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Risk factors associated with methicillin-resistant *Staphylococcus aureus* skin and soft tissue infections in hospitalized patients in Colombia

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ABSTRACT

Objectives: Methicillin-resistant *Staphylococcus aureus* (MRSA) skin and soft tissue infections (SSTIs) represent a major clinical problem in Colombia. The aim of this study was to evaluate the risk factors associated with MRSA SSTI in Colombia.

Methods: A multicenter cohort study with nested case–control design was performed. Patients with an SSTI with at least 48 h of inpatient care were included. Patients with an MRSA SSTI were considered the case group and patients with either a non-MRSA SSTI or with an Methicillin-susceptible S. aureus (MSSA) SSTI were the control groups. A multivariate logistic regression approach was used to evaluate risk factors associated with MRSA SSTI with two different statistical models.

Results: A total 1134 patients were included. Cultures were positive for 498 patients, of which 52% ($n = 259$) were *Staphylococcus aureus*. MRSA was confirmed in 68.3% of the *S. aureus* cultures. In the first model, independent risk factors for MRSA SSTI were identified as the presence of abscess ($P < 0.0001$), cellulitis ($P = 0.0007$), age 18–44 years ($P = 0.001$), and previous outpatient treatment in the previous index visit ($P = 0.003$); surgical site infection was a protective factor ($P = 0.008$). In the second model, the main risk factor found was previous outpatient treatment in the previous index visit ($P = 0.013$).

Conclusions: Community-acquired SSTIs in Colombia are commonly caused by MRSA. Therefore, clinicians should consider MRSA when designing the initial empirical treatment for purulent SSTI in Colombia, although there seems to be low awareness of this fact.

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Introduction

Skin and soft tissue infections (SSTI) cause a high burden of disease and are a common medical complaint worldwide. According to the HealthCore Integrated Research Database (HIRD), the incidence of SSTI in the USA between 2005 and 2010 was 47.9–48.5 cases per 1000 person-years, representing approximately two times the incidence of urinary tract infections and tenfold the incidence of pneumonia for the same period (Ray et al., 2013a; Miller et al., 2015b; Esposito et al., 2016).

Although in many cases of SSTI, specimens for culture or microbiological isolates are difficult to obtain, *Staphylococcus aureus* appears to be the leading causal agent. Indeed the SENTRY antimicrobial surveillance program report, which gathered SSTI data from different hospitals in three continents (North America, Latin America, and Europe) over a 7-year period (1998–2004), described *S. aureus* as the most frequently isolated etiological agent in SSTIs (33.5%).

In 1993, Udo reported the presence of an endemic strain of methicillin-resistant *S. aureus* (MRSA) in Australian patients who had not had any previous contact with medical settings (Udo, 1993), indicating the emergence of community-associated MRSA (CA-MRSA). Between 1993 and 2005, there was a sharp increase in the number of CA-MRSA SSTIs (Ray et al., 2013b). Currently this represents the main cause of this type of infection in emergency rooms in the USA (Skov and Jensen, 2009; Miller et al., 2015a; Talan et al., 2016). After performing molecular epidemiological studies, the remarkable increase in MRSA SSTIs in the USA was attributed to the rise of the USA300 MRSA clone (Carrel et al., 2015).

In South America, the USA300 Latin American variant (USA300-LV), first identified in 2005, has substituted the previously predominant healthcare-associated (HA)-MRSA Cordobes/Chilean clone, and has spread throughout community and hospital settings, especially in Colombia, Venezuela, and Ecuador (Reyes et al., 2009; Alvarez et al., 2010; Jiménez et al., 2012; Planet et al., 2015). Currently, the prevalence of infections caused by MRSA in Colombia is reported to be as high as 45–51%, and these are predominantly SSTIs (Reyes et al., 2009; Escobar-Perez et al., 2014).

Risk factors for SSTIs that require hospitalization have been described in multiple international studies. Some of the most relevant of these are diabetes mellitus, MRSA colonization or previous infection, immunosuppression, and trauma (Skiest et al., 2007; Stenstrom et al., 2009; Lipsky et al., 2012; Ray et al., 2013a). Other studies have described young age and purulent infections as risk factors for MRSA SSTIs (Ray et al., 2013a; Haysom et al., 2018). In Latin America, risk factors for MRSA SSTIs have not yet been characterized and this is required in order to make recommendations for the management of these infections in general practice. Due to the scarcity of data on MRSA causing SSTIs in Colombia, a multicenter retrospective study was performed to evaluate the clinical and epidemiological risk factors associated with this condition.

Methods

A multicenter retrospective cohort study with a nested case–control design was conducted from January 2009 to December 2016. The study population included all patients aged ≥18 years with a clinical diagnosis of SSTI who required hospitalization for ≥48 h and who were treated with antimicrobials. The diagnosis of SSTI was performed by a clinician based on clinical data at the time of patient admission. Infection was defined as having a diagnosis in the medical records related to SSTI in accordance with the International Classification of Diseases 10th Revision (ICD 10), including: impetiginization of other dermatoses (L01), cutaneous abscess, furuncle and carbuncle (L02), cellulitis and acute lymphangitis (L03), erysipelas (A46), furunculosis (L02.42), tenosynovitis (M68), necrotizing fasciitis (M72.6), pyomyositis (M60), superficial or deep surgical site infection (SSI) (T81.4), diabetic foot (E10.5), and pressure ulcer with SSTI (L89). Patients with suspected or confirmed bone or joint involvement, superficial vein infections, or the presence of a human or animal bite (excluding insect bite) at the infection site were excluded.

Thirteen Colombian hospitals in seven Colombian cities were included, as follows: Hospital Universitario San Ignacio (Bogotá), Fundación Clínica Shaio (Bogotá), Hospital Santa Clara (Bogotá), La Clínica de la Mujer (Bogotá), Hospital Universitario Hernando Moncaleano (Neiva), Hospital Rosario Pumarejo-López (Valledupar), Clínica Médicos LTDA (Valledupar), Clínica Laura Daniela (Valledupar), Clínica Universitaria San Juan de Dios (Cartagena), Clínica El Rosario (Medellín), Clínica CES (Medellín), Hospital Universitario del Valle (Cali). The Institutional Review Board (IRB) of each healthcare institution granted approval to the research project with an informed consent waiver, as no interventions or therapeutic modifications were made.

Data collection

The medical records were reviewed by healthcare professionals trained in the diagnosis of SSTI, following the definitions of the US Food and Drug Administration (FDA) and the Infectious Diseases Society of America (IDSA) (Moran et al., 2006; Skiest et al., 2007). The data collected from the medical records were de-identified and uploaded into a database for analysis. To ensure information reliability and safety, data were first recorded manually and then uploaded to an online database with registration filters and restrictions. Data quality and reliability were reviewed weekly by one of the principal investigators in the participating centers.

Variables analyzed as risk factors included age, sex, comorbidities, precipitating factors, history of previous surgeries, CA- or HA-SSTI, previous use of antibiotics, antimicrobial treatment in the previous index visit, type of infection, duration of symptoms, and clinical manifestations. Other variables included were sepsis, admission to an intensive care unit (ICU), length of hospital stay, use of appropriate antimicrobial therapy, improvement over a 72-h period, duration of therapy, complications, and death.

Microbiological procedures

All bacterial isolates registered in the medical records as the etiological agent of the SSTI were included in the analysis. All superficial samples (pustules, wounds) and deep samples (abscess drainage and biopsies) were cultured on blood, MacConkey, and chocolate agar (Becton-Dickinson, Sparks, MD, USA). All cultures were incubated at 35 °C for 18–24 h. Blood samples were inoculated into blood culture bottles (Bactec Plus Aerobic and Bactec Plus Anaerobic), incubated in the Bactec 9240 system (Becton-Dickinson, Sparks, MD, USA) until positivity, and later cultured on blood and chocolate agar.

Upon bacterial growth in the respective agar, culture purification was performed if required prior to microbiological identification and susceptibility testing by microdilution. Microbiological identification and antimicrobial susceptibility testing were performed with the automated bacterial identification and susceptibility analysis system Microscan Walkaway 96 Plus (Beckman Coulter, Brea, CA, USA). Minimum inhibitory concentrations (MICs) were interpreted in accordance with the M100 Performance Standards for Antimicrobial Susceptibility Testing of the Clinical and Laboratory Standards Institute (CLSI) guidelines valid for the year when the test was performed. Methicillin resistance was investigated with the cefoxitin test by disk diffusion method. The following antimicrobial susceptibility patterns were identified: MRSA community phenotype (oxacillin-resistant, sensitive to

Table 1
Demographic and epidemiological risk factors in patients with SSTI.

Variable	Cases MRSA SSTI (n = 177)		Control 1 Without MRSA SSTI (n = 321)		p-Value	Control 2 MSSA SSTI (n = 82)		p-Value
	n	%	n	%		n	%	
Age, years								
18–44	96	54.2	102	31.78	Ref.	36	44.0	Ref.
45–65	52	29.4	104	32.4	0.004	32	39.0	0.096
>65	29	16.4	115	35.83	<0.001	14	17.1	0.506
Sex								
Male	95	53.7	173	53.89	0.726	42	51.2	0.588
Female	82	46.3	148	46.11		40	48.8	
Regions								
Central	91	51.41	146	45.48	0.121	42	51.22	0.769
Caribbean	73	41.24	134	41.74	Ref.	31	37.8	Ref.
Antioquia	8	4.52	17	5.3	0.94	9	10.98	0.067
Valle del Cauca	5	2.82	24	7.48	0.42	0	0	–
Comorbidities								
Diabetes mellitus	24	13.6	101	31.46	<0.001	15	18.3	0.323
Chronic kidney disease	8	4.5	25	7.79	0.166	2	2.4	0.426
COPD	3	1.7	10	3.12	0.349	2	2.4	0.687
Obesity	6	3.4	24	7.48	0.074	1	1.2	0.337
Cancer	3	3.4	19	5.92	0.222	4	4.9	0.565
Transplant	1	0.6	2	0.62	0.936	0	0	–
HIV	2	1.1	5	1.56	0.699	1	1.2	0.95
Malnutrition	1	0.6	11	3.43	0.081	1	1.2	0.585
Precipitating factors								
None	101	57.1	131	40.81	0.001	38	46.3	0.108
Trauma	37	20.9	54	16.82	0.16	15	18.3	0.626
Insect bite	18	10.2	12	3.74	0.005	5	6.1	0.289
Puncture injury	12	6.8	86	26.79	<0.001	7	8.5	0.615
Surgery	3	1.7	29	9.03	0.004	1	1.2	0.774
Ulcer	3	1.7	9	2.8	0.445	1	1.2	0.114
Sports	1	0.6	0	0	–	0	0	–
Mesotherapy	1	0.6	1	0.31	0.673	0	0	–
Fishbone	1	0.6	1	0.31	0.673	1	1.2	0.585
Infection origin								
Healthcare-associated infections[a]	27	15.2	117	36.45		7	8.5	
Community	150	84.7	204	63.55	<0.001	75	91.5	0.142
History of previous surgery[b]	33	18.64	132	41.12	<0.001	16	19.51	0.868
Previous treatment in the previous index visit[c]								
No previous treatment	92	52.0	198	61.68	Ref.	48	58.5	Ref.
Previous outpatient treatment	44	24.9	50	15.58	0.008	8	9.8	0.013
Previous emergency room treatment	30	16.9	43	13.4	0.131	24	29.3	0.191
Previous hospitalization treatment	11	6.2	30	9.35	0.527	2	2.4	0.182
Previous use of antibiotics								
Penicillins	43	24.3	37	11.53	<0.001	18	22.0	0.680
Cephalosporins	21	11.9	38	11.84	0.993	12	14.6	0.535
Quinolones	3	1.7	4	1.25	0.685	0	0	–
TMP–SMX	1	0.6	1	0.31	0.673	0	0	–
Clindamycin	4	2.3	10	3.12	0.582	2	2.4	0.929
Other[d]	17	9.6	53	16.51	0.036	8	9.8	0.969
Type of infection								
Abscess	93	52.5	84	26.17	<0.001	51	62.2	0.147
Cellulitis[e]	51	28.8	99	30.84	<0.001	15	18.3	0.867
Furunculosis	4	2.3	0	0	–	0	0	–
Erysipelas	0	0	5	1.56	–	2	2.4	–
Tenosynovitis	5	2.8	4	1.25	0.218	3	3.7	0.719
Pyomyositis	0	0	0	0	–	2	2.4	–
Necrotizing fasciitis	6	3.5	5	1.56	0.699	1	1.2	0.95
Surgical site infection	11	6.2	81	25.23	<0.001	6	7.3	0.739
Diabetic foot	4	2.3	33	10.28	0.003	1	1.2	0.577
Infected pressure ulcer	3	1.69	31	9.66	0.003	1	1.2	0.774
Duration of symptoms[f]								
Less than 48 h	16	9.5	49	15.96	Ref.	8	9.9	Ref.
48 h to 7 days	92	54.4	141	45.93	0.029	44	54.3	0.925
More than 7 days	61	36.1	117	38.11	0.154	29	35.8	0.918
Clinical manifestations								
Fever	50	28.2	114	35.51	0.099	20	24.4	0.516
Erythema	127	71.7	183	57.01	0.001	67	81.7	0.088
Edema	142	80.2	216	67.29	0.002	72	87.8	0.138
Pain	154	87.0	239	74.45	0.001	74	90.2	0.457
Heat	115	65.0	160	49.84	0.001	55	67.1	0.741
Purulence	64	36.2	185	57.63	<0.001	33	40.2	0.528
Ecchymosis	2	1.1	1	0.31	0.291	0	0	–
Necrosis	9	5.1	52	16.2	0.001	0	0	–
Bullous lesions	9	5.1	8	2.49	0.135	0	0	–

Table 1 (*Continued*)

Variable	Cases MRSA SSTI (*n* = 177)		Control 1 Without MRSA SSTI (*n* = 321)		*p*-Value	Control 2 MSSA SSTI (*n* = 82)		*p*-Value
	n	%	*n*	%		*n*	%	
Disproportionate pain	1	0.6	2	0.62	0.936	0	0	–
Hypoesthesia	0	0	5	1.56	–	0	0	–

MRSA, methicillin-resistant *Staphylococcus aureus*; SSTI, skin and soft tissue infections; MSSA, methicillin-susceptible *Staphylococcus aureus*; COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus; TMP–SMX, trimethoprim–sulfamethoxazole.

[a] Healthcare-associated SSTI was defined as any of the following: hospitalization in the past 3 months, having nursing care at home, being in a program of hemodialysis, attending a chronic care unit, antibiotic treatment in the past 30 days, or hospital-acquired infections (infections that appeared ≥48 h after admission).

[b] Surgery in the last 30 days.

[c] Patients with a previous index visit for the same SSTI, with empiric antibiotic treatment.

[d] Other antibiotics include vancomycin, aminoglycosides, macrolides, carbapenems, and other β-lactams.

[e] Purulent cellulitis (cellulitis associated with purulent drainage or exudate in the absence of a drainable abscess) was included.

[f] Time of onset of symptoms of SSTI prior to hospitalization.

clindamycin and erythromycin), MRSA hospital phenotype (resistant to oxacillin, clindamycin, and erythromycin).

Statistical analysis

All variables were described with adequate univariate statistics using Stata 13 software. Nominal variables were described as percentages, while ordinal variables were described as proportions and quartiles. For continuous variables, arithmetic means and medians were used according to the data distribution. The Chi-square test for dichotomous variables was used to compare cases and controls; the Mann–Whitney test was used to compare ranges for continuous variables. The strength of association between dependent and independent variables was measured using the relative indirect risk, and the odds ratio (OR) and 95% confidence interval (95% CI) were calculated. Two models were applied to identify variables significantly associated with MRSA SSTI. In the first model, patients with MRSA SSTI formed the case group and patients with non-MRSA positive cultures formed the control group. In the second model, patients with MRSA SSTI constituted the case group and patients with MSSA SSTI were allocated to the control group. Variables with a *p*-value of <0.2 in the univariate analysis were selected for the multivariate analysis. A logistic regression model for multiple variable analysis was used. This method allowed the evaluation of multiple co-variables. An overall level of 5% was considered the cut-off for statistical significance.

Results

Study population

A total 1134 patients attending 13 Colombian hospitals during the years 2009 to 2016 were recruited into the study. The population was 50.7% male (*n* = 576). The median age was 52 years (range 18–91 years). The most frequent comorbidity was diabetes mellitus (22.0%, *n* = 250). Cultures were processed for 706 patients, out of which 71% (*n* = 498) were positive; three patients had more than one culture available. Most cultures were from superficial samples (45.4%, *n* = 318), followed by deep samples (44.4%, *n* = 311), blood cultures (11.7%, *n* = 82), and biopsy (0.6%, *n* = 4). The most frequently isolated microorganism was *S. aureus* (52%, 259/498), followed by *Escherichia coli* (11.6%, 58/498) and *Klebsiella pneumoniae* (6.42%, 32/498). Most cultures with *S. aureus* were either superficial (43%) or taken from deep tissue (53%). A total of 177 (68.3%) *S. aureus* isolates were MRSA, out of which 74% were susceptible to clindamycin, erythromycin, and trimethoprim–sulfamethoxazole.

SSTI caused by MRSA

The median age of patients with SSTI caused by MRSA was 40 years (range 18–82 years); 53.7% (*n* = 95) were male. Most patients (59.8%, *n* = 106) had no comorbidities or precipitating factors (57%, *n* = 101). CA infections were present in 84.7% (*n* = 150) of patients with MRSA, and 30.5% (*n* = 54) of patients had previously received β-lactam antibiotics. The predominant type of infection was abscess, occurring in 52.5% of patients (*n* = 93) (Table 1). Inappropriate therapy was observed in 57% of patients (*n* = 130), and 60% (*n* = 107) required therapy adjustment, a finding that was significantly higher compared to the non-MRSA group ($P < 0.001$). Sepsis was documented in 13.6% (*n* = 24) of patients; only 3.4% (*n* = 6) were admitted to the ICU, and no patients died. No significant difference in long hospital stay (>7 days) or SSTI complications was observed between the MRSA and non-MRSA SSTI groups (Table 2).

Model 1: MRSA SSTI vs. non-MRSA SSTI

In the multivariate model, risk factors associated with SSTI caused by MRSA were abscess (OR 2.60, 95% CI 1.44–4.69), cellulitis (OR 2.25, 95% CI 1.24–4.08), age 18–44 years (OR 2.60, 95% CI 1.49–4.54), and outpatient treatment in the previous index visit (OR 2.30, 95% CI 1.32–4.01). Surgical site infections (OR 0.3, 95% CI 0.12–0.72) represented a protective factor for MRSA SSTI. Table 3 depicts the multivariate models.

Model 2: MRSA SSTI vs. MSSA SSTI

In the multivariate analysis, the only risk factor associated with SSTI caused by MRSA vs. MSSA was outpatient treatment for the SSTI in the previous index visit (OR 2.87, 95% CI 1.25–6.58) (Table 3).

Discussion

S. aureus has become the most common pathogen causing SSTI in adults (Moran et al., 2006; Ray et al., 2013a; Ahmad and Asrar, 2014; Ensinck et al., 2018). The results of the present study are consistent with findings from the SENTRY study in regards to the prevalence of *S. aureus* isolates (52%); however, we found a higher rate of MRSA SSTI in Colombia compared to the SENTRY data for Latin America (68.3% vs. 29.4%). Similarly, the rate of MRSA SSTI was higher in our study than in Europe, where the reported frequency in the REACH study involving 11 countries was 26.7% (Garau et al., 2013). Interestingly, in the USA, where the North American variant of USA300 is present, the frequency of MRSA

Table 2
SSTI outcomes in patients with MRSA SSTI vs. MSSA SSTI.

Variable	MRSA SSTI (*n* = 177)		MSSA SSTI (*n* = 82)		*p*-Value
	n	%	*n*	%	
Sepsis					
No sepsis	153	86.44	68	82.93	Ref.
Sepsis	24	13.56	14	17.07	0.458
Septic shock	0	0	0	0	–
ICU admission	6	3.39	0	0	–
Length of hospital stay in days, median (IQR)	11.54 (6–14)		9.59 (4–11)		0.162
72-h clinical improvement	134	76.71	56	68.29	0.211
Treatment adjustment					
No	70	39.55	52	63.41	Ref.
<72 h	51	28.81	9	10.98	<0.0001
≥72 h	56	31.64	21	25.61	0.03
Duration of therapy					0.664
≤7 days	85	48.02	37	45.12	
>7 days	92	51.98	45	54.88	
Complications					
None	84	47.46	40	48.78	0.843
Drainage	85	48.02	40	48.78	0.91
Amputation	3	1.69	0	0	–
Acute kidney injury	2	1.13	0	0	–
Renal replacement therapy	1	0.56	0	0	–
Mortality	0	0	0	0	–

MRSA, methicillin-resistant *Staphylococcus aureus*; SSTI, skin and soft tissue infections; MSSA, methicillin-susceptible *Staphylococcus aureus*; ICU, intensive care unit; IQR, interquartile range.

Table 3
Multivariate logistic regression analysis of risk factors associated with MRSA SSTI (Model 1: MRSA SSTI vs. without MRSA SSTI; Model 2: MRSA SSTI vs. MSSA SSTI).

Risk factor	Model 1 (MRSA SSTI vs. without MRSA SSTI)			Model 2 (MRSA SSTI vs. MSSA SSTI)		
	OR	95% CI	*p*-Value	OR	95% CI	*p*-Value
Abscess	2.60	1.44–4.69	<0.001		NS	
Cellulitis	2.25	1.24–4.08	0.007		NS	
Age 18–44 years	2.60	1.49–4.54	0.001		NS	
Age 45–65 years	1.41	0.78–2.53	0.093		NS	
Previous treatment in the previous index visit[a]						
Previous outpatient treatment	2.30	1.32–4.01	0.003	2.87	1.25–6.58	0.013
Previous emergency room treatment	0.94	0.52–1.69	0.848	0.65	0.34–1.24	0.191
Previous hospitalization treatment	1.09	0.46–2.56	0.835	2.87	0.61–13.47	0.182
Surgical site infection	0.30	0.12–0.72	0.008		NS	

MRSA, methicillin-resistant *Staphylococcus aureus*; SSTI, skin and soft tissue infections; MSSA, methicillin-sensitive *Staphylococcus aureus*; OR, odds ratio; CI, confidence interval; NS, non-significant.
[a] Patients with a previous index visit for the same SSTI, with empiric antibiotic treatment.

causing SSTI seems to be higher than in other regions. Recently, Daum et al., Talan et al., and Miller et al., in different clinical trials, reported a frequency of MRSA of 73.6%, 73.6%, and 77%, respectively, from all *S. aureus* SSTI (Miller et al., 2015a; Talan et al., 2016; Daum et al., 2017), results that are comparable to the present study findings.

In Colombia, a study analyzing 1570 *S. aureus* isolates from different sources, out of which 45% were MRSA, described a prevalence of CA-MRSA of 31% (Reyes et al., 2009), which is low compared to our findings. Conversely, a recent study analyzing bloodstream infection isolates recovered from three Colombian hospitals showed that most MRSA isolates belonged to the USA300-LV (Arias et al., 2017), confirming that USA300-LV is prevalent not only in the community, but also in hospitals.

In this study it was found that the risk factors for MRSA vs. non-MRSA SSTI in hospitalized patients were the presence of abscess, cellulitis, age of 18–44 years, and previous outpatient antibiotic treatment. Some of the risk factors identified in this study are similar to those reported in other studies performed in the USA, Canada, and Taiwan, in which purulent infections (abscesses and purulent cellulitis) (Moran et al., 2006; Haysom et al., 2018) and previous use of antibiotics were associated with MRSA (Moran et al., 2006; Skiest et al., 2007; Stenstrom et al., 2009; Chou et al., 2015). In the present study, diabetes, intravenous drug use, female sex, HIV infection, and athletic team participation (Hota et al., 2007) were not associated with MRSA SSTI, in contrast to the findings of studies in the USA, Canada, and the Middle East (Stenstrom et al., 2009; Ray et al., 2013a; Al Jalaf et al., 2018).

Cellulitis was also a risk factor for MRSA SSTI in patients with a positive culture. It is assumed that most of these patients had purulent cellulitis (Liu et al., 2011), given that cellulitis is not sampled for culture unless purulence is observed, and the percentage of biopsy cultures was only 0.6% (*n* = 4). This indicates that purulent SSTI should be treated with antimicrobials with activity against MRSA (which is a recommendation in the SSTI and MRSA guidelines of Infectious Diseases Society of America), whereas non-purulent non-complicated SSTIs should not be treated for MRSA, taking into account that most of these infections are caused by β-hemolytic streptococci (Jeng et al., 2010) and clinical trials have not shown the superiority of MRSA coverage in this scenario (Pallin et al., 2013; Moran et al., 2017).

Interestingly, it seems that in Colombia there is no clear association between HA infections and a higher rate of infection by multidrug-resistant organisms in SSTIs. This is supported by the

finding that SSI was a protective factor for MRSA SSTI, and MRSA was the most relevant etiological agent in CA-SSTI. However, MRSA should not be overlooked in HA infections (Márquez-Ortiz et al., 2014; Ocampo et al., 2014).

In the multivariate analysis comparing MRSA vs. MSSA SSTI, the only risk factor for MRSA SSTI was antimicrobial outpatient treatment in the previous index visit. In hospitalized patients with *S. aureus* infections (89% with SSTI), Miller et al. did not find clinical variables that had sufficient predictive capacity to distinguish between an infection by MRSA and an infection by MSSA (Miller et al., 2007). This finding suggests that empiric treatment for MRSA SSTI should be based on the presence of abscess or purulent drainage and epidemiological data.

An elevated frequency of inappropriate therapy (57%) was observed in this study. In Colombia, it is common for clinicians to prescribe penicillins for SSTIs, specifically amoxicillin, amoxicillin–clavulanic acid, and dicloxacillin. This finding is similar to those of studies performed in the Middle East and Asia (Chou et al., 2015; Al Jalaf et al., 2018) and in contrast to the findings of other studies in Europe and the USA (Lipsky et al., 2007; Macía-Rodríguez et al., 2017), where an increase in prescription of antibiotics active against MRSA (Szumowski et al., 2007; Hersh, 2008) was noted in emergency rooms in the last decades (Pallin et al., 2008). A systematic review by Abetz et al. reported a frequency of treatment failure of 15–38% in SSTI, and an MRSA infection was implicated in this outcome (Abetz et al., 2018). Macía-Rodríguez et al. reported that an inadequate empirical therapy of SSTI resulted in greater mortality (OR 44.74, 95% CI 5.40–370.73) (Macía-Rodríguez et al., 2017). Although the present study data did not show an increase in hospital stay, complications, or mortality for patients with MRSA SSTI, which may be explained by younger age and fewer comorbidities in the MRSA SSTI group and limited power in our sample, it confirms the need for MRSA coverage in purulent SSTI to attempt to improve microbiological cure (Stevens et al., 2014; Kwak et al., 2017). More studies are needed to assess the impact of inappropriate initial therapy on outcomes.

Several limitations of this study are worth mentioning. First, there is a possibility that MRSA was present in patients with no culture availability. Nonetheless, MRSA appears to be less common in non-purulent infections (Moran et al., 2006; Jeng et al., 2010) where a culture is more difficult to obtain. For this reason, we excluded negative culture SSTI from the risk factor analysis of MRSA vs. non-MRSA SSTI. Second, previous contact with someone with a similar skin condition or surgery, nasal carriage of MRSA, and a history of SSTI were not assessed, which have been described as risk factors for MRSA SSTI (Skiest et al., 2007; Stenstrom et al., 2009; Chou et al., 2015). Third, this study did not include molecular analysis to confirm the characteristics of the MRSA isolates, since the isolates were not stored for further characterization. Despite this limitation, the demographic and phenotypic data suggest that the infections were most probably caused by the USA300-LV strain of CA-MRSA, given the susceptibility profiles and the fact that the infections occurred in otherwise healthy and young patients (Dryden 2010; Haysom et al., 2018). Indeed, 74% of the isolates USA300-LV were susceptible to clindamycin, macrolides, and trimethoprim–sulfamethoxazole, a phenotype frequently associated with the community strain in Colombia (Reyes et al., 2009). Fourth, as the nature of this study was retrospective, the diagnosis of SSTI was performed by a clinician based on clinical data. Furthermore, the bacteria that the clinician considered to be the etiological agent were included in this study. This may have resulted in the inclusion of some isolates that may not have been the causal agent.

In summary, CA-SSTIs in Colombia are commonly caused by MRSA, affecting mainly young people, and MRSA is the principal cause of purulent infections from the community. Outpatient treatment in the previous index visit was found to be an important risk factor for MRSA SSTI. Moreover, most hospitalized patients with purulent SSTIs received inadequate antimicrobial therapy for MRSA. Although clinicians should consider MRSA when designing the initial empirical treatment for purulent SSTI, in Colombia, there seems to be a low awareness of this fact.

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Ethical approval

The Ethics Committee of the Hospital Universitario San Ignacio approved the study.

Conflict of interest

Dr Sandra L. Valderrama has given lectures for pharmaceutical companies, including Pfizer, Merck Sharp and Dohme, and Stendhal. Dr Carlos Alvarez has given lectures for pharmaceutical companies, including Pfizer, Merck, Stendhal, and Abbvie. Dr Cesar A. Arias has received grant support from Merck and MeMed diagnostics. Other authors have no conflicts of interest to declare.

Author contributions

SV, CAM, CAA designed the study; FG, AR designed the methodology and analyzed the data; SG, JR, JO, IT, CG, GA, IB, EM, provided patient cases for the study and helped design the study; SM, MC, AZ gathered the clinical and microbiological data; GC analyzed the microbiological data; AD, SV, SM, CAA analyzed the results and structured the discussion.

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