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Evaluation of Children with *Ralstonia pickkettii* Bacteraemia

Ralstonia pickettii Bakteriyemili Çocuk Olguların Değerlendirilmesi

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Abstract

Objective: *Ralstonia pickettii* is an opportunistic pathogen that is often considered to be contaminant. It can cause infection due to colonisation in infusion solutions and disinfectants. Although rare, it can lead to nosocomial outbreaks, so this agent should not be ignored. In this study, it was aimed to evaluate the growth of *R. pickettii* in blood cultures taken in the pediatric wards of our hospital, to analyze the outbreaks by *R. pickettii* and to discuss the precautions to prevent the outbreaks.

Material and Methods: Patients with *Ralstonia picketti* in blood cultures, who were admitted in the pediatric intensive care unit (PICU; n= 46, 81%), neonatal intensive care unit (n= 7, 12%) and other pediatric wards (n= 4, 7%) between February 2014 and December 2017 were included into the study. Patient's data, the relation between the outbreaks and culture growths, and the sources and the prevention of potential outbreaks were evaluated. Recurrent growths were defined as a single episode.

Results: *Ralstonia pickettii* detected in 57 different specimens in 38 different episodes in a total of 35 patients. Of the fifty-seven blood samples, 67% (n= 38) were peripheral blood cultures, 33% (n= 19) were catheter blood cultures and 74% of the samples lead to infection. Of the 38 episodes, 63% (n= 24) were considered as infection and 37% (n= 14) was contamination. Median age of the patients were seven (0-180) months, and the major underlying comorbidity was congenital heart disease. Of 57 specimens with Raltstonia pickettii growth, 16 (28%) had only *R. pickettii* growth, and the remaining 41 (71%) cultured growths were polymicrobial. Among these, the most common accompanying microorganisms were *Stenotrophomonas maltophilia* and *Burkholderia* species. Of 38 ep-

Öz

Giriş: *Ralstonia pickettii* çoğunlukla kontaminan kabul edilen fırsatçı bir patojendir. İnfüzyon solüsyonlarında, dezenfektanlarda kolonize olarak enfeksiyona neden olabilir. Nadir de olsa nozokomiyal salgınlara yol açabileceği için göz ardı edilmemesi gereken bir etkendir. Bu çalışmada hastanemiz çocuk servislerinde alınan kan kültürlerindeki *R. pickettii* üremelerinin değerlendirilmesi, *R. pickettii*'nin neden olabileceği salgınların analizi ve engellemek için alınması gereken önlemlerden bahsetmek amaçlanmıştır.

Gereç ve Yöntemler: Hastanemizin çocuk yoğun bakım ünitesi (ÇYBÜ; n= 46, %81), yenidoğan yoğun bakım ünitesi (n= 7, %12) ve diğer çocuk sağlığı ve hastalıkları kliniklerinde (n= 4, %7) Şubat 2014 ile Aralık 2017 tarihleri arasında yatmış olan hastalardan, kan kültürlerinde *Ralstonia picketti* üremesi olan olgular çalışmaya dahil edildi. Olguların verilerinin irdelenmesi, üremelerin salgınla ilişkisi, kaynağı ve potansiyel salgınların önlenmesi yaklaşımları değerlendirildi. Ardışık üremeler tek epizod olarak tanımlandı.

Bulgular: Toplam 35 hastada, 38 farklı epizodda, 57 kan kültüründe *R. pickettii* üremesi tespit edildi. Elli yedi kan örneğinin %67 (n= 38)'si periferik kan kültürü, %33 (n= 19)'ü kateterden alınan kan kültürü olup örneklerin %74 (n= 42)'ü anlamlıydı. Otuz sekiz epizoddan %63 (n= 24)'ü anlamlı, %37 (n= 14)'si kontaminasyon olarak kabul edildi. Hastaların yaşları medyan yedi (0-180) ay olup, altta yatan major komorbidite konjenital kalp hastalığıydı. *Raltstonia pickettii* üremesi olan 57 örneğin 16'sında (%28) sadece *R. pickettii* üremesi olup kalan 41 (%71) kültür üremesi polimikrobiyaldi. Bunlar içerisinde en sık eşlik

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isodes, 58% (n= 22) had a central venous catheter (CVC), of which 64% (n= 14) developed catheter-related bloodstream infection due to *R. picketti*. Eighty-one percent of the specimens were detected in the pediatric intensive care unit, and the outbreak situation was examined. Twenty-three (61%) of a total of 57 growths were associated with an outbreak of healthcare-associated infection in three separate periods. *Ralstonia pickettii* was not detected in environment scans. Antibiogram features of the growths were similar and they were thought to be of the same isolate, no molecular study was applied. Three patients died within the first 30 days after the growth.

Conclusion: Our study has the largest case series reported in a pediatric population in Türkiye and the world. The mortality rate due to *R. pickettii* was low. Eighty-one percent of the specimens were in the pediatric intensive care unit and 61% was associated with the outbreak. The importance of hospital infection control measures in preventing *R. pickettii* and similar outbreaks were emphasized. A limited number of studies have been conducted on this subject in Türkiye, and we believe that our study will contribute to the literature.

Keywords: Bacteriaemia, childhood, gram-negative bacilli, *Ralstonia picketti*

eden mikroorganizmalar *Stenotrophomonas maltophilia* ve *Burkholderia* spp. türleri idi. Otuz sekiz epizoddan %58 (n= 22)'inde santral venöz kateter (SVK) mevcut olup, bunların %64 (n= 14)'ünde *R. pickettii*'ye bağlı kateter ilişkili kan dolaşım enfeksiyonu gelişti. Üremelerin %81'i çocuk yoğun bakım ünitesinde tespit edilmiş olup salgın durumu incelendi. Toplam 57 üremenin 23 (%61)'ü üç ayrı dönemde sağlık bakımı ile ilişkili enfeksiyon salgını ile ilişkilendirildi. Ortam taramalarında *R. pickettii* saptanmadı. Üremelerin antibiyogram özellikleri birbirine benzer olup aynı izolat olduğu düşünüldü, moleküler çalışma uygulanmadı. Üç hasta üreme sonrası ilk 30 gün içerisinde kaybedildi.

Sonuç: Çalışmamız Türkiye ve dünyada çocuk olgularda bildirilen en geniş seriydi. *R. pickettii*'ye bağlı mortalite oranı düşük bulundu. Üremelerin %81'i çocuk yoğun bakım ünitesinde olup %61'i salgınla ilişkiliydi. Hastane enfeksiyon kontrol önlemlerinin *R. pickettii* ve benzer salgınların önlemesindeki önemi vurgulandı. Türkiye'de bu konuda kısıtlı sayıda çalışma yapılmış olup, çalışmamızın literatüre katkı sağlayacağı kanaatindeyiz.

Anahtar Kelimeler: Bakteriyemi, çocukluk dönemi, gram-negatif basil, *Ralstonia pickettii*

Introduction

Ralstonia picketti is an opportunistic pathogen with non-fermentative gram-negative bacilli, previously known as *Burkholderia pickettii* and *Pseudomonas picketti*. Due to its low virulence, it is usually associated with pseudobacteremia and asymptomatic colonization (1). However, it can cause infection ranging from minor skin infection to septicemia. *R. pickettii*, which is a water-borne bacterium, is often transmitted from solutions such as contaminated saline and water for injections (1-4). Since *Ralstonia pickettii* can pass through 0.45 mm and 0.2 mm filters, contamination usually occurs during product preparation in the factory. In addition, *R. pickettii* can survive in hospital disinfectants such as chlorhexidine and ethacridine lactate (5).

The *Burkholderia* family began to be defined towards the end of the 1970s, and the information that it was a different isolate from *Pseudomonas* spp. became widespread. In taxonomy, *Burkholderia* species is represented by *Burkholderia cepacian*, which is the main type. *Burkholderia cepacia* has clinical importance, especially in patients with cystic fibrosis, as it can colonize and cause infection. Apart from *Burkholderia cepacia*, there are also other *B. cepacia* related species such as *B. pickettii*, *B. gladioli*, and *B. mallei* (6). While *Ralstonia pickettii* was named as *Pseudomonas pickettii* before the 1990s, it took its place in the taxonomy as *Burkholderia pickettii* in 1992 and as *Ralstonia pickettii* in 1995 (6). In routine laboratory systems, complex isolates of *B. cepacia*, *B. gladioli*, *S. maltophilia* or *Ralstonia* spp. may be misidentified. These bacteria can be distinguished from each other according to some features such as oxidation and decarboxylation (6).

When the literature was examined, it was observed that endophthalmitis developed due to contaminated methotrexate solution in two cases in which intravitreal methotrexate infusion was applied (5). In addition, *R. pickettii* infections have been detected due to contaminated solutions such as iv ranitidine, saline solutions, and water for injections (2). It has been shown in a study by Boutros et al. that it can cause infection by colonizing blood culture bottles as well (1). Although it is a bacterium with low virulence, it can cause bacteremia in immunosuppressed patients.

Patients hospitalized in our hospital's pediatric health and diseases clinics (PHDC) between February 2014 and December 2017 with *Ralstonia picketti* growth in their cultures were included in the study. It was aimed to examine the data of these cases, to determine the relation of reproduction with an epidemic, its emergence, source and role in the prevention of potential epidemics, and to ensure that this bacterium, which can cause epidemics although rarely, is not ignored.

Materials and Methods

Department of pediatric health and diseases of our university is an accredited tertiary care practice and research hospital, and it is a 131-bed clinic with a total of nine services, mainly neonatal intensive care unit, pediatric intensive care unit, hematology and oncology hospital and pediatric infection service. The pediatric intensive care unit has a capacity of 10 beds, four of which are isolated.

In our hospital, soap containing 2% chlorhexidine gluconate is used as hand disinfectant, and water containing 1000 ppm chlorine is used for surface disinfection. Handwashing activities are checked at regular intervals in all services. Paper towels are used in our institution, and patients in the pediatric intensive care unit are washed twice a week. Disinfection rules training is given to each newly appointed assistant/nurse/personnel under the name of the institution orientation program.

Infection control committee meetings are held quarterly. In these meetings, mortality rates of intensive care units and the relation between mortality and infection are also evaluated. Health personnel trainings are organized in line with the recommendations of the infection control committee, especially during periods of increased infection rates or outbreaks, and environmental scans are carried out in units that are considered to be outbreaks.

In this study, out of the cases aged 0-18 years and hospitalized in the pediatrics clinics of our hospital between February 2014 and December 201, those with *Ralstonia picketti* growth in their blood, catheter, other sterile body fluids, and/or tracheal aspirate fluid, and urine cultures were examined. Those who were found to have growth in their blood and/or catheter cultures were included in the study. Data such as clinical findings (admission diagnosis, comorbid disease), laboratory data, infection risk factors (central venous catheter, urinary catheter, intubation status, total parenteral nutrition intake, etc.), mortality status of these cases were evaluated. The relation between *Ralstonia pickettii* reproduction and outbreak was investigated.

In our study, a single episode was evaluated in patients who developed more than one episode of bacteremia. Cases with reported growth were followed up in the isolation room, following isolation precautions. Colonization status was defined as the presence of proliferating microorganisms in a culture area but the absence of inflammation in the host. Infection was defined as the presence of proliferating microorganisms and the presence of inflammation in the host.

Bacteria identification and antibiotic susceptibility tests are performed in the BD Phoenix 100 (Becton Dickinson, USA) system in the bacteriology laboratory of our hospital. Antibiotic susceptibility tests are performed according to EUCAST (European Committee on Antimicrobial Susceptibility Testing) recommendations (7-9).

CDC (Centers for Disease Control and Prevention, USA) criteria were used for definitions (10-11). Re-isolation of the same organism from the same source from a patient was considered a single episode. The isolation of more than one microorganism in a bacteremic episode was termed polymicrobial bacteremia. Contaminant bacterial growth in the blood culture, lack of clinical significance and negative acute phase reactants were considered as contamination.

Ethics Committee approval was received from Uludağ University Faculty of Medicine Clinical Research Ethics Committee (Decision no: 2018-3/22, Date: 06.02.2018).

SPSS 17.0 program was used for statistical analysis. Descriptive statistics were given as mean, standard deviation, median, minimum and maximum. In comparison of the data, the "paired samples T test" was used for normally distributed variables in dependent groups, and "non-parametric Wilcoxon test" was used for the variables that did not show normal distribution. In order to compare the difference between three or more independent means in a normally distributed series, one-way analysis of variance (Anova) was used in normally distributed series and Kruskal Wallis analysis was used in the non-normally distributed series. In statistical comparisons, the level of significance was determined as $p< 0.05$.

Results

Between February 2014 and December 2017, *R. pickettii* growth was detected in a total of 35 patients, in 38 different episodes, and in 57 blood cultures. *R. pickettii* overgrowth occurred in two different episodes in three patients during different hospitalization periods. More than one reproduction occurred in eight (21%) of a total of 38 episodes. In eight episodes in which *Ralstonia pickettii* was re-isolated, mean reproduction number was 3 ± 1.5 (median 2.2-6). Of the 57 cultures, 67% (n= 38) were peripheral blood cultures, 33% (n= 19) were blood cultures taken from the catheter, and 74% (n= 42) of the samples were considered significant. Of the 38 episodes, 63% (n= 24) were considered significant and 37% (n= 14) were considered as contamination. Colonization was accepted because of the absence of clinical findings in six catheter blood cultures, and cultures of these cases were taken on the day of insertion of the catheter (Table 1).

Demographic and clinical data of the patients are shown in Table 2.

First 30-day mortality was observed in three (8%) patients, and polymicrobial growths of *B. cepacia*, *R. pickettii* and *S. maltophilia* were detected in all three. This polymicrobial growth was observed in the blood cultures of a total of 11 patients, 10 of which were considered clinically significant, and three patients (27%) died. Polymicrobial growth of *Burkholderia cepacia*, *R. pickettii* and *S. maltophilia* was found to be associated with mortality (p= 0.018). When mortality risk factors associated with *Ralstonia pickettii* were compared, it was observed that there was no significant difference between the two groups although the number of data was low (Table 3).

While *R. pickettii* was the sole agent in 16 (28%) of the 57 specimens with growth of *R. pickettii*, growth was polymicrobial in the remaining 41 (72%) cultures. Among these, the most common accompanying microorganisms were *Stenotrophomonas maltophilia* (44%, n= 25), *Burkholderia cepacia* and other *Burkholderia* species (42%, n= 24), *Acinetobacter lwolfi* (0.2%, n= 1), *Corynebacterium* spp. (0.2%, n= 1), *Achromabacter* species (0.2%, n= 1) and *Comamonas testosteroni* (0.2%, n= 1). Among the cases, there were those with prolonged intubation, but there was no case with prior microorganism growth belonging to the *Burkholderia* spp. family in respiratory tract cultures. There was no case diagnosed with cystic fibrosis.

Table 1. Number of patients, episodes and *Ralstonia pickettii* bacteremia growth

	Total n (%)	Significant	Contamination/Colonization
Number of patients Number of patients detected with more than one growth	35 (100) 3 (9)		
Number of episodes Number of episodes detected with more than one growth	38 8 (21)	24 (63)	14 (37)
Blood culture	57 (100)		
Peripheral	38 (67)	29	9
Catheter	19 (33)	13	6

Table 2. Some clinical and demographic characteristics of the patients

	Median (min-max)	n (%)
Total number of patients		35 (%100)
Age (months)	7 (0-180)	
Sex (male)		20 (%57)
Number of patients in the ICU[a]		32 (%91)
Length of hospital stay (day)	37 (9-210)	
Length of stay with growth (day)	9 (0-165)	
Major comorbidity[b]		
CHD		12 (%34)
Cerebral palsy		6 (%18)
Metabolic disease		4 (%11)
Prematurity		4 (%11)
Malignancy		3 (%9)
Immune deficiency		2 (%6)
Other		4 (%11)
Mortality due to growths[c]		3 (%8)

Min: Minimum, Max: Maximum, Med: Median, ICU: Intensive care unit, CHD: Congenital heart disease.
[a]Includes total number of patients in the pediatric intensive care and neonatal intensive care units.
[b]All patients had a major comorbidity.
[c]First 30-day mortality.

At the time the cultures were taken, 31 (81%) of 38 episodes were hospitalized in the pediatric intensive care unit, four (10%) in the neonatal intensive care unit, two (6%) in the pediatric health and diseases clinic, and one (3%) in the pediatric hematology and oncology clinic.

Of 38 episodes, 58% (n= 22) had a central venous catheter, of which 64% (n= 14) developed a catheter-related bloodstream infection due to *R. pickettii*. The catheters of the patients who developed catheter-related bacteremia were removed. Colonization was accepted due to the absence of clinical findings in six catheter blood cultures. According to CDC diagnostic criteria, 48 hours must elapse from the day of insertion of the catheter to be considered a catheter-related bloodstream infection. Catheter blood cultures considered colonized were obtained on the day of insertion of the catheter. In addition, cultures were not considered significant since the cases did not have clinical signs and symptoms of infection and laboratory acute phase symptoms were negative.

Of the cases, 79% (n= 30) had a nasogastric tube, 21% (n= 8) had a urinary catheter, 76% (n= 29) were being followed on an intubated mechanical ventilator, 29% (n= 11) were receiving TPN, and 2% (n= 1) were neutropenic.

Antimicrobial susceptibilities of the strains are given in Table 4. All strains tested for ampicillin sulbactam, amoxicillin clavunate, ceftriaxone, aztreonam and colistin were found to be 100% resistant to these antibiotics. The strains were 100% susceptible to cefepime and levofloxacin, 94% to piperacillin-tazobactam, 88% to ciprofloxacin, 70% to imipenem, 50% to ceftazidime 50%, and 40% to meropenem.

It was determined that *R. pickettii* clustered in certain periods in 23 (61%) of 38 episodes. Clusters were all observed in the PICU. When these periods were examined in detail, it was determined that the first clustering was in six patients in total in the pediatric intensive care unit between October and December 2015 (Figure 1). When this cluster was examined, three of the patients had CVC, five had a nasogastric (NG) tube, three had a urinary catheter, one was receiving TPN, and six patients were intubated. Five cultures were considered significant associated with the infection. Antibiogram characteristics of the growths were similar, and they were thought to be the same isolate. One patient died because of catheter-related bloodstream infection due to polymicrobial growth of *B. cepacia*, *R. pickettii* and *S. maltophilia*. Since the growths were higher than expected and clustered and the isolates had similar antibiograms, the growths were considered as outbreaks. The media was scanned from 70% alcohol, batikon and isotonic 100 cc solutions that were used in common, and no *R. pickettii* was detected in the scans. *S. maltophilia* grew in the heparin sample taken from the intensive care unit. No common source could be identified for *Ralstonia pickettii*.

The second cluster was observed in the pediatric intensive care unit between October-December 2016 and January 2017 (Figure 1). During this period, *R. pickettii* growths were detected in peripheral blood and catheter blood cultures in 10 patients. There was no patient loss. Three patients had CVC

Table 3. Comparison of mortality risk factors associated with *R. pickettii* of the cases with *Ralstonia pickettii* bacteremia

	Mortality (n= 3)	No mortality (n= 32)	p
Male	1 (%33)	19 (%59)	1
Age (median month)	5 months	7 months	1
Ward			
Neonatal intensive care unit	1 (%33)	3 (%9)	0.36
Pediatric intensive care unit	2 (%67)	27 (%82)	1
Other pediatric clinics	0	3 (%9)	1
Bloodstream infection*			
Bacteremia (peripheral blood culture)	1 (%33)	20 (%62)	1
Catheter-related bacteremia	2 (%67)	12 (%38)	0.61
Risk factors			
Central venous catheter	2 (%67)	20 (%62)	1
TPN	2 (%33)	7 (%22)	0.26
Neutropenia	0	1 (%3)	1
NG catheter	3 (%100)	20 (%63)	0.67
Urinary catheter	1 (%33)	7 (%22)	1
Mechanical ventilation	3 (%100)	23 (%72)	1
Use of broad-spectrum antibiotics	2 (%67)	21 (%66)	1
Length of hospital stay longer than 14 days	3 (%100)	11 (%34)	0.33

Table 4. Antimicrobial susceptibility and resistance percentages of *Ralstonia pickettii* strains

	Susceptible (%)	Moderately susceptible (%)	Resistant (%)
Amikacin	12	8	80
Gentamicin	0	0	100
Ceftazidime	50	0	50
Cefepime	100	0	0
Ciprofloxacin	88	0	12
Levofloxacin	100	0	0
Piperacillin tazobactam	94	0	6
Meropenem	40	24	36
İmipenem	70	16	14
Seftriakson	0	0	100
Colistin	0	0	100

and four patients were receiving TPN. Six patients had a history of prior blood transfusion and four patients had a history of prior surgery. All patients were serious patients who required high-level intensive care and had risk factors. Six of the growths were considered significant, and control blood cultures were found without growth in all patients. Antibiogram characteristics of the growths were similar, and they were thought to be the same isolate. MALDI-TOF (Matrix assisted laser desorption ionization time of flight massspectrometry) was performed for confirmation of stored samples that could be reproduced in the laboratory environment. However, further examination could not be performed with pulsed field gel electrophoresis (PFGE) to show clonal similarity. Culture analyzes of heparin, batikon solution, chlorhexidine solution and tap water taken while investigating the cause of the outbreak and used for the patient did not detect any growth. Some bacterial growths (coagulase negative *staphylococcus*, *Bacillus* species, *Enterobacter cloacae*) were detected from environmental cultures.

In December 2017, a total of 52 patients were followed up in the pediatric intensive care unit, and it was observed that 13% of the annual patient population was followed up in this period. It was observed that the number of hospitalized patients increased during the period when the reproduction was

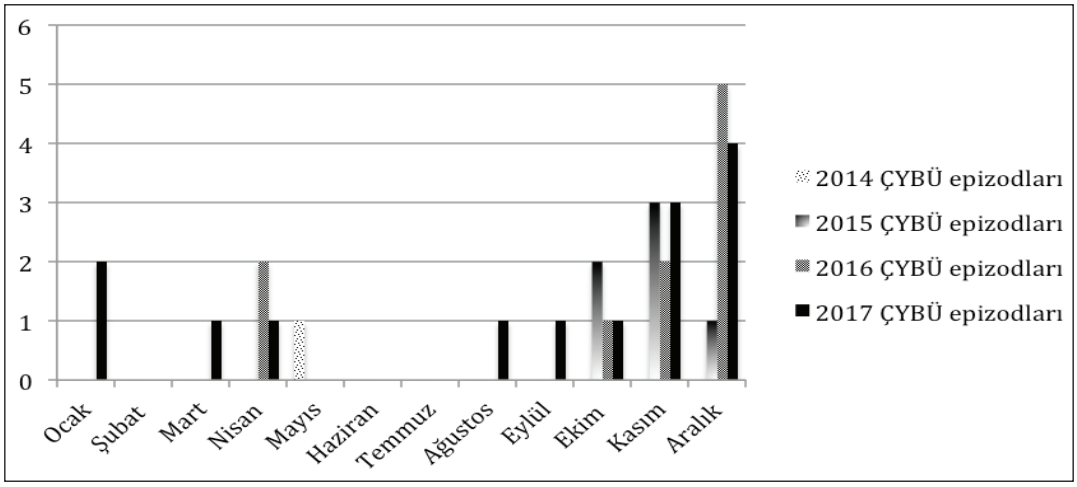

Figure 1. 2014-2017 pediatric intensive care unit detected episodes of *R. pickettii* (n= 31, 81%).

highest. The third cluster was seen in the pediatric intensive care unit in seven patients between November and December 2017 (Figure 1). During this period, five reproductions were evaluated as catheter-related bloodstream infections and were considered significant, and two reproductive colonizations were counted. One patient died because of catheter-associated bloodstream infection due to *B. cepacia*, *R. pickettii* and *S. maltophilia* strains. During this period, six patients had a central venous catheter, six patients had an intubation tube, seven patients had an NG catheter, one patient had a urinary catheter, and one patient was receiving TPN. Antibiogram characteristics of the growths were similar, and they were thought to be the same isolate.

Discussion

In our study, no increase in mortality was detected during the outbreak periods in mortality rate calculations, and the number of hospitalized and deceased patients in three-month periods was similar in the year-to-year comparison. In December 2017, a total of 52 patients were followed up in the pediatric intensive care unit, and it was observed that 13% of the annual patient population was followed up in this period. It was observed that the number of hospitalized patients increased during the period when the reproduction was highest. In all these periods, health personnel trainings were organized in line with the recommendations of the infection control committee, and environmental scans were carried out in units that were thought to have an outbreak. In our intensive care unit, the patient/nurse ratio was found to be over three, and it was aimed to avoid the use of central venous catheters, to pay attention to catheter care, and to ensure that the patient/nurse ratio was two.

Ralstonia pickettii bacteria can colonize in medical materials such as physiological saline, water for injection, and distilled water and cause infections (1-4). The use of these substances in the ventilator, humidifier, NG catheter and urinary catheter for irrigation, as well as the immunosuppression status of the patients such as neutropenia may predispose to infection. In our study, 79% (n= 30) of the patients had an NG catheter, 21% (n= 8) had a urinary catheter, 76% (n= 29) were intubated and followed on mechanical ventilator, 29% (n= 11) were receiving TPN, and 2% (n= 1) were neutropenic. Although the number of data is low, these risk factors were not shown to increase mortality (Table 3).

Various outbreaks, bacteremia and pseudobacteremia or localized organ involvement due to *Ralstonia pickettii* have been reported in the world (5,12). In an adult study published by Chen et al. published in 2017, an outbreak was observed due to physiological saline contamination in a total of 57 positive *R. pickettii* specimens in 30 patients, and it was proven that the epidemic was related to a molecularly similar isolate (4). In a different study by Stelzmueller et al., *R. pickettii* caused bacteremia and pneumonia in 38 patients with a median age of 35 (1.4-81), and the source could not be determined (13). Similar to our study, the resistance of the strains to aminoglycosides was found to be higher than 60%, and the resistance to ciprofloxacin was found to be low by 17% (13). In our study, aminoglycoside (amikacin, gentamicin) resistance was found 80% and above, ciprofloxacin resistance was 12%.

In another four-center study, 34 cases, 29 of which were children and five of which were adults, were affected and a 0.9% serum physiologic outbreak was observed, and five (15%) cases, three of whom were children, were lost (14). Mortality rates are higher compared to our study. In a study by Kimura et al., *R. pickettii* bacteremia and pneumonia due to heparin vial were observed in 18 newborns, and there was no patient loss (15). In the *R. pickettii* epidemic that occurred in three centers in Spain in 1993, nosocomial infections related to the use of intravenous ranitidine were reported (16). There are pediatric case reports or original studies with fewer patients (12,17,18).

In Türkiye, two pediatric oncology cases that caused catheter-related bacteremia and resolved with removal of the catheter and antibiotic therapy have been published (19). In an editorial letter written by Kendirli et al., *R. pickettii* growth has been detected in distilled water used in ventilator air humidifiers (20).

In a study by Demirdağ et al. in 2019, *R. pickettii* catheter-related blood stream infection was detected in 11 febrile neutropenic children in the pediatric hematology unit, and it was documented that they were the same clone as PFGE and associated with an outbreak. In addition, the growth of *R. pickettii* in saline solution was shown in the media scan. Unlike our study, molecular analysis could be performed and no mortality was observed due to this low virulence bacterium (21).

The limitation of our study is that the similarity of *R. pickettii* isolates and their association with an outbreak could not be made by molecular methods such as PFGE. During the study preparation process, the isolates stored in the microbiology laboratory were reproduced and redefined with MALDI-TOF. Molecular study was attempted in PFGE, which was planned to be made for the clonal similarities of the strains, but this analysis could not be carried out due to the lack of growth in most strains and the inability to sample for the molecular method planned for the growing strains. In our study, reproduction in the intensive care was associated with an outbreak due to the fact that *R. pickettii* strains were a factor other than conventional factors, there was an increase in *R. pickettii* reproductions especially in intensive care units at similar times, and the strains that grew had similar antibiograms.

Conclusion

Our study was the largest series reported in pediatric cases in Türkiye and in the world. Although *Ralstonia pickettii* has low virulence, it can cause hospital-acquired bloodstream infections and lead to outbreaks, especially in intensive care units. In our study, the first 30-day mortality rate (n= 3, 8%) was found to be low. Eighty-one percent of the reproductions were in the pediatric intensive care unit, and 61% of them were associated with the outbreak. In this article, the importance of hospital infection control measures in the prevention of *R. pickettii* and similar outbreaks is emphasized. A limited number of studies have been conducted on this subject in Türkiye, and we believe that our study will contribute to the literature.

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Informed Consent: Patient consent was obtained.

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