

Impact of A Mobile App For Antibiotic Stewardship on The Incidence of Nosocomial Infections With Multidrug Resistant Micro Organisms

Paulo Castañeda-Méndez*¹, Marco Villanueva-Reza², Luis Enrique Soto Ramírez³, Daniel Antonio Aguilar-Zapata³, María Lorena Cabrera-Ruiz³, Javier Reyes-Mar³, Israel Rojas-de Ita², Andrea Priscila Hernández-Pérez², Esperanza Aleman-Aguilar⁴ and Lorena Lanz-Zubiria⁵



¹Internal Medicine, Infectology Máster in infection control, Hospitalary Epidemiologic Vigilance Unit, Antibiotic Stewardship Program Coordinator, Clinical Foundation Medica Sur, Mexico

²Internal Medicine, Clinical Foundation Medica Sur, Mexico

³Internal Medicine, Infectology, Hospitalary Epidemiologic Vigilance Unit Chief, Clinical Foundation Medica Sur, Mexico

⁴Informatic degree, Hospitalary Epidemiologic Vigilance Unit. Clinical Foundation Medica Sur, Mexico

⁵General physician, Clinical Foundation Medica Sur, Mexico

***Corresponding author:** Paulo Castañeda-Méndez, Internal Medicine, Infectology, Master in infection control, Hospitalary Epidemiologic Vigilance Unit, Antibiotic Stewardship Program Coordinator, Clinical Foundation Medica Sur, Mexico

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ABSTRACT

Objectives: to determine the impact of a guideline for empiric antimicrobial treatment based on local data of microorganism resistance delivered via mobile app as a strategy of an antibiotic stewardship program on the incidence of nosocomial infections and isolation of multidrug resistant microorganisms.

Methods: retrospective, unicentric, observational study developed in a private hospital in Mexico City. We compared the incidence of nosocomial infections and isolation of multidrug resistant (MDR) microorganisms in 2013, year in which the local guidelines for empiric antimicrobial treatment were implemented as a strategy of the antibiotic stewardship program, with the incidence of 2018. We also determined the annual percentage of adherence to the guidelines.

Results: we observed progressive increase in guideline adherence and a progressive decrease in the incidence of nosocomial infections as well as the proportion of MDR microorganisms isolates.

Conclusion: similar to previous reports in other countries, the instauration of antibiotic stewardship programs contributed to the decrease in nosocomial infections and MDR bacteria isolates in a private hospital in Mexico City.

Abbreviations: MDR: Multi-Drug Resistant, ESBL: Extended Spectrum Beta-Lactamase, VRE: Vancomycin Resistant Enterococcus, NNIS: National Nosocomial Infections Surveillance, ESBL: Extended Spectrum Beta-Lactamase, BSI: Blood Stream Infections, UTI: Urinary Tract Infection

Introduction

Multi-Drug Resistant (MDR) microorganisms are defined as microorganisms, predominantly bacteria, resistant to one or more class of antimicrobial agents. Bacteria as Methicillin Resistant *Staphylococcus Aureus* (MRSA), high or intermediate level vancomycin resistant *Staphylococcus aureus*, Vancomycin Resistant *Enterococcus* (VRE), Extended Spectrum Beta-Lactamase (ESBL) producing enterobacteriaceae, *Acinetobacter baumannii* resistant to all antimicrobial agents, carbapenem resistant *Pseudomonas aeruginosa* or bacteria inherently resistant to broad spectrum antimicrobial agents, such as *Stenotrophomonas maltophilia*, *Burkholderia cepacia* and *Ralstonia pickettii*. Prevalence of MDR microorganisms is variable, depending on timing, geography and site of health care [1]. Infections associated with MDR microorganisms have increased in the last decades. For example, in healthcare facilities that report to the National Nosocomial Infections Surveillance (NNIS) System network in the United States of America, the percentage of *Staphylococcus aureus* isolates that were methicillin resistant increased from 36% in 1992 to 64% in 2003 [2].

Similarly, in the intensive care units of the same network, there was an increase of isolates of *Acinetobacter baumannii* from 4% in 1986 to 7% in 2003, with a significant increase in resistance profiles, as well as an increase of isolates of imipenem and ceftazidime resistant *Pseudomonas aeruginosa* and ESBL *Escherichia coli* [3]. In Mexico, the same trend towards increase in bacterial resistance has been reported, for example, one study group reported that *Acinetobacter baumannii* meropenem-sensitive decreased from 92% in 1999 to 12% in 2012 [4]. According to data from the Hospitalary Network of Epidemiological Vigilance (RHOVE) in 2015, there was an increase in isolates of ESBL *Escherichia coli*, *Klebsiella pneumoniae* y *Enterobacter cloacae*, as well as imipenem and quinolone resistant *Pseudomonas aeruginosa*, *Clostridioides difficile* and *Acinetobacter baumannii*. The lethality rate increased from 4.8% deaths in 2014 to 5.8% deaths in 2015 [5].

Rationale for rise in microorganism resistance is variable, depending on geographical situation and specific agents. However, the selective pressure secondary to indiscriminate antibiotic use that, in Mexico, could be purchased without medical prescription until 2010, inadequate infection control practices, increase in the amount of vulnerable patients associated to longer survival in chronic disease and disease associated with immunosuppression, antibiotic use in agriculture and farming industry for human consumption and globalization are some factors associated with increase in bacterial resistance [6]. Infections with multi-drug-resistant bacteria are associated with increase in hospitalization length, need of surgery to achieve infection control, delay in starting adequate antimicrobial therapy, the need for antimicrobial agents

with greater toxicity and rise in morbidity and mortality, that lead to higher health expenditure. In the United States of America the estimated total cost of antimicrobial resistance is 30 billion dollars a year [7].

In Spain, a retrospective study reported a higher all-cause mortality rate in individuals with nosocomial infections caused by MDR bacteria (OR 2.17) and a higher amount of emergency room visits for patients infected by MRSA and resistant strains of *Escherichia coli*; there was no rise in time of hospital stay, need for admission in general ward or intensive care unit, need for surgery or diagnostic tests, however, individuals infected with more than one multidrug-resistant microorganism and the ones with two or more episodes of infection during hospital stay were excluded [8]. Additionally, in low income countries, the access to certain antimicrobial drugs is limited by availability and cost. Antibiotic stewardship programs intent to reduce incidence of infections caused by MDR microorganism in healthcare facilities. The goals are antimicrobial drug use optimization, to reduce adverse effects and, ultimately, decrease mortality. Implementation of these programs proved to be associated with a decrease in isolates of resistant bacteria with adequate adherence to recommendations.

A study developed in Andalusia, Spain showed a 10% reduction in imipenem resistant *Pseudomonas aeruginosa* and a 13% decrease in ESBL *Klebsiella pneumoniae*, with a healthcare expenditure saving of 30,000 euro annually [9]. Other studies have similar findings, with decrease in incidence of MDR bacteria, *Clostridioides difficile* and also a decrease in antimicrobial defined daily dose [10-15]. The objective of this study was to determine the impact of a guidelines for empiric antimicrobial treatment delivered via mobile app, as a strategy of an antimicrobial stewardship program introduced in 2013 in the incidence of nosocomial infections and isolation of MDR microorganisms in a tertiary referral hospital in Mexico city.

Materials and Methods

Retrospective, observational, unicentric study developed in Medica Sur, a tertiary referral private hospital in Mexico city. All nosocomial infections from January 1st 2013 to December 31st 2018 registered by the epidemiological vigilance unit. MDR nosocomial infections were defined as hospital-acquired infections caused by ESBL *Escherichia coli*, ESBL *Klebsiella* spp, Carbapenem Resistant Enterobacteriaceae (CRE), carbapenem resistant *Pseudomonas* spp, Vancomycin Resistant *Enterococcus* Spp (VRE) or Methicillin-Resistant *Staphylococcus Aureus* (MRSA). We used definitions of Ventilator Associated Pneumonia (VAP), Hospital-Acquired Pneumonia (HAP), Urinary Tract Infection (UTI), Blood Stream Infections (BSI) and Soft Tissue Infection (STI) published by the World Health Organisation (WHO). Reports by year, infection site and MDR microorganism were obtained.

Local guidelines for empirical antimicrobial treatment are available as a mobile app in IOS and Android platforms since 2013 and contain recommendations for empiric antimicrobial treatment based on local bacterial resistance records. These guidelines include recommendations for the most common infectious disease in our insitution see (Table 1). The app, called PURA MS, was developed by the Epidemiological Vigilance Unit staff of our hospital and it is available for all healthcare professionals authorised to prescribe antibiotics in the hospital and who are trained twice a year in the

use PURA MS app; the contents are updated at least once a year. Adherence to local guidelines for empiric antimicrobial treatment are reported in percentage of adequate treatment of the total of empirical treatment registries. We assess 70 cases selected randomly every month. We compared the percentage of annual adherence to local guidelines for empiric antimicrobial treatment available in the PURA MS mobile app with the annual percentage of nosocomial infections caused by MDR bacteria.

Table 1: List of infections included in local guidelines of empiric antimicrobial treatment PURA MS.

Respiratory tract infections
Tracheobronchitis
Chronic obstructive pulmonary disease
Community acquired pneumonia
Pneumonia in special situations
Nosocomial pneumonia
Abdominal infections
Abdominal sepsis
Cholecystitis and cholangitis
Pancreatitis
Bacterial infections in cirrhotic patients
Acute and nosocomial diarrhea
Soft tissue and skin infections
Soft tissue and skin infections
Superficial infections of the skin
Necrotizing infections of skin and soft tissue
Animal bites
Surgical site infection
Diabetic foot
Osteo-articular infections
Septic arthritis
Prosthetic arthrhtis
Central nervous system infections
Meningitis
Urinary tract infections
Cystitis
Acute prostatitis
Acute pyelonephritis
Infections associated with a urinary catheter
Catheter-related infections
Blood stream infections associated with a central catheter

Results

We assessed 6 years, from 2013 to 2018. Avarage annual discharge rate was 13 824 to 15 754 patients/year. Initial adherence to local guidelines for empiric antimicrobial treatment was low (42.2%) in 2013 and progresively increased annually until 79.8% adherence in 2018, attributed to a systematic training of healthcare professionals authorised to prescribe antimicrobials in

the hospital and a handier access to guidelines. As the adherence to local guidelines increased, the percentage of nosocomial acquired infections caused by MDR bacteria decreased from 25% in 2013 to 15% in 2018 (Table 2) associated with an increase in adherence to local empiric antimicrobial treatment guidelines (Figure 1). During the study period, we observed a decrease in the incidence of MDR bacteria strains causing nosocomial infections in 2018 compared to 2013. Nosocomial infections caused by ESBL Escherichia coli

decreased by 10.7%, ESBL *Klebsiella* spp by 19%, carbapenem resistant *Pseudomonas aeruginosa* by 29.5%, methicilin resistant *Staphylococcus aureus* decreased from 55.6% to 0% in the same period of time (Table 3). By type of nosocomial infection caused

by MDR bacteria, hospital acquired pneumonia decreased by 20%, surgical site infection by 7.9%, blood stream infection diminished from 28.6% in 2013 to 0% in 2018 (Table 4).

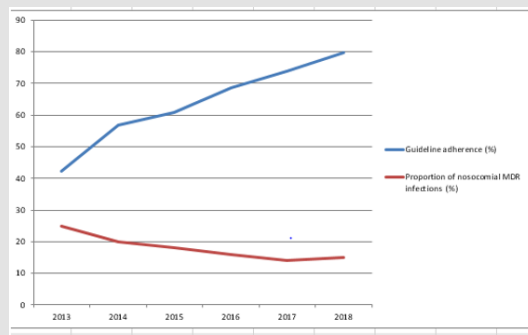


Figure 1: Annual adherence to local guidelines and percentage of nosocomial infections caused by MDR microorganisms.

Table 2: Annual percentage of nosocomial MDR microorganism infections from 2013 to 2018.

	Annual discharge	Guideline adherence (%)	Nosocomial infections (n)	Positive cultures (n)	Positive cultures (%)	MDR isolates (n)	Proportion of nosocomial MDR infections (%)	Proportion of MDR bacteria in positive cultures (%)
2013	15754	42.2	239	165	69	61	25	36
2014	14747	56.7	197	138	70	40	20	28
2015	14043	60.7	187	134	71	35	18	26
2016	13978	68.7	193	142	73	32	16	22
2017	13824	73.7	190	148	77	28	14	18
2018	14017	79.8	152	124	81	23	15	18
TOTAL	86363	63.3	1158	851	73	219	18	24.6

Table 3: Microorganisms and proportion of MDR status in nosocomial infections by year (2013-2018).

		2013	2014	2015	2016	2017	2018	TOTAL
<i>E. coli</i>	Total	53	33	24	35	35	29	209
	ESBL	29	23	17	20	14	13	116
	%	54.7	69.7	70	57	46	44	55
<i>Klebsiella spb.</i>	Total	21	11	5	8	8	13	66
	ESBL	12	3	3	4	6	5	33
	%	57	27	60	50	37.5	38	50
<i>Enterobacteriaceae</i>	Total	74	44	29	0	2	29	178
	CRE	0	0	1	0	2	1	4
	%	0	0	3.4	0	4.3	3.4	2
<i>Pseudomonas</i>	Total	13	19	20	13	13	12	90
	MDR	3	3	1	0	0	1	8
	%	23.1	15.8	5	0	0	8.2	8
<i>Pseudomonas</i>	Total	13	19	20	13	13	12	90
	CRE	6	4	10	5	5	2	32
	%	46.2	21.1	50	38	38	16.7	35
<i>Staphylococcus aureus</i>	Total	9	7	10	5	5	12	48
	MRSA	5	2	0	2	1	0	10

	%	55.6	28.6	0	40	16	0	20
<i>Enterococcus</i>	Total	0	0	9	15	15	10	49
VRE	VRE	0	0	1	0	0	1	2
	%	0	0	11	0	0	10	4

Table 4: Type of nosocomial infection by year (2013-2018).

2013	2014	2015	2016	2017	2018	TOTAL		
Ventilator associated pneumonia	Total	12	12	4	3	4	5	40
	MDR	5	6	2	0	1	1	15
	%	41	50	50	0	25	20	37
Hospital acquired pneumonia	Total	58	60	36	44	43	24	265
	MDR	5	5	2	1	1	3	17
	%	8.6	8.3	5.6	2.3	2.3	12.5	6
Urinary tract infection	Total	39	29	19	32	23	17	159
	MDR	17	13	8	11	8	7	64
	%	43.6	44.8	42.1	34.4	34	41.2	40
Surgical site infection	Total	76	39	54	57	47	41	314
	MDR	13	12	19	11	7	7	69
	%	25	30.6	35	19.3	14.9	17.1	21
Blood stream infection	Total	7	5	17	5	6	7	47
	MDR	2	0	4	2	1	0	9
	%	28.6	0	11.8	40	16.7	0	19

Discussion

Antimicrobial abuse generates selection pressure associated with the development of bacteria strain profiles with multiple drug resistance and some studies have shown that, in as much as 30-50% of cases, empirical antimicrobial selection of therapy, indication of treatment or duration are inadequate [14]. The development of resistant bacteria strains is already considered a public health issue that, in the United States, affects 2 million people of whom 23 000 die each year [15]. This study assessed the impact on bacterial resistance in our healthcare facility after implementation of local guidelines for empiric antimicrobial treatment developed in 2013 as a part of the antibiotic stewardship program, with a friendly interface and an handy access that guides healthcare professionals in the selection and duration of empiric antimicrobial treatment according to local bacterial resistance and international guidelines.

After the implementation of this guidelines, we observed a progressive increase in the percentage of adherence to the guidelines associated with a decrease in the percentage of nosocomial infections caused by MDR microorganisms, as well as decrease in the percentage of isolates of MDR bacteria. This results are similar to other published reports. We conclude that antibiotic stewardship programs that include use local guidelines for empiric antimicrobial

treatment delivered by friendly mobile phone interfaces are effective strategies for the control of nosocomial MDR bacterial infections. This study, along with other similar studies, support the use of antimicrobial stewardship programs as a standar of hospital care to slow down this public healthcare issue.

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Paulo Castañeda-Méndez. Biomed J Sci & Tech Res



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