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Original Article

Multidrug resistance and its association with Enterobacteriales and age among pregnant Peruvian women with- bacteremia

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Abstract

Introduction: This study aimed to assess the prevalence of multidrug resistance (MDR) and its associated factors among pregnant Peruvian women with bacteremia.

Methodology: In an 18-month cross-sectional study, all pregnant women were routinely tested with a presumptive diagnosis of sepsis admitted to the largest reference maternity hospital (Instituto Nacional Materno Perinatal) in Lima, Peru for bacteremia. Every isolate was tested for antimicrobial susceptibility as defined by the Institute of Clinical and Laboratory Standards (CLSI). Additionally, associated factors were assessed with MDR and the number of resistant antimicrobial categories using robust Poisson regression models with link log, especially focused on its association with age and bacterial families or species.

Results: A total of 236 blood cultures of pregnant women (33.4 ± 11.4 years old) was analyzed. The prevalence of MDR was 70% (95% confidence interval [CI]: 64%–76%). The main etiological agent was *Escherichia coli* (65%), showing an MDR rate of 74% (68%–81%). Overall, we observed that the MDR rate was associated with *Enterobacteriales* (adjusted prevalence rate, (aPR) = 1.29; 95% CI: 1.03–1.61) and age 35 or older (PR = 1.18; 95% CI: 1.01–1.39). However, the number of resistant antimicrobial categories was associated with *Enterobacteriales* (aPR = 1.44; 95% CI: 1.25–1.67) and hospital-acquired infections (PR = 0.81; 95% CI: 1.01–1.39).

Conclusions: The prevalence of MDR among pregnant women with sepsis was alarmingly high, being even higher among women age 35 or older and among those with hospital-acquired infections.

Key words: Pregnant women; drug resistance; anti-bacterial agents; bacteremia; multiple.

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Introduction

Bacterial bloodstream infection or bacteremia is one of the main causes of maternal mortality and morbidity [1, 2]. Bacteremia also represents a major cause of neonatal mortality and morbidity, including preterm birth and miscarriage [3, 4]. Inadequate treatment of bacteremia can lead to sepsis, with a high risk of death. However, the choice of the most adequate antibiotic must be made with caution because the pharmacokinetics and pharmacodynamic properties of antibiotics often change in pregnant women and may be harmful to the fetus [5], and there is an increasing threat of multidrug resistance (MDR).

The increasing prevalence of MDR is of major concern worldwide, particularly because of the increasing resistance to reserve antimicrobials [6]. Case-fatality rates associated with bacteremia range from 35% to 50% in patients admitted to intensive care units (ICU) and are commonly associated with MDR, extended-spectrum beta-lactamases (ESBL), and carbapenems resistant bacteria [7]. It is known that adequate antibiotic therapy for MDR has a substantial impact on reducing the length of hospitalization and the risk of mortality overall in adults, but little is known regarding its effects on pregnant women [8].

In Latin America and the Caribbean approximately 7.7% of all maternal deaths are due to maternal sepsis [9]. However, epidemiological data regarding MDR and its associated factors among pregnant women are needed to optimize empiric antibiotic treatment guidelines. Although the prevalence of MDR related to bacteremia is commonly reported as being high in Peru [10], there is little data available regarding the prevalence of MDR among pregnant women with bacteremia. Thus, the aim of the study was to characterize the bacterial etiological agents causing bacteremia among pregnant women, determine the prevalence of MDR and analyze the factors associated with its development.

Methodology

Study design and population

The study was conducted at the National Maternal-Perinatal Institute (INMP), which is the largest maternity reference hospital in Lima, Peru (> 20,000 births annually). During an 18-month period (January 2017 to June 2018) every pregnant woman was routinely tested with a presumptive diagnosis of sepsis for bacteremia using blood culture. Study exclusion criteria included blood cultures that were either contaminated or that did not grow, as well as blood cultures collected from patients who were receiving antibiotic treatment. Then, antimicrobial susceptibility was evaluated in every positive culture, especially focusing on the diagnosis of MDR (resistance to ≥ 3 antimicrobial classes) and the prevalence of ESBL. Finally, the demographic data and location of residence of all the women studied as potential factors associated with the development of MDR were assessed. Cases of sepsis were classified as community- if patient or hospital-acquired according the definitions: Community-acquired infections if patients had the infection at admission to the hospital and hospital-acquired when the infection occurred after almost 72h post admission.

Strain identification

All blood samples were cultured in two bottles per patient and incubated in a BD BACTEC automated blood culture system for seven days before reporting no growth. When growth was detected in blood samples, a Gram stain and sub-culture were performed using selective media in order to identify the causative agent according to conventional microbiology protocols. Specifically, we use Blood Agar and Mannitol Agar for Gram-positive cocci; blood agar and MacConkey for Gram-negative bacilli; and, Blood Agar, Agar Sabouraud, and CRHOM Candid Agar for yeast. In order to avoid introducing contaminating agents into the study, coagulase-negative *Staphylococci* (CoNS) was considered as a plausible etiological agent only when patients tested CoNS positive in two separate blood cultures.

Antimicrobial susceptibility

The antimicrobial susceptibility was evaluated using disc-diffusion on Mueller–Hinton agar plates and a conventional Kirby Bauer method with *Escherichia coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 as quality controls [11]. The results of each bacterial isolate were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines in the Laboratory of Microbiology of the INMP [11]. The antimicrobial agents tested were: ampicillin (10 mg); amoxicillin/clavulanic acid (20/10 mg); cefoxitin (30 mg); ceftriaxone (30 mg); ceftazidime (30 mg); imipenem (10 mg); meropenem (10 mg); gentamicin (10 mg); amikacin (30 mg); tetracycline (30 mg); chloramphenicol (30 mg); trimethoprim/sulfamethoxazole (1.25/23.75 mg); nalidixic acid (30 mg); ciprofloxacin (5 mg); rifampicin (5 mg); and azithromycin (15 mg).

MDR and MDR patterns

Any bacteria showing resistance to at least one agent in three or more antimicrobial categories was diagnosed as MDR [12], and the MDR rate was estimated. Then, we described the frequency of the patterns of antibiotic resistance by counting the number of resistant antimicrobial categories (with at least one positive resistant antibiotic agent).

ESBL phenotype detection

ESBL expression was assessed using the ESBL disk synergy test. Each disk contained cefotaxime, amoxicillin with clavulanic acid, and ceftazidime on Mueller–Hinton agar as described previously [11].

Data Entry and Quality Control

Data entry was conducted using the WHONET software, which is a free windows-based database software developed by the World Health Organization Collaborating Centre for Surveillance of Antimicrobial Resistance to facilitate antimicrobial susceptibility data entry and analysis [13]. With this software, we also incorporated several quality control procedures because WHONET comes with previous consensus categories or specific range values for each variable and several quality control protocols [13]. Regardless, an independent reviewer (GS) double checked for any possible data entry disagreements which were contrasted with the original test orders as the data source.

Statistical Analysis

We summarized each antimicrobial resistant descriptor and other categorical variables with their absolute and relative frequencies and summarized every numerical variable with its mean and standard deviation. Then, we estimated the MDR and EBSL rates by counting the total number of positives per 100 tested. In addition, we assessed the factors associated with MDR and the number of resistant antimicrobial categories using generalized linear models with a Poisson distribution, link log, and robust error variance.

Table 1. General characteristics of the study subjects.

Characteristic	MDR rate (95% CI)	No-MDR N = 71	MDR N = 165	Total N = 236
Age (Mean ± SD, years)		31.3 ± 8.9	34.2 ± 12.3	33.4 ± 11.4
< 35 years	65.8% (58.3–73.4)	53 (74.7%)	102 (61.8%)	155 (65.7%)
35 or older	77.8% (69.5–87.0)	18 (25.4%)	63 (38.2%)	81(34.3%)
Infection origin				
Community-acquired	74.3% (63.7–84.8)	18 (25.4%)	52 (31.5%)	70 (29.7%)
Hospital-acquired	68.5% (60.9–75.2)	53 (74.7%)	113 (68.5%)	166 (70.3%)
Bacteria family ‡				
Moraxellaceae	100% (N/A)	0 (0%)	1 (0.6%)	1 (0.4%)
Enterobacteriaceae	74.4% (67.8–81.0)	44 (62.0%)	128 (77.6%)	172 (72.9%)
Enterococcaceae	27.3% (-0.4–58.7)	8 (11.3%)	3 (1.8%)	11 (4.7%)
Streptococcaceae	68.8% (43.2–94.3)	5 (7.0%)	11 (6.7%)	16 (6.8%)
Pseudomonadaceae	100% (N/A)	0 (0%)	1 (0.6%)	1 (0.4%)
Staphylococcaceae	67.7% (50.3–85.2)	10 (14.1%)	21 (12.7%)	31 (13.1%)
Xanthomonadaceae	100% (N/A)	4 (5.6%)	0 (0%)	4 (1.7%)
Bacteria species †				
Acinetobacter	100% (N/A)	0 (0%)	1 (0.6%)	1 (0.4%)
Enterococcus spp.	27.3% (-4.1–58.7)	8 (11.3%)	3 (1.8%)	11 (4.7%)
E. coli	72.1% (64.9–79.2)	43 (60.6%)	111 (67.3%)	154 (65.3%)
Klebsiella spp.	91.7% (73.3–110)	1 (1.4%)	11 (6.7%)	12 (5.1%)
P. aeruginosa	100% (N/A)	0 (0%)	1 (0.6%)	1 (0.4%)
Proteus vulgaris.	100% (N/A)	0 (0%)	6 (3.6%)	6 (2.5%)
CoNS	67.9% (49.4–86.3)	9 (12.7%)	19 (11.5%)	28 (11.9%)
Staphylococcus aureus	66.7% (-77.8–210)	1 (1.4%)	2 (1.2%)	3 (1.3%)
Streptococcus spp.	68.8% (43.3–94.3)	5 (7.0%)	11 (6.7%)	16 (6.8%)
S. maltophilia	0% (N/A)	4 (5.6%)	0 (0%)	4 (1.7%)

MDR: Multidrug-resistant; SD: Standard deviation; CoNS: Coagulase-negative *Staphylococcus*; N/A: not applicable; †: valor p < 0.05; ‡: valor p < 0.001.

Table 2. Antibiotic resistance among the five most frequent isolates from pregnant women with bacteremia.

Antibiotics	Top 1 *E. coli* (n = 154)	Top 2 CoNS (n = 28)	Top 3 *Streptococcus* (n = 16)	Top 4 *Klebsiella* (n = 12)	Top 5 *Enterococcus* (n = 11)
	R/R + S (%)	R/R + S (%)	R/R + S (%)	R/R + S (%)	R/R + S (%)
Ampicillin	16/22 (72)		7/15 (47)	5/5 (100)	1/11 (9)
Amoxicillin/Clavulanic Acid	33/80 (41)			2/5 (40)	
Aztreonam	37/151 (25)			4/12 (33)	
Cefepime	45/148 (30)			4/11 (36)	
Cefotaxime	47/152 (30)	16/28 (57)		4/12 (33)	
Cefoxitin	5/152 (3)			0/12 (0)	
Ceftazidime	39/151 (26)			4/12 (33)	
Imipenem	0/148 (0)			0/11 (0)	
Meropenem	1/147 (1)			1/12 (8)	
Amikacin	21/147 (14)	7/28 (25)		2/12 (17)	
Gentamicin	33/152 (22)	15/27 (56)	4/7 (57)	3/12 (25)	
Nalidixic acid	102/145 (70)			5/12 (42)	
Ciprofloxacin	80/147 (54)	15/28 (54)		3/12 (25)	6/11 (55)
Levofloxacin	66/149 (44)	10/21 (48)	6/12 (50)	1/12 (8)	1/8 (13)
Clindamycin			13/15 (89)		
Erythromycin			15/15 (100)		8/11 (73)
Fosfomycin	66/149 (44)				
Nitrofuratoin	29/144 (20)	0/7 (0)		9/10 (90)	1/9 (11)
Rifampin		2/19 (11)			2/2 (100)
Tetracycline		2/2 (100)	1/2 (50)		
TMP/SMX	75/150 (50)	15/25 (60)		3/12 (25)	
Teicoplanin					1/10 (10)
Vancomycin			0/16 (0)		0/11 (0)

R: Resistant; S: Susceptible; CoNS: Coagulase-negative *Staphylococcus*; TMP/SMX: Trimethoprim-sulphamethoxazole.

For this purpose, we considered patient age, infection origin and bacterial families or species as potential associated factors. We conduced these analyses using STATA™ MP version 14.0 (Stata Corp., College Station, TX) and a confidence interval of 95% (95% CI) for our estimates.

Results

Study population

A total of 236 pregnant women (33 ± 11 years old) tested positive for bacterial bloodstream infections (BSI) during the study period (Table 1). Most of these pregnant women were under 35 years of age (66%) and tested bacteremia positive during hospitalization (70%), including 11% who tested bacterial bloodstream infections positive when admitted to ICUs.

Etiological strains among pregnant women with bacteremia

The most frequent etiological agent isolated among blood culture of pregnant women with bacterial bloodstream infections was *E. coli* (n = 154, 65%). Other isolates included coagulase-negative *Staphylococcus* (CoNS) (n = 28, 12%), *Streptococcus* spp. (n = 16, 7%), *Klebsiella* spp. (n = 12, 5%), *Enterococcus* spp. (n = 11, 5%), *Proteus vulgaris* (n = 6, 3%), followed by *Stenotrophomonas maltophilia*, *Staphylococcus aureus*, *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, each with frequency of 1% or less (Table 1).

Antimicrobial susceptibility and ESBL phenotype

The top five most frequent isolates (*E. coli*, CoNS, *Streptococcus*, *Klebsiella* and *Enterococcus*) among pregnant women with bacterial bloodstream infections presented a wide range of antibiotic resistance rates (range: 0% to 100%) (Table 2). Overall, only 22% (51 isolates) of the isolates studied were tested for ESBL production, including 45 *E. coli*, 4 *Klebsiella spp.*, and 2 *Proteus spp* isolates. Out of the 51, 98% (50/51; CI 95%: 90%–99%) were MDR positive.

MDR rates

Among pregnant women with bloodstream infection, the prevalence of MDR was 70% (95% CI: 64%–76%). Among the top five most frequent bacteria isolated we observed a significantly ($p<0.05$) higher prevalence of MDR due to *Klebsiella* spp. (92%; 95% CI: 73%–110%) and *E. coli* (72%; 95% CI: 65–79) compared with *Enterococcus* spp. (27%; 95% CI: -4–59%). Additionally, the prevalence of MDR was 100% among isolates of *Proteus* spp. (6/6), *S. aureus*. (3/3), *Acinetobacter* spp. (1/1) and *P. aeruginosa* (1/1).

MDR patterns

Overall, the MDR patterns among pregnant women with BSI were highly variable. Specifically, when we analyzed the two most frequent isolates, we observed that the most frequent antibiotic resistance pattern only represented 15% (top 1: *E. coli*) and 21% (top 2: CoNS)

Table 3. Antibiotic resistance patterns among pregnant women with bacteremia that tested positive to at least one antimicrobial category.

Antibiotic resistance pattern		N (%)
Escherichia coli **(n = 140/154)**		
Top 1	QNL	19 (14.5)
Top 2	QNL + DRI	13 (9.9)
Top 3	PPN	11 (8.4)
Top 4	DRI	10 (7.6)
Top 5	QNL + DRI + CFL3 + CFL4 + AMG	10 (7.6)
Top 6	QNL + DRI + PPN + CFL3 + CFL4	9 (6.9)
Top 7	Different combinations with frequencies < 5%	68 (45.0)
CoNS (n = 24/28)		
Top 1	DRI + AMG	5 (20.8)
Top 2	DRI + AMG + CFL2	5 (20.8)
Top 3	AMG + CFL2	4 (16.7)
Top 4	DRI + CFL2	3 (12.5)
Top 5	CFL2	2 (8.3)
Top 6	DRI	2 (8.3)
Top 7	Different combinations with frequencies < 5%	3 (12.5)
Streptococcus **spp. (n = 15/16)**		
Top 1	MCL	14 (93.3)
Top 4	TTC	1 (6.7)

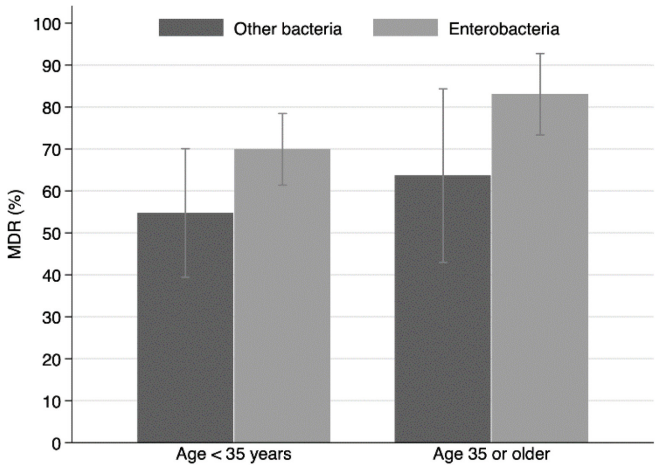
MDR: Multidrug-resistant; CoNS: Coagulase negative staphylococcus; QNL: quinolones; DRI: dihydrofolate reductase inhibitors; PPN: phosphonates; CFL2: second generation cephalosporins; CFL3: third generation cephalosporins; CFL4: fourth generation cephalosporins; AMG: aminoglycosides; MCL: macrolides; TTC: tetracyclines.

of all the different patterns observed. However, in the case of the third most frequent isolate the most frequent antibiotic resistant pattern represented 93% of all the possible antibiotic resistant patterns (Table 3).

Factors associated with the prevalence of MDR

Among pregnant women with BSI the prevalence of MDR was associated with *Enterobacteriales* infections (adjusted prevalence rate, (aPR) = 1.29; 95% CI: 1.03–1.61) and age 35 years of age or older (PR = 1.18; 95% CI: 1.01–1.39). When we analyzed the number of resistant antimicrobial categories, we found that these were associated with *Enterobacteriales* infections (PR = 1.44; 95% CI: 1.25–1.67) and hospital-acquired infections (PR = 1.20; 95% CI: 1.01–1.44) (Table 4) (Figure 1).

Figure 1. MDR rates for the top five most frequent bacteria isolated from pregnant women with bacteremia.



MDR: Multidrug-resistant.

Discussion

The main results of this study were the relevant importance of MDR in etiological agents related to bacterial bloodstream infections in pregnant women in the Peruvian maternal setting, highlighting *E. coli* as one of the most common organisms involved in bloodstream infection. Additionally, we found age (> 35 years old) and hospital-acquired infections to be factors associated with MDR acquisition in this setting.

Bacterial bloodstream infections during pregnancy is associated with a poor fetal outcome and a high mortality rate [14]. Usually, the sepsis varied, with half of the cases of sepsis occurring during postpartum, followed by intrapartum (36%), and most were related to the presence of pelvic infection source and antepartum (17%), with more commonly no pelvic in origin. [15]. The most frequent type of infection was that of the genital tract followed by the urinary tract [3]. The source of sepsis infection is important to guide the choice of the most adequate antibiotic treatment.

While taking antibiotics in pregnancy is not recommended due to possible side effects such as anaphylaxis or ruptured membranes, they are also sometimes overused and are given in cases without ruptured membranes or with non-symptomatic urinary tract infection (UTI) (even if leukocytes are present), thereby contributing to the emergence and selection of antibiotic resistance [5].When antibiotics are necessary, the choice of empirical antibiotics is selected based on the suspected source of infection, the microorganisms involved and local antibiotic resistance patterns.

In general, *Enterobacteriales* are the most important bacteria related to bacteremia in the general population and also during pregnancy [16]. *E. coli* is especially relevant inBSI in pregnant women and may be life-threatening for fetuses [14]. Thus, the etiological agent was linked to different outcomes, meanwhile *E.coli* was linked to preterm delivery, Group A

Table 4. Regression analyses for the multidrug resistance outcomes and number of resistant antimicrobial categories among pregnant women with bacteremia.

Associated factor	cPR (95% CI)	p-value	aPR (95% CI)	p-value
Outcome 1: MDR				
Enterobacteriales	1.28 (1.02 – 1.61)	0.030	1.29 (1.03 – 1.61)	0.029
Age 35 or older	1.18 (1.00 – 1.39)	0.044	1.18 (1.01 – 1.39)	0.041
Age (years)	1.01 (1.00 – 1.01)	0.023		
E. coli	1.09 (0.91 – 1.32)	0.338		
Hospital-acquired	1.09 (0.92 – 1.30)	0.323		
Outcome 2: Number of resistant antimicrobial categories				
Enterobacteriales	1.33 (1.16 – 1.55)	< 0.001	1.44 (1.25 – 1.67)	< 0.001
Hospital-acquired	1.09 (0.92 – 1.30)	0.323	1.20 (1.01 – 1.44)	0.001
E. coli	1.18 (1.04 – 1.36)	0.011		
Age (years)	1.09 (0.91 – 1.32)	0.338		
Age 35 or older	0.92 (0.77 – 1.09)	0.323		

MDR: Multidrug-resistant; cPR: crude prevalence ratio; aPR: adjusted prevalence ratio.

Streptococcus was related to postpartum sepsis at term and both were the most virulent microorganisms [3].

In general, we found high rates of MDR in this study, especially in *Enterobacteriales* and non-fermenting Gram-negative bacilli. Antibiotic resistance of *E.coli* to quinolones was high (54-70%), with 72% presenting resistance to ampicillin and 50% to sulfamethoxazole/trimethoprim. A previous study in BSI in a Peruvian population showed higher antibiotic resistance levels to quinolones (85% to ciprofloxacin and 86% to sulfamethoxazole/trimethoprim) [10]. Resistance to quinolones was high, especially to older quinolones (70%), although routine use of fluoroquinolones during pregnancy is still not recommended [17].

The rate of antibiotic resistance to amoxillicin-clavulanic acid was nearly 40% in *Enterobacteriales* (*E.coli* and *Klebsiella*). This antibiotic is frequently prescribed in the context of pregnancy with preterm premature rupture, although its use has been associated with a risk of necrotizing enterocolitis [18].

The rate of streptococcal infection in pregnant women is high. However, although the number of *Streptococcus* isolates was limited in the present study, high levels of resistance to clindamycin and erythromycin were found (89% and 100% respectively). Usually, the resistance levels to macrolides was high in *Streptococcus* [19], although, values obtained in this study are much higher than those previously reported in the country [20, 21]. These resistance rates may be related to overusage of antibiotics during pregnancy, since macrolides are one of the antibiotics of choice to treat preterm rupture of membranes, leading to the selection of antibiotic-resistant microorganisms [22]. Moreover, the origin of Group B *Streptococcus* is associated with colonization in pregnant women, presenting a rates between 10% to 30%, depending on different characteristics such as geographical area or age [23].

In the present study hospital-acquired infections and *Enterobacteriales* infection were related to more resistant antimicrobial categories in the isolates studied likely in response to the antibiotic resistance pressure related to hospitalization, especially in the ICU. Most of these infections were related to contamination and dissemination of microorganisms from ICUs surfaces or devices or from patients admitted for infectious processes or health care personnel [24]. The association of *Enterobacteriales* with more resistant antimicrobial categories is related to a greater presence of plasmids, contributing to rapid and easy dissemination among different species. Moreover, the elevated antibiotic resistance levels in *Klebsiella* species are due to their high capacity of adaptation generated by high carriage of plasmids and GC content [25].

We found the prevalence of MDR to be higher in community-acquired (74%) than hospital-acquired (69%) BSI. Some studies have suggested the importance of the prevention of community-acquired infections in order to reduce the cases of *E.coli* bacteremia, which are mainly related to underlying UTI. Indeed, prompt adequate treatment of UTI could reduce the prevalence of community-acquired *E.coli* bacteremia, since a high proportion of these bacterial bloodstream infections are due to treatment failure in UTIs [26]. Single-dose fosfomycin is recommended for the treatment of UTIs in pregnant women, and in this study, the levels of resistance to fosfomycin were 44%. Additionaly, the most frequent antibiotic resistance patterns in *E.coli* are to fosfomycin, together with quinolones and trimethroprim (15%). It has been reported that other antimicrobials such as amikacin, cephalosporins, and nitrofurantoin are not as effective in single doses for this population, but the levels of resistance found are slightly lower (40, 30 and 20% respectively).

In our study, age (35 years old or older) was found to be associated with higher rates of MDR. In previous study, age has been related to antibiotic resistance according to the target of the antimicrobial, with antibiotics targeting DNA synthesis showing higher antibiotic resistance rates in older populations, while this association is not found in other antimicrobial groups such as aminoglycosides or cephalosporins [27]. Similar to other middle and low-income countries, the emergence of MDR bacteria has spread rapidly across Peru. Such dissemination occurred mainly promoted by patient contamination, overwhelmed health-care workers, limited hospital infrastructure, poor hygiene control, and lack of infection control programs [28].

Regarding the study limitations, the main limitation of this study was the limited access we have to the patients ' clinical information. This lack of clinical data limited the scope of our MDR risk factors analysis to the minimum. Nonetheless, we managed to capture some vital signals and control the confounding bias by performing a multivariable regression analysis. Another significant limitation was the risk of selection bias since we restrain our investigation to only those participants with a presumptive diagnosis of sepsis for bacteremia using blood culture. To mitigate this risk, we assessed as many eligible participants as we can, analyzing the larger sample of pregnant women with bacterial

bloodstream infections published up to date in the region.

Conclusion

In conclusion, the prevalence of MDR among pregnant women with sepsis was alarmingly high, is even higher among women age 35 or older and those with hospital-acquired infections. Our study results could improve the use of antimicrobial treatments to avoid misuse of antibiotics and a further selection of antibiotic resistance. The levels of antibiotic resistance were high in both hospital- and community-acquired BSI, especially with *Enterobacteriales.*

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