ARTIGO ORIGINAL / *ORIGINAL ARTICLE*

Infeção e colonização por *Staphylococcus aureus* meticilino-resistente numa enfermaria de Medicina Interna

Methicillin-resistant Staphylococcus aureus *infection and colonization in a Portuguese Internal Medicine ward*

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/ Resumo

Objetivo: Caracterizar a infeção e colonização por *Staphylococcus aureus* meticilino-resistente numa enfermaria de Medicina Interna e identificar os fatores de risco para a sua aquisição.

Métodos: Estudo observacional retrospetivo dos isolamentos de MRSA numa enfermaria de Medicina Interna entre 2012 e 2014. A informação foi obtida através da base de dados do Departamento de Controlo de Infeção e do processo clínico hospitalar.

Resultados: Houve 56 isolamentos em 4908 admissões (1,1%), com incidência decrescente ao longo dos anos. A idade média foi de 77±10.94 anos, 64% do género masculino e 52% eram dependentes nas atividades de vida diária. Apresentavam numerosas comorbilidades e fatores de risco para a infeção por MRSA: 48% tinham realizado antibióticos, 63% foram hospitalizados nos 6 meses precedentes, 13% tinham uma cultura prévia positiva para MRSA e 88% apresentavam dispositivos médicos. O tempo médio entre a admissão e o isolamento de MRSA foi inferior a 5 dias em 25% dos casos e 20% dos isolamentos consideraram-se colonizações. Nos casos de infeção (n=45), a duração média de tratamento foi de 9.3±8.11 dias, com uma taxa de cura de 46% (n=21). O isolamento de MRSA associou-se a uma demora média superior (44.1±42.23 vs. 10.8±13.5, p<0.001) e a maior mortalidade intra-hospitalar (30% vs. 9%, p<0.001). A mortalidade aos 30 dias foi de 43% (n=24) e de 59% (n=33) aos 6 meses. Seis casos (11%) tiveram re-infeção por MRSA.

Conclusão: Este trabalho revelou uma incidência decrescente de casos com isolamento por MRSA na nossa enfermaria. A infeção por MRSA esteve associada a internamentos mais prolongados e a maior mortalidade, quer a curto, quer a longo prazo, o que evidencia a importância de medidas de prevenção eficazes.

Palavras-chave: infeção por MRSA; colonização por MRSA; Portugal; Medicina Interna; medidas de prevenção

/ Abstract

Objective: *To characterize MRSA infection, colonization rates and associated risk factors among inpatients in an Internal Medicine ward.*

Design, patients and methods: *Retrospective observational study of patients with MRSA-positive cultures in an Internal Medicine ward, between 2012 and 2014. Data were obtained from the Infection Control Department database and from the hospital clinical electronic database.*

Results: *There were 56 cases in 4908 admissions (1.1%), with decreasing incidence per year. The mean age was 77±10.94 years, 64% were male and 52% were dependent in daily life activities. Patients presented with many comorbidities and risk factors for MRSA infection: 48% had received antimicrobial therapy, 63% had been hospitalized in the preceding 6 months, 13% had a previous MRSA-positive culture, and 88% presented with medical devices. The mean time from admission to MRSA-positive culture was <5 days in 25% and 20% were considered colonization. In case of infection (n=45), the mean treatment duration was 9.3±8.11 days with a cure rate of 46% (n=21). Compared to all inpatients in the ward, MRSA-positive culture was associated with a higher mean length of hospital stay (44.1±42.23 vs. 10.8±13.5, p<0.001) and in-hospital mortality (30% vs 9%, p<0.001). All-cause mortality at 30 days was 43% (n=24) and at 6 months 59% (n=33). Six cases (11%) had MRSA reinfection.*

Conclusions: *This study showed a decreasing incidence of cases of MRSA-positive cultures in our ward. MRSA infection was associated with prolonged length of hospital stay and high short and long-term mortality, which highlights the importance of effective preventive measures.*

Keywords: *MRSA Infection, MRSA colonization, Portugal, Internal Medicine, preventive measures*

/ Introduction

Staphylococcus aureus is a human commensal bacteria that colonizes the nostrils, axilla, pharynx and skin. In susceptible hosts, it can cause a broad spectrum of infections, especially in the presence of wounds or invasive devices that disrupt the skin-blood barrier.[1]

Methicillin Resistant *Staphylococcus aureus* (MRSA) strains were first described in 1961[2, 3] and are now an important cause of community and nosocomial infections worldwide.[4, 5]

Because of its high virulence and pattern of antibiotic resistance, treatment options are limited and expensive, leading to increased morbidity and mortality, longer hospitalization and higher healthcare costs.[6-10]

MRSA colonization is associated with a high risk of nosocomial infection (up to 30%) and is a major source of transmission to other patients.[11, 12] To address this matter, several infection control and prevention policies are applied worldwide, including hand hygiene programs, carrier detection, contact precaution protocols, decolonization strategies and control of antibiotic prescription for multi-drug resistant infections.[13-18] Globally, the results of these policies are heterogeneous. Decolonization of MRSA carriers with nasal mupirocin and chlorhexidine baths has shown some effectiveness in reducing MRSA infection rates and controlling MRSA spreading.[19-23]

In Europe, the prevalence of MRSA infection ranges from 5 to more than 50%, with a high prevalence in Portugal (53.8%).[24,25] We intended to describe the pattern of MRSA infection and colonization in a medical ward of a central and tertiary-care hospital in Portugal.

/ Methods

Setting and Study design

We conducted a retrospective observational study in an Internal Medicine ward of a tertiary-care hospital in Lisbon, Portugal. All patients with MRSA-positive cultures between January 2012 and December 2014 were included.

Data Collection

Whenever a MRSA positive culture is detected in the laboratory, the Infection Control and Prevention Department is notified. This department subsequently notifies the ward, to allow for the implementation of adequate precaution measures. Patients with positive cultures were thus identified through the Infection Control Department database. The clinical record of each patient was then reviewed for data collection, using the hospital electronic clinical database. Information gathered from clinical records included: demographic characteristics; comorbidities; functional status (dependent/autonomous); residence prior to admission (home, long-term care facility, nursing home, other); hospitalization or ICU stay within the previous 6 months; surgical procedures in the preceding 90 days; antibiotic use in the preceding 6 months; skin ulcers; exposure to medical devices such as endotracheal intubation, central venous catheter, urinary catheter or feeding nasogastric tube; known previous MRSA colonization or infection; length of hospital stay; main diagnosis; type of sample (sputum, exudates, blood, urine or other); type and duration of antimicrobial therapy; treatment results (cure, failure, death); recurrence of MRSA positive cultures (date and site of isolation) and mortality at 30 days, 6 months and at the date of study conclusion (31st December 2015).

Microbiological standards in our center

Specimens for culture are obtained from blood, urine, wounds, invasive devices or other, whenever infection or colonization is suspected. They are also obtained by protocol at the time of a central venous catheter withdrawal.

The samples are analyzed by an automated detection system (GeneXpert®) in the microbiology laboratory. Susceptibility tests and minimum inhibitory concentration (MIC) results are in accordance with the European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards. Positive cases are communicated to and registered in the Infection Control Department database and subsequently reported to our ward to allow for the implementation of contact isolation measures. The specific treatment or decolonization strategy is decided by the physician in charge of the patient.

Case Definition

A patient with at least one MRSA-positive culture from any type of isolate/sample. A new positive culture from any sample after resolution of MRSA infection in non-colonized patients, either in the same hospital admission or a new one, was considered a new case.

Other Definitions

MRSA Infection was considered to be present if there was a positive culture in a patient with clinical and laboratorial results suggestive of active disease. If clinical symptoms were not present at admission nor within 48 hours after hospitalization, and if MRSA-positive cultures were detected later than 5 days after admission, MRSA infection was classified as nosocomial. Otherwise, it was considered to be community-acquired.

MRSA colonization was defined as any isolate in a patient without clinical and laboratorial results suggestive of active disease.

Treatment was considered successful whenever there was clinical and laboratorial improvement after antibiotic therapy; if there was no clinical improvement and if cultures remained positive, or if death occurred and was MRSA infection-related, it was considered a treatment failure.

Death was presumed to be caused by MRSA infection if the event death and MRSA infection were clinically and time correlated, in the absence of other clinical condition responsible for the fatal outcome.

Reinfection was defined by the presence of a positive culture from any type of sample after successful treatment, in a patient with clinical and laboratorial signs suggestive of active disease.

Mortality was defined as death from any cause from admission until the end of the study period. Cause of death was obtained from death certificates.

Statistical analysis

Continuous variables were described using mean and standard deviation; categorical variables were described as proportions. Length of hospital-stay and in-hospital mortality were compared between our sample and all inpatients in the ward in the same period, with independent unpaired student t-test and two-sample independent test of proportions, respectively. Data were analyzed using STATA®.

/ Results

During the study period there were a total of 56 cases of MRSA-positive culture in 53 patients, in a total of 4908 admissions (1.1%), with decreasing incidence per year (Figure 1). The patients were slightly older comparing to all inpatients in the ward (mean age of 77±10.9 vs 75±14.6 years; p= 0.246); and 64% were male (Table I). Forty-six were living at home (82%) and 9 (16%) in long-term care institutions. Twenty-nine (52%) were dependent in daily life activities before admission. The baseline characteristics and main comorbidities are presented in Table II. Regarding risk factors for MRSA infection, 27 (48%) had received antimicrobial therapy and 35 (63%) had been hospitalized in the preceding 6 months; 6 (11%) had surgery in the previous 90 days; 7 (13%) had a previous MRSA-positive culture; and 49 (88%) presented with medical devices when samples were collected for culture, mainly urinary and central venous catheters, and nasogastric tube.

Forty cases (71%) were admitted from the emergency department, while 16 (29%) had been previously admitted in an intensive care unit and 10 (18%) in an intermediate care unit.

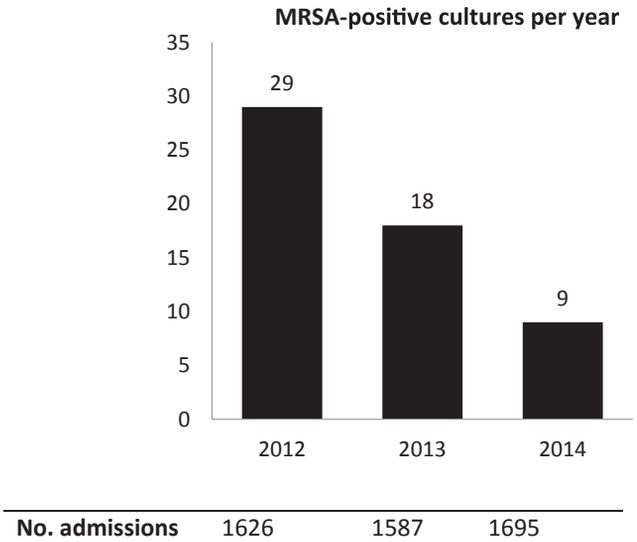

Figure 1 – Total number of admissions and MRSA positive cultures in the ward between 2012-2014

TABLE I – COMPARISON OF MRSA-INFECTION CASES AND ALL IN-PATIENTS IN THE WARD

	IN-PATIENTS (N=4908)	MRSA-INFECTION (N=56)
Age (years, mean +/- SD)	75±14.6	77±10.9
Gender (male, %)	47	64
Length of hospital-stay (days, mean +/- SD)	11±13.5	44±42.2
In-hospital mortality (%)	9	30

The mean time to MRSA-positive culture from admission was <5 days in 14 cases (25%). The types of culture samples are shown in Table III. Eleven cases (20%) were considered colonization (isolates from urine- 5, superficial wound swab – 4, rectal/nasal swab 2) and decontamination was done in 3 cases (with nasal mupirocine and clorohexidine baths for five days in all cases).

In 45 cases infection was considered to be present. The most frequent types were: respiratory tract (11), urinary (10), skin (10) and blood (9) infections, with mean treatment duration of 9.3±8.11 days. The most commonly used antibiotics were linezolid (n=27, 60%) and trimetoprim-sulfametoxazol (n=10, 22%). The pattern of antibiotic resistance was similar among all cases (Table IV).

The cure rate was 46% (n=21). In 5 cases (11%), cultures (4 from skin swabs and 1 from urine) remained positive after effective treatment despite the resolution of clinical and laboratorial signs of infection and were thus considered colonization (Table V).

The mean length of hospital-stay was significantly longer for patients with MRSA-positive culture, comparing to all inpatients in the ward in the same period (44±42.23 vs 11±13.50, p<0.001, Table I).

In-hospital mortality was 30% (n=17) (95% CI 17.99 – 42.00), two thirds of which were considered related to MRSA-infection (65%, n=11) (Table1) . MRSA-infection was associated with a significantly higher all-cause in-hospital mortality compared to all inpatients in the ward (30% vs 9%, p<0.001, Table I). All-cause mortality at 30 days after discharge was 43% (n=24) and at 6 months 59% (n=33). Six patients (11%) had MRSA reinfection after discharge (4 from skin, 1 from urine, 1 from bronchoalveolar lavage), three of which died.

TABLE II – BASELINE DEMOGRAPHIC AND RISK FACTORS DATA	MRSA -POSITIVE CASES
Age (years, mean ± SD)	77±10.9
Gender	
Male (%)	64
Female (%)	36
Comorbidities (%, n)	
Diabetes mellitus	46% (26)
Skin ulcer	41% (23)
Heart failure	30% (17)
CKD	21% (12)
Cancer	16% (8)
COPD	13% (7)
Previous systemic corticotherapy	11% (6)
Dependency before admission	52% (29)
Risk factors for MRSA infection (%, n)	
Antibiotics in the previous 6 m	48% (27)
Hospitalization in the previous 6 m	63% (35)
Surgery in the previous 90 days	11% (6)
Previous MRSA-positive culture	13% (7)
Medical devices*	88% (49)

CKD: Chronic kidney disease, COPD: Chronic Obstructive Pulmonary Disease

* urinary, central venous catheters, nasogastric tube and others

TABLE III – CULTURE SAMPLES	
TYPE OF SAMPLE	N (%)
Superficial exsudate	19 (34)
Urine	16 (29)
Blood	13 (23)
Others	14 (25)

TABLE IV – PATTERN OF ANTIBIOTIC RESISTANCE	
Gentamicin	Sensitive
Vancomycin	Sensitive (MIC:0.5-1 mcg/mL)
Teicoplanin	Sensitive
Ciprofloxacin	Resistant
Trimetoprim-sulfametoxazol	Sensitive
Linezolid	Sensitive
Erythromycin	Resistant

TABLE V – TREATMENT OUTCOME (NUMBER OF CASES)	
Outcome	**Cases (N)**
Cure	21
Colonization	11
Colonization after treatment	5
Inconclusive	2
Death	17
MRSA- related	11
Of other cause	6

/ Discussion

Identification and eradication of MRSA is of primordial importance since it has a high morbimortality. In contrast with other multi-resistant microorganisms, its transmission can be prevented by treating infections, implementing contact precautions and decolonization of carriers.[18] We observed a decreasing incidence of cases of MRSA-positive cultures in our ward during the study period, which could be due to increased awareness of this problem among physicians and effective implementation of contact precaution measures.

Although there is some controversy regarding the best decolonization strategy[16,17], it has been effective in reducing MRSA infection rates and spreading. In our hospital, there is no specific protocol and decolonization measures are applied under individualized medical decision. Despite the decrease in the incidence of MRSA isolates, there was a very low decolonization rate, perpetuating the carrier state and the consequent risk of infection. By the analysis of the clinical records we were not able to identify the reasons why decolonization was not performed. It is necessary to increase the number of nasal swabs requested for screening and to implement effective contact precautions and decolonization measures in high-risk populations.

We found MRSA isolates in elderly patients, mostly men, who presented a high burden of risk factors for MRSA acquisition which is consistent with the literature[10,26]: dependent patients, diabetes, heart failure and/or skin ulcers; a high rate of antibiotic use; hospitalization in the 6 months before admission; and more

than 60% had been admitted in intensive care or intermediate care units during the same hospital admission. The majority of isolates were nosocomial which reinforces the importance of implementing contact prevention measures and identifying and eradicating carriers.

Our data also points to the high virulence of MRSA, considering the associated low cure rates and high in-hospital and long-term mortality, with significantly higher in-hospital mortality rates compared to other inpatients. We also highlight the significantly longer length of hospital stay in MRSA-infected patients, with the inherent increase in costs and risk of other infectious and non-infectious complications.

This study was important to underline the pattern of MRSA infection in our ward and the burden of this infection on health care. The low rate of decolonization was unexpected, which may concur to the high rate of nosocomial MRSA infections.

To pursue the decreasing incidence of MRSA isolates of the previous years and avoid nosocomial infection, it is important to assure the use of decolonization strategies with quality-control measures and reinforce the contact precautions. Screening patients for MRSA carriage on admission could help in carrier's eradication and consequent prevention of MRSA spreading and reinfection.

This study has several limitations since it is a retrospective analysis with a small number of isolates. Furthermore, data were only collected from the clinical records of our center. Even though patients are usually hospitalized in their residential area, clinical and laboratorial data from admissions in other hospitals might have been missed. However, this study shows a significant clinical burden of MRSA infection which must be prevented.

To our knowledge this is the most recent study of MRSA infection and colonization in a Medical ward in Portugal where it is still an important clinical issue. Further studies are needed to understand the reality in other Portuguese hospitals countries with a similar income.

This study showed a decreasing incidence of cases of MRSA-positive cultures in our ward. The majority were nosocomial infections and occurred in patients with a high burden of risk factors. MRSA infection was associated with prolonged length of hospital stay and high short and long-term mortality. This highlights the importance of the implementation of effective preventive measures, especially protocolized decolonization strategies.

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