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Clinical factors associated to bacterial resistance at the North of Mexico

Factores clínicos asociados a la resistencia bacteriana en el Norte de México

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ABSTRACT

Objective: To identify associated factors to bacterial multidrug resistance in a hospital from the north of Mexico. **Material and methods:** A randomized study of cases (n = 75, patients with at least one bacterial isolate with multidrug resistance; MR) and controls (n = 33, with non-MR isolate) had place during 2016 to 2019. The variables included were previous admission and treatment, length of stay, site of infection, long-term antibiotic management, multiple antibiotic use, among others. Descriptive analysis, χ^2 and logistic regression were performed to search for association with bacterial resistance. **Results:** Previous admission ($p < 0.05$), previous treatment ($p < 0.05$) and days of antibiotic use ($p < 0.05$) were identified as risk factors; the latter factor behaved as an independent risk factor for multidrug resistance. **Conclusions:** The study provides knowledge on modifiable factors derived from prescription like previous admission, use of antibiotic and term of treatment, as critical risk factors for multidrug resistance.

RESUMEN

Objetivo: *Identificar factores clínicos asociados a multirresistencia bacteriana en un hospital del Norte de México.* ***Material y métodos:*** *Estudio aleatorizado de casos (n = 75, pacientes con al menos un aislado bacteriano con multirresistencia; MR) y controles (n = 33, con aislado no-MR) durante el periodo 2016 a 2019. Las variables incluyeron ingreso y tratamiento previos, días de estancia hospitalaria, sitio de infección, días de uso de antibiótico, uso de dos o más antibióticos, relación con infección nosocomial. Se efectuó análisis descriptivo, χ^2 y regresión logística para buscar asociación con resistencia bacteriana.* ***Resultados:*** *Los factores de riesgo significativos fueron ingreso previo ($p < 0.05$), tratamiento previo ($p < 0.05$) y días de uso de antibiótico ($p < 0.05$); siendo este último un factor de riesgo independiente para multirresistencia bacteriana.* ***Conclusiones:*** *Este estudio identifica al ingreso, tratamiento previo y días de uso de antibiótico como factores de riesgo para multirresistencia derivados de la prescripción y, por lo tanto, susceptibles de modificación.*

INTRODUCTION

Antibiotics are drugs that are used in the treatment of bacterial infections, when bacteria possess or develop mechanisms that make these drugs ineffective, they are said to be resistant to antibiotics.[1] According to a report by the Center for Disease Control and Prevention (CDC), efforts to prevent the threat of antibiotic resistance are improving, however, in 2019, the number of people suffering from an infectious disease caused by resistant bacteria in the United States remains close to three million;[2] worldwide, 2,000 people die every day from bacterial resistance.[3] At United Kingdom bacterial resistance generates a cumulative global cost of 100 trillion annually[4] and globally, bacterial

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resistant microorganisms could potentially kill more than 10 million people a year by 2050 if no more actions are generated.[5] Although some risk factors for generating multidrug resistance have already been identified, the sensitivity profiles and resistance mechanisms differ from one place to another, even from one service to another within the same hospital.[6-15] In Mexico, there is little information about bacterial resistance, which is essential to carry out interventions. In a previous study in a private tertiary hospital in northern Mexico, we reported that three out of four isolates presented multi-resistance, extended resistance, or pan-resistance.[16] This study aims to identify the clinical risk factors associated with said multi-resistance.

MATERIAL AND METHODS

An observational, analytical, case-control study was carried out in a private tertiary-care hospital, located in the city of Chihuahua, Chihuahua, Mexico, where, through the antibiotic susceptibility profile, clinical isolates of bacteria were classified as Non-multi-resistant (Non-MDR), multi-resistant, with extended resistance or with pan-resistance.[16] From these isolates, the corresponding clinical information was obtained from the records, including as variables: days of hospital stay, admission service, previous treatment, site of infection, infection associated with health care, days of antibiotic use and use of two or more antibiotics.

Statistical analysis

The patients who presented infection by any multi-resistant bacteria, extended resistance or pan-resistance were the cases; controls were selected by simple randomized sampling from hospitalized patients who presented infection by Non-MDR bacteria in the same

Table 1: Bivariate analysis of clinical factors.

Variable		Group		χ^2	p	OR	CI 95%	
		Cases (n, %)	Controls (n, %)				Min.	Max.
Previous admission	Yes	70 (42.20)	53 (31.9)	4.95	0.02	2.29	1.09	4.55
	No	16 (9.60)	27 (16.3)					
Previous antibiotic use	Yes	51 (30.70)	9 (5.4)	5.82	0.01	2.67	1.18	6.06
	No	72 (43.34)	34 (20.5)					
Hospital stay (days)	≤ 5 days	24 (14.50)	13 (7.8)	2.11	0.14	1.78	0.81	3.93
	> 6 days	99 (59.60)	30 (18.1)					
Simultaneous > 2 antibiotic prescription	Yes	108 (65.10)	33 (19.9)	3.04	0.81	2.18	0.98	5.31
	No	15 (9.00)	10 (6.0)					
Period of Antibiotic use (days)	≤ 10 days	44 (26.50)	27 (16.3)	9.50	0.00	3.03	1.47	6.22
	> 10 days	79 (47.60)	16 (9.6)					
Admission service	Surgery	17 (10.30)	6 (3.6)	13.23	0.02	NA	–	–
	Internal medicine	16 (9.60)	14 (8.4)					
	Gynecology	4 (2.40)	1 (0.6)					
	Pediatry	2 (1.20)	3 (1.8)					
	NICU	24 (14.50)	7 (4.3)					
	ICU	60 (36.10)	12 (7.2)					
HAIs	Yes	64 (38.60)	16 (9.6)	2.8	0.09	1.81	0.89	3.73
	No	59 (35.50)	27 (16.3)					

Analysis of the clinical variables potentially associated to antibiotic multi-resistance.
OR = odds ratio, HAIs = health-care associated infections, ICU = Intensive Care Unit, NICU = Neonatal Intensive Care Unit.

Table 2: Significant multivariate model variables.

Variable		Crude OR	CI 95% Min.	CI 95% Max.	Adjusted OR	CI 95% Min.	CI 95% Max.
Period of antibiotic use (days)	> 10 days	3.03	1.47	6.22	3.03	1.47	6.22
	≤ 10 days	1.00	-	-	1.00	-	-

OR = odds ratio.
Multivariate analysis of the antibiotic resistance significant variables.

period of time in a 2.8-1 proportion with cases. The relative frequencies of each variable were calculated, by means of the statistical χ^2 test, the comparisons of the variables studied were made and the Odds ratio (OR) were calculated with their respective 95% confidence interval (CI) and a significant p value < 0.05. Finally, a logistic regression was performed with the variables with significant associations according to the Hosmer-Lemeshow criterion ($p < 0.25$) to obtain the model that better explains the associations of the study variables with the event.

RESULTS

A total of 108 clinical records were included, corresponding to 123 isolates of multi-resistant bacteria (75 files) and 43 isolates of Non-MDR bacteria (33 files), sample of more than one kind was taken from 27 patients and ten clinical samples included two isolates. Previously, it had been characterized among the 166 bacteria included, 123 (74.1%) with multi-resistance and the rest (43 bacteria, 25.9%) without multi-resistance criteria.[16] The distribution by sex in the two study groups was similar ($p = 0.84$), the 57.4% (62 patients) of the patients were men; the average age was of 46 years and there were not significant differences between groups ($p = 0.33$). Among the clinical antecedents studied, previous admission, previous antibiotic treatment, days of antibiotic use and admission service behaved as risk factors with a significant difference ($p < 0.05$) *(Table 1)*. In the analysis, a higher exposure proportion was found in the cases than in the controls ($p = 0.01$) in the patients that had received antibiotic treatment in the previous 48 hours increased the risk (67%) of have a multidrug resistant bacteria, compared with those who were not exposed (OR = 2.67; 95% CI: 1.18-6.06). Previous admission of no more than three months was also a relevant variable for the presence of bacterial resistance ($p = 0.03$); having an increased the risk by 22% compared to those who had not a record of admission before the study, (OR = 2, 29; 95% CI: 1.09-4.51); the increase in the use of days of antibiotic prescription also showed a difference between groups ($p = 0.02$), the analysis showed that the use of more than 10 days increased the risk by 50% compared to those who were not exposed to long antibiotic therapy (OR = 3.03; 95% CI: 1.47-6.22). An association was found with the service where the patient was admitted ($p = 0.02$), there was an increased risk for those patients hospitalized in areas such as intensive care and neonatal intensive care units. The multivariate analysis was significant for the variable duration in days of antibiotic use (OR = 3.03; 95% CI: 1.47-6.22), which behaved as an independent risk factor for acquiring an infection by multi-resistant bacteria *(Table 2)*.

DISCUSSION

Previous exposure to antibiotics and prolonged use of them were significant risk factors for bacterial multi-resistance identified in this study; these factors could be translated into an inappropriate indication by the doctor, a misdiagnosis, inappropriate administration of the drug, misuse of the same and a lack of use of laboratory susceptibility reports.[17] In this study, the clinical records of the patients with multidrug resistance showed that the half of the clinical records with history of previous antibiotic therapy, were using at the time of admission an antibiotic for a microorganism non-susceptible to it, at other cases, on spite of presence of an antibiogram report, the prescription was not adjusted to it; the clinical records also showed that the prolonged use of antibiotic treatment was due, in most of the cases to

the non-simultaneous use of several antibiotics for the management of the same infection, directly relating it to previous antibiotic use. This finding agrees with the literature where previous exposure to antibiotics was a risk factor that increases on 34.48% the probability of infection due to multi-resistant bacteria was reported.[17] and more importantly, the identification of modifiable factors enclosed as unappropriated prescription gives a start point for future interventions.

The admission at intensive care and neonatal Intensive Care Units showed higher risk, this is related to the clinical complexity and the multiple infections that patients in these hospitalization areas more frequently show than at other hospital services, the multiple infections very often leads to the use of broad spectrum antibiotics as it was reported by Valderrama et al.[18]

Previous admission proved to be a significant constant ($p = 0.02$) for bacterial resistance, in this study the main cause of readmission was re-infection, encouragement of good hygienical practices at hospital and at community care can reduce the re-infections; as reported by Ossa et al.,[7] the higher risk of antibiotic multi-resistance by previous admission is explained by a greater exposure of the patient to an environment with resistant bacteria.

Age, sex, concomitant use of two or more antibiotics, site of infection and days of hospital stay were non-significant variables for the generation of multidrug resistance ($p \geq 0.05$), although other authors have described that more than five days of hospitalization increases the risk of acquiring multi-resistant bacteria infections due to exposure to many drugs and to the procedures to which they are subjected Londoño et al.,[6] at our study, the length of hospital stay in days turned out not to be a significant variable ($p \geq 0.05$) and will require further study of the variables related with it.

The identification of the factors that contribute to multidrug resistance makes it possible to directly influence on those that can be modified through better prescription practices and have more chance to impact the problem and, in the case of non-modifiable factors, the knowledge of them allows to stress in advance the adequate management of the patients with higher risk of multiple antibiotic resistance developing.

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