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Epidemiology and clinical characteristics of *Staphylococcus aureus* bloodstream infections in a tertiary-care center in Mexico City: 2003-2007

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ABSTRACT

Objective. *To compare the epidemiology, clinical variables, outcome and molecular characteristics between methicillin-resistant* Staphylococcus aureus *(MRSA) and methicillin-susceptible* S. aureus *(MSSA) bloodstream infections (BSI) of patients from a tertiary-care center.* ***Methods.*** *We conducted a five-year retrospective cohort analysis of all patients with at least one peripherally-drawn blood culture positive for* S. aureus. *Patient characteristics, clinical data and outcome were analyzed, as well as microbiologic data.* ***Results.*** *We included 444 isolates derived from 172 patients. The highest rate of MRSA BSI was observed in 2005 (4.9 cases per 1,000 patients). MRSA BSIs were more likely to be originated from a skin and soft tissue infection (OR 2.44, CI 95% 1.05-5.67, p = 0.03). The only significant risk factor for MRSA BSI was the mean length of hospital stay (OR 1.01; CI 95% 1.00-1.02, p = 0.002). A difference in inadequate initial treatment was noticed in MRSA BSI (OR 8.35 CI 95% 1.55-8.39, p = 0.002); but it had no impact on mortality. All MRSA isolates were SCC*mec *type II, and we did not find any resistance to vancomycin or linezolid.* ***Conclusion.*** *MRSA BSIs were associated with a prolonged hospital stay. We did not observe any difference in mortality between MRSA and MSSA BSIs. During the study period, we only identified SCC*mec *type II in MRSA isolates, which suggests that this infection was hospital- acquired.*

Epidemiología y características clínicas de las infecciones por* Staphylococcus aureus *en el torrente sanguíneo en un centro de atención tercer nivel en la ciudad de México: 2003-2007

RESUMEN

Objetivo. Comparar la epidemiología, las variables clínicas, el desenlace y las características moleculares entre las infecciones del torrente sanguíneo (ITS) por *Staphylococcus aureus* resistente a meticiilina (SARM) y *S. aureus* sensible a meticilina (SASM) ocurridas en pacientes de un hospital de tercer nivel. **Métodos**. Es un estudio de cohorte retrospectivo que incluyó un análisis de los episodios de ITS ocurridos durante cinco años. Incluímos a todos los pacientes hospitalizados, mayores de 16 años y con al menos un hemocultivo positivo para *S. aureus*. Se incluyeron características de los pacientes, datos clínicos y desenlace. Se realizaron pruebas de susceptibilidad antimicrobiana y de tipificación molecular en todos los aislados clínicos. **Resultados**. Durante el periodo de estudio hubo 6126 hemocultivos positivos, analizamos 444 de 172 pacientes. La proporción más elevada de ITS por SARM fue observada en 2005 (4.9 casos por 1,000 pacientes). ITS por SAMR fue más común en pacientes con infecciones de piel y tejidos blandos (RM 2.44, IC 95% 1.05-5.67, p = 0.03). La estancia hospitalaria promedio fue el único factor de riesgo significativo para ITS por SARM con una RM 1.01 por día adicional (IC95% 1.0-1.02, p = 0.002). Una diferencia significativa fue observada en los casos de ITS por SARM con tratamiento inadecuado (OR 8.35, CI 95% 1.55-8.39, p = 0.002); sin embargo, no hubo diferencia en la tasa de mortalidad entre los casos con ITS por SARM o por SASM. Todos los aislados de SARM fueron tipo SCCmec II, no encontramos resistencia

a vancomicina ni a linezolid. **Conclusiones**. Las ITS por SARM se asocciaron con una estancia hospitalaria prolongada. No hubo deferencias en el porcentaje de mortalidad al comparar los casos con SARM y SASM durante el periodo de estudio. Todos los aislados fueron genotipo SCCmec II como evidencia de adquisición nosocomial.

Key words. Staphylococcus aureus. *Methicillin-resistance. Blood culture. Methicillin. Vancomycin.*

Palabras clave. *Staphylococcus aureus*. Resistencia a meticilina. Hemocultivos. Meticilina. Vancomicina.

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) was detected for the first time in London in 1961.[1] Since then, it has disseminated worldwide, and accounts for approximately 50% of all staphylococcal bloodstream infections (BSI).[2] In intensive care units, nearly 25% of all patients are colonized. An increase in resistance has been observed from 22% in 1995 to 57% in 2001 in the United States.[3] Resistance is mediated by the *mecA* gene, which encodes for the penicillin-binding protein 2a. This gene is contained on a genetic island called the Staphylococcal chromosomal cassette *mec* (SCC*mec*). There are five types of SCC*mec*. Types I, II and III are related to hospital-acquired MRSA (HA-MRSA) and types IV (subtypes a, b, c and d) and V with community-acquired MRSA (CA-MRSA).[4-6] One of the most important differences between HA-MRSA and CA-MRSA is that the former has a structure that confers resistance to other antimicrobial agents such as trimethoprim-sulfamethoxazole and clindamycin, in contrast with CA-MRSA, which is usually susceptible to these antibiotics. [4-6]

A variety of risk factors have been associated to MRSA bacteremia, including previous antibiotic use, a prolonged hospital stay, the use of intravascular devices, severe underlying conditions, and MRSA nasal carriage.[2] Some studies have shown that MRSA bacteremia carries a higher mortality rate than bacteremia caused by methicillin-susceptible *S. aureus* (MSSA), and has been considered as an independent predictor of mortality.[3,5] Harbarth and colleges, on the other hand, failed to identify a significant difference in mortality between infections caused by MRSA or MSSA.[2] Therefore, the aim of this study was to compare the epidemiology, clinical variables, outcome and molecular characteristics between MRSA and MSSA BSI of patients from a tertiary-care center in Mexico City.

MATERIALS AND METHODS

Study population and setting

We conducted a retrospective cohort analysis during a five-year period. We included all patients older than 16 years admitted to our hospital (200 bed tertiary-care center) from January 2003 through December 2007 with at least one peripherally-drawn blood culture positive for *S. aureus*. A patient with recurrent bacteremia was counted as a single event. We recorded basic information, clinical variables, initial treatment and patient's outcome. We excluded patients in whom *S. aureus* was identified in a catheter-drawn blood culture without positive peripheral blood cultures and patients whose medical records were not available.

We used the following case definitions:

- *S. aureus*-bacteremia (SAB) as an episode of fever and at least one peripherally-drawn blood culture positive for *S. aureus*.
- Health-care associated *S. aureus*-bacteremia (HA-SAB) as a positive blood culture obtained ≥ 72 hrs after admission into the hospital or at any time during hospital stay if the patient had at least one of the following conditions: hospitalization, surgery, residency in a long-term care facility, hemodialysis or peritoneal dialysis, within a previous year; or an indwelling percutaneous device or catheter during the current admission.[7]
- Community-associated *S. aureus*-bacteremia (CA-SAB) if the blood culture was obtained in ambulatory patients at the emergency room or ≤ 72 hrs after hospitalization, without any of the above criteria.[8]

Inadequate initial treatment (IIT) for MRSA BSI was defined if the patient did not receive an antibiotic regimen that included intravenous (IV) van-

comycin (or other appropriate antibiotic) within the first 24 hrs after blood cultures were drawn. For MSSA BSI we defined IIT as a regimen that did not include an IV b-lactam (with adequate *S. aureus* activity) or vancomycin. Episodes of death were classified as: early, if the patient died <7 days after the diagnosis of BSI; during the first 30 days, if the patient died during the first month after diagnosis, and overall mortality, which included all deaths.

Blood cultures

Blood from at least two culture bottles from a febrile patient was inoculated in Bactec Plus Aerobic/F and/or BactecMyco/F-Lytic media (Becton Dickinson, Cockesville, MD, USA); all blood cultures were processed in the BACTEC 9240 Automated System (Becton Dickinson). After growth detection, initial identification and susceptibility tests were performed by conventional laboratory methods and with the VITEK System (bioMérieux, Lyon, France). Species identification was confirmed by the presence of the *nuc* gene determined by PCR (see below). All isolates were tested for antibiotic susceptibility using microbroth dilution following standard CLSI protocols.[9] Furthermore, methicillin resistance was confirmed by the presence of the *mecA* gene.

Bacterial selection and molecular typing

We only included the first isolate of each case of SAB if the other isolates were phenotypically identical. Determination of *nuc* and *mecA* genes and SCC*mec* type/subtype were performed using polymerase chain reaction (PCR), these procedures are briefly described:

- DNA isolation: Two to three colonies were suspended in 100 µL of 10^{-1} mM TE buffer. Then the suspension was heated to 95°C for 10 minutes. The samples were centrifuged, and the supernatant was separated.
- Amplification of the *nuc* and *mecA* genes were performed with a multiplex PCR (M-PCR) was performed as described previously; using *nuc*F5'GCGATTGATGGTGATACGGTT3', *nuc*R5'AGCCAAGCCTTGACGAACTAAAGC3'; *mecA*F5'AAAATCGATGGTAAAGGTTGGC3', *mecA*R5'AGTTCTGCAGTACCGGATTTGC3' as primers.[10]
- SCC*mec* type identification: Cassette amplification was determined by M-PCR, as described elsewhere.[11] We expected the following base pair sizes: 613 bp for SCCmec type I, 398 bp for type II, 280 bp for type III, 776bp for Type Iva, 493bp type IVb, 200bp IVc, 881bp type IVd and 325 bp for type V.
- Sequence analysis of the nucleotide product of 398 bp was done to confirm the cassette type. The 398 bp band was purified with the QIAquick Kit (Qiagen Gel Extraction, Qiagen, Stanford, CA, USA) and sequenced following the manufacturer instructions in an automated sequencer (Applied Biosystems, Foster City, CA USA). We used the VECTOR NTI Advance V. 10.3 software (Invitrogen Inc., Carlsbad, CA, USA) for alignment between the sequences. The sequence was compared and analyzed with GenBank/EMBL.[11]

Statistical analysis

For descriptive statistics, median, interval, frequencies and percentages were used. Univariate analysis was done using Mann-Whitney U, χ^2 or Fisher's exact tests as appropriate. Associations between variables were expressed as odds ratios with 95% confidence intervals (CIs). A value of $p \leq 0.05$ was considered statistically significant. SPPS v15.0 was used for analysis.

RESULTS

We detected 448 (7.3%) *S. aureus* out of 6126 positive blood cultures, derived from 176 patients. Four cultures (corresponding to 4 patients) were eliminated because they were not confirmed *S. aureus* (all of them showed absence of the *nuc* gene); therefore, we analyzed 444 positive blood cultures from 172 patients (a mean of 2.5 blood cultures per patient). A steady decline in the rate of MSSA BSI was observed since 2004, the year in which the highest rate was observed (5.2 cases per 1000 patients). For MRSA the highest rate was 4.9 cases per 1000 patients in 2005, followed by a decrease in the rates (3.2 and 3.3 cases per 1000 patients in 2006 and 2007, respectively) (Figure 1).

Resistance to methicillin among *S. aureus* bloodsteam isolates was: 40% in 2003, 37.5% in 2004, 53.6% in 2005, 43.7% in 2006, and 51.7% in 2007. None of the isolates expressed resistance to vancomycin or linezolid during the study period (Table 1). Baseline characteristics are described in table 2. There were no significant differences in age, type of hospital admission and origin of the bacteremia.

Of 28 patients with SAB originated from a skin and soft tissue infection (SSTI), 18 were MRSA and 10 were MSSA (OR 2.44, CI 95% 1.05-5.67, p = 0.03). Follow-up blood cultures were taken if the patient remained febrile between the third and fifth day in 75 patients (44 in the MSSA group, and in 31 in the MRSA group) and were positive in 9 (20.4%) and 11 (35.4%), respectively. *S. aureus* grew in urine cultures in 6 of 50 (12%) patients of the MSSA group and 1 of 30 (3.3%) patients of the MRSA group. Polymicrobial bacteremia was documented in three patients (3.2%) with MSSA (*Streptococcus spp.* 1, *Staphylococcus spp.* 1 and *Klebsiella pneumoniae* 1) and four (5.0%) with MRSA (*Escherichia coli* 1, *Staphylococcus spp.* 2, and *Enterococcus faecalis* 1).

A significant difference was observed in the inadequacy of the initial antimicrobial therapy between MSSA and MRSA BSIs, this situation was seen in 9.6% of MSSA BSIs and 27.8% of MRSA BSIs (OR 8.35 CI 95% 1.55-8.39, p = 0.002). In the MSSA group, treatment was started with vancomycin in 41 patients (44%) and in 14 of them the therapy was combined with an aminoglycoside. In the remaining 43 patients, the initial treatment included a β-lactam, and in 19 patients it was combined with an aminoglycoside. For MRSA infections, 72.1% of the cases received adequate initial therapy with vancomycin, 26 of them in combination with an aminoglycoside. Despite inadequacy in the initial treatment, there was not any significant difference between groups, in both early and overall mortality (OR 0.67 95% CI 0.02-0.87, p = 0.53).

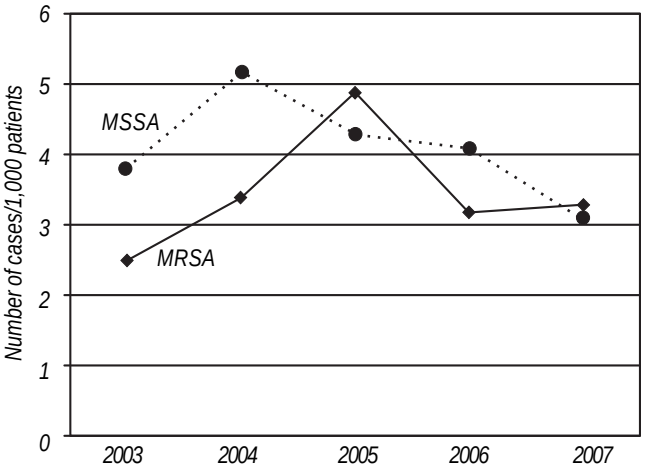

Figure 1. *Annual incidence of bloodstream infections caused by methicillin-susceptible (MSSA) and methicillin-resistant (MRSA)* Staphylococcus aureus.

After multivariate analysis, the only significant risk factor for the development of an MRSA infection was the mean hospital stay with an OR 1.01 (95% CI 1.00-1.02, p = 0.002) (Table 3).

Four clinical isolates were not recovered for molecular analysis (3 MRSA and 1 MSSA); the 168 remaining *S. aureus* isolates were fully PCR-tested for *nuc*, *mecA* and SCC*mec* cassette type; all MSSA were *nuc* (+) and *mecA* (-) and none had SSC*mec* genes. All MRSA isolates were *nuc* (+) and *mecA* (+), and all of them were SCC*mec* cassette type II. We did not identify any other cassette types in this study. The 398 bp sequenced-product correlated with the SSC*mec* type II isolate N315 access number Gene Bank D86934. Using epidemiological definitions, 153 out of 168 cultures (91.0%) were HA-SAB and 15 (8.9%) were classified as CA-SAB. Of the 153 *S. aureus* HCAB (49.0%) were MRSA and 78 (50.9%) were MSSA. From the 15 cases defined as community-associated *S. aureus* bacteremia, 14 were MSSA and only one was MRSA.

DISCUSSION

Our data showed a steady increase in the incidence of hospital-acquired MRSA BSIs in our hospital. However, we also identified a very low mortality rate of these infections despite a substantial number of patients under inadequate initial treatment. We did not find any isolate resistant to vancomycin or linezolid, and all MRSA isolates contained the SCC*mec* type II cassette. Previous studies in our institution had shown that methicillin resistance in

Table 1. Antibiotic resistance of *Staphylococcus aureus* blood isolates according to the year of isolation.

	Percentage of resistance					
	Vancomycin	Teicoplanin	Trimethoprim/sulfamethoxazole	Ciprofloxacin	Levofloxacin	Oxacillin
2003 (n = 30)	0	0	0	0	27.2	40.0
2004 (n = 40)	0	0	2.5	30.0	37.5	37.5
2005 (n = 41)	0	0	7.3	58.5	60.9	53.6
2006 (n = 32)	0	0	6.2	28.1	28.1	43.7
2007 (n = 29)	0	0	10.3	51.7	62.0	51.7

S. aureus bloodstream infections had been stable before 2000, when a significant increase was observed from ~10% to 26.1%. Since then, the rate of MRSA has almost doubled (~50%) which concurs with our findings.[12,13] In our study, we found a 10-fold higher rate of MRSA in comparison with tertiary-care centers from some European countries.[14,15] Hospital length of stay and prolonged hospital stay after diagnosis were significantly different between MRSA (median 46.2 and 15 days respectively) and MSSA (median of 27.3 and 14 days, respectively), similar to that observed in other settings.[16-18]

More patients with an MRSA infection received an inadequate initial treatment; however, we did

Table 2. Clinical characteristics of patients with methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *S. aureus* bloodstream infections.

Characteristic	All n = 172 (%)	MSSA n = 93 (%)	MRSA n = 79 (%)	OR	95%CI	P value
Male (%)	89 (51.7)	48 (51.6)	41 (51.9)	0.98	0.54 - 1.80	0.97
Median age	46 (17-86)	44 (17-86)	51 (20-83)	–	–	0.16
Non surgical disease	125 (72.6)	73 (78.5)	52 (65.8)	0.52	0.26 - 1.04	0.06
Hospitalization ≤ 6 weeks	80 (46.5)	42 (45.2)	38 (48.1)	1.12	0.61 - 2.05	0.70
Site of infection						
Catheter related	70 (40.7)	38 (40.9)	32 (40.5)	0.98	0.53 - 1.81	0.96
Skin/Soft-tissue	28 (16.2)	10 (10.8)	18 (22.8)	2.44	1.05 - 5.67	0.03
Deep abscess	19 (11.0)	9 (9.7)	10 (12.7)	1.35	0.52 - 3.51	0.53
Pneumonia	45 (26.1)	21 (22.6)	24 (30.4)	1.49	0.75 - 2.96	0.24
Endocarditis	8 (4.6)	3 (3.2)	5 (6.3)	2.02	0.46 - 8.76	0.47
Osteomyelitis/ Septic arthritis	10 (5.8)	3 (3.2)	7 (8.9)	2.91	0.72 - 11.06	0.11
UTI	12 (6.9)	9 (9.7)	3 (3.8)	0.36	0.09 - 1.41	0.13
Other	27 (15.6)	17 (18.3)	10 (12.7)	0.64	0.27 - 1.51	0.31
Comorbidities						
Diabetes mellitus	54 (31.3)	29 (31.2)	25 (31.6)	1.02	0.53 - 1.94	0.94
Cirrhosis of the liver	17 (9.8)	10 (10.6)	7 (8.9)	0.80	0.29 - 2.22	0.67
Human immunodeficiency virus (+)	1 (0.5)	1 (0.1)	0 (0)	0.53	0.46 - 0.61	0.54
Immunosupression**	69 (40.1)	35 (37.6)	34 (43)	1.25	0.67 - 2.30	0.47
Cancer	46 (26.7)	20 (21.5)	26 (32.9)	1.79	0.90 - 3.54	0.09
Transplant recipient	9 (5.2)	4 (4.3)	5 (6.3)	1.50	0.39 - 5.80	0.55

** Patients with chronic rheumatic conditions on immunosuppressive therapy are also included.

Table 3. Clinical outcome of patients with methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *S. aureus* bloodstream infections.

Clinical outcome	All n = 172	MSSA n = 93	MRSA n = 79	OR	95% CI	P value
Mean hospital stay (min-max)	27 (0 - 585)	21 (0 - 140)	31 (1 - 585)	–	–	0.003
Hospital stay after diagnosis (min-max)	14 (0 - 584)	14 (0 - 84)	15 (1 - 584)	–	–	0.001
Acute renal failure (%)	42 (24.1)	21 (22.6)	21 (26.6)	1.24	0.61 - 2.49	0.54
Acute respiratory failure (%)	52 (30.2)	27 (29)	25 (31.6)	1.13	0.59 - 2.17	0.71
Admitted to ICU (%)	57 (33.1)	35 (37.6)	22 (27.8)	0.64	0.33 - 1.22	0.17
Inadequate initial treatment (%)	31 (18.0)	9 (9.7)	22 (27.8)	8.35	1.55 - 8.39	0.002
Mortality (%)						
≤ 7 days	18 (10.4)	13 (14.0)	5 (6.3)	0.41	0.14 - 1.22	0.08
30 - day mortality	37 (21.5)	20 (21.5)	17 (21.5)	1.00	0.48 - 2.07	0.99
Overall mortality	61 (35.5)	32 (34.4)	29 (36.7)	1.10	0.59 - 2.06	0.75

not find a significant difference in mortality between these groups. Other authors have also found that there is not a significant difference in mortality between MRSA and MSSA BSIs,[19] even if the patients did not receive an active agent during the initial 48 h after diagnosis. Moreover, this agent is commonly used in combination with aminoglycosides, but this common practice has not demonstrated any reduction in mortality rates, although it has shown a reduction in the duration of the bacteremia (~1 day) in patients with native-valve endocarditis.[20-22] Combination of vancomycin and aminoglycosides was recorded in 14/41 patients with MSSA-BSI and in 26/57 with MRSA-BSI. No differences in ≤ 7 day and in-hospital mortality between MRSA and MSSA BSI patients were observed. Only a slight trend was noted with MSSA BSI mortality. These findings are similar to those found by Harbarth, *et al*.[2] They reported that there was not any difference in crude mortality between MRSA and MSSA BSIs, and mortality was equal when the groups were adjusted for comorbidities and confounding factors. Other studies have noticed a trend towards a higher mortality in patients with MRSA BSI.[3,5,23] Our results showed similar outcomes in patients with both types of organisms.

CA-MRSA has been associated with severe community acquired infections (skin and soft tissue,[24,25] pneumonia,[26,27] etc.) and this type of isolates have caused severe disease in hospitalized patients in some centers.[28] However, our results showed that almost all of the organisms isolated were HA-MRSA, similar to the findings reported by several hospitals in Mexico.[29,30]

In conclusion our data demonstrated a very high incidence rate of hospital acquired MRSA BSI in association with a prolonged hospital stay. Surprisingly, there was not a major difference in the rate of crude mortality between MRSA and MSSA BSIs in patients with adequate or inadequate initial treatment.

REFERENCES

1. Tomic V, Svetina Sorli P, Trinkaus D, Sorli J, Widmer AF, Trampuz A. Comprehensive strategy to prevent nosocomial spread of methicillin-resistant Staphylococcus aureus in a highly endemic setting. *Arch Intern Med* 2004; 164: 2038-43.
2. Harbarth S, Rutschmann O, Sudre P, Pittet D. Impact of methicillin resistance on the outcome of patients with bacteremia caused by Staphylococcus aureus. *Arch Intern Med* 1998; 158: 182-9.
3. Tverdek FP, Crank CW, Segreti J. Antibiotic therapy of methicillin-resistant Staphylococcus aureus in critical care. *Crit Care Clin* 2008; 24: 249-60.
4. Crum NF, Lee RU, Thornton SA, et al. Fifteen-year study of the changing epidemiology of methicillin-resistant Staphylococcus aureus. *Am J Med* 2006; 119: 943-51.
5. Romero-Vivas J, Rubio M, Fernandez C, Picazo JJ. Mortality associated with nosocomial bacteremia due to methicillin-resistant Staphylococcus aureus. *Clin Infect Dis* 1995; 21: 1417-23.
6. Wallin TR, Hern HG, Frazee BW. Community-associated methicillin-resistant Staphylococcus aureus. *Emerg Med Clin N Am* 2008; 26: 431-55.
7. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008; 36: 309-32.
8. Maree CL, Daum RS, Boyle-Vavra S, Matayoshi K, Miller LG. Community-associated methicillin-resistant Staphylococcus aureus isolates causing healthcare-associated infections. *Emerg Infect Dis* 2007; 13: 236-42.
9. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; sixteenth informational supplement. 2006; 26(3): 118-23, table 2c.
10. Louie L, Goodfellow J, Mathieu P, Glatt A, Louie M, Simor AE. Rapid detection of methicillin-resistant Staphylococci from blood culture bottles by using a multiplex PCR assay. *J Clin Microbiol* 2002; 40: 2786-90.
11. Zhang K, McClure JA, Elsayed S, Louie T, Conly JM. Novel multiplex PCR assay for characterization and concomitant subtyping of staphylococcal cassette chromosome mec types I to V in methicillin-resistant Staphylococcus aureus. *J Clin Microbiol* 2005; 43: 5026-33.
12. Sifuentes-Osornio J, Guerrero-Almeida MC, Ponce de León-Garduño LA, Guerrero-Almeida ML. Trends for bacteremia and risk factors for death in a tertiary hospital in Mexico City. 1981-1992. *Gac Med Mex* 2001; 137: 191-202.
13. Kato-Maeda M, Bautista-Alavez A, Rolón-Montes-de-Oca AL,et al. Increasing trend of antimicrobial drug-resistance in organisms causing bacteremia at a tertiary-care hospital: 1995 to 2000. *Rev Invest Clin* 2003; 55: 600-05.
14. Kluytmans J, Struelens M. Meticillin resistant Staphylococcus aureus in the hospital. *BMJ* 2009; 338: b364.
15. Khatib R, Schaffer C, Johnson LB. Staphylococcus aureus in a single positive blood culture: causes and outcome. *Scand J Infect Dis* 2002; 34: 645-7.
16. Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, Carmeli Y. The impact of methicillin resistance in Staphylococcus aureus bacteremia on patient outcomes: mortality, length of stay, and hospital charges. *Infect Control Hosp Epidemiol* 2005; 26: 166-74.
17. Cosgrove SE, Fowler VG. Management of methicillin-resistant Staphylococcus aureus bacteremia. *Clin Infect Dis* 2008; 46: S386-S393.
18. Fowler VG Jr, Boucher HW, Corey GR, et al. Daptomycin versus standard therapy for bacteremia and endocarditis caused by Staphylococcus aureus. *N Engl J Med* 2006; 355: 653-65.
19. Wang JL, Chen SY, Wang JT. Comparison of both clinical features and mortality risk associated with bacteremia due to community-acquired methicillin-resistant Staphylococcus aureus and methicillin-susceptible S. aureus. *Clin Infect Dis* 2008; 46: 799-806.
20. Abrams B, Sklaver A, Hoffman T, Greenman R. Single or combination therapy of staphylococcal endocarditis in intravenous drug abusers. *Ann Intern Med* 1979; 90: 789-91.
21. González C, Rubio M, Romero-Vivas J, González M, Picazo JJ. Bacteremic pneumonia due to Staphylococcus aureus: A comparison of disease caused by methicillin-resistant and methicillin-susceptible organisms. *Clin Infect Dis* 1999; 29: 1171-7.

22. Wyllie DH, Crook DW, Peto TE. Mortality after Staphylococcus aureus bacteremia in two hospitals in Oxfordshire, 1997-2003: cohort study. *BMJ* doi:10.1136/bmj.38834.421713.2F (published 23 June 2006).
23. Francis JF, Doherty MC, Lopatin, et al. Severe community-onset pneumonia in healthy adults caused by methicillin-resistant staphylococcus aureus carrying the panton-valentine leukocidin genes. *Clin Infect Dis* 2005; 40: 100-07.
24. Daum RS. Clinical practice. Skin and soft-tissue infections caused by methicillin-resistant Staphylococcus aureus. *N Engl J Med* 2007; 357: 380-90.
25. Diep BA, Sensabaugh GF, Somboona NS, Carleton HA, Perdreau-Remington F. Widespread skin and soft-tissue infections due to two methicillin-resistant Staphylococcus aureus strains harboring the genes for Panton-Valentine leucocidin. *J ClinMicrobiol* 2004; 42: 2080-4.
26. Rubinstein E, Kollef MH, Nathwani D. Pneumonia caused by methicillin-resistant Staphylococcus aureus. *Clin Infect Dis* 2008; 46(Suppl 5): S378-S385.
27. O'Brien FG, Pearman JW, Gracey M, Riley TV, Grubb WB. Community strain of methicillin-resistant Staphylococcus aureus involved in a hospital outbreak. *J Clin Microbiol* 1999; 37: 2858-62.
28. Borer A, Gilad J, Yagupsky P. et al. Community-acquired methicillin-resistant Staphylococcus aureus in institutionalized adults with developmental disabilities. *Emerg Infect Dis* 2002; 8: 966-70.
29. Echániz-Aviles G, Velázquez-Meza ME, Aires-de-Sousa M. et al. Molecular characterization of a dominant methicillin-resistant Staphylococcus aureus (MRSA) clone in a Mexican hospital (1999-2003). *Clin Microbiol Infect* 2006; 12: 22-8.
30. Velazquez-Meza ME, Aires de Sousa M, Echaniz-Aviles G. et al. Surveillance of methicillin-resistant Staphylococcus aureus in a pediatric hospital in Mexico City during a 7-year period (1997 to 2003): clonal evolution and impact of infection control. *J Clin Microbiol* 2004; 42: 3877-80.

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