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RESISTANT MICROORGANISMS IN A PEDIATRIC AND NEONATAL INTENSIVE CARE UNIT

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Abstract: Background: Health Care Associated Infections (HAIs) present high rates in Pediatric and Neonatal Intensive Care Units worldwide and in the Pediatric, Cardiothoracic and Neonatal Intensive Care Units (ICU) of the Baca Pediatric Hospital. Ortiz, - Ecuador. The microorganisms that cause HAIs increase morbidity and mortality in ICUs. They present bacterial resistance that the World Health Organization aims to eliminate. **Objective:** Determine the microorganisms causing HAIs and bacterial resistance in the Pediatric, Cardiothoracic and Neonatal Intensive Units of the Baca Ortiz Pediatric Hospital Materials and **Methods:** Observational, Descriptive, Retrospective and documentary design lasting one year. The results were obtained through the epidemiology and infection control department. **Results:** A sample of 1,188 patients was obtained, 228 total Health Care Associated Infections (119 in the Pediatric and Cardiothoracic Intensive Care Units and 34 Neonatal Intensive Care Units), with a sample validity of 99%. We determined the microorganisms that cause HAIs, the microorganism with the highest frequency of recovery is *Klebsiella pneumoniae ESBL (extended spectrum ß-lactamases)*. Bacterial resistance to antibiotics was determined, of the microorganisms *Klebsiella pneumoniae* (63.9%) and *Pseudomona aeroginosa* (44.3%) resistant to Carbapenems. Multidrug-resistant *Staphylococcus aureus* (35.6%). **Discussion:** the microorganisms present in Neonatal Pediatric Intensive Care Units are present in a higher percentage than those determined worldwide. Bacterial resistance occurs in low-spectrum antibiotics. **Conclusion:** The microorganism causing HAIs in ICUs predominates *Klebsiella pneumoniae* ESBL. The measures used in ICUs must be aimed at controlling multidrug-resistant bacteria and eliminating them.

Keywords: Hospital Infection, Bacterial Drug Resistance, Multiple Bacterial Drug Resistance, Pediatric Intensive Care Unit Neonatal Intensive Care Units.

INTRODUCTION

Bacterial resistance to antimicrobials (AMR) has become a global problem. Mutations of the microorganism transform medicines into obsolete and less effective weapons. It is one of the threats to Public Health. Organizations have focused their objective on the fight against this phenomenon(1,2).

There were 4.95 million deaths associated with bacterial AMR in 2019 and 1.27 million deaths attributable to bacterial AMR. The highest mortality is attributed to Western Sub-Saharan Africa, with 27.3 deaths per 100,000 inhabitants and the lowest in Australasia, which has 6.5 deaths per 100,000 inhabitants. Lower respiratory tract infections (infectious syndrome) are the most serious (1.5 million deaths associated with mortality – 2019). The six pathogens associated with resistance and attributable mortalities are: *Escherichia coli*, followed by *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, *Acinetobacter baumannii* (3).

Antibiotic resistance is analyzed worldwide, where the figures are alarming, *Klebsiella pneumoniae* determined resistance to amikacin (40.8%), aztreonam (73.3%), ceftazidime (75.7%), ciprofloxacin (59.8%), colistin (2.9%), cefotaxime (79.2%) [95% CI 68.0-87.2], cefepime (72.6) and imipenem (65.6%) (3). *Methicillin* Resistant *Staphylococcus aureus* (MRSA) and *Methicillin Resistant Coagulase Negative Staphylococcus* (MRCoNS) is effectively treated with linezolid, daptomycin and tigecycline effectively inhibit (99.9%) MRSA (4). *Acinetobacter baumannii* with combined frequency of resistance to carbapenems was 85.1%(5).

The World Health Organization has implemented efficient measures to reduce morbidity and mortality attributed to microorganisms and their resistance (6). The "Global Plan for Bacterial Resistance" was proposed (7,8). Emphasis is placed on epidemiological surveillance studies and measures to eliminate bacterial residence (9,10). This study aims to determine the microorganisms causing HAIs and bacterial resistance in the Pediatric, Cardiothoracic and Neonatal Intensive Units of the Baca Pediatric Hospital. Ortiz.

MATERIALS AND METHODS

A quantitative, descriptive, retrospective research design was carried out on patients with Health Care Associated Infections; from the period to January – December 2019. The data was obtained under the foundations of the *Manual of Procedures of the SIVE Hospital Surveillance Subsystem - Infections Associated with Health Care - IAAS of the year 2019 (11).*

The population subjected to the study are users consecutively admitted to the Pediatric, Cardiothoracic and Neonatal Intensive Care Unit (ICU) of the "Baca Ortiz" Pediatric Hospital in the city of Quito – Ecuador. Purposive sampling was carried out. The readability criteria are patients admitted to the ICU, absence of IAAS upon admission and presence of invasive medical devices. The age of the population ranges from 0 to 29 days in newborns and 30 days to 15 years in patients. The two age groups include cardiac patients.

The first stage collects data from the departments of the *Department of Epidemiology, Microbiology, Pharmacovigilance, Intensive Care Unit* rooms, *Surgical Center, and Department of Statistics*. The second stage, the information was collected and consolidated in the instrument of each of the departments, the information was verified (Stage 3). The information was analyzed (Stage 4.5)

using the Health Care Associated Infections (HAIs) surveillance components and the Microorganism Resistance Surveillance Indicators (12). Descriptive statistics were used, analyzing measures of central tendency, dispersion and distribution.

RESULTS

MICROORGANISMS CAUSING HAIS IN PEDIATRIC INTENSIVE CARE UNITS

MICROORGANISMS CAUSING PNEUMONIA ASSOCIATED WITH MECHANICAL VENTILATION

The bacteria that cause Healthcare Associated Pneumonia are *Klebsiella pneumoniae ESBL (extended spectrum ß-lactamases)* with 30%; *Escherichia coli* ESBL (extended *spectrum ß-lactamases*). *Enterobacter cloacae* Amp-C, *Methicillin*-resistant *Staphylococcus aureus* MRSA present 6.7%; Multiresistant bacteria (1.7%) were also determined: *Pseudomonas aeruginosa* resistant to Imipenem (Carbapenems) and *Acinetobacter baumannii* resistant to ceftazidime (third generation cephalosporin) (Table 1*).*

MICROORGANISMS CAUSING URINARY TRACT INFECTIONS

The bacteria that cause Urinary Tract Infections are predominantly *Klebsiella pneumoniae ESBL (extended spectrum ß-lactamases)* with 21.9%; 31.3% of cases of *Candida albicans* were determined (Table 1*).*

MICROORGANISMS CAUSING BLOODSTREAM INFECTIONS CAUSED BY CENTRAL VENOUS CATHETER

The *Klebsiella pneumoniae ESBL* microorganism (extended *spectrum ß-lactamases*) is the cause of 30.1% and 10.8% of *Candida albicans*, they are the bacteria with the highest incidence causing Bloodstream Infections caused by Central Venous Catheter in the UNCP and UCIC (Table *1).*

THE MICROORGANISMS THAT CAUSE IAAS IN NEONATAL INTENSIVE CARE UNITS

26.1% of the bacteremias in neonates were isolated and were caused by *Klebsiella pneumoniae ESBL (extended spectrum ß-lactamases)*, 13% by *S. aureus*; *Candida parapsilosis* and *Klebsiella pneumoniae* were recovered in 8.7% of cases. *Staphylococcus epidermidis* causes 42.9% of conjunctivitis in neonates. Multidrug-resistant bacteria such as *Enterobacter cloacae*, resistant to Imipenem (Carbapenems), are the cause of an episode of meningitis. The increase in multidrug-resistant bacteria is present with *Serratia marcescens* resistant to Imipenen (Carbapenems) with 6.5% and *Klebsiella pneumoniae* producing *Carbapenemase (KPC)* with 2.2% (Table 1).

MICROORGANISMS THAT CAUSE SURGICAL SITE INFECTIONS

The analysis of the microorganisms causing Surgical Site Infections in the Intensive Care Units, *Klebsiella pneumoniae ESBL (extended spectrum ß-lactamases)* was the cause of 36.8% of the infections in the Pediatric ICU and 37. 5% in Neonatal ICUs. Followed by *Methicillin-resistant Staphylococcus aureus* (MRSA) with 15.8%. The resistance of *Klebsiella pneumoniae* is 5.9% to third generation cephalosporins (Table *1).*

ETIOLOGICAL AGENT	INTENSIVE CARE UNITS						
	PEDIATRIC				NEONATAL		
	Microorganisms causing Health Care-Associated Infections						
	Pneumonia Associated with Mechanical Ventilation	Urinary tract infection	Bacteremia	Bacteremia	Healthcare Associated Pneumonia	Conjunctivitis	Meningitis
	%						
Escherichia coli		3,1		4,3			
Escherichia coli Amp-C (beta-lactamases)	1,7	3,1					
Escherichia coli ESBL (extended spectrum ß-lactamases)	6,7	6,3	9,6	26,1			
Escherichia coli resistant to Cefepime (Cephalosporins 4° G)			2,4				
Klebsiella pneumoniae	3,3	3,1	2,4	8,7			
Staphylococcus epidermidis						42,9	
Klebsiella pneumoniae BLEE (ß- lactamasas de espectro extendido)	30	21,9	30,1				
Klebsiella pneumoniae productora de Carbapenemasa (KPC)			1,2	2,2			
Klebsiella oxytoca	1,7	3,1	1,2	8,7			
Staphylococcus aureus	3,3		3,6	13	100	28,6	
Staphylococcus aureus meticilino resistente SARM	6,7	3,1	3,6	2,2			
Staphylococcus epidermidis	1,7		6				
Staphylococcus epidermidis meticilino resistente SARM	3,3		3,6				
Staphylococcus capitis			1,2				
Staphylococcus hominis			1,2				
Staphylococcus haemolyticus				2,2			
Pseudomonas aeruginosa	3,3	9,4	1,2				
Pseudomonas aeruginosa resistente a Ciprofloxacina (Quinolonas)	1,7	3,1					
Pseudomonas aeruginosa resistente a Imipenem (Carbapenémicos)	1,7						
Acinetobacter baumannii	5			2,2			
Acinetobacter baumannii resistente a ceftazidime (Cefalosporina de tercera generación)	1,7		1,2				
Candida albicans	3,3	31,3	10,8				
Candida lusitaniae		3,1	1,2				
Candida tropicalis			2,4				
Candida parapsilosis			3,6	8,7			
Stenotrophomonas maltophilia	1,7		1,2				
Stenotrophomonas maltophilia resistente a Amikacina (Aminoglucósidos)	1,7						
Serratia marcesnens	5						
Serratia marcesnens resistente a Imipenen (Carbapenemicos)	3,3	3,1	2,4	6,5			100
Serratia Liquefaciens				2,2			
Enterobacter cloacae	3,3	3,1	2,4	2,2			
Enterobacter cloacae Amp-C	6,7			6,5			

Enterococcus faecalis		3,1	2,4	2,2			
Proteus mirabilis				2,2			
Citrobacter freundii	3,3						
Aeromonas sp			1,2				
Haemophilus influenzae			1,2			28,6	
Burkhololderia cepacia			1,2				
Salmonella entérica			1,2				
Total	100	100	100	100	100	100	
n=	60	32	83	46	1	7	

Table 1. Microorganisms Causing HAI in Pediatric and Neonatal Intensive Care Units.

Source: Department of Epidemiology and Statistics. IAAS Control Subdirectorate. HPBO Intensive Care Units.

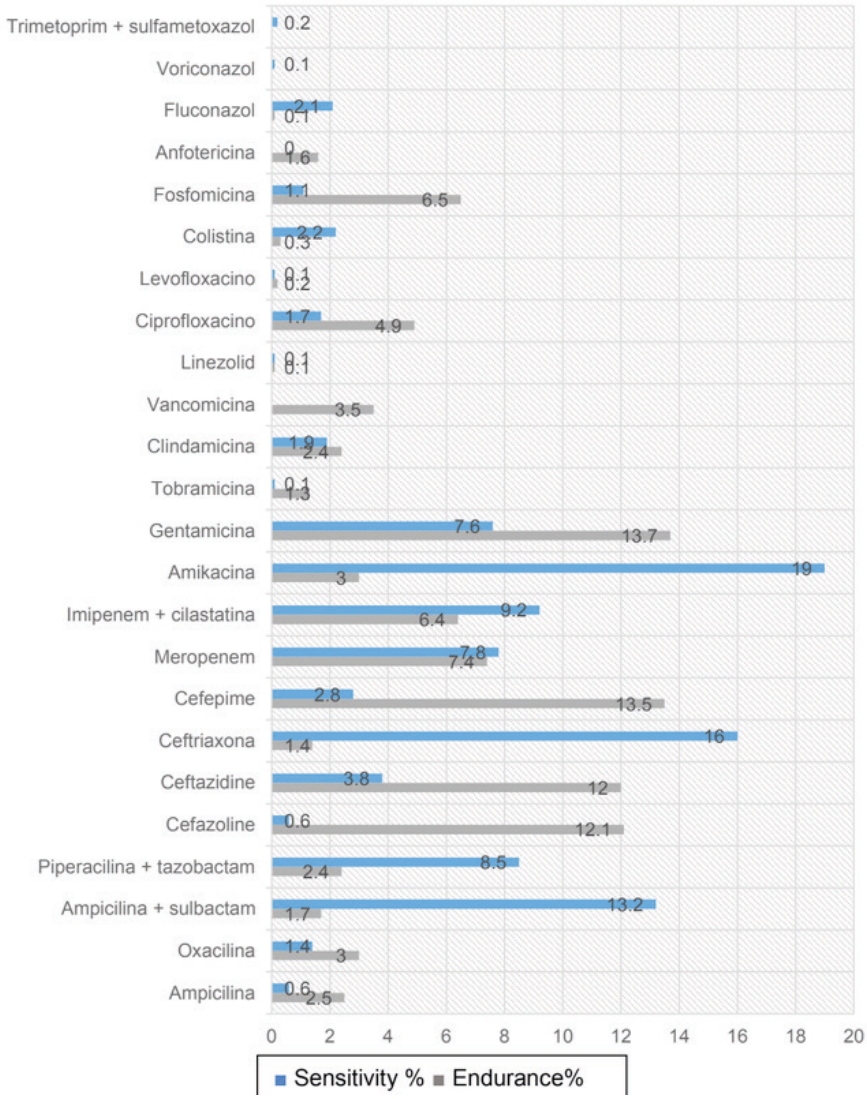

Table 2. Sensitivity and Resistance to Antibiotics of Microorganisms Causing Health Care-Associated Infections in Intensive Care Units

BACTERIAL SENSITIVITY AND RESISTANCE TO ANTIBIOTICS

The analysis of the Sensitivity and Resistance to Antibiotics of the Microorganisms Causing Infections Associated with Health Care in the Intensive Care Units of the Baca Ortiz Pediatric Hospital, 322 samples of tracheal secretion, blood and urine were taken and analyzed (Table 2*)*.

The analysis of the samples revealed resistance to antibiotics described by groups of drugs: Beta-lactams (Ampicillin, Oxacillin, Ampicillin + Sulbactam, Piperacillin + Tazobactam) present a low resistance of 1.7 to 3%, the sensitivity of the bacteria analyzed is evident in ampicillin + sulbactam with 13.2% (n=133) and piperacillin + tazobactam 8.5% (n=85) (Table 2*)*.

Resistance to Carbapenems reveals 7.4% resistant to Meropenem and 6.4% resistant to Imipenen + Cilastatin. The sensitivity is 7.8% (Meropenem) and 9.2% (Imipenem + Cilastatin) (Table 3). The aminoglycide group reports resistance to Amikacin 3%; Gentamicin 13.7% and Tobramycin 1.3%. The highest sensitivity was obtained by Amikacin (19%). Macrolides with their Clindamycin representative reported a resistance of 2.4%. Vancomycin represents 3.5% resistance, no bacteria sensitive to this glycopeptide were reported, linezolid presented a resistance and sensitivity of 0.1%. Quinolones represent a resistance to ciprofloxacin of 4.9% and to levofloxacin of 0.2% (Table *2)*.

Colistin showed 0.3% resistance, fosfomycin 6.5% resistance, and amphotericin B 1.6% resistance. 0.1% resistance for both fluconazole and voriconazole (Table *2)*.

BACTERIAL SENSITIVITY AND RESISTANCE TO BROAD SPECTRUM ANTIBIOTICS

Bacterial sensitivity and resistance to broad-spectrum antibiotics in HAIs in HPBO was determined: %), carbapenem-resistant *Klebsiella pneumoniae* (KPC) (57.1%). *Pseudomona aeruginosa* resistant to quinolones (48.4%) and resistant to cefepime (37.8%). *Klebsiella pneumoniae* resistant to third-generation cephalosporins (45.1%). *Echerichia coli* resistant to third-generation cephalosporins (27.3%) (Graph 1*)*.

The most relevant bacteria in Pneumonia Associated with Mechanical Ventilation are: *Pseudomona aeruginosa* resistant to quinolones (39.1%) and *Klebsiella pneumoniae* resistant to carbapenems (KPC) (24.5%) (Graph 1*)*.

The most relevant bacteria in Pneumonia Associated with Mechanical Ventilation are: *Methicillin*-resistant *Staphylococcus aureus* (15.6%). Carbapenem-resistant *Pseudomona aeruginosa* (41%), carbapenem-resistant *Klebsiella pneumoniae* (KPC) (57.1%), *Acinetobacter baumannii* (21.4%) (Graph 1*)*.

Urinary Tract Infection Associated with Indwelling Urinary Catheter is caused by carbapenem-resistant *Klebsiella pneumoniae* (KPC) (23.5%), quinolone-resistant *Pseudomonas aeruginosa* (9.4%) (Graph 1*)*.

Bloodstream infections caused by Venous Catheter are *Klebsiella pneumoniae* (KPC) (29.9%) and *Echerichia coli* resistant to third generation cephalosporins (12.1%) (Table 2*)*.

The sensitivity (Table 2) according to the microorganisms causing HAIs, in the Intensive Care Units, determined that 225 strains representing 100% of the isolates, *Methicillin*-resistant *Staphylococcus aureus* was recovered (35.6%); *Klebsiella pneumonaie* resistant to carbapenems (57.1%) and resistant to third generation cephalosporins (46.1%). *Pseudomona aeruginosa* showed resistance

to cefepime in 37.8% and resistance to quinolones (48.4%). *Acinetobacter baumannii* was resistant to carbapenems (46.8%) and resistant to quinolones (88.9%).

In the literature, in post-surgical pediatric patients with congenital heart disease, IAAs must be considered due to their ability to complicate and prolong the post-surgical recovery process and association of antibiotic regimens (13). Surgical site infection, caused mainly by gram-positive bacteria, was identified as the main cause of HAIs (14). *Acinetobacter baumanni* is the cause of SSIs (11,1%).

DISCUSSION

According to literature data on gram-negative bacilli, the majority of carbapenemase-producing strains correspond to clinical isolates of *K. pneumoniae and Escherichia coli*. The threat posed by carbapenemase-producing bacteria is manifested in the reports provided by the World Health Organization (WHO).(15).

Thus, in 2014, the World Health Organization reported that strains of *K. pneumoniae* resistant to carbapenems have spread worldwide, which has produced an increase in the rate of resistance to carbapenems above 50%, which leads to an increase of mortality and morbidity in patients with carbapenem-resistant *K. pneumoniae* infections (15).

In early 2017, the WHO published a list of priority pathogens that pose the greatest threat to human health. Bacteria resistant to carbapenem antimicrobials such as *A. baumannii, P.* aeruginosa and carbapenem-resistant extended-spectrum β-lactamases (ESBL)-producing enterobacteria stand out in the critical group (16).

The European Antimicrobial Resistance Surveillance Network (EARS-Net) reported in 2019 that the most frequently reported bacterial species was *Echerichia coli* (44.2%), followed by *S. aureus* (20.6%), *K. pneumoniae* (11.3%), *E. faecalis* (6.8%), *P. aeruginosa* (5.6%), *S. pneumoniae* (5.3%), *E. faecium* (4.5%) and *Acinetobacter* species (1.7%) (17). Resistance of A. baumannii has been determined up to 85%, which has been increasing (18)

Bacterial sensitivity and resistance, in *Bloodstream Infections caused by Central Venous Catheter*, was found to be produced by *Staphylococcus aureus*, Enterococuus faecalis, *Pseudomona aeruginosa*, *Klebsiella pneumonaie bacteria*; *Acinetobacter baumannii*; *Echerichia coli* (19).

In the HPBO ICUs, oxacillin-resistant *Staphylococcus aureus* bacteria were isolated in 35.9%; the Centers for Disease Control and Prevention and National Healthcare Safety Network (NHSN – CDC)(20,21) determined 50.7% and the International Nosocomial Infection Control Consorcian Foundation (INICC) (7) 64.6%; The data obtained in the HPBO are among the averages of the data presented internationally.

Klebsiella pneumonaie presented resistance according to the CDC of 28.8% (cephalosporins) 12.8% (carbapenem) and the INICC of 67.5% (cephalosporins) 36.1% (carbapenem); In the HPBO this bacteria was isolated, resistant to cephalosporins in 46.1% and 44.8% resistant to carbapenems. *Acinetobacter baumannii* presented a low resistance of 21.4% to carbapenems; For the INICC worldwide, there was a resistance of 73.4% and for the CDC, a resistance of 62.6% to carbapenems was found. *Echerichia coli* was isolated as a bacteria resistant to quinolones in 21.1%, low values for the data presented by the CDC (49.3%) and INICC (49.4%) (19).

The CDC in the 2018 report, in the Intensive Care Units reported that the bacteria causing Bloodstream Infections associated with Venous Catheter presented worldwide

Microorganism	Bacterial resistance	*Pneumonia Associated with Mechanical Ventilation*	*Urinary Tract Infections*	*Bloodstream Infections Caused by Venous Catheter*	*Surgical Wound Infection*	*IAAS UCI TOTAL*
		Resistance percentage				
Staphylococuus aureus	Oxacilina	3,1		10,7	1,8	15,6
Enterococcus faecium	Vancomicina			33,3		33,3
Pseudomona aeruginosa	Quinolonas	39,1	9,4			48,4
	Piperacilina + Tazobactam	34,5	5,5			40
	Amikacina	24,1	9,3			33,3
	Carbapenemicos	34,4	4,9		1,6	41
	Cefepime	30,5	7,3			37,8
Klebsiella pneumonaie	Ceftriaxona / Ceftazidine	3,9	23,5	11,8	5,9	45,1
	Carbapenemicos	24,5		29,9	2,7	57,1
Acinetobacter baumanii	Quinolonas				11,1	11,1
	Carbapenémicos	17,9		3,6		21,4
Echerichia coli	Ceftriaxona / Ceftazidine	15,2		12,1		27,3
	Carbapenemicos	11,1				11,1
	Quinolonas		14	7		21,1
TOTAL		238,3	73,9	108,4	23,1	443,6
n=		171	55	98	16	340

Table 2. Description of Resistance to broad-spectrum antibiotics according to the microorganisms causing Infections Associated with Health Care in Intensive Care Units

Source: HPBO Microbiology Department.

resistance to the Imipenem/Carbapenem-resistant *Acinetobacter baumannii* in 62.6%; oxacillin-resistant *Staphylococcus aureus* in 50.7%; quinolone-resistant *Echerichia coli* in 49.3%; resistant to ceftriaxone/ceftazidine in 19% and resistant to carbapenems in 1.9%; *Klebsiella pneumonaie* resistant to ceftriaxone/ceftazidine in 28.8%; resistant to Carbapenems in 12.8%; *Pseudomona aeruginosa* resistant to quinolones in 30.2%; resistant to carbapenems and cefepime in 26.1% (22).

The resistance marked worldwide by the INICC and the CDC in the United States, report higher percentages than in Ecuador in the Pediatric and Neonatal Intensive Care Units. Research considers that the incidence rates of HAIs are 10% higher in medium and low-developed countries, the mortality rate associated with HAIs is higher in developed countries. Multidrug-resistant Gram-negative species, especially *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* are predominant in high-income countries(23).

The results of this research suggest that patients hospitalized in critical pediatric units require highly specialized multidisciplinary management, which includes active surveillance, especially that proposed by the Ministry of Public Health of Ecuador, which will allow obtaining a diagnosis at any time. local and national level which will allow

structuring interventions for the prevention and control of HAIs, through the constant evaluation of the evidence-based measures used, using active behavior, early evaluating the need to use invasive procedures and justifying antimicrobial therapy.

It is essential to continue implementing strategies to reduce antimicrobial pressure, such as the rational use of antibiotics, the establishment of antimicrobial regimens used according to the resistance present in each institution, adherence to antimicrobial prophylaxis in surgery (in time and type of antibiotics). administered), strict programs for the prevention of infections associated with health care to ensure the appropriate and rational use of antibiotics, as well as continuing to monitor and report antimicrobial resistance in hospitals, among other measures such as the implementation cleaning protocols for hospital units(24).

According to the data from this research, the HAIs surveillance system proposed in Ecuador can be applied, however, it requires highly trained personnel in the surveillance system for its correct application, in addition to extensive knowledge in epidemiology and statistics, since the calculation of rates, especially those adjusted to specific risk factors, are difficult to execute.

It is important to highlight the "fundamental role" of nursing professionals, who participate in the epidemiological surveillance of HAIs, since they must incorporate strategies based on evidence, aimed at developing interventions that stimulate behaviors, to reduce the days of exposure of invasive procedures, or compliance with protective activities for the development of HAIs, given their influence and leadership in health teams.

CONCLUSIONS

1. The microorganism with the highest frequency of recovery in HAIs is *Klebsiella pneumoniae ESBL (extended spectrum ß-lactamases)*, in Intensive Care units.
2. The presence of microorganisms resistant to broad-spectrum antibiotics is low in developing countries.
3. Microbial resistance must be addressed globally through effective active surveillance programs.
4. Actions to prevent, control and eliminate HAIs are effective.

ETHICAL CONSIDERATIONS

Ethical aspects are relevant in the Code such as the Nuremberg Code (25) and Organizations such as the Council of International Organizations of Medical Sciences (COICM) that support health studies (26); The guide to the ethical principles of Ezekiel Emanuel was used (27).

The research that determines Microorganisms and Their Antimicrobial Resistance in a Pediatric and Neonatal Intensive Care Unit was PRESENTED and APPROVED by the Human Research Ethics Committee of the Carlos Andrade Marín Hospital (CEISH-HCAM) in the city of Quito.

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The author has no conflicts of interest.

AUTHOR CONTRIBUTIONS

This article is the total contribution of the author in the development of his academic growth.

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