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Microbial resistance associated with IPCSL in an adult ICU in Ceará

Resistência microbiana associada à IPCSL em UTI adulto no Ceará

Resistencia microbiana asociada a la IPCSL en unas UCI para adultos en Ceará

ABSTRACT

Objective: To describe the microbial resistance (MR) profile associated with laboratory-confirmed primary bloodstream infections (LCPBIs) reported in adult intensive care units (ICUs) in Ceará, from 2021 to 2023. **Methods:** A cross-sectional, descriptive, retrospective study with secondary data aggregated from the Brazilian Health Regulatory Agency (ANVISA), derived from notifications of healthcare-associated infections (HAIs) and MR; records with identified microorganisms and sensitivity testing were included. **Results:** The incidence density (ID) ranged from 3.45 to 10.51 per 1,000 patient-days. In Gram-negative bacteria, high resistance to cephalosporins (CEF) and carbapenems (CARB) was observed in Klebsiella pneumoniae, Acinetobacter spp., and Enterobacter spp., in addition to significant resistance to ceftazidime/avibactam (CAZ-AVI) in 2023. Among Gram-positive bacteria, resistance to vancomycin (VANCO) in enterococci and to oxacillin (OXA) in staphylococci stood out. **Conclusions:** The findings reinforce the surveillance of HAIs and the qualification of actions for prevention, control, and rational use of antimicrobials.

Keywords: *Drug resistance microbial; Sepsis; Health surveillance; Intensive care units.*

RESUMO

Objetivo: Descrever o perfil de resistência microbiana (RM) associado às infecções primárias de corrente sanguínea confirmadas laboratorialmente (IPCSL), notificadas em unidades de terapia intensiva (UTI) adulto no Ceará, de 2021 a 2023. **Método:** Estudo transversal, descritivo e retrospectivo, com dados secundários agregados da Agência Nacional de Vigilância Sanitária (ANVISA), oriundos das notificações de infecções relacionadas à assistência à saúde

(IRAS) e de RM; incluíram-se registros com microrganismo identificado e teste de sensibilidade. **Resultados:** A densidade de incidência (DI) variou de 3,45 a 10,51 por 1.000 pacientes-dia. Em gram-negativos, observou-se resistência elevada a cefalosporinas (CEF) e carbapenêmicos (CARB) em Klebsiella pneumoniae e Acinetobacter spp. e Enterobacter spp., além de resistência importante à ceftazidima/avibactam (CAZ-AVI) em 2023. Entre gram-positivos, destacaram-se resistência à vancomicina (VANCO) em enterococos, e à oxacilina (OXA) em estafilococos. **Conclusão:** Os achados reforçam a vigilância das IRAS e a qualificação das ações de prevenção, controle e uso racional de antimicrobianos.

Descritores: *Resistência microbiana a medicamentos; Sepse; Vigilância sanitária. Unidades de terapia intensiva.*

RESUMEN

Objetivo: Describir el perfil de resistencia microbiana (RM) asociado a las infecciones primarias del torrente sanguíneo confirmadas por laboratorio (IPCSL) notificadas en unidades de terapia intensiva (UTI) para adultos en Ceará, de 2021 a 2023. **Método:** Estudio transversal, descriptivo y retrospectivo, con datos secundarios agregados de la Agencia Nacional de Vigilancia Sanitaria (ANVISA), procedentes de notificaciones de infecciones relacionadas con la asistencia sanitaria (IRAS) y de RM; se incluyeron registros con microorganismos identificados y pruebas de sensibilidad. **Resultados:** La densidad de incidencia (DI) varió de 3,45 a 10,51 por cada 1000 pacientes-día. En los gramnegativos, se observó una elevada resistencia a las cefalosporinas (CEF) y a los carbapenémicos (CARB) en Klebsiella pneumoniae y Acinetobacter spp. y Enterobacter spp., además de una importante resistencia a la ceftazidima/avibactam (CAZ-AVI) en 2023. Entre los grampositivos, se destacó la resistencia a la vancomicina (VANCO) en enterococos y a la oxacilina (OXA) en estafilococos. **Conclusión:** Los hallazgos refuerzan la vigilancia de las IRAS y la calificación de las acciones de prevención, control y uso racional de los antimicrobianos.

Descriptores: *Farmacorresistencia microbiana; Sepsis; Vigilancia sanitaria; Unidades de cuidados intensivos.*

INTRODUCTION

Healthcare-associated infections (HAIs) represent one of the main challenges for patient safety, especially in Intensive Care Units (ICUs), where the severity of clinical conditions and the frequent use of invasive devices, such as central venous catheters, significantly increase the risk of infections. In this scenario, antimicrobial resistance (AMR) becomes an aggravating factor, reducing the effectiveness of antimicrobials, increasing morbidity and mortality rates, prolonging hospital stays, and increasing hospital costs[1,2].

Among healthcare-associated infections (HAIs), primary bloodstream infections (BSIs) are of particular concern because they are frequently associated with the presence of multidrug-resistant microorganisms, such as Klebsiella pneumoniae, Acinetobacter spp., and Pseudomonas aeruginosa, which exhibit increasing resistance to critical classes of antimicrobials, such as carbapenems (CARBs), polymyxins (POLIs), and glycopeptides[3].

Acute respiratory infections (ARDs) are considered a global public health emergency. According to estimates by the World Health Organization (WHO), by 2050, infections caused by multidrug-resistant microorganisms could become the leading cause of death worldwide, surpassing cancer and cardiovascular diseases. In the hospital setting, and especially in ICUs, the spread of these pathogens represents a growing threat to therapeutic effectiveness and patient safety[4].

In Brazil, between 40% and 60% of infectious diseases are already resistant to medication, according to the Organization for Economic Cooperation and Development (OECD, 2018)[5]. And currently, according to the WHO, approximately 700,000 people die each year worldwide due to antimicrobial-resistant infections[4].

In Brazil, the fight against these infections is conducted within the scope of the National Program for the Prevention and Control of Healthcare-Associated Infections (PNPCIRAS), coordinated by the National Health Surveillance Agency (ANVISA), which establishes guidelines for epidemiological surveillance and control of HAIs in health services[6]. In Ceará, the State Plan for the Prevention and Control of HAIs also reinforces the importance of monitoring HAIs, especially IPCS[7].

The analysis of the resistance profile (RM) in laboratory-confirmed primary bloodstream infections (BSIs) reported by adult ICU services is fundamental to supporting surveillance and control actions for healthcare-associated infections (HAIs), since the occurrence of multidrug-resistant microorganisms represents a serious risk to public health. In Ceará, aggregated data from notifications made by health services can allow the identification of resistance patterns and priority microorganisms, enabling the adoption of more effective interventions, as well as strengthening state surveillance and improving sanitary actions in the hospital setting. Therefore, the objective of this study is to describe the RM profile associated with BSIs reported in adult ICUs in Ceará.

METHODS

This is a cross-sectional, quantitative, descriptive, and retrospective study of IPCSL and RM notifications from healthcare services with adult ICUs in the State of Ceará.

The setting for this study was the state of Ceará, divided into five regional health superintendencies: Fortaleza (SRFOR), Sobral (SRNORTE), Juazeiro do Norte (SRSUL), Quixadá (SRCEN), and Limoeiro do Norte (SRLES). The state health structure is organized into 22 Decentralized Health Areas (ADS), encompassing municipalities such as Fortaleza, Caucaia, Juazeiro do Norte, Sobral, among others.

The analysis was based on notifications of HAIs and AMRs from healthcare facilities with adult ICU beds. According to the monitoring of According to the State Coordination for the Control of Healthcare-Associated Infections (CECIRAS), the state has 127 healthcare-associated infection reporting services, 63 of which have adult ICU beds.

These notifications are carried out monthly by the Hospital Infection Control Committees (CCIH), using standardized forms available in the LimeSurvey® system, according to guidelines established by ANVISA (Brazilian Health Regulatory Agency). The choice to focus exclusively on CLABSIs (Clinical and Stabilized Healthcare-Associated Infections) is justified by their high epidemiological relevance, their potential for clinical severity, and because they are included as priority indicators in the National Program for the Prevention and Control of Healthcare-Associated Infections (PNPCIRAS), as well as in the State Plan for the Prevention and Control of Healthcare-Associated Infections of Ceará. This focus aims to contribute to the monitoring of respiratory infections in critical settings, such as ICUs, promoting the improvement of hospital health surveillance.

The study included notifications of bloodstream infections (BSIs) registered in the national forms of ANVISA (Brazilian Health Regulatory Agency) between January 2021 and December 2023, originating exclusively from healthcare services located in the State of Ceará that have adult ICU beds. Furthermore, for the resistance profile analysis, only notifications that presented, in a complete manner, the identification of the isolated microorganism and its respective sensitivity or resistance profile to antimicrobials were considered. For epidemiological interpretation and comparability purposes, the analysis focused on the main microorganisms of epidemiological relevance in the context of ICU and bloodstream infection, defined as those with the highest frequency of isolation during the period and recognized importance for the surveillance of bloodstream infections.

Notifications from pediatric or neonatal ICUs were excluded from the study, as were those classified as Clinical Primary Bloodstream Infection, i.e., without laboratory confirmation. Notifications with incomplete data, such as the absence of identification of the etiological agent or resistance profile, as well as

duplicate records by the reporting services, were also disregarded—in these cases, the most recent notification was considered.

Annual data (2021 to 2023) were collected from the national HAI and AMR indicator forms for adult ICU services in Ceará. Data collection was performed directly from the Patient Safety and Quality in Health Services bulletins published on the ANVISA website.

The incidence density (ID) data for IPCSL, as well as the resistance profiles of the isolated microorganisms, were organized in spreadsheets using Microsoft Excel 365® software. The analysis was performed using descriptive statistics, with calculation of absolute and relative frequencies, in addition to the temporal distribution of cases and resistance patterns identified over the years.

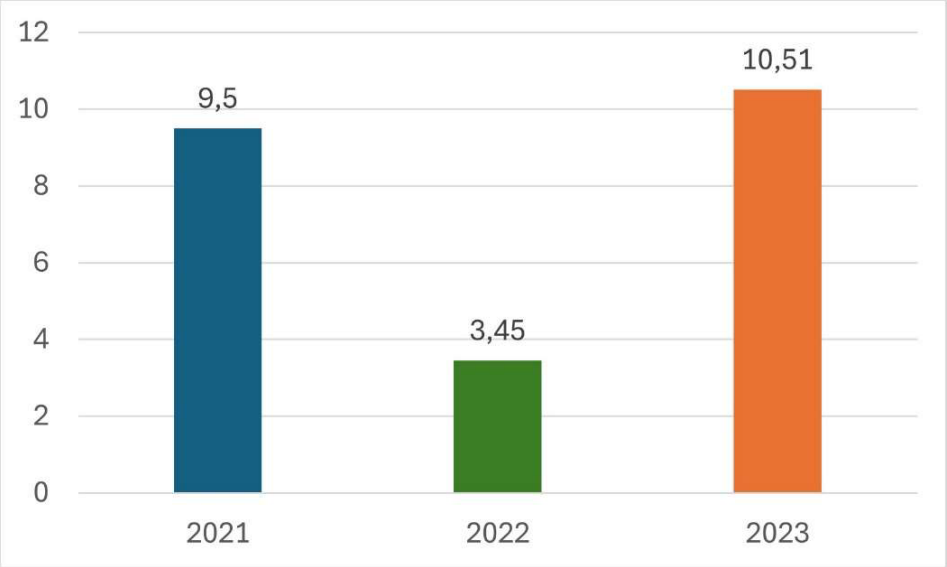
This study used secondary data from public databases made available by ANVISA (Brazilian Health Regulatory Agency), referring to aggregated notifications of HAIs (Healthcare-Associated Infections) and AKIs (Acute Respiratory Infections) in adult ICUs in the state of Ceará. No information was collected that would allow the direct or indirect identification of patients, thus ensuring the confidentiality and anonymity of the analyzed information.

Because it does not directly involve human beings and uses publicly available data, the research falls under the exceptions provided for in Resolution No. 510/2016 of the National Health Council, and is therefore exempt from the need for submission to the Research Ethics Committee. Even so, all stages of the study respected the ethical principles of scientific research, as established by Resolution No. 466/2012, safeguarding the precepts of autonomy, beneficence, non-maleficence, justice, and equity.

RESULTS

The annual incidence rate of IPCSL in adult ICUs in the State of Ceará varied between 2021 and 2023. In 2021, the incidence rate was 9.5 per thousand patient-days, with a significant reduction in 2022 (3.45 per thousand patient-days) and an increase in 2023 (10.51 per thousand patient-days) (Figure 1).

Figure 1 – Annual incidence density (per thousand patient-days) of Primary Bloodstream Infections (PBSI) in adult ICUs in the state of Ceará, from 2021 to 2023.



Source: Author's own work (2026).

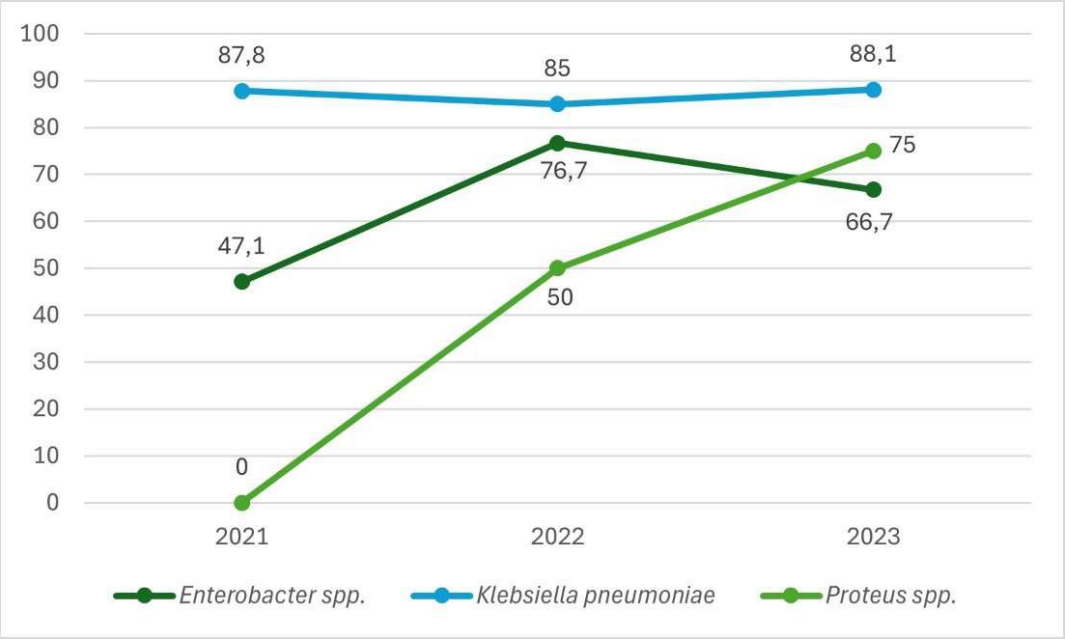
Regarding the resistance profile in Gram-negative bacteria, variations were observed among the microorganisms evaluated during the period (Chart 1; Figure 2). In Klebsiella pneumoniae, resistance to cephalosporins (CEFs) remained high throughout the three years, varying from 87.8% in 2021 to 85.0% in 2022 and 88.15% in 2023. In Enterobacter spp., there was an increase in resistance from 2021 to 2022, with a subsequent reduction in 2023, although it remained at a high level (47.1%, 76.7%, and 66.67%, respectively). For Proteus spp., resistance to CEFs increased from 50.0% in 2022 to 75.0% in 2023 (Figure 2).

Chart 1 – Antimicrobial resistance in adult ICUs in the state of Ceará, from 2021 to 2023.

GRAM NEGATIVE												
ANTIMICROBIAL RESISTANCE (%)												
	2021				2022				2023			
MO	CEF	CARB	POLI B e/ou E	CAZ-AVI	CEF	CARB	POLI B e/ou E	CAZ-AVI	CEF	CARB	POLI B e/ou E	CAZ-AVI
Acinetobacter	-	81,0	12,1	-	-	67,4	0,0	-	-	79,01	26,92	-
Enterobacter spp,	47,1	29,4	25,0	-	76,7	66,7	13,6	-	66,67	71,79	0,00	40,00
Klebsiella pneumoniae	87,8	75,7	54,1	-	85,0	72,7	24,5	50,0	88,15	80,65	41,18	58,82
Pseudomonas aeruginosa	-	46,9	17,6	-	-	32,8	11,4	-	-	52,94	16,67	-
Proteus spp,	-	-	-	-	50,0	30,0	-	-	75,00	59,09	-	37,50
GRAM POSITIVE												
ANTIMICROBIAL RESISTANCE (%)												
	2021				2022				2023			
MO	CEF	CARB	VANCO	OXA	CEF	CARB	VANCO	OXA	CEF	CARB	VANCO	OXA
Enterococcus faecalis	-	-	3,7	-	-	-	5,9	-	-	-	24,2	-
Enterococcus faecium	-	-	56,5	-	-	-	76,9	-	-	-	46,4	-
Enterococcus spp.	-	-	20,0	-	-	-	33,3	-	-	-	62,5	-
Staphylococcus aureus	-	-	12,2	-	-	-	6,3	54,3	-	-	-	40,9
Staphylococcus coagulase negativa	-	-	4,5	-	-	-	10,8	83,2	-	-	-	21,5

Source: ANVISA, 2021, 2022, 2023.

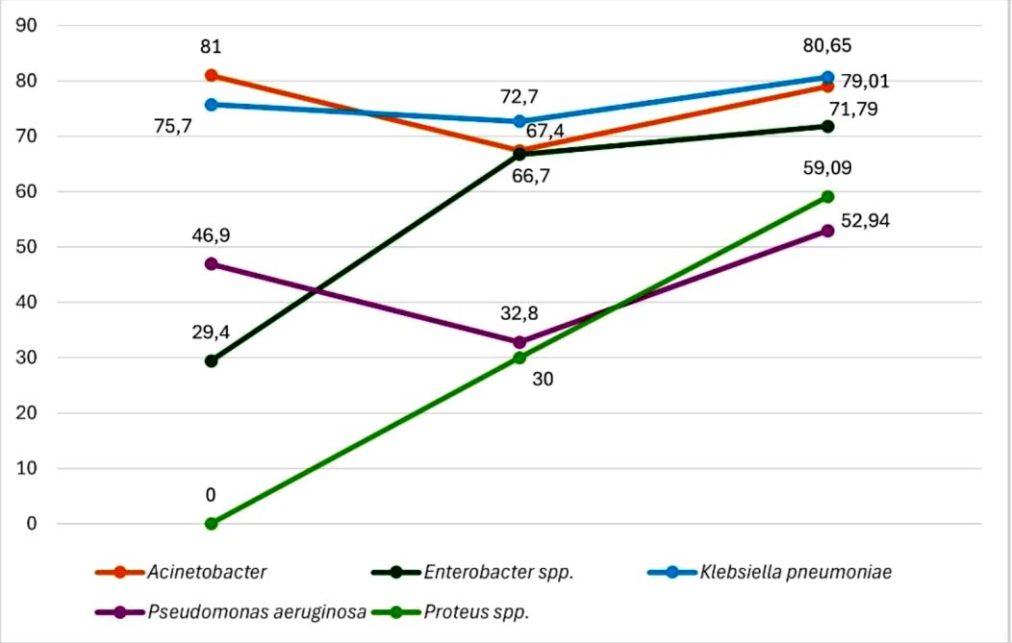
Figure 2 – Resistance rate to cephalosporins of the main Gram-negative microorganisms of CLABSI in adult ICUs in the state of Ceará, from 2021 to 2023.



Source: Author's own work (2026).

Carbapenem (CARB) resistance showed high levels and variable behavior among the agents analyzed (Figure 3). In Acinetobacter spp., resistance remained high throughout the period (81.0%, 67.4%, and 79.01%, respectively). In Enterobacter spp., a progressive increase was observed between 2021 and 2023 (29.4%, 66.7%, and 71.79%). For this group, resistance to ceftazidime/avibactam (CAZ-AVI) was also observed in 2023, with a rate of 40% (Figure 5).

Figure 3 – Carbapenem resistance rate of the main Gram-negative microorganisms of CLABSI in adult ICUs in the state of Ceará, from 2021 to 2023.

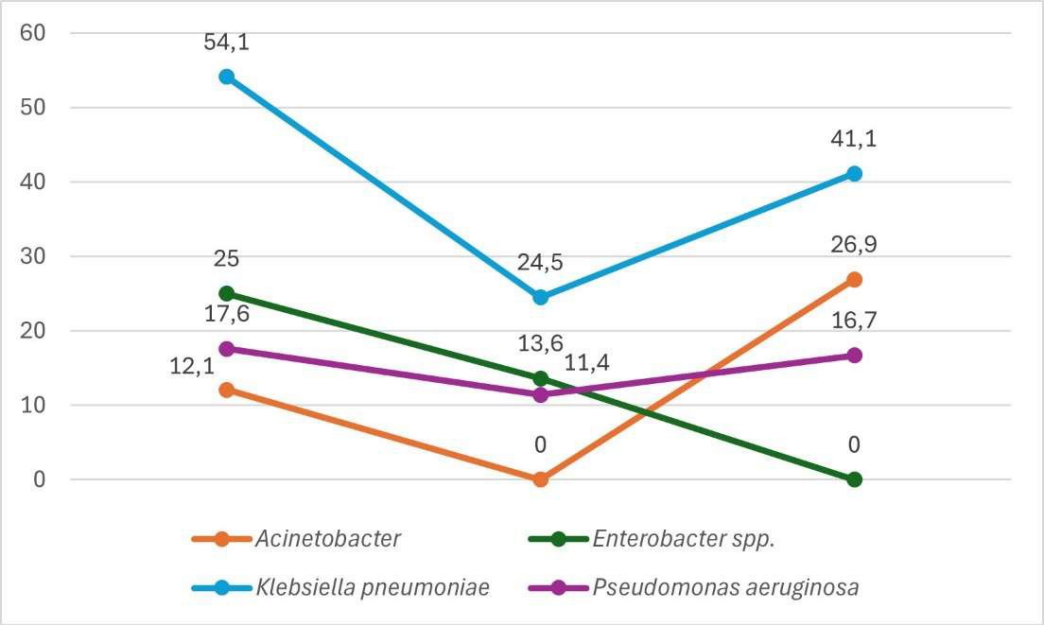


Source: Author's own work (2026).

In Klebsiella pneumoniae, CARB resistance remained high throughout the period, with rates of 75.7% in 2021, 72.7% in 2022, and 80.65% in 2023 (Figure 3). For CAZ-AVI, there was an increase from 50.0% in 2022 to 58.82% in 2023 (Figure 5).

In Pseudomonas aeruginosa, resistance to CARB varied from 46.9% in 2021 to 32.8% in 2022, increasing to 52.94% in 2023 (Figure 3). Resistance to polymyxins B and/or E (POLY B/E) varied during the period (17.6%, 11.4%, and 16.67%, respectively) (Figure 4).

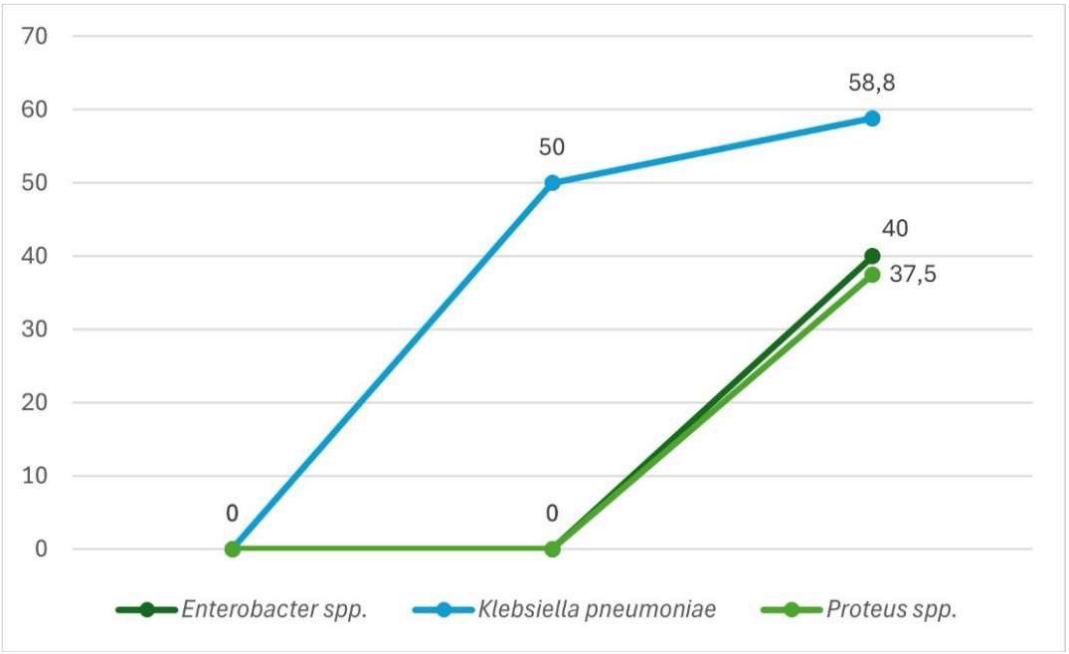
Figure 4 – Resistance rate to polymyxins B and/or E of the main Gram-negative microorganisms of CLABSI in adult ICUs in the state of Ceará, from 2021 to 2023.



Source: Author's own work (2026).

For Proteus spp., resistance to CARB increased from 30% in 2022 to 59.09% in 2023 (Figure 3); in 2023, resistance to CAZ-AVI was 37.5% (Figure 5).

Figure 5 – Resistance rate to ceftazidime/avibactam of the main Gram-negative microorganisms of CLABSI in adult ICUs in the state of Ceará, from 2021 to 2023.

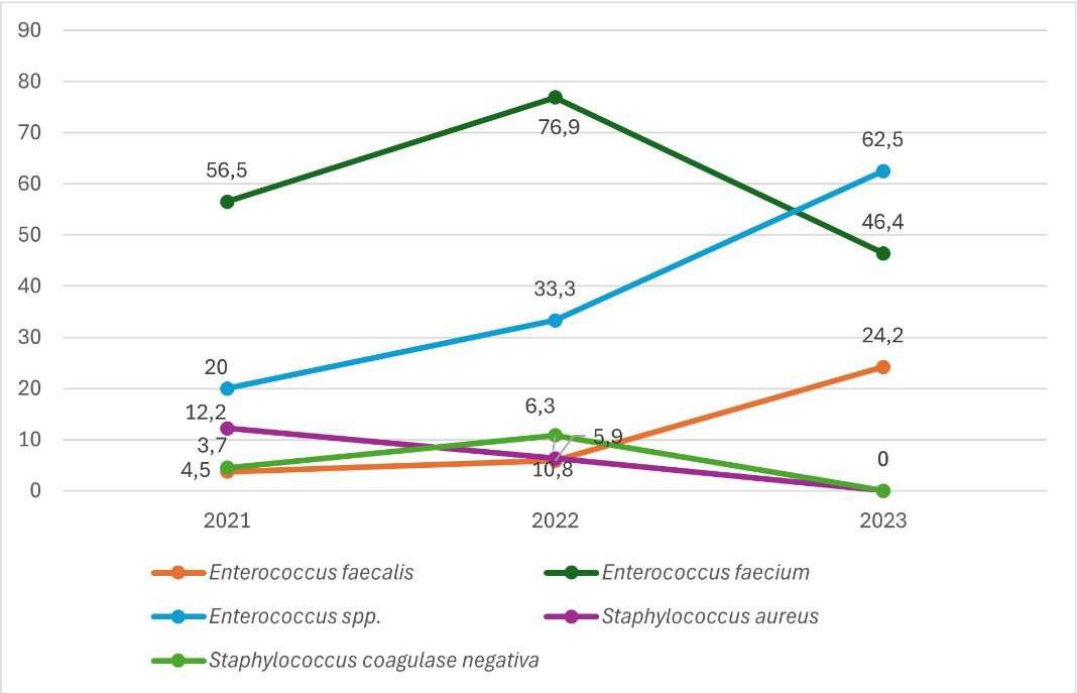


Source: Author's own work (2026).

Regarding Gram-positive bacteria, Enterococcus faecium showed vancomycin (VANCO) resistance of 56.5% in 2021, 76.9% in 2022, and 46.4% in

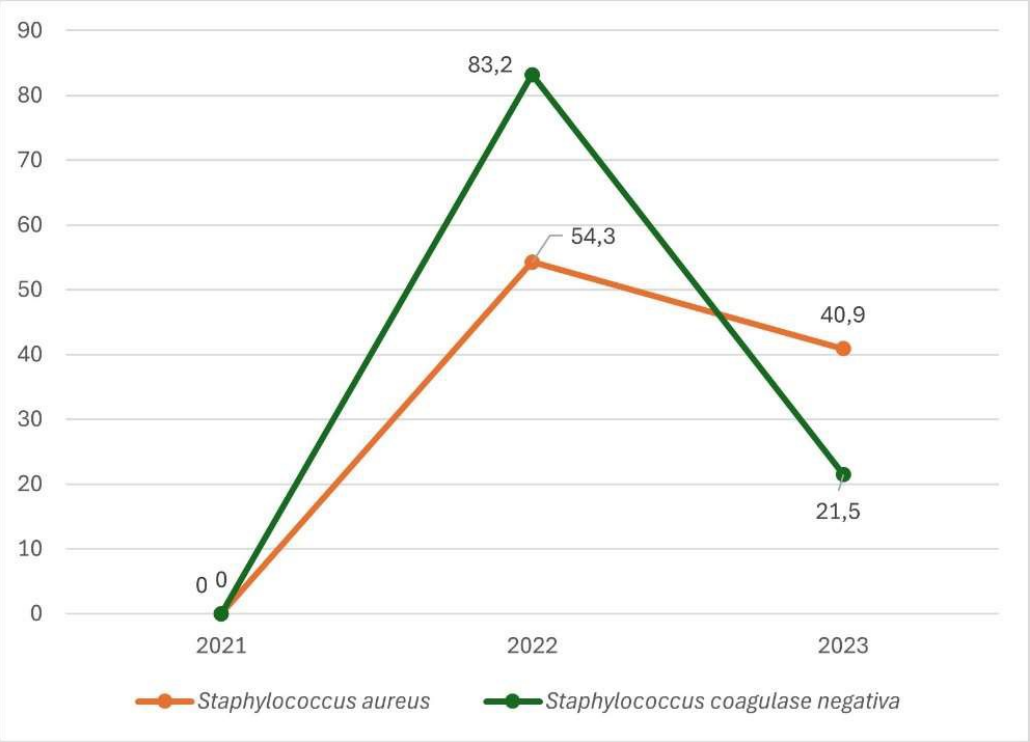
2023, while Enterococcus spp. reached 62.5% resistance in 2023 (Figure 6). In Staphylococcus aureus, oxacillin (OXA) resistance decreased from 54.3% in 2022 to 40.9%. In coagulase-negative staphylococci, OXA resistance was also lower in 2023 (from 83.2% in 2022 to 21.5% in 2023) (Figure 7).

Figure 6 – Vancomycin resistance rate of the main Gram-positive microorganisms of CLABSI in adult ICUs in the state of Ceará, from 2021 to 2023.



Source: Author's own work (2026).

Figure 7 – Oxacillin resistance rate of the main Gram-positive microorganisms of CLABSI in adult ICUs in the state of Ceará, from 2021 to 2023.



Source: Author's own work (2026).

DISCUSSION

The DI of IPCSL in adult ICUs in Ceará showed significant variation during the analyzed period, with a reduction in 2022 and a return to a high level in 2023, close to that observed in 2021. This behavior is consistent with a multifactorial phenomenon, in which fluctuations may reflect simultaneous changes in healthcare risk, use and duration of intravascular devices, patient profile and severity, and adherence to prevention practices, as well as variations in the sensitivity of surveillance and the quality/consistency of reported records[6,8,9].

The reduction observed in 2022 may be consistent with improvements in preventive measures, especially those focused on central venous catheter care, such as the implementation and maintenance of insertion and maintenance bundles, audits, and standardization of practices. However, it may also reflect variations in the population served, the length of hospital stay, and the capacity for detection and recording over time. Conversely, the increase in 2023 may be related to the loss of sustainability of interventions, greater clinical complexity and exposure time, or even to improvements in the collection and qualification of notifications[6,8,9].

Evidence produced in the context of the COVID-19 pandemic describes changes in healthcare-associated infections (HAIs) in critical care units, associated with changes in patient flow, healthcare overload, and fluctuations in adherence to preventive measures, which reinforces the plausibility of temporal variations in the indicators. From this perspective, surveillance should operate as

a continuous feedback system for services, guiding trend analysis and the implementation of corrective and sustainable actions[10].

In the microbiological component, the set of findings is consistent with high selective pressure in the ICU environment and with the circulation of resistant profiles in Gram-negative bacilli (GNB) frequently implicated in severe infections. The maintenance of very high resistance to CEF in Klebsiella pneumoniae, and the increase observed in Enterobacter spp. between 2021 and 2022, with maintenance of high levels in 2023, in addition to the increase seen in Proteus spp. from 2022 to 2023, suggest an unfavorable scenario for empirical regimens based on this class, especially in severe cases of CLABSI, in which the initial therapeutic adequacy plays a critical role in the outcome[11].

The significant increase in Enterobacter spp. between 2021 and 2022 suggests a possible event of selection or clonal dissemination (e.g., local outbreaks, change in species predominance within the group, regional variations), or even a change in the profile of antimicrobials used[12-15]. Even the decrease in 2023 (without returning to the 2021 level) maintains resistance at a high level, reinforcing that, even with annual fluctuations, the structural risk remains. In this context, the interpretation of trends should be integrated with local surveillance (antibiograms by service, outbreak monitoring, and prevention indicators), recognizing that aggregated data do not allow confirmation of specific mechanisms or clonality, but signal the need for investigation and timely response[13,14].

Resistance to CARBs also stood out, with high values and, in some microorganisms, a growing trend over the period. In Acinetobacter spp., the percentages remained high in all years, as well as in Klebsiella pneumoniae. In Enterobacter spp., a progressive increase was observed, and in Proteus spp., an increase between 2022 and 2023. This pattern is particularly relevant in IPCS in critically ill patients, because CARB resistance reduces therapeutic predictability and increases the risk of discordant empirical therapy in sepsis scenarios, where the initial adequacy of the antimicrobial is crucial for prognosis13,14. Furthermore, recent guidelines highlight that the management of CARB-resistant Gram-negative bacilli requires integration between local surveillance, risk stratification (by unit and patient profile), and antimicrobial use optimization programs, in order to balance clinical effectiveness and containment of selective pressure[14,16].

In Acinetobacter spp., high and persistent resistance is particularly concerning in ICUs, as microorganisms of this genus have a recognized ability to survive for extended periods on surfaces and to remain in environmental reservoirs of care, favoring cross-transmission and the occurrence of outbreaks when there are weaknesses in environmental hygiene and work processes[17,18]. From a public health perspective, this finding also aligns with the WHO's list of priority bacterial pathogens, in which CARB-resistant Gram-negative bacilli, such as Acinetobacter baumannii and Enterobacterales, have higher priority,

given the combination of high burden, clinical severity, and therapeutic limitations[3].

In Pseudomonas aeruginosa , the fluctuation in CARB resistance, with a lower percentage in 2022 and an increase in 2023, may be due to variations in the profile of critically ill patients, changes in selective pressure resulting from the use of antimicrobials, and possible aggregation events (e.g., concentration of cases in certain services or periods)[14,16]. In non-fermenting bacilli, annual fluctuations may reflect both changes in care practices and antimicrobial consumption, as well as transmission episodes and outbreaks, especially when there are failures in prevention and control measures in high-risk units[19].

Resistance to POLI, although variable, remained present and is clinically relevant because it involves a class often reserved for infections caused by multidrug-resistant Gram-negative bacteria with limited therapeutic alternatives[20]. Furthermore, the testing and interpretation of susceptibility to POLI itself requires methodological attention, which can contribute to heterogeneity between laboratories and reinforces the importance of standardization and quality assurance in microbiological surveillance[21].

The identification of resistance to CAZ-AVI in 2023, in both Enterobacter spp. and Proteus spp., and the increase observed in Klebsiella pneumoniae between 2022 and 2023, constitute relevant findings, as they involve an antimicrobial combination frequently reserved for the treatment of infections caused by multidrug-resistant Gram-negative bacilli, especially Enterobacterales resistant to CARB[22].

For Enterobacter spp. and Proteus spp., it was not possible to establish a temporal comparison with previous years due to the absence of testing in the preceding period, which imposes caution in the interpretation of trends and may reflect, in part, variations in laboratory routines and susceptibility panels adopted by the services9. Even so, the percentages observed reinforce the importance of systematic surveillance and judicious use of CAZ-AVI, in order to avoid premature loss of effectiveness[14,22].

Enterococcus faecium stand out, as does the percentage observed for Enterococcus spp. in 2023. Although the reduction in 2023 may reflect variations in the profile of the isolates evaluated and/or the effects of prevention and control measures, the level remains concerning in the ICU. The clinical and epidemiological relevance of VANCO-resistant enterococci in this scenario stems from the potential for colonization of the gastrointestinal tract, environmental persistence, and dissemination through contact, with a higher occurrence in contexts of prolonged hospitalization, high healthcare workload, and prior exposure to broad-spectrum antimicrobials[23].

For Staphylococcus aureus and coagulase-negative staphylococci, the reduction in OXA resistance in 2023 may suggest an improvement in the sensitivity profile but should be interpreted with caution. In aggregate analyses, this behavior may be influenced by variations in the number of isolates tested,

changes in the collection profile, laboratory methodological differences over time, or even regional/hospital variations "diluted" in the annual aggregate[24-25].

For coagulase-negative staphylococci, interpretation is particularly sensitive to aspects of the pre-analytical phase, since this group is among the main microorganisms associated with blood culture contamination. Thus, fluctuations in the volume of collections and the proportion of contaminated samples can influence both the denominator and the resistance estimates when the data are summarized. In this context, the reduction in the number of isolates tested in 2023 may have contributed to the magnitude of the observed variation[26].

This study uses aggregated secondary data and depends on the quality and standardization of notifications, which may introduce heterogeneity between services and in the analyzed period. It was not possible to adjust the findings for clinical and care variables (e.g., severity, use of invasive devices, patient profile, and prior exposure to antimicrobials), nor to assess the contribution of outbreaks or clonal dissemination, since there is no molecular typing within the scope of the database used. Finally, variations in the volume of cultures performed, in the request criteria, and in the panel of antimicrobials tested may influence the resistance estimates and the comparability between years, especially when the number of isolates is reduced[27, 28].

CONCLUSION

The findings indicate that CLABSIs in adult ICUs in Ceará showed significant variation in infection rate and a resistance profile consistent with high circulation of multidrug-resistant Gram-negative bacilli (GNBs), highlighting high resistance rates to CEF and CARB, and the identification of CAZ-AVI resistance in 2023. Among Gram-positive bacteria, VANCO resistance in enterococci remained significant, requiring continuous surveillance and integrated actions. Taken together, these results reinforce the need to strengthen, in a coordinated manner, CLABSI prevention, microbiological surveillance, and the rational use of antimicrobials, integrating the Infection Control Committee, laboratory, Antimicrobial Stewardship Program, and Sanitary Surveillance for a timely and sustained response.

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