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Original research

Bloodstream infections and antibiotic resistance at a regional hospital, Colombia, 2019–2021

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ABSTRACT

Objectives. To assess antibiotic susceptibility of World Health Organization (WHO) priority bacteria (*Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella* spp., *Staphylococcus aureus*, and *Streptococcus pneumoniae*) in blood cultures at the Orinoquía regional hospital in Colombia.

Methods. This was cross-sectional study using routine laboratory data for the period 2019–2021. Data on blood samples from patients suspected of a bloodstream infection were examined. We determined: the total number of blood cultures done and the proportion with culture yield; the characteristics of patients with priority bacteria; and the type of bacteria isolated and antibiotic resistance patterns.

Results. Of 25 469 blood cultures done, 1628 (6%) yielded bacteria; 774 (48%) of these bacteria were WHO priority pathogens. Most of the priority bacteria isolated (558; 72%) were gram-negative and 216 (28%) were gram-positive organisms. Most patients with priority bacteria (666; 86%) were hospitalized in wards other than the intensive care unit, 427 (55%) were male, and 321 (42%) were ≥ 60 years of age. Of the 216 gram-positive bacteria isolated, 205 (95%) were *Staphylococcus aureus*. Of the 558 gram-negative priority bacteria isolated, the three most common were *Escherichia coli* (34%), *Klebsiella pneumoniae* (28%), and *Acinetobacter baumannii* (20%). The highest resistance of *Staphylococcus aureus* was to oxacillin (41%). For gram-negative bacteria, resistance to antibiotics ranged from 4% (amikacin) to 72% (ampicillin).

Conclusions. Bacterial yield from blood cultures was low and could be improved. WHO priority bacteria were found in all hospital wards. This calls for rigorous infection prevention and control standards and continued surveillance of antibiotic resistance.

Keyword Sepsis; blood culture; anti-bacterial agents; drug resistance, microbial; Colombia.

Bloodstream infections (also known as sepsis) are life-threatening and need to be treated immediately. Mortality in cases of sepsis is estimated to be 15–30% (1–3). When sepsis is suspected, health care practitioners usually start patients on intravenous broad-spectrum antibiotics that cover various types of bacteria while waiting for the results of blood culture and antibiotic sensitivity testing. When these results become available, the treatment is tailored and an effective antibiotic is used (4). Timely availability of blood culture results promotes diagnostic stewardship and rational use of antibiotics (5, 6).

In 2015, the World Health Organization (WHO) introduced the Global Antimicrobial Resistance Surveillance System (GLASS) for monitoring antimicrobial resistance. In blood samples, surveillance is recommended for six priority pathogens. These pathogens include four gram-negative bacteria (*Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, and

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Salmonella spp.) and two gram-positive bacteria (*Staphylococcus aureus* and *Streptococcus pneumoniae*) (7).

A recent systematic review of 163 studies from low- and lower middle-income countries showed considerable heterogeneity between studies on antibiotic resistance in the priority pathogens (8). Pooled resistance proportions for gram-negative pathogens were higher in low- and lower middle-income countries than in high-income countries. Given the observed heterogeneity in the levels of resistance, the review recommended the need for improved national and subnational surveillance to detect differences in antibiotic resistance at various levels.

Previous studies from Colombia have also highlighted varying bacterial profiles and resistance patterns (9–11) and the importance of blood culture and antibiotic sensitivity testing, including the use of automated systems (6,12–14).

The Orinoquía regional tertiary hospital in Colombia has a quality-controlled laboratory that has data on antibiotic resistance in blood samples from patients suspected of sepsis. These data provide an opportunity to analyze culture yields and antibiotic resistance patterns for WHO priority bacteria. Such hospital-level data on antimicrobial resistance are vital to track evolving bacterial profiles and resistance, which in turn could inform and enhance infection prevention and control and stewardship programs.

We therefore aimed to assess the antibiotic susceptibility of WHO priority pathogens in blood samples at the Orinoquía regional tertiary hospital in Colombia. The specific objectives were to determine: (i) the total number of blood cultures done and the proportion with a culture yield; and (ii) the WHO priority bacteria and their antibiotic resistance patterns.

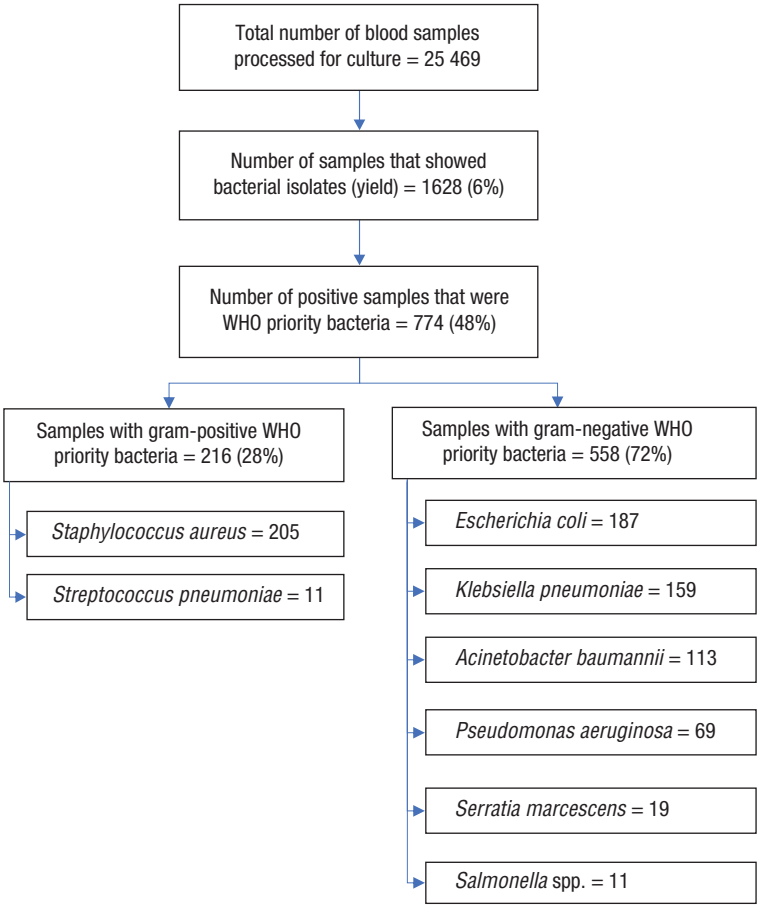
METHODS

Study design and setting

This was a cross-sectional descriptive study using routine hospital data.

The study was carried out at the Orinoquía regional tertiary hospital in Yopal, Colombia. Colombia has 2711 hospitals in the country with more than 78 000 hospital beds. The Orinoquía regional hospital was established in 1954 and it became a regional tertiary hospital in 2015. It has a catchment area of about 177 688 inhabitants. The hospital has 333 beds, 1234 health workers, and offers emergency services, outpatient consultation, hospitalization, and surgical services. The inpatient wards include internal medicine, surgery, orthopedics, obstetrics and gynecology, pediatrics, and neonatology. Before 2020, the hospital had only a neonatal intensive care unit (ICU). As a result of coronavirus disease 2019 (COVID-19) pandemic, the

FIGURE 1. Culture yield and WHO priority bacteria isolated from blood samples at Orinoquía hospital, Colombia, 2019-2021



WHO, World Health Organization.
Source: Prepared by authors from the results.

emergency unit was turned into an ICU to manage patients with severe COVID-19. The total number of ICU beds increased from four to 96 in 2020. The hospital has a laboratory that offers all the basic tests including biochemistry, hematology, blood culture, and antibiotic sensitivity testing. The hospital sends antimicrobial resistance information to the Colombian national health institute for antimicrobial surveillance.

Blood sample collection and blood culture

For patients suspected of blood stream infection – defined as individuals with fever, hypotension, tachycardia, and tachypnea (7) – two blood specimens are drawn by clinical and paramedical staff and sent to the hospital laboratory. Blood cultures and antibiotic sensitivity testing are done according to the guidelines of the Clinical and Laboratory Standards Institute (15).

Each of the two 10-mL blood specimens are transferred into 30 mL of brain–heart infusion broth and incubated for 5 days in a BACT/ALERT® 3D (bioMérieux) automated microbial detection system. Any signs of bacterial colonies are reported at 48 hours and the culture is then processed for identification of the bacteria and antibiotic sensitivity testing. All bacterial colonies are subcultured for purity and identified by colony morphology and biochemical tests. Isolates are confirmed using the VITEK® 2 isolation system (bioMérieux).

Antibiotic susceptibility testing

All isolated pathogens are tested for antibiotic susceptibility by the VITEK® 2 system and read according to recommendations of the Clinical and Laboratory Standards Institute (15). The results are expressed as sensitive, intermediate, or resistant. In cases of bacterial growth, a preliminary report is sent to the treating clinician and the final report is sent within 48 hours. Established quality-control measures are in place based on national standards.

All laboratory data were entered manually into the WHONET data platform (16) by a trained data-entry clerk who entered the data from an automated machine for culture and sensitivity testing. Data entry into WHONET was cross-validated by a microbiologist. Antibiotic resistance was categorized using the WHO classification of Access (first-line), Watch (restricted), Reserve (last resort) (AWaRe) antibiotics (17).

Study population and data collected

All blood cultures and antibiotic sensitivity testing that were done at the regional public hospital of Orinoquía, Colombia during January 2019 to December 2021 were included in our study.

Data on patient characteristics, type of ward, bacterial culture, bacterial pathogen identified, and antibiotic susceptibility results were retrieved from hospital records and transferred to the electronic database in Microsoft Excel format.

Statistical analysis

Microsoft Excel was imported into EpiData software v2.2.2.186 (EpiData Association, Odense, Denmark) for the analysis. Results are presented as numbers and percentages.

Ethics approval

Permission to use the laboratory data was sought from the Chief of the Investigation Group of Orinoquía hospital. National approval was obtained from the health research ethics committee of Orinoquía hospital (Acta 005 2021). International ethics approval was obtained from the ethics advisory group of the International Union against Tuberculosis and Lung Disease, Paris, France (EAG 24/21) and the Pan American Health Organization (0385.01 2021). The study used anonymized program data and therefore individual informed consent did not apply.

TABLE 1. Characteristics of patients with WHO priority bacteria isolated from blood cultures at Orinoquía hospital, Colombia, 2019–2021

Characteristic	n (%)			
	2019 (*n* = 274)	2020 (*n* = 214)	2021 (*n* = 286)	Total (*n* = 774)
Age, in years				
≤ 1 (infant)	17 (6)	11 (5)	9 (3)	37 (5)
1–4 (under-5)	34 (12)	18 (8)	11 (4)	63 (8)
5–18 (pediatric)	38 (14)	20 (9)	15 (5)	73 (9)
19–59 (adult)	83 (30)	70 (33)	126 (44)	279 (36)
≥ 60 (elderly)	101 (37)	95 (44)	125 (44)	321 (42)
Sex				
Male	160 (58)	108 (50)	159 (56)	427 (55)
Female	113 (41)	106 (50)	127 (44)	346 (45)
Ward admitted to				
Intensive care unit	4 (2)	8 (4)	96 (34)	108 (14)
Others	270 (98)	206 (96)	190 (66)	666 (86)

WHO, World Health Organization.
Note: Data were missing on age and sex for one bacterium.
Source: Prepared by authors from the results.

TABLE 2. WHO priority bacteria isolated from blood cultures at Orinoquía hospital, Colombia, 2019–2021

WHO priority bacteria	2019	2020	2021	Total
	n	n	n	n (%)
Gram-positive				
Staphylococcus aureus	64	65	76	205 (95)
Streptococcus pneumoniae	5	5	1	11 (5)
Total	**69**	**70**	**77**	**216**
Gram-negative				
Escherichia coli	64	65	58	187 (34)
Klebsiella pneumoniae	53	34	72	159 (28)
Acinetobacter baumannii	64	23	26	113 (20)
Pseudomonas aeruginosa	15	18	36	69 (12)
Serratia marcescens	3	3	13	19 (3)
Salmonella spp.	6	1	4	11 (2)
Total	**205**	**144**	**209**	**558**

WHO, World Health Organization.
Source: Prepared by authors from the results.

RESULTS

Culture yield and WHO priority bacteria isolated

Of a total of 25 469 blood samples that were processed for culture, 1628 (6%) yielded bacteria and 774 (3%) were WHO priority bacteria. Of the priority pathogens, 558 (72%) were gram-negative and 216 (28%) were gram-positive organisms (Figure 1).

Characteristics of patients infected with WHO priority bacteria

Of patients infected with WHO priority bacteria, the greatest proportion were older than 60 years (42%), were male (55%), and were hospitalized in general wards (86%) (Table 1).

WHO priority bacteria isolated and their antibiotic resistance patterns

Of the 216 gram-positive WHO priority bacteria isolated, 205 (95%) were *Staphylococcus aureus.* The three most common gram-negative bacteria were *Escherichia coli* (34%), *Klebsiella pneumoniae* (28%), and *Acinetobacter baumannii* (20%) (Table 2). *Pseudomonas aeruginosa, Serratia marcescens*, and *Salmonella* spp. made up the remaining gram-negative bacteria (Table 2).

Table 3 shows the antibiotic resistance patterns of the gram-positive WHO priority bacteria. Of the *Staphylococcus aureus* samples tested, the highest resistance was to oxacillin (41%), an Access group antibiotic. No resistance was found to vancomycin and linezolid (Watch group antibiotics) (17).

Table 4 shows antibiotic resistance patterns of gram-negative WHO priority bacteria. For all gram-negative bacteria, resistance to amikacin (Access group antibiotic) (17) was low (0–9%). Overall, resistance was highest to ampicillin (67%). In the Watch group antibiotics, resistance to all tested antibiotics ranged from 0% to 42%**.** Overall, resistance was highest to ciprofloxacin.

DISCUSSION

This 3-year study of all blood samples (25 469) processed in a regional tertiary hospital in Colombia showed that only 6% had a bacterial culture yield and WHO priority bacteria were isolated in patients from all hospital wards.

The study strengths are that data covered a 3-year period, laboratory quality standards were ensured and reporting was in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (18). The study also had some limitations. We had no data on how blood sample collection, transport, and storage were done, and this might have influenced culture yields. We also used two blood specimens instead of the recommended three and this might have negatively influenced the culture yield. Laboratory turn-around times, which are important for clinical decision-making, were also not available in the database. Going forwards, this element should be added to the database. Finally, we did not include Reserve antibiotics for resistance testing and this could be considered in future studies.

The study findings have a number of implications. First, the finding of WHO priority bacteria in all general hospital wards is concerning. This may be explained by the reorganization of the hospital wards to accommodate severely ill patients without COVID-19 in the general wards as the ICU was overloaded with COVID-19 patients. Understandably, general wards do not have the same infection prevention and control standards as specialized ICUs, and acquisition and transmission of WHO priority pathogens become more possible in this context. Whatever the reasons for this finding, the priority now is to ensure high infection prevention and control standards and continued vigilance in the general wards.

Second, our culture yield was 6%, which is low. Although blood culture yields are known to be generally low, this figure is lower than reports from India (9%) (19), Europe (14%) (20), and Cameroon (28%) (21). The underlying message here is to try to achieve higher culture positivity rates. A number of factors can influence the yield of blood cultures. These factors include

TABLE 3. Antibiotic resistance patterns for gram-positive WHO priority bacteria isolated from blood cultures at Orinoquía hospital, Colombia, 2019–2021

Antibiotic	Gram-positive		*Staphylococcus aureus*		*Streptococcus pneumoniae*	
	Tested	Resistant	Tested	Resistant	Tested	Resistant
	n	n (%)	*n*	n (%)	*n*	n (%)
Access						
Clindamycin	212	8 (4)	205	6 (3)	7	2 (29)
Gentamicin	207	8 (4)	205	7 (3)	2	1 (50)
Oxacillin	198	82 (41)	198	82 (41)	0	NA
Sulfamethoxazole + trimethoprim	212	5 (2)	205	5 (2)	7	1 (14)
Watch						
Ciprofloxacin	205	7 (3)	205	7 (3)	0	NA
Erythromycin	211	46 (22)	203	44 (22)	8	2 (25)
Vancomycin	213	0 (0)	205	0 (0)	8	0 (0)
Linezolid	213	0 (0)	205	0 (0)	8	0 (0)

WHO, World Health Organization; NA, not applicable.
Note: Not all samples were tested for all antibiotics because of technical issues with the VITEK® cards.
Source: Prepared by authors from the results.

adherence to: the criteria of suspected bloodstream infection (sepsis) before use of antibiotics; the volume of blood drawn; the frequency with which culture samples are drawn; and the site from which the culture samples are taken (22). Handling of cultures in the microbiology laboratory and the type of blood culture system used also influence blood culture yield (22). Other factors include challenges in sample collection and transportation, and higher storage temperatures before incubation (23). Determining the exact reasons behind the low culture yield would allow the institution of take corrective measures but requires additional specific research.

Finally, the main pathogens isolated in our study included *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Acinetobacter baumannii*, which is similar to the pattern reported in other hospitals in Colombia (24). However, resistance patterns of WHO priority bacteria (gram-positive and

TABLE 4. Antibiotic resistance patterns of gram-negative WHO priority bacteria isolated from blood cultures at Orinoquía hospital, Colombia, 2019–2021

Antibiotic	Total gram-negative		*Escherichia coli*		*Klebsiella pneumoniae*		*Acinetobacter baumannii*		*Pseudomonas aeruginosa*		*Serratia marcescens*		*Salmonella spp.*	
	Tested	Resistant	Tested	Resistant	Tested	Resistant	Tested	Resistant	Tested	Resistant	Tested	Resistant	Tested	Resistant
	n	n (%)	*n*	n (%)	*n*	n (%)	*n*	n (%)	*n*	n (%)	*n*	n (%)	*n*	n (%)
Access														
Amikacin	445	17 (4)	187	0 (0)	159	11 (7)	0	NA	69	6 (9)	19	0 (0)	11	0 (0)
Ampicillin	66	44 (67)	35	21 (60)	27	23 (85)	0	NA	0	NA	0	NA	4	0 (0)
Ampicillin + sulbactam	470	159 (34)	187	64 (34)	159	71 (45)	113	13 (12)	0	NA	0	NA	11	0 (0)
Gentamicin	557	77 (14)	187	33 (18)	159	27 (17)	113	4 (4)	69	17 (25)	19	2 (11)	11	1 (9)
Sulfamethoxazole + trimethoprim	295	46 (16)	187	17 (9)	27	10 (37)	66	18 (27)	0	NA	10	1 (10)	4	0 (0)
Watch														
Cefepime	558	53 (9)	187	8 (4)	159	24 (15)	113	6 (5)	69	10 (14)	19	7 (37)	11	0 (0)
Ceftriaxone	558	126 (23)	186	50 (27)	159	51 (32)	113	17 (15)	0	NA	19	8 (42)	11	0 (0)
Ceftazidime	558	63 (11)	187	20 (11)	159	21 (13)	113	4 (4)	69	9 (13)	18	8 (44)	11	0 (0)
Ciprofloxacin	558	145 (26)	187	68 (36)	159	54 (34)	113	3 (3)	69	11 (16)	19	8 (42)	11	1 (9)
Ertapenem	382	28 (7)	186	3 (2)	159	23 (14)	0	NA	0	NA	19	0 (0)	11	0 (0)
Meropenem	557	53 (10)	186	3 (2)	159	29 (18)	113	6 (5)	69	15 (22)	19	0 (0)	11	0 (0)
Piperacillin + tazobactam	512	87 (17)	178	17 (10)	150	41 (27)	108	11 (10)	68	10 (15)	0	NA	8	0 (0)

WHO, World Health Organization; NA, not applicable.
Note: Not all samples were tested for all antibiotics because of technical issues with the VITEK® cards.
Source: Prepared by authors from the results.

gram-negative) were generally low compared to the patterns reported in other low- and middle-income countries (8). For gram-positive bacteria, oxacillin resistance was highest (41%) and they showed the presence of methicillin-resistant *Staphylococcus aureus* (MRSA). Encouragingly, as reported in a recent review from other countries, we found no resistance to vancomycin or linezolid, which may be linked to the fact that their use is restricted in the community (25). In gram-negative bacteria, resistance to third-generation cephalosporins was less than 23%, which contrasts with other settings where the pooled prevalence of resistance was 75% (8). Ciprofloxacin resistance was the highest in our study (42%). This drug is commonly used orally with reports of frequent use in the community during COVID-19.

Another point to take into account is that the low levels of antimicrobial resistance in *Acinetobacter baumannii* and *Pseudomonas aeruginosa* may be associated with low access to broad-spectrum antibiotics and the level of care of the hospital.

In conclusion, our findings are important as they show that WHO priority bacteria are circulating in general wards. This highlights the urgent need to ensure infection, prevention and control standards for patients, visitors, and health care workers and for continued surveillance of antimicrobial resistance. In addition, the yield from bacterial culture of blood samples was relatively low which could be improved.

Author contributions. JCS, LGA, and DF were involved in the conception or design of the work, and data acquisition. JCS, AA, and PT analysed and interpreted the data. JCS, AA, PT, and CT drafted the manuscript. AA, PT, JR, and RZ critically reviewed and revised the manuscript. All authors reviewed and approved the final version.

Conflicts of interest. None declared.

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Infecciones del torrente sanguíneo y resistencia a los antibióticos en un hospital regional en Colombia, 2019-2021

RESUMEN

Objetivos. Evaluar la sensibilidad a los antibióticos de las bacterias incluidas en la lista prioritaria de la Organización Mundial de la Salud (OMS) (*Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella* spp., *Staphylococcus aureus* y *Streptococcus pneumoniae*) en hemocultivos en el Hospital Regional de la Orinoquía en Colombia.

Métodos. Se trata de un estudio transversal que empleó datos rutinarios de laboratorio del período comprendido entre los años 2019 y 2021. Se examinaron datos de muestras de sangre de pacientes con presunción clínica de infección del torrente sanguíneo. Se determinó el número total de hemocultivos realizados y la proporción cultivos con resultados, las características de los pacientes con bacterias prioritarias, así como el tipo de bacterias aisladas y los patrones de resistencia a los antibióticos.

Resultados. De 25 469 hemocultivos realizados, se aislaron bacterias en 1628 (6%); 774 (48%) con agentes patógenos prioritarios de la OMS. La mayoría de las cepas bacterianas prioritarias aisladas (558; 72%) eran gramnegativas y 216 (28%), organismos grampositivos. La mayoría de los pacientes con bacterias prioritarias (666; 86%) fueron hospitalizados en salas distintas de la unidad de cuidados intensivos, 427 (55%) eran varones y 321 (42%) tenían 60 años o más. De las 216 bacterias grampositivas aisladas, 205 (95%) eran *Staphylococcus aureus*. De las 558 bacterias prioritarias gramnegativas aisladas, las tres más comunes fueron *Escherichia coli* (34%), *Klebsiella pneumoniae* (28%) y *Acinetobacter baumannii* (20%). La mayor resistencia de *Staphylococcus aureus* fue a la oxacilina (41%). Entre las bacterias gramnegativas, la resistencia a los antibióticos varió del 4% (amikacina) al 72% (ampicilina).

Conclusiones. El aislamiento de bacterias en los hemocultivos fue bajo y podría mejorarse. Se encontraron bacterias de la lista prioritaria de la OMS en todas las salas del hospital, por lo que es necesario aplicar rigurosas normas de prevención y control de infecciones y realizar una vigilancia continua de la resistencia a los antibióticos.

Palabras clave Sepsis; cultivo de sangre; antibacterianos; farmacorresistencia microbiana; Colombia.

Infecções de corrente sanguínea e resistência a antibióticos em um hospital regional, Colômbia, 2019-2021

RESUMO

Objetivos. Avaliar a suscetibilidade a antibióticos das bactérias consideradas prioritárias pela Organização Mundial da Saúde (OMS) (*Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella* spp., *Staphylococcus aureus* e *Streptococcus pneumoniae*) em hemoculturas coletadas no hospital regional de Orinoquía na Colômbia.

Métodos. Estudo transversal utilizando dados laboratoriais de rotina do período 2019-2021. Foram examinados os dados de amostras de sangue de pacientes com suspeita de infecção de corrente sanguínea. Determinamos o número total de hemoculturas realizadas e a proporção de culturas com rendimento, as características dos pacientes com bactérias prioritárias, e o tipo de bactéria isolada e padrões de resistência a antibióticos.

Resultados. Das 25.469 hemoculturas realizadas, 1.628 (6%) foram positivas para bactérias, sendo que 774 (48%) dessas bactérias eram da lista de agentes patogênicos prioritários da OMS. A maioria das bactérias prioritárias isoladas (558; 72%) eram gram-negativas e 216 (28%) eram gram-positivas. A maioria dos pacientes com bactérias prioritárias (666; 86%) estava internada em enfermaria, e não em unidade de terapia intensiva. 427 (55%) eram homens e 321 (42%) tinham ≥ 60 anos de idade. Das 216 bactérias gram-positivas isoladas, 205 (95%) eram *Staphylococcus aureus*. Das 558 bactérias gram-negativas prioritárias isoladas, as três mais frequentes foram *Escherichia coli* (34%), *Klebsiella pneumoniae* (28%) e *Acinetobacter baumannii* (20%). O *Staphylococcus aureus* apresentou maior resistência à oxacilina (41%). Entre as bactérias gram-negativas, a resistência aos antibióticos variou entre 4% (amicacina) e 72% (ampicilina).

Conclusões. O rendimento bacteriano das hemoculturas foi baixo e pode ser melhorado. As bactérias consideradas prioritárias pela OMS foram encontradas em todas as enfermarias do hospital. Os achados exigem normas rigorosas de prevenção e controle de infecção, e vigilância contínua da resistência bacteriana a antibióticos.

Palavras-chave Sepse; hemocultura; antibacterianos; resistência microbiana a medicamentos; Colômbia.