Antimicrobial resistance and antibiotic consumption in Mexico.

Flores-Moreno K, Miranda-Novales G, Rodríguez-Álvarez M, López-Vidal Y, Arredondo-Hernández L, Ponce de León-Rosales S and PUCRA network members, Facultad de Medicina UNAM, Mexico City, Mexico.
sponcedeleonr@gmail.com

Background: The Universidad Nacional Autónoma de México (UNAM), aware of the challenge that this problem represents for the public health, has proposed through the University Program of Health Research (Programa Universitario de Investigación en Salud, PUIS), an action plan to control antimicrobial resistance in Mexico (PUCRA). As part of the initial activities of this plan, health personnel were invited to collect and share information to establish the current status of antimicrobial resistance and obtained basal data on antibiotic consumption in a network of hospitals in Mexico. **The objectives** of these study were: a) to establish the current situation of antimicrobial resistance in Mexico in isolates obtained from blood and urine cultures. b) to calculate the defined Daily Dose (DDD) of antibiotic consumption /100 occupied beds (OB).

Methods: Second and tertiary-care level hospitals were invited to participate in the network. Selection of participant centers was by convenience. A retrospective observational study was conducted with the information of the antimicrobial resistance patterns of isolated microorganisms from blood cultures from 2017 to 2018, focused on the ESKAPE group pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterobacter spp*.). Also, antimicrobial resistance patterns of *Escherichia coli* and *Klebsiella pneumoniae* isolates obtained from urine cultures in the same period were registered. Bacterial isolates were identified by automated microbial identification systems, including MALDI TOF VITEK MS, VITEK 2, (bioMérieux Marcy l' Etoile, France), BD Phoenix (Becton-Dickinson Sparks, MD, USA), MicroScan autoSCAN-4, WalkAway 96 plus, (Beckman Coulter Brea, California, USA), and Aris Sensititre in one (Thermo-Fisher Scientific Waltham, Massachusetts, USA). Hospitals reported indicators (number of beds, occupancy rate, and discharges). Antibiotic consumption (J01 systemic use) was calculated for each hospital and expressed in defined daily dose (DDD)/100 occupied bed-days (OBD), according to the formula: DDD/100 OBD= (consumption/DDD) x (100/OBD). Antibiotic consumption (J01 systemic use) was calculated for each hospital and expressed in defined daily dose (DDD)/100 occupied bed-days (OBD), according to the formula: DDD/100 OBD= (consumption/DDD) x (100/OBD). Statistical analysis: Numeral data was expressed with median, percentages and minimum and maximum values. For antimicrobial consumption data was expressed in median and 95% confidence intervals.

Results: Twenty five hospitals in eleven states of the Mexican Republic provided information for the 2017 and 2018 period. Of the total of 10,324 isolates in blood, *E. coli* and *K. pneumoniae* were the most frequently isolated, resistance was high; only amikacin and carbapenems maintain good *in vitro* activity (<10% resistance) (Table 1). The highest resistance was registered in *A. baumannii* (> 40% for all drugs) (Table 2). Oxacillin resistance in *S. aureus* was >20% (Table 3).

Table 1. Antimicrobial resistance in enterobacteria isolated from blood cultures.

Antimicrobial	*E. coli*		*K. pneumoniae*		*E. cloacae*	
	2017 n=1,467	2018 n=1,720	2017 n=886	2018 n=1,193	2017 n=278	2018 n=370
Ampicilin	88	87	IR		IR	
Amikacin	2	2	7	4	0	0
Piperacilin / Tazobactam	23	18	26	24	24	22
Cefepime	69	65	65	67	17	14
Ceftriaxone	69	65	65	67	35	33
Ertapenem	0	0	0	0	0	0
Meropenem	0	0	4	2	3	0
Ciprofloxacin	70	64	41	50	5	15

IR: Intrinsic Resistance

Table 2. Antimicrobial resistance in non-fermenting Gram-negative bacilli isolated from blood cultures.

Antimicrobial	*P. aeruginosa*		*A. baumannii*	
	2017 n=586	2018 n=670	2017 n=317	2018 n=405
Amikacin	15	12	47	49
Ampicilin/ Sulbactam	IR		44	64
Piperacilin/ Tazobactam	22	19	60	40
Cefepime	22	26	68	87
Ceftazidime	24	23	ND	52
Meropenem	30	31	44	64
Ciprofloxacin	18	21	71	61

IR: Intrinsic Resistance

Table 3. Antimicrobial resistance *in S. aureus* and *E. faecium* strains isolated from blood cultures

Antimicrobial	*S. aureus*		*E. faecium*	
	2017 n=848	2018 n=1,221	2017 n=197	2018 n=166
Ampicilin	ND		29	50
Ciprofloxacin	33	27	25	62
Gentamicin	10	8	NA	
Gentamicin HL	NA		0	10
Clindamycin	36	25	IR	
Erytromycin	35	30	87	94
Streptomycin HL	NA		13	53
Levofloxacin	ND		14	52
Linezolid	0	0	0	0
Oxacilin	21	22	NA	
Penicilin	ND		29	79
Q/D	ND		50	0
Rifampin	0	0	NA	
Tetracycline	ND		50	50
TMP/SMX	5	6	NA	
Vancomycin	0	0	0	28

IR: Intrinsic Resistance NA: Not applicable
ND: No data available, Q/D: Quinupristin/dalfopristin
TMP/SMX: Trimethoprim/Sulfamethoxazole

Urine cultures: of 57,497 isolates, 90% corresponded to *E. coli;* resistance to ciprofloxacin, cephalosporins and TMP/SMZ was> 47%, with good activity to nitrofurantoin, amikacin and carbapenems. For *K. pneumoniae* only amikacin and carbapenems had resistance <10% (Table 4).

Table 4. Antimicrobial resistance in *Escherichia coli* and *Klebsiella pneumoniae* isolated from urine cultures.

Antimicrobial	*E. coli*		*K. pneumoniae*	
	2017 n=11,056	2018 n=40,120	2017 n=1,095	2018 n=5,226
Ampicilin	81	82	100	99
Amikacin	3	4	5	3
Cefepime	48	47	58	51
Ceftriaxone	48	47	58	52
Imipenem	1	0	9	0
Meropenem	1	0	7	1
Nitrofurantoin	9	8	52	49
TMP/SMX	57	59	63	56
Ciprofloxacin	65	61	49	40

TMP/SMX: Trimethoprim/Sulfamethoxazole

Antimicrobial consumption: Hospitals were divided according to number of beds. Group I (100-200 beds) had higher antibiotic consumption during 2017. During 2018 a slight decrease in the total median DDD/100 OB was noted, with the Group I being responsable (Table 5). Main antibiotics consumed were cephalosporins, carbapenems and vancomycin (Table 6).

Table 5. Antibiotic consumption in DDD/100 BD according to size of the hospital.

Hospitals according to size (Nº of beds)	Median of antibiotic consumption	
	2017	2018
Group I (100-200)	75.6	57.0
Group II (201-499)	47.8	57.9
Group III (≥500)	47.7	49.5
Total	57.0	54.8

Table 6. Median consumption (DDD / 100 OB) of main antibiotics.

Antibiotic	2017		2018	
	Median	Min-Max	Median	Min-Max
Cephalosporins	17.8	2.86-37.07	18.33	4.55-35.8
Carbapenems	7.1	1.13-23.20	8.7	1.42-34.47
Vancomycin	4.5	1.12-8.23	4.1	0.81-8.52
Penicilins	4.5	0.08-9.45	1.5	0.15-4.41
Quinolones	3.6	0.30-12.12	0.63	0.27-5.58

Discussion and conclusions: This study has several limitations: 1) Participation of hospitals was voluntary, so this is not a representative sample of our country, however, the number of participating states offers a wide geographical distribution. 2) There is a variability in the size of the participating hospitals and the characteristics of the underlying diseases of the patients attended by each center. 3) Bacterial identification systems and susceptibility methods are not identical in all hospitals, however, virtually all used automated systems and internal quality controls are carried out periodically. 4) The information on annual antibiotic consumption offers at this moment raw descriptive data, 5) In this report, the bacterial isolates of health-care associated infections could not be presented and analyzed separately.

While this report is not representative of the entire country, it gives us a perspective on the seriousness of the problem of antimicrobial resistance and antibiotic consumption. Results are similar to those published recently by Garza E. et al. There are useful as a reference to propose and evaluate immediate interventions aimed at reducing the use of wide spectrum antibiotics and contain the dissemination of resistant strains.

References:
1. O'Neill J. Tackling Drug-Resistant Infections Globally: final report and recommendations. The review on antimicrobial resistance. UK: Wellcome Trust, HM Government, 2016
2. Garza-González E, Morfín-Otero R, Mendoza-Olazarán S, et al. A snapshot of antimicrobial resistance in Mexico. Results from 47 centers from 20 states during a six-month period. PLoS ONE. 2019;14(3):e0209865