



ORIGINAL ARTICLE

Rate of methicillin-resistant *Staphylococcus aureus* in pediatric emergency departments in Spain^{☆,☆☆}



Lucía Garriga Ferrer-Bergua^{a,*}, Anna María Borrull Senra^b,
Carmen Pérez Velasco^c, Cristina Montero Valladares^d, Iris Collazo Vallduriola^e,
Sandra Moya Villanueva^f, Roberto Velasco Zúñiga^g, Marta Pérez Alba^h,
Mercedes de la Torre Espí^a, en representación del Grupo de Trabajo de Enfermedades
Infecciosas de la SEUP

^a Hospital Universitario Infantil Niño Jesús, Madrid, Spain

^b Hospital Sant Joan de Déu, Barcelona, Spain

^c Hospital Son Espases, Palma, Spain

^d Hospital Universitario Virgen del Rocío, Sevilla, Spain

^e Hospital de Mataró, Mataró, Barcelona, Spain

^f Corporació Sanitaria Parc Taulí, Sabadell, Barcelona, Spain

^g Hospital Río Hortega, Valladolid, Spain

^h Hospital de Cabueñes, Gijón, Spain

Received 12 May 2021; accepted 17 June 2021

Available online 1 July 2022

KEYWORDS

Methicillin-resistant
*Staphylococcus
aureus*;
Pediatric emergency
care;
Microbiological
isolation

Abstract

Introduction: *Staphylococcus aureus* is a common germ in bacterial infections in children. The rate of methicillin-resistant *S. aureus* (MRSA) is increasing lately.

Objectives: The main aim is to know the rate of positive cultures to MRSA in Spanish pediatric emergency departments. The secondary aims are to analyse the risk factors for MRSA isolation (patient origin, history of hospitalization or surgery in the previous 90 days, antibiotherapy in the previous 60 days, presence of comorbidity, invasive devices, prior MRSA isolation) and to analyse the morbidity of these infections.

Methodology: Retrospective multicenter study (07/01/2017–06/30/2018) with review of patient histories with isolation of *S. aureus* in samples of any origin obtained in 8 pediatric emergency departments of the Infectious Diseases Working Group of the Spanish Society of pediatric Emergencies.

[☆] Please cite this article as: Garriga Ferrer-Bergua L, Borrull Senra AM, Pérez Velasco C, Montero Valladares C, Collazo Vallduriola I, Moya Villanueva S, et al. Tasa de *Staphylococcus aureus* resistentes a metilicina en urgencias pediátricas en España. An Pediatr (Barc). 2022;97:95–102.

^{☆☆} Previous presentation: this study was presented at the XXV Annual Meeting of the Sociedad Española de Urgencias de Pediatría (online, March 3–6, 2021).

* Corresponding author.

E-mail address: lgarferg@gobiernodecanarias.org (L. Garriga Ferrer-Bergua).

Results: During this period, *S. aureus* was detected in 403 patients (average age 75.8 ± 59.2 months; 54.8% male): 28.8% hospital-related infections (HRI) and 71.2% community-related infections (CRI). Overall, MRSA rate was 16.6% (95% CI: 13–20.2%); 18.1% in HRI and 16.2% in CRI ($p > 0.05$). The highest rates of MRSA were obtained in skin abscesses (29.3%, CI 95%: 21.8–36.8%), patients not born in Spain (52%; CI 95%: 32–72%) or patients with a previous MRSA infection (90%; CI 95% 71.4–100%).

167 (41%) patients were admitted, 12 (3%) had complications and 4 (1%) suffered sequels. There were no deaths.

Conclusions: The overall MRSA rate was one in 6 staphylococcal infections. Higher MRSA rates were detected in samples of suppurating skin injuries and in foreign children or in children with a history of previous MRSA infection. In suppurative skin lesions, early drainage is essential and the change to an antibiotic with MRSA coverage should be considered if the evolution is inadequate.

© 2021 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

PALABRAS CLAVE

Staphylococcus aureus
meticilín-resistente;
Urgencias
pediátricas;
Aislamiento
microbiológico

Tasa de *Staphylococcus aureus* resistentes a meticilina en urgencias pediátricas en España

Resumen

Introducción: *S. aureus* es un germen frecuente en las infecciones bacterianas infantiles. Últimamente la tasa de *S. aureus* resistente a meticilina (SAMR) está aumentando.

Objetivos: Principal: conocer la tasa de cultivos positivos a SAMR en los servicios de urgencias pediátricos (SUP) españoles.

Secundarios: analizar factores de riesgo de aislamiento de SAMR (procedencia del paciente, antecedentes de hospitalización o cirugía en los 90 días previos, de antibioterapia en los 60 días previos, presencia de comorbilidad, dispositivos invasivos, aislamiento SAMR previo) y la morbilidad de estas infecciones.

Metodología: Estudio retrospectivo multicéntrico (1/07/2017-30/06/2018) con revisión de historias de pacientes con aislamiento de *S. aureus* en muestras de cualquier origen obtenidas en 8 SUP del Grupo de Trabajo de Enfermedades Infecciosas de la Sociedad Española de Urgencias de Pediatría.

Resultados: Durante dicho periodo se aisló *S. aureus* en 403 pacientes (edad media $75,8 \pm 59,2$ meses; 54,8% hombres): 28,8% infecciones relacionadas con el hospital (IRH) y 71,2% con la comunidad (IRC).

Tasa global de SAMR: 16,6% (IC95%: 13-20,2%); 18,1% en IRH y 16,2% en IRC ($p > 0,05$). Las tasas más altas de SAMR se obtuvieron en abscesos cutáneos (29,3%, IC95%: 21,8-36,8%), pacientes no nacidos en España (52%; IC95%: 32-72%) o con una infección previa por SAMR (90%; IC95% 71,4-100%).

Ingresaron 167 pacientes (41%), presentaron complicaciones 12 (3%) y secuelas 4 (1%). No hubo fallecimientos.

Conclusiones: La tasa global de SAMR afectó a una de cada 6 infecciones estafilocócicas. Las tasas más altas de SAMR se han producido en muestras de lesiones supuradas de piel y en niños extranjeros o con antecedentes de infección previa por SAMR. En las lesiones supuradas de piel es principal su drenaje precoz y valorar el cambio a antibiótico con cobertura frente a SAMR si la evolución no es la adecuada.

© 2021 Asociación Española de Pediatría. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Staphylococcus aureus is one of the pathogens involved most frequently in bacterial infections in children. These infections are of variable severity, ranging from mild forms like superficial cutaneous infections and soft tissue abscesses to

severe forms of invasive infection (necrotising pneumonia, pyomyositis, osteomyelitis, sepsis) that carry a high morbidity and may be life-threatening¹.

In the late 1990s, there was a marked increase in the prevalence of methicillin-resistant *S. aureus* (MRSA), reflecting the emergence of resistant strains that spread

both inside and outside hospitals, and both nosocomial and community-acquired MRSA infections have since become frequent. Some of the studies in the literature have noted that the increased prevalence of MRSA may be particularly important in the paediatric population^{2–4}.

In Europe, the knowledge of the prevalence of methicillin-resistant *Staphylococcus* infections throughout the continent is obtained through the European Antimicrobial Resistance Surveillance Network (EARSnet), which started operations in year 1999⁵. This network collects data on episodes of bacteraemia caused by different bacterial species, including *S. aureus*. Based on the 2019 EARSnet report, the percentage of bacteraemia isolates corresponding to MRSA was 19.2%, which, while lower compared to the 2015 report (25%), continued to be above the European mean (15.5%). The prevalence of MRSA is greater in older individuals (age >65 years: 22.8%), but it is still considerable in the paediatric population (age 0–4 years: 12%; age 5–18 years: 15.7%)⁶.

The EARSnet focuses on the prevalence of bacteraemia by different species and strains, including MRSA; but there is no system at the European level for epidemiological surveillance of MRSA isolates from samples other than blood.

In Spain, 6 studies have been devoted to the prevalence of *Staphylococcus* species since 1986 (1986, 1991, 1994, 1996, 2002, 2006) through the analysis in the same single laboratory of all *Staphylococcus* strains isolated from different types of clinical samples in a single day in every participating hospital, with representation of every region in the country^{7,8}. These studies evinced an increase in the prevalence of MRSA from 1.5% in year 1986 to 31.2% in 2002, followed by stabilization at 29.2% in 2006. The studies included both community-acquired and nosocomial infections.

Data regarding the evolution of antimicrobial drug resistance in bacteria has a substantial influence on the development of strategies for the selection of empirical antibiotherapy. Although the aforementioned nationwide prevalence studies could reflect temporal trends in the prevalence of MRSA, the study universe was the adult population, and therefore the results cannot be extrapolated to the paediatric population.

As regards community-acquired infection by MRSA in children in Spain, the first case series was published in 2006⁹. Later on, other series have been published in different geographical regions. The described infections mainly involved the skin and soft tissues, some were severe (cases of pneumonia and necrotising fasciitis, bacteraemia)^{10–15}. In Spain, only one multicentre study, published in 2009, has assessed the prevalence of MRSA in the paediatric population. This study included all infections by *S. aureus* in children managed in 4 Spanish hospitals (Barcelona, Madrid, Palma de Mallorca and A Coruña), and found a proportion of community-acquired MRSA infection of 8.8%¹⁶.

The primary objective of our study was to determine the proportion of cultures positive for MRSA among the patients managed in paediatric emergency departments (PEDs) in Spain. The secondary objectives were to identify risk factors associated with an increased probability of MRSA isolation and to analyse the morbidity associated with these infections.

Material and methods

We conducted a multicentre retrospective study in 8 PEDs included in the Working Group on Infectious Diseases of the Sociedad Española de Urgencias de Pediatría (SEUP, Spanish Society of Paediatric Emergency Care) (Hospital Infantil Universitario Niño Jesús in Madrid, Hospital Sant Joan de Déu in Barcelona, Corporació Sanitària Parc Taulí in Sabadell, Hospital de Mataró, Hospital de Cabueñes in Gijón, Hospital Virgen del Rocío in Seville, Hospital Río Hortega in Valladolid and Hospital Son Espases in Mallorca) of patients managed between 1/07/2017 and 30/06/2018 in whom *S. aureus* had been isolated from culture from samples obtained from any site.

The identification of *S. aureus* isolates was performed at the microbiology laboratories of each hospital. Later on, we reviewed the health records of patients to select those that met the inclusion criteria.

Inclusion criteria

Patients aged 0–16 years managed in PEDs.

Isolation of *S. aureus* from any sample obtained at the PED or drainage of an abscess, mastoiditis or any other purulent secretion in the 6 h following hospital admission from the PED.

Exclusion criteria

Patients that were not admitted to hospital from the PED and those admitted from the PED in whom the sample was obtained from drainage of an abscess, mastoiditis or another purulent secretion more than 6 h after admission.

We collected data on demographic variables (age, sex), microbiological variables (source of sample, empirical antibiotherapy), potential risk factors associated with methicillin resistance^{8,17–19} (origin of patient, history of hospitalization or surgery in the past 60 days, comorbidities, invasive devices and history of previous MRSA isolation) and outcome variables (need of admission, complications, sequelae and death).

Infections by *S. aureus* were classified based on criteria established by the Centers for Disease Control and Prevention (CDC)¹⁸:

- **Hospital-associated MRSA infection** – Infection in patients with any of the following risk factors: use of percutaneous catheter at the time of infection, previous isolation of MRSA, history of hospitalization, surgery or dialysis or presence of chronic disease.
- **Community-associated MRSA** – infections with onset in the community or in the first 48 hours of hospitalization in the absence of any of the risk factors described above.

The principal investigator in each participating hospital completed the data in the Google drive[®] form designed for the purpose. The data for each of the hospitals was pooled in a single Excel[®] spreadsheet that was only accessible to principal investigators. To guarantee the confidentiality of the patients, we did not collect any personal identifiable information.

Table 1 Reported episodes with isolation of *S. aureus* by hospital and autonomous community and proportion of methicillin resistance.

Hospital	<i>n</i>	Autonomous community	<i>n</i> (%)	Methicillin resistance, <i>n</i> (%; 95% CI)	<i>P</i>
H. Infantil Universitario Niño Jesús (Madrid)	98	Madrid	98 (24.3)	16 (16.3; 8.9–23.6)	>.05
H. Sant Joan de Déu (Barcelona)	133	Cataluña	183 (45.4)	32 (17.5; 11.9–23)	
Consorci Corporació Sanitaria Parc Taulí (Sabadell)	24				
H. de Mataró (Mataró)	26				
H. Universitario Río Hortega (Valladolid)	18	Castilla y León	18 (4.5)	1 (5.5)	
H. Universitario Son Espases (Majorca)	58	Baleares	58 (14.4)	14 (24.1;13.1–35.1)	
H. Universitario de Cabueñes (Gijón)	11	Asturias	11 (2.7)	0	
H. Universitario Virgen del Rocío (Seville)	35	Andalucía	35 (8.7)	4 (11.4; 0.9–21.9)	
Total	403		403 (100)	67 (16.6; 13–20.2)	

The research project was approved by the Ethics and Clinical Research Committee of the Hospital Infantil Universitario Niño Jesús on 28/05/2019 (under in-house code R-0028/19).

Statistical analysis

The statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) version 21 (Chicago, IL, USA).

In the descriptive analysis, we summarised continuous data as mean and standard deviation. We assessed the normality of the distribution of the variables using the Shapiro-Wilk test. We summarised categorial data as absolute and relative frequencies (counts and percentages). We calculated the prevalence of methicillin resistance in the overall sample, in each participating hospital and in each of the autonomous communities represented in the study.

Later, we performed an inferential statistical analysis to identify potential risk factors associated with a greater probability of methicillin resistance and to assess the morbidity and mortality associated with these infections. To this end, we used the chi square test and the Mann-Whitney *U* test as applicable. We also calculated 95% confidence intervals (CIs) for proportions using the Wilson method and odds ratios (ORs) for the risk factors under study. In every case, we defined statistical significance as a *P* value of 0.05 or less.

Results

In the period under study, *S. aureus* was isolated from 403 samples. Table 1 presents the number of episodes with isolation of *S. aureus* reported by each PED and by autonomous community in Spain.

The mean age of patients was 75.8 months (standard deviation, 59.2), 54.8% were male. Comorbidities were present in 59 children (14.6%), the most frequent of which

were: altered immunity (immunodeficiency, steroid therapy at a dose ≥ 2 mg/kg/day or immunosuppression) (*n* = 8), severe atopic dermatitis (*n* = 6), congenital heart disease (*n* = 6), cancer (*n* = 6; 3 of these patients also had indwelling central venous catheters); neurogenic bladder (*n* = 4), cystic fibrosis (*n* = 3) and preterm birth (*n* = 3).

Thirty-six patients (8.9%) were using invasive medical devices: 16 osteosynthesis material, 7 gastrostomy tubes; 5 central venous catheters, 2 urinary catheters, 2 ventriculo-peritoneal shunts, 1 a urinary catheter and a gastrostomy tube, 1 a cochlear implant and 2 cardiac stents.

The overall proportion of MRSA was 16.6% (67/403; 95% CI, 13–20.2%); Table 1 presents the proportions of MRSA isolates by autonomous community.

Out of the 403 staphylococcus infections, 116 (28.8%) were hospital-associated, and 287 (71.2%) community-associated, with a respective prevalence of MRSA of 18.1% and 16.2% (*P* > .05).

We proceed to present the results on the anatomical site of the samples, the potential risk factors for methicillin resistance and outcomes of patients with isolation of methicillin-sensitive and methicillin-resistant *S. aureus*.

Table 2 presents the anatomical sites of the samples from which *S. aureus* was isolated and the proportion of MRSA isolation by site. The proportion of MRSA isolates was higher in samples obtained from cutaneous abscesses compared to samples obtained from blood, conjunctiva, skin or the ear (*P* < .05). Fifty percent of reported *S. aureus* blood culture isolates were associated with osteoarticular infections. The overall prevalence of MRSA in osteoarticular infections was 7.7% (2/16 blood cultures, 0/10 joint drainage cultures).

The proportion of infections caused by MRSA in children born in Spain was 13.3% (95% CI, 9.4–17.2) versus 52% (95% CI, 32–72) in those born outside Spain (*P* < .01). Methicillin-resistant *S. aureus* grew in 90% (95% CI, 71.4–108.6) of cultures of patients with a previous history of MRSA infection, compared to 13% (95% CI, 9.6–16.4) of patients without

Table 2 Anatomical site of sample and proportion of MRSA by site.

Anatomical site of sample	n (%)	MRSA
		n (%; 95% CI)
Cellulitis/cutaneous abscess (drainage)	140 (34.7)	41 (29.3; 21.8–36.8)
Conjunctiva	14 (3.5)	4 (28.6; 4.9–52.3)
Blood culture of peripheral blood draw sample	32 (7.9)	4 (12.5; 1–24)
Skin	59 (14.6)	6 (10.2; 0–34.3)
Ear	66 (16.4)	6 (9.1; 0–32.1)
Surgical wound	19 (4.7)	0
Joint fluid	10 (2.5)	0
Urine culture	3 (0.7)	0
Blood culture of catheter sample	1 (0.3)	0
Other	59 (14.6)	6 (10.2; 0–34.4)
Total	403 (100)	67 (16.6; 13–20.2)

Table 3 Proportion of MRSA and risk factors for methicillin resistance (univariate analysis).

Risk factors for methicillin resistance	(n)	Proportion of MRSA, % (95% CI)	P
Patient nationality	Spanish (293)	13.3 (9.4–17.2)	<.01
	Not Spanish (25)	52 (32–72)	
	Unknown (85)		
History of hospitalization in past 90 days	Yes (63)	9.5 (0–16.7)	>.05
	No (338)	18 (13.9–22.1)	
	Unknown (2)		
History of surgery in the previous 90 days	Yes (42)	7.1 (0–14.9)	>.05
	No (360)	17.8 (13.9–21.8)	
	Unknown (1)		
History of antibiotherapy in the previous 60 days	Yes (153)	18.3 (12.2–24.4)	>.05
	No (240)	15.8 (11.2–20.4)	
	Unknown: 10		
Comorbidity	Yes (59)	17 (7.4–26.6)	>.05
	No (344)	16.6 (12.7–20.5)	
Medical devices	Yes (36)	13.9 (2.6–25.2)	>.05
	No (367)	16.9 (13.1–20.7)	
Previous MRSA	Yes (10)	90 (71.4–100)	.01
	No (366)	13 (9.6–16.4)	
	Unknown (27)		

that history ($P < .01$). We found a greater probability of methicillin resistance in foreign-born children (OR, 7; 95% CI, 3%–16.6%) and in children with a previous MRSA infection (OR, 59.6; 95% CI, 7.4%–481.2%). Table 3 presents the comparative analysis of MRSA isolation based on the presence or absence of each of the risk factors under study.

Antibiotherapy was administered to 369 children (91.5%) before culture results were available, in 215 (58.3%) amoxicillin-clavulanic acid and in 20 (4.9%) an antibiotic that covered MRSA (vancomycin, clindamycin or cotrimoxazole).

When it came to patient outcomes in the total sample (403), 167 (41.4%) were admitted to hospital, and 12 (3%) developed complications: poor outcome with need of surgical reintervention in 4 children with postoperative wound infection (with removal of osteosynthesis material in 2 of them), 2 with cutaneous abscesses, 1 with osteomyelitis, 1 with superficial venous thrombosis, 1 with cutaneous necro-

sis secondary to cellulitis that required surgery, 1 with sepsis in the context of necrotising fasciitis, 1 with osteomyelitis following a cutaneous abscess and 1 with osteomyelitis that progressed with extensive involvement of the femur. The proportion of complications in patients was 3.4% (10/296) in cases in which *S. aureus* was sensitive to the antibiotic prescribed in the PED and 2.8% (2/73) in the cases in which it was resistant ($P > .05$).

There were sequelae in 4 children in the sample: genu flexum following osteoarticular infection ($n = 2$), bone erosion in joint margin ($n = 1$) and chronic otorrhoea with conductive hearing loss following suppurative otitis media ($n = 1$). There were no deaths directly associated with the staphylococcus infection. Table 4 presents the comparison of outcomes (admission, complications, sequelae) based on methicillin sensibility.

Table 4 Comparison of patient outcomes based on methicillin sensitivity of *S. aureus*.

Outcome	% (95% CI)	P
Admission	MRSA: 50.7 (38.7–62.7)	>.05
	MSSA: 39.6 (34.4–44.8)	
Complications	MRSA: 3 (0–7.1)	>.05
	MSSA: 3 (1.2–4.8)	
Sequelae	MRSA: 0	>.05
	MSSA: 1.2 (0.2–2.8)	
Death	0%	

MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-sensitive *S. aureus*.

Discussion

This is the first multicentre study conducted in Spain that analyses the prevalence of MRSA in cultures of samples collected from paediatric patients managed in PEDs. We found an overall proportion of methicillin resistance of 16.6%, practically double the proportion of MRSA in community-acquired *S. aureus* infections (8.8%) found in the only multicentre study ever conducted in Spain in the paediatric population, in 2009¹⁶, although the latter did not only include cultures of samples collected in emergency departments or hospital-associated infections. The MRSA prevalence data reported for Spain by the EARSnet in the 2017 report broken by paediatric age group, which ranged from 14.9% (0–5 years) to 16.4% (5–18 years)²⁰, could be extrapolated to ours. Although the EARSnet only analyses isolates from blood stream infections, this is the only source at the European level that is available to follow temporal trends in the prevalence of methicillin resistance in Europe overall and in each participating country.

Several publications have alerted of the spread of MRSA strains in outpatient and community settings in Spain^{21–23}, a phenomenon that extends to the paediatric population^{9,16} and corroborated by our study, as we did not find statistically significant differences in the proportion of MRSA between hospital-associated *S. aureus* infections (18.1%) and community-associated infections (16.2%). In Spain, the COSACO study,²⁴ conducted recently, has contributed relevant and interesting knowledge regarding nasal colonization by MRSA in the Spanish paediatric population. The authors estimated the prevalence of nasal colonization by MRSA at 1.4%, which they considered high compared to the prevalence in European children and adults^{25–28}. The prevalence of nasal colonization by MRSA, a known risk factor for future infection^{24,29}, and the proportion of MRSA out of all *S. aureus* isolates in the PED setting are not directly comparable. Still, the detection of a high prevalence of nasal carriage of MRSA is consistent with the frequency of methicillin resistance in community-associated staphylococcus infections found in the paediatric population.

The prevalence of methicillin resistance found in our study did not vary significantly between participating autonomous communities, although the sample did not include patients from all autonomous communities and the representation of those that participated was also not optimal, which limits the extrapolation of our results.

Infections by *S. aureus* most frequently involve skin and subcutaneous tissue^{7,30,31}. In countries with a high prevalence of MRSA, this has become one of the main causal agents involved in these community-acquired infections^{29,32–36}. At the same time, skin and soft tissue infections are the most frequent form of community-acquired MRSA infection²⁹, so it is not surprising that we found the highest prevalence of MRSA in these infections in our sample, with 30% of MRSA isolates corresponding to samples obtained from suppurative cutaneous lesions. This proportion of methicillin resistance was significantly higher compared to the proportion in skin samples in cases of infection that did not require drainage (10.2%). However, we cannot infer that methicillin resistance itself is the factor that promotes suppuration. In fact, there is evidence of an association with the presence of Pantone-Valentine leukocidin, independently of the sensitivity or resistance to methicillin^{12,14,31}. In addition, this factor did not affect patient outcomes in infections caused by MRSA, in whom the frequency of complications or sequelae were not higher (Table 4).

The high prevalence of MRSA detected in cutaneous abscess cases does not call for a change in clinical management as regards initiation of empirical antibiotic therapy (an antibiotic that covered MRSA was only given to 5% of the patients) but it does call for performance of drainage as early as possible and the use of antibiotics that cover MRSA if the patient is not improving as expected.

On the other hand, invasive infections account for a minority of the total community-associated MRSA infections²⁹. The 12.5% prevalence of MRSA found in blood cultures of peripheral blood draws in our study (4/32) stood out in relation to the proportions reported in previous studies in Spain: 0% (0/57) in the prospective study conducted in the 2007–2010 period in patients aged less than 16 years by Barrado et al in a tertiary care hospital in Madrid³⁷, and 3% in the 2010–2012 period in the retrospective study conducted in Barcelona in patients aged less than 16 years by Cobos-Carrascosa et al.¹⁵ The prevalence of MRSA isolated from blood culture in our study (12.5%) was, however, consistent with the frequencies by age group reported by the EARSnet for Spain in 2019, which can be consulted online in the Surveillance Atlas of Infectious Disease (an open-access resource of the European Centre for Disease Prevention and Control available at <http://atlas.ecdc.europa.eu/public/index.aspx>): prevalence of bacteraemia caused by MRSA of 12% in the 0–4 years age group and 15.7% in the 5–18 years group. Although the prevalence of MRSA isolation from blood culture in our sample was high, this was not associated with poorer outcomes or a higher incidence of complications or sequelae (Table 4).

As regards the risk factors for methicillin resistance, we only found an association with the origin of the patients (higher prevalence in children born outside Spain) and the history of previous isolation of MRSA.

In our study, we found a higher proportion of MRSA in children who were not native Spaniards (52% in children of other nationalities vs 13.3% in Spanish children; $P = .000$), which was not unexpected, as studies conducted by the European Network for the Surveillance of Imported *S. aureus* have

found a high frequency of skin and soft-tissue infections by *S. aureus* in travellers that return to Europe (67%), with a documented prevalence of methicillin resistance of 14% in the isolates of these imported cases¹⁷. The probability of methicillin resistance in imported *S. aureus* cases varied between regions and was highest for Latin America¹⁷. In our study, we did not analyse the region of origin in children of foreign nationality.

As for the higher prevalence of methicillin resistance found in our study in patients with a previous history of MRSA isolation (90% compared to 13.3% in children without previous MRSA isolation), we ought to note that this is not a surprising finding, as previous MRSA isolation is a thoroughly-documented risk factor for methicillin resistance¹⁹. Therefore, it is important to always explore this history in patients that present to the PED with a suspected staphylococcal infection.

The staphylococcus infections managed in PEDs, independently of methicillin susceptibility or resistance, were severe: nearly half the patients required hospital admission and 1 in 30 developed complications. Although methicillin resistance does not make *S. aureus* more virulent, an aspect that rather appears to be associated with the presence of the Panton-Valentine leukocidin, as noted above^{12,14,31,38}, it is important to document and monitor the prevalence of MRSA in children to know which antibiotics offer the best treatment option in the case of infection of a likely staphylococcal aetiology.

Limitations

There are several limitations to our study. First, it had a retrospective design, with the limitations that this entails in obtaining complete data for the variables included in the analysis. On the other hand, it only allowed us to determine the prevalence of methicillin resistance in the current time point. Time series analysis studies in the paediatric population would be needed to gain a better perspective of the problem and be able to act on it. Lastly, the extrapolation of the results to the entirety of Spain is restricted by the limited representation of different autonomous communities in the study.

Conclusion

The overall prevalence of MRSA in cultures of samples obtained in PEDs in Spain was significant: 1 in every 6 isolates. The highest frequencies of MRSA corresponded to children born outside of Spain, children with a previous history of MRSA isolation and samples obtained from cutaneous abscess and subcutaneous tissue. In the case of suppurative lesions of skin and soft tissues, it is important to perform early drainage and to consider switching to an antibiotic that covers MRSA if treatment does not achieve an adequate outcome.

Prospective studies in larger samples and with representation of more regions in Spain are required to more accurately estimate the prevalence of MRSA in cultures of samples obtained in Spanish PEDs.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgments

We thank Dr Mercedes Alonso Sanz (Department of Microbiology of the Hospital Infantil Universitario Niño Jesús, Madrid), Dr Enrique Ruiz de Gopegui (Department of Microbiology of the Hospital Son Espases, Palma de Mallorca), Dr Marta Arias Temprano (Department of Microbiology of the Hospital de Cabueñes, Asturias) and Dr Goretti Sauca Subias (Department of Microbiology of the Hospital de Mataró, Barcelona) for their contributions to the development of this research project.

References

1. Fritz SA, Garbutt J, Elward A, Shannon W, Storch GA. Prevalencia y factores de riesgo de colonización por *Staphylococcus aureus* resistente y sensible a metilina adquirido en la comunidad en niños visitados en una consulta de pediatría afiliada a una red de investigación basada en consultorios. *Pediatrics* (Ed esp). 2008;65:291–9.
2. Chaves F. Emergencia de infecciones pediátricas por *Staphylococcus aureus* resistente a metilina asociadas a la comunidad: ¿debemos dar la alerta? *Enferm Infecc Microbiol Clin*. 2010;28:672–4.
3. Kaplan SL, Hulten KG, Gonzalez BE, Hammerman WA, Lamberth L, Versalovic J, et al. Three-year surveillance of community-acquired *Staphylococcus aureus* infections in children. *Clin Infect Dis*. 2005;40:1785–91.
4. Fridkin SK, Hageman JC, Morrison M, Thomson Sanza L, Como-Sabetti K, Jernigan JA, et al. Methicillin-resistant *S. aureus* disease in 3 communities. *N Engl J Med*. 2005;352:1436–44.
5. Johnson AP. Methicillin-resistant *Staphylococcus aureus*: the European landscape. *J Antimicrob Chemother*. 2011;66 Suppl 4:iv43–8.
6. European Centre for Disease Prevention and Control. Antimicrobial resistance in the EU/EEA (EARS-Net) - Annual Epidemiological Report 2019. Stockholm: ECDC; 2020.
7. Cuevas O, Cercenado E, Goyanes MJ, Vindel A, Trincado P, Boquete T, et al. Evolution of the antimicrobial resistance of *Staphylococcus* spp. in Spain: five nationwide prevalence studies, 1986 to 2002. *Antimicrob Agents Chemother*. 2004;48:4240–5.
8. Cuevas O, Cercenado E, Goyanes MJ, Vindel A, Trincado P, Boquete T, et al. *Staphylococcus* spp. en España: situación actual y evolución de la resistencia a antimicrobianos (1986–2006). *Enferm Infecc Microbiol Clin*. 2008;26:269–77.
9. Broseta A, Chaves F, Rojo P, Otero JR. Emergence of a single clone of community-associated methicillin-resistant *Staphylococcus aureus* in southern Madrid children. *Enferm Infecc Microbiol Clin*. 2006;24:31–5.
10. Cercenado E, Cuevas O, Marín M, Bouza E, Trincado P, Boquete T, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in Madrid, Spain: transcontinental importation and polyclonal emergence of Panton-Valentine leukocidin-positive isolates. *Diagn Microbiol Infect Dis*. 2008;61:143–9.
11. Barrios M, Alcolea A, Negreira S, Chaves F. Necrotizing pneumonia due to community-acquired methicillin resistant *Staphylococcus aureus* in a pediatric patient. *Enferm Infecc Microbiol Clin*. 2008;26:398–9.
12. Daskalaki M, Rojo P, Marín-Ferrer M, Barrios M, Otero JR, Chaves F, et al. Panton-Valentine leukocidin-positive *Staphylococcus*

- aureus* skin and soft tissue infections among children in an emergency department in Madrid, Spain. *Clin Microbiol Infect.* 2010;16:74–7.
13. Frick MA, Moraga-Llop FA, Bartolomé R, Larrosa N, Campins M, Roman Y, et al. Infecciones por *Staphylococcus aureus* resistente a meticilina adquirido en la comunidad en niños. *Enferm Infecc Microbiol Clin.* 2010;28:675–9.
 14. Rojo P, Barrios M, Palacios A, Gómez C, Chaves F. Community-associated *Staphylococcus aureus* infections in children. *Expert Rev Anti Infect Ther.* 2010;8:541–54.
 15. Cobos-Carrascosa E, Soler-Palacín P, Larrosa MN, Bartolomé R, Martín-Nalda A, Frick MA, et al. *Staphylococcus aureus* bacteremia in children. Changes during eighteen years. *Pediatr Infect Dis J.* 2015;34:1329–34.
 16. Gómez-González C, Larrosa N, Ruiz de Gopegui E, Fernández A, Palacios A, Moraga F, et al. 479: Infecciones por *Staphylococcus aureus* resistente a meticilina asociado a la comunidad en población pediátrica: estudio multicéntrico. XIV Congreso de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC). *Enferm Infecc Microbiol Clin.* 2010;28(Espec Cong 1):223–4.
 17. Nurjadi D, Fleck R, Lindner A, Schäfer J, Gertler M, Mueller A, et al. Import of community-associated, methicillin-resistant *Staphylococcus aureus* to Europe through skin and soft-tissue infection in intercontinental travellers, 2011–2016. *Clin Microbiol Infect.* 2019;25:739–46.
 18. ABCs Report: Methicillin-Resistant *Staphylococcus aureus*, 2008. Active Bacterial Core Surveillance: Emerging Infections Program Network www.cdc.gov/abcs/reportsfindings/survreports/mrsa08.htm.
 19. File TM. Impact of community-acquired methicillin-resistant *Staphylococcus aureus* in the hospital setting. *Cleveland Clin J Med.* 2007;74 Suppl. IV:S6–11.
 20. European Centre for Disease Prevention and Control. Antimicrobial resistance in the EU/EEA (EARS-Net) - Annual Epidemiological Report 2017. Stockholm: ECDC; 2018.
 21. López-Aguilar C, Perez-Roth E, Méndez-Álvarez S, Moreno A, Duran MC, Casanova C, et al. Association between the presence of the Pantone-Valentine leukocidin-encoding gene and a lower rate of survival among hospitalized pulmonary patients with staphylococcal disease. *J Clin Microbiol.* 2007;45:274–6.
 22. Cercenado E, Marín M, Vindel A, Padilla B, Cuevas O, Navarro A, et al. First report of infection with community-acquired methicillin-resistant *Staphylococcus aureus* in Spain. In: 16th European Congress of Clinical Microbiology and Infectious Diseases. 2006. Abstract P-466.
 23. Pérez S, Torres E, Treviño M, Fernández B, Otero I, Barbeyto L, et al. Complejos clonales de *Staphylococcus aureus* resistente a meticilina predominantes en Galicia. Caracterización de los aislados comunitarios detectados. XII Reunión de la Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica (SEIMC). La Coruña, 9–11 de mayo de 2007. Abstract 43.
 24. Del Rosal T, Méndez-Echevarría A, García-Vera C, Escosa-García L, Agud M, Chaves F, et al. *Staphylococcus aureus* nasal colonization in Spanish children. The COSACO Nationwide Surveillance Study. *Infect Drug Resist.* 2020;13:4643–51.
 25. Den Heijer CD, van Bijnen EM, Paget WJ, Pringle M, Goossens H, Bruggeman CA, et al. Prevalence and resistance of commensal *Staphylococcus aureus*, including methicillin-resistant *S. aureus*, in nine European countries: a cross-sectional study. *Lancet Infect Dis.* 2013;13:409–15, [http://dx.doi.org/10.1016/S1473-3099\(13\)70036-7](http://dx.doi.org/10.1016/S1473-3099(13)70036-7).
 26. Laub K, Tóthpál A, Kovács E, Sahin-Tóht J, Horváth A, Kardos S, et al. High prevalence of *Staphylococcus aureus* nasal carriage among children in Szolnok, Hungary. *Acta Microbiol Immunol Hung.* 2018;65:59–72.
 27. Tavares DA, Sá-Leão R, Miragaia M, de Lencastre H. Large screening of CA-MRSA among *Staphylococcus aureus* colonizing healthy young children living in two areas (urban and rural) of Portugal. *BMC Infect Dis.* 2010;10, <http://dx.doi.org/10.1186/1471-2334-10-110>.
 28. Esposito S, Terranova L, Zampiero A, Lerardi V, Rios WP, Pelucchi C, et al. Oropharyngeal and nasal carriage by healthy children. *BMC Infect Dis.* 2014;14:1, <http://dx.doi.org/10.1186/s12879-014-0723-933>.
 29. Gorwitz R. Community-associated methicillin-resistant *Staphylococcus aureus* epidemiology and update. *Pediatr Infect Dis J.* 2008;27:925–30.
 30. Trilla A, Miró JM. Identifying high risk patients for *Staphylococcus aureus* infections: skin and soft tissue infections. *J Chemother.* 1995;7 Suppl 3:37–43.
 31. Barrios López M, Gómez González C, Ángeles Orellana M, Chaves F, Rojo P. *Staphylococcus aureus* abscesses: methicillin resistance or Pantone-Valentine leukocidin presence? *Arch Dis Child.* 2013;98:608–10.
 32. Herold BC, Immergluck LC, Marana MC, Lauderdale DS, Gaskin RE, Boyle-Vavra SE, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. *JAMA.* 1998;279:593–8.
 33. Moran GJ, Krishnadasan A, Gorwitz RJ, Fosheim GE, McDougal LK, Carey RB, et al. Methicillin-resistant *S. aureus* infections among patients in the emergency department. *N Engl J Med.* 2006;355:666–74.
 34. Chen A, Goldstein M, Carroll K, Song X, Perl TM, Siberry GK. Evolving epidemiology of pediatric *Staphylococcus aureus* cutaneous infections in a Baltimore hospital. *Pediatr Emerg Care.* 2006;22:717–23.
 35. Pallin DJ, Egan DJ, Pelletier AJ, Espinola JA, Hooper DC, Camargo CA Jr. Increased US emergency department visits for skin and soft tissue infections, and changes in antibiotic choices, during the emergence of community-associated methicillin-resistant *Staphylococcus aureus*. *Ann Emerg Med.* 2008;51:291–8.
 36. Szczesniak JM, Shermock KM, Murtaza UI, Siberry GK. No decrease in clindamycin susceptibility despite increased use of clindamycin for pediatric community-associated methicillin-resistant *Staphylococcus aureus* skin infections. *Pediatr Infect Dis J.* 2007;26:852–4.
 37. Barrado L, Brañas P, Rojo P, Gómez-González C, Barrios M, Orellana MA, et al. Molecular epidemiology of *Staphylococcus aureus* bacteremia in children, Spain: low risk of methicillin resistance. *J Infect.* 2014;68:195–8.
 38. Gillet Y, Etienne J, Lina G, Vandenesch F. Association of necrotizing pneumonia with Pantone-Valentine leukocidin-producing *Staphylococcus aureus*, regardless of methicillin resistance. *Clin Infect Dis.* 2008;47:985–6.