Original research

Epidemiology of antimicrobial resistance in bacteria isolated from inpatient and outpatient samples, Ecuador, 2018

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ABSTRACT

Objective. To compare the epidemiology of antimicrobial resistance in bacteria isolated from inpatient and outpatient samples in Ecuador.

Methods. A secondary analysis was done of data on bacteria isolated from inpatient and outpatient samples. Data were taken from the 2018 national antimicrobial resistance surveillance database of the National Reference Center for Antimicrobial Resistance. The variables included were: age, sex, inpatient versus outpatient setting, type of specimen, bacterial species identified, pattern of resistance to antibiotics, and geographic area.

Results. Data from 57 305 bacterial isolates were included in the study: 48.8% were from hospitalized patients, 55.7% were from women, and 60.1% were from patients older than 45 years. Urine (42.9%) and blood (12.4%) were the most common clinical samples. Overall, 77.1% of bacterial isolates were gram-negative (83% and 71% in outpatients and inpatients, respectively). The most common gram-positive and gram-negative species were *Staphylococcus aureus* and *Escherichia coli*, respectively. Antimicrobial resistance levels were high (up to 80% for some antimicrobial drugs), and were higher in hospitalized patients compared with outpatients. A variety of carbapenemases were found to confer resistance to carbapenems (antibiotics of last resort) in gram-negative bacteria.

Conclusions. The study findings provide an important baseline on antimicrobial resistance in Ecuador. This will allow the strengthening of guidelines of the surveillance system, the creation of public policies for standardization of laboratory methodologies, the proper handling of information, and the development of empirical therapy guidelines based on local epidemiology.

Keywords Drug resistance, bacterial; anti-bacterial agents; inpatients; outpatients; Ecuador.

Globally, antimicrobial resistance (AMR) is a growing public health threat. In 2019, around 1.27 million deaths were attributable to AMR worldwide (1, 2). With the rising levels of AMR, it is estimated that it will be one of the leading causes of death by 2050, surpassing cancer (1, 2). AMR occurs because of adaptive changes in microorganisms that make them resistant to currently effective antimicrobial drugs, causing infections that are difficult to treat (3). The main drivers of AMR are the

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misuse and overuse of antimicrobial drugs in both humans and animals, inadequate clean water, sanitation and hygiene, and poor infection, prevention and control measures in health care facilities (4–6). In addition, poor access to accurate and timely diagnosis exacerbates the causes and consequences of AMR (7).

Prevention, control, and treatment of infections caused by multiresistant pathogens require reliable data and the coordinated multisectoral efforts of various governmental and nongovernmental institutions (5, 7). To obtain accurate and timely AMR data, a comprehensive population-based AMR surveillance system is required at the national and international level (8). Such systems will help monitor short-term and long-term trends in AMR, provide early warnings of emerging threats, and guide antimicrobial stewardship at the national and international level (5, 9). Since 1996, the World Health Organization (WHO), through the Latin American AMR Surveillance Network (ReLAVRA), has been promoting at the regional level the use of standardized methodologies and improvement in data quality with the use of digital tools such as WHONET software (10). Another important strategy to tackle AMR is to promote research with different approaches to AMR because the availability of clear, up-to-date and reliable information will allow evidence-based public policies to be improved.

In Ecuador, an upper middle-income country in South America, information on the AMR burden and morbidity and mortality caused by AMR is limited (11–13). Available information shows widespread inappropriate antibiotic use in humans and livestock (14–18), and higher rates of health care associated infections compared with other countries in the region (12). Since 2014, the National Reference Center for Antimicrobial Resistance has been in charge of AMR surveillance in Ecuador. The center confirms resistance patterns and mechanisms, manages information from the hospitals in the network that report data on microorganisms and AMR using WHONET software, and issues surveillance guidelines. In addition, the National Reference Center for Antimicrobial Resistance has conducted studies that indicate high rates of resistant bacterial isolates obtained from patients seeking medical care in hospital outpatient departments or primary health care centers, and even higher rates of resistance in isolates obtained from hospitalized patients (19–21).

The 2018 AMR surveillance database provides a nationally representative sample of bacterial AMR that will help assess future trends and improve surveillance variables. In this operational research study, we describe the demographic characteristics of patients whose clinical samples were positive on bacterial culture, the bacterial species isolated, and the antibiotic resistance patterns of certain clinically important bacterial species, according to the WHO list of priority pathogens (22).

METHODS

Study design and setting

This was a secondary analysis of data from the 2018 national AMR surveillance database of the National Reference Center for Antimicrobial Resistance.

Ecuador had an estimated population of 17 268 000 in 2020. The Integral Health System in Ecuador includes public and private institutions of different levels of complexity. Public hospitals provide free services and are spread over the country. There are 4165 health facilities, of which 3539 are primary health care centers that primarily provide ambulatory outpatient care and 626 are hospitals with different medical specialties that also provide inpatient care. A patient referral system is in place between the primary health facilities and hospitals with referral depending on disease severity and the complexity of medical care needed for the diagnosis and treatment of patients. Ecuador is divided into nine administrative zones according to population density, called zonal coordinations, which allow the planning, coordination, and articulation of public health policies. The zones include urban and rural populations. Zone 9 corresponds to the metropolitan district of Quito (capital of the country) and zone 8 corresponds to Guayaquil; these two zones have the largest populations in the country.

Not all patients suspected of bacterial infection have samples taken for culture and antibiogram profiling; this is a measure the treating physician can prescribe in case of non-response to empirical treatment. Microbiology laboratories that perform bacterial culture and antimicrobial susceptibility testing are predominantly located in hospitals. In these laboratories, identification of bacterial species and antimicrobial susceptibility testing are performed using manual and automated methods. Some of these laboratories also perform ancillary tests to detect specific AMR mechanisms. Laboratories in Ecuador have been standardizing workflows for testing and reporting results according to species and using the National Reference Center for Antimicrobial Resistance surveillance technical manual (23). For AMR surveillance, a register has been established in each laboratory using the WHONET software (24). Data on positive bacterial isolates, along with the antimicrobial susceptibility patterns, are sent to a national AMR database every month. Certain bacterial isolates with epidemiologically important resistance patterns are sent to the National Reference Center for Antimicrobial Resistance for confirmation. If the resistance mechanism of these isolates has not been reported before, a national alert is issued by the Ministry of Public Health.

National Reference Center for Antimicrobial Resistance

The National Reference Center for Antimicrobial Resistance is responsible for the AMR national laboratory network of Ecuador. The number of laboratories in the network has been increasing every year. In 2022, 72 microbiology laboratories were included in the network; theses laboratories are located in hospitals with different complexity levels in various parts of the country. The National Reference Center for Antimicrobial Resistance maintains the national AMR database that contains information on positive bacterial culture results from the network of laboratories reported through the WHONET software. Bacterial isolates are classified into two categories based on the source or origin of the clinical samples: 1) from inpatients, if the source of the clinical sample is from hospitalized patients (including those admitted to intensive care units) and 2) from outpatients, if the source of the clinical sample is from ambulatory patients seeking care at outpatient departments and emergency rooms of health facilities; this includes patients referred from primary care.

Study population and period

The study includes results of the first bacterial isolates obtained from clinical samples of inpatients and outpatients in

Ecuador (adults and children) and antimicrobial susceptibility results submitted to the national AMR surveillance database at National Reference Center for Antimicrobial Resistance during 2018. Data analysis was conducted between July 2021 and May 2022. The decision to include the AMR surveillance data only for 2018 was based on system interruptions and limitations in health care facilities as a result of the coronavirus disease 2019 (COVID-19) pandemic. Isolates with no data for species identification or origin, or duplicate data were excluded from the analysis.

Data source and variables

The main data source was the national AMR database maintained in the National Reference Center for Antimicrobial Resistance in WHONET format. The variables included were: age, sex, patient's health care setting (inpatient or outpatient setting), type of specimen, bacterial species identified, pattern of resistance to antibiotics, and geographic area (zonal coordination). For the resistance mechanism (e.g., carbapenemases), data were taken from the isolates confirmed by the National Reference Center for Antimicrobial Resistance.

Data analysis

Data were downloaded from the WHONET software to Microsoft Excel 2010 (Microsoft, Redmond, WA, USA). The data were then imported into EpiData (version 2.2.3.187, EpiData partnership, Odense, Denmark) for further analysis. We used numbers and percentages to summarize the data variables. To describe the AMR levels in the clinical samples from inpatients and outpatients, we chose four gram-positive species (*Staphylococcus aureus, Staphylococcus* other than *Staphylococcus aureus, Enterococcus faecalis*, and *Enterococcus faecium*) and four gram-negative species (*Klebsiella pneumoniae*, *Escherichia coli*, *Acinetobacter calcoaceticus–baumannii* complex and *Pseudomonas aeruginosa*) based on their frequency and clinical relevance. The differences in proportions between inpatients and outpatients were assessed using the chi-squared test for proportions. A p-value < 0.05 was considered statistically significant.

Ethics

Permission was obtained from the authorities of the National Institute of Public Health of Ecuador to use the 2018 AMR surveillance database, which was provided anonymously under internal protocols of the institution. Ethical approval for the study was obtained from the Ethics Committee of the Pan American Health Organization (no. PAHOERC.0388.01) and the Union Ethics Advisory Group of the International Union against Tuberculosis and Lung Disease, Paris, France (no. 20/21).

RESULTS

In 2018, 59 156 clinical samples had a positive bacteriological culture. Of these, 1851 (3.1%) records with missing data on species or origin of the patient (inpatient or outpatient) as well as duplicates were excluded from the study. Of the remaining 57 305 samples, 27 941 (48.8%) were from inpatient settings and 29 364 (51.2%) from outpatient settings.

The demographic characteristics of the patients disaggregated by the origin (inpatient or outpatient) are presented in Table 1. Overall, 60.1% of the samples were from patients older than 45 years and 55.7% were from females. Urine (42.9%), blood (12.4%), unspecified secretions (7.3%), tracheal aspirates (6.7%), and sputum (6.4%) were the most common clinical samples. Most of the samples (81.8%) were from geographical zones 8 and 9. Significant differences were found between the characteristics of inpatients and outpatients ($p < 0.001$).

The bacterial species isolated from the clinical samples are given in Table 2. Overall, 22.9% of the isolates were gram-positive bacteria and the remaining 77.1% were gram-negative bacteria. The most common gram-positive bacterial species were *Staphylococcus aureus* (41.5%), followed by *Staphylococcus epidermidis* (26.9%). The most common gram-negative bacterial species were *Escherichia coli* (50.3%), *Klebsiella pneumoniae* (19.7%), and *Pseudomonas aeruginosa* (8.5%). There were statistically significant differences in species isolated from outpatient settings compared with inpatient settings, with *Escherichia coli* accounting for 68.7% of isolates from outpatient settings compared with 27.9% from inpatient settings.

Figure 1 shows the AMR patterns of the four selected gram-positive species in inpatient and outpatient samples. For almost all antimicrobial agents, the resistance levels of isolates from inpatients were higher than those from outpatient settings. More than 30% of *Staphylococcus aureus* isolates (Figure 1, panel A) from hospital and community settings were resistant to cefoxitin and oxacillin, the latter being considered methicillin-resistant *Staphylococcus aureus* (MRSA). About 40% of the *Staphylococcus aureus* isolates were resistant to trimethoprim–sulfamethoxazole and erythromycin and about 20% were resistant to clindamycin. No resistance to vancomycin or linezolid was reported among *Staphylococcus aureus* isolates. For *Staphylococcus* other than *Staphylococcus aureus* isolates (Figure 1, panel B) the resistance levels in both settings were higher than with *Staphylococcus aureus* for all drugs tested, except for vancomycin and linezolid where no resistance was found.

For *Enterococcus*, aminoglycoside resistance was found in 42% of *Enterococcus faecalis* isolates (Figure 1, panel C) and 34% of *Enterococcus faecium* isolates (Figure 1, panel D) in hospital settings using a high-load gentamicin susceptibility method. With regard to ampicillin, *Enterococcus faecium* isolates showed marked resistance, both in hospitalized patients (82%) and outpatients (72%); for *Enterococcus faecalis*, resistance to ampicillin was much lower – 5% for inpatients and 2% for outpatients. Vancomycin resistance in *Enterococcus faecium* was seen in 18% of isolates from inpatients. Resistance levels to linezolid were low (1–2%) in both *Enterococcus faecalis* and *Enterococcus faecium* isolates, regardless of the setting.

The levels of resistance of the four selected gram-negative bacteria are shown in Figure 2. For *Klebsiella pneumoniae* (Figure 2, panel A), high levels of resistance (> 30%) were observed to third-generation cephalosporins (ceftazidime and ceftriaxone), fourth-generation cephalosporins (cefepime) and β-lactam/β-lactamase inhibitor combination agents (piperacillin–tazobactam and ampicillin–sulbactam). A significant degree of resistance to carbapenems (imipenem, meropenem, and ertapenem) was seen in hospitalized patients – 38%, 37%, and 32%, respectively – associated with the presence of carbapenemases such as *Klebsiella pneumoniae* carbapenemase (Figure 3, panel A).

Escherichia coli isolates (Figure 2, panel B) showed high levels of resistance (> 40%) to ampicillin–sulbactam and ciprofloxacin, and resistance levels ranged from 12% to 38% for

TABLE 1. Demographic and clinical characteristics of patients (inpatients and outpatients) with positive bacterial cultures, Ecuador, 2018

Characteristic	Total	Inpatients	Outpatients
	n (%)	n (%)	n (%)
Total	57 305 (100)	27 941 (100)	29 364 (100)
Age group, in years			
< 1	3 333 (6.1)	2 520 (9.4)	813 (2.9)
1–5	2 873 (5.3)	1 351 (5.0)	1 522 (5.5)
6–18	4 354 (8.0)	1 959 (7.3)	2 395 (8.7)
19–45	9 484 (17.4)	4 201 (15.6)	5 283 (19.2)
46–64	17 940 (32.9)	8 609 (32.0)	9 331 (33.9)
> 65	16 498 (30.3)	8 281 (30.8)	8 217 (29.8)
Not recorded	2 823 (4.9)	1 020 (3.7)	1 803 (6.1)
Sex			
Male	24 049 (43.0)	15 209 (56.0)	8 840 (30.7)
Female	31 892 (57.0)	11 973 (44.0)	19 919 (69.3)
Not recorded	1 364 (2.4)	759 (2.7)	605 (2.1)
Clinical specimen			
Urine	24 590 (44.5)	5 250 (19.7)	19 340 (67.7)
Blood	7 127 (12.9)	5 105 (19.1)	2 022 (7.1)
Secretions	4 171 (7.5)	2 903 (10.9)	1 268 (4.4)
Tracheal aspirates	3 866 (7.0)	3 314 (12.4)	552 (1.9)
Sputum	3 670 (6.6)	2 292 (8.6)	1 378 (4.8)
Wound	2 772 (5.0)	1 652 (6.2)	1 120 (3.9)
Abscess	2 139 (3.9)	1 561 (5.8)	578 (2.0)
Catheter	807 (1.5)	729 (2.7)	78 (0.3)
Rectum	750 (1.4)	694 (2.6)	56 (0.2)
Abdominal fluid	756 (1.4)	601 (2.3)	155 (0.5)
Stool	488 (0.9)	355 (1.3)	133 (0.5)
Vagina	387 (0.7)	60 (0.2)	327 (1.1)
Cerebrospinal fluid	251 (0.5)	208 (0.8)	43 (0.2)
Pleural fluid	257 (0.5)	152 (0.6)	105 (0.4)
Catheter, central	227 (0.4)	72 (0.3)	155 (0.5)
Other	2 994 (5.4)	1 749 (6.6)	1 245 (4.4)
Not recorded	2 053 (3.6)	1 244 (4.5)	809 (2.8)
Geographical location, zonal coordination			
1	1 312 (2.3)	636 (2.3)	676 (2.3)
2	1 767 (3.1)	366 (1.3)	1 401 (4.8)
3	963 (1.7)	295 (1.1)	668 (2.3)
6	2 682 (4.7)	1 086 (3.9)	1 596 (5.4)
7	3 690 (6.4)	1 241 (4.4)	2 449 (8.3)
8	14 581 (25.4)	8 084 (28.9)	6 497 (22.1)
9	32 310 (56.4)	16 233 (58.1)	16 077 (54.8)

Note: All differences between inpatients and outpatients were statistically significant because of the large number of isolates, $p \leq 0.001$.
Source: Prepared by authors from the results.

TABLE 2. Bacterial species identified in positive bacterial cultures from inpatient and outpatient samples, Ecuador, 2018

Species	Total	Inpatients	Outpatients
	n (%)	n (%)	n (%)
Gram-positive species			
Total	13 075 (100)	8 034 (100)	5 041 (100)
Staphylococcus aureus	5 423 (41.5)	3 581 (44.6)	1 842 (36.5)
Staphylococcus epidermidis	3 517 (26.9)	2 345 (29.2)	1 172 (23.2)
Enterococcus faecalis	1 135 (8.7)	573 (7.1)	562 (11.1)
Staphylococcus hominis	773 (5.9)	513 (6.4)	260 (5.2)
Enterococcus faecium	271 (2.1)	201 (2.5)	70 (1.4)
Streptococcus pneumoniae	267 (2.0)	160 (2.0)	107 (2.1)
Staphylococcus warneri	136 (1.0)	75 (0.9)	61 (1.2)
Other	1 553 (11.9)	586 (7.3)	967 (19.2)
Gram-negative species			
Total	44 073 (100)	19 912 (100)	24 161 (100)
Escherichia coli	22 156 (50.3)	5 565 (27.9)	16 591 (68.7)
Klebsiella pneumoniae	8 683 (19.7)	5 958 (29.9)	2 725 (11.3)
Pseudomonas aeruginosa	3 753 (8.5)	2 592 (13.0)	1 161 (4.8)
Proteus mirabilis	1 680 (3.8)	707 (3.6)	973 (4.0)
Enterobacter cloacae complex	1 558 (3.5)	1 062 (5.3)	496 (2.1)
Acinetobacter calcoaceticus–baumannii complex	1 336 (3.0)	1 106 (5.6)	230 (1.0)
Serratia marcescens	772 (1.8)	524 (2.6)	248 (1.0)
Shigella sp.	705 (1.6)	477 (2.4)	228 (0.9)
Klebsiella oxytoca	658 (1.5)	341 (1.7)	317 (1.3)
Citrobacter freundii	379 (0.9)	177 (0.9)	202 (0.8)
Klebsiella aerogenes	359 (0.8)	211 (1.1)	148 (0.6)
Stenotrophomonas maltophilia	231 (0.5)	197 (1.0)	34 (0.1)
Proteus vulgaris	133 (0.3)	47 (0.2)	86 (0.4)
Providencia rettgeri	121 (0.3)	52 (0.3)	69 (0.3)
Salmonella sp.	111 (0.3)	72 (0.4)	39 (0.2)
Other	1 438 (3.3)	824 (4.1)	614 (2.5)

Note: For 157 samples, data on species were missing and are not included in the table. All observed differences between inpatients and outpatients were statistically significant because of the large number of isolates, $p \leq 0.001$.
Source: Prepared by authors from the results.

cephalosporins (ceftriaxone and ceftazidime). The resistance to cephalosporins was due to the presence of extended-spectrum β-lactamases. However, resistance to carbapenems, amikacin, and tigecycline was very low.

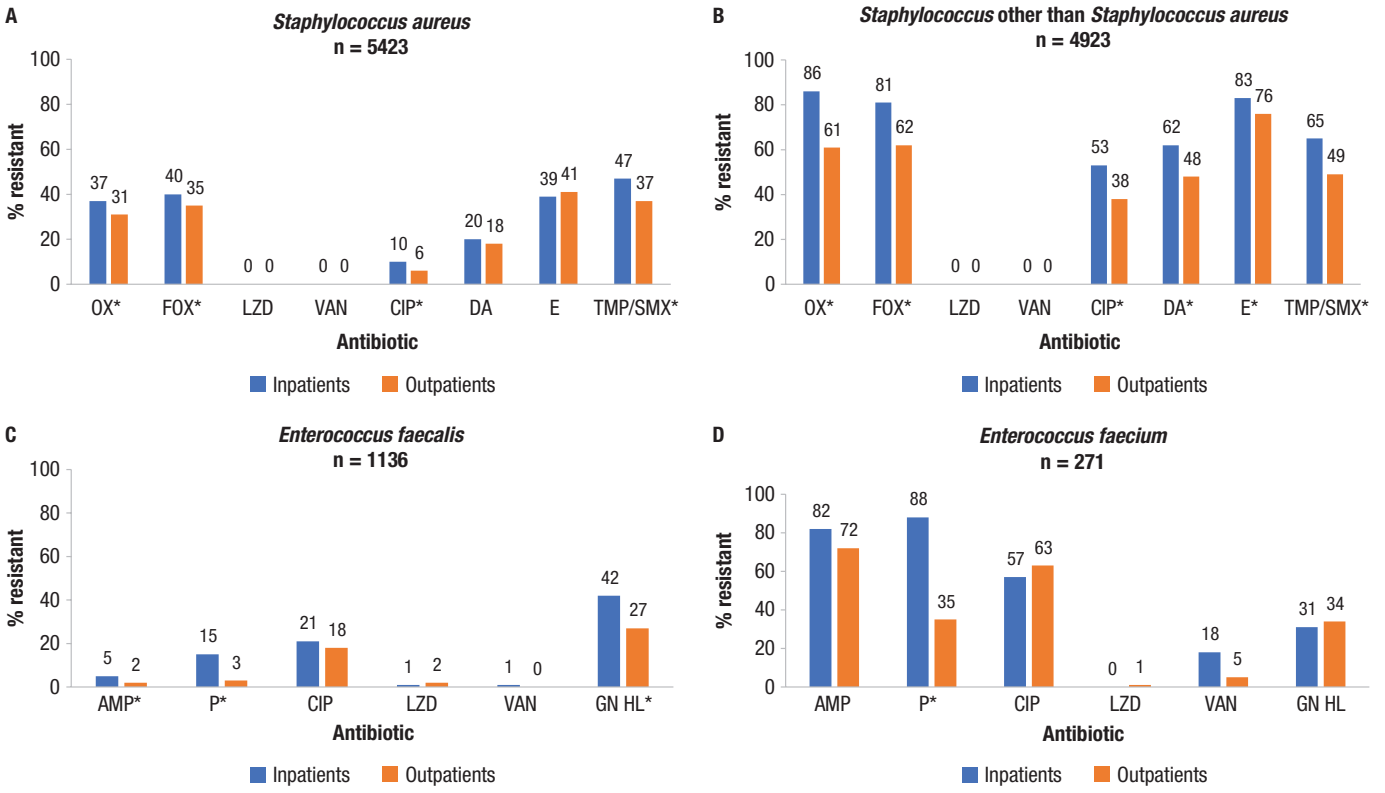
Acinetobacter calcoaceticus–baumannii complex isolates (Figure 2, panel C) had high levels of resistance (ranging from 39% to 72%) to β-lactams, including carbapenems. The mechanism of resistance to carbapenems was mostly due to the presence of carbapenemases (oxacillinases) in these species (Figure 3, panel B). The mechanisms of resistance to carbapenems were derived from a non-random sub-sample of isolates by molecular biology techniques performed in the National Reference Center for Antimicrobial Resistance.

Pseudomonas aeruginosa showed resistance, ranging from 9% to 35%, to the main antipseudomonal drugs such as aztreonam, ceftazidime, piperacillin–tazobactam, ceftriazone, and amikacin (Figure 2, panel D). This resistance was mostly due to the presence of metallo-β lactamases (Figure 3, panel C).

DISCUSSION

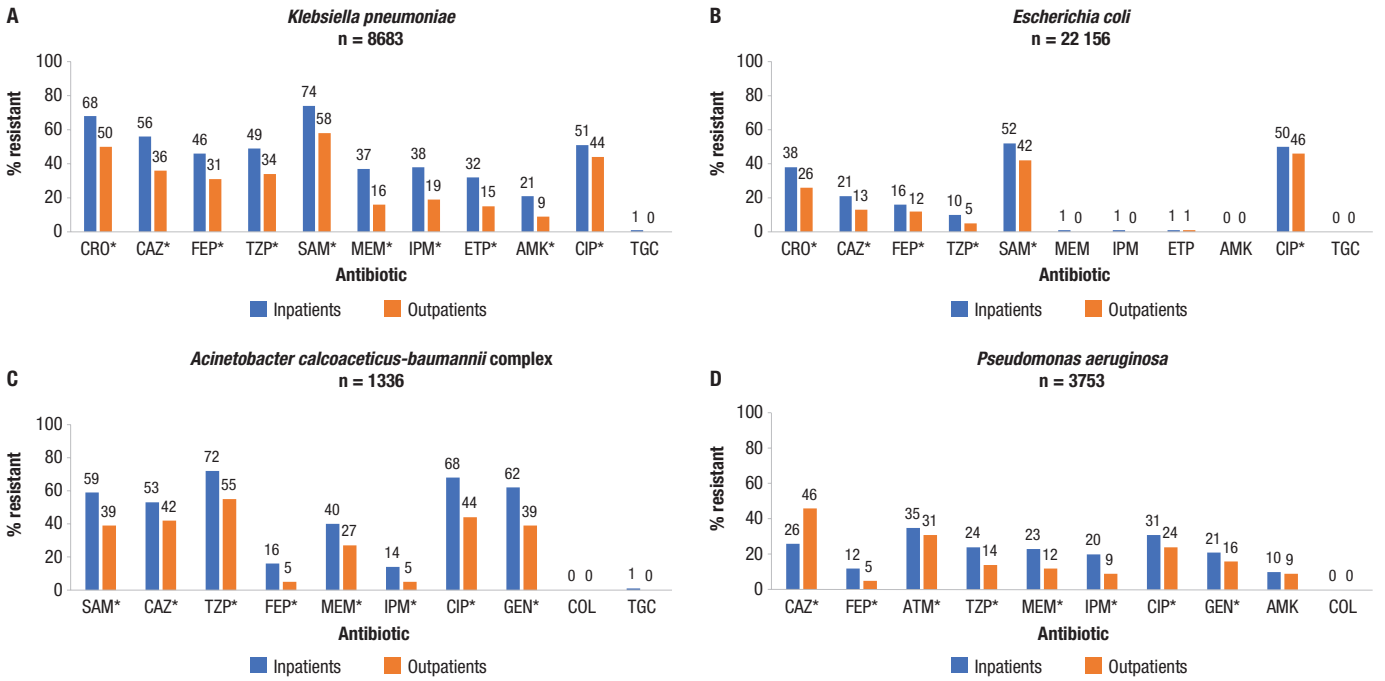
This is the first study from Ecuador providing a comprehensive overview of the bacterial profile and AMR pattern from

FIGURE 1. Resistance patterns of the main gram-positive species obtained from inpatient and outpatient samples, Ecuador, 2018



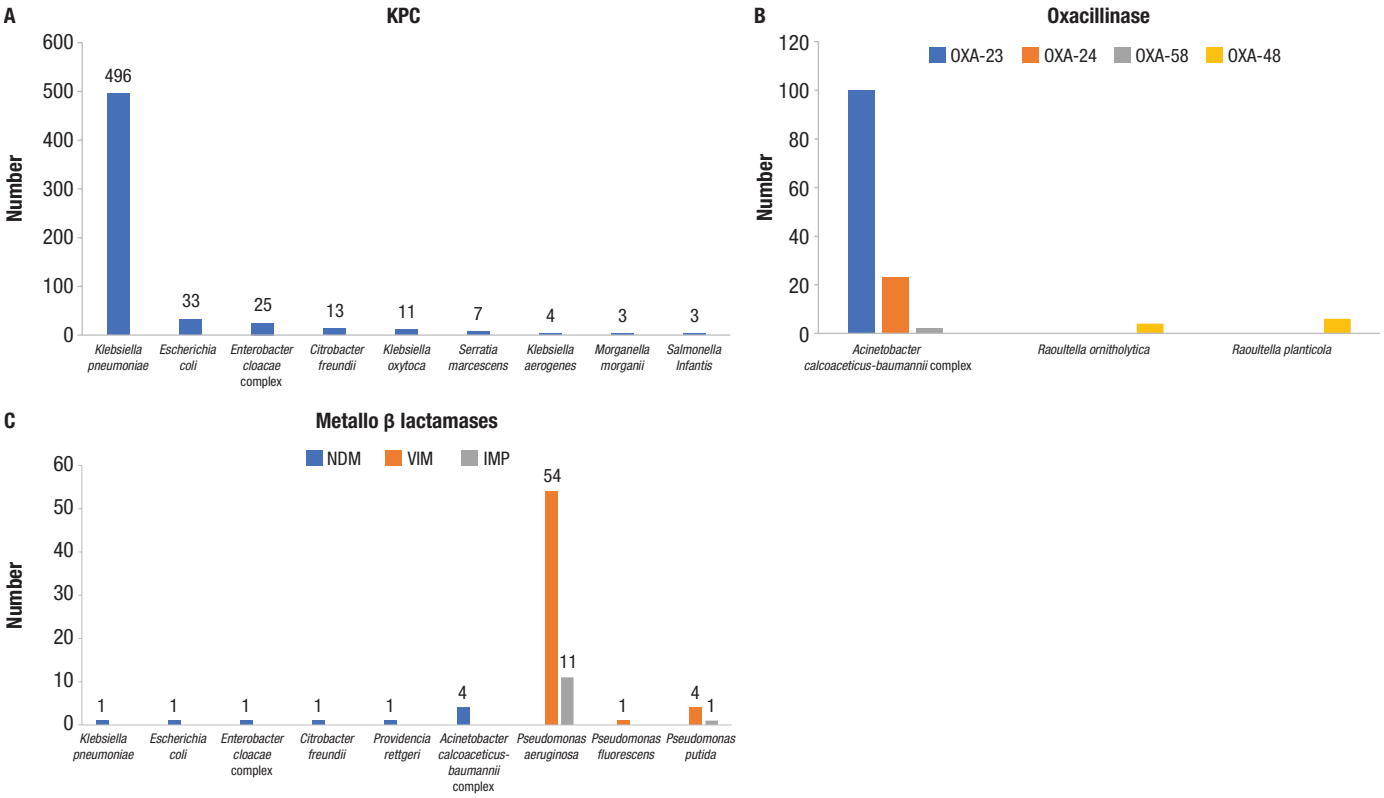
OX, oxacillin; FOX, cefoxitin; LZD, linezolid; VAN, vancomycin; CIP, ciprofloxacin; DA, clindamycin; ERY, erythromycin; TMP–SMX, trimethoprim–sulfamethoxazole; AMP, ampicillin; P, penicillin; GN HL, gentamicin high load.
*Differences between inpatients and outpatients were statistically significant, $p < 0.05$.
Source: Prepared by authors from the results.

FIGURE 2. Resistance patterns of the main gram-negative species obtained from inpatient and outpatient samples, Ecuador, 2018



SAM, ampicillin–sulbactam; TZP, piperacillin–tazobactam; CRO, ceftriaxone; CAZ, ceftazidime; FEP, cefepime; ETP, ertapenem; IPM, imipenem; MEM, meropenem; CIP, ciprofloxacin; AMK, amikacin; TGC, tigecycline; COL, colistin; ATM, aztreonam; GEN, gentamicin.
*Differences between inpatients and outpatients were statistically significant, $p < 0.05$.
Source: Prepared by authors from the results.

FIGURE 3. Frequency of carbapenemase-producing organisms reported in 1889 isolates referred to the National Reference Center for Antimicrobial Resistance, Ecuador, 2018



KPC, *Klebsiella pneumoniae* carbapenemase; OXA, oxacillinase; NDM, New Delhi metallo-β-lactamase; VIM, Verona integron-encoded metallo-β-lactamase; IMP, active against imipenem.
Source: Prepared by authors from the results.

inpatients and outpatients seeking medical care at various health facilities across the country.

The AMR surveillance system was able to capture information from a relatively large number of patients. Nearly 97% of the data in the surveillance system was complete, with only 3% of the records having missing data on the key variables (bacterial species and source of the clinical specimen) indicating that good quality data had been captured through the system. The demographic profile of the patients whose clinical samples were positive on bacterial culture indicates representation from all age groups and both sexes.

There was over-representation of samples from two geographic zones with zonal coordination 8 and zonal coordination 9 contributing nearly 80% of the data in the surveillance system. In contrast, few data were from zones 4 and 5. Zones 8 and 9 are two of the largest areas of the country with many health facilities and laboratories that are part of the AMR surveillance system, which explains the over-representation. The number of laboratories participating in the national AMR surveillance system is increasing every year, therefore this deficiency is being addressed. Analysis of data in the future is likely to provide more representative information about the bacterial species and AMR levels in various parts of the country.

Gram-negative bacteria constituted more than 75% of the bacteria identified by the AMR surveillance system. The isolation of gram-negative bacteria was higher from clinical outpatient samples (83%; 24 161/29 202) than from clinical inpatient samples (71%; 19 912/27 946). Previous studies of data from AMR surveillance systems from other countries in the region have found similar findings (25, 26). This finding is driven largely by the type of clinical samples obtained for culture. From outpatients, the clinical samples were predominantly urine samples that are more likely to yield gram-negative bacteria than clinical samples from inpatients which have a higher proportion of respiratory and blood samples.

The following implications can be drawn from the levels of resistance reported in our study for gram-positive bacteria, which may aid in the clinical management of infections with these bacteria. More than 30% of *Staphylococcus aureus* isolates can be classified as MRSA, which is similar to what has been reported in Argentina (37%) (27). Because MRSA is difficult to treat, this proportion is considered high and clinically significant (22, 28). However, all *Staphylococcus aureus* isolates in our study were sensitive to linezolid and vancomycin and more than 80% of isolates were sensitive to clindamycin. Therefore, care must be taken to use these antibiotics judiciously in order to prevent the emergence of resistance to these drugs.

Enterococcus faecalis isolates, especially those isolated from inpatients, had high levels of resistance to high-load gentamicin. The levels of resistance are comparable to those reported in studies elsewhere (8, 29). Antibiotics such as ampicillin, penicillin, ciprofloxacin, vancomycin, and linezolid may be tried in the treatment of these infections. *Enterococcus faecium*, however, showed high levels of resistance to ampicillin, penicillin, ciprofloxacin, and high-load gentamicin; therefore, the use of these drugs should be guided by antibiotic susceptibility results. In

the presence of resistance to these drugs, linezolid and vancomycin may be considered. It should be noted, however, that 20% of *Enterococcus faecium* strains in our study were resistant to vancomycin.

Klebsiella pneumoniae showed high levels of resistance to several drugs, so antibiotic susceptibility testing should always be done when infection with this bacterium is suspected in order to choose the best treatment option. *Escherichia coli* showed high levels of resistance to ciprofloxacin, ampicillin–sulbactam, and ceftriaxone, therefore these antibiotics should be avoided for empiric treatment. Instead, meropenem, imipenem, ertapenem, amikacin, and tigecycline may be alternative drugs to use depending on the severity and source of infection. *Acinetobacter calcoaceticus–baumannii* complex showed high levels of resistance to most of the antibiotics considered for treatment, with the exception of colistin and tigecycline, to which it had low levels of resistance. In patients with suspected *Pseudomonas aeruginosa* infections, aztreonam, ceftazidime, and ciprofloxacin should be avoided, with amikacin, cefepime, and colistin preferred instead.

The data in the surveillance system also provide insights into the mechanisms of resistance. *Klebsiella pneumoniae*, the most frequent pathogen identified in hospitalized patients, showed almost 70% resistance to third-generation cephalosporins and about 40% resistance to carbapenems. The available data indicate the presence of carbapenemases in *Klebsiella pneumoniae* and this enzyme is efficiently transmitted by plasmids and clonal worldwide dissemination, especially in South American countries (30, 31) Our study also shows that carbapenem-resistant isolates of *Pseudomonas aeruginosa* express predominantly metallo-β-lactamases such as Verona integron-encoded metallo-β-lactamase and some activity against imipenem. Isolates of *Acinetobacter calcoaceticus-baumannii* complex showed very high resistance rates (> 50%) to β-lactams which was mostly mediated by oxacillinase-type enzymes such as oxacillinase-23 and oxacillinase-24 and other mechanisms, such as porin closure. These resistance mechanisms affect the activity of imipenem and efflux pumps to the entire β-lactam family (32). The resistance levels of *Enterococcus faecium* to ampicillin and vancomycin was higher than expected, and mostly mediated by PBP-5 mutations for ampicillin resistance, and *vanA/vanB* gene acquisition for vancomycin resistance (this was not ascertained and reported in the surveillance system). Linezolid resistance among the bacteria included in this study is an area of concern because of increasing reports of *poxtA* and *optrA* genes in these species (33, 34). Understanding the underlying mechanisms of resistance will help to optimize clinical outcomes by providing better guidance on the choice of drugs that can be used. In addition, it will facilitate a better understanding of the potential for the rapid spread of resistance between and among bacterial species that are causing infection outbreaks.

The main strength of the study is that we used nationwide data from the routine surveillance system. Therefore, the results reflect the ground level realities. Another strength of the study is the reporting in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines (35). A limitation of the study is that the methods used to determine the antibiotic resistance profile in the laboratories within the AMR surveillance network were not the same. In addition, there were some concerns about the quality of the data; for example, outpatients had a relatively large number of clinical samples labelled as central catheter which perhaps points to problems in classification. Another limitation is the lack of inclusion of *Salmonella* sp., *Shigella* sp., *Streptococcus pneumoniae* and *Neisseria gonorrhoeae* in the surveillance system because these pathogens should be monitored according to the WHO classification (22).

The study has several important implications. The study findings provide comprehensive information on AMR that can inform public policy. This highlights the importance of continuous monitoring of AMR and the need to ensure adequate resourcing of the network, even in times of pandemics and other health emergencies. The findings call for standardization of the testing methods used and the recording and reporting of bacterial culture and AMR results across the country.

In conclusion, the information provided in this study will play an important role in establishing a national baseline to assess future trends in AMR, updating the policies of antimicrobial surveillance, and improving the antibiotic stewardship program. We believe that our findings will help in defining criteria for referring hospital and community isolates to the National Reference Center for Antimicrobial Resistance for further evaluation to determine the accuracy of resistance levels in specific bacteria and identify drug-resistance mechanisms. The findings will also encourage continued training of health care personnel in technical issues, such as microbiology and molecular biology, as well as in the use of the WHONET for data management and analysis in laboratories across the country.

Author contributions. All authors contributed to the concept and design of the study; CS undertook the data collection; CS, SS, GE, KS, HD, and AM analysed the data; and CS, SS, GE, HD, and AM prepared the first draft of the paper. All authors critically reviewed the paper and approved the final draft.

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Características epidemiológicas de la resistencia antimicrobiana en cepas bacterianas aisladas en pacientes de servicios hospitalarios y ambulatorios de Ecuador, 2018

RESUMEN

Objetivo. Comparar las características epidemiológicas de la resistencia a los antimicrobianos en cepas bacterianas aisladas de muestras de pacientes de servicios hospitalarios y ambulatorios en Ecuador.

Métodos. Se realizó un análisis secundario de los datos sobre cepas bacterianas aisladas en muestras de pacientes de servicios hospitalarios y ambulatorios. Se recogieron los datos de la base de datos nacional del 2018 para la vigilancia de la resistencia a los antimicrobianos del Centro de Referencia Nacional para la Resistencia a los Antimicrobianos. Las variables incluidas fueron: edad, sexo, entorno hospitalario frente a entorno ambulatorio, tipo de muestra, especies bacterianas detectadas, patrón de resistencia a los antibióticos y zona geográfica.

Resultados. En el estudio se incluyeron datos de 57 305 cepas aislamientos bacterianos: 48,8% fueron de pacientes hospitalizados, 55,7% fueron de mujeres y 60,1% fueron de pacientes mayores de 45 años. La orina (42,9%) y la sangre (12,4%) fueron las muestras clínicas más comunes. En general, 77,1% de las cepas bacterianas aisladas fueron gramnegativas (83% y 71% en pacientes de servicios ambulatorios y hospitalarios, respectivamente). Las especies grampositivas y gramnegativas más comunes fueron *Staphylococcus aureus* y *Escherichia coli*, respectivamente. Los niveles de resistencia a los antimicrobianos fueron elevados (hasta 80% en el caso de algunos fármacos antimicrobianos) y fueron más elevados en los pacientes de servicios hospitalarios en comparación con los pacientes de servicios ambulatorios. Se encontró que una variedad de carbapenemasas confiere resistencia a los carbapenémicos (antibióticos de último recurso) en bacterias gramnegativas.

Conclusiones. Los resultados del estudio proporcionan una línea de base importante sobre la resistencia a los antimicrobianos en Ecuador, que permitirá el fortalecimiento de las directrices del sistema de vigilancia, la creación de políticas públicas para la estandarización de los métodos de laboratorio, una adecuada gestión de la información y la elaboración de orientaciones de tratamiento empírico basadas en las características epidemiológicas locales.

Palabras clave Farmacorresistencia bacteriana; antibacterianos; pacientes internos; pacientes ambulatorios; Ecuador.

Epidemiologia da resistência aos antimicrobianos em bactérias isoladas de amostras hospitalares e ambulatoriais no Equador, 2018

RESUMO

Objetivo. Comparar a epidemiologia da resistência aos antimicrobianos em bactérias isoladas de amostras hospitalares e ambulatoriais no Equador.

Métodos. Foi feita uma análise secundária de dados sobre bactérias isoladas de amostras hospitalares e ambulatoriais. Os dados foram obtidos do banco de dados nacional de vigilância da resistência aos antimicrobianos de 2018 do Centro Nacional de Referência para a Resistência aos Antimicrobianos. As variáveis incluídas foram: idade, sexo, ambiente hospitalar versus ambiente ambulatorial, tipo de espécime, espécies bacterianas identificadas, padrão de resistência a antibióticos e área geográfica.

Resultados. Foram incluídos no estudo os dados de 57 305 isolados bacterianos: 48,8% eram de pacientes hospitalizados, 55,7% eram de mulheres e 60,1% eram de pacientes com mais de 45 anos. As amostras clínicas mais comuns foram urina (42,9%) e sangue (12,4%). No total, 77,1% dos isolados bacterianos eram gram-negativos (83% e 71% em pacientes ambulatoriais e pacientes internados, respectivamente). As espécies gram-positivas e gram-negativas mais comuns foram *Staphylococcus aureus* e *Escherichia coli*, respectivamente. Os níveis de resistência aos antimicrobianos foram elevados (até 80% para alguns antimicrobianos) e foram mais elevados em pacientes hospitalizados em comparação com pacientes ambulatoriais. Foram encontradas várias carbapenemases que conferem resistência aos carbapenêmicos (antibióticos de último recurso) em bactérias gram-negativas.

Conclusões. Os resultados do estudo fornecem uma importante linha de base sobre a resistência aos antimicrobianos no Equador. Isto permitirá o fortalecimento das diretrizes do sistema de vigilância, a criação de políticas públicas para padronização de metodologias laboratoriais, o manejo adequado de informações e o desenvolvimento de diretrizes para a antibioticoterapia empírica com base na epidemiologia local.

Palavras-chave Farmacorresistência bacteriana; antibacteriano; pacientes internados; pacientes ambulatoriais; Equador.