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Serratia spp. Infections Outside An Outbreak Scenario: A Five-year Review of Patients in A University Hospital

Salgın Senaryosunun Dışındaki *Serratia* spp. Enfeksiyonları: Bir Üniversite Hastanesindeki Hastaların Beş Yıllık Değerlendirmesi

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ABSTRACT

Background: *Serratia* spp. are Gram-negative bacilli commonly found in soil and water, causing opportunistic infections particularly in hospital settings.

Materials and Methods: A hospital review of patients hospitalized from 2017 to 2022 was made to identify patients whose clinical cultures grew *Serratia* spp. Inclusion criteria were age ≥18 years and isolation of one or more positive blood cultures for *Serratia* spp. Bacteremia was classified into two groups: Primary hospital-acquired bacteremia detected after 48 hours of hospitalization and bacteremia detected within the first 48 hours that was associated with previous healthcare facilities or applications.

Results: During the study period, *Serratia* spp. were identified in blood cultures of 46 patients (52.7% males; mean age 60.7±17.6 years). Thirty-one patients (67.4%) had hospital-acquired bacteremia, while 15 patients had bacteremia acquired from previous healthcare facilities or applications. Thirty-five patients (76.1%) were infected by *Serratia marcescens*. All patients had predisposing risk factors for bacteremia, the most common being malignancies (n=19), followed by cardiac diseases (n=16), and diabetes mellitus (n=13). A history of antibiotic treatment in the past month was common (67.4%). Compared with patients who acquired bacteremia from previous healthcare facilities or applications, the rate of prior antibiotic use was significantly higher in patients with hospital-acquired bacteremia (p<0.01), so was the rate of appropriate empirical antibiotic use (p=0.01). Resistance to piperacillin/tazobactam was significantly more common among patients who acquired bacteremia from previous healthcare facilities or applications (p=0.02). Resistance to carbapenem in this group was also higher than expected (20%). During hospitalization, sepsis developed in 27 patients (58.7%). Within 30 days after laboratory detection of *Serratia* spp., mortality occurred in 16 patients (34.8%).

Conclusion: The rate of healthcare-associated bacteremia is alarmingly high among hospitalized patients, which requires a meticulous inquiry into previous histories.

Keywords: *Serratia marcescens*, *Serratia* spp., healthcare-associated infection, bacteremia

ÖZ

Amaç: *Serratia* türleri toprakta ve suda yaygın olarak bulunan ve özellikle hastane ortamlarında fırsatçı enfeksiyonlara neden olan Gram-negatif basillerdir.

Gereç ve Yöntemler: Klinik kültürlerinde *Serratia* spp. üremesi olan hastaları belirlemek için 2017-2022 yılları arasında yatırılarak izlenen hastalar değerlendirmeye alındı. Dahil edilme kriterleri ≥18 yaş ve bir veya daha fazla kan kültüründe *Serratia* spp. üremesi olan hastalar olarak belirlendi. Hastaneye yattıktan 48 saat sonra saptanan primer hastane kaynaklı bakteriyemiler ve daha önceki sağlık kuruluşu başvuruları veya sağlık uygulamaları ile ilişkili olan ve ilk 48 saat içinde saptanan bakteriyemiler olmak üzere bakteriyemiler iki gruba ayrıldı.

Bulgular: Çalışma süresi boyunca, 46 hastanın (%52,7'si erkek; ortalama yaş 60,7±17,6) kan kültürlerinde *Serratia* spp. saptandı. Hastaların 31'inde (%67,4) hastane kaynaklı bakteriyemi, 15 hastada ise daha önceki sağlık kuruluşu başvuruları veya sağlık uygulamalarından kaynaklanan bakteriyemi vardı. Otuz beş hasta (%76,1) *Serratia marcescens* ile enfekteydi. Tüm hastalarda bakteriyemi için predispozan risk faktörleri vardı; en sık görülen risk faktörleri sırasıyla maligniteler (n=19), kalp hastalıkları

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(n=16) ve diyabet (n=13) idi. Son bir ayda antibiyotik tedavisi alma öyküsü yaygındı (%67,4). Hastane kökenli bakteriyemisi olan hastalarda önceki sağlık kuruluşu başvuruları veya sağlık uygulamaları kaynaklı bakteriyemisi olan hastalara kıyasla bakteriyemi öncesi antibiyotik kullanma oranı ve uygun ampirik antibiyotik kullanma oranı anlamlı derecede yüksekti (sırasıyla p<0,01, p=0,01). Piperasilin/tazobaktama direnç, önceki sağlık kuruluşu başvuruları veya sağlık uygulamaları kaynaklı bakteriyemisi olan hastalarda anlamlı olarak daha yüksekti (p=0,02). Bu grupta karbapenem direnci de beklenenden daha yüksekti (%20). Hastaneye yatış sırasında 27 hastada sepsis gelişti. *Serratia* spp.'nin laboratuvarda tespit edilmesinden sonraki 30 gün içinde 16 hastada (%34,8) ölüm meydana geldi.

Sonuç: Hastanede yatan hastalar arasında sağlık hizmetiyle ilişkili bakteriyemi oranı endişe verici derecede yüksektir ve bu da hastaların geçmiş öykülerin titiz bir şekilde araştırılmasını gerektirir.

Anahtar Kelimeler: *Serratia marcescens*, *Serratia* spp., sağlık hizmeti ilişkili enfeksiyon, bakteriyemi

Introduction

Serratia spp. are Gram-negative bacilli commonly found in soil and water (1,2). Although it had long been considered a nonpathogenic agent, *Serratia* spp. has now been recognized as an infectious agent since the 1970s and has been reported as a source of community- and hospital-acquired and even healthcare-associated infections (3,4). *Serratia* spp. accounts for 1-2% of all hospital-acquired infections in a wide variety of hospital settings, particularly in adult intensive care and neonatal intensive care units (ICU) (5,6). A large number of reports are about hospital outbreaks caused *by Serratia* spp. leading to bacteremia, urinary tract, respiratory tract and wound-site infections, endocarditis, and osteomyelitis which originate from use of central venous catheters and some medications (heparin, magnesium sulphate, propofol, etc.) as well as human sanitary neglect (7,8,9,10,11,12,13,14,15,16,17,18). There have also been individual case reports on *Serratia* spp.-associated endocarditis (19), meningitis (20,21), and soft-tissue infections (22,23). In addition, intrinsic or emerging resistance of *Serratia* spp. to commonly used beta-lactam antibiotics is a growing concern among healthcare professionals (5).

Due to the ubiquitous presence of the organism in the nature, some authors proposed to seek the actual source of *Serratia* bacteremia detected in primary hospital settings from those acquired from community or previous healthcare facilities or applications (7,24,25). Indeed, healthcare-associated infections other than acquired in a primary hospital setting are a growing problem worldwide, contributing to antibiotic resistance, and complicating establishment of appropriate antibiotic therapy as well as increasing morbidity and mortality (9,24). This makes this differentiation important when examining patient populations with respect to the actual source of infections and their appropriate treatment.

This study was designed to determine individual cases of *Serratia* spp. bacteremia in a tertiary health care center over a five-year period and to document laboratory and clinical characteristics of patients, with emphasis on the need for differentiation of bacteremia acquired in a primary hospital setting and that acquired from previous healthcare facilities or applications.

Material and Methods

A hospital review of patients hospitalized from February 2017 to 2022 was made to identify patients whose clinical cultures grew *Serratia* spp.. Our 900-bed university hospital includes six adult ICUs and newborn and pediatric ICUs. After a comprensive search from hospital electronic records and patient charts, patients were identified whose one or more blood cultures grew *Serratia* spp. and those who were 18 years of age or older were selected as eligible participants.

Exclusion criteria included patients whose clinical data were absent or missing and those with community-acquired bacteremia, as defined by the absence of a previous history of any healthcare service within the past 30 days despite positive cultures detected within the first 48 hours of hospitalization.

Patients with positive cultures for *Serratia* spp. were further analyzed with respect to socio-demographic characteristics, the length of hospitalization until detection of *Serratia* spp., diagnosis at admission, comorbidities, recent histories of admission, treatment and interventions prior to the current hospitalization, antibiotic treatments prior to and after the detection of *Serratia* spp. becteremia, and hospital setting at the time of growth of *Serratia* spp.. Blood samples were processed using the automated Phoenix™ system (Becton Dickinson Diagnostics, USA).

The study was approved by the institutional review board of Pamukkale University (04.01.2023/E.310937) and was conducted in accordance with the Declaration of Helsinki. Analysis and reporting of the results are in compliance with

the Strengthening the Reporting of Observational Studies in Epidemiology (STOBE) checklist.

Definitions

Bacteremia of hospital origin were defined according to the National Nosocomial Infections Surveillance Network (UHESA) (26).

Bacteremia was classified into two groups: Primary hospital-acquired bacteremia and bacteremia associated with previous healthcare facilities or applications. The former was defined as at least one positive blood culture taken from a patient after any time following 48 hours of hospitalization. The latter was defined as any positive blood culture obtained within the first 48 hours of hospitalization from a patient who had been receiving hemodialysis, wound care, chemotherapy, intravenous therapy, or nursing/home care, or who had applied to a hospital clinic within the past 30 days, or who had a history of hospitalization in the previous 90 days for ⩾2 days, or those living in a long-term care facility.

Primary bacteremia was defined as the detection of a positive blood culture for *Serratia* spp. in the absence of any other positive culture (urine, bronchoalveolar lavage, sputum, soft tissue). If *Serratia* spp. grew in any culture along with blood cultures, the primary site of infection was assumed to be the source where the positive culture had been obtained; thus, secondary bacteremia. The isolation of more than one organism from the same blood cultures was defined as polymicrobial bacteremia.

A disease outbreak was defined based on the World Health Organization criteria, as the occurrence and abrupt onset of affected cases of disease confirmed by positive cultures, exceeding what would normally be expected in a healthcare facility (27).

Previous antibiotic use was defined as use of an antibiotic for at least 48 h within the past month prior to the bacteremia episode. Appropriate therapy was defined as antibiotic therapy given based on the results of final blood cultures. Hypoalbuminemia was defined as a serum albumin level of less than 3.0 g/dL at the time of bacteremia.

The primary outcome was all-cause 30-day mortality after the first detection of *Serratia* spp. bacteremia.

Statistical Analysis

Data were processed with using Statistical Package for the Social Sciences (SPSS) 25 (IBM, Nyc, USA). Demographic and clinical characteristics and laboratory data of patients with primary hospital acquired bacteremia and those determined to have bacteremia possibly acquired from other healthcare facilities were compared. Categorical variables were presented as numbers (percentage), continuous variables were presented as means (standard deviation). The Kolmogorov-Smirnov test was used to analyze the normality of the distribution of parameters. Variables without normal distribution were presented as medians with interquartile range (IQR). The non-parametric Mann-Whitney U test was used for comparison of numerical data, and the chi-squared test or Fisher's Exact test was used for comparison of categorical data. A p-value of less than 0.05 was considered significant.

Results

During the study period, *Serratia* spp. was sporadically identified in blood cultures of 47 patients. One patient who met the criteria for community-acquired bacteremia was excluded. Socio-demographic and clinical characteristics of 46 patients with primary hospital-acquired or with bacteremia acquired from previous healthcare facilities are summarized in Table 1. The majority of the patients were males (52.7%). The mean age of the patients was 60.7±17.6 years. The median hospital stay was 19.5 (IQR 8.8-55.8) days. Thirty-five patients (76.1%) were infected by *Serratia marcessens* (Table 1). All patients had predisposing risk factors for bacteremia, the most common being malignancies (n=19), followed by cardiac diseases (n=16), and diabetes mellitus (n=13) (Table 1).

Primary Hospital-acquired Bacteremia

Based on the inclusion criteria, 31 patients (67.4%) acquired *Serratia* spp. bacteremia while hospitalized at 13 diverse clinical and ICU settings, with anesthesia ICU being the most common (n=9), followed by cardio-vascular surgery (ICU) (n=5). Time from admission to laboratory detection of *Serratia* spp. ranged from 3 to 195 days (median 19; IQR 6-53). Detection of *Serratia* spp. fell into diverse time periods in all the 31 patients, with the shortest period being one month apart, ruling out the possibility of an outbreak. In this group the most common predisposing risk factors for bacteremia were being malignancies (n=13), cardiac diseases (n=12), and diabetes mellitus (n=9) (Table 1).

Bacteremia Acquired from Previous Healthcare Facilities

Within the first 48 hours of admission, blood cultures of 15 patients (32.6%) grew *Serratia* spp., all of whom had previous histories of healthcare: four patients had been receiving hemodialysis, three had been receiving chemotherapy, four had undergone major (n=2) or minor (n=2) surgical interventions, two had undergone urological interventions, one had been receiving homecare, and one had a history of hospitalization at another center. Of note, two patients also had a history of anesthesia with propofol for minor surgical interventions. In addition, five patients

had a previous history of antibiotic treatment in the past month.

Antibiotic Treatment

A history of antibiotic treatment in the past month was common (67.4%); 26 patients who acquired bacteremia in hospital settings had also taken antibiotics. All but one patient received empirical antibiotic therapy prior to or upon detection of *Serratia* spp. The rate of prior antibiotic use was significantly higher in patients with primary hospital-acquired bacteremia (p<0.01), so was the rate of appropriate empirical antibiotic use (p=0.01). Based on culture results and susceptibility testing, antibiotic therapy was revised so that 34 patients received appropriate antibiotic therapy.

Source of Bacteremia

The majority of cases (60.9%) were considered primary bacteremia, the remaining cases had respiratory tract infections (23.9%), urinary tract infections (6.5%) and surgical site infections (8.7%) responsible for *Serratia*

Table 1. Demographic and clinical characteristics of patients with *Serratia* spp. bacteremia

	Total (n=46)	Primary hospital-acquired bacteremia (n=31)	Bacteremia associated with previous healthcare facilities or applications (n=15)	p-value
Age (years), mean ± SD	60.7±17.6	60.3±16.1	61.6±21.1	0.57
Male, n (%)	24 (52.2)	17 (54.8)	7 (46.7)	0.60
Comorbidities n (%)	43 (93.5)	30 (96.8.0)	13 (86.7)	0.24
Malignancies	19 (41.3)	13 (41.9)	6 (40.0)	0.90
Cardiac diseases	16 (34.8)	12 (38.7)	4 (26.7)	0.42
Diabetes mellitus	13 (28.3)	9 (29.0)	4 (26.7)	0.87
Neurologic disorder	9 (19.6)	6 (19.4)	3 (20.0)	0.62
Chronic kidney disease	8 (17.4)	3 (9.7)	5 (33.3)	0.61
Chronic obstructive pulmonary disease	4 (8.7)	2 (6.5)	2 (13.3)	0.40
Source of bacteremia, n (%)				
Primary bacteremia	28 (60.9)	16 (51.6)	12 (80)	0.06
Secondary to respiratory tract infections	11 (23.9)	11 (35.5)	0 (0)	0.006
Secondary to urinary tract infections	3 (6.5)	1 (3.2)	2 (13.3)	0.24
Secondary to surgical-site infections	4 (8.7)	3 (9.7)	1 (6.7)	0.61
Polymicrobial bacteremia, n (%)	21 (45.7)	16 (51.6)	5 (33.3)	0.24
Sepsis	27 (58.7)	16 (51.6)	11 (73.3)	0.16
Monomicrobial bacteremia, n (%)	14 (51.9)	7 (43.8)	7 (63.6)	0.31
Polymicrobial bacteremia, n (%)	13 (48.1)	9 (56.2)	4 (36.4)	0.34
Hospital stay, median (IQR)	19.5 (8.8-55.8)	42 (18-82)	6 (2-12)	0.00
Time to positive cultures (days), median (IQR)	NA	19.0 (6.0-53.0)	NA	NA
Antibiotic treatment				
Antibiotic treatment in the past month, n (%)	31 (67.4)	26 (83.9)	5 (33.3)	0.001
Appropriate empirical antibiotic therapy, n (%)	27 (58.7)	22 (71.0)	5 (33.3)	0.01
Appropriate definitive antibiotic therapy, n (%)	34 (73.9)	23 (74.2)	11 (73.3)	0.61
Laboratory findings				
Hypoalbuminemia, n (%)	30 (65.2)	21 (67.7)	9 (60.0)	0.61
Procalcitonin, median (IQR)	9.1 (2.0-31.7)	8.8 (2.8-14.8)	24.4 (1.9-65.0)	0.26
Leukocyte count (×1000/uL), median (IQR)	14.29 (7.14-21.60)	13.10 (5.76-20.07)	18.01 (9.24-26.25)	0.24
Serum CRP (mg/L), median (IQR)	107.0 (24.5-261.0)	126 (27-261)	87 (10-261)	0.31
30-day mortality after detection of positive cultures	14 (30.4)	9 (29.0)	5 (33.3)	0.51

NA: Not applicable, CRP: C-reactive protein, IQR: Interquartile range, SD: Standard deviation

spp. bacteremia. Nearly half of the patients (45.7) had polymicrobial bacteremia, the great majority (76.2%) of whom acquired the infection in hospital settings. The most common coexisting bacterium was *Enterococcus* spp. (n=6), followed by *Pseudomonas* spp. (n=5).

Bacterial Resistance

On susceptibility testing, the highest rates of resistance were found to piperacillin/tazobactam (19.6%) and to carbapenems (19.6%) (Table 2). Resistance to piperacillin/tazobactam was significantly more common among patients with bacteremia previously acquired from healthcare facilities (p=0.02). Resistance to carbapenem among these cases was also higher than expected (20%).

Hospital Outcomes

During hospitalization, sepsis developed in 27 patients (58.7%). Within 30 days after laboratory detection of *Serratia* spp., mortality occurred in 14 patients (30.4%), with three patients dying within the first 24 hours of hospitalization.

Discussion

In our five-year review of *Serratia* spp., we identified 46 infected patients with primary hospital-acquired bacteremia or bacteremia acquired from previous healthcare facilities, all detected at diverse time points, highly excluding the possibility of an outbreak. Importantly, nearly a third of the cases (32.6%) were found to be associated with previous healthcare. Consistent with the literature reports, *Serratia* spp. bacteremia mostly developed in patients with comorbidities, in particular with malignancies, and in those having a previous history of antibiotic use (28,29,30).

Reports on *Serratia* spp. has been mainly concerned with hospital outbreaks, with reports on individual occurrences being rare (7,8,9,10,11,12,13,14,15,16,17,18). The outbreaks were mainly associated with therapeutic administration of contaminated magnesium sulphate (16), contaminated prefilled saline and/or heparin syringes (31), administration of propofol for anesthesia (11,12), use of contaminated pressure monitoring equipment (17), and use of contaminated epoetin alfa during hemodialysis (18).

Sunenshine et al. (16) documented a U.S. multistate outbreak of healthcare-acquired bloodstream infections in 18 patients from 5 states caused by *S. marcescens* transmitted via a contaminated commercial magnesium sulfate compound used for therapeutic purposes. During investigations for outbreaks of bloodstream infections, the authors emphasized the need to review the quality standards and use of commercial parenteral medications, such as magnesium sulfate, that are commonly used in hospital settings. Another U.S. multistate report of *S. marcescens* outbreak was concerned with bloodstream infections detected in 162 patients in whom contaminated prefilled saline and/or heparin syringes were used (31). In addition, as another source, outbreaks of *S. marcescens* emerged from inappropriate preparation, handling, storage, and use of propofol (11,12,13). Following detection of postoperative systemic inflammatory response syndrome in seven patients, *Klebsiella pneumoniae* and *S. marcescens* grew in cultures obtained from opened vials of propofol (12). The authors addressed problems concerning aseptic preparation, handling and storage of propofol that resulted in extrinsic contamination, particularly the use of a single-use vial for multiple patients. Another sepsis outbreak caused by *S. marcescens* from contaminated propofol was reported in three patients following chest surgery (11). These literature reports on *Serratia* spp. outbreaks clearly demonstrate that, whenever there has been a lapse or neglect in the sanitary standards and therapeutic applications, development of bacteremia is likely to be encountered in every setting of clinical practice. Harnett et al. (17) found contamination with *S. liquefaciens* in syringes and connector tubing of intravascular line pressure monitoring equipment, leading to positive blood cultures in 11 patients receiving adult critical care. The authors implicated lapses in hand hygiene during intravascular pressure monitoring. Finally, another outbreak of *S. liquefaciens* emerged from multiple use of preservative-free, single-use vials of epoetin alfa, where

Table 2. Antimicrobial resistance profile of all *Serratia* spp. isolates

Antimicrobial agents	All *Serratia* spp. isolates (n=46)	Primary hospital-acquired bacteremia (n=31)	Bacteremia associated with previous healthcare facilities or applications (n=15)	p-value
	Resistance rates, n (%)			
Quinolones	8 (17.4)	4 (12.9)	4 (26.7)	0.23
Third-generation cephalosporins	8 (17.4)	3 (9.7)	5 (33.3)	0.06
Carbapenems	9 (19.6)	6 (19.4)	3 (20.0)	0.62
Piperacillin/tazobactam	9 (19.6)	3 (9.7)	6 (40.0)	**0.02**
Trimethoprim/sulfamethoxazole	7 (15.2)	3 (9.7)	4 (26.7)	0.14

residual epoetin alfa was not discarded, but pooled and reused again in hemodialysis patients (18). The authors drew attention to the appropriate use of medication vials so that they contain a sufficient amount of medication for clinical need.

Despite a large number of hospital outbreaks reported associated with contaminated use of hospital medications and equipment, there has been a growing interest in attributing a greater role to community- or other healthcare-associated sources as the origin of *Serratia* spp. bacteremia. Two population-based studies reported considerably high rates of community-acquired or previously healthcare-associated *Serratia* spp. bacteremia (24,25). A laboratory surveillance study for *Serratia* spp. isolates in a large Canadian cohort over a six-year period found that 65% of incident *Serratia* spp. isolates were of community onset (25). Another population-based study from Australia over 10 years found that 29% of *Serratia* spp. bacteremia episodes were purely community-associated and a further 18% of episodes originated from community, but were in particular healthcare-associated (24). These findings about the community and/or previous healthcare origin of *Serratia* spp. bacteremia make our findings even more important and relevant, because, after a meticulous inquiry into the sources of cases, we found that 32.6% of our cases contracted bacteremia from healthcare delivered previously. This differentiation is particularly important in designing antibiotic treatment for these cases, as demonstrated by the significantly lower rate of appropriate empirical antibiotic therapy, addressing the need for a more comprehensive history taking about previous treatments and interventions in this patient group.

Concerning the source of bacteremia, 60.9% of patients had primary bacteremia, while 18 patients (39.1%) had secondary bacteremia. In addition, nearly half of the patients (45.7%) had polymicrobial bacteremia. The rates of both secondary bacteremia and polymicrobial bacteremia were higher in patients who acquired bacteremia at the hospital settings (Table 1). The high rate of polymicrobial bacteremia may be due to the presence of secondary bacteremia and longer hospital stays that may predispose patients to infections caused by other bacteria. Cultures of patients with polymicrobial bacteremia showed no growth of organisms suggestive of a possible contamination.

In our series, more than half of the patients (58.7%) developed sepsis, and mortality occurred in 30.4%. The rates of previously acquired *Serratia* spp. bacteremia from healtcare facilities and overall mortality were considerably higher compared to those reported in a similar study (for bacteremia, 32.6% vs. 18.4%; for mortality 30.4% vs. 22.4%) (32).

To our knowledge, there has been no report on comparative frequencies of *Serratia* spp. resistance to antibiotics in previously healthcare-associated and primarily hospital-acquired bacteremia. Our findings showed similar rates in the two bacteremia groups except for resistance to piperacillin/tazobactam, which was significantly more common (40% vs. 9.7%, p=0.02) among patients with previously healthcare-acquired bacteremia. Interestingly, resistance to carbapenem was even higher (20.0% vs. 19.4%) in this patient group (Table 2). These differences may result from the relatively small size of the two patient groups, the presence of long-term use of healthcare applications, such as hemodialysis (n=4) and chemotherapy (n=3) that may render the patients susceptible to antibiotic resistance, and the increased likelihood of lack or insufficiency of surveillance on antibiotic use or resistance in these healthcare facilities.

Study Limitations

The main limitation of the study is its retrospective design. The sample size is also smaller than other reported serious. Another limitation may be that, had a more comprehensive history concerning long-term previous use of antibiotics been obtained, a more detailed analysis and a more satisfactory explanation would have been possible about the differences in the rates of antibiotic resistance between the two groups.

Conclusion

The rate of bacteremia acquired previously from healthcare facilities is alarmingly high among hospitalized patients, which requires a meticulous inquiry into previous histories of patients so that appropriate empirical antibiotic therapy considering high rates of resistance can be designed and initiated. Whether or not detected during an outbreak, further comparative studies are required about the actual prevalence of *Serratia* spp. bacteremia acquired from community or from healthcare facilities other than the primary hospital setting.

Ethics

Ethics Committee Approval: The study was approved by the institutional review board of Pamukkale University with the decision numbered E. 310937 on 04.01.2023.

Informed Consent: Retrospective study.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.D., S.O.K., F.S., A.K., İ.K., Concept: S.D., S.O.K., A.K., İ.K., Design: S.D., S.O.K., F.S., A.K., İ.K., Data Collection or Processing: S.D., S.O.K., F.S., A.K., İ.K.,

Analysis or Interpretation: S.D., S.O.K., F.S., A.K., İ.K., Literature Search: S.D., S.O.K., Writing: S.D., S.O.K.

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