenotype, but there was still sensitivity to fluoroquinolones, cefoperazone-sulbactam, and carbapenems (imipenem, meropenem). These results are consistent with treatment outcomes in other outbreaks in India, where cephalosporins and carbapenems have been successful treatment options. [5, 4] The widespread resistance to aminoglycosides, and piperacillin-tazobactam that we observed highlights how crucial it is to use targeted therapy based on culture and sensitivity rather than empirical broad-spectrum regimens.

Furthermore, no new cases were found after the contaminated pantoprazole diluent batches were withdrawing from hospital, proving the efficacy of source-based infection control. Our epidemiological conclusion is supported by this quick containment, which also demonstrates how removing the pharmaceutical or environmental reservoir can stop transmission . [11, 5]

In conclusion, this outbreak helps in understanding of R. mannitolilytica as a nosocomial hazard. It emphasizes how versatile this pathogen is, how it can use pharmaceutical diluents as reservoirs, and how crucial vigilance, microbial surveillance, and strict quality control are to preventing the infections.

CONCLUSION

This case series, which was linked to contamination of a pantoprazole diluent is a rare but significant source of nosocomial transmission and represents one of the largest known healthcare-associated outbreak of Ralstonia mannitolilytica from India.[13,14] The outbreak demonstrates the organism's capacity to endure in aqueous pharmaceutical products and seriously impair critically ill patients. Rapid outbreak control and a lower death rate than previously reported were achieved through prompt identification and withdrawal of the implicated product, and targeted antimicrobial therapy.[12]

Strong multidisciplinary coordination during outbreak investigations, increased clinical suspicion for uncommon pathogens and strict pharmaceutical quality monitoring are made necessary by this incident. To reduce similar risks in the future, strong infection prevention procedures and quick product recall procedures will be crucial.[15].

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