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Major Article

# Epidemiologic surveillance of multidrug-resistant bacteria in a teaching hospital: A 3-year experience

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**Key Words:** *Surveillance program; multidrug-resistant organism; dissemination;:* hospital infection

***Background:*** The objective of this prospective study was to verify the effectiveness of a multidisciplinary surveillance program that was implemented in a teaching hospital in southern Brazil, to prevent and control the spread of multidrug-resistant organisms.

***Methods:*** The program implemented involved establishment of prevention guidelines, hand-hygiene promotion, isolation of patients colonized or infected by such organisms, enforced contact precautions, and terminal cleaning and disinfection of isolation rooms. A microbiology service, previously provided by an external laboratory, was established in the hospital. Detection of bacteria-resistant genes and molecular typing were performed also.

***Results:*** Statistically significant differences were observed between the pre- and post-intervention periods ($P = .00198$). Control measures were effective in blocking the dissemination of a previously endemic clone of *Acinetobacter baumannii*. Changes were observed in the dissemination pattern, from a monoclonal to a polyclonal mode. The incidence of vancomycin-resistant *Enterococcus* during the surveillance period was low. Only 2 isolates of $BLA_{KPC}$-positive *Klebsiella pneumoniae* (distinct profiles), and 5 isolates of $BLA_{SPM}$-positive *Pseudomonas aeruginosa* (a single cluster), were detected.

***Conclusions:*** These results indicate that the surveillance program implemented was effective in preventing the spread of multidrug-resistant organisms in the hospital.



Surveillance programs are important tools for controlling the emergence and dissemination of multidrug-resistant organisms (MDROs) because they can provide important information to guide control measures in various institutions.[1] Some countries have national surveillance programs to monitor antibiotic resistance, whereas others can obtain information only from isolated studies by local researchers.[2] Although official technical norms for the isolation of carbapenem-resistant Enterobacteriaceae have been issued by Brazilian government agencies,[3] the control of MDROs in Brazilian hospitals is hampered by other factors, most of which are related to lack of human resources and inadequate infrastructure.[4–6]

Nonetheless, data on bacterial resistance are very important for a better understanding of the dynamics of hospital infections and for guiding implementation of governmental programs to improve health care. Thus, the objective of the present study was to verify the effectiveness of a multidisciplinary surveillance program implemented in a teaching hospital in southern Brazil to prevent and control the spread of MDROs.

## MATERIALS AND METHODS

### *Settings*

This prospective epidemiologic study was conducted at Maringá University Hospital, in Maringá, Brazil. This 123-bed public teaching

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hospital provides general and advanced medical and diagnostic services and public health care to about 750,000 residents of Maringá and surrounding towns. Monitoring of MDROs could only be initiated in 2011, after implementation of a microbiologic service in the Clinical Analysis Laboratory of the hospital. Between 2005 and 2010, microbiologic diagnostic tests were performed by an external laboratory.

With the emergence of *Klebsiella pneumoniae* carbapenemase (KPC)–producing bacteria worldwide, a priority surveillance program was established in 2011 that included the following measures: (1) issuance of guidelines to prevent transmission of hospital pathogens; (2) annual educational campaigns on hand hygiene, including lectures, workplace reminders, feedback, and training on antiseptic hand scrubbing; (3) isolation of patients colonized or infected with MDROs, in a single room, with enforced contact precautions and terminal cleaning and disinfection of the rooms, performed twice, by different teams on separate days; (4) implementation of surveillance cultures for the pathogens KPC-producing bacteria, vancomycin-resistant *Enterococcus* (VRE), and methicillin-resistant *Staphylococcus aureus* (MRSA); and (5) detection of bacteria-resistant genes and molecular typing of clinical and surveillance isolates.

### *Bacterial samples*

During a 36-month period, subdivided into 3 periods of 12 months (March 2011–February 2012, March 2012–February 2013, March 2013–February 2014), microorganisms were isolated from clinical and surveillance cultures from inpatients. This process took place in the following hospital units: emergency care; clinical care (medical clinic, surgery, pediatrics, and obstetrics and gynecology); adult, pediatric, and neonatal intensive and semi-intensive care units (ICUs); and outpatient clinics (blood center and ambulatory clinic). Collection of surveillance cultures was performed according to a protocol established by the Hospital Infection Control Commission.

### *Culture on admission*

The protocol was as follows: Rectal swab samples were collected for VRE/KPC detection, from adult and pediatric patients who were hospitalized for more than 48 hours in the preceding 30 days, had stayed in the ICU in the preceding 6 months, or were on dialysis. Nasal swabs, for MRSA detection, were collected from pediatric patients. Rectal swabs for VRE/KPC detection, and nasal swabs for MRSA detection, were collected from all newborns who came from other services, regardless of their length of stay.

### *Cultures during hospitalization*

At the request of the Hospital Infection Control Commission, biweekly rectal swabs were collected for VRE/KPC detection in adults, in addition to nasal swabs for MRSA detection in pediatric patients and newborns.

### *Phenotypic identification and antimicrobial susceptibility testing*

The phenotypic identification and antibiotic sensitivity profile of the isolates were performed using the BD Phoenix Automated Microbiology System (BD Diagnostic Systems, Sparks, MD). Interpretation of the criteria for antimicrobial sensitivity was performed as recommended by the Clinical Laboratory Standards Institute (CLSI).[7] The screening and detection of KPC-producing Enterobacteriaceae were performed according to the Brazilian National Health Surveillance Agency.[3]

### *Detection of resistance genes*

The investigation of metallo-β-lactamase and $BLA_{KPC}$ genes was performed using multiplex polymerase chain reaction (PCR), according to Poirel et al.[8] The Enterobacteriaceae $BLA_{KPC}$ and $BLA_{NDM}$ genes, *Pseudomonas aeruginosa* $BLA_{GIM}$, $BLA_{IMP}$, $BLA_{SPM}$, $BLA_{NDM}$, and $BLA_{KPC}$ genes, and *Acinetobacter baumannii* $BLA_{GIM}$, $BLA_{IMP}$, $BLA_{SIM}$, $BLA_{VIM}$, $BLA_{SPM}$, $BLA_{NDM}$, and $BLA_{KPC}$ genes were investigated.

In addition, oxacillinase genes ($BLA_{oxa51\text{-}like}$, $BLA_{oxa23\text{-}like}$, $BLA_{oxa24\text{-}like}$, $BLA_{oxa58\text{-}like}$, and $BLA_{oxa143\text{-}like}$) for *A. baumannii* were also investigated, according to Woodford et al.[9] Isolates of *S. aureus* were investigated for the presence of the *mec*A gene according to Vannuffel et al.[10] The *van*A and *van*B genes in Enterococci were investigated, according to Patel et al.[11]

### *Molecular typing*

All of the isolates of carbapenemase-producing *Klebsiella spp*, *Enterobacter spp*, and *P. aeruginosa* were selected for molecular typing. For *A. baumannii*, the first isolate recovered from patients in the adult ICU was selected. For *S. aureus*, only one isolate from each patient was included. In cases of duplicate samples, only those obtained from sterile sites were selected. Two samples from the same patient were used only when a change in the antibiotic resistance profile was observed. Only VRE isolates were selected. For Gram-negative bacilli, molecular typing was performed by enterobacterial repetitive intergenic consensus (ERIC)-PCR, according to Silbert et al.[12] For *S. aureus*, repetitive extragenic palindromic (REP)-PCR was used with the RW3A oligonucleotide, according to Del Vecchio et al.[13] Band patterns were interpreted using BioNumerics 6.5 software (Applied Maths, Sint-Martens-Latem, Belgium). Isolates were considered to belong to the same clone when the Dice similarity coefficient was ≥0.9 for Gram-negative bacilli, and ≥0.8 for *S. aureus*.[14]

### *Hospital infection rates*

Annual hospital infection rates were calculated over a 12-year period (2005–2016) that was subdivided into pre-intervention (2005–2010) and postintervention (2011–2016) periods. A Student *t*-test was used to compare general hospital infection rates between the pre- and post-intervention periods.

## RESULTS

During the study period, a total of 2472 microorganisms were isolated. The pathogens that were isolated frequently are *Escherichia coli* (21%), *S. aureus* (16%), *Staphylococcus epidermidis* (13%), *P. aeruginosa* (11%), *Klebsiella* spp (11%), *Enterococcus* spp (7%), *Enterobacter* spp (7%), *A. baumannii* (6%), *Candida albicans* (5%), and *Staphylococcus haemolyticus* (3%).

The most important resistant pathogens that were isolated were *S. aureus*, *P. aeruginosa*, *Klebsiella* spp, *Enterococcus* spp, *Enterobacter* spp, and *A. baumannii*. The number of patients who had the same bacterial species in both clinical and surveillance cultures was highest for *P. aeruginosa* (31), followed by *A. baumannii* (19), *Klebsiella* spp (15), *Enterobacter* spp (7), *S. aureus* (2), and *Enterococcus* spp (1).

Vancomycin, daptomycin, and linezolid presented good activity against *S. aureus*. Surveillance isolates (MRSA) had higher antimicrobial minimum inhibitory concentrations (MICs) than did clinical isolates. One clinical isolate and 8 surveillance isolates of *Enterococcus faecium* were resistant to vancomycin ($MIC_{90} > 32$ μg/ml). All of the clinical isolates of *E. faecalis* ($n = 107$) were susceptible to vancomycin, and only one surveillance isolate was resistant to vancomycin. Ampicillin presented good activity against isolates of *E. faecalis* ($MIC_{50} = 1$ μg/ml; $MIC_{90} = 2$ μg/ml). Only one clinical isolate