ORIGINAL RESEARCH

Point Prevalence Survey of Antimicrobial Use in Four Tertiary Care Hospitals in Mexico

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Purpose: To describe the antimicrobial use in four tertiary care hospitals in Mexico.

Patients and Methods: Point prevalence surveys (PPSs) were conducted on medical records of hospitalized patients with prescribed antimicrobials (AMs) in four tertiary care hospitals in Mexico in 2019. Prevalence estimates and descriptive statistics were used to present the collected data on antimicrobial prescribing and microbiological studies.

Results: The prevalence of patients with prescribed AMs among the hospitals ranged from 47.1% to 91.3%. Antibiotics for systemic use (J01s) were the most prescribed (84.6%, [95% CI: 81.5–87.3]), mainly extended-spectrum J01s: third-generation cephalosporins 19.8% [95% CI: 16.8–23.1], and carbapenems 17.0% [95% CI: 14.2–20.2]. Antibiotic treatments were largely empirical, with no planned duration or review dates. The ceftriaxone use was excessive and prolonged. No formal reference guidelines for antimicrobial prescribing were available in the hospitals. Multidrug-resistant *Escherichia coli* and ESKAPE pathogens were identified in all hospitals.

Conclusion: This study describes the extensive use of antimicrobials and broad-spectrum antibiotics for systemic use in Mexican hospitals, along with the presence of resistant pathogens to the antibiotics frequently used in the hospitals surveyed.

Keywords: PPSs, antimicrobial use, antibiotics, Mexican hospitals

Introduction

Antimicrobials (AMs) are the pharmacological health-care standard against infectious diseases. Any usage of antimicrobials, mainly antibacterials (antibiotics) contributes to the selection of antimicrobial resistance (AMR), but their misuse and overuse worsens it.[1] Antimicrobial-resistant infections cause serious illnesses and prolonged hospital stays, increasing health-care costs, treatment failures, and morbi-mortality rates.[2,3]

In the US alone, a conservative estimate indicates that more than two million people every year are affected with antimicrobial-resistant infections, with at least 23,000 dying as a result.[4] Although it has been estimated that a continued rise in AMR by 2050 would lead to 10 million deaths every year worldwide,[5] the fact that infectious diseases can no longer be treated with antimicrobials could represent an even bleaker future. Given the serious threat that AMR represents to global public health, the efforts to reduce the irrational antibiotic use are becoming an increasing priority.[6]

Inadequate antibiotic therapies are common in hospitals regarding the agent's selection for microorganism type, routes of administration or treatments duration.[7] Thus, the majority of hospitalized patients are exposed either to potentially serious

adverse effects or the acquisition of resistant or difficult-to-treat pathogens (ie, *Clostridium difficile*), without any therapeutic benefit.[8,9]

Selection of antibiotic-resistant bacteria in hospitals may be aggravated by the frequent extended-spectrum antibiotics usage (eg, cephalosporins and carbapenems), and concentrated in common causal agents of hospital-associated infections (HAIs), such as those of the ESKAPE group (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter spp*), driven to a vicious cycle of greater use of extended-spectrum antibiotics.[10,11]

The World Health Organization (WHO) global action plan on AMR seeks to strengthen surveillance and optimize antimicrobial prescribing.[6] These actions are promoted in hospitals with antimicrobial stewardship programs (ASPs) through interventions to improve clinical outcomes, ensure the antimicrobial therapy's cost-effectiveness, and reduce unintended use consequences.[12] However, the needed effort, coordination, and resources for active monitoring of antimicrobial prescribing behavior in hospitals are high.

In Mexico, there is still little information on the antimicrobial use in general, and in the hospital environment in particular. Earlier studies focused on national consumption of antibiotics, based on retail sales.[13] More recently, the main focus has been on the epidemiology of HAIs, which usually report also some valuable data on antimicrobial use.[14,15] One of these studies, using the one-day point prevalence approach for HAIs, included four Mexican hospitals within a study in four Latin-American countries. This study reported that Mexican hospitals had the highest prevalence of patients on antibiotics (59.3%) among the four countries, and a relatively extensive use of third-generation cephalosporins, and carbapenems.[14] A related topic for research has been the bacterial pathogens and AMR.[16,17] These studies report a high frequency of AMR in both Gram-negative and Gram-positive bacteria, including high levels of multi-drug resistance in some strains. Besides, the antibiotic use for surgical prophylaxis is of particular concern. Several studies have shown the worrisome low frequency of good clinical practices in this regard. In one particular hospital, the level of compliance with international guidelines for surgical prophylaxis was 6.5%.[18] In another study, also in a single hospital, only 3.9% of surgical patients received the recommended antimicrobial prophylaxis.[19] Even after a multi-centric improvement

initiative, inappropriate prophylaxis regimens were found in 75.3% of surgical patients, and inappropriate dosages in 51.2%.[20] To date, in spite of this worrisome panorama, there are not official programs to analyze and improve the patterns of antibiotic use in Mexico. Besides, comprehensive studies on the characteristics of antimicrobial prescription and use are also lacking.

Point prevalence surveys (PPSs) are a useful method to study the antimicrobial prescription patterns in order to identify objectives for optimization on antibiotic use.[21–23] Therefore, the Global-PPS initiative and WHO (WPPS) have proposed standardized methodologies to conduct PPSs in hospitals.[23,24]

The aim of this study is to describe the antimicrobial use in four tertiary care hospitals in Mexico by means of PPSs.

Materials and Methods
PPS Protocol and Hospitals Characteristics

The protocol for this study was based on the Global-PPS and the WPPS methodologies[23,24] with a few modifications previously standardized.[25] Four third-care hospitals were selected for the PPSs. Hospitals will be described with anonymous nomenclature as H1, H2, H3 and H4.

H1 and H2 are highly specialized national referral institutions located in Mexico City, with 167 and 119 beds, respectively. Annually, each one provides healthcare to around five thousand patients. H3 is a referral hospital located in the State of Mexico, with 246 beds, and each year provides specialized clinical and surgical care to nearly six thousand patients. H4 is a general hospital located in a state in the northeast of Mexico, it has 120 beds and provides specialized medical care to approximately 4500 low-income patients. Regarding antimicrobial stewardship activities in the hospitals surveyed, H1 reported educational activities on antibiotics and pharmacovigilance interventions; H2 has implemented some interventions to improve the antibiotic prescribing; H3 reported having surveillance activities of resistant-ESKAPE pathogens. However, no hospital reported to have specific funding or personnel for these activities, neither documents or records to support any formally established ASP were found or available. No data were available on antimicrobial stewardship activities or AMR surveillance in H4.

Observer Team

The PPSs were conducted in all hospitals by the same multidisciplinary observer team, integrated by three

professionals with expertise in health surveys, supported by the principal investigators and the health-care providers of the hospitals. The observers were trained for one week on the PPS method, the study's aims, the characteristics and content of the questionnaires, and the procedures for data collection and management. The team was under the direct supervision of at least one principal investigator during the pilot studies and the PPSs.

PPS Pilot Studies

Pilot studies were conducted in each hospital at least one week in advance of the PPSs to identify the data sources and to allow corrective action. Anonymized data were collected in REDCap from two questionnaires based on the variables set proposed by the WPPS. Each pilot study included 15 patients hospitalized at 8:00 am on a - particular day. Inter-observer agreement was assessed on the total variables of both questionnaires.

The preparation, coordination, and data collection difficulties faced during our pilot studies, as well as the identified gaps in WPPS guidance to address common challenges for PPS implementation are reported in our previous work.[25]

PPSs in the Hospitals

The PPSs were conducted in August, October, November, and December 2019. Data were collected from patients with at least one AM prescribed, any age, hospitalized at 8:00 am on the day of the surveys in the medical and surgical wards, and the intensive-care units (ICUs). Data from outpatients or patients with surgery on the same day of the PPSs were not included.

Data collection was from 8:00 am to 8:00 pm, any day between Monday and Friday for patient selection, but data corroboration for selected patients was followed for two weeks. Written data on antimicrobial prescribing found in prescription sheets, medical notes, Kardex and nursing notes, nutrition records, hospital census, surgical scheduling sheets, and laboratory reports were collected.

Anonymized recorded data on the patients' age, sex, admission date, clinical diagnoses, wards/units of care, invasive devices presence, and the type of indication (therapeutic or prophylactic) were collected. The patients' type of infection (HAIs or community-acquired infections (CAIs)) defined in the medical records was collected. The observer team corroborated the onset dates of infections' first signs or symptoms after admission in the patients' medical records. When these dates were not

found, the date the antimicrobial treatment was started or the date the first sample was taken was considered according to the WPPS recommendations for classification of HAI versus CAI. The recorded data in the medical records on microbiological studies and antimicrobial susceptibility testing (AST) also was collected.

The name, number, and ATC codes (Anatomical Therapeutic Chemical classification system) of the AMs prescribed were collected,[26] as well as the reasons for the antimicrobial prescription, the type of treatments (empirical or targeted), routes of administration, doses, duration and review dates of treatments. Data on topical or ophthalmologic AMs were not included.

The observer team was instructed to notify the principal investigators when the medical record data were not clear to them or when there were doubts about capturing the information.

Data Management and Analysis

The PPSs data collected were exported to the SPSS v25 statistical package for cleaning and analysis.[27] The prevalence by hospital, wards and units was defined as the percentages of the number of patients with AMs, and antibiotics for systemic use (ATC level 2: J01s) prescribed, divided by the total number of patients admitted on the day of the PPSs. As appropriate, descriptive statistics (frequencies, proportions, and ranges between hospitals surveyed) were used to examine the data on patients, clinical diagnoses, prescribed agents (ATC levels 3, 4 and 5), routes of administration, types of indication, infection and treatments, surgical prophylaxis dose-day schedules, microbiological studies, and ASTs, by hospital, wards and units. The 95% confidence intervals [95% CI] were calculated using GraphPad QuickCalcs.[28]

Results
Most of the Hospitalized Patients Received AMs

PPSs detected a total of 525 patients, and 348 (66.3%, [95% CI: 62.1–70.2]) of them were receiving AMs in the four hospitals. The mean age of the patients with AMs was between 37 and 50 years. All patients were adults in H1. The highest children proportion was 18.6% in H3, including a neonatal ward (4.1%). The proportions by gender were similar, except for H4 where more male patients were found (68.2%) (Annex 1). Pneumonia and intra-abdominal sepsis were the most frequent clinical

diagnoses of patients receiving AMs. Nonetheless, the clinical diagnosis was documented in less than half of the patients in two of the four hospitals (Annex 2).

The prevalence of patients with AMs prescribed in the hospitals surveyed ranged from 47.1% to 91.3%. The prevalence of patients who had received J01s was in similar ranges, from 46.2% to 82.6%. The prevalence of patients with AMs prescribed among the wards/units ranged from 55.6% to 89.4%, almost equal to the range of patients who had received J01s (55.1% to 89.4%).

The volume of prescription was high in three of the hospitals (H1-H3), the medical wards, and ICUs, with prescription of three or more AMs by patient (Table 1).

Extensive Use of AMs Was Based on Empirical Decisions

The average number of days of AM treatments in patients ranged from 4.1 to 7.7 days among hospitals, and 5.9 (medical wards) to 7.5 days (ICUs) among wards/units. At the day of PPSs data collection, between 61.9% and 90.5% of patients with AMs were treated empirically, and between 60.5% and 91.8% of those who had received J01s. Besides, between 81.1% and 91.9% of the AMs were administered parenterally. Parenteral J01s was above 90% in all hospitals. In addition, almost all AMs and J01s used in the ICUs and surgical wards were administered parenterally (Table 2).

The AMs and J01s indication use were documented in most cases. However, none of the hospitals was

documented a planned duration and review dates of the antibiotic therapies. There was also no evidence of formal reference guidelines for antimicrobial prescribing in the four hospitals, but in three of them there were specialists qualified in infectious diseases with different authority levels to control or recommend the prescription of some antibiotics.

The J01s Was the Main Group of AMs Used in Hospitalized Patients

Overall, six hundred and six prescriptions of AMs were issued, and 84.6% [95% CI: 81.5–87.3] of these corresponded to J01s (n = 513), mainly beta-lactam antibiotics (ATC level 3: J01D). Almost all AMs used in H4, the surgical wards, and ICUs were J01s. Other AM groups (ATC level 2) prescribed in the hospitals in much smaller proportions were: antimycotics (J02: 7.9%, [95% CI: 6.0–10.3]), and antivirals for systemic use (J05: 5.8%, [95% CI: 4.1–7.9]), anti-diarrheal, intestinal anti-inflammatory /anti-infective agents (A07: 0.8%, [95% CI: 0.2–1.9]), anti-mycobacterials (J04: 0.5%, [95% CI: 0.1–1.5]), and anti-parasite agents (P02C: 0.3%, [95% CI: 0.1–1.2]) (Table 3).

The J01s were mainly used for therapeutic indications (ie, HAIs, and CAIs) in three of the hospitals (Table 2). The use of J01s for medical prophylaxis ranged from 4.2% to 27.3%, whereas, for surgical prophylaxis it ranged from 14.4% to 25.0%. All or most of the surgical prophylaxis in the hospitals comprised

Table 1 Prevalence and Volume of Use of AMs and J01s in the Hospitals and Wards/Units Surveyed

		Hospitals				Wards/Units – All Hospitals		
		H1	**H2**	**H3**	**H4**	**Medical**	**Surgery**	**ICUs**
		n (%) [95% CI]	n (%) [95% CI]	n (%) [95% CI]	n (%) [95% CI]	n (%) [95% CI]	n (%) [95% CI]	n (%) [95% CI]
Prevalence rates	Patients with AMs	84 (91.3) [83.5–95.7]	56 (47.1) [38.3–55.9]	145 (64.7) [58.2–70.7]	63 (70.0) [59.8–78.5]	174 (69.0) [63.0–74.4]	115 (55.6) [48.7–62.1]	59 (89.4) [79.4–95.0]
	Patients with J01s	76 (82.6) [73.5–89.1]	55 (46.2) [37.5–55.1]	143 (63.8) [57.3–69.8]	61 (67.7) [57.5–76.5]	162 (64.3) [58.1–69.9]	114 (55.1) [48.2–61.7]	59 (89.4) [79.4–95.0]
Patients per number of AMs	One AM	16 (19.0)	12 (21.4)	38 (26.2)	27 (42.9)	39 (22.4)	43 (37.4)	11 (18.6)
	Two AMs	24 (28.6)	16 (28.6)	41 (28.3)	25 (39.7)	50 (28.7)	38 (33.0)	18 (30.5)
	≥ Three AMs	44 (52.4)	28 (50.0)	66 (45.5)	11 (17.5)	85 (48.9)	34 (29.6)	30 (50.8)
Average number of prescriptions per patient	AMs	1.9 [164/84]	2.0 [112/56]	1.6 [234/145]	1.5 [96/63]	1.8 [315/174]	1.5 [176/115]	1.9 [115/59]
	J01s	1.4 [120/84]	1.5 [86/56]	1.5 [217/145]	1.4 [90/63]	1.4 [239/174]	1.5 [171/115]	1.7 [103/59]

Notes: AM prescribed groups (ATC level 2): Antibacterials for systemic use (J01); Antimycotics for systemic use (J02); Antimycobacterials (J04); Antivirals for systemic use (J05); Anti-diarrheal, intestinal anti-inflammatory/anti-infective agents (A07); Anti-parasite agents (P02C). H1 does not have surgery ward. H4 did not have patients admitted in ICU.
Abbreviations: AMs, antimicrobials (all identified groups); J01s, antibacterials for systemic use.

Table 2 Characteristics of Prescription of AMs and J01s in the Hospitals and Wards/Units Surveyed

			Hospitals				Wards/Units – All Hospitals		
			H1	H2	H3	H4	Medical	Surgery	ICUs
			n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Average number of days of treatment in patients		AMs	7.7	4.1	6.3	6.0	5.9	6.1	7.5
Patients per type of treatment	Empiric	AMs	52 (61.9)	45 (80.4)	97 (66.9)	57 (90.5)	127 (73.0)	92 (80.0)	32 (54.2)
		J01s	46 (60.5)	44 (80.0)	95 (66.4)	56 (91.8)	117 (72.2)	92 (80.7)	32 (54.2)
	Target	AMs	32 (38.1)	11 (19.6)	48 (33.1)	6 (9.5)	47 (27.0)	23 (20.0)	27 (45.8)
		J01s	30 (39.5)	11 (20.0)	48 (33.6)	5 (8.2)	45 (27.8)	22 (19.3)	27 (45.8)
Route of administration/prescriptions	Parenteral	AMs	133 (81.1)	94 (83.9)	215 (91.9)	88 (91.7)	246 (78.1)	172 (97.7)	112 (97.4)
		J01s	114 (95.0)	79 (91.9)	209 (96.3)	86 (95.6)	217 (90.8)	169 (98.8)	102 (99.0)
	Oral	AMs	31 (18.9)	18 (16.1)	19 (8.1)	8 (8.3)	69 (21.9)	4 (2.3)	3 (2.6)
		J01s	6 (5.0)	7 (8.1)	8 (3.7)	4 (4.4)	22 (9.2)	2 (1.2)	1 (1.0)
Documented indication/prescriptions		AMs	163 (99.4)	74 (66.1)	233 (99.6)	96 (100)	281 (89.2)	174 (98.9)	111 (96.5)
		J01s	120 (100)	57 (69.8)	216 (99.5)	90 (100)	214 (89.5)	169 (98.8)	100 (97.1)
J01 prescriptions by type of indication	Hospital-associated infections		79 (65.8)	15 (26.3)	65 (30.1)	20 (22.2)	72 (33.6)	61 (36.1)	46 (46.0)
	Community-acquired infections		36 (30.0)	23 (40.4)	38 (17.6)	44 (48.9)	91 (42.5)	33 (19.5)	17 (17.0)
	Medical prophylaxis		5 (4.2)	10 (17.5)	59 (27.3)	13 (14.4)	46 (21.5)	20 (11.8)	21 (21.0)
	Surgical prophylaxis		N/A	9 (15.8)	54 (25.0)	13 (14.4)	5 (2.3)	55 (32.5)	16 (16.0)
	– Single dose			2 (22.2)	1 (1.9)	-	1 (20.0)	2 (3.6)	-
	– Multiple dose 1 day			-	9 (16.7)	-	-	1 (1.8)	8 (50.0)
	– Multiple dose >1 day			7 (77.8)	44 (81.5)	13 (100)	4 (80.0)	52 (94.5)	8 (50.0)
Expected duration or revision date recorded		AMs	-	-	-	-	-	-	-
		J01s	-	-	-	-	-	-	-

Notes: Prescribed groups (ATC level 2): Antibacterials for systemic use (J01); Antimycotics for systemic use (J02); Antimycobacterials (J04); Antivirals for systemic use (J05); Anti-diarrheal, intestinal anti-inflammatory/anti-infective agents (A07); Anti-parasite agents (P02C). N/A: H1 does not have surgery ward. H4 did not have patients admitted in ICU.
Abbreviations: AMs, antimicrobials (all prescribed groups); J01s, antibacterials for systemic use; ICUs, intensive care units.

Table 3 Prevalence of AMs Prescriptions at ATC Level 2, 3 and 4 in the Hospitals and Wards/Units Surveyed

AM Groups (ATC Level 2, 3 and 4)	Hospitals				Wards/Units – All Hospitals			Global
	H1	H2	H3	H4	Medical	Surgery	ICUs	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%) [95% CI]
J01 Antibacterials for systemic use	120 (73.2)	86 (76.8)	217 (92.7)	90 (93.7)	239 (75.9)	171 (97.2)	103 (89.6)	513 (84.6) [81.5–87.3]
J01A Tetracyclines	1 (0.6)	-	2 (0.9)	-	1 (0.3)	-	2 (1.7)	3 (0.5) [0.1–1.5]
J01C Beta-lactam, penicillins								
– J01CA Extended-spectrum penicillins	25 (15.2)	11 (9.8)	14 (6.0)	-	33 (10.5)	7 (4.0)	10 (8.7)	50 (8.2) [6.3–10.7]
– J01CF Beta-lactamase resistant penicillins	-	-	-	3 (3.1)	-	3 (1.7)	-	3 (0.5) [0.1–1.5]
– J01CE Beta-lactamase sensitive penicillins	2 (1.2)	-	-	-	1 (0.3)	-	1 (0.9)	2 (0.3) [0.01–1.2]
J01D Other beta-lactams								
– J01DB First generation cephalosporins	5 (3.0)	1 (0.9)	10 (4.3)	-	7 (2.2)	7 (4.0)	2 (1.7)	16 (2.6) [1.6–4.2]
– J01DD Third generation cephalosporins	5 (3.0)	19 (17.0)	54 (23.1)	42 (43.8)	42 (13.3)	65 (36.9)	13 (11.3)	120 (19.8) [16.8–23.1]
– J01DE Fourth generation cephalosporins	-	-	4 (1.7)	-	2 (0.6)	1 (0.6)	1 (0.9)	4 (0.7) [0.1–1.7]
– J01DH Carbapenems	31 (18.9)	22 (19.6)	40 (17.1)	10 (10.4)	58 (18.4)	21 (11.9)	24 (20.9)	103 (17.0) [14.2–20.2]
J01E Sulfonamides and trimethoprim								
– J01EE Combinations of sulfonamides and trimethoprim	13 (7.9)	8 (7.1)	6 (2.6)	-	18 (5.7)	-	9 (7.8)	27 (4.5) [3.0–6.4]
J01F Macrolides, lincosamides and streptogramins								
– J01FA Macrolides	6 (3.7)	2 (1.8)	1 (0.4)	3 (3.1)	10 (3.2)	1 (0.6)	1 (0.9)	12 (2.0) [1.1–3.4]
– J01FF Lincosamides	-	3 (2.7)	18 (7.7)	16 (16.7)	9 (2.9)	21 (11.9)	7 (6.1)	37 (6.1) [4.4–8.3]
J01G Aminoglycoside								
– J01GB Other	1 (0.6)	1 (0.9)	12 (5.1)	3 (3.1)	3 (1.0)	7 (4.0)	7 (6.1)	17 (2.8) [1.7–4.4]
J01M Quinolones								
– J01MA Fluoroquinolones	2 (1.2)	2 (1.8)	6 (2.6)	2 (2.1)	4 (1.3)	7 (4.0)	1 (0.9)	12 (2.0) [1.1–3.4]
J01X Other								
– J01XA Glycopeptides	17 (10.4)	6 (5.4)	26 (11.1)	8 (8.3)	31 (9.8)	10 (5.7)	16 (13.9)	57 (9.4) [7.3–12.0]
– J01XB Polymyxins	4 (2.4)	2 (1.8)	1 (0.4)	-	5 (1.6)	1 (0.6)	1 (0.9)	7 (1.2) [0.5–2.4]
– J01XD Imidazole derivatives	1 (0.6)	7 (6.3)	21 (9.0)	3 (3.1)	11 (3.5)	18 (10.2)	3 (2.6)	32 (5.3) [3.7–7.3]
– J01XX Other antibacterials	7 (4.3)	2 (1.8)	2 (0.9)	-	4 (1.3)	2 (1.1)	5 (4.3)	11 (1.8) [0.9–3.2]
J02 Antimycotics for systemic use	21 (12.8)	16 (14.3)	9 (3.8)	2 (2.1)	35 (11.1)	3 (1.7)	10 (8.7)	48 (7.9) [6.0–10.3]
J04 Antimycobacterials	1 (0.6)	1 (0.9)	-	1 (1.0)	3 (1.0)	-	-	3 (0.5) [0.1–1.5]
J05 Antivirals for systemic use	19 (11.6)	8 (7.1)	6 (2.6)	2 (2.1)	33 (10.5)	-	2 (1.7)	35 (5.8) [4.1–7.9]
A07 Anti-diarrheal, intestinal anti-inflammatory/anti-infective agents	3 (1.8)	1 (0.9)	1 (0.4)	-	5 (1.6)	-	-	5 (0.8) [0.2–1.9]

P02C Anti-parasite agents	-	-	-	1 (0.4)	1 (1.0)	-	2 (1.1)	-	2 (0.3) [0.01–1.2]
Total prescriptions	164 (100)	112 (100)	234 (100)	96 (100)	315 (100)	176 (100)	115 (100)	606 (100)

Notes: H1 does not have surgery ward. H4 did not have patients admitted in ICU.
**Abbreviation:** ICUs, intensive care units.

multiple applications of antibiotics for more than one day. Ninety-four percent of surgical prophylaxis was under this schedule (Table 2).

Numerous Prescriptions of Four Groups of Extended-Spectrum J01s

Regarding the total prescriptions of AMs (n = 606), the highest proportion corresponded to the J01 groups (ATC level 4): third-generation cephalosporins 19.8% [95% CI: 16.8–23.1], carbapenems 17.0% [95% CI: 14.2–20.2], glycopeptides 9.4% [95% CI: 7.3–12.0], and extended-spectrum penicillins 8.2% [95% CI: 6.3–10.7] (Table 3). These four groups of antibiotics represented more than 60% of total J01 prescriptions in the hospitals, and wards/units surveyed (Figure 1). The third-generation cephalosporins were the most prescribed AM group in H3, H4, and within the surgical wards, while the carbapenems were most used in H1, H2, the medical wards, and ICUs (Table 3). The five most used J01s (ATC level 5) in the hospitals were ceftriaxone 21.0% [95% CI: 17.7–24.8], meropenem 14.2% [95% CI: 11.4–17.5], vancomycin 11.1% [95% CI: 8.6–14.1], piperacillin 8.0% [95% CI: 5.9–10.6], and clindamycin 7.2% [95% CI: 5.2–9.8]. Ceftriaxone prescriptions accounted for almost half of total J01 prescriptions in H4. Ceftriaxone was also the most used antibiotic in the surgery and the medical wards. A similarly high proportion of meropenem prescriptions was also observed in the medical wards. Meropenem was also the most used antibiotic in the ICUs (Annex 3).

Ceftriaxone and Meropenem Extensive Use for Any Type of Indication or Infection

The carbapenems were most frequently used to treat HAIs (Table 4), as well as the following antibiotics: meropenem, ceftriaxone, imipenem and cilastatin, and piperacillin (Annex 4). Fifty-six percent of the total prescriptions for HAIs were empirical, mainly for ceftriaxone, imipenem and cilastatin, and piperacillin (Annex 5). The empirical treatments for HAIs in the hospitals ranged from 52.3% to 85.0%. The third-generation cephalosporins were mostly prescribed for patients with CAI in three of the hospitals (Table 4). Ceftriaxone, piperacillin, and sulfamethoxazole and trimethoprim were the most used antibiotics to treat CAIs. Ceftriaxone prescriptions accounted for almost half of total J01 prescriptions for CAIs in H4 (Annex 4). The overall proportion of empirical prescriptions for CAIs was
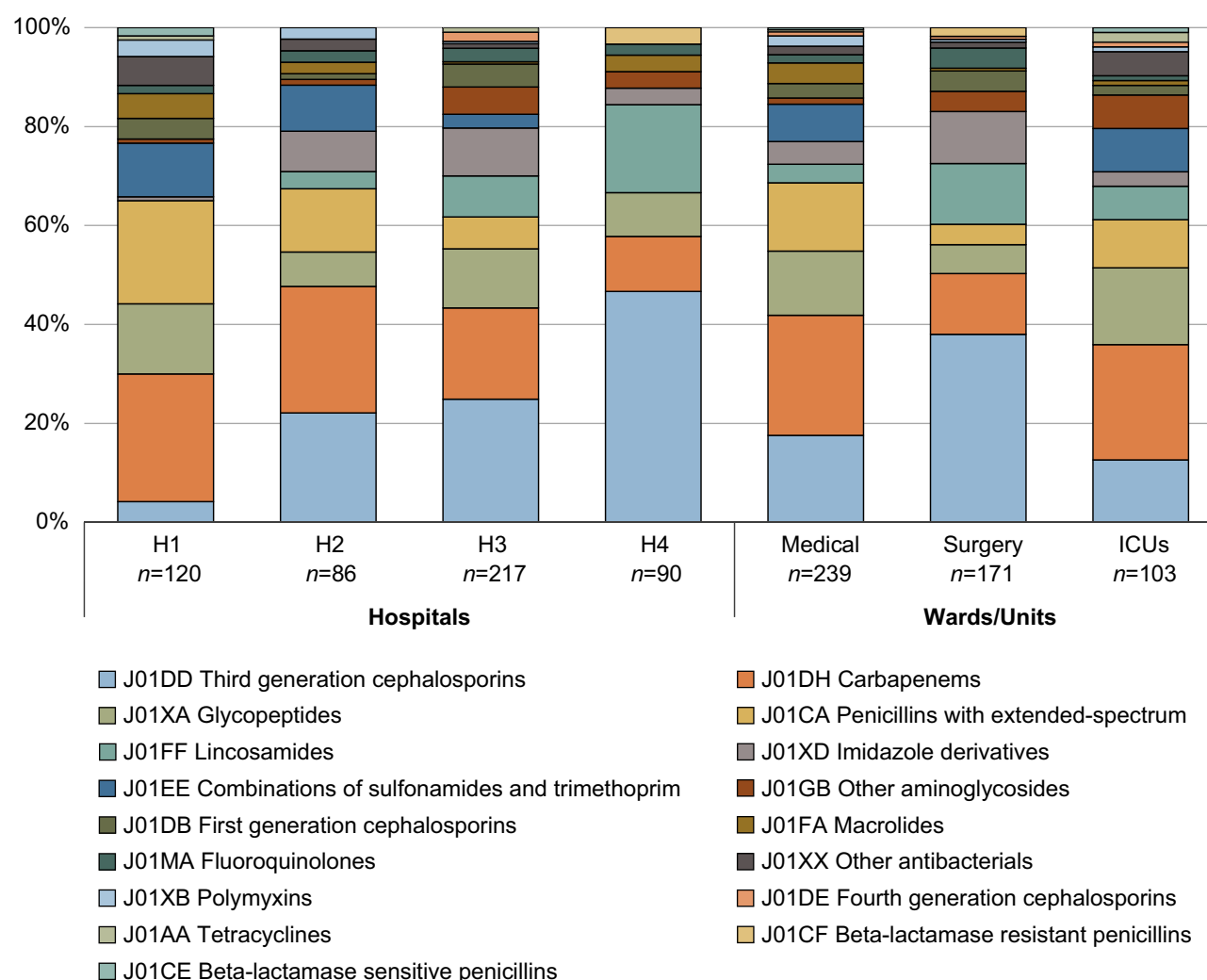
Figure 1 Percentage of J01 prescriptions at ATC level 4 in the hospitals and wards/units surveyed.

higher than for HAIs, mainly for ceftriaxone, piperacillin, and clarithromycin (Annex 6). Empirical prescriptions for CAI were also common in all hospitals, ranging from 66.7% to 88.6% (Table 4).

The third-generation cephalosporins, carbapenems, glycopeptides, and the combinations of sulfonamides and trimethoprim were the most used for medical prophylaxis (Table 4), as well as the following antibiotics: ceftriaxone, meropenem, vancomycin, and sulfamethoxazole and trimethoprim (Annex 4). The third-generation cephalosporins were also the most used for surgical prophylaxis (Table 4). Between 24.1% and 92.3% of total surgical prophylaxis prescriptions corresponded to ceftriaxone, which was predominantly prescribed in multiple doses for more than one day (Annex 4, 7).

The patients with pneumonia were treated mostly with ceftriaxone, piperacillin, meropenem, and vancomycin.

Whereas the antibiotics imipenem and cilastatin, meropenem, ertapenem, and clindamycin were commonly used for the patients with sepsis' treatment (Annex 8).

Resistant *Escherichia coli* and ESKAPE Pathogens Were Frequently Identified in the Hospitals

A wide variation in the proportion of patients with microbiological cultures was observed between the hospitals, ranging from 30.2% to 91.7%. The number of species, genus or families of microorganisms isolated also varied considerably, from 11 to 81 per hospital. Gram-negative bacterial species/genus were frequently identified, which accounted for 48.8% to 91.3% of the total isolates. Positive isolates for *E. coli, P. aeruginosa* and *K. pneumoniae* were found in all hospitals (Table 5).

Table 4 Prevalence of J01 Prescriptions at ATC Level 4 by Type of Indication

J01 Groups (ATC Level 4)	Hospital-Associated Infections				Community-Acquired Infections				Medical Prophylaxis				Surgical Prophylaxis		
	H1	H2	H3	H4	H1	H2	H3	H4	H1	H2	H3	H4	H2	H3	H4
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
J01DD Third generation cephalosporins	2 (2.5)	3 (20.0)	11 (16.9)	4 (20.0)	3 (8.3)	7 (30.4)	10 (26.3)	20 (45.4)	-	-	16 (27.1)	6 (46.1)	5 (55.6)	16 (29.6)	12 (92.3)
J01DH Carbapenems	21 (26.6)	6 (40.0)	19 (29.2)	6 (30.0)	8 (22.2)	4 (17.4)	4 (10.5)	4 (9.1)	2 (40.0)	2 (20.0)	11 (18.6)	-	-	6 (11.1)	-
J01XA Glycopeptide antibacterials	11 (13.9)	3 (20.0)	8 (12.3)	3 (15.0)	4 (11.1)	1 (4.3)	3 (7.9)	5 (11.4)	2 (40.0)	-	8 (13.6)	-	-	7 (12.9)	-
J01CA Extended-spectrum penicillins	18 (22.8)	2 (13.3)	1 (1.5)	-	7 (19.4)	5 (21.7)	6 (15.8)	-	-	-	5 (8.5)	4 (30.8)	1 (11.1)	2 (3.7)	-
J01FF Lincosamides	-	-	6 (9.2)	3 (15.0)	-	1 (4.3)	3 (7.9)	8 (18.2)	-	1 (10.0)	4 (6.8)	-	1 (11.1)	5 (9.3)	1 (7.7)
J01XD Imidazole derivatives	1 (1.3)	1 (6.7)	7 (10.8)	2 (10.0)	-	3 (13)	3 (7.9)	1 (2.3)	-	-	4 (6.8)	-	1 (11.1)	7 (13)	-
J01EE Combinations of sulfonamides and trimethoprim	6 (7.6)	-	2 (3.1)	-	6 (16.7)	-	2 (5.3)	-	1 (20.0)	6 (60.0)	2 (3.4)	-	-	-	-
J01DB First generation cephalosporins	5 (6.3)	-	-	-	-	-	1 (2.6)	1 (2.3)	-	-	-	-	1 (11.1)	9 (16.7)	-
J01GB Other aminoglycosides	1 (1.3)	-	4 (6.1)	2 (10.0)	-	-	1 (2.6)	1 (2.3)	-	-	6 (10.2)	-	-	1 (1.8)	-
J01MA Fluoroquinolones	1 (1.3)	-	2 (3.1)	-	1 (2.8)	1 (4.3)	2 (5.3)	2 (4.5)	-	-	2 (3.4)	-	-	-	-
J01XX Other antibacterials	6 (7.6)	-	2 (3.1)	-	1 (2.8)	1 (4.3)	-	-	-	1 (10.0)	-	-	-	-	-
J01FA Macrolides	1 (1.3)	-	-	-	5 (13.9)	-	1 (2.6)	3 (6.8)	-	-	-	-	-	-	-
J01XB Polymyxins	4 (5.1)	-	1 (1.5)	-	-	-	-	-	-	-	-	-	-	-	-
J01DE Fourth generation cephalosporins	-	-	1 (1.5)	-	-	-	2 (5.3)	-	-	-	-	-	-	1 (1.8)	-
J01AA Tetracyclines	1 (1.3)	-	1 (1.5)	-	-	-	-	-	-	-	1 (1.7)	-	-	-	-
J01CF Beta-lactamase resistant penicillins	-	-	-	-	-	-	-	-	-	-	-	3 (23.1)	-	-	-
J01CE Beta-lactamase sensitive penicillins	1 (1.3)	-	-	-	1 (2.8)	-	-	-	-	-	-	-	-	-	-
Total prescriptions	79 (100)	15 (100)	65 (100)	20 (100)	36 (100)	23 (100)	38 (100)	44 (100)	5 (100)	10 (100)	59 (100)	13 (100)	9 (100)	54 (100)	13 (100)
% over total indications by hospital	65.8	26.3	30.1	22.2	30.0	40.4	17.6	48.9	4.2	17.5	27.3	14.4	15.8	25.0	14.4
% of empiric treatments for therapeutic indications by hospital	53.2	53.3	52.3	85.0	66.7	73.9	86.8	88.6	-	-	-	-	-	-	-

Note: H1 does not have surgery ward.
Abbreviation: J01s, antibacterials for systemic use.

Table 5 General Characteristics of Isolations of Microorganisms in the Hospitals Surveyed

	Hospitals			
	H1	H2	H3	H4
	n (%)	n (%)	n (%)	n (%)
Patients on AMs with Clinical Culture	**77 (91.7%)**	**42 (75.0%)**	**92 (78.0%)**	**19 (30.2%)**
Number of Specimens for Culture	**n=199**	**n=74**	**n=159**	**n=29**
Microorganisms isolated				
Gram negatives	21 (48.8)	21 (91.3)	40 (49.4)	8 (72.7)
– Escherichia coli	7 (16.3)	8 (34.8)	14 (17.5)	4 (36.4)
– Pseudomonas aeruginosa	5 (11.6)	1 (4.3)	3 (3.7)	3 (27.3)
– Klebsiella pneumoniae	2 (4.6)	3 (13.0)	3 (3.7)	1 (9.1)
– Other Citrobacter spp	–	–	5 (6.2)	–
– Klebsiella oxytoca	2 (4.6)	1 (4.3)	2 (2.5)	–
– Eikenella corrodens	–	3 (13.0)	1 (1.2)	–
– Gram-negative bacilli	-	-	3 (3.7)	-
– Enterobacter cloacae	-	2 (8.7)	-	-
– Stenotrophomonas maltophilia	2 (4.6)	-	-	-
– Other Gram-negative bacilli	-	2 (8.7)	-	-
– Prevotella spp	-	-	2 (2.5)	-
– Other Gram-negative cocci	-	-	1 (1.2)	-
– Other Enterobacter spp	-	-	1 (1.2)	-
– Other Klebsiella spp	1 (2.3)	-	-	-
– Salmonella spp, not specified	1 (2.3)	-	-	-
– Other Salmonella spp	1 (2.3)	-	-	-
– Acinetobacter baumannii	-	-	1 (1.2)	-
– Acinetobacter haemolyticus	-	1 (4.3)	-	-
– Burkholderia cepacia	-	-	1 (1.2)	-
– Other Pseudomonadaceae family	-	-	1 (1.2)	-
– Pseudomonadaceae family, not specified	-	-	1 (1.2)	-
– Morganella morganii	-	-	1 (1.2)	-
Gram positives	11 (25.6)	2 (8.7)	36 (44.4)	-
– Enterococcus faecalis	1 (2.3)	-	10 (12.5)	-
– Staphylococcus epidermidis	1 (2.3)	-	8 (10.0)	-
– Staphylococcus aureus	3 (7.0)	-	5 (6.2)	-
– Enterococcus faecium	5 (11.6)	-	3 (3.7)	-
– Streptococcus spp	-	-	5 (6.2)	-
– Gram-positive cocci, not specified	-	-	2 (2.5)	-
– Clostridium difficile	-	2 (8.7)	-	-
– Other Clostridium	-	-	1 (1.2)	-
– Staphylococcus haemolyticus	-	-	1 (1.2)	-
– Enterococcus spp	1 (2.3)	-	-	-
– Actinomyces spp	-	-	1 (1.2)	-
Fungi	11 (25.6)	-	4 (5.0)	3 (27.3)
– Candida spp	9 (20.9)	-	4 (5.0)	2 (18.2)
– Aspergillus fumigatus	2 (4.6)	-	-	-
– Cryptococcus spp	-	-	-	1 (9.1)
Total isolations	43 (100)	23 (100)	81 (100)	11 (100)

Table 6 Species/Genus of Bacteria with Antimicrobial Susceptibility Testing (AST) in the Hospitals Surveyed

Hospitals	Species/Genus of Bacteria with Resistance Results	J01s at ATC Level 5 (>1 AST Result)
H1	*Escherichia coli*	J01DD04 Ceftriaxone (3) | J01MA02 Ciprofloxacin (2) | J01CA12 Piperacillin | J01EE01 Sulfamethoxazole and trimethoprim
	Pseudomonas aeruginosa	J01DB03 Cefalotin (2) | J01DH02 Meropenem | J01CA12 Piperacillin | J01AA12 Tigecycline
	Enterococcus faecium	J01MA02 Ciprofloxacin | J01XA01 Vancomycin (3)
	Staphylococcus epidermidis	J01CF04 Oxacillin | J01FF01 Clindamycin
	Klebsiella pneumoniae	J01CA12 Piperacillin | J01EE01 Sulfamethoxazole and trimethoprim
	Klebsiella oxytoca	J01DD04 Ceftriaxone | J01CA12 Piperacillin
	Other Klebsiella spp	J01CA12 Piperacillin
	Salmonella spp, not specified	J01MB02 Nalidixic acid
	Other Salmonella spp	J01MB02 Nalidixic acid
H3	*Staphylococcus epidermidis*	J01FA01 Erythromycin | J01GB03 Gentamicin (3) | J01CF04 Oxacillin | J01FF01 Clindamycin (6)
	Other Citrobacter spp	J01DD02 Ceftazidime (2) | J01DD04 Ceftriaxone (2) | J01MA02 Ciprofloxacin
	Escherichia coli	J01DD04 Ceftriaxone (5)
	Staphylococcus haemolyticus	J01MA02 Ciprofloxacin | J01GB03 Gentamicin | J01MA12 Levofloxacin
	Staphylococcus aureus	J01MA02 Ciprofloxacin | J01FF01 Clindamycin
	Enterococcus faecalis	J01GB03 Gentamicin (2)
	Klebsiella oxytoca	J01DD04 Ceftriaxone (2)
	Streptococcus spp	J01FF01 Clindamycin
	Klebsiella pneumoniae	J01DD04 Ceftriaxone
	Morganella morganii	J01MA02 Ciprofloxacin
H4	*Escherichia coli*	J01CA01 Ampicillin (4) | J01DE01 Cefepime (3) | J01DD04 Ceftriaxone | J01MA02 Ciprofloxacin | J01CR04 Sultamicillin (3)
	Klebsiella pneumoniae	J01CA01 Ampicillin | J01DE01 Cefepime | J01CR04 Sultamicillin
	Pseudomonas aeruginosa	J01CA12 Piperacillin | J01DF01 Aztreonam | Pan-drug resistance

Notes: Data on the specific AST methods performed were not available in clinical records. H2 had no data of AST.
Abbreviations: AST, antimicrobial susceptibility testing; J01s, antibacterials for systemic use.

Data on AST were only found in three hospitals (H1, H3, H4). Multidrug-resistant *E. coli*, and at least two species of ESKAPE pathogens: *K. pneumoniae, P. aeruginosa, S. aureus* or *E. faecium* were identified in all hospitals with AST data (Table 6). Aztreonam-resistant and pan-drogo-resistant *P. aeruginosa* strains were also identified (H4), as well as vancomycin-resistant *E. faecium* strains (H1). *E. coli* and ESKAPE pathogens were mostly resistant to ceftriaxone, ampicillin, piperacillin, and ciprofloxacin.

Discussion

The PPSs showed variability in the prevalence of AMs use among the hospitals surveyed (47.1% to 91.3%). This variability could possibly be related to differences in the case-mix, and particular structural characteristics of the hospitals, such as the type and balance of medical specialties, that are not part of the data included in the PPS

protocol. No matter that variability, our data revealed a wide use of AMs in the hospitals surveyed exceeding those used in hospitals of Europe (29.0%), Latin America (36.8%), and US (49.9%).[22,23,29] Furthermore, our results were higher than those reported previously by other tertiary care Mexican hospitals (59.3%, 51.5%).[14,30] Our findings also describe the extensive use of broad-spectrum J01s such as ceftriaxone, meropenem, vancomycin, piperacillin, and clindamycin. These results are consistent with trends in the use of these antibiotics in Mexico and Latin America.[13,14,17,23,30,31] Nevertheless, we identified even greater use proportions of these five antibiotics than those commonly found in Latin America, mainly ceftriaxone and meropenem.[23] These last two antibiotics belong to the WHO "Watch" group, only recommended for a specific and limited number of indications due to their elevated risk of resistant-bacteria selection.[32] Thus, the fact that almost half of the antibiotics used in

one of the hospitals surveyed (H4) were ceftriaxone, suggests that at least a proportion of these prescriptions were inappropriate. Furthermore, ceftriaxone was predominantly prescribed in multiple doses for more than one day for surgical prophylaxis, contrary to the conventional recommendation of a single dose of cephalosporins (eg, cefazolin), 1 h before surgical incision for most surgical procedures.[33] Besides, although the microbiology laboratories' role and rate of antimicrobial cultures per patient varied widely among the hospitals surveyed, none of them appears to have used the culture results and AST data for de-escalation of the antibiotic therapies, as recommended to reduce detrimental effects on patients as well as to minimize the development of AMR.[34]

All the above could represent a common scenario associated to the recurrent identification of MDR *E. coli* and ESKAPE pathogens in the hospitals surveyed, as well as in other Mexican hospitals.[16,17,35,36]

We consider that our findings could be partly explained by the absence of formally established ASPs in the hospitals surveyed. ASPs consist of a variety of systematic activities and interventions aimed to optimize the antimicrobial use. The core elements of this type of program have been defined,[37] and a set of possible activities identified and positively analyzed in systematic reviews.[38,39] Professionals associations and both national and international health agencies strongly support the implementation of these programs.[37,40,41] In recent years, the WHO has pushed forward this approach for low- and middle-income countries by publishing guidelines for implementing ASPs in these settings.[41] However, the hospitals surveyed did not have guidelines for antimicrobial prescribing or formal evidence of other possible interventions to improve the antimicrobial use. Therefore, we consider it urgent to plan and implement ASP programs in these Mexican hospitals, or at least devise and ensure the formal implementation of some of the interventions that have proven effective for controlling and improving the antimicrobial use. These interventions could include implementing international or local antimicrobial prescription guidelines, educational, audit, and feedback strategies, managing the use of broad-spectrum antibiotics, improving the quality of surgical prophylaxis, and reinforcing the implementation of planned duration treatments, among others.[12,38,39,42–45] The absence of a defined strategy and plan for improving the antimicrobial use at the health system level is not helping either. We may argue that the absence of ASPs in Mexican public hospitals, like the ones we have studied,

could be partially due to the lack of an official, explicit, and operative policy to improve the antimicrobial use in the Mexican health-care system.

The results of this study show the potential usefulness of raising of awareness about routine AM prescription at the patient level. The strength of our results is based on the data collection uniformity, achieved by conducting pilot studies in the four hospitals prior to the PPSs.[25] However, our study is not exempt of limitations. Some of them are intrinsic to the PPS method: data are transversal but collected at different months of the year (between August and December); long-term treatments may be overrepresented; and it is not possible to identify the patients' cases combination, changes in the incidence and prevalence of different infections, or institutional factors, all of which may influence the antimicrobial prescribing patterns. Our findings also do not reflect the prescribing practices of other hospitals in Mexico, particularly in pediatric' hospitals.

Conclusions

Our PPSs reveal the extensive use of broad-spectrum antibiotics for systemic use for empirical treatments, with no planned duration or review dates, and the excessive and prolonged use of certain antibiotics (ie, ceftriaxone). Furthermore, we identified the recurrent presence of *E. coli* and ESKAPE pathogens, which many of them are resistant to the antibiotics frequently used in the hospitals surveyed, suggesting that a vicious cycle of prescribers used to particular patterns of antibiotic prescription has been created.

The first step to improve the antimicrobial prescribing behavior in hospitals is to provide enough evidence of their prescription patterns aiming at the identification of objectives for optimization on antibiotic use. Thereby, can be prioritized specific aims to optimize the day-to-day antibiotic prescribing on patients. PPSs at the hospital or at priority wards/units' level could be a useful method for this purpose.

Abbreviations

PPSs, point prevalence surveys; AMs, antimicrobials; J01s, antibiotics for systemic use; AMR, antimicrobial resistance; ESKAPE, *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp*; WHO, World Health Organization; ASPs, antimicrobial stewardship programs; WPPS, WHO methodology for point prevalence survey on antibiotic use in hospitals; H1, hospital 1; H2,

hospital 2; H3, hospital 3; H4, hospital 4; ICUs, intensive-care units; HAIs, hospital-associated infections; CAIs, community-acquired infections; AST, antimicrobial susceptibility testing; ATC, Anatomical Therapeutic Chemical classification system; MDR, multidrug-resistant.

Ethical Approval

The protocol of this study was approved by the research ethics committee of the National Institute of Public Health of Mexico (RF. 17CEI00420160708). This study did not include any interaction with patients. Informed consents to review the patient´s medical records were not required since all collected patients' data was anonymous. All the authors assume the obligation to protect the individual' privacy and maintain the confidentiality of the patients' data in compliance with the Declaration of Helsinki, and the Regulation of the General Health Law on Health Research of Mexico.

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Disclosure

The authors report no conflicts of interest in this work.

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