



Does the COVID-19 pandemic have influenced the profile of primary bloodstream infections in critically ill neonates?

A pandemia de COVID-19 influenciou o perfil das infecções primárias de corrente sanguínea em neonatos críticos?

¿La pandemia de COVID-19 ha influido en el perfil de las infecciones primarias de la corriente sanguínea en neonatos críticos?

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ABSTRACT

Introduction: Primary Bloodstream Infection (PBSI) associated with Central Venous Catheters (CVC) is the primary site of healthcare-associated infections in Neonatal Intensive Care Units (NICUs). **Aim:** To assess the occurrence of PBSI associated with Peripherally Inserted Central Catheters (PICC) in neonates, before and during the COVID-19 pandemic. **Outlining:** We conducted a retrospective cohort analysis in the NICU of a teaching hospital in the Federal District, Brazil. The sample included 169 neonates who used PICCs from 2018 to 2021. **Results:** There were 16 primary bloodstream infections, with 50% occurring in the pre-pandemic period and 50% during the pandemic. Additionally, 267 blood cultures were performed, of which 17.23% were positive, including 61.7% gram-positive microorganisms and 36.17% gram-negative. The primary microorganisms identified were *Klebsiella* spp. and coagulase-negative *Staphylococcus*, with one microorganism exhibiting oxacillin resistance. **Implications:** We emphasize the importance of monitoring and maintaining continuous surveillance of PBSI associated with CVC, especially during events like the COVID-19 pandemic. Stringent infection control measures should be implemented to minimize the risk of infection and improve care in neonatal intensive care units.

DESCRIPTORS

Catheter-Related Infections; Intensive Care Units; Neonatal; Cross Infection.

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INTRODUCTION

Peripherally Inserted Central Catheters (PICC) are extensively used in neonatal intensive care units (NICU) and facilitate the administration of parenteral nutrition, transfusion of blood products, high-concentration medications, reducing the necessity for multiple venous punctures, as well as the risk of phlebitis, infiltration, and extravasation.¹⁻⁴

Primary bloodstream infection (PBSI) associated with the Central Venous Catheter (CVC) is the primary site of Healthcare-Associated Infections (HAI) in NICUs.⁵ The estimated incidence of PBSI in developed countries ranges from 8.4% to 26%, while in Brazil, these rates range from 18.9% to 57.7%.⁶ However, a reduction in infection rates has been observed after implementing prevention and control measures, as demonstrated in various recent studies. For example, a study⁷ conducted in Australia in 2018 showed a decrease in infection rates from 8.8 to 4.9 per 1,000 catheter-days. A study in Canada⁸ in 2019 reported a decrease from 14.2% to 9.2% in infection rates over a 6-year period, while a study in Kuwait⁹ in 2022 showed a reduction from 7.5 to 3.0 per 1,000 catheter-days. Another study in Belgium¹⁰ in 2022 found that greater adherence to catheter insertion guidelines was associated with a decreased risk of PBSI.

Among the microorganisms isolated in PBSI, notable ones include *Acinetobacter* sp., *Pseudomonas* sp., *Klebsiella* sp., coagulase-negative *Staphylococcus*, methicillin/oxacillin-resistant *Staphylococcus aureus* (MRSA), and *Escherichia coli*.^{8,11-15} It's worth mentioning that coagulase-negative *Staphylococcus* (CNS), a microorganism naturally found on the skin, has shown antimicrobial resistance and the ability to colonize surfaces and form biofilms on intravascular devices.¹⁶⁻¹⁸

From birth to 28 days of age, neonates⁵ are susceptible to infections due to their naturally immature immune system, even under the best conditions. Neonates admitted to the NICU are mostly

premature, with low birth weight, and frequently undergo invasive procedures, making them even more susceptible to infections.^{10-11,19-20}

The year 2020 marked a pivotal moment in human history with the onset of the COVID-19 pandemic, caused by the novel coronavirus (SARS-CoV-2).²¹ The public health crisis required a restructuring of healthcare systems and processes, especially in hospital services. The increased workload, the complexity of care, and the severity of COVID-19 patients in intensive care, along with the suspension of elective surgeries and other pandemic-related developments, had a significant impact on surveillance, diagnosis, and increased rates of HAI and microbial resistance in Brazil and the Federal District.²²

In this complex and diverse clinical and institutional context, it is crucial to identify microorganisms and maintain a biologically safe PICC. It should be noted that these patients, in addition to their unfavorable clinical condition, are progressively exposed to influences from the hospital environment, especially in the ICU. Therefore, this study aims to assess neonates using a PICC in intensive care regarding the occurrence of PBSI associated with the catheter, both before and during the COVID-19 pandemic.

METHOD

This is a retrospective cohort study. The study utilized data from neonates hospitalized between 2018 and 2021 and was conducted in the Neonatal Intensive Care Unit (NICU) of a teaching hospital in the Federal District.

Eligibility Criteria

Inclusion criteria: Neonates using a PICC with a minimum usage time of 48 hours and up to 24 hours after its removal.

Exclusion criteria: Neonates who had the PICC inserted in another hospital, neonates with accidental removal of the PICC, and neonates using a

PICC simultaneously with another central venous or umbilical catheter.

Data Collection

Data collection occurred in four stages between January and December 2022.

In the first stage, the protocol was presented to the Hospital's Education and Research Management to obtain authorization for access to the institution and data collection from medical records.

In the second stage, the research protocol and objectives were presented to the managers of the NICU, the microbiology laboratory, and the Hospital Infection Control Committee (CCIH).

In the third stage, a report containing information on all patients admitted to the NICU between 2018 and 2021 was requested from the hospital's Information Technology Service. Subsequently, 1,373 electronic medical records were evaluated to identify patients who used the PICC, totaling 321 neonates. After simple random sampling, 175 patients were selected and divided into two groups proportionally: the pre-pandemic group with 86 patients (years 2018 and 2019) and the pandemic group with 89 patients (years 2020 and 2021). It's important to note that six patients, three from each group, were excluded from the study after applying the eligibility criteria.

In the fourth stage, data for the 169 selected patients were collected by reviewing electronic medical records, accessing the Hospital University Management Application System (AGHU), and examining Hemoculture and Antimicrobial Sensitivity Test (AST) reports through the Comprehensive Laboratory Management System (Complab Advanced). Additionally, physical medical records in the hospital's archive were analyzed to complement the collected data. The outcome assessment, including discharge, transfer to another hospital unit, or death, occurred at the end of the NICU hospitalization period by accessing the patient's electronic medical record. All

information was recorded on a form containing details about the neonate, hospitalization, and clinical and laboratory examinations of the neonate.

Data Treatment and Analysis

After data collection and tabulation, the database underwent data cleaning and standardization, followed by analysis using the statistical software R version 4.1.3²³, applying a statistical significance level of $p \leq 0.05$.

Descriptive analysis involved calculating the absolute and relative frequencies of qualitative variables, while for quantitative variables, measures of position, central tendency, and dispersion were calculated, including median, mean, standard error, and percentiles 25 and 75.

For inferential analysis, the Kruskal-Wallis test was used due to the data's identified asymmetry through the Shapiro-Wilk test.

Ethical Aspects

This study was approved by the Research Ethics Committee of the Faculty of Ceilândia at the University of Brasília (CEP/FCE/UnB), under the number CAAE: 32477420.2.0000.8093, in accordance with Resolution 466/2012 of the National Health Council.

RESULTS

The sample consisted of 169 neonates who used a PICC between the years 2018 and 2021. There was a predominance of male neonates, 66.27% during the pre-pandemic period, with a shift during the pandemic, with 52.94% being female (Table 1).

Preterm birth was the most frequent in both periods, 49.4% and 58.14%. Additionally, it is observed that in both the pre-pandemic and pandemic periods, neonates with a birth weight between 1,500g and 2,499g were more prevalent, with 33.73% (n=28) and 33.72% (n=29), respectively.

Table 1 - Demographic characteristics of neonates using PICC catheters in the NICU, Brasília, from 2018 to 2021.

Variable		Period		Total
		Pre-Pandemic N (%)	Pandemic N (%)	
*Sex	Male	55 (66.27)	40 (47.06)	95
	Female	28 (33.73)	45 (52.94)	73
Gestational age	Preterm	41 (49.4)	50 (58.14)	91
	Late preterm	15 (18.1)	7 (8.14)	22
	Early term	14 (16.9)	11 (12.79)	25
	Full term	10 (12)	17 (19.77)	27
	Late term	3 (3.6)	1 (1.16)	4
	< 750g	1 (1.21)	3 (3.49)	4
Birth weight (grams)	750 to 999g	7 (8.43)	9 (10.47)	16
	1,000 to 1,499g	23 (27.71)	22 (25.58)	45
	1,500 to 2,499g	28 (33.73)	29 (33.72)	57
	> 2,500g	24 (28.92)	23 (26.74)	47

*In one medical record, the information was missing.

Source: Prepared by the authors.

Regarding the reasons for admission to the NICU, we observed that the most frequent reason for admission, both in the pre-pandemic and pandemic periods, was early respiratory distress, with 50% (n=49) and 55.8% (n=53), respectively (Table 2).

As for the indication for the use of PICC, it is possible to notice that in both periods, the indication for parenteral nutrition (NPT) and medication stands

out, with 44.6% (n=37) and 53.5% (n=46), respectively.

In contrast, the indication for medication decreased by approximately 3% between the two periods, and there were no indications for venous hydration with the catheter during the pandemic. Additionally, all neonates underwent another invasive procedure.

Table 2 - Clinical characteristics of neonates using PICC catheters in the NICU, Brasília, from 2018 to 2021.

Variable		Period		Total
		Pre-Pandemic N (%)	Pandemic N (%)	
Reason for hospitalization	Early Respiratory Distress	49 (50.0)	53 (55.8)	102
	Early Neonatal Sepsis	21 (21.4)	17 (17.9)	38
	Congenital Heart Disease	8 (8.16)	3 (3.2)	11
	Neonatal Asphyxia	6 (6.12)	8 (8.4)	14
	Extreme Prematurity	6 (6.12)	4 (4.2)	10
	Hyaline Membrane Disease	4 (4.1)	6 (6.3)	10
	Twin Birth	4 (4.1)	4 (4.2)	8
PICC indication	VH	5 (6.0)	-	5
	VH and Medication	4 (4.8)	2 (2.3)	6
	VH and PN	-	1 (1.2)	1
	Medication	32 (38.6)	29 (33.7)	61
	PN	5 (6.0)	8 (9.3)	13
	PN and Medication	37 (44.6)	46 (53.5)	83

Invasive procedures	Nasogastric Tube	17 (12.2)	23 (19.5)	40
	Orogastric Tube	73 (52.5)	59 (50)	131
	Indwelling Urinary Catheter	6 (4.3)	5 (4.2)	11
	Endotracheal Tube	43 (31.0)	31 (26.3)	74

Note 1: Some neonates had more than one reason for admission. Note 2: Compiled with available data. Legend: Venous Hydration (VH) and Parenteral Nutrition (PN).

Source: Compiled by the authors.

It can be observed that there were 16 PBSIs, with 50% occurring in the pre-pandemic period and 50% during the pandemic (Table 3).

Table 3 - Frequency of PBSI occurrence in neonates using PICC catheters in the NICU, Brasília, from 2018 to 2021.

Period	Infection	Frequency N (%)
Pandemic	Yes	8 (50)
Pre-Pandemic	Yes	8 (50)
Total		16 (100)

Source: Compiled by the authors.

There is no association between PBSI and birth weight; however, there is a tendency for

infection in neonates with low birth weight, i.e., less than 2499g (Table 4).

Table 4 - Association between PBSI and birth weight in neonates using PICC catheters in the NICU, Brasília, from 2018 to 2021.

Variable	Pre-Pandemic				p-value ¹	
	Yes		No			
	N	%	N	%		
Birth weight (grams)	< 750g	1	33.3	2	66.7	0.301
	750 to 999g	3	42.9	4	57.1	
	1000 to 1499g	1	5.88	16	94.12	
	1500 to 2499g	2	7.7	24	92.3	
	> 2500g	1	3.85	25	96.15	
Birth weight (grams)	< 750g	-	-	1	100.0	0.681
	750 to 999g	2	25.0	6	75.0	
	1000 to 1499g	5	20	20	80.0	
	1500 to 2499g	1	3.85	25	96.15	
	> 2500g	-	-	20	100.0	

Note: Compiled using available data. 1 Kruskal-Wallis test.

Source: Compiled by the authors.

Despite the eight cases of confirmed PBSI during the study period by the CCIH, 267 blood cultures were performed, with a positivity rate of 17.23% (n=46), including one blood culture with simultaneous growth of two microorganisms.

A total of 61.7% (n=29) of gram-positive microorganisms were identified: 36.17% (n=17) were

gram-negative, and 2.13% (n=1) were fungi. Among the gram-positives, 72.42% (n=21) were coagulase-negative *Staphylococcus* (SCN), and among the gram-negatives, 47.1% (n=8) were *Klebsiella* spp (Table 5).

Regarding the microorganisms that exhibited resistance in the AST, it is noteworthy that there

were two oxacillin-resistant *S. aureus* (pre-pandemic), nine oxacillin-resistant SCN (five from the pre-pandemic period and four from the pandemic period), but none were resistant to

vancomycin. On the other hand, among the gram-negatives, one *E. coli* (pre-pandemic) showed resistance to third-generation cephalosporins (ceftazidime and ceftriaxone) and fluoroquinolones (ciprofloxacin and levofloxacin).

Table 5 - Microorganisms identified in blood cultures in neonates using PICC catheters in the NICU, Brasília, in the pre-pandemic period from 2018 to 2021.

Microorganisms	Period		Total
	Pre-Pandemic N (%)	Pandemic N (%)	
<i>Enterobacter cloacae</i>	-	1 (4)	1
<i>Enterococcus faecalis</i>	1 (4.54)	-	1
<i>Escherichia coli</i>	2 (9.1)	2 (8)	4
<i>Klebsiella oxytoca</i>	3 (13.64)	1 (4)	4
<i>Klebsiella pneumoniae</i>	-	1 (4)	1
<i>Klebsiella pneumoniae ssp ozaenae</i>	1 (4.54)	-	1
<i>Klebsiella pneumoniae ssp pneumoniae</i>	2 (9.1)	-	2
<i>Pseudomonas aeruginosa</i>	-	1 (4)	1
<i>Rhodotorula mucilaginosa</i> (leveduras)	-	1 (4)	1
<i>Serratia marcescens</i>	-	3 (12)	3
<i>Staphylococcus aureus</i>	5 (22.73)	2 (8)	7
<i>Staphylococcus capitis</i>	1 (4.54)	3 (12)	4
<i>Staphylococcus epidermidis</i>	5 (22.73)	8 (32)	13
<i>Staphylococcus gallinarum</i>	-	1 (4)	1
<i>Staphylococcus haemolyticus</i>	1(4.54)	-	1
<i>Staphylococcus hominis</i>	1 (4.54)	1 (4)	2
Total	22	25	47

Source: Compiled by the authors.

DISCUSSION

In this study, we evaluated neonates in intensive care who were using PICC lines for the occurrence of Catheter-Associated Bloodstream Infections (PBSI) before and during the COVID-19 pandemic. The aim was to support the improvement of healthcare quality and patient safety. Several factors contribute to an increased risk of critical neonates developing PBSIs, especially prematurity, low birth weight, and the performance of invasive procedures.²⁴ A study conducted in China¹⁹ concluded that premature newborns with low birth weight and more extended PICC usage may face a higher risk of PBSIs. Although prematurity is a vulnerability factor for infections and was significantly prevalent in the

study, it did not show a significant association with PBSIs in the evaluated population. Other studies from Australia²⁵ and Brazil²⁰ corroborate our findings, particularly regarding critical neonates using PICC who exhibited higher rates of early respiratory distress and preterm birth.

Our study aligns with the scientific literature regarding the reasons for PICC usage. In both periods, the predominant indication was medication and Parenteral Nutrition (NPT).^{2,26-27}

Regarding the prevalence of identified microorganisms in this investigation, 61.7% were gram-positive bacteria, with Coagulase-Negative *Staphylococcus* (SCN) accounting for 72.42% of these cases. We also identified 36.7% of gram-negative bacteria, with *Klebsiella* spp. being notable at 47.1%

of cases. These findings are supported by existing literature, as research conducted in various hospitals in the United States¹⁴ reported that *Staphylococcus* spp. accounted for 46% of the microorganisms in NICUs. In another study, 71.4% of the isolated microorganisms were identified as SCN, followed by *E. coli* (5.9%) and *S. aureus* (5.6%).²⁵

As for the influence of COVID-19, our study couldn't determine its impact on PBSI rates, primarily because only two pregnant women were confirmed to have COVID-19. However, other studies conducted in ICUs found an increase in PBSI rates during the pandemic compared to the pre-pandemic period. For example, a study in 78 hospitals in Saudi Arabia reported a 16% increase from 2020-2021 compared to 2019.²⁸ Another study in 21 Brazilian hospitals found a significant increase ($p=0.002$) in the incidence of PBSIs during the pandemic.²⁹ Several explanations for the increased PBSI rates were suggested, including reduced catheter care during insertion and maintenance due to overwhelmed healthcare teams.²⁸

During the pandemic, particularly in its early stages, infection control teams reported a fivefold increase in consultations, mainly focused on isolating individuals exposed to COVID-19. This resulted in less time dedicated to catheter surveillance and care. To manage the increased demand for healthcare, nursing teams were rapidly trained and assigned to assist in caring for COVID-19 patients in ICUs. Finally, the excessive use of immunosuppressive drugs among COVID-19 patients may have also contributed to an increased susceptibility to infections, including PBSIs.

²⁸

In a study³⁰ conducted between January 2018 and December 2021, a significant decrease was observed in cases of infections caused by gram-positive bacteria (from 70.5% to 48.6%) during the pandemic period. Furthermore, there was a notable reduction in the fatality rate of these infections, decreasing from 38% to 15.45% during the pandemic. The authors believe that this phenomenon

may be attributed to better compliance with infection control and prevention measures in the NICUs.

Additionally, despite finding microorganisms resistant to certain antimicrobials, we did not identify multidrug-resistant microorganisms, which are resistant to more than one class of antimicrobials.²⁴ This aligns with other studies that indicate lower infection rates caused by resistant microorganisms in NICUs.^{14,31} This finding may be due to the reduced exposure of these patients to healthcare environments and antimicrobials compared to adult patients.^{14,31} However, despite the decreasing rates of antimicrobial-resistant gram-positive bacteria in NICUs, other microorganisms, such as *Candida auris* and antimicrobial-resistant gram-negative bacteria, especially carbapenem-resistant strains, have increased among neonates, particularly in developing countries.²⁴

Epidemiological surveillance related to PICC usage, especially in NICUs, facilitates establishing strategies and objectives to reduce adverse events. In this context, understanding the incidence of major microorganisms and their antimicrobial resistance patterns can help define targets for antimicrobial management programs and provide better guidance for infection prevention.

Limitations

This is a retrospective study, data obtained from medical records made it challenging to establish a temporal relationship between risk factors and infection occurrence. Another limitation was the lack of PICC insertion, maintenance, and removal records. When this information was recorded, the lack of standardization made identifying and interpreting relevant information for catheter monitoring difficult.

CONCLUSION

The results of this study demonstrated an incidence of 9.46% of Catheter-Associated Bloodstream Infections (IPCS) related to PICC line usage, equally distributed in the pre-pandemic and COVID-19 pandemic periods. Thus far, the study has shown that the pandemic does not significantly contribute to the influence of catheter-related bloodstream infections in critical neonates using PICCs. In this context, it is essential to emphasize the importance of epidemiological surveillance related to

PICC usage at the hospital under study. Despite the increased workload during the pandemic, surveillance remained active, and no increase in IPCS was determined.

The variables associated with IPCS occurrence were gestational age, birth weight, and early respiratory distress. The primary microorganisms identified in infection cases were *Klebsiella* spp. and Coagulase-Negative *Staphylococcus* (SCN), with one microorganism displaying resistance to oxacillin.

RESUMO

Introdução: A Infecção Primária da Corrente Sanguínea (IPCS) Associada ao Cateter Venoso Central (CVC) é a principal topografia de infecção relacionada à assistência à saúde em Unidades de Terapia Intensiva Neonatais (UTIN). **Objetivo:** avaliar a ocorrência de IPCS associada ao Cateter Central de Inserção Periférica em neonatos, tanto antes quanto durante a pandemia de COVID-19. **Delineamento:** Realizamos uma análise retrospectiva de coorte na UTIN de um hospital de ensino no Distrito Federal, Brasil. A amostra incluiu 169 neonatos que utilizaram cateter central de inserção periférica no período de 2018 a 2021. **Resultados:** Ocorreram 16 infecções primárias da corrente sanguínea, sendo 50% no período pré-pandemia e 50% no período de pandemia. Além disso, foram realizadas 267 hemoculturas, sendo 17,23% positivas, das quais, 61,7% de microrganismos gram-positivos e 36,17% gram-negativos. Os principais microrganismos identificados nos casos de infecção foram *Klebsiella* spp. e *Staphylococcus* coagulase negativa, com um microrganismo identificado com perfil de resistência à oxacilina. **Implicações:** Destacamos a importância de monitorar e manter a vigilância contínua em relação à (IPCS) associada a CVC, especialmente durante eventos como a pandemia de COVID-19. Medidas rigorosas de controle de infecções devem ser implementadas para minimizar o risco de infecção e melhorar os cuidados em unidades de terapia intensiva neonatais.

DESCRITORES

Infecções Relacionadas a Cateter; Unidades de Terapia Intensiva Neonatal; Infecção Hospitalar.

RESUMEN

Introducción: La Infección Primaria de la Corriente Sanguínea (IPCS) Asociada a Catéteres Venosos Centrales (CVC) es la principal localización de infecciones relacionadas con la atención médica en Unidades de Cuidados Intensivos neonatales (UCIN). **Objetivo:** Evaluar la ocurrencia de IPCS asociada a Catéter Central de Inserción Periférica en neonatos, tanto antes como durante la pandemia de COVID-19. **Delineación:** Realizamos un análisis retrospectivo de cohorte en la UCIN de un hospital de enseñanza en el Distrito Federal, Brasil. La muestra incluyó a 169 neonatos que utilizaron CVC en el período de 2018 a 2021. **Resultados:** Se registraron 16 infecciones primarias de la corriente sanguínea, siendo el 50% en el período previo a la pandemia y el 50% durante la pandemia. Además, se realizaron 267 cultivos de sangre, de los cuales el 17.23% resultó positivo, con un 61.7% de microorganismos gram-positivos y un 36.17% gram-negativos. Los principales microorganismos identificados en los casos de infección fueron *Klebsiella* spp. y *Staphylococcus* coagulasa negativa, con un microorganismo identificado con resistencia a oxacilina. **Implicaciones:** Destacamos la importancia de monitorear y mantener una vigilancia continua en relación a la IPCS asociada a CVC, especialmente durante eventos como la pandemia de COVID-19. Deben implementarse medidas rigurosas de control de infecciones para minimizar el riesgo de infección y mejorar la atención en unidades de cuidados intensivos neonatales.

DESCRIPTORES

Infecciones Relacionadas con Catéteres; Unidades de Cuidado Intensivo Neonatal; Infección Hospitalaria.

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COLLABORATIONS

HSJ: Substantial contributions to data acquisition, analysis, interpretation of results, and manuscript writing. ZSFR: Substantial contributions to data acquisition, analysis, interpretation of results, and critical manuscript review. JKSC: Substantial contributions to critical manuscript review and manuscript formatting. PSPS: Substantial contributions to data acquisition and manuscript formatting. TFC: Substantial contributions to data acquisition and manuscript formatting. PRSH: Substantial contributions to the conception and design of the study. **All authors agree and are responsible for the content of this version of the manuscript to be published.**

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AVAILABILITY OF DATA

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CONFLICTS OF INTEREST

There are no conflicts of interest to declare.