



Economic Impact of Severe Multidrug-Resistant Infections in a Tertiary Public Hospital in Brazil

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INTRODUCTION

The increase in multidrug-resistant infections by 2050 can lead to an additional 10 million deaths per year worldwide, a reduction of 2.0 to 3.5% of GDP and a cost of up to US \$ 100 trillion [1].

However, studies that have assessed the impact of infections on economic and clinical outcomes in developing countries are lacking [2].

Our main objective was to assess the impact of infections by multidrug-resistant organisms (**MDR**) on patient-level hospital costs in a public tertiary hospital located in Brazil. In addition, we aimed to compare the range of results obtained using two different statistical approaches.

This research is a pilot study of the "MDR IMPACT Program", a national study on the impact of infections caused by MDR in Brazil, supported by the Brazilian Ministry of Health and the Brazilian Sanitary and Health Surveillance Regulatory Agency (ANVISA).

METHODS

Study Design

Retrospective observational study.

Population

All patients admitted to the ICU of a Brazilian public hospital in São Paulo/Brazil, from 2016 to 2018.

All healthcare-associated infections (**HAI**) were assessed but, due to the low densities observed, only patients presenting Central Line Associated Blood Stream Infections (**CLABSI**) were included in the analysis.

Patients were classified as MDR cases when the etiological agents listed below were found (Table1).

<i>Acinetobacter baumannii</i> resistant to carbapenems and/or polymyxins;
<i>Pseudomonas aeruginosa</i> resistant to carbapenems and/or polymyxins;
<i>Enterobacteriaceae</i> resistant to third and fourth generation cephalosporins, carbapenems and/or polymyxins;
<i>Enterococcus faecium</i> resistant to vancomycin;
<i>Staphylococcus aureus</i> resistant to methicillin;
<i>Coagulase negative Staphylococcus</i> resistant to methicillin;
<i>Candida</i> species resistant to imidazoles.

Table 1. Bacteria and fungi defined as MDR microorganisms

Costing Methodology

Absorption Costing Methodology was used to assess hospital patient-level costs. Data were extracted using an integrated hospital system (Business Intelligence).

Costs are segmented through different categories (materials, drugs, tests, labor, daily rates). Costs of materials, drugs and exams are directly allocated (patient-level), and the other costs such as direct labor, and others (depreciation, maintenance) are allocated according to the length of stay. Indirect costs are allocated by specific cost drivers.

Hospital costs were dollarized [3], considering the average dollar of the year 2018 (the last analyzed data collection period), considering the amount of R\$ 3.0576 per dollar according to the history of quotes from the Central Bank of Brazil.

Statistical Analysis

All categorical data are presented as absolute numbers and percentages and compared using the chi-square test or Fisher's test, as appropriate. All continuous data are presented as means and standard deviations and compared with the independent t test.

Two propensity score models [4] were fit, both using nearest neighbor metric to match patient groups based on two different sets of pre-defined features: set1 - age, sex, Charlson Comorbidity index, SAPS3 (severity index), hospital readmission and year of admission; set2: the same above, excluding sex, and year of admission.

RESULTS

A total of 2009 patients/ICU admissions were analyzed in the period.

987 (49.1%) patients had a central venous catheter placed; and 4.6% (45) of them presented CLABSI.

45 CLABSI were found: MDR infections (n = 20), and non-MDR patients (n = 25). 1964 patients presented with no CLABSI during the hospital stay and were excluded from the analysis.

Table 1. Table 1. Patients' Characteristics and Costs - model 1

	NO INFECTION (N = 15)	MDR CLABSI (N = 11)	P-VALUE
Age (means, sd)	45,87 (21,40)	52,55 (18,66)	0,42
Charlson (means, sd)	1,13 (1,06)	1,18 (1,40)	0,92
SAPS 3	51,00 (21,48)	54,27 (14,49)	0,67
Readmission	No 11 (73,33%)	7 (63,63%)	0,43
	Yes 4 (26,67%)	4 (36,36%)	
Cost (means, sd)	\$ 18,736.68 (\$ 17,967.27)	\$ 81,153.98 (\$ 52,321,13)	<0,01
Deceased	5	2	<0,01
Hospital LOS (means, sd)	15,20 (11,52)	59,45 (39,21)	<0,01

Table 2. Patients' characteristics and costs - model 2

	NO CLABSI (N = 21)	MDR CLABSI (N = 20)	P-VALUE
Sex (Male)	11 (52,38%)	12 (60%)	0.49
Sex (Female)	10 (47,61%)	8 (40%)	
Discharge (Alive)	21 (100%)	16 (80%)	0.83
Discharge (Deceased)	0 (0%)	4 (20%)	
Age (means, sd)	54.10 (14.81)	53.35 (15.45)	0.88
BMI (means, sd)	19.79 (10.43)	22.24 (8.43)	0.43
Hospital LOS (means, sd)	24.90 (26.45)	46.00 (33.30)	0.03
ICU LOS (means, sd)	6.95 (7.60)	9.50 (10.81)	0.40
SAPS 3 (means, sd)	49.48 (13.34)	49.15 (13.58)	0.94
Charlson (means, sd)	2.05 (1.79)	1.95 (1.77)	0.86
Costs (means, sd)			
Daily rates	\$ 19,534.64 (\$ 21,761.20)	\$ 32,949.23 (\$ 23,368.11)	<0.01
Nursing	\$ 10,353.02 (\$ 19,523.59)	\$ 13,511.60 (\$ 11,037.54)	0.01
Drugs	\$ 2,714.25 (\$ 3,445.28)	\$ 4,980.05 (\$ 3,765.87)	<0.01
Additional Services	\$ 2,449.29 (\$ 3,738.78)	\$ 4,781.97 (\$ 5,827.74)	<0.01
Materials	\$ 1,952.14 (\$ 2,529.92)	\$ 3,463.74 (\$ 3,701.31)	0.01
Exams	\$ 3,274.22 (\$ 5,922.15)	\$ 2,352.85 (\$ 1,443.17)	<0.01
Procedures	\$ 2,092.43 (\$ 5,958.86)	\$ 2,210.96 (\$ 2,477.79)	0.19
Fees	\$ 1,323.17 (\$ 2,902.48)	\$ 1,285.77 (\$ 1,108.03)	0.96
Gasotherapy	\$ 427.77 (\$ 1,397.66)	\$ 435.37 (\$ 835.13)	0.15
Honoraries	\$ 167.89 (\$ 248.69)	\$ 245.50 (\$ 259.65)	0.25
Total Cost (means, sd)	\$ 44,288.88 (\$ 62,879.27)	\$ 66,218.17 (\$ 44,567.73)	<0.01

Note: LOS - length of stay; ICU - Intensive Care Unit; SAPS3 - Simplified Acute Physiology Score (severity index). Costs categories: additional services: respiratory/physical therapist costs, psychology consultation, nutrition service, consultation with other medical specialties, and dialysis; nursing: emergency nursing, continuous hemodiafiltration nursing; honoraries: anaesthesia professional (surgery or small surgical procedures); procedures: blood bank, respiratory therapy fee, endoscopy, nasoenteral tube placement; fees: surgical/obstetrics room rates, chemotherapy room rate, hemodynamics room rates, ambulance (patient transfer).

Patients with MDR-CLABSI had higher average costs mainly due to longer ICU and hospital stays (69% higher). Other associated factors included (in absolute terms): nursing (31% higher), drugs (83% higher), services (95% higher), and materials (77% higher).

Incremental length of stay ranged from 21.10 days to 44.25 days, and incremental costs per patient admission ranged from US\$ 21,929.29 to 62,417.30, depending on the

model chosen (Incremental Cost-Effectiveness Ratio - ICER ranged from corresponding to additional costs ranging from US\$ 1,039.30 to US\$ 1,410.56/patient/day).

DISCUSSION

MDR-CLABSI were associated to significant increased costs and length of stay in a general ICU population in a public hospital in Brazil. Daily rates are the main component of such costs (human resources: physicians and nurses), but medicines, and other services (respiratory/physical therapist costs, psychology consultation, nutrition service, consultation with other medical specialties, and dialysis) are additional drivers.

Expressive incremental costs associated with MDR-CLABSI may reach more than 400% of paired admissions without infections. Each infection prevented can generate US\$ 1,410.56 daily savings per patient.

Using different methodological approaches may yield significant differences (in our experiment, they reached about 100% and 200%, in terms of outcomes and costs, respectively).

The importance of policies to prevent the acquisition of nosocomial infections are present in the daily practice of health professionals, but it appears that it is still possible to optimize health expenditures considering that any acquisition of infection in the hospital environment is a potential case of prevention, justifying a study in other hospitals in the country to analyze the heterogeneity of the rate of acquisition of these infections in other hospital centers [5].

CONCLUSION

Expressive incremental costs and incremental length of stay were associated with MDR-CLABSI in a public hospital in Brazil.

Each infection prevented may generated generate US\$ 1,410.56 daily savings per patient.

In this particular scenario, incremental costs calculations are complex (mainly due to several sources of heterogeneity among patients) and methodologies and its parameters may directly and significantly influence on the magnitude of the measured impact.

REFERENCES

1. Neill JO'. Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations The Review on Antimicrobial Resistance Chaired. 2014;(December).
2. Serra-Burriel M, Keys M, Campillo-Artero C, et al. Impact of multi-drug resistant bacteria on economic and clinical outcomes of healthcare-associated infections in adults:

Systematic review and meta-analysis. PLoS One. 2020;15(1):1-14.

3. Vieira, Fabrício AC, Márcio Holland, and Marco F. Resende. "Financial dollarization and systemic risks: New empirical evidence." *Journal of International Money and Finance* 31.6 (2012): 1695-1714.

4. Lee, Jaehoon, and Todd D. Little. "A practical guide to propensity score analysis for applied clinical research." *Behaviour research and therapy* 98 (2017): 76-90.

5. Leal JR, Conly J, Henderson EA, Manns BJ. How externalities impact an evaluation of strategies to prevent antimicrobial resistance in health care organizations. *Antimicrob Resist Infect Control*. 2017;6(1):1-11. doi:10.1186/s137.