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# *Staphylococcus aureus* infections and factors associated with resistance to methicillin in a hospital emergency department

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## ABSTRACT

**Objective.** Assessment of the characteristics of patients with *Staphylococcus aureus* (SA) infections, and factors associated with resistance to methicillin in a hospital emergency department (ED) in Spain.

**Materials and Methods.** All adult patients admitted between January 2007 and December 2010 with a SA infection confirmed by a positive culture in a sample obtained in the hospital emergency department were selected for enrolment. Epidemiological, clinical, therapeutic and microbiological variables were retrospectively collected from the patients' medical charts. The variable assessed within the primary outcome of the study was the isolation of methicillin resistant *Staphylococcus aureus* (MRSA). For the purpose of the analysis, the sample was divided in terms of the presence or not of the resistance to methicillin and a logistic regression analysis was performed to identify the factors associated with isolation and empirical antibiotic coverage of MRSA.

**Results.** A total of 207 patients with a confirmed SA infection were included in the study analysis, with a mean age of 64.7 (SD 20) years. MRSA was isolated in a total of 63 (30.4%) patients, and a linear incremental trend was observed over the course of the study ( $p=0.047$ ). MRSA was empirically covered in the emergency department on an average rate of one in three patients. Independent factors associated with the isolation of MRSA were: age above 65 years [OR 2.97 (95% CI 1.24 to 7.1),  $P = 0.014$ ], severe baseline functional dependence [OR 2.41 (95 % 1.02 to 5.69),  $P = 0.045$ ], chronic obstructive pulmonary disease [OR 4.83 (95% CI 1.88 to 12.42),  $P = 0.001$ ], history of antibiotic treatment within the previous 2 months [OR 4.94 (95% CI 2.27 to 10.76),  $P < 0.001$ ] and a confirmed urinary infection [OR 5.98 (95% CI 1.65 to 21.69)  $p = 0.007$ ]. Independent factors associated with empiric coverage of MR-

SA in the ED were history of antibiotic treatment within the previous 2 months [OR 3.88 (95% CI 1.76 to 8.57),  $P < 0.001$ ] and the presence of a catheter device [OR 6.28 (95% CI 1.64 to 24.07),  $P = 0.007$ ].

**Conclusions.** Resistance to methicillin appears to be increasingly frequent in patients infected with SA admitted in our emergency department and there appears to be a need for a more optimal empiric antibiotic treatment in these patients.

## Infección por *Staphylococcus aureus* y factores asociados con la resistencia a meticilina en un servicio de urgencias hospitalario

## RESUMEN

**Objetivo.** Determinar las características de los pacientes con infección estafilocócica, y los factores asociados a la resistencia a meticilina en un servicio de urgencias hospitalario (SUH) en España.

**Material y Métodos.** Se seleccionaron todos los casos de adultos ingresados por una infección causada por *Staphylococcus aureus* (SA) demostrada mediante un cultivo positivo en la muestra obtenida en un servicio de urgencias hospitalario entre enero de 2007 y diciembre de 2010. Se recogieron de forma retrospectiva variables epidemiológicas, clínicas, terapéuticas y microbiológicas de la historia clínica. La variable resultado principal fue el aislamiento de SARM. Para el análisis, la muestra se dividió en función de la presencia o no de la resistencia meticilina y se realizó un análisis de regresión logística con el fin de identificar los factores asociados al aislamiento y la cobertura antibiótica empírica de SARM.

**Resultados.** Se incluyeron 207 pacientes infectados por SA con una edad media de 64,7 (DE 20) años. El SARM se aisló en un total de 63 (30,4%) pacientes. La cobertura empírica en urgencias para SARM se realizó en uno de cada tres casos. Los factores independientes asociados al aislamiento de SARM fueron: el tener más de 65 años [OR 2,97 (IC95% 1,24-7,1);  $p=0,014$ ], la dependencia funcional basal

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grave [OR 2,41 (IC95% 1,02-5,69);  $p=0,045$ ], la enfermedad pulmonar obstructiva crónica [OR 4,83 (IC95% 1,88-12,42);  $p=0,001$ ], la toma de antibióticos los 2 meses previos [OR 4,94 (IC95% 2,27-10,76);  $p < 0,001$ ] y el foco infeccioso urinario [OR 5,98 (IC95% 1,65-21,69)  $p=0,007$ ]. Los factores independientes asociados a la cobertura empírica para SARM en urgencias fueron la toma de antibióticos en los dos meses previos [OR 3,88 (IC95% 1,76-8,57);  $p<0,001$ ] y el ser portador de catéter [OR 6,28 (IC95% 1,64-24,07);  $p=0,007$ ].

**Conclusiones.** La resistencia a metilina es cada vez más frecuente en las infecciones estafilocócicas, y existe la necesidad de realizar una mejor adecuación antibiótica en el tratamiento empírico en los servicios de urgencias.

## INTRODUCTION

*Staphylococcus aureus* (SA) is one of the most frequently isolated microorganisms in humans, causing a broad spectrum of infectious conditions ranging from sepsis to infections of skin and soft tissue, endocarditis, bacteraemia associated with indwelling medical devices, necrotizing pneumonia, urinary tract infections, as well as arthritis and osteomyelitis. Recent studies have documented a high rate of resistance to antibiotics in SA isolates in Spain, and especially resistance to methicillin<sup>1</sup>. This fact, in conjunction with a possible misuse of antibiotics, the ability of bacteria to exchange the genetic material conferring antimicrobial resistance, as well as the effect of globalization, emphasize the overall importance of the treatment of the infections caused by SA as a major healthcare problem.

Traditionally, the MRSA as a pathogen has primarily been associated with the infections acquired within hospital settings. However, in recent years an increased prevalence of community acquired MRSA infections has been reported<sup>2-4</sup>. These results may be related both to the high prevalence of colonization in patients admitted to nursing homes or long-term care facilities<sup>5-7</sup>, as well as the increasing incidence of MRSA necrotizing infections in young adults with no known risk factors or contact with the healthcare environment<sup>8-9</sup>. Furthermore, community acquired infections by MRSA appear to be an emerging issue worldwide, specially in United States<sup>10</sup>, whilst the exact risk factors still appear to be insufficiently elaborated. Taking all this into account, a different approach to the empiric antibiotic treatment of staphylococcal community acquired infections appears to be warranted.

Infections constitute one of the primary pathologies diagnosed in the hospital emergency departments (ED). The ED is also considered a gateway to the hospital, whilst it also reflects in a reliable manner the social and health-related changes occurring in the community. Here, for example, as a consequence of an aging population as well as the overall developments within the healthcare system, an increasing prevalence of elderly or immunocompromised patients, as well as patients with indwelling medical devices, institutionalized patients or those originating from nursing or long-term care centers are being

admitted in the ED. On the other hand, an important percentage of antimicrobial treatments are initiated during the very stay in the ED, most of these being done empirically, due to the limited availability of the rapid microbiological techniques that might enable a more directed antibiotic treatment<sup>11-12</sup>. Furthermore, this situation may also be influenced by the absence of an enabling environment in the ED, due to periods of saturation and the difficulty in obtaining the adequate information regarding the MRSA risk factors<sup>13-14</sup>. Finally, an improper selection of the initial antibiotic treatment leads to an increased mortality regardless of the subsequent modifications in correlation with the results of the microbiology testing<sup>15-16</sup>. In addition to the aspects related to the posterior clinical evolution of these patients, an inadequate empirical antimicrobial treatment against MRSA is also associated with a longer hospital stay and a higher overall treatment cost<sup>17-19</sup>.

Previous studies reported an increased prevalence of MRSA in EDs<sup>20-22</sup>, but there appears to be a lack of data regarding the exact nature of the predictive factors associated with an MRSA infection in the ED. The aim of this study was therefore to determine the characteristics of the patients with SA infection and factors associated with resistance to methicillin admitted in an ED in Spain.

## METHODOLOGY

**Patient selection.** A retrospective case series study was performed involving all adult patients hospitalized for a SA infection confirmed by a positive culture in samples obtained in the emergency department of a tertiary hospital center during the period of January 2007 through December 2010. Patients were identified through a Microbiology Department database and only a single episode per patient was considered during the study period.

**Study Setting.** The San Carlos Clinical Hospital is a tertiary, urban, teaching hospital, with an assigned area of approximately 500,000 patients in the Autonomous Community of Madrid. The ED attends an average of 450 patients per day, with one out of four being elderly patients.

**Variables.** Epidemiological, clinical, microbiological and therapeutic variables were retrospectively collected from patient's medical charts. The independent variables analyzed in the study included age, patient personal history (including the history of diabetes mellitus, renal failure, chronic liver disease, chronic obstructive pulmonary disease, rheumatoid arthritis, HIV infection, solid organ and/or hematological malignancies, or intravenous drug abuse), treatment (chronic corticosteroid therapy, biological therapy and/or chemotherapy), patient's provenience prior to the ED admission (home, long-term care institution, nursing home), the degree of baseline functional dependence status as per the Barthel index, prior hospital admissions within the previous month, history of antibiotic treatment in the last two months, including the class of antibiotic administered (beta-lactam, quinolone, macrolide, aminoglycoside, combination therapy or other), prior colonization by SA, the type

of infection (urinary infection, skin and soft tissue, respiratory, infections associated with an indwelling medical device, or other infections), hospital ward of the subsequent hospital admission upon ED discharge (medical, surgical, intensive care unit, short stay unit), the empirical antibiotic treatment initiated in the ED, the risk factors for multidrug-resistant Gram-positive microorganisms<sup>23</sup> (the presence of a catheter device or prostheses, hemodialysis and/or the presence of skin ulcers) and the type of sample obtained in the ED for microbiology analysis (sputum, exudates, blood, urine or other). The collection and processing of the samples was performed according to the procedures established by the Department of Microbiology. The study primary outcome variable was the isolation of MRSA in the clinical sample cultures taken in the ED. We included indistinctively both the infections by clonal variants of the hospital strains of MRSA (HA-MRSA), usually isolated in healthcare related infections (patients originating from day hospitals, undergoing dialysis or homecare of skin ulcers, patients with indwelling medical devices, or receiving previous antibiotic treatment, etc.), as well as the infections by the community acquired variants of methicillin-resistant *Staphylococcus aureus* (CA-MRSA), usually causing community acquired necrotizing infections in patients with no known recent contact with the healthcare setting<sup>23</sup>.

**Microbiology assessments.** Biologic samples proceeding from ED were cultured in standart culture media (BioMérieux®). We identified *Staphylococcus aureus* using VITEK panels (bioMérieux SA, Marcy l'Etoile, France), MicroScan panels (Dade MicroScan, West Sacramento, California, USA), WIDER system (Francisco Soria Melguizo SA, Madrid, Spain) or MALDI-TOF (Bruker Microflex LT Biotyper). The MICs were confirmed using agar dilution methods following the guidelines of the Clinical and Laboratory Standards Institute

**Statistical analysis.** With respect to the statistical analysis, the qualitative variables were presented as absolute numbers and their frequency distribution. Quantitative variables were presented as mean and standard deviation (SD). For the purpose of the analysis, the sample was divided in terms of the presence or absence of resistance to methicillin. We used the Student t test for quantitative variables, whilst for the analysis of the qualitative variables a chi-square test was performed, or the Fisher's exact test in case that more than 25% of the expected frequencies were less than 5. To identify factors associated with isolation and empiric antibiotic coverage of MRSA, we performed a logistic regression analysis to control the effects of the confounding factors. We calculated the odds ratio (OR) and confidence intervals at 95% (CI95%). Differences were considered to be significant for  $p < 0.05$ . The processing and analysis of the data was performed using the SPSS 15.0 statistical software.

## RESULTS

A total of 207 patients with a confirmed SA infection were included in the study, resulting in a mean age of the population analyzed of 64.7 (SD 20) years. Noteworthy, one in four patients on an average scale had some degree of functional dependency and only an average of one patient in ten patients analyzed was referred from a nursing home or a long-term stay center. The most common type of infection in the overall population was skin and soft tissue infections (42%). Additionally, MRSA was isolated in a total of 63 (30.4%) patients, whilst the most common types of MRSA confirmed infections were respiratory infections in 23 cases (36.5%), followed by infections of the skin and soft tissue in 20 cases (32%) and urinary tract infections in 11

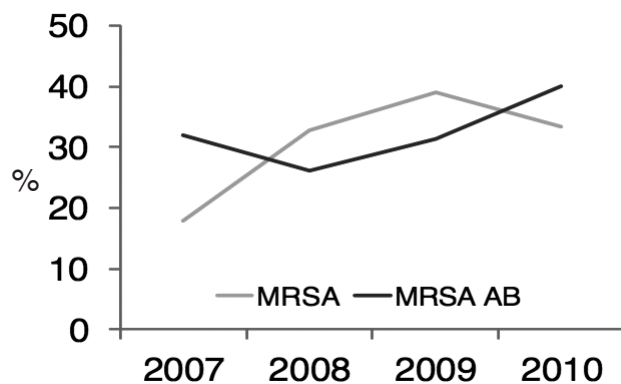


Figure 1

Isolation of MRSA and empiric antibiotic coverage. MRSA. Methicillin-resistant *Staphylococcus aureus*; MRSA AB: Antibiotic active against methicillin-resistant *Staphylococcus aureus*. Linear association of the isolation of MRSA ( $p=0,047$ )

**Table 1** Patient characteristics and factors associated with an MRSA infection

	Total sample	MSSA	MRSA	P
n	207	144	63	
Age	64,7 (SD 20)	60,95 (SD 21,5)	73,29 (SD 13,6)	< 0,001
<b>Type of infection</b>				<b>0,008</b>
Skin and soft tissue	88 (42,51)	68 (47,2)	20 (31,7)	
Indwelling medical devices	19 (9,17)	17 (11,8)	2 (3,2)	
Bone and joint infections	12 (5,79)	8 (5,6)	4 (6,3)	
Respiratory	57 (27,53)	34 (23,6)	23 (36,5)	
Urinary	19 (9,17)	8 (5,6)	11 (17,5)	
Other	12 (9,17)	9 (6,3)	3 (4,8)	
<b>Patient origin</b>				0,198
Home	181 (87,4)	129 (89,6)	52 (82,5)	
Nursing home	9 (4,3)	4 (2,8)	5 (7,9)	
Long-term care center	9 (4,3)	7 (4,9)	2 (3,2)	
Other	8 (3,9)	4 (2,8)	4 (6,3)	
<b>Previous hospitalization</b>	67 (32,4)	39 (27,1)	28 (44,4)	<b>0,014</b>
<b>History of antibiotic treatment</b>	72 (34,8)	37 (26,1)	35 (55,6)	< 0,001
<b>SA Colonization</b>	21 (10,1)	15 (10,4)	6 (9,5)	0,845
<b>Basal functional status</b>				<b>0,004</b>
Independent	158 (76,3)	118 (81,9)	40 (63,5)	
Partially dependent	31 (15)	19 (13,2)	12 (19)	
Dependent	18 (8,7)	7 (4,9)	11 (17,5)	
<b>Co-morbidities</b>				
Onco-haematological	50 (24,2)	30 (20,8)	20 (31,7)	0,097
Diabetes mellitus	53 (25,6)	32 (22,2)	21 (33,3)	0,097
Renal insufficiency	50 (24,2)	28 (19,4)	22 (34,9)	<b>0,018</b>
Chronic hepatic disease	26 (12,6)	20 (13,9)	6 (9,5)	0,374
COPD	38 (18,4)	16 (11,1)	22 (34,9)	< 0,001
Rheumatoid arthritis	11 (5,3)	7 (4,9)	4 (6,3)	0,669
HIV	9 (4,3)	8 (5,6)	1 (1,6)	0,195
<b>Risk factors</b>				
Presence of a catheter device	27 (13)	19 (13,2)	8 (12,7)	0,908
Dialysis	18 (8,7)	16 (11,1)	2 (3,2)	0,061
Chronic ulcers	28 (13,5)	18 (12,5)	10 (15,9)	0,498
Presence of a urinary catheter	12 (5,8)	5 (3,5)	7 (11,1)	<b>0,032</b>
Intravenous drug abuse	8 (3,9)	8 (5,6)	0 (0)	0,056
Prosthesis	17 (8,2)	12 (8,3)	5 (7,9)	0,913
Chronic corticosteroid therapy	46 (22,2)	21 (14,6)	25 (39,7)	< 0,001
Biologic therapy	11 (5,3)	8 (5,6)	3 (4,8)	0,815
Chemotherapy	25 (12,1)	16 (11,1)	9 (14,3)	0,531

**Table 1** Patient characteristics and factors associated with an MRSA infection (cont.)

	Total sample	MSSA	MRSA	P
<b>Sample type</b>				<b>0,006</b>
Sputum	32 (15,5)	19 (13,2)	13 (20,6)	
Exudates	32 (15,5)	30 (20,8)	2 (3,2)	
Blood	63 (30,4)	44 (30,6)	19 (30,2)	
Urine	13 (6,3)	6 (4,2)	7 (11,1)	
Other	67 (32,1)	45 (31,3)	22 (34,9)	
<b>Type of antibiotic administered in the ED</b>				<b>&lt; 0,001</b>
Beta-lactam	46 (25,7)	28 (22,4)	18 (33,3)	
Quinolone	27 (15,1)	20 (16,0)	7 (13,0)	
Macrolide	6 (3,4)	6 (4,8)	0 (0)	
Cloxacillin	26 (14,5)	24 (19,2)	2 (3,7)	
Vancomycin	36 (20,1)	28 (22,4)	8 (14,8)	
Teicoplanin	7 (3,9)	4 (3,2)	3 (5,6)	
Linezolid	11 (6,1)	3 (2,4)	8 (14,8)	
Daptomycin	2 (1,1)	1 (0,8)	1 (1,9)	
Other	14 (7,8)	11 (8,8)	3 (5,6)	
<b>MRSA coverage</b>	<b>56 (27,1)</b>	<b>36 (25)</b>	<b>20 (31,7)</b>	<b>0,151</b>

Quantitative variables are expressed as media  $\pm$  standard deviation, and qualitative as total number (percentage). The functional status was classified in accordance with the Barthel scale as: independent (100 points), partially dependent (99-61), y dependent ( $\leq 60$ ). SA: *Staphylococcus aureus*; MSSA: methicillin sensitive *Staphylococcus aureus*; MRSA: methicillin resistant *Staphylococcus aureus*; ED: emergency department; COPD: chronic obstructive pulmonary disease; SD: standard deviation.

cases (17.5%). The most frequent empirical antibiotic treatment in the overall population was beta-lactams in 46 cases (26%), followed by vancomycin in 36 cases (20%) and quinolones in 27 (15%). Empirical antibiotic treatment with coverage of MRSA was initiated in a total of 56 (27%) patients (table 1).

With respect to the evolution of the prevalence of the SA isolates resistant to methicillin in terms of years, a linear growth trend ( $p = 0.047$ ) was documented throughout the study period. Additionally, an increase in the prescription of antimicrobial coverage against MRSA was also observed in this period, although the correlation failed to achieve statistical significance ( $p = 0.463$ ) (figure 1).

Regarding the factors associated with the isolation of MRSA, we detected the following: age ( $p < 0.001$ ), the patient's baseline functional status ( $p = 0.004$ ), history of renal failure ( $p = 0.018$ ), chronic obstructive pulmonary disease ( $p < 0.001$ ), the presence of a urinary catheter ( $p = 0.032$ ), chronic corticosteroid therapy ( $p < 0.001$ ), type of infection ( $p = 0.008$ ), previous hospitalization with the past month ( $p = 0.014$ ) and history of antibiotic treatment within the 2 previous months ( $p < 0.001$ ) (table 1).

Furthermore, the multivariate analysis confirmed five independent factors associated with the isolation of MRSA: age above 65 years [OR 2.97 (95% CI 1.24 to 7.1),  $P = 0.014$ ], severe baseline functional dependence [OR 2.41 (95% CI 1.02 to

5.69),  $P = 0.045$ ], chronic obstructive pulmonary disease [OR 4.83 (95% CI 1.88 to 12.42),  $P = 0.001$ ], history of antibiotic treatment within the 2 previous months [OR 4.94 (95% CI 2.27 to 10.76),  $P < 0.001$ ] and a urinary infection [OR 5.98 (95% CI 1.65 to 21.69)  $p = 0.007$ ] (table 2).

When analyzing the antibiotic treatments initiated in patients with a confirmed MRSA infection, it should be noted that on an average scale, the empiric coverage of this microorganism was considered in only one out of three cases admitted in our ED (table 1). After performing the multivariate analysis, were identified the following independent factors associated with the MRSA empirical coverage: history of antibiotic treatment within the 2 previous months [OR 3.88 (95% CI 1.76 to 8.57),  $P < 0.001$ ] and the presence of a catheter device [OR 6.28 (95% CI 1.64 to 24.07),  $P = 0.007$ ], as well as a positive trend in patients with indwelling medical devices [OR 4.46 (95% CI 0.83-23, 91),  $P = 0.081$ ] (table 3).

## DISCUSSION

The present study documents that on an average, one in three patients admitted in our emergency department for a confirmed SA infection presented resistance to oxacillin, whilst this percentage also showed a linear increasing trend over the years of the study.

**Table 2** Factors associated with MRSA isolation. Multivariate Analysis

Variable	OR	CI 95%	P
Age > 65 years	2,97	1,24-7,10	<b>0,014</b>
Functional dependence	2,41	1,02-5,69	<b>0,045</b>
COPD	4,83	1,88-12,42	<b>0,001</b>
History of antibiotic therapy	4,94	2,27-10,76	<b>&lt; 0,001</b>
Renal insufficiency	2,34	0,96-5,68	0,061
Urinary infection	5,98	1,65-21,69	<b>0,007</b>
Respiratory infection	1,57	0,63-3,91	0,330
Indwelling medical device	0,27	0,48-1,52	0,138
Bone and joint infection	3,65	0,80-16,62	0,094
Other	1,21	0,20-7,17	0,834
Skin and soft tissue infection	Reference		

COPD: chronic obstructive pulmonary disease. The variables included in the analysis were age, type of infection, prior hospitalization, history of antibiotic treatment, patient's functional status, renal failure, chronic obstructive pulmonary disease, presence of a urinary catheter, chronic corticosteroids therapy.

In a recent publication, Hadler et al.<sup>10</sup> show a general reduction in MRSA isolates. It could be related with hospital measures control. In this work, authors find an increase, but around 5% of CA-MRSA and a decrease of nosocomial MRSA under 10%. The percentage of HA-MRSA remains constantly around 15% of isolates. This decrease was also reported specifically in MRSA nosocomial pneumonia<sup>23</sup>, however, these studies are biased owing to selection by culture positivity, which are only requested in less than 15% of cases.

In Spain, an increase in the percentage of CA-MRSA in the emergency departments, especially in infections of skin and soft tissue, was described<sup>24-26</sup>. None the less, based on the results of this study, in our health area most of the community acquired MRSA infections appear to belong to the group of infections previously denominated as healthcare related, given the overall profile of the population included in our study reporting a higher mean age, a significant degree of comorbidity and/or baseline functional dependence, and a high percentage of previous hospital admission and a recent history of antibiotic treatment. It should also be noted that although in our setting, the prevalence of resistance to methicillin in these infections is not negligible, it still remains far from the results reported in the epidemiological studies performed in the US emergency departments, where the prevalence of MRSA infection of skin and soft tissue appears to round some 60% in certain cases<sup>27</sup>. Still, our results do support the notion that the presence of MRSA is to be taken into consideration when it comes to staphylococcal infections in the emergency departments in Spain, and consequently should also be taken into account when starting the empirical antibiotic prescription in these patients.

As previously noted, the principal independent risk factors associated with an MRSA infection in our study were age above

65 years, certain degree of functional dependence, chronic obstructive pulmonary disease, history of antibiotic treatment in the previous two months and the presence of a urinary infection. Previous studies performed in similar patient populations already highlighted the age and the recent history of antibiotic treatment as a risk factor for MRSA skin and soft tissue infection<sup>28-31</sup>, as well as to some degree the level of functional dependence and chronic pulmonary comorbidity<sup>31</sup>. Here we consider it to be important to point out that the presence of a chronic obstructive pulmonary disease and baseline functional impairment could also be explained as variables closely related to an increased number of cycles of antibiotics therapy, frequent hospitalizations and other forms of healthcare, which on the other hand has by itself been associated with and increased prevalence of MRSA colonization in ED<sup>28-29</sup>. In our population none the less, and unlike these results previously reported in other ED populations, there appeared to be no association of a history of diabetes mellitus, previous MRSA infection or MRSA colonization or patient provenance from geriatric or long-term stay centers, as risk factor for a subsequent MRSA infection. Still, this may be also related to the limited sample size, the small number of nursing homes in our health area and the lack of practice of MRSA screening for colonization in our population.

In our study, the most frequent forms of the MRSA infection were respiratory infections, and not skin and soft tissue infections as reported in previous epidemiological studies of staphylococcal infections in the emergency departments<sup>31</sup>. This may be a result of a frequent outpatient management of the skin and soft tissue infections in our area, as well as the high prevalence of respiratory pathology in our emergency department, being this also a condition with a higher likelihood for a posterior hospital admission, as well as a higher probability for adequate microbiological sputum and blood sampling compared to other infections. We would also like to note that

**Table 3** Factors associated with an empirical coverage of MRSA in the emergency department

Variable	OR	CI 95%	P
History of antibiotic treatment	3,88	1,76-8,57	<0,001
Presence of a catheter device	6,28	1,64-24,07	0,007
Urinary infection	0,24	0,04-1,33	0,104
Respiratory infection	0,50	0,18-1,36	0,173
Presence of an indwelling medical device	4,46	0,83-23,91	0,081
Bone and joint infection	2,04	0,48-8,55	0,331
Other	0,84	0,19-3,75	0,815
Skin and soft tissue infection	Reference		

The variables included in the model were: chronic renal failure, dialysis, History of antibiotic treatment, presence of a catheter device and the type of infection.

staphylococcal infection of urinary origin was also identified as an independent factor for the isolation of MRSA. In conjunction to this finding, previous studies have also reported that SA causes urinary tract infections in patients with urinary catheters and that the majority of these cases tends to be resistant to methicillin<sup>32</sup>.

According to the findings of this study, the empirical antibiotic coverage was appropriate in not more than one in three patients with an MRSA infection in our ED. These data are consistent with previous studies that have demonstrated the low rates of prediction of methicillin resistance in staphylococcus infections in emergency departments<sup>31,33</sup>. Furthermore, we would also like to highlight the linear increase in the prevalence of MRSA infections observed throughout the study period, coupled with an increase in the prescription of antibiotics against resistant Gram-positive microorganisms in the ED, though the latter lacking statistical significance. These data are also consistent with the data reported in the literature regarding the empirical treatment against MRSA in ED, which is estimated to be inappropriate in some 50–70% of the cases<sup>34–36</sup>. Many of the factors independently associated with an appropriate empirical antibiotic coverage against MRSA in the ED patients with a suspected staphylococcal infection found in our study were previously described in the literature, such as the presence of a catheter device, or an infection of skin and soft tissue, or infections associated with the presence of indwelling medical devices. However, our series does detect other, not so frequently reported though just as logical factors, taking into account their associated comorbidity and possible floral disruption, such as advanced age coupled with functional impairment, or even some specific forms of staphylococcus infection, such as exacerbations of COPD or urinary tract infections. Therefore, we consider that additional, prospective and multicentre studies are warranted in order to further clarify the risk of MRSA infections with respect to the presence of chronic obstructive pulmonary disease, patient functional dependency and type of infection, specifically urinary tract infections.

Our study also has certain limitations. First, this was a retrospective study, conducted in patients admitted for staphylococcus infections from a single emergency department, in a tertiary level hospital center covering an urban area. Secondly, given that the study was conducted under conditions of routine clinical practice in an ED with high attendance rate, this may have introduced undesired variability in the decision making process regarding the correct microbiological sampling and sample processing, which may have consequently limited the overall sensitivity of the microbiology results. Thirdly, being our work a retrospective prevalence study, there was not able to adequately assess certain factors such as colonization by SA and the temporal relationship between the acquisition of SA and the emergency medical care. Finally, MRSA strains were not genotyped and we used epidemiology, clinical picture and phenotype susceptibility patterns to establish an approximated classification between CA-MRSA and HA-MRSA. MRSA strains were considered as healthcare-associated (HA-MRSA) when were obtained from patients with previous admission, recent antimicrobial therapy or when were resistant to ciprofloxacin, erythromycin or clindamycin. MRSA were considered as community-acquired when strains were isolated from complicated pulmonary or soft tissue infections, in patients without previous admission and were susceptible to ciprofloxacin, erythromycin or clindamycin. Despite all this, we do consider that the results presented in this study provide valuable findings regarding the characteristics of staphylococcal infections and the factors associated with methicillin resistance in patients admitted in the emergency department in Spain.

In conclusion to our findings, our study detected a 30% rate of methicillin resistance in staphylococcal infections admitted in the emergency department, whilst only 1 in 3 patients with MRSA infection received appropriate initial antibiotic treatment. Furthermore, we also conclude that there is a need for prospective multicenter studies that allow us to determine the overall prevalence of MRSA in Spanish EDs, as well as the associated risk factors, in order to optimize the empirical antibiotic therapy against this pathogen. This would allow

us not only to improve the adequacy of the initial treatment of these patients, but also help avoid the excessive antibiotic usage that could increase the selection pressure and resistance rates in this and other pathogens.

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## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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