

# Infection or colonization with resistant microorganisms: identification of predictors

Infecção ou colonização por micro-organismos resistentes: identificação de preditores

Graciana Maria de Moraes<sup>1</sup>

Frederico Molina Cohrs<sup>2</sup>

Ruth Ester Assayag Batista<sup>2</sup>

Renato Satovschi Grinbaum<sup>1</sup>

## Keywords

Nursing assessment; Nursing research;  
Infection/nursing; Risk factors;  
Forecasting

## Descritores

Avaliação em enfermagem;  
Pesquisa em enfermagem; Infecção/  
enfermagem; Fatores de risco;  
Previsões

## Submitted

June 10, 2012

## Accepted

March 27, 2013

## Abstract

**Objective:** Identifying predictors of infection or colonization with resistant microorganisms.

**Methods:** A quantitative study of prospective cohort was carried out. A descriptive analysis was performed in order to know the population of the study and a discriminant analysis was performed to identify the predictors.

**Results:** In this study were included 85 patients with infections caused by resistant microorganisms: carbapenem-resistant *Pseudomonas aeruginosas* (24.7%); carbapenem-resistant *Acinetobacter* (21.2%); methicillin-resistant *Staphylococcus aureus* (25.9%), vancomycin-resistant *Enterococcus* spp (17.6%) and carbapenem-resistant *Klebsiella pneumonia* (10.6%). The discriminant analysis identified transfers from other hospitals and hospitalization in intensive care unit as predictors for the occurrence of infections by the following groups: *S. aureus* resistant to methicillin, *Acinetobacter* resistant to carbapenems and *K. pneumoniae* resistant to carbapenems. None of the studied variables was discriminant for vancomycin-resistant *Enterococcus* spp. and carbapenem-resistant *P. aeruginosas*.

**Conclusion:** The predictors found were: ICU hospitalization and transfers from other hospitals.

## Resumo

**Objetivo:** Identificar os fatores preditores de infecção ou colonização por micro-organismos resistentes.

**Métodos:** Foi realizado estudo quantitativo de coorte prospectivo. Foram realizadas a análise descritiva, para conhecimento da população do estudo, e a análise discriminante, para identificação dos fatores preditores.

**Resultados:** Foram incluídos 85 pacientes com infecções por micro-organismos resistentes: *Pseudomonas aeruginosas* resistente aos carbapenêmicos (24,7%), *Acinetobacter* resistente aos carbapenêmicos (21,2%), *Staphylococcus aureus* resistente à metilina (25,9%), *Enterococcus* spp. resistente à vancomicina (17,6%) e *Klebsiella pneumoniae* resistente aos carbapenêmicos (10,6%). A análise discriminante identificou transferências de outros hospitais e internação na Unidade de Terapia Intensiva como fatores preditores para ocorrência de infecção pelos grupos *S. aureus* resistente à metilina, *Acinetobacter* resistente aos carbapenêmicos e *K. pneumoniae* resistente aos carbapenêmicos. Nenhuma das variáveis estudadas foi discriminante para *Enterococcus* spp. resistente à vancomicina e *P. aeruginosas* resistente aos carbapenêmicos.

**Conclusão:** Os fatores preditores encontrados foram: internação na UTI e a transferências de outros hospitais.

## Corresponding author

Graciana Maria de Moraes  
Napoleão de Barros street, 754, Vila  
Clementino, São Paulo, SP, Brazil. Zip  
Code: 04024-002  
graci\_moraes@ig.com.br

<sup>1</sup>Instituto de Assistência Médica ao Servidor Público Estadual, São Paulo, SP, Brazil.

<sup>2</sup>Universidade Federal de São Paulo, São Paulo, SP, Brazil.

**Conflicts of interest:** Batista REA is an associate editor of Acta Paulista de Enfermagem and did not participate in the review process of the manuscript.

## Introduction

Infections related to healthcare caused by microorganisms resistant to multiple antimicrobials (MDRO, multidrug-resistant organisms) are increasingly prevalent in hospitals. The severity and extent of the diseases caused by these pathogens varies according to the affected population and the institution in which they are found.<sup>(1)</sup> According to estimates from the European Center for Disease Prevention and Control (ECDC), the MDRO infections affect one in every 20 hospitalized patients.<sup>(2)</sup> The increased morbidity and mortality as a consequence of these infections is directly related with the difficult treatment due to the limited availability of effective drugs.<sup>(3)</sup>

The colonization or infection with resistant microorganisms in hospitalized patients has been receiving increasing attention from the services of hospital infection control.<sup>(4,5)</sup> The impact of this infectious complications in the hospital environment turns into longer hospitalization, readmission, sequels, inability to work, cost increases and mortality. There are no accurate estimates for the global impact of these infections.<sup>(6)</sup>

Infections associated with health assistance constitute an important problem worldwide and represent a major threat to the safety of patients.<sup>(7)</sup>

The Centers for Disease and Control and Prevention (CDC) recommends the implementation of contact precautions for this population. However, several studies show low adherence to such strategy.<sup>(8-10)</sup> Besides, there is the risk of delay in the diagnosis of colonization or infection, which increases the possibilities of transmission among patients.

The virulence and transmissibility of some microorganisms has evidenced the inability of eradicating these agents, hence the need for searching new methods of control.<sup>(11)</sup> Studies show it is useful to perform epidemiological surveillance cultures to know the real extent of the resistance problem in healthcare facilities.<sup>(12)</sup>

Surveillance cultures must be performed in order to diagnose colonized or infected patients, who are a reservoir for dissemination of these microorganisms. The purpose of this collection is the

early identification of MDRO colonized or infected patients and the immediate deploy of infection control strategies, reducing cross-contamination and the risk of developing subsequent infections.<sup>(11)</sup> However, this practice is only strongly recommended in outbreak situations, in endemic cases that are not controllable with protocol measures or in risk populations because surveillance cultures consume material and human resources and have high costs.<sup>(2)</sup> Moreover, the influx of MDRO colonized patients does not change and there is a delay in obtaining culture test results, favoring the spread of these agents.

Experts recommend deploying contact precautions with the predictors criterion<sup>(2,13)</sup> as a strategy to control MDRO dissemination. The objective of this study was to identify the predictors of infection or colonization with resistant microorganisms.

## Methods

The selected design for the study was cohort, conducted in a tertiary public school hospital which has 979 beds for clinical and surgical treatment, located in São Paulo (SP). The Grupo Executivo de Controle de Infecção Hospitalar, GECIH (Executive Group for Hospital Infection Control) develops the program of hospital infection control based on a methodology called National Nosocomial Infection Surveillance System (NNIS).<sup>(14)</sup>

Data collection was conducted between August 2007 and January 2008 through active search, after the resistant microorganism was identified by the microbiology laboratory of the hospital, in accordance with conventional methods of bacterial isolation and identification. The researcher was notified of the positive result for surveillance culture and then conducted the follow-up with patients by filling up a special form until their discharge or death. When the patient had more than one resistant microorganism, it was considered the first to be identified.

The demographic data collected were the ones cited in literature as risk factors for contracting MDRO: age, gender, origin, underlying disease,

date of hospital admission, length of hospital stay, antibiotic use, invasive procedures, surgical procedures in the past 30 days, date of the infection related to healthcare and its location, associated diseases, previous hospitalization, admission to intensive care unit, contact with patients with MDRO and clinical evolution.<sup>(2,5)</sup>

MDROs were defined as: methicillin-resistant *Staphylococcus aureus* (MRSA); vancomycin-resistant *Enterococcus* spp. (VRE); carbapenem-resistant *Pseudomonas aeruginosa* (PCR); carbapenem-resistant *Acinetobacter* (ARC); carbapenem-resistant *Klebsiella pneumoniae* (KRC).

After collection data were processed using the Statistical Package for Social Science (SPSS), version 17.0. Initially a descriptive analysis was carried out to know the population of the study. Afterwards a discriminant analysis was performed to identify the predictive factors.

The development of the study met both national and international ethical standards of research involving human beings.

## Results

During the study period all the patients with MDRO were included (n=85). The average age of patients with microorganisms was 68.7 years with a standard deviation of 16.4 (Table 1).

The MRSA, ARC and KRC groups showed equally predictive variables as follows: hospitalization in intensive care units and transfers from other hospitals (Table 2). Data show that in the relation between the predictive variables and the ARC group there was a classification in 94.4% of cases while with the MRSA group it was 54.5% and with KRC group it was 44.4%. It is also noteworthy that none of the elements of the study with predictors was related with PCR and VRE.

Table 2 shows two discriminant functions. The second function best discriminates “transfers from other hospitals” as a predictor, while the first function best discriminates the “ICU hospitalization”.

Data in table 3 show the best classification for the ARC group with 94.4% of accuracy, followed

by the MRSA group with 54.5% and by the KRC group with 44.4% for the variables “transfers from other hospitals” and “ICU hospitalization”, identified as predictive factors.

## Discussion

This study was limited by the number of patients included and its conduction in an only healthcare center, which compromises the generalization of data.

The results of this study in relation to the resistant microorganisms identified are similar to those in literature when compared to the population of ICU patients in other institutions. The prevalent resistant microorganisms found were: *P. aeruginosa*, *Acinetobacter baumannii*, *S. aureus*, *K. pneumoniae* and *Enterobacter cloacae*.<sup>(15)</sup>

The prevalence of resistant microorganisms that frequently cause nosocomial infections is modified according to the study site, with rates between 58 and 71% of PRC and between 43 and 59% of MRSA.<sup>(11,15)</sup> In this study however, prevalence of these agents was lower: 24.7% for PRC and 25.9% for MRSA.

Previous use of antimicrobial, prior hospitalization and acute kidney injury are identified by several studies as risk factors for colonization with VRE.<sup>(16,17)</sup> Regarding the PRC, some studies have shown as predictors of colonization the following: presence of cancer, previous use of antimicrobial and surgery in the prior four weeks.<sup>(18,19)</sup> In this study, none of these variables was discriminant for VRE and PRC, probably because of the sample size or due to interference of extrinsic factors. Although this latter case was not studied the transmission of microbial agents among patients may have occurred.

Studies show previous use of antimicrobial and prior hospitalization as risk factors for MRSA colonization; for KRC they indicate the presence of cancer, ICU admission and use of antimicrobials; for ARC the presence of cancer, high APACHE II score, ICU admission and exposure to antimicrobials.<sup>(17,20-22)</sup> In this study, through discriminant canonical function coefficients of resistant micro-

**Table 1.** Characteristics of patients colonized or infected with resistant microorganisms

Variables	MRSA n(%)	VRE n(%)	PRC n(%)	ARC n(%)	KRC n(%)
Gender					
Male	11(50.0)	11(73.3)	9(42.8)	10(55.6)	5(55.6)
Origin					
Transfer from other hospitals	2(9.1)	-	1 (4.8)	1(5.6)	4(44.4)
Previous hospitalization in the past 30 days	9(40.9)	10(66.7)	8(38.1)	9(50.0)	3(33.3)
ICU hospitalization	10(45.4)	9 (60.0)	15(71.4)	18(100.0)	8(88.9)
Invasive procedures					
Use of indwelling urinary catheter	12(54.5)	12(80.0)	15(71.4)	18(100.0)	9(100.0)
Use of central venous catheter	12(54.5)	12(80.0)	15(71.4)	18(100.0)	9(100.0)
Use of mechanical ventilation	11(50.0)	10(66.7)	13(61.9)	18(100.0)	9(100.0)
Surgery in the past 30 days	3(13.6)	2(13.3)	5(23.8)	3(16.7)	1(11.1)
Material					
Catheter	1(4.5)	1(6.7)	1(4.8)	4(22.2)	1(11.1)
Blood	14(63.6)	13(86.7)	9(42.9)	7(38.9)	7(77.8)
Secretions	6(27.1)	-	7(33.3)	6(33.4)	1(11.1)
Tendon	1(4.5)	-	1(4.8)	-	-
Urine	-	1(6.7)	3 (14.3)	1 (5.6)	-
Diseases					
Diabetes mellitus	12(54.5)	5(33.3)	4(19.1)	4 (22.2)	2 (22.2)
Neoplasia	1 (4.5)	1(6.7)	1(4.8)	2 (11.1)	1(11.1)
Chronic renal failure	3(13.6)	4(26.7)	4(19.1)	5 (27.8)	2(22.2)
Acute renal failure	4(18.2)	4(26.7)	3(14.3)	4 (22.2)	1(11.1)
Neurological disease	4(18.2)	5(33.3)	1(4.8)	1(5.5)	1(11.1)
Corticotherapy	5(22.7)	1(6.7)	2(9.52)	5(27.8)	1(11.1)
Type of infection					
Urinary tract	3(16.7)	3(18.8)	8(27.6)	1(5.0)	3(33.3)
Wound	1(5.6)	2(12.5)	8(27.6)	6(30.0)	-
Peritonitis	-	-	1(3.4)	-	-
Blood stream	4(22.2)	1 (6.3)	3(10.3)	-	-
Pneumonia	7(38.9)	10(62.5)	9(31.0)	12(60.0)	6(66.7)
Skin or soft tissue	1(5.6)	-	-	1(5.0)	-
Abdominal focused	1(5.6)	-	-	-	-
Meningitis	1(5.6)	-	-	-	-
Evolution					
Hospital discharge	10(45.4)	3(20.0)	10(47.6)	5(27.8)	1(11.1)
Death	12(54.5)	12(80.0)	11(52.4)	13(72.2)	8(88.9)
Total	22 (25.9)	15 (17.6)	21 (24.7)	18 (21.2)	9 (10.6)

Legend: MRSA – *Staphylococcus aureus* resistant to methicillin; VRE – *Enterococcus* spp. resistant to vancomycin; PRC – *Pseudomonas aeruginosa* resistant to carbapenems; ARC – *Acinetobacter* resistant to carbapenems; KRC – *Klebsiella pneumoniae* resistant to carbapenems; ICU – intensive care unit

**Table 2.** Canonical discriminant function coefficients of resistant microorganisms

Predictive factors	Function	
	1	2
Transfers from other hospitals	2.119	3.015
ICU hospitalization	1.818	-1.538
(Constant)	-1.482	0.802

Legend: Discriminant analysis was used to identify predictors. ICU – intensive care unit

**Table 3.** Classification results of resistant microorganisms

Group	MRSA n(%)	VRE n(%)	PRC n(%)	ARC n(%)	KRC n(%)	Total
MRSA	12(54.5)	0(0.0)	0(0.0)	8(36.4)	2(9.1)	22(100.0)
VRE	6(40.0)	0(0.0)	0(0.0)	9(60.0)	0(0.0)	15(100.0)
PRC	6(28.6)	0(0.0)	0(0.0)	14(66.7)	1(4.8)	21(100.0)
ARC	0(0.0)	0(0.0)	0(0.0)	17(94.4)	1(5.6)	18(100.0)
KRC	0(0.0)	0(0.0)	0(0.0)	5(55.6)	4(44.4)	9(100.0)

Legend: Discriminant analysis was used to classify the resistant microorganisms. MRSA – methicillin-resistant *Staphylococcus aureus*; VRE – vancomycin-resistant *Enterococcus* spp.; PRC – carbapenem-resistant *Pseudomonas aeruginosa*; ARC – carbapenem-resistant *Acinetobacter*; KRC – carbapenem-resistant *Klebsiella pneumoniae*

organisms, transfers from other hospitals and ICU hospitalization were identified as predictive factors for positive culture for MRSA, ARC and KRC. Even antibiotics use, no matter what class studied, did not lead to the occurrence of a particular microorganism, suggesting that the selection promoted by the use of broad-spectrum antimicrobials is homogeneous, regardless of resistance mechanism.

Multiple predisposing factors have been linked to emergence and spread of resistant microorganisms, such as declining age, length of hospital stay, severity of underlying disease, enteral feeding, transfers between units and hospitals, surgeries, exposure to invasive procedures and use of antibiotics.<sup>(23)</sup>

The results of ICU admission as a predictor for MDRO positive culture are compatible with other studies. ICUs are places where many invasive procedures take place and that concentrate the severest medical and surgical patients admitted in hospitals, with higher infection rates, which leads to a widespread use of antimicrobial, factors that

contribute to the increase of nosocomial infections and bacterial resistance. Therefore, these units are the main source of resistant micro-organisms outbreaks. These patients are at increased risk for bloodstream infections, pneumonia and urinary tract infection, having different microorganisms as etiologic agents.<sup>(24,25)</sup> Thus, ICUs are the epicenter of MDRO infections, which can be disseminated throughout the hospital. Yet, another challenge is to control the spread outside the hospital environment, in other words, the community, in long stay institutions or in other places of patients transfers after hospital discharge.<sup>(5)</sup>

In this study transfers from other hospitals were found as predictors for colonization or infection with MDROs, a factor previously shown in other studies. Patients transferred from other hospitals or who have stayed more than 24 hours in another hospital for examinations or procedures may be colonized or infected with resistant microorganisms and, upon entering the institution, may show clinical infection by the agent or transmit it horizontally.

Infection control practices have arisen over the years, to prevent the spread of infections by epidemiologically important microorganisms. Great part of researches by the Society of Healthcare Epidemiology of America (SHEA) has been highlighted in the guidelines of infection. Practical guidelines include contact precautions for MDRO infected patients, sterile barrier precautions during implementation of central venous catheter, hand hygiene with alcoholic solutions, surveillance and routine precautions for MRSA and VRE in areas where high risk patients are hospitalized.<sup>(26)</sup>

Thus, patients transferred from other hospitals should be kept in contact precautions in order to take cultures of invasive devices, lesion and rectal swab. Infected and colonized patients should remain in precaution until discharge. For patients who had contact with colonized or infected patients it is also recommended to take cultures of invasive devices, lesions and rectal swab. ICU colonized or infected patients must remain in contact precautions until discharge and when transferred to the hospitalization unit should remain isolated until the end of treatment, in cases of infection or colonization.<sup>(1)</sup>

The early implementation of contact precautions is extremely important to contain the spread of resistant microorganisms in healthcare environments. The high cost of culture tests together with the delay in obtaining results make the identification of predictor variables, as in this study, a valuable tool.<sup>(1)</sup>

## Conclusion

The predictive variables for colonization or infection with MRSA, ARC and KRC found in this study were transfers from other hospitals and ICU hospitalization. None of the variables studied was discriminant for colonization or infection with VRE and PCR.

## Collaborations

Moraes GM participated in the conception and design, analysis and interpretation of data, drafting the article, revising it critically for important intellectual content and final approval of the version to be published. Cohrs FM collaborated with the conception and design, analysis and interpretation of data. REA Batista collaborated in the writing, revising it critically for important intellectual content and final approval of the version to be published. Grinbaum RS participated in the conception and design, analysis and interpretation of data, drafting the article, revising it critically for important intellectual content and final approval of the version to be published.

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