Mortality among critically ill patients with methicillin-resistant *Staphylococcus aureus* bacteremia: a multicenter cohort study in Colombia

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ABSTRACT

Objective. *To evaluate risk factors associated with methicillin-resistant* Staphylococcus aureus *(MRSA) bacteremia emergence, its prognosis, and mortality-determining factors in critically ill patients in Colombia.*

Methods. *A multicenter, retrospective cohort study conducted in 2005–2008 at 16 public and private reference health care institutions in Bogotá, Colombia, that form part of a national epidemiological surveillance network and a hospital network with 4 469 beds. Methicillin-resistant emergence and mortality were analyzed using descriptive and time-to-event analysis; a multivariate Cox proportional hazard regression model was built to test the association between methicillin resistance and mortality.*

Results. *A total of 372 patients were studied: 186 with MRSA bacteremia, randomly matched with 186 with methicillin-susceptible* Staphylococcus aureus *(MSSA) bacteremia. Previous surgery, antibiotic exposure, and hospital-acquired infections were independently associated with methicillin resistance. MRSA caused longer hospital stays among survivors (median 24 versus 18 days,* P = *0.014). Mortality predictors were: patient age, creatinine level over 1.21mg/dl at ICU admission, severe sepsis, and inotropic requirement. Appropriate antimicrobial therapy and antimicrobial therapy change were independent protective factors, as was male gender.*

Conclusions. *Methicillin resistance per se was not a mortality-independent prognostic factor. Previous conditions, such as age, baseline renal impairment, severe sepsis, and inotropy demand explained the observed mortality. Appropriate antimicrobial therapy remained a protective factor. A call to improve infection control measures in Colombia is mandatory.*

Key words Bacterial infections; methicillin-resistant *Staphylococcus aureus*; outcome assessment (health care); risk factors; mortality; Colombia.

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Since its emergence in hospital environments (1), methicillin-resistant *Staphylococcus aureus* (MRSA) has become a serious public health problem that has spread worldwide. In most countries, MRSA is an important con-

cern for hospital infection-control programs, especially in the Intensive Care Units (ICU), where it can cause severe complications (2–4). As a cause of bacteremia, an MRSA can be related to poor outcomes for the patient, the patient's family, and the healthcare providers (5, 6).

The relationships between methicillin resistance and mortality, morbidity, prolonged length of stay, and higher hospital costs have been widely studied (7–9). Risk factors for MRSA development in the ICU setting have been analyzed, and invasive device exposure, hospital acquired infections, and previous antimicrobial treatment are well recognized as predisposing conditions (5, 10). On the other hand, some reports have studied the effect of MRSA on clinical outcomes, especially mortality (11). However, there has been wide variability in methodology, sample size, confounding variables, and data analysis strategies (12–20).

A consistent conclusion on MRSA-associated mortality in the ICU cannot be reached with the available evidence; however, some prognosis factors have been established for negative outcomes of MRSA bacteremia. Some reports have discussed the role of baseline comorbidities, illness severity, cardiovascular impairment, and multiorganic dysfunction as predictors of hospital mortality (12–15, 17). Recent literature has brought into question the protective function of adequate, initial antimicrobial therapy, and its timely implementation after bacteremia onset (20–22).

The present study evaluates risk factors associated with MRSA bacteremia emergence, its prognosis, and mortality-determining factors in critically ill patients in Colombia.

METHODS

Study setting

A retrospective cohort study was conducted at 16 public and private reference health care institutions in Bogotá, Colombia. All institutions belonged to an epidemiological surveillance network that receives and processes microbiological data from hospitals around the country. During the observation period, the hospital network had 4 469 beds and reported 347 active beds for medical, cardiovascular, pediatric, and burn intensive care services. Hospital capacity ranged from 46–630 beds.

Data collection

All critical care isolations of MRSA bacteremia among in-patients at least 16 years of age at participating institutions in January 2005–December 2008 were identified and matched (1:1 ratio), by hospital and year, with a randomly-selected sample of patients with methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia. Clinical information was extracted from medical records by a team of trained physicians who consulted with one of the infectious disease specialists in the group (JAC, CAA, ALL). A list of random numbers was used to select the unexposed group in each participating institution. Patients with polymicrobial bacteremias were excluded.

Sample size was calculated assuming an effect size for oxacillin equivalent to a hazard ratio (HR) of 1.5, with a theoretical event frequency of 50%, an alpha value of 0.05, and a sample power of 80% for a two-tailed hypothesis test. In a 1:1 ratio, a sample size of 382 subjects was adequately powered to observe a difference in the survival function expressed by an HR of 1.5.

The institutional review board of the School of Medicine at the Universidad Nacional de Colombia (National University of Colombia, Bogotá, Colombia) approved the study protocol in August 2007. In addition, all participating institutions independently approved their own participation in the study.

Definitions and variables

An episode of *S. aureus* bacteremia was defined according to the criteria established by the Centers for Disease Control and Prevention (CDC, Atlanta, Georgia, United States) as an isolation of the target pathogen with signs or symptoms of infection and without other simultaneous micro-organisms. The source of bacteremia, as well as of co-infections, was defined using the same guidelines (23). Furthermore, the source of infection was classified as eradicable and non-eradicable according to the availability of any intervention intended to remove it (i.e., catheter withdrawal, peritoneal lavage, abscess drainage, tissue resection, prosthesis removal, and others.)

Health care-associated infection was defined using Friedman's criteria (24). Bacteremia occurring 48 hours after hospitalization was considered nosocomial, and so were infections related to an implant or device used in the previous year.

Death was considered directly attributable to bacteremia if the patient, in the absence of any other reasonable explanation, presented signs or symptoms of bacteremia in the 7 days preceding death or had an active infection in another location caused by the same micro-organism (25). If the patient did not present a likely cause of death, bacteremia was still considered the probable cause of death (7).

Adequate antimicrobial treatment was defined as administration of the microbiological agent pertinent to reported resistance profile within the first 48 hours of the bacteremia onset in the appropriate manner, frequency, dose, and duration.

Comorbidity

Baseline risk of death and severity of disease at ICU admission time was assessed using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score and the McCabe classification, respectively (26, 27). Comorbid conditions were measured using the Charlson index (28). International Sepsis Definition Conference criteria were used for all infection-related outcomes (29). Patients were considered immunocompromised if any pre-stated conditions (i.e., acquired immunodeficiency syndrome, autoimmune disease, cancer, chemotherapy, chronic renal failure, cirrhosis, high-dose steroid treatment, severe burns, severe malnourishment, transplantation, or uncontrolled diabetes mellitus) were documented in the 30-day period preceding bacteremia. Clinical background, such as hospitalizations, invasive devices, use of antibiotics, and surgical procedures, were also recorded.

Microbiological methods

Staphylococcus aureus isolation and typing were done in all participating laboratories according to standardized techniques. Antimicrobial susceptibility

was performed by an automated microdilution method using either VITEK® (bioMérieux Inc., Marcy l'Étoile, France) or MicroScan® (Siemens Healthcare Diagnostics Inc., Tarrytown, New York, United States).

Methicillin resistance was defined as a minimum inhibitory concentration of 4 mg/L accordingly to Clinical and Laboratory Standards Institute criteria (30). Participating hospitals did not routinely perform a Cefoxitin confirmatory test.

Statistical analyses

The main outcome was overall mortality, defined as death by any cause during the first 30 days of bacteremia. Discrete variables were expressed as frequencies (percentages) and continuous variables as means (with standard deviation) or medians (with inter-quartile range) according to data distribution. Comparative analyses between proportions were done with the Chi-square test or Fisher's exact test; and the Student's t test or Wilcoxon's rank sum test were used for the continuous variables, as appropriate.

To evaluate variables associated with MRSA resistance, logistic regression was done using resistance or susceptible micro-organisms as outcome. To study the influence of methicillin resistance and other variables on overall mortality, a Cox proportional hazard regression was performed. Survival rates per 1 000 patients/day were calculated, and Kaplan Meier survivor functions were estimated and compared between different groups using the log rank test. Variables with P value < 0.10 in bivariate analyses or those with a plausible biological relationship to the outcome were considered in multivariate modeling. Starting from a full model, variables were added and removed using a stepwise approach (31). Some predictors were restricted according to correlation test in order to avoid collinearity using a correlation coefficient greater than 0.70. Two independent models were constructed, one forcing the introduction of methicillin resistance and the other without the presence of this variable; models were contrasted with a likelihood ratio test. Hazard ratios with 95% Confidence Intervals (95%CI) were reported. Proportional hazard assumption was evaluated both graphically and statistically using Schoenfeld residuals, and time dependent covariates were considered in final models. All tests were two-tailed and $P < 0.05$ was considered to indicate statistical significance. All analyses were performed using Stata® version 11.1 (StataCorp LP, College Station, Texas, United States).

RESULTS

A total of 372 patients were included in the study; 186 with MRSA bacteremia matched 1:1 with 186 with MSSA. Of the study population, those 65 years of age and older represented 43.8%. No important differences in age, sex, or baseline severity were observed; however, previous surgery, previous antibiotic use, invasive devices, or hospital environment exposure were more frequent in MRSA patients. Comparison of baseline characteristics among exposed groups is shown in Table 1. Logistic regression showed that previous surgery (Odds Ratio [OR] = 2.55; 95%CI: 1.59–4.08), previous antibiotic exposure (OR = 4.05; 95%CI: 2.31–7.14), and hospital-related bacteremia were risk factors for MRSA emergence (Table 2).

Median survival time was 28 days for the entire cohort. Compared to MSSA-infected patients, MRSA was associated with longer hospital stays among survivors (median 30 days vs. 21 days, $P < 0.001$) and a higher risk of global hospital mortality (57% vs. 46.2%, $P = 0.038$). A total of 192 patients died during hospitalization, corresponding to a general mortality rate of 29.64 per 1 000 patient-days. A clinical, but not statistically significant, attributable mortality was observed in MRSA contrasted with MSSA (71.7 vs. 57%, $P = 0.097$). Mortality rates were significantly higher in women (40.02 per 1 000 patient-days), patients 65 years of age and older (43.10), and those with septic shock (53.91), multiple organ failure (65.88), creatinine more than 1.21 mg/dL at ICU admission (46.31), and initial inappropriate treatment (43.54) (Table 3). Despite the presence of a gradient according to risk categories for severity indicators, such as APACHE II and McCabe at ICU admission, these differences were not statistically significant.

Cox proportional hazard model results are summarized in Table 4. Variables associated with an increased risk of overall mortality were older age, creatinine level at ICU admission more than 1.21 mg/dL, presence of severe sepsis, and inotropic requirement. Methicillin resistance was not an independent prognostic factor for mortality once adjusted for other predictors. Independent protective factors were initial, adequate treatment; antibiotic change during infection; and being male.

DISCUSSION

This study showed a clinical, but not statistically-significant, difference in mortality in MRSA bloodstream infections when compared to MSSA bacteremia in critical care patients. Risk factors for methicillin resistance identification were related to previous health care exposure. Risk factors for mortality among patients with *S. aureus* bacteremia can be classified into three categories: those related to the micro-organism, those related to the affected individual (comorbidity), and those related to the severity of the infection (clinical status at admission). Contrasted with previous research in critical care settings (13, 15, 16, 18, 32), these results did not register an independent effect of methicillin resistance phenotypes on overall mortality. Lack of methicillin resistance effect on unfavorable outcomes could be explained by the effect of other predictors as set out in non-exclusive ICU comparisons (6, 8) and ICU comparisons (19). On the other hand, initial adequate treatment, as reported in previous studies, represented an important protective factor against MRSA mortality (20) and an indirect indicator of the effect of the antimicrobial resistance. Previous evidence suggests that MRSA isolation and length of hospital stay are important risk factors in the event of inappropriate empirical antimicrobial treatment (33). Independent effect of recognized mortality predictors, such as age (10, 13, 19, 34), gender (35), creatinine level at ICU admission (36), shock, and sepsis with at least one organ impairment (33), were seen in critical care patient populations.

These findings, however, agreed with other multicenter studies, and confirmed the prognostic significance of severity gradation from sepsis, severe sepsis, and shock as forms to evaluate clinical presentation at admission (37). Some correlation between severe sepsis and multiorganic dysfunction; and septic shock and inotropic requirement was documented. It leads to restriction of

TABLE 1. Comparison of patients' baseline characteristics according to their methicillin resistance profile in a hospital network in Colombia, 2005–2008

Characteristic[a]	MSSA[b] (*n* = 186)		MRSA[c] (*n* = 186)		Total (*n* = 372)		
	No.	%	No.	%	No.	%	*P* value
Age in years [mean (SE[d])]	57.9	1.4	57.7	1.4	57.8	3.0	0.900
Sex (male)	105	56.5	116	62.4	221	59.4	0.245
Referred	83	44.6	90	48.4	173	46.5	0.467
Type of referring institution							0.247
Hospital	77	92.8	77	86.5	154	89.5	
Home care service	0	0	2	2.2	2	1.2	
Ambulatory	6	7.2	10	11.2	16	9.3	
Clinical background							
Immunosuppression	85	45.7	94	50.5	179	48.1	0.350
Previous surgery	73	39.2	125	67.2	198	53.2	< 0.001
Hospitalization in the last year	87	46.8	103	55.4	190	51.1	0.312
Previous antibiotic exposure	115	62.5	164	88.6	279	75.6	< 0.001
Previous invasive device	160	86	179	96.2	339	91.1	0.001
LOS[e] before bacteremia (days) [median (IQR[f])]	5	(1–9)	12	(2–15)	7	(13–13)	< 0.001
APACHE II score [median (IQR[f])]	15	(10–20)	15	(11–22)	15	(11–21)	0.4085
Charlson score > 3	94	50.5	94	50.5	188	50.5	1.000
Baseline serum creatinine (mg/dL)	1.1	1.41	1.07	1.18	1.1	1.23	0.406
McCabe classification							0.571
Rapidly fatal	11	5.9	9	4.8	20	5.4	
Ultimately fatal	80	43	72	38.7	152	40.9	
Nonfatal	95	51.1	105	56.5	200	53.8	
Place of bacteremia acquisition							0.005
Community or AH[g]	36	19.3	13	7	49	13.2	
Referent institution	26	14	26	14	52	14	
Index hospital, non ICU	34	18.3	42	22.6	77	20.7	
Index hospital, ICU	90	48.4	105	56.4	194	52.1	
Source of bacteremia							0.348
Central venous catheter	67	50.7	72	56.7	139	53.6	
Respiratory tract	32	24.2	24	18.9	56	21.6	
Surgical site	4	3	8	6.3	12	4.6	
Skin and soft tissue	12	9.1	10	7.9	22	8.5	
Unknown	54	29	59	31.7	113	30.4	
Classification of source							0.998
Eradicable	86	47	85	46.7	171	46.8	
Non-eradicable	97	53	97	53.3	194	53.2	

[a] Variables are stated as frequency (number and percentage) unless otherwise specified.
[b] Methicillin-susceptible *Staphylococcus aureus*.
[c] Methicillin-resistant *Staphylococcus aureus*.
[d] Standard error.
[e] Length of stay.
[f] Inter-quartile range (25th percentile–75th percentile).
[g] Ambulatory health care.

TABLE 2. Bivariate and multivariate analysis of risk factors related to methicillin resistant *Staphylococcus aureus* bacteremia in a hospital network in Colombia, 2005–2008

Risk factor	OR[a]	95%CI[b]	AOR[c]	95%CI
Age (> 65 years)	1.16	0.77–1.76	—	—
Sex (male)	1.28	0.84–1.94	—	—
Immunosuppression	1.21	0.81–1.82	—	—
Hospitalization in the last year	1.32	0.77–2.26	—	—
LOS[d] before bacteremia (day)	1.08	1.06–1.11	—	—
Previous invasive device	4.16	1.76–9.83	—	—
Previous surgery	3.17	2.08–4.85	2.55	1.59–4.08
Previous antibiotic exposure	4.69	2.72–8.07	4.06	2.31–7.14
Place of bacteremia acquisition				
Community or AH[e]	1	1	1	1
Referent institution	2.77	1.20–6.38	2.77	1.15–6.70
Index hospital, non-ICU[f]	3.42	1.57–7.45	2.68	1.17–6.14
Index hospital, ICU	3.23	1.61–6.47	2.65	1.27–5.54

[a] Odds ratio.
[b] 95% confidence interval.
[c] Adjusted odds ratio.
[d] Length of stay.
[e] Ambulatory health care.
[f] Intensive care unit.

less significant predictors in the final model. Although some limitations can be expected from a non-standardized procedure for measurement of creatinine levels, this factor and sepsis severity constituted important predictors of general mortality and do not show collinearity with other predictors. Some controversy exists in recent literature regarding gender differences in mortality (10, 38); biological factors and comorbid conditions can be reasonable explanations for this discrepancy.

Some studies have found an explanatory effect of baseline severity on hospital mortality rate (13, 19). The present study did not observe any important, independent effect of the McCabe classification or the APACHE II score on mortality. Nonetheless, with bivariate

TABLE 3. Bivariate analysis of mortality rates by predictor for *Staphylococcus aureus* bloodstream infections in critically ill patients from a hospital network in Colombia, 2005–2008

Mortality predictor	Patients	Mortality rate[a]	95%CI[b]	*P* value[c]
Overall	372	29.64	25.4–34.59	
Sex				0.0052
Male	151	24.17	19.57–29.86	
Female	221	40.02	31.92–50.19	
Age (years)				< 0.0001
15–64	209	21.23	16.83–26.79	
≥ 65	163	43.10	35.06–53.00	
Methicillin resistance				0.0697
Susceptible	186	25.73	20.29–32.63	
Resistant	186	33.34	27.21–40.86	
Previous surgery				0.0797
No	174	35.09	28.18–43.68	
Yes	198	25.70	20.67–31.95	
Multiple organ failure				< 0.0001
No	184	9.54	6.74–13.49	
Yes	167	65.88	54.96–78.96	
Classification of source				0.0973
Eradicable	194	33.03	26.86–40.61	
Non eradicable	171	25.58	20.13–32.50	
Immunosuppressant condition				0.6968
No	193	28.91	23.19–36.04	
Yes	179	30.38	24.47–37.72	
McCabe classification				0.2612
Rapidly fatal	20	41.52	23.58–73.11	
Ultimately fatal	152	31.88	25.18–40.37	
Nonfatal	200	26.85	21.57–33.43	
APACHE II score				0.0683
< 10	61	20.41	13.02–31.20	
10–19	160	28.51	22.40–36.29	
> 20	151	34.77	27.77–43.53	
Nature of bacteremia				0.0298
ICU[d] acquired	198	24.97	20.00–31.17	
ICU treated[e]	166	35.67	28.61–44.46	
Severe sepsis				< 0.0001
No	104	3.32	1.49–7.38	
Yes	264	43.09	36.77–50.48	
Septic shock				< 0.0001
No	160	8.33	5.58–12.43	
Yes	201	53.91	45.42–63.98	
Inotropic requirement				< 0.0001
No	20	8.54	5.51–13.24	
Yes	136	47.47	40.13–56.16	
Creatinine				< 0.0001
< 1.20 mg/dl	203	22.86	18.17–28.75	
>1.21 mg/dl	145	46.31	37.25–57.58	
Antibiotic change during infection				0.0026
No	86	36.09	16.14–26.77	
Yes	60	20.78	29.21–44.58	
Initial adequate treatment				0.0002
No	102	43.54	33.59–56.45	
Yes	247	23.21	18.95–28.45	

[a] 30-day hospital mortality rate per 1 000 patient / days, starting from bacteremia onset.
[b] 95% Confidence Interval.
[c] Log rank test was used for hypothesis testing.
[d] Intensive Care Unit.
[e] Bacteremia acquired outside the ICU; main cause of ICU admission.

analysis, some kind of gradient was observed in mortality rates. Despite the balanced severity between exposed groups, a plausible relationship between severity of disease at ICU admission and the later outcome can be suspected.

A significant difference was seen in mortality rates between ICU and non-ICU-acquired bacteremia. Length of stay prior to bacteremia, reported as a predictor of mortality in previous studies, did not show a differential effect among resistant and susceptible strains in this analysis.

Etiologic factors for acquisition of methicillin-resistance concurred with widely accepted knowledge that regards previous invasive devices, procedures, and antibiotic exposure as important factors related to hospital-acquired MRSA. In this study's context, the highest rate of invasive procedures was related to *Staphylococcus aureus* infections, particularly methicillin-resistant ones (39).

The high nosocomial origin registered in this cohort was related to the predominant presence of MRSA in the hospital environment during the study period. Recent reports suggest the emergence of MRSA varieties of community origin as the causative agent of health care-associated infections, with important mortality rates associated with USA 300 clones (40).

Study limitations

A residual confusion could be related to retrospective nature of the research, especially related to molecular characteristics of some strains that could be related to worse outcomes and were not studied. Prospective studies could lead to a better characterization of widely known molecular diversity of MRSA strains in Latin American countries (41).

This study's main limitation is its retrospective nature, which could lead to some degree of information bias, potentially controlled by the participating institutions' standardization of definitions. Validation by local experts (infection control committees at each institution) and a centralized review committee created to validate the study date attempted to improve information quality.

Another limitation could be the sample size. The study had a sample of 10 subjects less than originally planned. Differences in mortality attributable to methicillin resistance profiles less than a 1.51 hazard ratio could be difficult to see with this sample size. It is worth noting, however, that this study represents one of the largest samples reported to date in the literature.

One of this study's strengths is its exposure-matching by cohorts in a 1:1 ratio within the same institution for the same year (using a random selection process). This allowed for controlling unidentified differences in each hospital environment and health care delivery.

TABLE 4. Bivariate and multivariate analysis of hospital mortality predictors for *Staphylococcus aureus* bloodstream infections in critically ill patients in a hospital network in Colombia, 2005–2008

Variable	Unadjusted hazard ratio (bivariate)	Adjusted hazard ratio[a] (with methicillin resistance)	Adjusted hazard ratio[b] (without methicillin resistance)
Methicillin resistance	1.31 (0.96–1.79)	0.90 (0.62–1.30)	—
Nosocomial bacteremia	0.65 (0.44–0.95)	—	—
Catheter-related bacteremia	0.57 (0.41–0.79)	—	—
APACHE II score[c]	1.04 (1.02–1.07)	—	—
Multiple organ failure[d]	6.03 (4.09–8.90)	—	—
Inotropic requirement[d]	5.22 (3.26–8.36)	2.58 (1.48–4.51)	2.63 (1.51–4.58)
Severe sepsis[d]	10.70 (5.02–22.83)	6.19 (2.16–17.78)	6.05 (2.11–17.33)
Septic shock[d]	5.74 (3.74–8.82)	—	—
Sex	0.66 (0.48–0.90)	0.64 (0.45–0.91)	0.64 (0.45–0.90)
Creatinine (> 1.21 mg/dL)	1.87 (1.36–2.57)	2.14 (1.50–3.06)	2.13 (1.49–3.04)
Age (years)[d]	1.02 (1.01–1.03)	1.01 (1.00–1.02)	1.01 (1.00–1.02)
Antibiotic change during infection	0.61 (0.44–0.85)	0.49 (0.34–0.71)	0.51 (0.36–0.72)
Source of infection eradicated	0.74 (0.53–1.02)	—	—
Initial adequate treatment	0.56 (0.40–0.77)	0.50 (0.34–0.73)	0.52 (0.36–0.74)

[a] Multivariate analysis forcing methicillin resistance inclusion.
[b] Model without methicillin resistance inclusion.
[c] Acute Physiology and Chronic Health Evaluation II.
[d] Statistical correlated variables avoided in the final model.
[d] Age was introduced in the model centered on its mean to achieve a natural zero value.

Conclusions

This study fills a gap in the Latin American literature on the impact of MRSA in bloodstream infections and confirms the importance of *S. aureus* as a causative pathogen. High mortality rates and increased length of stay confronts health care delivery with a public health problem within the hospital environment itself. Proper microbiological detection, improvement of surveillance networks, and timely control and treatment strategies are some measures that could assist with *S. aureus* containment. Resistance suspicion, source eradication, and suitable antibiotics must complement institutional control programs and infection control policies in Latin America.

There is a widespread need to improve all infection control measures in order to reduce the impact of MRSA in hospital environments. High mortality rates for resistant and susceptible strains justify the need for a broad empirical therapy, rational and controlled, and for the containment of this and other multiresistant micro-organisms, through well established infection control strategies.

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RESUMEN

Mortalidad en pacientes gravemente enfermos con bacteriemia por *Staphylococcus aureus* resistente a la meticilina: un estudio multicéntrico de cohortes en Colombia

Objetivo. Evaluar los factores de riesgo asociados con la aparición de bacteriemia por *Staphylococcus aureus* resistente a la meticilina (MRSA), su pronóstico y los factores determinantes de la mortalidad en pacientes gravemente enfermos en Colombia.
Métodos. Estudio retrospectivo multicéntrico de cohortes realizado en el período del 2005 al 2008 en 16 instituciones de atención de salud de referencia públicas y privadas de Bogotá, Colombia, que forman parte de una red nacional de vigilancia epidemiológica y de una red hospitalaria de 4 469 camas. Se analizaron la aparición de resistencia a la meticilina y la mortalidad mediante análisis descriptivos y de tiempo transcurrido hasta un suceso; se estableció un modelo multifactorial de regresión de riesgos proporcionales de Cox para evaluar la asociación entre la resistencia a la meticilina y la mortalidad.
Resultados. Se estudiaron 372 pacientes: 186 con bacteriemia por MRSA, apareados aleatoriamente con 186 con bacteriemia por *Staphylococcus aureus* sensible a la meticilina (MSSA). La cirugía previa, el tratamiento con antibióticos y las infecciones intrahospitalarias se asociaron independientemente con la resistencia a la meticilina. El MRSA provocó hospitalizaciones más prolongadas en los sobrevivientes (mediana de 24 frente a 18 días, $P = 0{,}014$). Los factores predictivos de mortalidad fueron: la edad del paciente, un nivel de creatinina superior a 1,21 mg/dl al ingresar en la UCI, la septicemia grave y el requerimiento de inotrópicos. El tratamiento antimicrobiano apropiado y el cambio de tratamiento antimicrobiano constituyeron factores protectores independientes, igual que el sexo masculino.
Conclusiones. La resistencia a la meticilina per se no fue un factor pronóstico independiente de la mortalidad. Las condiciones previas, como la edad, la insuficiencia renal inicial, la septicemia grave y el requerimiento de inotrópicos explicaron la mortalidad observada. El tratamiento antimicrobiano apropiado seguía siendo un factor protector. Es obligatorio hacer un llamamiento para mejorar las medidas de control de las infecciones en Colombia y en otros contextos similares.

Palabras clave Infecciones bacterianas; *Staphylococcus aureus* resistente a meticilina; evaluación de resultado (atención de salud); factores de riesgo; mortalidad; Colombia.