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ORIGINAL ARTICLE

Multidrug resistant organisms' incidence in a university Hospital in Porto Alegre

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ABSTRACT

Introduction: Multidrug-resistant organisms (MDRO) are a growing worldwide public health problem. Few therapeutic options remain available to treat infections caused by MDRO. Local actions should be implemented to reduce bacterial resistance and MDRO diffusion. **Objective:** Evaluate the incidence of MDRO in the institution and assess the outcome of patients. **Methods:** Was performed a prospective cohort. Were included patients hospitalized between June 2010 and May 2011, with microbiological isolates, classified according to 2010 Hospital Infection Control Committee criteria. Patients were followed until their outcomes. **Results:** Were identified 981 multidrug-resistant organisms in 808 patients. The median length of stay for the identification of the MDRO was 12 days (IQR 25-75%, 3-26 days). The monthly rate came to minimal and maximal amplitude of, respectively, 2.7 and 5.9 MDRO/1000 patient-days per period. During the studied period was not observed a significant increase in the incidence rate of MDRO at institution. **Conclusion:** Our findings show that MDRO with major incidence was extended-spectrum β-lactamase-producing organism and the vancomicin-resistant *Enterococcus* spp. The definition of a local epidemiologic profile of resistant organisms is important to drive preventive and therapeutic actions inside the institution.
Keywords: Multidrug resistance. Bacterial resistance. Incidence. Multidrug-resistant organisms.

INTRODUCTION

Multidrug-resistant organisms (MDRO) are a growing public health problem worldwide and few therapeutic options are available to treat infections caused by those organisms. Consequently, a multidisciplinary approach (infection control procedures, bacterial surveillance, patient isolation and antimicrobial stewardship) should be implemented to reduce those microorganisms dissemination[1].

Hospital-acquired infection is one of the most common hospital complications[2,3], and, when caused by MDRO, they increase hospital costs, length of stay and also patient morbidity and mortality[4,5]. The rise in resistant organisms, non-responsive to conventional treatment, emphasizes the need for new antibiotics development6. In the past 40 years, only four new classes of antibiotics have been launched and few pharmaceutical companies show interest in research and develop this kind of drugs[7].

Emergence of MDRO is mostly associated with inappropriate use of antibiotics, which promotes selective pressure on microorganisms[8]. Bacteria have the ability of easily transfer genes, which contributes to perpetuation of the resistant species, and the expression of resistance genes reduces treatment options[9].

Facing the growing problem of bacterial resistance, the aim of this study was evaluate the MDRO incidence at Hospital de Clínicas de Porto Alegre (HCPA), to provide information to plan new actions to control these organisms spread.

METHODS

Setting - Hospital de Clínicas de Porto Alegre, a 790-bed, university affiliated, tertiary level public hospital, is located in the city of Porto Alegre, in southern Brazil. All hospital units, i.e., intensive care units (adult, neonatal and pediatric), clinical and surgical wards were included. The study was approved by the institution's Ethics Committee under number 110129.

Study design and definitions - We performed a prospective cohort study, from June 2010 to May 2011.

Data were collected daily, by the review of the microbiological laboratory report and hospital electronic database for patient clinical and demographic data. The identification of bacterial species was performed according to standard laboratory protocols. Susceptibility data was tested by disc-diffusion method, interpreted according to Clinical and Laboratory Standards Institute guidelines[10].

The first microbiological MDRO isolate per patient was included, irrespective of the body site from which the specimen was obtained. If the same isolate was cultured after 10 days of the first identification, it was considered a new microorganism and included in the study. Patients re-hospitalized with the same MDRO isolate created a second entrance in the database. Patients were followed until their outcomes.

Resistance Data - Bacterial resistance was classified according to 2010 Hospital Infection Control Committee criteria, and included the following: carbapenem-resistant *Acinetobacter* spp., *Citrobacter* spp., *Enterobacter* spp., *Pseudomonas* spp. and *Serratia marcescens*; extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli*, *Klebsiella* spp. and *Proteus* spp.; sulfamethoxazole/trimethoprim resistant *Stenotrophomonas maltophilia*; vancomycin-resistant *Enterococcus* spp. (VRE); methicillin-resistant *Staphylococcus aureus* (MRSA); any *Clostridium difficile* and *Burkholderia cepacea*. Isolates with intermediate susceptibility were considered resistant.

Statistical analysis - Bacterial resistance rate was calculated by dividing the number of isolates for each species by the entire hospital number of patient-days multiplying the quotient by 1000. Data were reported on a monthly basis. Data normally distributed was shown as mean and standard deviation and otherwise distribution was shown as median and interquartile ranges (IQR). To determine the distribution pattern of the variables, the Kolmogorov-Smirnov test was performed. Linear regression was used to measure the curve trends of MDRO incidence. Statistical significance in all analyses was defined as $P < 0.05$. Data was analyzed with *Statistical Package for Social Science* (SPSS) 18.0.

RESULTS

In this study, we identify 981 MDRO in 808 patients. Most patients were men 56.4% (N=456), 92.1% were white (N=744), and 5.2% were black (N=42). The median age was 57 years (IQR25-75%, 37-69 years). From 808 patients, 17.3% had respiratory disease (N=140), 14.9% cardiovascular disease (N=120), 13.0% renal disease (N=105), 11.6% solid organ cancer (N=94), 9.8% gastrointestinal disease (N=79), 8.3% cystic fibrosis (N=67), 7.4% of patients were transplanted (N=60), 6.8% had hematology cancer (N=55) and 32.3% had other comorbidities (N=261).

The median length of stay of patients with MDRO was 31 days (IQR 25-75%, 17-56 days). The median time for identification of the organisms was twelve days (IQR 25-75%, 3-26 days). Considering the 808 patients, 69.1% (N=558) had been hospitalized before at HCPA. Thirty percent (N=247) of patients were readmitted to HCPA within 60 days after hospital discharge.

Monthly incidence of MDRO identified as infection or colonization, from hospital or community origin is shown in Figure 1. The trend curve shows no significant increase in MDRO in the studied period (P=0.16).

Among the 981 identified multiresistant organisms, 232 were *Enterococcus* spp. (23.6%), 224 were *Klebsiella* spp. (22.8%), 162 were *Staphylococcus aureus* (16.5%), 133 were *E. coli* (13.6%), 112 were *Pseudomonas aeruginosa* (11.4%), 63 were *Acinetobacter* spp. (6.4%), 18 were *Clostridium difficile* (1.8%), 16 were *Burkholderia cepacea* (1.6%), 10 were *Proteus* spp. (1.0%), 7 were *Stenotrophomonas maltophilia*. (0.7%) and 4 were *Enterobacter* spp. (0.4%). *Monthly incidence* of MDRO stratified by the main bacterial species is shown in Figure 2.

DISCUSSION

The aim of this study was to evaluate the MDRO incidence in HCPA. Our findings show that MDRO with major incidence was ESBL-producing organisms, VRE, MRSA, and carbapenem-resistant *Pseudomonas aeruginosa*. Patients with MDRO had a long hospital stay, compared to the mean entire hospital length of stay (8.13 days; personal communication) and a significant percentage of re-admissions. During the study period, there was no increase in trend of identification of MDRO.

Many studies show an increase of bacterial resistance to antibiotics. For instance, studies in Latin America observed that 48.3% of *Staphylococcus aureus* were resistant to methicillin, 21.4% of *Acinetobacter* spp. were resistant to carbapenems and 36.7% *Klebsiella pneumonia* and 20.8% *E. coli* were ESBL-producers11. Furthermore, the rate of *Enterococcus* spp. resistant to vancomycin increased from 5.0% in 2003 to 15.5% in 2008[12]. In Europe, there is an increasing incidence of ESBL, VRE, *Acinetobacter* spp., *Pseudomonas* spp., and others[13,14].

In our study, the global monthly incidence of MDRO shows some oscillations in the period. The monthly rate came to minimal and maximal amplitude of, respectively, 2.7 and 5.9 MDRO/1000 patient-days per period. These variations may be related to the new measures taken by Hospital Infection Control Committee (HICC) through the observed period, in an attempt to decrease MDRO incidence. Some of the measures include: the campaign involving patient empowerment and hand hygiene compliance initiated in August 2010; the at distance learning course about hand hygiene directed to the hospital assistant team in December 2010; and the creation of a unit for cohorting patients with MDRO in March 2011. Those interventions were not controlled in this study.

These differences in MDRO incidence may be the evidence that measures taken for the global MDRO reduction may have distinct effect for each microorganism. If we stratify incidence by microorganisms, we can see two distinct incidence profiles, one of them with few oscillation and the other with more variations in specific periods. MRSA and carbapenem-resistant *Pseudomonas aeruginosa* show an incidence profile with few variations, the other bacteria show a profile with more oscillations in specific periods of time (Figure 2). Studies show the importance of hand contamination for dissemination of MRSA or the environment for spread of *C. difficile*, VRE and *Acinetobacter* spp., therefore measures that aim hand hygiene or environment disinfection can affect rates of MDRO differently[5,15-17]. Another interesting observation was the reduction in MDRO incidence in December, for almost all microorganisms, which might be related to the at distance learning course on hand hygiene, although our study was not design to confirm this hypothesis.

This study has some limitations. Seasonality may have affected the incidence of certain bacteria in the period, like, for instance, *Acinetobacter* spp., whose incidence increases at summer time[18]. It was not possible to identify the rate resistance profile for each bacteria, because we included in this cohort only the resistant bacteria, which makes the comparison to other studies not possible. The mortality of patients cannot be attributed directly to colonization/infection by MDRO, since the study was not designed to evaluate this outcome.

The profile of bacterial resistance in HCPA shows predominance of ESBL-producing organisms and the VRE. There was not a significant increase in MDRO incidence rate in the period. The definition of a local epidemiologic profile of resistant organisms is important to drive preventive and therapeutic actions inside the institution.

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Figure 1. Monthly incidence from infection or colonization by MDRO (community or hospital acquired) at HCPA per 1000 patient-days.

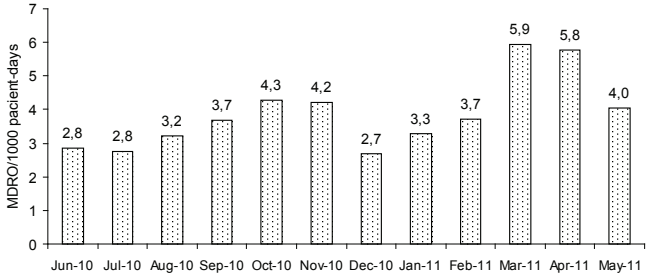
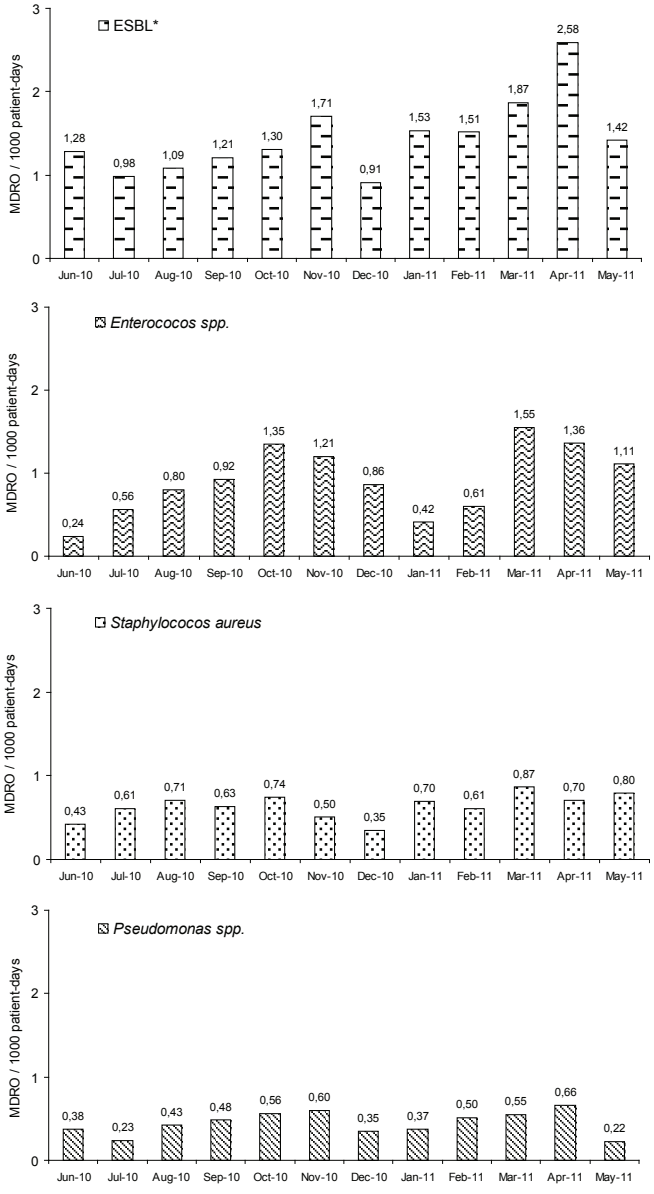
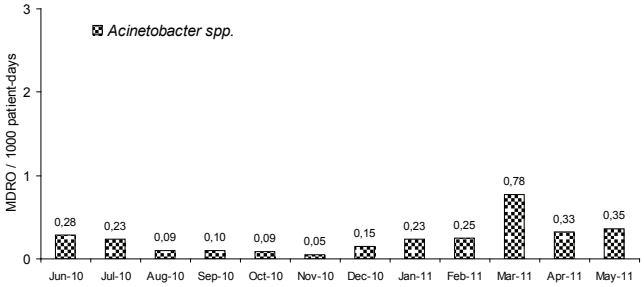


Figure 2. Monthly incidence from infection or colonization, stratified by MDRO (community or hospital acquired) at HCPA, per 1000 patient-days.





**ESBL (Klebsiella spp., E. coli, Proteus spp.)*

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