#### **Brief communication**

# Antimicrobial susceptibility profiles of extended-spectrum beta-lactamaseproducing bacteria

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Abstract

Introduction. Bacterial resistance is a worldwide problem, with bacteria such as Escherichia coli and Klebsiella pneumoniae showing increasing resistance rates. Objective. Characterize the antimicrobial susceptibility profiles of patients with infection by extended-spectrum beta-lactamase-producing Escherichia coli or Klebsiella pneumoniae bacteria in two hospitals of the public network of El Salvador, 2022. Methodology. Descriptive cross-sectional study of the characteristics and antimicrobial susceptibility profiles of a retrospective cohort of 989 patients with Escherichia coli or Klebsiella pneumoniae infection. Results. 50.1 % of patients had an infection with extended-spectrum beta-lactamase-producing Escherichia coli or Klebsiella pneumoniae, and of these, 34.1 % died at 30-day follow-up. The percentage of resistant susceptibility for these bacteria was 46.0 % and 13.0 %, respectively. The percentages of resistance were higher for ampicillin (100 %) and ceftriaxone (43 %-98 %), although carbapenemics also showed resistance (3 %-5 %). Conclusion. Severe complications and outcomes were more frequent in patients with infection by extended-spectrum beta-lactamase-producing bacteria with a higher susceptibility to cephalosporins and penicillins.

Keywords

Drug Resistance, Bacterial, beta-Lactamases, Escherichia coli, Klebsiella pneumoniae.

#### Resumen

Introducción. La resistencia bacteriana es un problema mundial, ya que las bacterias como Escherichia coli y Klebsiella pneumoniae presentan tasas de resistencia cada vez más altas. Objetivo. Caracterizar los perfiles de susceptibilidad antimicrobiana de los pacientes con infección por bacterias Escherichia coli o Klebsiella pneumoniae productoras de betalactamasas de espectro extendido en dos hospitales de la red pública de El Salvador, 2022. Metodología. Estudio descriptivo transversal de las características y perfiles de susceptibilidad antimicrobiana de una cohorte retrospectiva con 989 pacientes con infección por Escherichia coli o Klebsiella pneumoniae. Resultados. El 50,1 % de pacientes cursó con una infección por Escherichia coli o Klebsiella pneumoniae productoras de betalactamasas de espectro extendido, y de estos, el 34,1 % falleció en el seguimiento a 30 días. Para estas bacterias el porcentaje de susceptibilidad resistente fue de 46,0 % y 13,0 % respectivamente. Los porcentajes de resistencia fueron mayores para ampicilina (100 %) y ceftriaxona (43 %- 98 %), aunque los carbapenémicos también presentaron resistencia (3 %- 5 %). Conclusion. Las complicaciones y desenlaces graves fueron más frecuentes en los pacientes con infección por bacterias productoras de betalactamasas de espectro extendido con una susceptibilidad resistente mayor para cefalosporinas y penicilinas.

#### Palabras clave

Farmacorresistencia Bacteriana, beta-Lactamasas, Escherichia coli, Klebsiella pneumoniae.

## Introduction

Antimicrobial resistance (AMR) has increased worldwide in recent decades, causing an increase in medical complications, deaths,

and the need for increasingly potent antibiotics, which in turn increases healthcare costs.<sup>i</sup>Therefore, AMR has been cataloged as a serious problem and one of the ten main public health threats.<sup>i,ii</sup>





#### Perfiles de susceptibilidad antimicrobiana de bacterias productoras de betalactamasas de espectro extendido

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LPEM<sup>1</sup>, ZIAdeM<sup>2</sup>, CAVA<sup>3</sup>: study conception, LPEM<sup>1</sup>: manuscript design, and literature search, LPEM<sup>1</sup>, ZIAdeM<sup>2</sup>: data collection and data or software management. LPEM1, ZIAdeM<sup>2</sup>, CAVA<sup>3</sup>, EWMR<sup>4</sup>: data analysis, LPEM<sup>1</sup>, ZIAdeM<sup>2</sup>: writing, revising and editing.

Conflicts of interest: No conflicts of interest. Thus, the World Health Organization (WHO) has created priority lists of multidrug-resistant pathogens; where in critical priority one are: Acinetobacter baumanni (A. baumannii), Pseudomona aeruginosa (P. aeruginosa), Klebsiella pneumoniae (K. pneumoniae) and Escherichia coli (E. coli). These last two are part of the group of enterobacteria, which may present as one of their resistance mechanisms for the production of extended-spectrum beta-lactamases (ESBL).<sup>iii,iv</sup>

In the last report of the Global Antimicrobial Resistance Surveillance System (GLASS), in which 127 countries participated, levels of resistance were found to be above 50% of the total number of septicemias reported for *K. pneumoniae or Acinetobacter* spp, of which 8% had resistance to carbapenemics.<sup>iv</sup> For urinary tract infections caused by *E. coli*, 20% had resistance to first and second-line drugs.<sup>iv</sup>

In El Salvador, 1652 isolates from 26 hospitals were described during 2018. The most frequently isolated agents were *A. baumannii, K. pneumonia, P. aeruginosa, and E. coli.* The percentage of multi-resistance was 87.5 % of all isolates.<sup>vi</sup> Consequently, it is necessary to delimit the information according to the type of bacteria and resistance mechanism present.

This study describes *E. coli* and *K. pneumonia*, which WHO has identified as critical enterobacteria due to their resistance, including ESBL and carbapenemases.<sup>iii,jv</sup>

Both bacteria are responsible for nosocomial and community infections, highlighting the importance of antimicrobial surveillance in hospitals. In 2022, we characterized the antimicrobial susceptibility profiles and characteristics of patients infected with *E. coli or K. pneumoniae* bacteria producing extended-spectrum beta-lactamases in two public hospitals in El Salvador.

### Methodology

A cross-sectional study was conducted to describe the clinical characteristics of hospitalized patients with *E. coli and K. pneumoniae* infections, as well as to characterize the susceptibility profiles of ESBL-producing bacteria. The study was carried out in hospitals of the public health system of El Salvador, of the second and third level of care, respectively, with data corresponding to the year 2022. The database of bacterial isolates wa provided by the Directorate of Information and Communication Technologies, whose susceptibility results are by the latest modification of the European Com-

mittee for Antimicrobial Susceptibility Testing, "susceptible, intermediate susceptibility and resistant".vii This database consisted of 2048 isolates for the second-level hospital and 8259 for the third-level hospital. After the individualization of each patient in the database, the selection of bacteria and samples of interest was carried out, as well as the elimination of repeated records and incomplete data. A total of 989 individuals were identified.

All patients hospitalized during 2022 with positive bacteriologic cultures for *E. coli* or *K. pneumoniae* in blood, urine, and bronchial secretions were included. Those with insufficient information (lack of essential data for analysis) recorded in the physical and digital clinical record were excluded. Data collection was performed using a structured digital form in KoboToolbox version 2.023.21.

The study variables were defined according to the WHO GLASS guidelines, guaranteeing the data's standardization and comparability. Demographic variables (sex and age), clinical characteristics (hospital admission service, previous hospital admission, prolonged hospital stay, surgical procedure prior to culture collection, type of surgical procedure, use of invasive devices, presence of immunosuppression, clinical complications on admission, need for intensive care unit (ICU), Charlson comorbidity classification, discharge condition, and 30-day follow-up after culture collection) were collected. Thirty-day mortality was defined as death of the patient within 30 calendar days after the date of positive culture; infections were classified according to their probable origin as: community-acquired, present or incubating on admission, with no recent medical history; and healthcare-associated infections (HAIs), acquired during hospitalization or with a history of medical care, invasive devices or recent antibiotic use.

In addition, microbiological variables were used (type of sample, microorganism isolated, origin of the infection, susceptibility of the isolated agent, Betalactamaseproducing bacteria positive (ESBL+), and Betalactamase-producing bacteria negative (ESBL-), polymicrobial isolation and infection by other agents), antibiotic therapy received (in previous admissions to in the last 90 days, 48 hours prior to admission where the infection was isolated by E. coli and/or K. pneumoniae), empirical antibiotic treatment (antibiotic that the patient received to treat the infection before obtaining the microbiological result),<sup>v</sup> adequate empirical antibiotic treatment (empirical treatment whose active ingredient was sensitive to the isolated microorganism, according to the

antibiogram) and adequate targeted antibiotic treatment (treatment adjusted after the antibiogram result, considering sensitivity, route, dose and correct duration).

Frequencies and proportions were calculated for qualitative variables, while the Anderson-Darling normality test was performed for quantitative variables. For the differences in proportions between ESBL+ and ESBL- groups, Chi-square was used (pvalue < 0.05 as statistically significant). Epi-Info 7.2.6.0 and Microsoft Excel 365 with its XRealStats.xlam and XLSTAT 2023 add-in were used for data processing and analysis.

The Ethics Committee of each hospital authorized the study. The corresponding registration numbers are File No. 24/2023, Rosales National Hospital, and File No. 8-2023, San Rafael National Hospital.

## Results

### Characteristics of the population

Of the 989 patients analyzed, 58.4 % were female, and 40 % were aged 60 years or older. The median age was 39 years (RI: 2-67) for the second-level hospital and 57 years (RI: 42-69) for the third-level hospital. The service with the highest number of isolations was Internal Medicine, with 60.0 %. The most frequent type of specimen was urine, with 64.2 %, and the bacterium isolated with the highest proportion was *E. coli*, with 67.7 %. Community infections (52.7 %) were concentrated in urine samples. HAIs (47.3%) were most frequently present in blood and bronchial secretions. 24.1 % of patients had previous admissions, 29.9 % had undergone a surgical procedure, 84.5 % had exposure to invasive devices, 58.6 % required a prolonged hospital stay (> 7 days), and 52.4 % experienced complications during hospitalization. Of the 50.1 % who had an infection by BLEE+ bacteria, 34.1 % died during the 30-day follow-up after the culture was taken.

Of the 400 patients at the secondary care hospital, 39 % were infected with ESBL+ strains, 72.4 % were *E. coli*, and 27.5 % were *K. pneumoniae*. Regarding age, it was more common in patients over 60 years of age, at 50.6 %. However, this resistance mechanism was also identified in 17.9 % of children under 5 years of age (Table 1). 59.6 % were of community origin, and 76.2 % had no comorbidities according to the Charlson index, which relates 10-year life expectancy to a patient's comorbidities (Table 2).

Regarding treatment, 96.7 % received empirical antibiotic therapy, 48.7 % received appropriate treatment, and 62.1 % received adequate targeted antibiotic therapy according to the result of the antibiogram (Table 2).

In the 30-day follow-up after culture, mortality in the group with ESBL+ enterobacteria infection was 25.0 %, while in the group with ESBL- enterobacteria infection, it was 11.0 % (Table 2); this difference was statistically significant (p < 0.001).

In the tertiary care hospital, 589 patients were included, of whom 57.5 % presented infections caused by ESBL+ bacteria. Of these infections, *E. coli* was isolated in 54.0 % of the cases and *K. pneumoniae* in 46.0 %. 44.8 % of resistant cases occurred in patients older than 60 years. Furthermore, 66.1% of infections were of nosocomial origin, and 44.2 % of patients had high comorbidity according to the Charlson index (Table 2).

Regarding treatment, 72 % of the patients received empirical antibiotic therapy at the beginning of the management, which was appropriate in 15.3 % of the cases. A total of 68.1 % received adequate targeted antibiotic therapy based on antibiogram results, and 43.1 % required admission to the ICU (Table 2).

At the 30-day follow-up after culture collection, the mortality rate was 38.3% in the ESBL+ group and 30% in the ESBL-group, which represented a significant difference in these proportions (p < 0.04).

# Antimicrobial susceptibility profiles

Of the total samples analyzed for ESBL+ *E. coli* and *K. pneumoniae*, the susceptibility percentages were resistant in 46.0 % and 13.0 %; intermediate in 3.4 % and 50.4 %; and susceptible in 50.6 % and 36.9 %, respectively, for each bacterium.

In the secondary care hospital, the most frequently prescribed antibiotics for 48-hour pretreatment and empirical therapy were cephalosporins (37.2 % and 41.9 %, respectively), primarily ceftriaxone (32.4 % and 40.1%). Penicillins were prescribed for appropriate targeted therapy (38.0 %, mainly ampicillin) (72.0 %).

In *E. coli* and *K. pneumoniae* ESBL+ isolates, resistance was reported in 31.0 % and 42.8 % of the samples analyzed, respectively. Both bacteria showed 100 % resistance to ampicillin, and ampicillin-sulbactam showed both resistance (54 %, 75 %) and intermediate susceptibility for both bacteria (22 %, 4 %). For *E. coli* ESBL+, other antibiotics with a significant percentage of resistance were tetracycline (67 %), trimethoprim-sulfamethoxazole (64 %), levofloxacin (53 %), ciprofloxacin (52 %) and some **Table 1.** Sociodemographic characteristics of patients admitted with *Escherichia coli* or *Klebsiella pneumoniae* infection according to BLEE production, 2022.

	Second lev	el hospital	Third level hospital			
Características	ESBL- (n=244)	ESBL+ (n=156)	ESBL- (n=250)	ESBL+ (n=339)		
	fr(%)	fr(%)	fr(%)	fr(%)		
Sex						
Female	179 (73.4)	98 (62.8)	138 (55.2)	163 (48.1)		
Male	65 (26.6)	58 (37.2)	112 (44.8)	176 (51.9)		
Age groups (years)						
Under 1	61 (25.0)	24 (15.4)	-	-		
1 to 4	20 (8.2)	4 (2.6)	-	-		
5 to 9	5 (2.1)	-	-	-		
10 to 19	21 (8.6)	3 (1.9)	16 (6.4)	12 (3.5)		
20 to 29	33 (13.5)	6 (3.9)	23 (9.2)	27 (8.0)		
30 to 39	15 (6.1)	8 (5.1)	20 (8.0)	34 (10.0)		
40 to 49	13 (5.3)	8 (5.1)	36 (14.4)	50 (14.8)		
50 to 59	18 (7.4)	24 (15.4)	48 (19.2)	64 (18.9)		
Over 60	58 (23.8)	79 (50.6)	107 (42.8)	152 (44.8)		

ESBL-: beta-lactamase negative bacteria, ESBL+: beta-lactamase positive bacteria.

cephalosporins such as ceftazidime, ceftriaxone, cefepime, cephalothin, cefazolin (42-50 %). Moreover, carbapenemics such as imipenem (4 %) and meropenem (3 %) also reported resistance for *K. pneumoniae* ESBL+, cephalothin (79 %), cefepime, cefazolin, and ceftriaxone (69 %) were reported. Imipenem and meropenem were sensitive (100 %) (Table 1).

In the tertiary care hospital, cephalosporins were most frequently prescribed in preand empirical antibiotic therapy (78.1%, 50.9 %), with ceftriaxone being the most frequently used antibiotic, with 54.0 % and 40.9 %, respectively. Inappropriate targeted therapy, carbapenems were used at 50.6 %, mainly meropenem at 57.9 %.

Of the ESBL+ *E. coli* and *K. pneumoniae* samples tested, 55.7 % and 5.3 %, respectively, were resistant to one or more antibiotics, with 100 % resistant susceptibility to ampicillin and aztreonam. Furthermore, ESBL+ *E. coli* samples had percentages 98 % of resistance to cephalothin, cefazolin, cefepime, cefoxitin, and ceftriaxone, and 3 % resistance to imipenem and meropenem. ESBL+ *K. pneumoniae* samples were 98 % resistant to cephalothin, cefazolin, cefepime, cefoxitin, and ceftriaxone, 4 % resistent to imipenem and 5 % resistent to meropenem (Table 3).

## Discussion

In this study, the ESBL+ resistance mechanism was found to be present in half of all infections. In this group, more than onethird of the population died within 30 days of culture collection, a proportion that represents almost twice the mortality observed in the group with infections caused by non-ESBL-producing bacteria, suggesting that the presence of this resistance mechanism could influence the unfavorable prognosis of patients.<sup>viii, ix</sup>

In other studies, during the same 30day follow-up period in patients with *E. coli* and *K. pneumoniae* bacteremia, mortality is generallly higher when the ESBL resistance mechanism is present than when it is absent, and patients may even die before starting adequate antibiotic treatment.<sup>v,x,xi</sup>

The presence of this resistance mechanism has varied from 18.1% in an analysis of pediatric patients in Mexico to 46% in patients with urinary tract infections reported in Jordan and 96% in the case of Iran.<sup>xii</sup> The percentage and outcome vary according to the complexity of the hospital evaluated, the isolation samples, and the characteristics of the population analyzed, such as age, sex, comorbidities, and previous antibiotic therapy, among others.<sup>v,xii,xiii</sup> Thus, as in this study, the percentage of infections by ESBL+ bacteria was higher in the third-level hospital.

The most frequent characteristics present in the group with infection by ESBL+ bacteria in this research were similar to those identified in other studies, such as the older age of the patient, between the fifth and sixth decade of life, the presence of complications such as sepsis or septic

decording to ESDE production, 2	Second	level hospital	Third level hospital				
Features	ESBL- (n=244)	ESBL+ (n=156)	ESBL- (n=250)	ESBL+ (n=339)			
	fr(%)	fr(%)	fr(%)	fr(%)			
Clinics							
Hospital service							
Internal Medicine	91 (37.3)	100 (64.1)	179 (71.6)	216 (63.7)			
Surgery	14 (5.7)	20 (12.8)	71 (28.4)	123 (36.3)			
Pediatrics	67 (27.5)	13 (8.3)	-	-			
Obstetrics and Gynecology	52 (21.3)	8 (5.1)	-	-			
Neonatology	20 (8.2)	15 (9.6)	-	-			
Previous income	33 (13.5)	41 (26.3)	69 (27.6)	96 (28.3)			
Extended stay	61 (25.0)	92 (59.0)	171 (68.4)	256 (75.5)			
Surgical procedure	15 (6.1)	27 (17.3)	95 (38.0)	159 (46.9)			
Minimally invasive	2 (0.8)	6 (3.8)	17 (6.8)	22 (6.5)			
Invasive	13 (5.3)	22 (14.1)	78 (31.2)	137 (40.4)			
Invasive device	216 (88.5)	147 (94.2)	185 (74.0)	288 (85.0)			
Immunosuppression	6 (2.5)	11 (7.1)	129 (51.6)	179 (52.8)			
Presence of complications	43 (17.6)	67 (42.9)	157 (62.8)	252 (74.3)			
Admission to ICU	-	-	82 (32.8)	146 (43.1)			
Charlson comorbidity							
Absent	216 (88.5)	119 (76.3)	64 (25.6)	72 (21.2)			
Download	14 (5.7)	15 (9.6)	74 (29.6)	117 (34.5)			
High	14 (5.7)	22 (14.1)	112 (44.8)	150 (44.2			
Exit condition							
Alive	219 (89.8)	119 (76.3)	170 (68.0)	204 (60.5)			
Deceased	25 (10.2)	37 (23.7)	80 (32.0)	135 (39.8)			
30-day follow-up							
Alive	208 (85.2)	114 (73.1)	169 (67.6)	205 (60.2)			
Deceased	27 (11.1)	39 (25.0)	75 (30.0)	130 (38.3)			
Unknown	9 (3.7)	3 (1.9)	6 (2.4)	4 (1.2)			
Microbiological							
Type of sample							
Urine	212 (86.9)	114 (73.1)	139 (55.6)	170 (50.1)			
Blood	24 (9.8)	32 (20.5)	60 (24.0)	91 (26.8)			
Bronchial secretion	8 (3.3)	10 (6.4)	51 (20.4)	78 (23.0)			
Isolated microorganism							
Escherichia coli	214 (87.7)	113 (72.4)	160 (64.0)	183 (54.0)			
Klebsiella pneumoniae	30 (12.3)	43 (27.6)	90 (36.0)	156 (46.0)			
Origin of infection							
Community	208 (85.2)	93 (59.6)	105 (42.0)	115 (33.9)			
HAI	36 (14.8)	63 (40.4)	145 (58.0)	224 (66.1)			
Polymicrobial isolation	1 (0.4)	1 (0.6)	8 (3.2)	19 (5.6)			
Infection by other agents	4 (1.6)	7 (4.5)	48 (19.2)	75 (22.1)			
Antibiotic treatment							
Previous entry (90 days)	23 (9.4)	27 (17.3)	69 (27.6)	94 (27.7)			
Prior to admission (48 hours)	21 (8.6)	22 (14.1)	190 (76.0)	94 (27.7)			
Empirical	238 (97.5)	151 (96.8)	184 (73.6)	244 (72.0)			
Appropriate empirical	190 (77.9)	76 (48.7)	87 (34.8)	52 (15.3)			
Adequately addressed	203 (83.2)	97 (62.2)	201 (80.4)	231 (68.1)			

**Table 2.** Clinical characteristics of patients admitted with *Escherichia coli* or *Klebsiella pneumoniae* infection according to ESBL production, 2022.

ESBL-: beta-lactamase negative bacteria, ESBL+: beta-lactamase positive bacteria, ICU: Intensive Care Unit. HAI: Healthcare-associated infections

	<i>E. coli</i> ESBL+ (%)					K. pneumoniae ESBL+ (%)						
Antibiotic	2nd level (n=113)		3	3rd level (n=183)		2	2nd level (n=43)		3 (I	3rd level (n=156)		
	R	Ι	S	R	I	S	R	I	S	R	Ι	S
Amikacin	2	0	98	1	0	99	0	4	96	1	3	96
Amoxicillin/Clavulanic Acid	27	60	13	21	63	16	9	-	55	29	64	7
Ampicillin	100	0	0	-	0	0	-	0	0	-	0	0
Ampicillin-sulbactam	54	22	25	84	6	10	75	4	21	87	7	6
Aztreonam	56	0	44	-	0	0	55	0	45	-	0	0
Cephalothin	46	20	34	99	1	0	79	7	14	-	0	0
Cefazolin	50	0	50	89	0	11	69	0	31	99	0	1
Cefepime	43	0	57	99	0	1	69	0	31	99	0	1
Ceftazidime	42	0	58	99	0	1	54	0	46	99	0	1
Ceftriaxone	43	0	57	99	0	1	69	0	31	99	0	1
Ciprofloxacin	52	20	28	91	5	4	66	3	31	89	7	4
Ertapenem	6	0	94	2	1	96	3	0	97	6	0	94
Fosfomycin	3	1	96	4	0	96	-	-	-	0	0	-
Gentamicin	28	0	72	43	0	57	49	0	51	69	4	27
Imipenem	4	0	96	3	0	97	0	0	100	4	1	94
Levofloxacin	53	27	20	95	5	0	18	-	55	57	43	0
Meropenem	3	0	97	3	0	97	0	0	100	4	0	96
Nitrofurantoin	1	5	94	9	12	78	24	-	32	45	40	15
Piperacillin-Tazobactam	20	10	71	17	11	72	14	0	86	16	10	74
Tetracycline	67	0	33	89	0	11	55	0	45	93	0	7
Tigecycline	0	0	-	2	0	98	0	0	100	4	0	94
Trimethoprim-sulfamethox- azole	64	0	36	73	0	27	68	0	32	90	0	10

**Table 3.** Antimicrobial susceptibility profiles of-producing bacteria in the second and third level of care hospital, 2022.

R: Resistant, I: Intermediate, S: Susceptible, S: Sensitive

shock, exposure to invasive devices, previous admissions, prolonged hospital stay, immunosuppression, history of previous and empirical antibiotic therapy.<sup>v,xii</sup> One of the differences identified in the second-level hospital was that the absence of comorbidities and the community origin of the infection was the most frequent within the ESBL+ group, unlike the third-level hospital and other studies where a high Charlson index and the origin of nosocomial infection predominate.<sup>v,x,xv</sup> This is possibly explained by the complexity of the hospital, such as the tertiary level hospital in this study, which attends to patients with comorbidities and more serious complications, as well as longstanding diseases and a predominantly adult population.

The profiles for both bacteria reported a higher percentage of resistance for penicillins and cephalosporins. In contrast, for some drugs, all the samples analyzed were resistant, such as ampicillin in both hospitals. This is consistent with previous studies that point to the widespread use of these antibiotics as a key factor in the proliferation of ESBL+ strains.<sup>xvi,xvii</sup>

In addition, a percentage of resistance between 3 % and 4 % was presented for potent drugs such as imipenem and meropenem. This is in agreement with WHO reports and other studies where antibiotics used as first-line are ineffective due to the high resistance reported, and those considered as last choice antibiotics such as carbapenemics already have reports of resistance to them by some bacteria.<sup>v,xiixviii,xx</sup> In the case of K. pneumoniae, it presented higher percentages of resistance for most drugs, compared to *E. coli*, which is different from that reported in other countries where it is E. coli that presents higher percentages of resistance.<sup>xii</sup> Due to the increasing prevalence of antibiotic resistance, the development of new antibiotics and alternative therapies, improvements in infection control, and antibiotic optimization programs should be considered.<sup>xxi</sup> In addition, evidence-based guidelines for empirical treatment and restricting the use of third-generation cephalosporins are the most successful measures to control the severity of ESBL+ microbial pathogens.<sup>xvii</sup>

As this is a retrospective study, data collection depends on the quality and availability of previous medical records, which limits the researchers' ability to control this information. Furthermore, the impossibility of controlling the quality of the collection, handling, transport, and processing of biological samples must be considered. Therefore, the GLASS protocol was chosen, as it standardizes variable definitions and reduces the risk of data bias.

## Conclusion

Infections caused by ESBL-producing bacteria continue to represent a significant clinical challenge in second-third-level care hospitals in El Salvador. *Klebsiella pneumoniae* ESBL+ showed resistance to cephalosporins, quinolones and carbapenemics, especially in HAIs, underscoring the need to review and optimize treatment guidelines. *Escherichia coli* ESBL+ showed resistance in urinary tract infections of community origin, suggesting spread of resistance beyond the hospital setting.

Patients with ESBL+ infections presented higher mortality. These findings emphasize the importance of implementing more effective control and prevention measures adapted to the local context of resistance. Furthermore, it is necessary to develop and integrate therapeutic strategies that consider the growing resistance to carbapenems, prioritizing early identification and continuous monitoring of these pathogens.

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