



The Impact of the COVID-19 Pandemic on Bloodstream Infections in Hospitalized Patients

COVID-19 Pandemisinin Hastanede Yatarak Tedavi Gören Hastalarda Kan Dolaşımı Enfeksiyonlarına Etkisi

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ABSTRACT

Introduction: As a result of stricter adherence to hygiene rules during the coronavirus diseases-2019 pandemic, changes are expected in the epidemiology of infectious diseases in society, especially in etiological agent profiles and frequency rankings. This study aims to compare the microorganisms detected in bloodstream infections in our patients treated during the pandemic with the pre-pandemic period.

Materials and Methods: The study included patients aged ≥ 1 month to ≤ 18 years who were hospitalized in the pediatric ward or pediatric intensive care unit between April 1, 2018, and May 31, 2022, and had positive blood cultures. Pre-pandemic and pandemic period data were compared statistically.

Results: Of the patients included in the study, 129 (72.9%) were from the pre-pandemic period, and 48 (27.1%) were from the pandemic period. The most common reasons for hospitalization in both periods were lower respiratory tract infection and gastroenteritis. The most common comorbid conditions were cerebral palsy, immunodeficiency, and epilepsy. When all cases were evaluated together, it was determined that 25% of the cases received mechanical ventilation, 16% had a central venous catheter, and 6% had a ventriculoperitoneal shunt. The most frequently isolated causative agents in both periods were coagulase-negative staphylococci.

Conclusion: In our center, it was observed that the pandemic did not affect the causative microorganisms' profile in bloodstream infections. Although coagulase-negative staphylococci are the most common causative agents in catheter-related bloodstream infections, they are also frequently responsible for contamination. Clinical interpretation is important. Regular microbial monitoring is necessary to effectively control infections, and every healthcare center should undertake this responsibility.

Key Words: COVID-19; Bloodstream infection; Pandemic; Microbiological surveillance

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ÖZ

COVID-19 Pandemisinin Hastanede Yatarak Tedavi Gören Hastalarda Kan Dolaşımı Enfeksiyonlarına EtkisiŞeyma KESKİN¹, Mustafa AKÇAM², Füsün Zeynep AKÇAM³¹ Süleyman Demirel Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Isparta, Türkiye² Süleyman Demirel Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Gastroenteroloji Hepatoloji ve Beslenme Bilim Dalı, Isparta, Türkiye³ Süleyman Demirel Üniversitesi Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Isparta, Türkiye

Giriş: Koronavirüs hastalığı 2019 pandemisi sürecinde hijyen kurallarına daha sıkı uyulması sonucunda toplumda bulaşıcı hastalıkların epidemiyolojisinde, özellikle etiyolojik etken profillerinde ve sıklık sıralamalarında değişiklikler beklenmektedir. Bu çalışmanın amacı, pandemi döneminde yatarak tedavi gören hastalardaki kan dolaşımı enfeksiyonlarında saptanan mikroorganizmaların pandemi öncesi dönemle karşılaştırılmasıdır.

Materyal ve Metod: 1 Nisan 2018-31 Mayıs 2022 tarihleri arasında çocuk servisinde ve çocuk yoğun bakım ünitesinde yatan, ≥ 1 ay ve ≤ 18 yaş aralığında olan ve kan kültürlerinde pozitiflik saptanan hastalar çalışmaya alındı. Pandemi öncesi ve pandemi dönemi verileri istatistiksel olarak karşılaştırıldı.

Bulgular: Çalışmaya alınan hastaların 129 (%72.9)'u pandemi öncesi dönemde, 48 (%27.1)'i pandemi dönemindeydi. Her iki dönemde de hastaneye yatışların en sık nedenleri alt solunum yolu enfeksiyonu ve gastroenterit idi. En sık eşlik eden hastalıklar serebral palsy, immün yetmezlik ve epilepsi idi. Olguların tümü birarada değerlendirildiğinde %25'inde mekanik ventilasyon uygulandığı, %16'sında santral venöz kateter ve %6'sında ventriküloperitoneal şant olduğu belirlendi. Her iki dönemde de en sık izole edilen etken koagülaz negatif stafilokoklardı.

Sonuç: Merkezimizde pandeminin kan dolaşımı enfeksiyonlarındaki etken mikroorganizma profili üzerinde bir etkisi olmadığı gözlemlendi. Koagülaz negatif stafilokoklar kateterle ilişkili kan dolaşımı enfeksiyonlarında en sık etken olsa da sıklıkla kontaminasyondan da sorumludur. Klinik yorum önemlidir. Enfeksiyonları etkili bir şekilde kontrol etmek için düzenli mikrobiyal izleme çalışmaları gereklidir ve her sağlık merkezi bu sorumluluğu üstlenmelidir.

Anahtar Kelimeler: COVID-19; Kan dolaşımı enfeksiyonu; Pandemi; Mikrobiyolojik sürveyans

INTRODUCTION

Primary bloodstream infections (BSIs) are defined as laboratory-confirmed infections that are not secondary to another infection site in the body. These cases involve at least one of the following symptoms: fever or hypothermia, chills, or hypotension, along with the isolation of a pathogenic microorganism in a blood culture, without any identifiable infection focus elsewhere in the body^[1].

The epidemiology of BSIs has evolved in recent years due to various factors, including shifts in population demographics, healthcare delivery models, and increased global connectivity^[2]. Among the most impactful events influencing this change was the recent coronavirus diseases-2019 (COVID-19) pandemic. Since the outbreak began in early 2020, strict public health measures worldwide have altered

patterns of pathogen transmission, subsequently affecting the epidemiology of infectious diseases.

First identified in December 2019 in Wuhan, China, the novel coronavirus infection spread rapidly and was declared a global pandemic by the World Health Organization (WHO) on March 11, 2020. As of April 2023, 684.906.699 confirmed cases, 657.635.742 recoveries, and 6.837.598 deaths had been reported globally^[3]. On May 5, 2023, the WHO officially declared that the pandemic no longer constituted a global emergency. Given the widespread implementation of hygiene and infection prevention measures during this time, shifts in the frequency and distribution of infectious diseases were expected—especially in terms of pathogen profiles and ranking.

To evaluate the impact of this global event on our local context, we aimed to compare the

microorganisms responsible for bloodstream infections among hospitalized pediatric patients before and during the COVID-19 pandemic.

MATERIALS and METHODS

Study Population

This study included patients aged ≥ 1 month and ≤ 18 years who were hospitalized in either the pediatric ward or the pediatric intensive care unit (PICU) between April 1, 2018, and May 31, 2022, and had blood cultures positive for gram-positive bacteria (GPB), gram-negative bacteria (GNB), or fungi.

Ethical approval for this study was obtained from our regional clinical research ethics committee on September 28, 2022 (decision number: 263).

Study Periods and Patient Selection

The study was divided into two periods. The pre-pandemic period (PPP) was defined as April 1, 2018, to March 31, 2020, while the pandemic period (PP) was defined as April 1, 2020, to May 31, 2022. The start date corresponds to the first confirmed COVID-19 case in our province.

Primary BSIs were defined as the isolation of a pathogenic microorganism in one or more blood cultures with no evident focus of infection elsewhere in the body. Contamination was defined as the growth of skin flora organisms in only one of multiple blood culture sets without clinical or microbiological evidence of bacteremia.

Patients with blood cultures suggestive of secondary bacteremia, as well as repeated cultures from the same patient within a 14-day interval, were excluded from the analysis.

Demographic information, reasons for hospitalization, comorbidities, and potential BSI risk factors were recorded. Isolated microorganisms were noted.

Microbiological Methods

Bacterial identification was carried out using both conventional methods and the BD Phoenix 100 automated system (Becton-Dickinson, New Jersey, United States of America).

Statistical Analysis

Student's t-test was used for continuous variables with normal distribution. All statistical analyses were performed using SPSS version 29.0 for Windows (IBM Corp., Armonk, NY, USA). Categorical variables were compared using the Chi-square test or Fisher's exact test when expected counts were < 5 . For continuous variables not meeting normal distribution assumptions, the Mann-Whitney U test was applied. A p-value of < 0.05 was considered statistically significant.

RESULTS

During the PPP, a total of 2003 blood cultures were collected from patients hospitalized in the pediatric ward and the PICU of our hospital, compared to 1217 blood cultures collected during the PP. Of these, 316 cultures (10.1%) showed microbial growth-203 in the PPP and 113 in the PP. Following a retrospective review of medical records, 177 patients with complete data and no evidence of contamination were included in the study.

Of the included patients, 129 (72.9%) were from the PPP, and 48 (27.1%) from the PP. The most common reason for hospitalization in both periods was lower respiratory tract infections, with a frequency of 82.2% in the PPP and 41.7% in the PP.

The most frequently observed comorbidities were cerebral palsy (CP), immunodeficiency, epilepsy, squamous cell carcinoma, acute lymphoblastic leukemia, and diabetes mellitus. In the PPP, 22 patients (40%) had CP, 22 (40%) had epilepsy, six (10.9%) had immunodeficiency, and five patients had other comorbidities. In the PP, CP was again the most common comorbidity, followed by immunodeficiency and epilepsy. Notably, two patients (18.2%) in the PP had brucellosis, a condition not observed in the PPP group.

Risk factors for BSIs in this study included the presence of a ventriculoperitoneal (VP) shunt, central venous catheter (CVC), and mechanical ventilation (MV). Patient demographics, hospitalization indications, comorbid conditions, and risk factors are summarized in Table 1. Statistically significant differences between the two periods

Table 1. Sex, age, hospital wards, reasons for admission, comorbid conditions, and risk factors of patients with BSIs in PPP and PP

		PPP (n)	%	PP (n)	%	p
Sex	Female	66	51.2	16	33.3	0.042
	Male	63	48.8	32	66.7	
Age	Mean $\pm$ SD	4.54 $\pm$ 2.00		5.04 $\pm$ 2.50		0.408
	Min-max (median)	0-17 (5)		1-17 (5)		
Clinical Setting	Ward	71	55.0	31	64.6	0.306
	Intensive care	58	45.0	17	35.4	
Reason for Admission						
	Lower respiratory tract infection	106	82.2	20	41.7	0.005
	Gastroenteritis	20	15.5	12	25	0.126
	Urinary tract infection	12	9.3	0	0	0.040
	Cardiac causes	6	4.7	1	2.1	0.682
	Syndromic patients	6	4.7	1	2.1	0.682
	Meningitis	5	3.9	3	6.3	0.417
	Upper respiratory tract infection	3	2.3	2	4.2	0.601
	Soft tissue infection	2	1.6	1	2.1	0.807
	Other	2	1.6	14	25.2	0.005
Comorbid Conditions						
	Cerebral palsy	22	40.0	5	45.4	0.275
	Epilepsy	22	40.0	2	18.2	0.020
	Immunodeficiency	6	10.9	2	18.2	0.890
	Other (SCC, ALL, DM, Brucellosis)	5	8.0	2	18.2	0.271
Risk Factors						
	Mechanical ventilation	37	61.0	8	36.0	0.103
	Central catheter	18	29.5	10	46.0	0.265
	VP shunt catheter	6	9.8	4	18.0	0.346

SD: Standard deviation, SCC: Squamous cell carcinoma, ALL: Acute lymphoblastic leukemia, DM: Diabetes mellitus, VP: Ventriculoperitoneal.

were observed in gender distribution ($p= 0.042$), urinary tract infections ($p= 0.040$), other causes of hospitalization ($p= 0.005$), and the presence of epilepsy ($p= 0.020$).

The mean duration of hospitalization was 20 days (range= 1-180) during the PPP and 18 days (range= 2-81) during the PP ($p= 0.543$). The mean time from hospital admission to the development of BSI was 5.84 ± 15.36 days in the PPP and 4.92 ± 7.14 days in the PP ($p= 0.543$). The average time to microbial growth in cultures was 2.77 ± 1.92 days in the PPP and 3.27 ± 1.39 days in the PP, with this difference reaching statistical significance ($p= 0.018$).

The most frequently isolated pathogen in both periods was coagulase-negative staphylococci (CoNS). The most commonly observed risk factors were CVC and MV. Among patients receiving MV, CoNS was isolated in 35 cultures, *Candida albicans* in three, *Klebsiella pneumoniae* in two, and *Pseudomonas aeruginosa*, *Serratia marcescens*, *Acinetobacter baumannii*, and *Streptococcus* spp. in one each. Among those with CVCs, CoNS was isolated in 21 cultures, *Streptococcus* spp. in two, and *C. albicans*, *P. aeruginosa*, and *S. marcescens* in one each. In patients with VP shunts, CoNS was found in eight cultures, while *Escherichia*

Table 2. Microorganisms isolated from the pediatric ward and PICU during the PPP and PP

	Pre-Pandemic Period			Pandemic Period			p
	Ward	Intensive Care	Total	Ward	Intensive Care	Total	
Pre-Pandemic Period	n	n	n= 129	n	n	n= 48	
Coagulase-negative staphylococci	44	43	87	22	15	37	0.288
<i>Streptococcus</i> species	16	3	19	0	1	1	0.036
<i>Staphylococcus aureus</i>	0	0	0	3	0	3	0.027
<i>Escherichia coli</i>	3	1	4	0	0	0	0.505
<i>Enterococcus faecium</i>	1	2	3	1	0	1	1.000
<i>Candida albicans</i>	1	1	2	0	1	1	1.000
<i>Moraxella</i> species	1	0	1	0	0	0	1.000
<i>Proteus mirabilis</i>	1	0	1	0	0	0	1.000
<i>Citrobacter freundii</i>	1	0	1	1	0	1	0.469
<i>Stenotrophomonas maltophilia</i>	1	0	1	0	0	0	1.000
<i>Streptococcus mutans</i>	1	0	1	0	0	0	1.000
Gram-negative non-fermenter bacilli	1	0	1	0	0	0	1.000
<i>Klebsiella pneumoniae</i>	0	3	3	0	0	0	0.681
<i>Pseudomonas aeruginosa</i>	0	1	1	1	0	1	0.469
<i>Acinetobacter baumannii</i>	0	1	1	0	0	0	1.000
<i>Acinetobacter lwoffii</i>	0	0	0	1	0	1	0.605
<i>Serratia marcescens</i>	0	1	1	0	0	0	1.000
<i>Streptococcus pneumoniae</i>	0	1	1	1	0	1	0.469
<i>Streptococcus pyogenes</i>	0	1	1	0	0	0	1.000
<i>Streptococcus</i> species	0	0	0	0	1	1	1.000
<i>Brucella</i> species	0	0	0	1	0	1	0.605

coli and *Streptococcus* spp. were found in one culture each.

Microorganisms isolated from patients in the pediatric ward and PICU during both study periods are presented in Table 2. When comparing the PPP and PP, statistically significant differences were observed in the isolation of *Streptococcus* species ($p= 0.036$) and *Staphylococcus aureus* ($p= 0.027$).

In the PPP, 113 patients (87.6%) were discharged with recovery, and five patients (3.9%) died. In the PP, 33 patients (68.8%) recovered, while eight patients (16.7%) died.

DISCUSSION

During the COVID-19 pandemic, restrictions on mobility led to a notable decline in hospi-

tal admissions across all age groups, including pediatric patients. One study reported a 68.5% reduction in annual pediatric department visits during the pandemic, with the majority of admissions occurring through emergency departments^[4]. Consistently, our study also found a decrease in both patient numbers and hospital admissions during the pandemic compared to the pre-pandemic period.

While we did not identify any studies comparing pediatric ward and PICU admissions directly, our data showed that 55% of patients were hospitalized in the pediatric ward and 45% in the PICU during the pre-pandemic period. During the pandemic, these proportions shifted to 65% and 35%, respectively. In a study by Söğütü et al., respiratory and neurological

disorders were the most common causes of PICU admission during both periods, whereas Yogaraj et al. additionally reported cardiovascular diseases as frequent admission reasons^[5,6]. In our study, respiratory infections were the most prevalent cause of hospitalization in both periods, regardless of care unit. This aligns with the findings of Aşiloğlu et al., who identified respiratory tract infections, poisonings, and infectious diseases as common reasons for pediatric hospitalization^[7].

Invasive procedures are major risk factors for bloodstream infections (BSIs), largely due to disruption of the host's physical barriers^[8]. According to the National Nosocomial Infection Surveillance system, 91% of pediatric patients with BSIs had central venous catheters^[9]. In our study, 61.0% of children with BSIs were on mechanical ventilation, 29.5% had CVCs, and 9.8% had VP shunts. During the pandemic, both comorbid conditions and BSIs were observed less frequently, which may be attributable to reduced hospital attendance by high-risk patients due to fear of COVID-19 exposure or simply to lower admission rates.

Primary BSIs are usually catheter-related, whereas secondary BSIs are usually associated with hospital-acquired pneumonia, ventilator-associated pneumonia, intra-abdominal infections, urinary tract infections, surgical site infections, or osteoarticular infections^[10,11]. In our study, no other source of infection was detected in patients with primary bloodstream infections. Blood culture results in patients hospitalized with infection were not associated with their current infection. Pneumonia was the most common cause of hospitalization in both periods in our study (82.2% PPP, 41.7% PP). This is consistent with the findings in the literature. For example, in a study conducted in Brazil, the incidence of primary BSI in children hospitalized in the pediatric intensive care unit and diagnosed with pneumonia was over 19%^[12]. These data indicate that children with lower respiratory tract infections should be carefully monitored for BSI.

Jarvis et al. demonstrated a strong positive correlation between ICU length of stay and infection rates in a study involving 165,000 adult and pediatric patients^[13]. Longer hospitalizations

increase exposure to invasive procedures and nosocomial pathogens, further elevating the risk of infection. Our findings are consistent with this, as prolonged hospital stay was associated with increased BSI risk.

Dierig et al. reported that the median time to blood culture positivity in septic children was 12 hours (range= 8-109), with no association with age, sex, or comorbidities^[14]. Although clinical evaluation remains central to differentiating true infection from contamination, especially in CoNS isolations, several studies suggest that time to culture positivity may aid in diagnosis^[15,16]. In our study, the mean time to microbial isolation was significantly longer during the pandemic (3.27 ± 1.39 days) than in the pre-pandemic period (2.77 ± 1.92 days). This delay could be attributed to heightened anxiety among health-care workers during the pandemic, which may have affected adherence to aseptic techniques.

The distribution of microorganisms responsible for BSIs can vary not only between countries but also among different hospital units. Babay et al. reported GPBs in 78.6% of isolates and GNBs in 20%, with *E. coli* and *K. pneumoniae* being the most common GNBs^[17]. Gündoğdu et al. reported a reverse pattern, with GNBs comprising 68% and *A. baumannii* being the most frequently isolated pathogen^[18]. In a study by Gülmez et al., GPBs accounted for 68.8%, GNBs 21.4%, and fungi 10.8% of isolates, with CoNS being the most frequent^[19]. Similarly, Duman et al. found GPBs in 63.3% and GNBs in 34.1% of cultures^[20]. In line with national data, our study found GPBs in 87.5% and GNBs in 12.5% of BSIs^[20-23]. In the pre-pandemic period, the most common isolates were CoNS (67.4%), *Streptococcus* spp. (14.7%), and *E. coli* (3.1%). During the pandemic, CoNS (77.1%), *S. aureus* (6.3%), and *Streptococcus* spp. (4.2%) predominated. Among the patients with CoNS growth in their blood cultures, 12 had a CVC before the pandemic and nine during the pandemic period, totaling 21 patients.

Fungal bloodstream infections, although less common, also warrant attention. Özçetin et al. reported fungi in 12.5% of pediatric BSIs, while Copur et al. observed *Candida* spp. in 3% of

isolates^[23,24]. *C. albicans* is the most commonly isolated species in pediatric fungal infections, with risk factors including neutropenia, prematurity, surgery, and use of intravenous catheters^[25,26]. In our study, *C. albicans* was isolated in 1.5% of pre-pandemic and 2% of pandemic-period cases.

In this study, the presence of central venous catheter (CVC), mechanical ventilation (MV), and ventriculoperitoneal (VP) shunt were found to be significant risk factors for the development of BSI. This finding is also supported by previous studies; for example, the use of CVC in COVID-19 patients was reported to increase the risk of BSI^[27].

It is also noteworthy that brucellosis, which was not observed before the pandemic, emerged during the pandemic period. This increase may be a result of the effect of COVID-19 on the spread of zoonotic diseases and the restriction of access to health services. Since our country is endemic for brucellosis, it has led to the opinion that this issue should be examined separately.

In this study, a significant increase in the mortality rate was observed during the pandemic period (16.7%). This finding may be attributed to both the direct effects of COVID-19 and indirect factors, such as restricted access to healthcare services during the pandemic and patients presenting with more advanced illness. Similarly, a study conducted in Spain reported that the incidence of invasive bacterial infections increased in 2020, but this rate decreased in 2021 and 2022^[28].

In conclusion, the limitations of our study include its single-center design and retrospective nature. Due to the retrospective nature of the study, case definitions and contamination assessments may have been limited. However, ongoing microbiological surveillance is vital for infection prevention and control. Each center has a responsibility to contribute data and respond accordingly. Although limited by its single-center design and relatively small sample size, our study provides useful insights and can serve as a foundation for future multicenter studies with larger populations.

ETHICS COMMITTEE APPROVAL

This study was approved by the Süleyman Demirel University Faculty of Medicine Clinical Research Ethics Committee (Decision no: 263, Date: 28.09.2022).

CONFLICT of INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: ŞK, MA

Analysis/Interpretation: All of authors

Data Collection or Processing: ŞK, MA

Writing: All of authors

Review and Correction: All of authors

Final Approval: All of authors

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