Differences Between Methicillin-susceptible Versus Methicillin-resistant *Staphylococcus aureus* Infections in Pediatrics

Multicenter Cohort Study Conducted in Bogotá, Colombia, 2014–2018

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Background: The epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) has changed in recent years. The present article is intended to establish differences between clinical, laboratory and imaging findings and outcomes of MSSA and MRSA infections, as well as among subgroups of infection such as skin and soft tissue infection, osteoarticular, bacteremia or pneumonia in a pediatric population from Bogota, Colombia.

Methods: Retrospective cohort study using clinical records of patients under 18 years of age treated at the participating centers in Bogota, Colombia, between 2014 and 2018. The first positive *S. aureus* culture was studied. MSSA and MRSA were compared. The χ^2 test, Fisher exact test, and Kruskal-Wallis test were calculated, and the statistical significance was presented using the difference and its 95% CI.

Results: Five hundred fifty-one patients were included; 211 (38%) corresponded to MRSA and 340 (62%) to MSSA for a total of 703 cultures. A significantly higher probability of having an MSSA infection than MRSA was found in patients with previous heart disease (3.3% vs. 0.5%), neurologic disease (5.9% vs. 2.5%), recent major surgeries (11% vs. 5%) or who has an implanted device (11% vs. 4%). In contrast, in severe MRSA infections (bacteremia, osteoarticular infections and pneumonia), a higher rate of complications was seen (admission to the pediatric intensive care unit, mechanical ventilation and vasoactive support), and in osteoarticular MRSA, more than 1 surgery per case was seen (89% vs. 61%). Laboratory results and mortality were similar.

Conclusions: MRSA was associated with a more severe course in bacteremia, osteoarticular infections and pneumonia. Some classical risk factors associated with MRSA infections were found to be related to MSSA. In general, with the exception of skin and soft tissue infection, there was an increased risk of pediatric intensive care unit admission and mechanical and inotropic support with MRSA in a pediatric population.

Key Words: *Staphylococcus aureus*, staphylococcal infections, pediatrics, bacterial drug resistance, methicillin-resistant *Staphylococcus aureus*

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Unlike methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *S. aureus* (MRSA) has been associated with increased antibiotic exposure, prolonged hospital stays, and admission to the pediatric intensive care unit (PICU).[1–4] Until the 1990s, most MRSA infections occurred in a hospital setting. However, an increase in *S. aureus* isolates, particularly community-acquired (CA) MRSA, was reported worldwide by 2000.[5,6] However, a fall in the incidence of MRSA was reported in Europe where it went from 23% in 2009 to 16% in 2018.[7] In the United States of America, a progressive decrease in MRSA isolates in pediatrics has also been reported.[8,9] The epidemiologic records for Colombia prepared by the Group for Bacterial Resistance Control in Bogota reported that *S. aureus* was the second most frequently isolated bacteria in hospitals in 2018 while MRSA frequency was between 40% and 45% from 2010 to 2018.[10]

CA-MRSA as a cause of infection in children has been associated with greater severity, possibly due to the presence of more virulence factors related to the USA300 strain in the Colombian pediatric population.[11] MRSA infections can manifest with skin and soft tissue infection (SSTI),[12,13] bacteremia (20%–25%),[14,15] osteoarticular infections (OIs), deep infections[16–18] or pneumonia.[19]

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Attempts to predict methicillin susceptibility based on clinical or demographic factors have been unsuccessful. Finding the differences between these types of infections will facilitate timely diagnosis, and having this information could help guide the start of timely antibiotic treatment.[20–22] The present article is intended to compare clinical, laboratory and imaging findings and outcomes of MSSA and MRSA infections.

MATERIALS AND METHODS

Study Design

This is a multicenter, historical, cohort study that used the medical records of patients with *S. aureus* infection treated at 6 tertiary-level university centers in Bogota, Colombia, 2 of which were children-only.

Case Selection

Cases were identified based on a positive *S. aureus* culture, under 18 years of age, and diagnosed between January 1, 2014, and December 31, 2018. The information was extracted from the culture databases of the microbiology laboratories using the WHONET 18 software and automated identification methods that included MicroScan, VITEK 2 XL, VITEK MS, VIRTUO, and Phoenix depending on the center. Patients with cultures that lacked pathologic relevance (colonization or contamination), were less than 1 month old or lacked clinical records (to avoid measurement bias) were excluded.

Infections were classified into (1) SSTI in patients with clinical signs of SSTI and *S. aureus* in cultures of spontaneous secretion or surgical drainage. In cases of nonsuppurative cutaneous infections, clinical symptoms plus the presence of a positive culture for *S. aureus* from nasal cavities were considered SSTI; (2) bacteremia in patients with *S. aureus* in blood cultures (primary) or secondary to another infection (osteoarticular, pneumonia, SSTI or other foci); (3) OI in patients with clinical signs of infection in bones or joints accompanied by suggestive imaging scans and *S. aureus* in a culture of secretion or blood culture. Finally, (4) pneumonia included patients with clinical signs of lower respiratory tract infection associated with suggestive imaging scans and identification of *S. aureus* in pleural culture or blood culture. A patient may have multiple cultures from various sites during an infection.

For this analysis, if there was more than 1 positive culture, only the first positive culture from each location was used. Each was categorized as either MSSA or MSRA, and they were compared with each other based on their origin (SSTI, bacteremia, osteoarticular and pneumonia).

Sociodemographic variables (age, sex and center) and underlying diseases (immunodeficiencies, prematurity, neoplasms, autoimmune diseases, congenital heart disease, genetic syndromes, malnutrition, chronic lung disease, neurologic disease, atopic dermatitis or kidney disease) were identified. Risk factors previously described in the literature, such as major surgeries within 6 months of infection, a more than 3-day hospital stay and implanted medical devices (osteosynthesis material, central venous catheter, gastrostomy, ventriculoperitoneal shunt and peritoneal dialysis catheter) were also evaluated. Finally, community-onset infection was defined as a positive culture obtained <72 hours after hospital admission. Clinical and severe manifestations on admission (hypotension, impaired capillary refill or impaired consciousness), lab test results, imaging studies, number of surgeries, and outcomes were also described.

Statistical Analysis

A 40% prevalence reported by Group for Bacterial Resistance Control in Bogota in 2018 was used to estimate sample size.[11] Estimated risk factors with frequencies greater than 15% were expected, and calculations were done to detect differences with an odds ratio greater than 2, a power of 80% and an α error of 0.05. As a result, at least 492 cases (351 cases of MSSA and 141 cases of MRSA) were required. A descriptive analysis was carried out, and the qualitative variables showed absolute and relative frequencies. Regarding quantitative variables, central tendency and dispersion measures were used based on the distribution of the data. For comparisons between MSSA and MRSA cultures, the χ^2 test was used for categorical variables, Fisher exact test for small sample sizes ($n<5$) and nonparametric (Kruskal-Wallis) test for continuous variables. Missing data were not imputed for laboratory data, and statistical significance was presented using the difference and its 95% CI. The study was approved by the research committee and the ethics committees for human subject research at all the participating centers.

RESULTS

A total sample of 1045 available cases was obtained of which 494 were excluded because 181 corresponded to colonization or contamination, 210 had incomplete information or were repeat cultures, and 103 were neonatal infections. The final analysis included 551 cases with 703 positive cultures. Fig. 1 describes the selection flowchart. Of the cases found, 211 (38%) were MRSA and 340 (62%) were MSSA. These showed slight variations over the years, but the differences were not statistically significant (Table 1; Fig. 2). Age and sex distribution between categories was similar, and no differences were seen in connection with the center. With respect to comorbidities, a statistically significant frequency was seen in heart disease (MRSA 0.5% vs. MSSA 3.3%), neurologic disease (MRSA 2.4% vs. MSSA 5.9%) and other diseases (MRSA 10.9% vs. MSSA 17.7%; Table 1). The presence of major surgery in the last 6 months (MRSA 5% vs. MSSA 11%), device use (MRSA 3% vs. MSSA 11%) and hospital stays of more than 3 days (MRSA 11% vs. MSSA 17%) prior to the current clinical picture were found to be significantly associated with MSSA (Table 2).

On admission, 27 cases presented some evidence of severity, 14 (4%) had MSSA, and 13 (6%) had MRSA (Diff, 2%; 95% CI −2% to 6%). No differences were found in patients with hypotension [7 (2%) MSSA vs. 7 (3%) MRSA], respiratory distress [5 (1%) MSSA vs. 5 (2%) MRSA −1% to 3%], altered consciousness [0 (0%) MSSA vs. 2 (1%) MRSA 0% to 2%] or prolonged capillary refill [0 (0%) MSSA vs. 1 (0%) MRSA] by type of resistance. Regarding laboratory findings, no major differences were found. There was only a higher number of median absolute neutrophil counts [MRSA 8500 cells/mm^3 (interquartile range [IQR], 8720–16,000) vs. MSSA 7522 cells/mm^3 (IQR 8720–16,000); P=0.047; Table 3].

The median overall hospital stay was 10 days (IQR 6–17 days) for MRSA and 8 days (IQR 5–15 days) for MSSA; 14% (77/551) of infections required admission to PICU with stays of 8 days (IQR 6–11 days) for MRSA and 6 days (IQR 3–13 days) for MSSA. Of the total number of patients, 53% (41/77) received assisted ventilation with a median of $7^{4–9}$ days for MRSA and $9^{4–11}$ days for MSSA while inotropic agents were used in 77% (48/62) of the patients for $4^{3–7}$ days with MRSA and $6^{2–9}$ days with MSSA. With respect to the number of days of hospitalization, a longer stay in hospital was only found in the group of MRSA OIs (P = 0.0006), and no significant differences were found in the number of days spent in the PICU. Mortality was reported in 3 MRSA cases (1%) and 7 MSSA cases (2%). None of these differences were significant. Regarding the type of infection, 356 cases presented with SSTI infection (associated or not with bacteremia), 136 with OIs that may or may not have been associated with other infections, 45

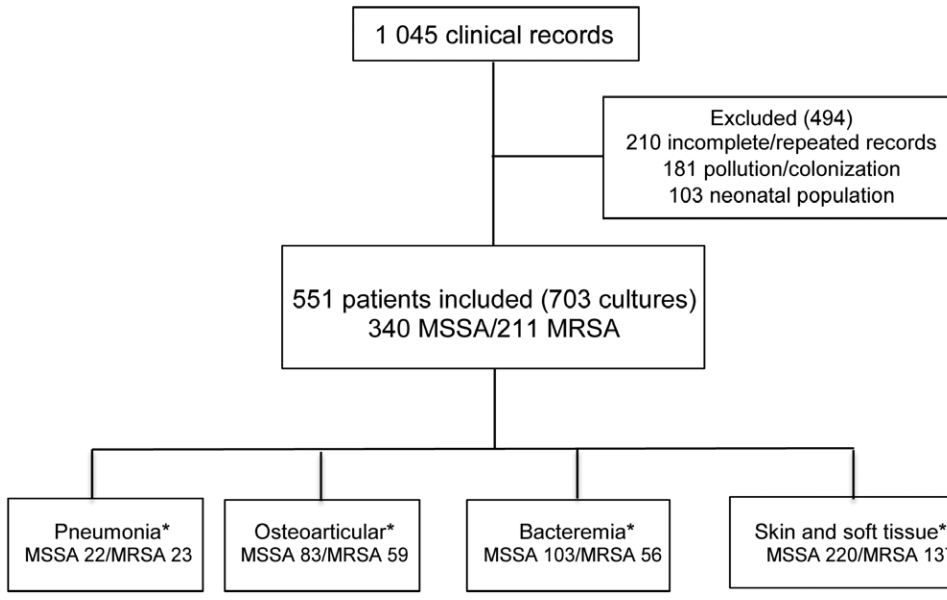

FIGURE 1. Case selection flowchart. *The most important infection was chosen in cases with more than 1 positive culture (osteoarticular > pneumonia > skin and soft tissues > bacteremia).

TABLE 1. Demographic Characteristics Based on the Presence or Absence of Resistance

	MRSA, n = 211 (38%)	MSSA, n = 340 (62%)	Diff (95% CI) [*P*]*
Male sex, n (%)	119 (56%)	183 (54%)	3 (−6 to 11)%
Age, median (IQR)	97 (30 to 162)	92 (23 to 155)	[0.254]
1–12 mo	30 (14%)	56 (16%)	−2 (−8 to 4)%
1–4 yr	47 (22%)	78 (23%)	−1 (−8 to 6)%
5–11 yr	63 (30%)	107 (31%)	−1 (−9 to 7)%
12–17 yr	71 (34%)	99 (29%)	5 (−3 to 13)%
Underling diseases, n (%)	71 (34%)	140 (42%)	−8 (−16 to 3)%
Immunodeficiency	4 (1.9%)	10 (3.0%)	−1.1 (−3.7 to 1.5)%
Prematurity	13 (6.2%)	25 (7.4%)	−1.2 (−5.5 to 3.1)%
Malignancy	6 (2.8%)	18 (5.3%)	−2.5 (−5.8 to 7.6)%
Autoimmune	4 (1.9%)	5 (1.0%)	0.9 (−1.2 to 3.0)%
Heart disease	**1 (0.5%)**	**11 (3.3%)**	**−2.8 (−4.9 to −0.7)%**
Undernutrition	6 (2.9%)	12 (3.6%)	−0.7 (−3.4 to 2.3)%
Genetic disease	5 (2.4%)	16 (4.7%)	−2.3 (−5.4 to 7.5)%
Chronic lung disease	7 (3.3%)	13 (3.8%)	−0.5 (−3.7 to 2.7)%
Neurologic disease	**5 (2.4%)**	**20 (5.9%)**	**−3.5 (−6.7 to −0.3)%**
Atopic dermatitis	13 (6.2%)	26 (7.7%)	−1.5 (−5.8 to 2.8)%
Renal disease	3 (1.4%)	12 (3.6%)	−2.2 (−4.7 to 0.3)%
Other diseases†	**23 (10.9%)**	**60 (17.7%)**	**−6.8 (−12.6 to −1.0)%**

NEC indicates necrotizing enterocolitis. Bold means statistically significant.

*Differences and 95% CIs calculated as the percentage with MRSA minus the percentage with MSSA. Negative values represent a higher proportion of patients with MSSA for the given variable. *P* values for continuous data using a nonparametric (Kruskal-Wallis) test.

†Other diseases such as the Kawasaki syndrome, achalasia, syphoscoliosis, postextubation laryngeal stenosis, HIV-positive mother, short bowel, history of NEC, history of total colectomy, right perinsular pop hemispherectomy for craniotomy, severe dengue, ileostomy, obesity, polycystic ovary, constipation, allergic rhinitis, hip dysplasia, hypoacusis, headache, giant nevus, sickle cell anemia, psychoactive substance use, esophageal atresia, chicken pox, cirrhosis, hemophilia A and hypothyroidism.

with pneumonia not associated with OI and 21 with bacteremia not associated with any of the infections described above. More than one focus of infection was identified in 22 cases: 13 cases presented with OI and SSTI simultaneously; 5 cases with pneumonia and OI; 1 case with pneumonia and SSTI and 3 cases had OI, pneumonia, and SSTI infection. Each group is described below based on the type of infection; a case may be included in more than 1 group (Table 4).

Skin and Soft Tissue Infections

There were 356 cases of SSTI of which 137 (38.5%) were MRSA and 219 (61.5%) MSSA. In the MRSA group, 137 (65%) presented with SSTI and 219 (64%) in the MSSA group (Table 4). No differences were found between the type of infection either between surgical drainage and spontaneous drainage based on susceptibility. The presence of nonsuppurative infections (without

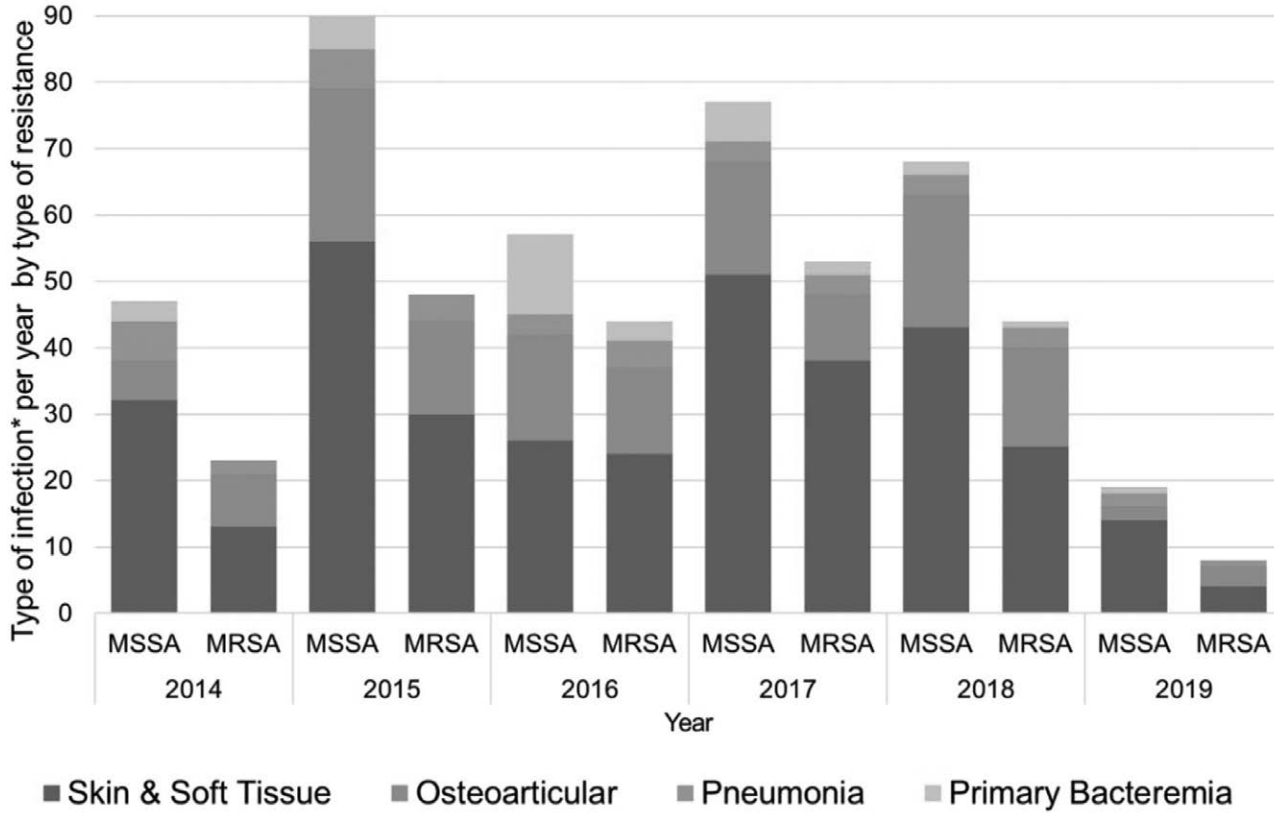

FIGURE 2. Comparison of MSSA and MRSA cases per type of infection. full color online

TABLE 2. Risk Factors Based on the Presence or Absence of Resistance

	MRSA, n = 211 (38%)	MSSA, n = 340 (62%)	Diff (95% CI)*
Some factor (a, b or c)	**28 (13%)**	**83 (24%)**	**−11 (−17 to −5)%**
a. Major surgery (n = 549)	**10 (5%)**	**37 (11%)**	**−6 (−10 to −2)%**
Type of major surgery			
None	**201 (95%)**	**303 (89%)**	**6 (2 to 10)%**
Central nervous system	2 (1.0%)	4 (1.2%)	−0.2 (−2.0 to 1.6)%
Cardiothoracic	1 (0.5%)	2 (0.6%)	−0.1 (−1.4 to 1.2)%
Abdomen	3 (1.4%)	5 (1.5%)	−0.1 (−2.1 to 1.9)%
Osteoarticular	**2 (1.0%)**	**18 (5.3%)**	**−4.3 (−7.0 to −1.6)%**
Skin and soft tissues	2 (1.0%)	5 (1.5%)	−0.5 (−2.4 to 1.4)%
Others	0 (0.0%)	3 (0.9%)	−0.9 (−1.9 to 0.1)%
b. Hospital stay (>3 days), n = 527	**21 (11%)**	**54 (17%)**	**−6 (−11.8 to −0.2)%**
c. Device use (n = 548)	**7 (4%)**	**38 (11%)**	**−7 (−11 to −3%)%**
Device type			
None	**204 (97%)**	**302 (89%)**	**8.0 (4.0 to 12.0)%**
Osteosynthesis material	3 (1.4%)	12 (3.5%)	−2.1 (−4.6 to 0.4)%
Central venous catheter	**2 (1.0%)**	**16 (4.7%)**	**−3.7 (−6.3 to −1.0)%**
Gastrostomy	1 (0.5%)	3 (0.9%)	−0.4 (−1.8 to 1.0)%
Peritoneal ventricular shunt	0 (0.0%)	1 (0.5%)	−0.5 (−1.2 to 0.2)%
Peritoneal dialysis catheter	1 (0.5%)	2 (0.6%)	−0.1 (−1.4 to 1.2)%
Others	0 (0.0%)	4 (1.2%)	−1.2 (−2.4 to 0.4)%

*Differences and 95% CIs calculated as the percentage with MRSA minus the percentage with MSSA. Negative values represent a higher proportion of patients with MSSA for the given variable.

drainage) was statistically more frequent in MSSA (14%) than in MRSA (7%; Table 4).

Bacteremia

One hundred fifty-nine (159) cases of bacteremia were found. Of these, 84 (52%) were associated with OI, 19 (13%) with pneumonia, 21 (13%) with SSTI and 14 (9%) with other foci; 21 (13%) had no identified focus (primary). In the MSSA group, 103 cases (30%) had bacteriemia and 56 (27%) did in the MRSA group. Bacteremia secondary to OI was more frequently associated with methicillin resistance (MRSA 73% vs. MSSA 53%) and SSTIs with methicillin-sensitive *S. aureus* (MRSA 6% vs. MSSA

TABLE 3. Laboratory Findings at the Time of Infection Based on the Presence or Absence of Resistance

	MRSA, n = 211 (38%)	MSSA, n = 340 (62%)	Diff (95% CI) [*P*]*
Complete blood count performed	177 (84%)	300 (88%)	−4 (−10 to 2)%
Missing	1	0	
Leukocytes (cell/mm^3), median (IQR)	13,104 (9200 to 18,035)	11,990 (8720 to 16,000)	[0.061]
Neutrophils (cell/mm^3), median (IQR)	**8500 (8720 to 16,000)**	**7522 (8720 to 16,000)**	**[0.047]**
Platelets (cell/mm^3), median (IQR)	344,000 (8720 to 16,000)	338,000 (8720 to 16,000)	[0.947]
C-reactive protein (mg/L), median (IQR)	53.7 (12.8 to 167.8)	39.0 (9.6 to 105)	[0.057]
Not done	*61*	*83*	
ESR (mm/h), median (IQR)	31 (16 to 45)	30 (13 to 48)	[0.669]
Blood cultures done	86 (41%)	153 (45%)	−1 (−12 to 4)%
Positive	56 (65%)†	103 (67%)†	−2 (−15 to 11)%

*Differences and 95% CIs calculated as the percentage with MRSA minus the percentage with MSSA. Negative values represent a higher proportion of patients with MSSA for the given variable. *P* values for continuous data using a nonparametric (Kruskal-Wallis) test.

†Percentage of the complete blood count or blood cultures drawn.

21%). PICU admission (MRSA 52% vs. MSSA 28%), mechanical ventilation (MRSA 30% vs. MSSA 13%), and vasoactive support (MRSA 38% vs. MSSA 17%) were statistically more frequent in the MRSA group (Table 4).

OIs

One hundred thirty-six (136) cases were found: 59 (43.4%) due to MRSA and 77 (56.6%) to MSSA. In the MRSA group, 59 (28%) had OI and 77 (23%) did in the MSSA group with no differences regarding the type of infection [osteomyelitis (OM), AS or septic arthritis, and OM; Table 4]. Positive blood cultures in 38 (64%) were associated with MRSA and 40 (52%) with MSSA (Diff, 12%; 95% CI −5% to 29%). In 116 (92.8%), tissue cultures were positive, with no differences between MRSA [52 (96.3%)] and MSSA [64 (90.4%); Diff, 6%; 95% CI −3% to 15%]. It is significant that patients with MRSA isolation required more than 3 surgical procedures (MRSA 45% vs. MSSA 24%). In addition, there were significantly more PICU admissions (36% vs. 12%), more mechanical ventilation (19% vs. 3%), more vasoactive support (27% vs. 5%) and more days of hospitalization [20 (15–31) vs. 15 (11–21)] related to MRSA.

Pneumonia

Forty-five (45) cases were identified of which 23 (51%) were associated with MRSA and 22 (49%) with MSSA. Chest radiographs showed differences in lobar and multilobar consolidation patterns (MRSA 96% vs. MSSA 62%) and complicated pneumonia (MRSA 57% vs. MSSA 24%). Admission to PICU (74% vs. 50%) and the need for mechanical ventilation (61% vs. 32%) was more frequent in the MRSA group.

DISCUSSION

The present study found a relationship between OIs, secondary bacteremia, complicated pneumonia, and the presence of MRSA with no differences in SSTI. Some of the risk factors previously described in MRSA infections in this series were interestingly associated with MSSA infections (previous major surgery, use of any implanted device and recent hospitalization).

Finding risk factors associated with MSSA such as major surgery in the last 6 months or the presence of implanted medical devices was rare,[23] but this is consistent with the most recent study by Vallejo et al of neurosurgical patients, where greater susceptibility to oxacillin was observed in infections in patients with ventriculoperitoneal shunts (70%).[24] Likewise, in 2019, Foster et al reported that MSSA was the primary agent in infections associated with orthopedic implants (72%).[25]

Regarding SSTI, a higher frequency of MSSA was identified in the study population while no significant differences were found by year and demographic profile compared with MRSA. The Texas Children's Hospital demonstrated a significant decline in invasive and SSTI from CA-MRSA and suggested that CA-MSSA could be a reemerging pathogen in this type of infection.[26] This decrease in CA-MRSA is partially attributed to the possible acquisition of herd immunity to the endemic clone USA300 of CA-MSSA, which could protect against invasive infections.[26] In this study, no differences were identified based on the type of infection (abscess or cellulitis). However, as Elliott et al described, MSSA was more frequent in nonsuppurative skin infections in accordance with recent studies in which no differences were seen in the treatment with β-lactam versus other antibiotics with MRSA activity.[27] This is similar to our findings that nonsuppurative skin infections seem to be more frequently associated with MSSA or *Streptococcus pyogenes*.[28,29]

Most cases of bacteremia were caused by CA-MSSA and, to a lesser extent, by hospital-acquired MRSA. These findings are consistent with the usual behavior in bacteremia due to MSSA[30] and MRSA.[31] In children, community-based *S. aureus* bacteremia is more frequent and is associated with concomitant foci of infection[30,32] while healthcare-associated bacteremia is more commonly observed in neonates under the age of one and usually related to intravascular devices.[33] Significant risk factors were found based on the origin of secondary bacteremia; osteoarticular and pulmonary foci are at increased risk of secondary bacteremia due to MRSA. Hamdy et al also demonstrated that foci such as OM (31%), catheter-related infection (22%), SSTI (16%) and pneumonia (9%) are predominant[31] in a cohort of children with bacteremia caused by MRSA. Abernethy et al, in turn, reported that most bacteremia cases caused by MSSA originated from SSTI[33]; this is similar to what has been reported in this study.

OIs due to MRSA were more severe than MSSA infections. They required more than 3 surgical interventions, coinciding with Arnold et al, and others, who stated that patients with MRSA needed surgical procedures more frequently (91%) than cases with MSSA (62%; $P < 0.001$).[16,34–36] In contrast to the findings of this study, reports from Finland and France, where MSSA predominates, describe less need for surgical procedures.[37,38] Kaplan reported differences in the United States (minor surgeries, shorter duration of antibiotics) possibly due to the predominance of MSSA and the lower frequency of virulence factors, particularly the presence of Panton-Valentine leucocidin.[39] Longer hospital stays for MRSA compared with MSSA are described in the literature as generally associated with greater medical complications,[16] which is similar to our findings (MRSA $20^{15–31}$ vs. MSSA $15^{11–21}$; $P < 0.001$). In this study, MRSA significantly predicted the requirement of additional

TABLE 4. Infection Groups Depending on the Presence or Not of Resistance

	MRSA, n (%) 211	MSSA, n (%) 340	Diff (95% CI)*/*P* value†
Skin and soft tissues	137 (65%)	219 (64%)	1 (−9 to 8)%
Blood cultures done	25 (18%)	52 (24%)	−6 (−15 to 3)%
Positive blood cultures	**6 (24%)**‡	**25 (48%)**‡	**−24 (−46 to −2)%**
Treatment			
Surgical treatment only	61 (46%)	89 (42%)	4 (−7 to 15)%
Spontaneous drainage only	60 (45%)	86 (40%)	5 (−6 to 16)%
Surgical and spontaneous drainage	4 (3%)	9 (4%)	−1 (−5 to 3)%
No drainage	**9 (7%)**	**29 (14%)**	**−7 (−13 to −1)%**
Missing	3	6	
Localization			
Face, head and neck	**28 (21%)**	**71 (33%)**	**−12 (−21 to −3)%**
Upper limbs	25 (19%)	45 (21%)	−2 (−11 to 5)%
Lower limbs	**51 (38%)**	**57 (26%)**	**12 (2 to 22)%**
Chest	17 (13%)	23 (11%)	2 (−5 to 9)%
Abdomen	4 (3%)	8 (4%)	−1 (−5 to 3)%
Hip	6 (4%)	7 (3%)	1 (−3 to 5)%
Genitalia	3 (2%)	7 (3%)	−1 (−4 to 2)%
Missing	2	3	
Duration of hospital stay (days), median (IQR)	7 (5 to 9)	5 (4 to 8)	[*P* = 0.1175]
PICU admission	7 (4%)	8 (5%)	−1 (−5 to 3)%
Length of stay (days), median (IQR)	8 (5 to 51)	9 (8 to 12)	[*P* = 0.8975]
Mechanical ventilation	5 (4%)	3 (1%)	3% (−1 to 7)%
Vasoactive support	5 (4%)	5 (2%)	2% (−2 to 6)%
Bacteremia	56 (27%)	103 (30%)	−3 (−11 to 4) %
Origin			
Health care–associated infection	8 (14%)	22 (21%)	−7 (−20 to 5)%
Community-onset infection	46 (85%)	76 (78%)	7 (−6 to 20)%
Missing	2	5	—
Type			
Primary	4 (7%)	17 (17%)	−10 (−20 to 0)%
Secondary	52 (93%)	86 (84%)	9 (−1 to 19) %
Secondary infection			
Osteoarticular	**38 (73%)**‡	**46 (53%)**‡	**20 (4 to 36)%**
Pulmonary	9 (17%)‡	10 (12%)‡	5 (−7 to 17)%
SSTI	**3 (6%)**‡	**18 (21%)**‡	**−15% (−26 to −4)%**
Others	**2 (4%)**‡	**12 (14%)**‡	**−10 (−19 to −1)%**
PICU admission	**29 (52%)**	**29 (28%)**	**24 (8 to 40)%**
Length of stay (days), median (IQR)	14 (8 to 23)	5 (2 to 15)	[*P* = 0.2429]
Mechanical ventilation	**17 (30%)**	**13 (13%)**	**17 (3 to 31)%**
Vasoactive support	**21 (38%)**	**18 (17%)**	**21 (6 to 36)%**
Osteoarticular	59 (28%)	77 (23%)	5 (−3 to 13)%
Diagnosis			
OM	24 (41%)	36 (43%)	−2 (−19 to 15) %
SA	18 (31%)	27 (33%)	−2 (−18 to 14)%
Both (SA and OM)	16 (27%)	13 (16%)	11 (−3 to 25)%
Missing	4	9	
ICU admission	**21 (36%)**	**9 (12%)**	**24 (10 to 38)%**
Length of stay (days), median (IQR)	8 (6 to 10)	4 (2 to 15)	[*P* = 0.648]
Mechanical ventilation	**11 (19%)**	**2 (3%)**	**16 (5 to 27)%**
Vasoactive support	**16 (27%)**	**4 (5%)**	**22 (10 to 34)%**
Surgical treatment	55 (93%)	70 (91%)	2 (−7 to 11)%
More than 1 surgical procedure‡	**49 (89%)**‡	**43 (61%)**‡	**28 (14 to 42)%**
More than 3 surgical procedures‡	**25 (45%)**‡	**17 (24%)**‡	**21 (4 to 38)%**
Pneumonia	23 (11%)	22 (6%)	5 (0 to 10)%
Chest radiographs			
Interstitial and alveolar pattern	**1 (4%)**	**8 (38%)**	**−34 (−56 to −12)%**
Lobar and multilobar consolidation	**22 (96%)**	**13 (62%)**	**34 (12 to 56)%**
Complicated pneumonia§	**13 (57%)**	**5 (24%)**	**33 (6 to 60) %**
Missing	0	1	
Duration of hospital stay (days), median (IQR)	17.5 (13.5 to 24)	18 (12 to 35)	[*P* = 0.7244]
ICU admission	**17 (74%)**	**11 (50%)**	**24 (−3 to 52)%**
Length of stay (days), median (IQR)	8 (4 to 13)	6 (5 to 10)	[*P* = 0.7612]
Mechanical ventilation	**14 (61%)**	**7 (32%)**	**29 (1 to 57)%**
Vasoactive support	**12 (52%)**	**6 (27%)**	**25 (−3 to 53)%**

OM indicates osteomyelitis; SA, septic arthritis.

*Differences and 95% CIs calculated as the percentage with MRSA minus the percentage with MSSA. Negative values represent a higher proportion of patients with MSSA for the given variable.

†*P* value by Kruskal-Wallis; statistical significance, $P<0.05$.

‡Percentage of the blood cultures, secondary bacteremia or surgical treatment.

§Complicated pneumonia defined as the presence of empyema, pneumatoceles, pleural effusion, necrotizing pneumonia or cavitation.

surgical procedures for the treatment of OIs and a more severe clinical course.

In our study, MRSA was slightly more frequent in bacteremia secondary to pneumonia, and this coincides with other populations where higher rates of complications and mortality have also been described.[40] Pneumonia caused by MRSA is associated with a higher rate of complications such as pleural effusion, pleural thickening, increased requirement for tube placement, pneumatoceles and high mortality rates with no differences in demographic data, days with fever, tachypnea, hypoxia, and length of hospital stay.[41,42] In this study, a higher frequency of complicated pneumonia was found [MRSA 13 (57%) vs. MSSA 5 (24%)]. Some studies have already described a particularly higher frequency of lung abscess and necrotizing pneumonia.[43–45] The literature describes a higher frequency of complications, need for PICU, hospital stay, etc. in MRSA infections that are attributed, in part, to the presence of Panton-Valentine leucocidin, a cytotoxin that destroys leukocytes and causes tissue necrosis.[38] Panton-Valentine leucocidin has been most frequently associated with abscess formation, tissue inflammation, pulmonary complications and the possibility of septic thrombophlebitis, especially in OM.[46] It is most commonly found in MRSA cases, especially in the USA300 strain[47] or in others depending on the geographical region.[10,48]

Finally, regarding the behavior of *S. aureus* in the study period, no differences were found in the presence of MRSA by year or by type of infection studied. This contrasts with Sutter et al, who, from 2005 to 2014, described a decrease in the frequency of MRSA in 39,207 children in the United States while reporting 59.4% susceptibility to oxacillin in 2005 and 68.4% in 2014.[7] Similarly, Hulten et al reported a 60.4% drop in MRSA infections in the Texas Children's Hospital between 2007 and 2014.[23] Considering the current findings, future changes in the behavior of MRSA in children may be expected. It is, therefore, essential to promote surveillance of *S. aureus* infections in the pediatric population across the country.

Some of the limitations of the present study include the retrospective nature of the data collection process and the failure to carry out molecular studies to describe virulence genes.

CONCLUSION

This study raises the importance of active monitoring of *S. aureus* infections in pediatrics in our region.

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