Revista portuguesa de saúde pública

www.elsevier.pt/rpsp

Artigo original

Methicillin-Resistant *Staphylococcus Aureus* (MRSA) in a Portuguese hospital and its risk perception by health care professionals

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ARTICLE INFO

ABSTRACT

Objective: To describe the epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA) and to assess its perception by healthcare professionals.

Design: Survey, through a two-part questionnaire.

Setting: A 441-bed district general hospital.

Participants: Part I - Inpatients over 16 years of age, in whom a non-nasal MRSA was isolated between February and August of 2005. Part II - nurses and doctors responsible for these patients.

Methods: Part I – Demographic and clinical data collected from medical notes. Part II – Perception of doctors and nurses. Observed agreement and "Kappa" statistic were used to compare perceptions. A P value lower than 0.05 was considered to be statistically significant.

Results: Of the 111 patients identified, 50.9% had history of hospitalization during the previous year, with high exposure to antimicrobial therapy and invasive procedures. Hospital stay was 4.5 times higher than the average inpatients and mortality 5.5 times higher. Proportion of MRSA was 60.0%, with an incidence density of 1.66%.

Although agreement between nurses and doctors was low, the majority admitted nosocomial origin of the MRSA and its transmission through the hands of professionals. Reinforcement of hand hygiene was considered important to manage these patients by 69.4% of nurses and 64.9% of doctors. Additionally, all nurses and 89.4% of doctors agreed on the need to isolate these patients.

Conclusions: High endemic level of MRSA detected in a susceptible population, associated with a lower awareness of management of these patients by doctors, compared with nurses, justifies a global programme to control MRSA. This programme should include consensus-based measures for management of patients, rational use of antimicrobials, and dynamic and focused educational programmes.

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Staphylococcus Aureus Resistente à Meticilina (MRSA) num hospital distrital do Grande Porto e percepção do risco pelos profissionais de saúde

R E S U M O

Palavras-chave:
MRSA
Controlo da infecção
Percepção do risco
Portugal

Objectivo: Descrever e analisar a epidemiologia do *Staphyloccocus aureus* resistente à meticilina (MRSA) num hospital distrital de 441 camas do Grande Porto, bem como a percepção que enfermeiros e médicos têm do problema.

Desenho do estudo: Estudo transversal descritivo, através da aplicação de um inquérito de duas partes.

Definição: Um hospital distrital de 441 camas.

Participantes: Parte I - doentes internados com mais de 16 anos em que foi detectado MRSA não nasal, entre Fevereiro e Agosto de 2005. Parte II – enfermeiros e médicos responsáveis pela prestação de cuidados aos referidos doentes.

Métodos: Parte I - recolha de dados demográficos, clínicos e factores de risco dos processos dos doentes. Parte II - aplicação de um inquérito a enfermeiros e médicos para análise das suas percepções. O acordo observado e a estatística "Kappa" foram utilizados para comparar as respostas entre classes de profissionais. O nível de significância adoptado foi de 5%.

Resultados: Dos 111 casos estudados, 50,9% tinham historial de internamentos até há um ano atrás e 83,8% haviam estado expostos a antibioticoterapia prévia. O tempo de internamento foi 4,5 vezes maior que a média da população internada neste hospital, e a mortalidade 5,5 vezes maior.

A prevalência de MRSA foi de 60,0% e a densidade de incidência de 1,66 casos por mil dias de internamento. A grande maioria dos profissionais admite que o MRSA é adquirido no ambiente hospitalar e que são as mãos dos profissionais de saúde a principal via de transmissão. Como medidas para gerir doentes com MRSA, 69,4% dos enfermeiros e 64,9% dos médicos referem o reforço da higienização das mãos, a totalidade dos enfermeiros e 89,4% dos médicos concordam com a necessidade de algum tipo de medidas de isolamento.

Conclusões: Constatou-se a existência de altos valores endémicos de MRSA. Os profissionais têm a percepção da associação do MRSA aos cuidados de saúde, bem como a importância das mãos dos profissionais como veículo de transmissão, no entanto a classe médica está menos sensibilizada para as medidas de gestão para estes doentes. Parece justificar-se um programa global para controlo deste microrganismo, na gestão de doentes colonizados ou infectados por MRSA, na utilização racional dos antibióticos, bem como a formação dos profissionais de saúde, com um carácter mais dinâmico e dirigido.

Introduction

Staphylococcus aureus is a Gram-positive bacterium that colonizes the skin of about 30% of healthy humans, although mainly a harmless coloniser, S. *aureus* can cause severe infection. Its oxacillin-resistant form (Methicillin-Resistant S. *aureus*, MRSA) is the most important cause of antibiotic-resistant healthcare-associated infections worldwide.[1] Of the expected 2 billion individuals carrying S. *aureus* worldwide, conservative estimates, based on either Dutch or United States of America (USA) prevalence figures, would predict that between 2 million and 53 million carry MRSA.[2] There are several studies which conclude that nosocomial MRSA infection increases morbidity, mortality, length of stay and costs.[3-7] Historically, MRSA isolates have been associated with nosocomial infections, however, in recent years, different strains with unique phenotypes have emerged in the community, and the reservoir of this community-associated MRSA (CA-MRSA) is rapidly expanding.[8] Mathematical models have shown that CA-MRSA has a high potential to become endemic in the community, and this will impact significantly on the control of MRSA in the hospital setting.[9]

For healthcare facilities, surveillance is an important and approved method to assess the incidence of infection due to multidrug-resistant bacteria and to improve infection control measures, if necessary.[10] Various protocols and guidelines have been developed in an attempt to prevent the development and slow down in the transmission of nosocomial MRSA. If healthcare professionals (HCP's) are to be successful in this objective, then understanding the epidemiology, pathogenesis and routes of transmission of MRSA in healthcare facilities

becomes critically important.[11] In this study we describe the epidemiologic characteristics of the MRSA in a Portuguese district general hospital, as well as its perception by the HCP's.

Methods

Study setting and infection control practices

This study was conducted at Pedro Hispano Hospital, a district general hospital in the north of Portugal with 441 beds. This facility, that serves a population of approximately 430,000, is part of a "local healthcare unit", which integrates the management of primary healthcare resources of the city of Matosinhos. Information about multirresistant microorganisms, including the MRSA (which is endemic in this facility) is available annually.

All patients with results positive for MRSA were treated with contact isolation measures, as recommended by the local infection control manual, based on the "Center for Disease Control and Prevention" (CDC) guidelines available at the time of the study.[12] Intensive care patients of both existing units were screened for nasal colonization at admission and every 4 days and, if positive for MRSA, decolonization was attempted with topical agents (nasal mupirocin and chlorhexidine bathing).

Participants and data collection

Between February 21 and August 31, 2005 (192 days), the prospective infection surveillance system, based on laboratory results, identified all cultures positive for MRSA. Patients were excluded from the study if they: (a) were less than 16 years old, (b) had only nasal colonization detected, (c) had died or been discharged when the result was known or (d) were treated in ambulatory care. A two part questionnaire was applied to the 111 cases who met the criteria, after it was pretested and approved by the institutional ethics board.

In the first part, the investigators recovered demographic and clinical data from the medical record of each patient and, in the second part, the questionnaire was administered to the doctors and nurses responsible for this patient, in order to assess their perception of the epidemiology of MRSA (meaning of the strain identified, source and route of transmission) as well as the proper conduct to be followed to take care of this patient.

Definitions and terms

The risk factors associated with the use of indwelling devices (peripheral and central vascular catheters, urinary catheter, gastrointestinal tube, wound drainage device, endotracheal tube or tracheostoma and hemodialysis) were considered if they were present during the last 4 days, exposure to antibiotics during the last 7 days and, in case of a surgical procedure, during the last 30 days before the recovery of the sample which detected the MRSA.

"Immunodeficiency" was considered when the patient had any immunological disease or immunosuppressive therapy (chemotherapy, radiotherapy or steroids) in high doses during at least 15 days before the recovery of the sample which detected the MRSA.[13]

The terms "single-room isolation" (isolation of patients in a single-bedded room), "cohorting" (physical segregation of a group of patients with MRSA from the other patients in a geographically distinct area of the same ward) and "barrier nursing" (use of aprons or gowns, gloves and, in some cases masks, by the HCP as the only physical barrier to transmission) were used to refer to the level of isolation, as recommended by an extensive systematic review on isolation policies.[14]

"Morbidity" estimation was based on the indicators proposed by Ducel et al.[15] and Horan and Gaynes[16], MRSA rates, using three different denominators: proportion of MRSA (percentage of strains resistant to methicillin within the total of *S. aureus* identified), the incidence (number of MRSA per 1,000 admissions) and incidence density (number of MRSA per 1,000 patient-days).

Microbiological methods

Isolates were grown on blood and chocolate agar and confirmed as *S. aureus* by colony morphology, Gram stain, catalase test and through the rapid method "Staph aureus fumouze" (Fumouze Diagnostics, Paris, France). The antimicrobial susceptibility testing was determined by the automatic system "Vitek 2" (bioMérieux, Marcy l'Etoile, France). In case of doubt, confirmation of the minimum inhibitory concentration result was performed through "E-test" (AB Biodisk, Solna, Sweden). Strains with minimum inhibitory concentrations of 4 µg/mL of oxacillin or greater were considered resistant and 2 µg/mL or less, sensitive, according to the "Clinical and Laboratory Standards Institute" guidelines.[17]

Statistical analysis

Statistical analysis was performed using the "Statistical Package for the Social Sciences" (SPSS Inc., Chicago, USA) version 13.0. Categorical variables were compared using the chi-square or Fisher's exact test. To evaluate agreement between doctors and nurses, responsible for each patient, observed agreement and the "Kappa" statistic were applied. "Kappa" statistic was assessed to quantify the extent of agreement beyond chance achieved by the two groups of HCP's considered. The level of significance adopted was 5%.

Results

Demographic characteristics and risk factors

During the 192 day study period, 111 cases were detected. The demographic characteristics of these are listed in table 1. The male gender predominated (60.4% of the studied population) and almost half (47.8%) were between 60 and

Table 1 – Demographic characteristics of the studied population (n=111)

Characteristic	N (%)
Gender	
Female	44 (39.6)
Male	67 (60.4)
Age (years)	
20-39	13 (11.7)
40-59	21 (18.9)
60-79	53 (47.8)
≥80	24 (21.6)
Origin	
Community	86 (77.5)
Acute care facility	17 (15.3)
Long-term care facility	8 (7.2)

79 years old. The majority of the patients came from the community (77.5%), but 17 of them (12.6%) were transferred from other hospitals and 8 (7.2%) from long-term care facilities.

According to table 2, more than half (50.9%) of the patients had a history of hospitalization during the previous year and almost 10% had previously been detected with MRSA. The majority of cases were identified in medical specialities (38.7%) followed by surgical (19.8%) and intermediate/intensive care department (16.2%). However it should be taken into account that 28.8% of the patients had been transferred from another ward, before the one where the MRSA was identified. A vast majority (83.8%) were exposed to antimicrobial therapy during the week before, with quinolones in 35.5% of the cases and

Table 2 – Risk factors present in the studied population (n=111)

	N (%)
General	
Hospitalization history (< 1 year)	58 (50.9[a])
MRSA history	6 (9.5[b])
Department of diagnosis	
Medical	43 (38.7)
Surgical	22 (19.8)
Intermediate/ Intensive care	18 (16.2)
Transfer from other department	32 (28.8)
Antibiotic exposure (total)	93 (83.8)
Quinolones	33 (35.5[c])
Cephalosporins	27 (29.0[c])
Macrolides	5 (5.4[c])
Immunodeficiency	14 (12.6)
Invasive Procedure Associated	
Peripheral vascular catheter	91 (82.0)
Central vascular catheter	19 (17.1)
Urinary catheter	57 (51.4)
Gastrointestinal tube	34 (30.6)
Wound drainage device	15 (13.5)
Endotracheal tube	13 (11.7)
Tracheostoma	6 (5.4)
Previous surgery (< 30 days)	54 (48.6)
Hemodialysis	7 (6.3)

[a]n=106 / [b]n=63 / [c]n=93.

cephalosporins in 29.0%. With respect to the risk factors associated with invasive procedures, 82.0% had a peripheral venous catheter and 51.4% an urinary catheter. Almost half (48.6%) had been subjected to a surgical procedure in the last thirty days and 17.1% had a central vascular catheter.

Morbidity and mortality

As listed in table 3, the mean length of stay was 40.7 days (median 31.5; range 5-182) with 20 patients (18.0%) who stayed more than 60 days.

More than one quarter of the studied population (27.0%) died in the hospital and 8 (7.2%) were transferred to other healthcare facilities. In 72.1% of the patients the MRSA was detected 48 hours after admission. The proportion of MRSA detected was 60.0%, the incidence was 11.9 per 1,000 admissions and incidence density revealed 1.66 cases per 1,000 patient-days.

Perception of the healthcare professionals

Table 4 shows the perception of the HCP's about the epidemiology of the MRSA, as well as the measures considered adequate to manage patients with positive cultures. More than 70% of the doctors and nurses considered the identified strains as hospital acquired infections, however, in the remaining cases, nurses referred twice as frequently as the doctors that the strains could be community acquired. For this question, the observed agreement was 74.2% and the Kappa value of 0.336, which corresponds to a "fair agreement" between observers.[18]

For the second question (perception about the source of the strain), 44.2% of the nurses answered the "environment", followed by 28.4% of these professionals who thought

Table 3 – Morbidity and mortality in the studied population: general and MRSA specific (n=111)

Data	N (%)
Length of stay	
Mean (days)	40.7
≤ 14	15 (13.5)
15-29	37 (33.3)
30-59	39 (35.2)
≥ 60	20 (18.0)
Type of discharge	
Home	73 (65.8)
Other hospital	8 (7.2)
Died	30 (27.0)
MRSA detection	
≤ 48 hours	31 (27.9)
> 48 hours	80 (72.1)
MRSA rates	
Proportion*	60.0 %
Incidence	11.9 ‰
Incidence density	1.66 ‰

*The proportion value is based on the CLSI definition "first isolate per patient"[17], considering the exclusion criteria of this study.

the source was a HCP. More doctors (39.8%) agreed to the hypothesis of the source being a HCP, 25.8% chose the option "own patient" and 18 doctors (19.4%) answered the "environment". For this question the observed agreement was low (22.5%) and the Kappa value (-0.045) compatible to "by chance" agreement between these two groups of professionals.

For the perception of the route of transmission, more than half of both nurses and doctors referred the hands as the main route (60.4 and 62.9%, respectively). Within this category, it was the "hands of a HCP" which was indicated most frequently (61.8% of nurses and 66.1% of the doctors). The second

option was "airborne" for nurses (22.0%) and "contaminated instrument" for doctors (21.3%). The observed agreement was 45.8% and the Kappa value (0.004) was, again, compatible to "by chance" agreement.

When asked about the conduct to be followed for the care of MRSA positive patients, two (2.1%) doctors answered "none specifically". The response "reinforce hand hygiene" was chosen by almost 70% of the nurses and by 64.9% of the doctors. All the nurses (100%) and 89.4% of the doctors agreed that the patient needed some type of isolation. Within this category, the first option was "barrier nursing" (79.6% of the nurses and 72.6% of the doctors) followed by single-room isolation (13.3% and 15.5%, respectively). The need to alter/implement antibiotic therapy was assumed by 66 doctors (70.2%).

Table 4 – Perception of nurses and doctors of the epidemiology of MRSA and measures to manage positive patients

Question	Nurses N (%)	Doctors N (%)
What do you think is the meaning of the identification of this strain?		
Observed Agreement: 74.2%	K=0.336 (p<0.001)	
Colonization	11 (11.2)	14 (14.9)
Hospital acquired infection	71 (72.5)	73 (77.7)
Community acquired infection	16 (16.3)	7 (7.4)
TOTAL	98 (100.0)	94 (100.0)
What do you think was the source of this strain?		
Observed Agreement: 22.5%	K=–0.045 (p=0.45)	
Other patient	12 (12.6)	14 (15.0)
Own patient	14 (14.8)	24 (25.8)
Healthcare professional (HCP)	27 (28.4)	37 (39.8)
Environment	42 (44.2)	18 (19.4)
TOTAL	95 (100.0)	93 (100.0)
What do you think was the route of transmission?		
Observed Agreement: 45.8%	K=0.004 (p=0.96)	
Contaminated solution	1 (1.1)	1 (1.1)
Hands (total)	55 (60.4)	56 (62.9)
Patient	13 (23.7[a])	7 (12.5[b])
HCP	34 (61.8[a])	37 (66.1[b])
Visitor	1 (1.8[a])	0 (0.0)
(doesn´t specify)	7 (12.7[a])	12 (21.4[b])
Contaminated instrument	15 (16.5)	19 (21.3)
Airborne	20 (22.0)	13 (14.6)
TOTAL	91 (100.0)	89 (100.0)
What conduct should be followed to take care of this patient?		
None in specific	0 (0.0)	2 (2.1)
Reinforce hand hygiene	68 (69.4)	61 (64.9)
Isolation of the patient (total)	98 (100.0)	84 (89.4)
Single-room isolation	13 (13.2[c])	13 (15.5[d])
Barrier nursing	78 (79.6[c])	61 (72.6[d])
Cohorting	4 (4.1[c])	3 (3.6[d])
(doesn´t specify)	3 (3.1[c])	7 (8.3[d])
Alter/ implement antibiotic therapy	– (–)	66 (70.2)
TOTAL	98 (100.0)	94 (100.0)

[a] n=55 / [b] n=56 / [c] n=98 / [d] n=84.

Kappa value calculations only considered the four main options: contaminated solution, hands, contaminated instrument and airborne.

Total values exceed 100% because participants could choose more than one option.

Discussion and conclusions

More than half of the studied sample had a history of hospitalization during the previous year and almost 10% had been previously diagnosed with MRSA, similarly to the 14.4% found by a study conducted in two terciary-care centers in Saudi Arabia.[19]

Interestingly, in the present study we found that it was in the medical department where most cases were detected, followed by surgical wards and intermediate/intensive care units, in contrast to other studies where the intensive care units (ICU) were in the first place.[19-21] This difference could be explained by the aggressive strategy to control the MRSA in both ICU's of this hospital (we are not aware if this occurred in the other studies). This information should be interpreted carefully, considering the exclusion criteria of this study, namely the fact that patients who had died when the result was known were not studied, since this could have had an influence in the number of critical patients included. Other sources of bias could be the different ratios ICU/general beds in the hospitals studied and the mobility of the patients within the facilities: we identified that 28.8% of the patients had been in other wards before the one where the MRSA was identified. A Spanish study detected an even higher value: 37.8% in patients with bacteraemia by MRSA.[22]

Monnet et al.[23] described several studies which conclude that exposure to cephalosporins, quinolones and macrolides constitutes risk factors for colonization or infection by MRSA. Similarly to our investigation, two other studies[20,22] detected an exposure to antibiotics of over 70% in a population with MRSA and, in another hospital, around 66%.[24] In contrast with the 35.5% described by us, a 640 bed USA hospital study[25] identified an exposure of 67.6% of MRSA positive patients to quinolones.

With the respect to the risk factors associated with invasive procedures, Montesinos et al.[20] likewise detected a similar proportion of patients with intravascular catheter (79%) and subjected to a previous surgical intervention (51%) but a higher exposure to urinary catheters (77%). In a Swiss study,[24] 45.7% of the MRSA colonized patients had a not specified indwelling device and 54.3% a history of surgery in the last thirty days.

The length of stay of the studied individuals was 4.5 times higher when compared to the general adult hospitalized population in this hospital (40.7 versus 9.0 days). This value

was higher than the difference found in a USA study developed in an acute care military facility, where MRSA patients had a length of stay 3.3 times higher.[26]

Although the mortality value we described may not be directly related to the mortality caused by MRSA, it may be an indication of the morbidity associated with this microorganism, as well as the susceptibility of the population it affects. For this indicator a 5.5 fold difference was found between the studied population and the general adult hospitalized population (27.0% *versus* 4.9%). Madani *et al.*[19] described a general mortality of 53.7% in a population infected with MRSA, but regarded as mortality directly associated with this infection 36.4% of the cases.

Usually an infection is considered acquired at a healthcare facility when it appears 48 hours after the admission.[16] In this study 31 patients (27.9%) were identified as MRSA positive less than 48 hours after admission, which could lead us to consider a community origin. A Portuguese study[27] involving 3,266 healthy individuals from the community detected low prevalence of MRSA nasal colonization (0.7%). However, all but 3 of our patients had classical risk factors for MRSA carriage: 6 came from other acute care facilities, 4 from long term care facilities and 18 had a history of hospitalization during the previous year.

MRSA rates in Portugal are know to be high: in 2005 the "European Antimicrobial Resistance Surveillance System" detected a proportion of resistance of 46.6% in Portugal,[1] which is in agreement with the 47.5% of resistance reported in a Portuguese study involving 9 hospitals.[28] Both values were still lower than the 60.0% detected in our study. A German study[29] identified an average value of incidence density of 2.77‰ in 38 ICU's and a French multicenter study[30] described a rise of this indicator from 0.71 to 0.96‰ between 1996 and 2000. Richet *et al.*[31] studied 90 healthcare facilities around the world and detected median values of 0.40‰ for Western Europe and hospital category<500 beds. Once again the values found were lower than the one in our study (1.66‰).

The majority of the HCP's had the perception that this MRSA strains were hospital acquired, but Kappa value identified just a "fair agreement" between nurses and doctors. A possible explanation for this would be the HCP's not taking into account the 48 hour timing generally used to distinguish hospital from community acquired infection. Considering the changing epidemiology of the MRSA, Klevens *et al.*[32] proposed a different classification of cases into three mutually exclusive groups: (a) healthcare-associated community-onset; (b) healthcare-associated hospital-onset and (c) community-associated. This is an interesting approach and should be considered in future research in this area.

Nurses identified first the "environment" and then a "member of the staff" as the possible source (opposed to the doctors who chose "member of the staff" first), perhaps because nurses spend more time on the wards and recognize the limitations of the cleaning procedures. Both groups of HCP's are concerned about being themselves the source of the MRSA, more than the option "other patient". Bearing in mind that clinical microbiological cultures fail to identify up to 85% of MRSA-colonized patients,[33] if the HCP has the perception that the other patients are not likely to be the source, this could have serious implications on the adherence to the Standard Precautions.

Slightly more doctors than nurses thought the route of transmission was the hands of a HCP. This is an interesting result considering that fewer doctors chose the option "reinforce hand hygiene" when asked about the management of MRSA positive patients. It would seem that there is a difference between the knowledge and importance of this practice and its day-to-day application. One study[34] recognized that 62% of the doctors and 72% of nurses have the perception that they practice hand hygiene more than 80% of the times before and after contact with patients, concluding that HCP's perception of the compliance with infection control measures are better than their actual practice, as demonstrated by observational studies. CDC guidelines[35] also indicate physician status as an observed risk factor for poor adherence to recommended hand-hygiene practices. It is interesting to see that a substantial number of HCP's identified the air as possible route of transmission (22% of the nurses and 14.6% of doctors). Although some studies[36,37] suggest that MRSA is recirculated in the air, especially after movement, such as in bedmaking, it is considered that the transmission of MRSA within healthcare facilities primarily occurs via carriage on the hands of healthcare workers.[11]

The fact that two doctors and none of the nurses agreed that no specific measures were necessary to take care of MRSA positive patients and that 100% nurses identified the need to isolate these patients, in contrast with just 89.4% of the doctors, is in agreement with other studies. Afif *et al.*[38] referred that the compliance to MRSA precautions is worse among doctors as compared to nurses (Odds Ratio 0.35; 95% confidence interval, 0.14 to 0.86). Seaton and Montazeri[39] described, in a population of British doctors, that 10% did not agree with the use of gloves when examining patients with MRSA and 34% did not believe in the efficacy of alcohol hand rub solutions in reducing MRSA transmission, concluding that "there is scope for improvement in awareness and knowledge about MRSA and its management". Acknowledging this problem, the recent CDC guidelines[40] advise that "improvement requires that the organizational leadership make prevention an institutional priority and integrate infection control practices into the organization's safety culture".

The high endemic values detected in our study as well as differences in the perception of the HCP's about the epidemiology and management of MRSA positive patients justify the need to implement a global infection control programme for MRSA, with consensus-based measures for management of colonized and infected patients, more effective strategies for the rational use of antimicrobials, as well as more dynamic and focused educational programmes for healthcare professionals.

Acknowledgments

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