Original Investigation / *Özgün Araştırma*

DOI: 10.5578/ced.20250402 • *J Pediatr Inf 2025;19(4):e228-e232*

Salmonella Bacteremia and Antibiotic Resistance Profile in Pediatric Patients at a Tertiary Care Hospital

Üçüncü Basamak Bir Hastanede Çocuk Hastalarda *Salmonella* Bakteriyemisi ve Antibiyotik Direnç Profili

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Cite this article as: Çetin FT, Çay Ü, Bakanoğlu E, Ünal A, Oğuz G, Kılınç F, et al. *Salmonella* bacteremia and antibiotic resistance profile in pediatric patients at a tertiary care hospital. J Pediatr Inf 2025;19(4):e228-e232.

Abstract

Objective: This study aims to investigate the demographic and clinical characteristics, as well as the antibiotic resistance profiles, of pediatric patients diagnosed with *Salmonella* bacteremia in a tertiary care hospital.

Material and Methods: This cross-sectional retrospective study included pediatric patients under the age of 18 with positive blood cultures for *Salmonella* spp. at Çukurova University Balcalı Hospital between September 2016 and February 2025. Sociodemographic and clinical data of the patients, serogroup distribution of *Salmonella* isolates, and antibiotic resistance profiles were recorded.

Results: A total of 16 patients were included, with a median age of 65.4 months (range= 8-204 months); 4 (25%) were female, and 12 (75%) were male (F/M ratio= 1:3). Nine (56.25%) patients were under five years of age, and 7 (43.75%) were five years or older. The most common symptom was fever (75%). Seasonal distribution showed that 6 (37.5%) cases occurred in summer, 3 (18.75%) in autumn, 5 (31.25%) in winter, and 2 (12.5%) in spring. The majority of patients (81.25%) had underlying immunodeficiency or hematologic-oncologic conditions. Among the *Salmonella* spp. isolates, one was identified as serogroup B, four as serogroup C, and four as serogroup D; serogroup typing was not performed in seven cases. The highest number of *Salmonella* bacteremia cases occurred in 2019. Antibiotic resistance rates were as follows: ampicillin (54.5%), ceftriaxone

Öz

Giriş: Bu çalışmanın amacı, üçüncü basamak bir hastanede *Salmonella* bakteriyemisi tanısı alan çocuk hastaların demografik ve klinik özellikleriyle antibiyotik direnç profilini incelemektir.

Gereç ve Yöntemler: Bu kesitsel retrospektif çalışmaya, Eylül 2016 ve Şubat 2025 tarihleri arasında Çukurova Üniversitesi Balcalı Hastanesi kan kültüründe *Salmonella* üremesi olan 18 yaş altı çocuk hastalar dahil edilmiştir. Hastaların sosyodemografik, klinik özellikleri, *Salmonella* suşlarının serotip dağılımı, antibiyotik direnç profili kaydedilmiştir.

Bulgular: Çalışmaya ortanca yaşı 65.4 ay (8-204 ay) olan 4 (%25)'ü kadın, 12 (%75)'si erkek (E/K= 3) olan toplam 16 hasta dahil edildi. Hastaların 9 (%56.25)'u beş yaş altında, 7 (%43.75)'si beş yaş ve üzeriydi. En sık görülen bulgu (%75) ateşti. Mevsimlere göre 6 (%37.5) hastada yaz, 3 (%18.75) hastada sonbahar, 5 (%31.25) hastada kış, 2 (%12.5) hastada ilkbaharda üreme vardı. Hastaların çoğuna (%81.25) immün yetmezlik veya hematolojik-onkolojik hastalık eşlik ediyordu. *Salmonella* spp. tiplendirilmesinde birinde serogrup B, dördünde serogrup C, dördünde serogrup D üremiş olup yedisinde tiplendirme yapılmamıştı. Yıllara göre *Salmonella* spp. kan üremesi en sık 2019 yılında görüldü. İzole edilen *Salmonella* spp.'de ampisilin direnci %54.5, seftriakson direnci %50.0, siprofloksasin direnci %50.0, trimethoprim sulfametaksazol direnci %6.25, meropenem direnci %6.25 olarak saptandı. Hastaların tedavide daha sık meropenem,

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Received: 26.07.2025 **Accepted:** 21.09.2025
Available Online Date: 25.12.2025

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

(50.0%), ciprofloxacin (50.0%), trimethoprim-sulfamethoxazole (6.25%), and meropenem (6.25%). The most frequently used antibiotics in treatment were meropenem, ceftriaxone/cefotaxime, and ciprofloxacin. Three patients (18.75%) died during hospitalization.

Conclusion: *Salmonella* remains a common cause of bloodstream infections in developing countries and is often clinically indistinguishable from other febrile bacteremia pathogens. It is associated with high mortality, especially in immunocompromised and hematologic-oncologic pediatric patients. Increasing rates of antibiotic resistance in recent years have further complicated treatment protocols. Therefore, expanded studies focusing on serogroup identification and antibiotic resistance profiles are urgently needed.

Keywords: *Salmonella* spp. infections, antibiotic resistance, bacteremia, child

seftriakson/sefotaksim ve siprofloksasin kullanıldığı görüldü. Üç (%18.75) hastanın hayatını kaybettiği saptandı.

Sonuç: *Salmonella*, gelişmekte olan ülkelerde kan dolaşımı enfeksiyonlarının yaygın nedenlerinden biridir. Diğer ateşli seyreden bakteriyemi nedenlerinden ayırt edilmeleri zordur. Özellikle immün yetmezlik ve hematolojik-onkolojik hastalarda yüksek ölüm oranı ile ilişkilidir. Son yıllarda antibiyotik direnç oranlarının da artmasıyla beraber tedavi rejimleri zorlaşmaktadır. Bu nedenle serogrup tayini, antibiyotik direnç profili ile ilgili daha çok çalışmaya gereksinim vardır.

Anahtar Kelimeler: *Salmonella* spp. enfeksiyonları, antibiyotik direnci, bakteriyemi, çocuk

Introduction

Salmonella is a pathogen transmitted primarily through contaminated food or water, and it is responsible for over 150.000 deaths annually (1,2). Common sources of *Salmonella* infection include eggs, poultry, meat products, raw or unpasteurized dairy, and inadequately cooked fruits and vegetables (3). Clinical symptoms typically include abdominal pain, diarrhea, nausea, vomiting, fever, and headache. *Salmonella* can cause a range of infections, including enteric fever (a systemic illness characterized by fever and abdominal symptoms), gastroenteritis, bacteremia, endovascular infections, osteomyelitis, abscesses, and chronic asymptomatic carrier states. Severe infections such as meningitis and bacteremia may occur in patients with sickle cell anemia, asplenia or splenic dysfunction, immunodeficiencies, malignancies, human immunodeficiency virus infection, or those receiving immunosuppressive therapies. Diagnosis is primarily based on the culture of the causative organism, although serological tests may be used for diagnosing enteric fever. Treatment options include third-generation cephalosporins, azithromycin, and fluoroquinolones (2,4).

Salmonella infections can be more severe, especially in patients with compromised immune systems. Appropriate empirical treatment remains crucial. Therefore, our study aimed to determine the demographic, clinical characteristics, and antibiotic resistance status of patients with *Salmonella* bacteremia.

Materials and Methods

Study Protocol

This study included pediatric patients aged 18 years and younger with *Salmonella* spp. growth in blood culture between September 1, 2016, and February 1, 2025. Data were retrospectively obtained from medical records and the microbiology laboratory. The sociodemographic and clinical characteristics of the patients, as well as the antibiotic resistance profile of the isolated strains, were recorded. Ethical approval for this study was obtained from the Ethics Committee of Çukurova University (Date: 16.05.2025, Decision no: 155).

Microbiology

Blood cultures were incubated for five days in the BD Bactec FX blood culture system (Becton, Dickinson, Franklin Lakes, NJ). Samples were taken from blood culture bottles showing positive signals, and both Gram staining and inoculation onto 5% sheep blood agar, chocolate agar, and MacConkey agar were performed. Plates were incubated at 37 °C for 24-48 hours. Gram staining and oxidase tests were performed on colonies growing on the media, for the identification of gram-negative bacteria, fully automated VITEK-2 system gram-negative bacteria identification (GN-ID) cards (Biomerieux, France) were used. For bacteria identified as *Salmonella* using the VITEK-2 system, serotyping was performed using polyvalent and monovalent *Salmonella* antiserums. Denka Seiken (Tokyo, Japan) *Salmonella* Antisera Set 1 (2 mL x 18; Code: 293855) was used.

Statistical Analysis

In statistical analysis, categorical measurements were summarized as numbers and percentages, while numerical measurements were summarized as mean and standard deviation, median, and 25th and 75th percentiles. Chi-square test statistic was used to compare categorical measurements between groups. IBM SPSS Statistics version 20.0 software was used for the statistical analysis of the data. The statistical significance level was set at 0.05 for all tests (5).

Results

Of the 16 patients with *Salmonella* spp. growth in blood culture, 4 (25%) were female and 12 (75%) were male. According to age distribution, 5 (31.25%) patients were aged 0-2 years, 4 (25%) were aged 2-5 years, and 7 (43.75%) were aged 5-18 years. Thirteen (81.25%) patients had underlying chronic conditions. Of these, six had malignancy, and seven had immunodeficiency (Table 1). Six (37.5%) patients were admitted to the pediatric hematology and oncology department, 2 (12.5%) to the pediatric infection department,

Table 1. Distribution of underlying diseases

Underlying Disease	n (%)
Hodgkin lymphoma	1 (6.25)
Acute leukemia	4 (25.0)
Hemophagocytic lymphohistiocytosis	1 (6.25)
Chronic granulomatous disease	2 (12.50)
Severe combined immunodeficiency	1 (6.25)
Severe combined immunodeficiency + BMT	1 (6.25)
Thalassemia major + BMT	1 (6.25)
Chronic granulomatous disease + BMT	1 (6.25)

BMT: Bone marrow transplantation.

Table 2. *Salmonella* strains serogroup distribution

Salmonella spp. Serogroup	n (%)
Group B	1 (6.25)
Group C	4 (25.0)
Group D	4 (25.0)
Untypeable	7 (43.75)

6 (37.5%) to other pediatric departments, and 2 (12.5%) to the pediatric intensive care unit. None of the patients had asplenia, splenic dysfunction, sickle cell anemia, or carriage of *Salmonella* spp.

The findings observed in patients were primarily fever (75%), followed by diarrhea (18.75%), convulsions (6.25%), and epididymoorchitis (6.25%). According to seasons, 6 (37.5%) patients had reproduction in summer, 3 (18.75%) in autumn, 5 (31.25%) in winter, and 2 (12.5%) in spring. In only 1 (6.25%) of all patients, *Pseudomonas aeruginosa* growth was present in addition to *Salmonella* spp. growth. *Salmonella* spp. growth was detected simultaneously in the peripheral blood culture and central venous catheter culture of 1 (6.25%) patient and in the blood and stool of 2 (12.5%) patients. In the typing of *Salmonella* spp., serogroup B was isolated in one case, serogroup C in four cases, and serogroup D in four cases, while typing was not performed in 7 (43.75%) cases (Table 2). The highest incidence was observed in 2019 (Figure 1). laboratory values of the patients are also presented in Table 3. The average time between hospitalization and culture growth was 3.75 days (range: 1-20 days). Patients received an average of 15.6 (1-23) days of treatment. The average time to negative blood culture after treatment was 3.4 (2-13) days. The most used antibiotics in treatment were meropenem, ceftriaxone/cefotaxime, and ciprofloxacin.

Table 3. Laboratory values of patients

WBC/µL	7198.1 ± 10562.9
ANS/µl	4300 ± 7800.4
ALS/µL	700 (27.5-3625)
Hemoglobin g/dL	9.5 ± 2.3
Platelet/µL	93062.5 ± 93562.4
CRP (mg/L)	111.8 ± 74.5
Procalcitonin ng/mL	1.6 (0.7-10)
AST U/L	45.5 (31.5-224.3)
ALT U/L	52.5 (17.3-113)
BUN mg/dL	14.3 ± 12
Creatinine mg/dL	0.4 ± 0.4
Albumin g/dL	29.8 ± 7.8

Data are expressed as either the mean ± standard deviation or the median (IQR_{25-75}), as appropriate according to distribution.
WBC: White Blood Count, ANS: Absolute neutrophil count, ALS: Absolute lymphocyte count,CRP: C-reactive protein, AST: Aspartate transaminase, .

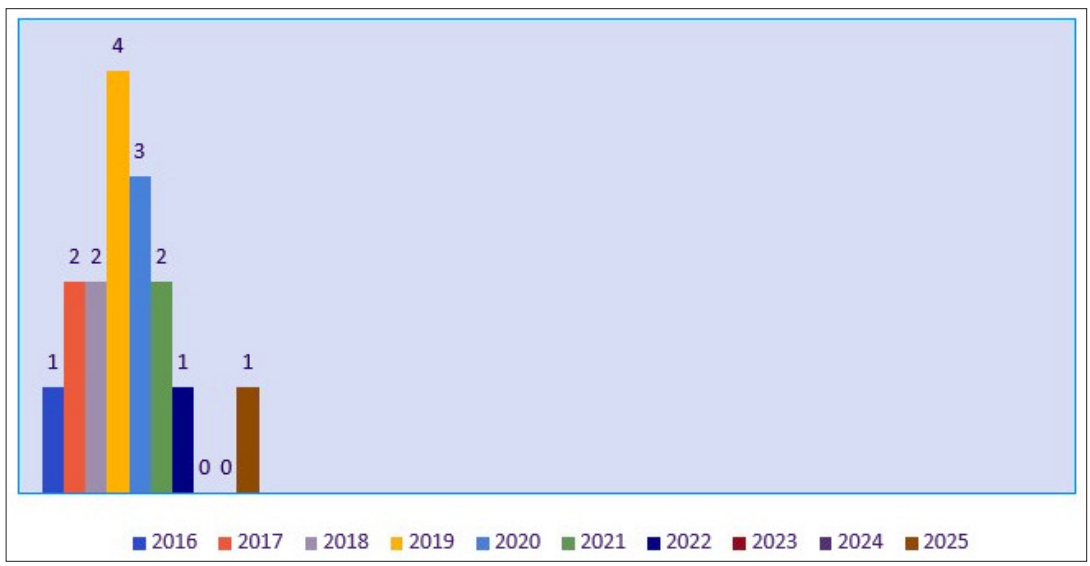

Figure 1. *Salmonella* spp. reproduction frequency.

Table 4. Antibiotic resistance rate of *Salmonella* strains grown in blood cultures

Antibiotic	Resistance Percentage (%)
Gentamicin	92.85
Amikacin	87.50
Ampicillin	54.50
Ceftriaxone	50.00
Amoxicillin-clavulanate	50.00
Ciprofloxacin	50.00
Ceftazidime	33.33
Piperacillin-tazobactam	15.40
Trimethoprim-sulfamethoxazole	6.25
Meropenem	6.25
Imipenem	0.00

Three (18.75%) patients were found to have died. While two of these patients received appropriate treatment, one died before the results of the blood culture for *Salmonella* spp. were finalized. Of the three patients who died, one had severe neutropenic Hodgkin lymphoma, one had severe neutropenic acute leukemia, and one had thalassemia major with mild neutropenia and had undergone bone marrow transplantation. The patient with mild neutropenia and thalassemia major who had undergone bone marrow transplantation had *Salmonella* spp. growth in both blood and catheter, while the patient with severe neutropenic Hodgkin lymphoma had growth of *Salmonella*, accompanied by *P. aeruginosa*. In the *Salmonella* typing of the deceased patients, two were identified as serogroup D, and one could not be typed. The deceased patient with *Salmonella* spp. growth in both blood and catheter was also identified as serogroup D.

When examining antibiotic resistance profiles of *Salmonella* species, it was found that four were susceptible to ceftriaxone, four were resistant, eight were susceptible to ciprofloxacin, eight were resistant, 15 were susceptible to meropenem, one was resistant, four were susceptible to amoxicillin-clavulanate, and four were resistant. Imipenem resistance was studied in five of 16 patients and all isolates were found to be susceptible to imipenem and meropenem. Resistance rates are presented in Table 4. No significant difference was found between ciprofloxacin, meropenem, amoxicillin-clavulanate, gentamicin resistance and patients with leukemia, lymphoma, immunodeficiency and bone marrow transplantation (p values 0.200, 0.437, 0.429, >0.999, respectively).

Discussion

Salmonella is a common cause of bloodstream infections in developing countries. It is difficult to distinguish it from other causes of febrile bacteremia and is associated with a high mortality rate (6). In our study, 16 cases of *Salmonella* bacteremia were identified over nine years, with a mortality rate of 18.75%. Although *Salmonella* spp. most commonly causes gastroenteritis in children, it poses a serious risk of bacteremia in patients with underlying immunodeficiency or hematological-oncological diseases (7). Patients with impaired cellular immunity, those receiving immunosuppressive therapy, and those who have undergone lymphoproliferative organ or bone marrow transplantation are at risk, and 81.25% of our patients fell into this group (8). A study has reported that *Salmonella* infection causes longer-lasting fever and longer hospital stays in immunocompromised children compared to healthy children (9).

Although *Salmonella* infection typically presents as gastroenteritis with symptoms such as nausea, vomiting, diarrhea, fever, and abdominal cramps, there are also reports of *Salmonella* species causing epididymoorchitis (10,11). In our study, 75% of patients had fever, and 18.75% had diarrhea. One patient also had epididymo-orchitis.

In our study, *Salmonella* serogroups C and D were the most common in the classified group. In another study, serogroup A was the most common, followed by serogroup B, serogroup C, and serogroup D, with serogroup A accounting for 25.7% (7). In a study conducted in Saudi Arabia, serogroup D was the most common (37%) (12). In a study by Tang and colleagues, 75% of the four adult patients with catheter-associated *Salmonella* infection were serogroup D, and 25% were serogroup C (13). In our study, the patient with catheter-associated *Salmonella* infection was serogroup D.

In our study, ampicillin resistance was found to be 54.5%, ceftriaxone resistance 50.0%, ciprofloxacin resistance 50.0%, trimethoprim-sulfamethoxazole resistance 6.25%, and meropenem resistance 6.25% in the isolated *Salmonella* spp. When examining ciprofloxacin resistance, it was found to be 100% in serogroup B, 75% in serogroup C, and 50% in serogroup D. In a study conducted in our country in 2012 on pediatric patients, resistance to ampicillin, trimethoprim-sulfamethoxazole, ceftriaxone, and ciprofloxacin was determined to be 25.8%, 7.0%, 4.7%, and 0.3%, respectively (14). In a study conducted in Kuwait, approximately one-quarter of *Salmonella* isolates were found to be multidrug-resistant (15). In a study by Xu and colleagues, 85.2% of *Salmonella* isolates isolated from patients were found to be multidrug-resistant (16). In our study, 31.25% were found to be multidrug resistant (MDR). Gentamicin resistance was found in 92.85% of patients. *Salmonella* spp. can form biofilms and develop resistance to gentamicin. Furthermore, the efflux pump found in *Salmonella* spp. can excrete gentamicin and amikacin and induce resistance (17). In our study, resistance to ceftriaxone and ciprofloxacin was observed to be much lower than to gentamicin. Third-generation cephalosporins and fluoroquinolones should be preferred for empirical treatment, and treatment should be adjusted according to the antibiogram during follow-up. In particular, the emergence of

Salmonella strains resistant to multiple antibiotics, particularly in recent years due to the widespread use of antibiotics, has made it challenging to select effective antibiotics for treatment. In MDR-*Salmonella* infections, especially in invasive cases (e.g., sepsis and meningitis), the ineffectiveness of empirical treatment protocols reduces treatment success. Infections caused by resistant strains can be more severe, require longer treatment periods, increase costs, and increase morbidity and mortality rates. This complicates treatment and leads to longer duration of infections, increased complications, and a greater burden on the healthcare system. MDR-*Salmonella* infections are generally transmitted to humans through contaminated animal products (meat, milk, eggs). This can cause widespread outbreaks. The uncontrolled use of antibiotics in animal husbandry triggers the emergence of MDR-strains. This poses a threat to both animal health and human health. MDR-*Salmonella* strains cross borders through food trade and international travel, becoming a global public health problem (18,19).

Conclusion

Salmonella spp. is an agent that can be invasive enough to require hospitalization and can cause death, especially in patients with immunodeficiency and hematological-oncological diseases. With increasing rates of antibiotic resistance in recent years, treatment regimens have become more challenging. Therefore, there is a need for more studies on serogroup identification and antibiotic resistance profiles. The sample size in our study was limited, which was the limitation of the study. Multicenter studies are needed to determine the correct empirical treatment.

Ethics Committe Approval: This study was approved by the T.C. Çukurova University Faculty of Medicine Clinical Research Ethics Committee (Decision no: 155, Date: 16.05.2025).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - FTÇ, ÜÇ, EB, ÖÖG, DA; Design - FTÇ, ÜÇ, ÖÖG, DA, AÜ; Supervision - FTÇ, ÜÇ, ÖÖG, DA; Resource - FTÇ, EB, AÜ, GO, FK; Data Collection and/or processing - FTÇ, ÜÇ, EB, AÜ, GO, FK; Analysis and/or interpretation - FTÇ, ÜÇ, FK, NT, ÖÖG, DA; Literature search - FTÇ, ÜÇ, EB, AÜ, FK, FK; Writing - FTÇ, ÜÇ, NT, FK; Critical review - All of authors.

Conflict of Interest: All authors declare that they have no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

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