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Original Article

Community-acquired *S. aureus* infection in childhood: a multi-center study

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ABSTRACT

Background. The prevalence of community-acquired methicillin-resistant *S. aureus* (CA-MRSA) has been increasing worldwide. We aimed to investigate the prevalence of MRSA in community-acquired *S. aureus* infections, the risk factors for CA-MRSA infection and the clinical features of CA-MRSA.

Methods. A multi-center study with prospective and retrospective sections was conducted. Patients ≥ 3 months old and ≤18 years of age who were diagnosed with community-acquired *S. aureus* infections were included in this study and the patients' information were reviewed from the medical and microbiological database of the hospital. A standard question form about living conditions and exposure risk factors was administered to the parents of patients. The CA-MRSA infections were compared with the methicillin-susceptible *S. aureus* (CA-MSSA) infections in terms of the queried risk factors and clinical variables.

Results. We identified 334 pediatric patients with *S. aureus* infection, 58 (17.4%) had an infection with CA-MRSA. The refugee rate was higher in the CA-MRSA group. There was no significant difference regarding the exposure risk. The treatment modalities and outcomes were similar.

Conclusions. The study was not able to show reliable clinical variables or epidemiological risk factors except for being a refugee for CA-MRSA infections. Empirical antibiotic treatment should therefore be determined according to the local CA-MRSA prevalence in patients presenting with a possible staphylococcus infection.

Key words: cellulitis, bacteremia, sulbactam ampicillin, refugee, immigrant.

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Staphylococcus aureus is an important etiologic agent of community-acquired infections, mainly involving the skin and soft tissue but also including bacteremia, endocarditis, osteomyelitis, pyomyositis, and necrotizing pneumonia. Less frequently, it can cause staphylococcal toxic shock syndrome, sepsis, and meningitis.[1] The most important issue when planning the treatment of *S. aureus* infections is whether the isolate is sensitive or resistant to methicillin, because beta lactam antibiotics are not effective on methicillin resistant *S. aureus*.

Methicillin-resistant *S. aureus* (MRSA) isolates produce penicillin-binding protein 2A (PBP2A) which is encoded by the *mecA* gene. PBP2A has a low affinity for methicillin and other β-lactam drugs, and MRSA isolates are therefore intrinsically resistant to almost all β-lactam antibiotics.[2] MRSA isolates were first described as hospital-acquired pathogens, and community-acquired *S. aureus* isolates (CA-MRSA) appeared later on.[2] CA-MRSA is susceptible to several antimicrobial agents, unlike hospital acquired MRSA (HA-MRSA). The prevalence of CA-MRSA varies from country to country and has been increasing for a long time. In the United States, the percentage of CA-MRSA has increased to 76%.[3] There is no active surveillance programme for CA-MRSA in Türkiye and the data on the frequency of CA-MRSA in the country is inadequate. The methicillin resistance rate for community-acquired *S. aureus* needs to be considered when planning empirical treatment of *S. aureus* infections. We therefore conducted this three-year multi-center surveillance study aiming to investigate the prevalence of CA-MRSA, the resistance patterns of community-acquired *S. aureus* isolates, and the risk factors for the acquisition of CA-MRSA infection.

Material and Methods

A multi-center study with prospective and retrospective sections was conducted. The study was conducted at the pediatric infectious disease departments of 7 regional pediatric referral hospitals from 4 cities (Ankara, İstanbul, Konya, Trabzon). Cases of laboratory-confirmed community-acquired *S. aureus* infections were included.

Patients ≥3 months old and ≤18 years of age who presented with an infectious disease complaint to the outpatient clinics and whose clinical isolates grew *S. aureus*, or hospitalized patients with clinical presentation compatible with infectious disease where *S. aureus* grew in the clinical isolates within 72 hours of hospitalization, who did not have a history of hospital admission in the last 3 months were included in the study. Patients diagnosed with *S. aureus* infection between January 1st, 2017 and February 28th, 2018 were retrospectively evaluated from hospital medical data and national health registration data screened and included in the study while patients diagnosed with *S. aureus* infection between March 1st, 2018 and January 1st, 2020 were prospectively included.

Patients who had a history of catheter insertion or surgery within the last year, patients on dialysis, and patients with an acquired *S. aureus* infection after an intramuscular injection were not included in the study. The *S. aureus* infections related to foreign material, such as grafts and implants, and ventriculoperitoneal shunt-associated infections were also excluded from the study, as were patients with *S. aureus* growth in the urine culture.

The demographic features of the patients, medical history especially antibiotic usage, underlying skin disorders, infection type, anatomical localization of the infection, treatment information, whether the treatment was as an outpatient or inpatient, whether drainage was used, the antibiotic regimens, and the antibiogram results of the *S. aureus* isolates were reviewed from the medical and microbiological database of the hospitals for retrospectively included patients. The same information was recorded by the physician during the prospective phase. Patients included in the study prospectively were contacted

directly at the time of the diagnosis and a standard question form about living conditions and exposure risk factors was administered to the parents. The number of people living in the house, the number of showers per week, the history of attending a nursery or school, history of living with a health care worker, history of household contact with a person suffering from any cutaneous infection, the travel history, antibiotic usage in the last 3 months, the presence of an underlying skin disorder, and hospitalization in the last year were queried. The CA-MRSA infections were then compared with the methicillin-susceptible *S. aureus* (CA-MSSA) infections in terms of the queried risk factors.

The infections were classified as skin and soft tissue infections (SSTI) and invasive infections (II). Skin abscesses, furuncles, and cellulitis were classified as SSTI. Lymphadenitis/deep neck infection, osteomyelitis/septic arthritis, and bacteremia were classified as II.[4] Pyomyositis/ileopsoas abscess, otitis media, mastoiditis, thyroiditis, pneumonia, empyema, sepsis/staphylococcal toxic shock syndrome, and meningitis were also classified as II. The infection was also classified as II if the primary site of infection was the skin and soft tissue but *S. aureus* grew from blood cultures.

The samples for SSTI were retrieved by spontaneously draining material from the infection site or by needle puncture or surgical drainage of the infection site. The samples for lymphadenitis/deep neck infection were retrieved by needle puncture or surgical drainage. The samples for osteomyelitis/septic arthritis, pyomyositis/ileopsoas abscess, thyroiditis, and mastoiditis were retrieved surgically. *S. aureus* were isolated from the pus draining from the ear in otitis media, from the pleural fluid in empyema, from the sputum in pneumonia cases, from blood cultures in patients with sepsis/staphylococcal toxic shock syndrome, and from the cerebrospinal fluid in meningitis patients.

Antimicrobial susceptibility was determined using the disc diffusion method according to the European Committee on Antimicrobial Susceptibility Testing protocol. Isolates that were methicillin resistant and also those that were resistant to ≥3 antibiotic classes (tetracycline, erythromycin, trimethoprim-sulfamethoxazole, fusidic acid, mupirocin, ciprofloxacin, and gentamicin) were evaluated as multi-drug resistant strains.

Ethics committee approval was obtained from Yıldırım Beyazıt University Yenimahalle Training and Research Hospital Ethics Committee (approval reference number: 2018/30).

Results

We identified 334 pediatric patients infected with *S. aureus*. 276 (82.6%) of these 334 patients were infected with CA-MSSA, while 58 (17.4%) were infected with CA-MRSA.

The median age was 1 year (IQR 1-18 years). There were 163 (39%) girls and 171 (61%) boys. Patient demographic characteristics and their comparison between the MSSA and MRSA groups are presented in Table I. Age and gender distribution were similar in the CA-MSSA and CA-MRSA groups. The refugee rate was higher in the CA-MRSA group.

Table I. Demographic characteristics of patients with CA-MSSA and CA-MRSA infection.

Characteristics	Total N=334	MSSA N=276	MRSA N=58	*p* value
Age (y), median (IQR)	1 (0-18)	1 (0-18)	1 (0-17)	0.69
Gender, Female/Total	163/334	132/276	31/58	0.715
Refugee, n (%)	22 (6.6)	14 (5.1)	8 (13.8)	0.01

CA-MSSA: community-acquired methicillin-susceptible *S. aureus*, CA-MRSA community-acquired methicillin-resistant *S. aureus*, IQR: interquartile range

The comparison of living conditions and possible exposure to risk factors for MRSA between the patients with CA-MRSA and CA-MSSA infections is shown in Table II. There was no significant difference regarding the exposure risk. No difference was found between the two groups in terms of underlying skin disease.

SSTI (198 patients [59.6%]) cases were more common than invasive infections (134 patients [40.4%]), both in the entire study population and in the CA-MSSA and CA- MRSA groups. The most common invasive infection types in both the CA-MSSA and CA-MRSA groups were lymphadenitis/deep neck infection, musculoskeletal infection, and bacteremia. Table III shows the clinical presentations of the patients with MRSA and MSSA infections. According to age, there was no difference between SSTI and II (p= 0.33).

The treatments administered to the patients are shown in Table IV. A history of hospitalization was present in 50.5% of the patients. There was no statistically significant difference between the MRSA and MSSA groups in terms of the hospitalization rate, duration of antibiotic treatment, or drainage application rate. When looking for SSTT, hospitalization rate, duration of antibiotic treatment, or drainage application rate were similar in MRSA and MSSA groups (p=0.72, p=0.47, p=0.26); these were also similar between groups in II (p=0.22, p=0.40, p=0.36).

Systemic (intravenous or peroral) antibiotics were used for the treatment of 88.3% of the patients. Anti-MRSA antibiotic treatment was started empirically at admission for 66 (19.8%) patients. Of these 66 patients, 18 had SSTT and 48 had II. The most commonly started parenteral antibiotics at admission were sulbactam ampicillin/amoxicillin clavulanate and third generation cephalosporins. A total of 103 patients had initially received IV sulbactam ampicillin / amoxicillin clavulanate while 75 patients received sulbactam ampicillin / amoxicillin clavulanate alone; in the other patients, the antibiotic used in combination with an anti-MRSA antibiotic was clindamycin in 17 patients, teicoplanin in 4 patients, and vancomycin in 2 patients. A total of 60 patients had received ceftriaxone/

Table II. Risk factors/exposures associated with community-onset methicillin resistance among patients with CA-MSSA and CA-MRSA infection.

	Total N=334	MSSA N=276	MRSA N=58	*p* value
Number of people living in the house, mean ± SD	4.3 ± 1.6	4.2 ± 1.6	4.6 ± 1.6	0.19
Number of showers per week, median (IQR)	2 (1-7)	2 (1-7)	2 (1-4)	0.44
Currently attending nursery or school, n (%)	83 (24.8)	68 (24.6)	15 (25.8)	0.86
Living with a health care worker, n (%)	3 (0.9)	3 (1)	0 (0)	
Being in prison, n (%)	1 (0.3)	0 (0)	1 (1.7)	
Household contact with person with cutaneous infections, n (%)	11 (3.3)	10 (3.6)	1 (1.7)	
Travel history, n (%)	29 (8.7)	22 (8)	7 (12.1)	0.21
Antibiotic usage in the last 3 months, n (%)	7 (2.1)	7 (2.5)	0 (0)	0.31
Underlying skin disorder, n (%)	73 (21.9)	64 (23.2)	9 (15.5)	0.19
Eczema/ Atopic dermatitis/urticaria, n (%)	16 (4.8)	13 (4.7)	3 (5.2)	
Trauma/Abrasion/varicella, enteroviral rash, herpes simplex virus, n (%)	53 (15.9)	47 (17)	6 (10.3)	
Insect bite, n (%)	4 (1.2)	4 (1.4)	0 (0)	
Hospitalization in the last year, n (%)	36 (10.8)	30 (10.9)	6 (10.3)	0.22

CA-MSSA: community-acquired methicillin-susceptible *S. aureus*, CA-MRSA community-acquired methicillin-resistant *S. aureus*, IQR: interquartile range, SD: standard deviation

Table III. Duration, type, and localization of infections in the MSSA and MRSA groups.

	Total N=334	MSSA N=276	MRSA N=58	*p* value
Duration of symptoms (days), Mean ± SD	14 ± 56.5	15.3 ± 61.5	7.6 ± 10.2	0.38
Type of infection				
SSTI, n (%)	198 (59.6)	166 (60.1)	34 (58.6)	0.86
Invasive infection, n (%)	134 (40.1)	110 (39.8)	24 (41.4)	
Localization of SSTI				
Head and neck, n (%)	41 (12.2)	35 (12.6)	6 (10.3)	
Trunk, n (%)	65 (19.5)	49 (17.7)	16 (27.6)	
Genitalia, n (%)	7 (2.1)	7 (2.5)	0 (0)	
Perianal, n (%)	3 (0.9)	2 (0.7)	1 (1.7)	
Foot-leg, n (%)	34 (10.2)	29 (10.5)	5 (8.6)	
Hand-arm, n (%)	36 (10.8)	32 (11.6)	4 (6.9)	
Gluteus, n (%)	12 (3.6)	10 (3.6)	2 (3.4)	
Type of invasive infection				
Lymphadenitis / deep neck infection, n (%)	51 (15.3)	41 (14.9)	10 (17.2)	
Bacteremia, n (%)	44 (13.2)	40 (14.5)	4 (6.9)	
Osteomyelitis / septic arthritis, n (%)	19 (5.7)	15 (5.4)	4 (6.9)	
Otitis media, n (%)	14 (4.2)	11 (4)	3 (5.2)	
Sepsis/staphylococcal toxic shock syndrome, n (%)	4 (1.2)	4 (1.4)	0 (0)	
Pneumonia ± empyema, n (%)	4 (1.2)	3 (0.01)	1 (1.7)	
Mastoiditis, n (%)	1 (0.3)	1 (0.4)	0 (0)	
Thyroiditis, n (%)	1 (0.3)	1 (0.4)	0 (0)	
Pyomyositis / iliopsoas abscess, n (%)	2 (0.6)	2 (0.6)	0 (0)	
Infective endocarditis, n (%)	1 (0.3)	1 (0.3)	0 (0)	
Meningitis, n (%)	1 (0.0)	0 (0)	1 (1.7)	

CA-MSSA: community-acquired methicillin-susceptible *S. aureus*, CA-MRSA community-acquired methicillin-resistant *S. aureus*, SD: standard deviation, SSTI: skin and soft tissue infections

Table IV. Rate of hospitalization, route of antibiotic administered, duration of antibiotic treatment and drainage application, change of antibiotics according to the culture result in CA-MSSA and CA-MRSA groups.

	Total N=334	MSSA N=276	MRSA N=58	*p* value
Hospitalization and intravenous antibiotic treatment, n (%)	169 (50.5)	135 (48.9)	34 (58.6)	0.33
Local antibiotic treatment, n (%)	68 (20.4)	60 (21.7)	8 (13.7)	0.32
Drainage, n (%)	166 (49.7)	131 (47.5)	35 (60.3)	0.18
Intravenous antibiotic treatment duration (days), median (IQR)	9 (6-13)	9 (6-12)	8 (5-14)	0.9
Total treatment duration (days), median (IQR)	10 (2-77)	10 (2-77)	10 (4-36)	0.35
Antibiotic change after culture result, n (%)	50 (15)	37 (13.4)	13 (22.4)	**0.02**
Escalation, n (%)	25 (7.4)	15 (5.4)	10 (17.2)	
De-escalation, n (%)	25 (7.4)	22 (7.9)	3 (5.1)	

CA-MSSA: community-acquired methicillin-susceptible *S. aureus*, CA-MRSA community-acquired methicillin-resistant *S. aureus*, IQR: interquartile range

cefotaxime, 3 of these with vancomycin and 3 with clindamycin. A total of 68 patients had initially been given oral antibiotics, consisting of 60 patients receiving amoxicillin-clavulanate, 2 patients receiving amoxicillin, 1 patient receiving trimethoprim-sulfamethoxazole, 1 patient receiving clarithromycin, 2 patients receiving cefuroxime-axetil, and 2 patients receiving cefixime. One patient with CA-MSSA bacteremia and one patient with necrotizing pneumonia accompanying the bacteremia due to CA-MRSA died. All other patients recovered completely.

The antibiotic resistance profiles of CA-MRSA and CA-MSSA isolates are shown in Table V. The tests showed resistance to penicillin in 85.8% of the CA-MSSA isolates, to erythromycin in 2.7%, and to clindamycin in 3.8%. All of the CA-MRSA isolates were resistant to penicillin, while 42% were resistant to erythromycin, and 20% to clindamycin. All CA-MRSA and CA-MSSA isolates were sensitive to teicoplanin and vancomycin. There were 4 (6.9%) MRSA isolates (out of 58) that were resistant to three or more antibiotic classes.

Discussion

We found the MRSA prevalence among community-acquired *S. aureus* infections to be 17.4%, 17.2% in SSTI and 17.8% in II. The refugee rate was significantly higher in the CA-MRSA group, and we could not find any other exposure risk factor for CA-MRSA infection. When the patients infected with CA-MSSA and CA-MRSA were compared, we did not find any difference regarding the invasive infection rate, hospitalization rate, drainage rate, and antibiotic treatment duration. CA-MRSA isolates were frequently susceptible to non-beta-lactam antibiotics, especially clindamycin, ciprofloxacin, trimethoprim-sulfamethoxazole, and gentamycin.

A Turkish study conducted in 1997 found a prevalence of 26.4% for CA-MRSA infections during that year at a single medical center.[5] Another study conducted in Türkiye between 2014 and 2018 in a single center in the province of Izmir found that 31.25% of S.aureus-caused SSTI infections were caused by CA-MRSA.[6] When evaluated together with the results of our study, it seems that the frequency of MRSA has not increased in Türkiye since then while an increase is reported in several countries around the world. The reason for the lack of an increase in Türkiye can be clarified by illuminating the risk factors that play a role in the development of MRSA infections, which have been extensively studied. There are conflicting results in this regard. Some studies have reported antibiotic use in the last 6 months as a risk factor for MRSA infection while others report no such

Table V. Antibiotic susceptibilities (% susceptible) of the CA-MSSA and CA-MRSA isolates.

	MSSA N:276			MRSA N:58		
	Sensitive (%)	Intermediate (%)	Resistant (%)	Sensitive (%)	Intermediate (%)	Resistant (%)
PEN	3.5	0.7	85.8	0	0	100
CLI	87.2	3.8	9	76.3	3.7	20
ERY	81	2.7	16.3	56	2	42
SXT	98.4	0	1.6	78.4	4	17.6
CIP	95.4	1	3.6	84.5	2.2	13.3
TET	94.4	0	5.6	58.6	0	44.4
TEC	100	0	0	100	0	0
VAN	100	0	0	100	0	0
GEN	98.9	0.4	0.7	89.7	1.7	8.6

CA-MSSA: community-acquired methicillin-susceptible *S. aureus*, CA-MRSA community-acquired methicillin-resistant *S. aureus*, CIP: ciprofloxacin, CLI: clindamycin, ERY: erythromycin, GEN: gentamicin, SXT: trimethoprim/sulfamethoxazole, PEN: penicillin, TEC: teicoplanin, TET: tetracycline, VAN: vancomycin

relationship.[7-9] Similarly, some studies report day care attendance to be associated with MRSA transmission while others have found similar rates of day care attendance among those with MSSA and MRSA infections.[7,10,11] No relationship has been found between CA-MRSA infection and close contact with healthcare professionals, steroid use, underlying skin disease, sports activities, and travel abroad.[7,10] Current or previous homeless status, current or prior incarceration, and alcoholism have each been found to be more common in patients with MRSA infection compared to those with MSSA infection.[9] In the current study, the MRSA and MSSA groups were found to be similar in terms of the exposure risk factors. We had one imprisoned subject who was infected with MRSA.

CA-MRSA has been reported to be more common in minority groups. In a study conducted in Israel, Arab ethnicity was found to be a risk factor for CA-MRSA infection.[12] CA-MRSA has similarly been reported to be more common in Aborigines and those of Polynesian ethnicity in Australia.[13,14] In the USA, a higher proportion of CA-MRSA infections are found in African American patients than in white or Hispanic patients.[7,9] A study from Denmark has reported a higher incidence of CA-MRSA infections in those of non-Danish origin.[10] The CA-MRSA clone, which is predominant in Spain, has similarly been found to be more common in immigrants from South America than in the native Spanish population.[15] High rate of CA-MRSA colonization has been reported in the refugee population.[16] In the current study, being a refugee was found to be a risk factor for CA-MRSA infection but other exposure risks were similar between the groups. Although minority groups are reported as a risk factor for CA-MRSA in the literature, we are not aware of any other publication reporting being a refugee as such a risk factor. It is possible that a combination/interaction of many factors and not a single factor plays a role in minority groups and immigrants as regards development of MRSA infections. The long journeys during migration, accommodation in multiple locations, the difficult conditions of the migration routes, crowded home conditions, and lower hygiene conditions due to socioeconomic problems may be contributing factors for colonization of MRSA, thereby CA-MRSA infection. Considering the higher prevalence of CA-MRSA among the homeless and those with alcoholism, we believe that the residential environment is a very important factor in determining the risk of CA-MRSA infection.

Results from studies investigating the clinical picture caused by CA-MSSA and CA-MRSA in the literature are conflicting. CA-MSSA has been reported to be associated with a higher rate of invasive infections in some studies while CA-MRSA patients have been reported to have higher morbidity, mortality, and hospitalization rates than those with CA-MSSA infection in another study.[10,17,18] Some studies report no difference in severity between MSSA and MRSA infections.19 The most common type of infection with both MSSA and MRSA has been reported to be those of the skin and soft tissues.[10] The most common invasive infections caused by CA-MRSA isolates have been found to be musculoskeletal and pulmonary infections, while the most common ones caused by CA-MSSA have been reported as septic arthritis, bacteremia, osteomyelitis, and lymphadenitis.[17] Skin and soft tissue infections were most common with both CA-MSSA and CA-MRSA isolates in the current study, and the frequency of invasive infections was similar in the two groups, with the most common type of invasive infection caused by both CA-MSSA and CA-MRSA isolates found to be lymphadenitis/deep neck infection and bacteremia.

The optimal treatment for skin and soft tissue infections is drainage if the lesion is suitable. No difference has been reported between MSSA and MRSA infections in terms of drainage rates.[19] Drainage was used in half of the patients in the current study and most had received systemic antibiotic treatment. The rates of invasive infection, needing drainage,

and hospitalization, as well as the treatment duration were similar in our groups, indicating that methicillin resistance was not a factor that increased virulence. It was reported that the *S. aureus* virulence increases with virulence factors such as PVL, regardless of the methicillin resistance.[19]

CA-MRSA isolates have been reported to be highly susceptible to non-beta-lactam antibiotics, unlike hospital-acquired MRSA.[20] Clindamycin resistance has been increasing over the years in both CA-MRSA and CA-MSSA isolates.[17] The sensitivity rates to erythromycin and clindamycin, trimethoprim/sulfamethoxazole, and ciprofloxacin was higher in the current study than those reported in the literature.[10,17,21,22] Tetracycline sensitivity rates vary greatly in the literature (24.2-100%).[9,21] The CA-MSSA isolates were highly susceptible to tetracycline while half of the CA-MRSA isolates were resistant in the current study. CA-MSSA was found to be more sensitive to all the antibiotics tested when compared to CA-MRSA.

The strong points of our study are the prospective inclusion of patients who were queried about exposure risk factors, and evaluating both inpatients and outpatients for community-acquired *S. aureus* infection. Our study was conducted at seven health care centers in four cities and we therefore believe it is able to highly represent findings that may be generalized to our country. One of the limitations of this study is that we did not screen for the carrier state by nasal culture. We also did not investigate the living conditions and exposure risks in the retrospective part of our study. We found being a refugee to be a significant risk factor for CA-MRSA infection but we did not investigate the refugees' time of immigration, place of immigration, and living conditions in more detail. Therefore, our results cannot be generalized to all refugees. While our study was conducted in multiple centers, we did not include centers from all of Türkiye's geographical regions, which have varying climatic conditions, so our results may not be representative of other regions.

In conclusion, we found no reliable epidemiological risk factor except for being a refugee for CA-MRSA infections. We also did not find clinical variables that could differentiate between CA-MRSA and CA-MSSA infections at admission, before the culture results were available. Empirical antibiotic treatment should therefore be determined according to the local CA-MRSA prevalence in patients presenting with a possible staphylococcus infection. Further studies that focus on why CA-MRSA is more common in refugees are needed.

Ethical approval

Ethics committee approval was obtained (approval reference number: 2018/30) from Yıldırım Beyazıt University Yenimahalle Training and Research Hospital Ethics Committee for the study.

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: GİB, HA, FNO, OMA, BBD, ZGGA, data collection: GİB, UÇ, EÇT, FO; analysis and interpretation of results: UÇ, AK, OT, EÇ; draft manuscript preparation: AK, TAT, Eİ, GT. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Katz SE, Williams DJ. Pediatric community-acquired pneumonia in the United States: changing epidemiology, diagnostic and therapeutic challenges, and areas for future research. Infect Dis Clin North Am 2018; 32: 47-63. https://doi.org/10.1016/j.idc.2017.11.002
2. Que YA, Moreillon P. Staphylococcus aureus (Including Staphylococcal Toxic Shock Syndrome). In: Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 9th ed. Philadelphia: Elsevier; 2020: 2293-2431.
3. Kaplan SL, Hulten KG, Gonzalez BE, et al. Three-year surveillance of community-acquired Staphylococcus aureus infections in children. Clin Infect Dis 2005; 40: 1785-1791. https://doi.org/10.1086/430312
4. Penteado FD, Tubero TZ, Hein N, Gilio AE. Frequency of community-acquired methicillin-resistant staphylococcus aureus in pediatric population in a general hospital in São Paulo, Brazil, over 5 years. Pediatr Infect Dis J 2019; 38: e87-e89. https://doi.org/10.1097/INF.0000000000002158
5. Durmaz B, Durmaz R, Sahin K. Methicillin-resistance among Turkish isolates of Staphylococcus aureus strains from nosocomial and community infections and their resistance patterns using various antimicrobial agents. J Hosp Infect 1997; 37: 325-329. https://doi.org/10.1016/s0195-6701(97)90149-3
6. Böncüoğlu E, Kıymet E, Çağlar İ, et al. Upward trend in the frequency of community-acquired methicillin-resistant Staphylococcus aureus as a cause of pediatric skin and soft tissue infections over five years: a cross-sectional study. Turk J Pediatr 2021; 63: 200-205. https://doi.org/10.24953/turkjped.2021.02.003
7. Sattler CA, Mason EO Jr, Kaplan SL. Prospective comparison of risk factors and demographic and clinical characteristics of community-acquired, methicillin-resistant versus methicillin-susceptible Staphylococcus aureus infection in children. Pediatr Infect Dis J 2002; 21: 910-917. https://doi.org/10.1097/00006454-200210000-00005
8. Baggett HC, Hennessy TW, Leman R, et al. An outbreak of community-onset methicillin-resistant Staphylococcus aureus skin infections in southwestern Alaska. Infect Control Hosp Epidemiol 2003; 24: 397-402. https://doi.org/10.1086/502221
9. Skiest DJ, Brown K, Cooper TW, Hoffman-Roberts H, Mussa HR, Elliott AC. Prospective comparison of methicillin-susceptible and methicillin-resistant community-associated Staphylococcus aureus infections in hospitalized patients. J Infect 2007; 54: 427-434. https://doi.org/10.1016/j.jinf.2006.09.012
10. Böcher S, Gervelmeyer A, Monnet DL, Mølbak K, Skov RL; Danish CA-MRSA Study Group. Methicillin-resistant Staphylococcus aureus: risk factors associated with community-onset infections in Denmark. Clin Microbiol Infect 2008; 14: 942-948. https://doi.org/10.1111/j.1469-0691.2008.02055.x
11. Shahin R, Johnson IL, Jamieson F, McGeer A, Tolkin J, Ford-Jones EL. Methicillin-resistant Staphylococcus aureus carriage in a child care center following a case of disease. Toronto Child Care Center Study Group. Arch Pediatr Adolesc Med 1999; 153: 864-868. https://doi.org/10.1001/archpedi.153.8.864
12. Galper E, Bdolah-Abram T, Megged O. Assessment of infections rate due to community-acquired methicillin-resistant Staphylococcus aureus and evaluation of risk factors in the paediatric population. Acta Paediatr 2021; 110: 1579-1584. https://doi.org/10.1111/apa.15698
13. Nimmo GR, Coombs GW. Community-associated methicillin-resistant Staphylococcus aureus (MRSA) in Australia. Int J Antimicrob Agents 2008; 31: 401-410. https://doi.org/10.1016/j.ijantimicag.2007.08.011
14. Gosbell IB, Mercer JL, Neville SA, Chant KG, Munro R. Community-acquired, non-multiresistant oxacillin-resistant Staphylococcus aureus (NORSA) in South Western Sydney. Pathology 2001; 33: 206-210. https://doi.org/10.1080/00313020123439
15. Manzur A, Dominguez AM, Pujol M, et al. Community-acquired methicillin-resistant Staphylococcus aureus infections: an emerging threat in Spain. Clin Microbiol Infect 2008; 14: 377-380. https://doi.org/10.1111/j.1469-0691.2007.01934.x
16. Aro T, Kantele A. High rates of meticillin-resistant Staphylococcus aureus among asylum seekers and refugees admitted to Helsinki University Hospital, 2010 to 2017. Euro Surveill 2018; 23: 1700797. https://doi.org/10.2807/1560-7917.ES.2018.23.45.1700797
17. Hultén KG, Kaplan SL, Gonzalez BE, et al. Three-year surveillance of community onset health care-associated staphylococcus aureus infections in children. Pediatr Infect Dis J 2006; 25: 349-353. https://doi.org/10.1097/01.inf.0000207404.50143.1e
18. Gomes RT, Lyra TG, Alves NN, Caldas RM, Barberino MG, Nascimento-Carvalho CM. Methicillin-resistant and methicillin-susceptible community-acquired Staphylococcus aureus infection among children. Braz J Infect Dis 2013; 17: 573-578. https://doi.org/10.1016/j.bjid.2013.02.010
19. Bennett CM, Coombs GW, Wood GM, et al. Community-onset Staphylococcus aureus infections presenting to general practices in South-eastern Australia. Epidemiol Infect 2014; 142: 501-511. https://doi.org/10.1017/S0950268813001581

20. Groom AV, Wolsey DH, Naimi TS, et al. Community-acquired methicillin-resistant Staphylococcus aureus in a rural American Indian community. JAMA 2001; 286: 1201-1205. https://doi.org/10.1001/jama.286.10.1201

21. Wu D, Wang Q, Yang Y, et al. Epidemiology and molecular characteristics of community-associated methicillin-resistant and methicillin-susceptible Staphylococcus aureus from skin/soft tissue infections in a children's hospital in Beijing, China. Diagn Microbiol Infect Dis 2010; 67: 1-8. https://doi.org/10.1016/j.diagmicrobio.2009.12.006

22. Liu Y, Xu Z, Yang Z, Sun J, Ma L. Characterization of community-associated Staphylococcus aureus from skin and soft-tissue infections: a multicenter study in China. Emerg Microbes Infect 2016; 5: e127. https://doi.org/10.1038/emi.2016.128