M. Pilar Barrufet[1]
Ester Vendrell[1,2]
Lluis Force[1]
Goretti Sauca[3]
Sandra Rodriguez[1]
Encarna Martinez[1]
Elisabet Palomera[4]
Mateu Serra-Prat[4]
Josep Anton Capdevila[1,2]
Jordi Cornudella[5]
Anabel Llopis[6]
M. Asunción Robledo[7]
Crisóstomo Vazquez[8]

# Prevalence and risk factors for meticillin-resistant *Staphylococcus aureus* in an acute care hospital and long-term care facilities located in the same geographic area

[1]Internal Medicine Unit, Hospital de Mataró, Consorci Sanitari del Maresme. Mataró. Barcelona, Spain.
[2]Department of Medicine. Universitat Autònoma de Barcelona. Bellaterra (Cerdanyola del Vallès). Barcelona, Spain.
[3]Microbiology Laboratory. Hospital de Mataró, Consorci Sanitari del Maresme. Mataró. Barcelona, Spain.
[4]Epidemiology Unit, Hospital de Mataró, Consorci Sanitari del Maresme. Mataró. Barcelona, Spain.
[5]Geriatrics, El Casal de Curació. Vilassar de Mar. Barcelona, Spain.
[6]Geriatrics, Antic Hospital de Sant Jaume, Consorci Sanitari del Maresme. Mataró. Barcelona, Spain.
[7]Geriatrics, Centre Geriàtric Maresme, Mataró. Barcelona, Spain.
[8]Geriatrics, Residència Geriàtrica l'Estada. Sant Andreu de Llavaneres. Barcelona, Spain.

## ABSTRACT

To determine the prevalence and risk factors (RF) for methicillin-resistant *Staphylococcus aureus* (MRSA) during stay in 1 acute care hospital (ACH) and 4 long-term care facilities (LTCF). After obtaining the informed consent, nasal and skin ulcer swabs were taken and a survey was conducted to determine RF for MRSA. Six hundred and ninety nine patients were included, 413 LTCF and 286 ACH patients and MRSA prevalence were 22.5% and 7.3% respectively. MRSA was located in the nares, skin ulcers, and in both in 61.4%, 21.1%, and 17.5%. Among MRSA carriers, 81% of the ACH and 66.7% of the LTCF patients were only colonized. The multivariate analysis for the ACH revealed the following factors to be associated with MRSA: referral from an LTCF (OR 4.84), pressure ulcers (OR 4.32), a Barthel score < 60 (OR 2.60), and being male (OR 5.21). For the LTCF: urinary catheterisation (OR 3.53), pressure ulcers (OR 2.44), other skin lesions (OR 2.64), antibiotic treatment in ≤ 6 months, (OR 2.23), previous MRSA colonization (OR 2.15), and a Barthel score <20 (OR 1.28). Molecular typing identified 2 predominant clones Q, P, present in all centres. No relationship was found between clones and antibiotic susceptibility.

In conclusion: MRSA prevalence is high in all centres but is 3 times greater in LTCF. The risk factors most strongly associated with MRSA were pressure ulcers and a stay in an LTCF. We propose preventive isolation in these cases.

**Keywords: Methicillin-resistant *Staphylococcus aureus*, prevalence, risk factors, acute care hospital, long-term care facilities**

Correspondence:
M. Pilar Barrufet
Internal Medicine Unit. Hospital de Mataró
C/ Cirera sn. Mataró, 08304. Barcelona, SPAIN
Phone: +34 93 741770 Fax +34 93 7417702
E-mail: mbarrufet@csdm.cat

## Prevalencia y factores de riesgo de *Staphylococcus aureus* resistente a meticilina en un hospital de agudos y cuatro centros sociosanitarios de una misma área geográfica

## RESUMEN

El objetivo de este estudio es determinar la prevalencia y factores de riesgo de *Staphylococcus aureus* resistente a meticilina (SARM) en 1 hospital de agudos y 4 centros socio sanitarios (CSS) de la misma área geográfica. Después de obtener el consentimiento informado de los pacientes se efectuó un frotis nasal y de úlceras cutáneas a los pacientes ingresados en las 5 instituciones. Al mismo tiempo se pasó un cuestionario para establecer los factores de riesgo de SARM. Se estudiaron 699 enfermos, 413 en los CSS y 286 en el hospital. La prevalencia de SARM en los CSS fue del 22,5% y del 7,3% en el hospital. Las localizaciones fueron nasal 61,4%, úlceras de decúbito 21,1% y ambas localizaciones 17,5%. El 81% de los portadores de SARM en el hospital y el 66,7% en los CSS estaban exclusivamente colonizados. El análisis multivariado en el hospital mostró que eran factores independientemente asociados a SARM: proceder de un CSS o residencia (OR 4,84), tener úlceras de decúbito (OR 4,32), un índice de Barthel <60 (OR 2,60) y ser varón (OR 5,21). En los CSS los factores independientemente asociados a SARM eran el sondaje urinario (OR 3,53), las úlceras de decúbito (OR 2,44) y otras lesiones cutáneas (OR 2,64), haber tomado antibióticos en los últimos 6 meses (OR 2,23), la colonización previa por SARM (OR 2,15) y un índice de Barthel < 20 (OR 1,28). Mediante tipificación molecular se han identificado 2 clones epidémicos predominantes Q y P distribuidos en todos los centros. No se ha observado relación entre los genotipos y la sensibilidad antibiótica.

Conclusión: La prevalencia de SARM es alta en los 5 centros, siendo en los CSS tres veces superior a la del hospital. Las úlceras de decúbito y proceder de un CSS son los factores más fuertemente asociados a SARM por lo que proponemos que un aislamiento preventivo en estos pacientes.

**Palabras clave: *Staphylococcus aureus* resistente a meticilina, prevalencia, factores de riesgo, hospital agudos, centros socio sanitarios**

## INTRODUCTION

*Staphylococcus aureus* (SA) is an easily-transmitted, colonizing microorganism of the skin and mucosa. Its presence in the skin has been linked to a greater risk of infection[1], principally in patients with underlying diseases and/or patients undergoing invasive procedures[2].

The first strains of methicillin-resistant SA (MRSA) appeared in the 1960s. As MRSA spread from hospital to hospital, it increasingly became a source of nosocomial infection. MRSA is particularly likely to develop in older patients or patients with debilitating illnesses, causing skin and other serious infections[3]. In the 1990s, MRSA resistance to other antibiotics—such as macrolides, quinolones, aminoglycosides, rifampicin and glycopeptides —developed[4,5].

The ageing of the population and the chronicity of certain diseases have led to more patients being institutionalized in chronic care facilities. Colonization by MRSA is by now endemic in these institutions, with prevalence reported to be in the order of 20-25%[6]. These institutions have thus developed into important reservoirs of the microorganism and a potential source for spreading MRSA in both hospitals and the community.

Although the literature describes risk factors for colonization by MRSA, colonization prevalence tends to vary according to geographic area, type of healthcare institution, and the characteristics of the population receiving care. If a known carrier of MRSA is to be hospitalized, precautionary steps can be taken to minimize the spread of MRSA. Precautionary measures can also be implemented on the basis of an awareness of the factors that entail a high risk of colonization, even when it is not known whether or not a given patient is a carrier[7-11].

This study was designed to assess the prevalence and risk factors for MRSA in patients during stay in 1 acute care hospital (ACH) and 4 long-term care facilities (LTCF) in Barcelona (Spain). Patients from the 4 LTCF are referred to the ACH, and ACH patients are discharged to the LTCF for sub-acute and chronic treatments.

## METHODS

A cross-sectional study was conducted in December 2003 in the Hospital de Mataró (342 beds for acute patients) and in 4 long-term care centres (421 beds—ranging from 73 beds in the smallest centre to 124 beds in the largest centre).

The study was approved by the hospital Ethics and Clinical Research Committee. All patients agreed to participate in the study. Informed consent was obtained from the patients or, in the case of impaired mental state, from the responsible family member. After obtaining the informed consent, nasal and skin ulcer samples were taken from each patient and an epidemiological survey was administered in order to determine prevalence of MRSA colonization or infection during stay in the health care centres included in the study, and the factors related to the same.

The epidemiological survey, which was administered by the same medical staff, consisted of an interview and a structured review of patient medical records. In the case of patients with neurological diseases, who were not able to take part, the survey was given to the family member responsible for the patient

The epidemiological survey and the samples were obtained over a period of 15 days. Each bed was visited, and the patient examined, only once. Empty beds were not returned to. The hospital has all medical and surgical specialities, except thoracic and cardiac surgery and neurosurgery. All departments except pediatrics were included. Functional status was measured with the Barthel scale which classifies patients in the following dependency order: independent (score 100), slight (score 61-99), moderate (score 41-60), high (score 21-40) and severe (0-20).

A distinction was drawn between colonization and infection in accordance with CDC criteria[12].

Microbiological Studies: The same nursing staff took nasal and skin ulcer samples in each centre. The samples were obtained by means of a swab introduced in a tube containing a transport Stuart medium and were analyzed in the hospital microbiology laboratory.

The samples were routinely cultured by seeding in Colum-

**Table 1** Sex, age, and MRSA location for ACH and LTCF patients

| | All Patients n=699 | ACH Patients n=286 | LTCF Patients n=413 | P |
|---|---|---|---|---|
| Patients with MRSA | 114 | 21 (7.3%) | 93 (22.5%) | <0.001 |
| Women | 55.3% | 48.9% | 60.8% | |
| Age (mean±SD) | 76.1±11.9 | 72.9±13.3 | 76.6±12.9 | |
| Pressure ulcers | 111(15.9%) | 21(7.3%) | 90 (21.8%) | <0.001 |
| Location | | | | |
| Nares only | 70 (61.4%) | 13 (62%) | 57 (61.3%) | |
| Pressure ulcers only | 24 (21.1%) | 2 (9.5%) | 22 (23.6%) | |
| Both locations * | 20 (17.5%) | 6 (28.5%) | 14 (15.1%) | |
| Colonization | 70% | 81% | 66.7% | |
| Infection | 30% | 19% | 43.3% | |

*** Nares and pressure ulcers. ACH indicates acute care hospital; LTCF, long-term care facilities; SD, standard deviation**

**Table 2** **Factors associated with MRSA in the ACH: bivariate analysis**

| | OR | CI 95% | p |
|---|---|---|---|
| Referral from LTCF or residential centre | 6.75 | 2.10-21.67 | 0.004 |
| LTCF or residential centre admission, last 5 years | 5.73 | 2.15-15.25 | <0.001 |
| Pressure sores | 5.67 | 1.94-16.51 | <0.001 |
| Barthel score<60 | 3.19 | 1.14-8.89 | 0.027 |
| Being male | 2.72 | 1.02-7.22 | 0.038 |
| Hospital admission, last year (risk per day's stay) | 1.05 | 1.01-1.09 | 0.017 |

**ACH indicates acute care hospital; OR, odds ratio; CI, confidence interval; LTCF long-term care facilities**

**Table 3** **Factors associated with MRSA in LTCF: bivariate analysis**

| | OR | CI 95% | p |
|---|---|---|---|
| Vesical catheterisation | 7.18 | 3.06-16.88 | <0.001 |
| Nasogastric catheterisation | 7.13 | 1.28-39.59 | 0.033 |
| Previous MRSA colonization | 4.67 | 1.79-12.20 | 0.001 |
| Pressure ulcers | 4.28 | 2.42-7.56 | <0.001 |
| Other skin lesions | 3.50 | 1.70-7.18 | <0.001 |
| Treatment with antibiotics, last 6 months | 2.65 | 1.63-4.29 | <0.001 |
| Treatment with quinolones, last 6 months | 2.13 | 1.14-3.98 | 0.017 |
| Barthel score<20 | 2.10 | 1.20-3.69 | 0.046 |

**LTCF indicates long-term care facilities, OR, odds ratio; CI, confidence interval.**

bia blood-agar and blood-agar supplemented with antibiotics (Columbia CAN agar) for 48 hours. Isolates identified as SA underwent an antibiogram using the disk diffusion technique and applying the CLSI criteria guidance[13]. All the strains were typed by DNA analysis based on pulsed-field electrophoresis (genotyping was performed by macrorestriction analysis of *SmaI*-digested DNA by pulsed-field gel electrophoresis (PFGE)[14].

We analyzed the prevalence of MRSA, MRSA infection/colonization sites, and the infection and colonization percentages. A descriptive analysis was also made of the sensitivity and clone distribution patterns. A bivariate analysis was conducted in order to study the MRSA risk factors. For the categorical variables we used the chi-square test or Fisher exact test, and for the continuous variables we used the Student t test (for normally distributed variables) or Mann-Whitney U test (for non-normally distributed variables). The odds ratio (OR) for a confidence interval of 95%, was used as an association measure, estimated using logistic regression. All variables that were significant in the bivariate analysis were included in the multivariate analysis.

Patient Evaluation and Interventions: pre-established control measures were applied to the MRSA carriers at each centre, namely isolation and nasal decontamination. Patients with MRSA infections according to CDC criteria[12] were treated with antibiotics.

## RESULTS

A total of 699 patients were included in the study, 413 (59.1%) of whom were LTCF patients and 286 (40.9%) of whom were ACH patients. Women represented 58.1% of the total and mean age was 72.6±16.5 years (range 16.8-101.6).

Of the 413 LTCF patients, 63.4% were women, and mean age was 76.6±12.9 years. Of the 286 ACH patients, 50.3% were women, and mean age was 66.3±19.2 years ($P$<0.001). Given that the backgrounds and clinical characteristics of the ACH and LTCF patients were statistically different, the study of MRSA risk factors was performed separately for the 2 populations.

MRSA was isolated in 114 colonized or infected patients, 21 (18.4%) in the ACH and 93 (81.6%) in the LTCF ($P$<0.001). MRSA prevalence in the ACH was 7.3%, and in the LTCF was 22.5% (35.5%, 25.8%, 21.5% and 17.2% in each of the centres). Sex, age, proportion of patients with pressure ulcers and MRSA location for all included patients are shown in table 1.

The factors associated with MRSA in the bivariate analysis for the ACH and LTCF are shown in tables 2 and 3. In the ACH the multivariate analysis showed that the following factors were independently associated with MRSA: referral from a LTCF (OR 4.84), pressure ulcers (OR 4.32), a Barthel score < 60 (OR 2.60), and being male (OR 5.21) (table 4). In the LTCF multivariate analysis the factors independently associated with MRSA were: urinary catheterisation (OR 3.53), pressure ulcers (OR 2.44), other skin lesions (OR 2.64), antibiotic treatment within the previous 6 months (OR 2.23), previous MRSA colonization (OR 2.15), and a Barthel score < 20 (OR 1.28) (table 5).

Antibiotic sensitivity was studied for 155 strains, 38% of which were sensitive to erythromycin, 78% to clindamycin, 81% to gentamicin, and 100% to trimethoprim-sulfamethoxazole, rifampin, and vancomycin. All the strains were resistant to ciprofloxacin. Molecular typing of all the strains was performed by DNA analysis based on pulsed-field electrophoresis. The following clones were detected: Q, 53.8%; P, 27.6%; 1, 10.9 %, and 2, 3, 4 and 5, 7.7%. Clone Q was the most frequent in all the LTCF, and constituted 94.4% of all the clones detected at these centres. Clone P was also prevalent in 3 of the centres, being detected in around 41% of cases. Clone 1 was prevalent

**Table 4** Factors independently associated with MRSA in the ACH: multivariate analysis

| | OR | CI 95% | p |
|---|---|---|---|
| Being male | 5.21 | 1.38-19.65 | 0.015 |
| Referral from LTCF or residential centre | 4.84 | 1.00-23.51 | 0.050 |
| Pressure sores | 4.32 | 1.14-16.70 | 0.032 |
| Barthel score<60 | 2.60 | 0.87-7.79 | 0.087 |

ACH indicates acute care hospital; OR, odds ratio; CI, confidence interval; LTCF, long-term care facilities.

**Table 5** Factors associated with MRSA in the LTCF: multivariate analysis

| | OR | IC 95% | p |
|---|---|---|---|
| Vesical catheterisation | 3.53 | 1.36-9.18 | 0.009 |
| Other skin lesions | 2.64 | 1.09-6.41 | 0.003 |
| Pressure ulcers | 2.44 | 1.25-4.76 | 0.009 |
| Treatment with antibiotics, last 6 months | 2.23 | 1.31-3.79 | 0.003 |
| Previous MRSA colonization | 2.15 | 0.71-6.44 | 0.174 |
| Barthel score<20 | 1.28 | 0.69-2.39 | 0.438 |

LTCF indicates long-term care facilities OR, odds ratio; CI, confidence interval

in 1 LTCF in 32% of all cases. In the ACH, clones P and Q predominated, constituting 45.7% and 42.9% respectively of all clones detected. No relationship could be established between genotypes and antibiotic susceptibility.

## DISCUSSION

Few studies have been conducted in Spain on the prevalence of MRSA in ACH and LTCF, nor is it known to what degree LTCF have a bearing on the spread of MRSA to ACH and to the community[14,15].

The main strategy currently applied in Spanish hospitals and aimed at restricting the spread of MRSA is to monitor clinical samples that result positive for MRSA. A recently published study reveals that there are considerable differences among Spanish hospitals in applying MRSA control measures[15].

The results of our study indicate that MRSA prevalence is high, particularly in LTCF, with a prevalence rate—for our study—that was 3 times higher than in the ACH. These data, which corroborate the conclusions of other studies[6,16-18], attest to the fact that LTCF act as a reservoir for the SA microorganism and may contribute to the spread of MRSA in ACH and in the community.

In our study, the percentage of LTCF patients with MRSA identified as having infections is 33.3%, a higher percentage than described in other series of geriatric patients[16]. That a high level of infection may be associated with long-term colonization in LTCF patients is a conclusion which is corroborated by Muder et al,[19] who monitored patients admitted to LTCF over a period of 2 years and observed that colonization both preceded and increased the risk of infection (OR 3.7).

Confirming other studies[20,21] our results show that pressure ulcers, urinary catheterisation, treatment with antibiotics, and previous colonization are risk factors associated with MRSA in LTCF. Our finding of an association between colonization and poor functional status is also corroborated elsewhere[18]. With regard to antibiotic use, some studies have reported an association between MRSA colonization and the use of fluoroquinolones[22]. In our series, quinolone administration was not a factor that was independently associated with MRSA, although, when patients had taken quinolones, the relative risk of MRSA was 2.13. Pressure ulcers, poor functional status, being referred by an LTCF and being male were also independently associated with MRSA in ACH. Although this last finding corroborates those of other authors[9,11], the reason for the association is uncertain, and in an analysis of factors associated with sex, such as smoking and chronic obstructive bronchopneumopathy we found no confounding variable.

Most authors agree that patients colonized by MRSA have higher incidence of staphylococcal infections than non-colonized patients[7,8]. In an observational study of patients with first-time MRSA colonization, Huang et al[8] observed that, over a monitoring period of 18 months, 29% of patients had become infected due to SA. Identifying patients exposed to a greater risk of colonization would enable suitable control mechanisms to be established. MRSA screening in intensive care units has been shown to be cost effective[23]. However, screening in emergency departments is another matter, given that the circumstances in which care is provided imply significant functional difficulties and increased costs. Establishing which patients are at a high risk of being MRSA carriers would indicate when screening was appropriate. Given that, in our study, the existence of pressure ulcers and referral from a LTCF are both strongly associated with MRSA, we are of the opinion that patients with either of these risk factors should be screened for MRSA prior to admission to hospital. Preventative isolation is advisable until potential MRSA-carrier status has been established.

All the strains studied were resistant to ciprofloxacin, thus corroborating the high degree of resistance to quinolones described in other studies[24]. The clones Q, P were the most frequent detected in PFGE. These two predominant genotypes have been previously described as belonging to the clonal complex CC5[25] related with the pediatric clone ST5-IV[26]. The

first clones isolated from this clonal complex appeared in Spain in 1996[14]. About 18% of the strains (clones 1, 2, 3, and 4) could not be typed by pulsed-field electrophoresis with genes previously described.

For patients at a high risk of MRSA, sensitivity patterns need to be taken into account when empirically choosing an antibiotic to treat infection. Given that 100% of the strains were sensitive to rifampin and cotrimoxazole for our series, the combination of these antibiotics may represent an alternative therapy choice in certain circumstances in patients for which there is no suspicion of bacteraemia.

In conclusion, MRSA prevalence in the ACH and LTCF analyzed in our study is high. Given that pressure ulcers and stays in an LTCF are the 2 factors most strongly associated with colonization, it would seem logical to recommend systematic MRSA screening and preventative isolation of these categories of patients while awaiting screening results.

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