Journal of Statistics on Health Decision

EXTENDED ABSTRACT

A19 Bacterial multidrug resistance evolution analysis in Coimbra Burns Unit, 2016-2020

Leonor Rodrigues[1], Vera Afreixo[1,2], Ana H. Tavares[1,2], Marisa Caetano[3], Catarina Chaves[4], Luís Cabral[5]

[1]Department of Mathematics, University of Aveiro, Portugal
[2]Center for Research & Development in Mathematics and Applications (CIDMA), University of Aveiro, Portugal
[3]Pharmacy Department, Coimbra University Hospital Centre, Portugal
[4]Department of Clinical Pathology, Coimbra University Hospital Centre, Portugal
[5]Department of Plastic Surgery and Burns Unit, Coimbra University Hospital Centre, Portugal

Introduction:

Bacterial multidrug resistance has become one of the biggest challenges of modern medicine. If no action is taken, it is expected that in 2050 the number of deaths due to antibiotics resistance may reach 10 million per year [1]. In most cases, burn patients are immunosuppressed and have an increased risk of developing infections. Recent studies have shown that between 42% and 65% of deaths in burn patients are primarily caused by infection and the associated mortality is twice higher than the mortality of patients without infection [2]. Multiresistance is one of the main causes of the uncontrollability of these infections. This study focuses in understanding the factors that contribute to multidrug resistance as well as its behavior over time, in order to provide an adequate treatment to burn patients.

Methods:

The current study was carried out in Coimbra Burns Unit, a department of Coimbra University Hospital Centre, from 2016 to 2020. During this period, it was only considered the group of bacteria species that infected at least 50 patients from a universe of 468 in analysis, such as: *Staphylococcus aureus, Pseudomonas aeruginosa, Enterococcus faecalis, Klebsiella pneumoniae, Escherichia coli, Proteus mirabilis, Serratia marcescens, Enterobacter cloacae*. Bacteria species resistant to at least three antibiotic classes were considered to be multidrug-resistant. To perform this study, binary logistic regression models were used. Multiresistance was used as a dependent variable and as predictor variables the following parameters were considered: year, age, sex, burn degree, percentage of the burn body surface, total days of hospitalization, mechanical ventilation, and central venous catheter insertion. The selection criteria to integrate independent variables in the multivariate model was the p-value of each variable being less than 0.25 in the univariate model. The predictor variable year has always been included in multivariate models. Statistical hypothesis tests with a p-value less than 0.05 were considered significant. All statistical analyses were performed using R (version 4.1.0).

Results:

Out of the eight bacteria species studied, it was only found significant associations between the predictor variables and the multidrug resistance development in two bacteria species (*Staphylococcus aureus* and *Klebsiella pneumoniae*). In table 1 are depicted the results from the multivariate models of the two bacteria species mentioned. Regarding the *Staphylococcus aureus*, the risk of developing multiresistance

Table 1 - Multivariate models regarding to *Staphylococcus aureus* and *Klebsiella pneumoniae*

	Klebsiella pneumoniae			***Staphylococcus aureus***		
Predictor variables	**OR[1]**	**95% CI[2]**	**p-value**	**OR[1]**	**95% CI[2]**	**p-value**
Year						
2017	0.15	[0.02; 0.77]	0.032	1.22	[0.40; 3.83]	0.726
2018	0.58	[0.11; 3.01]	0.520	1.38	[0.46; 4.23]	0.566
2019	0.88	[0.16; 4.62]	0.879	0.61	[0.15; 2.20]	0.459
2020	0.36	[0.01; 6.78]	0.508	0.35	[0.02; 2.20]	0.344
Age (years)	-	-	-	1.02	[1.00; 1.05]	0.044
Burned body surface (%)	1.04	[1.01; 1.08]	0.020	-	-	-

[1]Odd Ratio; [2]95% Confidence Interval

Keywords:
Bacterial multidrug resistance, burn patients

Corresponding author:
Leonor Rodrigues
leonorcrodrigues@ua.pt

Conflict of interest:
The authors declare no conflict of interests.

First published: 22JUN2021

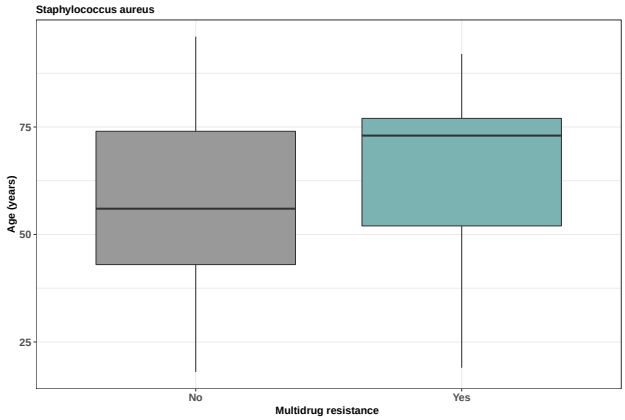

Figure 1 – Boxplot of the age in function of multidrug resistance – *Staphylococcus aureus*

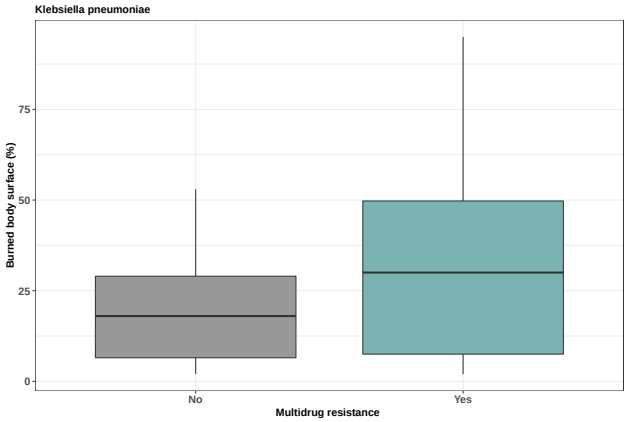

Figure 2 – Boxplot of the burned body surface (%) in function of multidrug resistance – *Klebsiella pneumoniae*

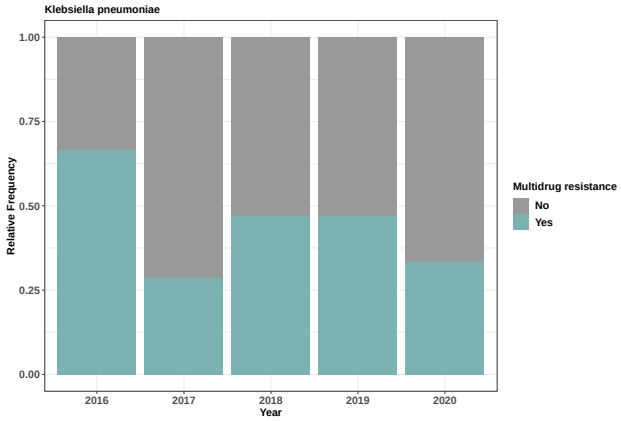

Figure 3 – Barplot of the multidrug resistance relative frequency in function of year – *Klebsiella pneumoniae*

increased with age (OR = 1.02; p-value = 0.044) (Figure 1). The area under the curve (AUC) associated with this model is 0.6455 (95% CI 0.5372 to 0.7539). In *Klebsiella pneumoniae*, the risk of developing multiresistances increased with the percentage of the burn body surface (OR = 1.04; p-value = 0.020) and it was lower in patients considered in 2017 when compared to the ones in 2016 (OR = 0.150; p-value = 0.032). The AUC associated with this model is 0.7230 (95% CI 0.5993 to 0.8467).

Discussion:

Regarding the *Staphylococcus aureus*, it was found that the risk of developing multidrug resistances increased with age. Older patients, in general, have already taken many antibiotics throughout their lives, so there is an increased risk for cumulative resistance. Multidrug resistance development is a natural phenomenon that results from the selective pressure exerted by the use of antibiotics[3,4]. In *Klebsiella pneumoniae* it was found that the risk of developing multidrug resistance increased with the percentage of the burned body surface. Patients with higher percentages of burn body surface are more likely to be immunosuppressed and are more exposed to nosocomial infections. Prolonged hospitalizations are also associated with the development of resistances[2]. Concerning the predictor variable

year, it was not observed any relevant argument towards the lower risk of developing multiresistance in 2017 when compared to the year 2016. Bacterial resistance to antibiotics is a growing concern to public health. It is very important to counter this trend: we may be heading towards a post-antibiotic era, in which common infection may be difficult to cure, leading to higher mortality. If no action is taken, the entire research effort may culminate in a huge failure.

References:

1. Robben PM, Ayalew MD, Chung KK, Ressner RA. Multi-Drug–Resistant Organisms in Burn Infections. Surg Infect (Larchmt). 2020;21(X):1-10. https://doi.org/10.1089/sur.2020.129
2. Lachiewicz AM, Hauck CG, Weber DJ, Cairns BA, Van Duin D. Bacterial Infections after Burn Injuries: Impact of Multidrug Resistance. Clin Infect Dis. 2017;65(12):2130-2136. https://doi.org/10.1093/cid/cix682
3. Yoshikawa TT. Antimicrobial resistance and aging: Beginning of the end of the antibiotic era? J Am Geriatr Soc. 2002;50(7 SUPPL.):226-229. https://doi.org/10.1046/j.1532-5415.50.7s.2.x
4. Loureiro RJ, Roque F, Teixeira Rodrigues A, Herdeiro MT, Ramalheira E. O uso de antibióticos e as resistências bacterianas: breves notas sobre a sua evolução. Rev Port Saúde Pública. 2016;34(1):77-84. https://doi.org/10.1016/j.rpsp.2015.11.003