Chula Med J Vol. 68 No. 3 July - September 2024; 161 - 172 DOI : 10.56808/2673-060X.5411

Original article

Trends of methicillin-resistant *Staphylococcus aureus* infections among Thai pediatric patients

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Abstract

Background: Although reductions in methicillin-resistant *Staphylococcus aureus* (MRSA) infections have been reported, vancomycin prescription rates remain high.
Objective: This study aimed to update trends in pediatric prevalence and antibiotic susceptibilities of MRSA infections.
Methods: This retrospective study analyzed patients aged <15 years who contracted *S. aureus* infections between 2016 and 2022 at a tertiary-care hospital in Thailand. MRSA was defined as resistance to cefoxitin or oxacillin minimal inhibitory concentration of >4 μg/mL. Patients with MRSA infections and their first isolates were classified into healthcare-associated (HA) or community-associated (CA) MRSA based on surveillance definitions. Antibiotic susceptibilities were tested using the VITEK 2XL automated system and disk diffusion method. The annual prevalence of MRSA was estimated and compared using the chi-square test for trend.
Results: Among 1,059 children with *S. aureus* infections, MRSA was identified in 82 (7.7%; 95% CI 6.2–9.6), consisting of 65 HA-MRSA and 17 CA-MRSA infections. MRSA prevalence exhibited a significantly downward trend ($P = 0.003$). MRSA isolates were fully susceptible to vancomycin, linezolid, and tigecycline, with high susceptibilities to fosfomycin and fusidic acid (> 90.0%), lower to trimethoprim-sulfamethoxazole (77.0%) and tetracycline (48.0%), and the least to clindamycin (18.0%).
Conclusion: A declining trend and low prevalence of MRSA infections were observed among pediatric patients, justifying the cautious use of vancomycin as empirical therapy for patients without MRSA risk. MRSA isolates remained highly susceptible to most current antibiotics, which further supports the effectiveness of these treatments against MRSA infections.

Keywords: Antibiotic susceptibility, children, MRSA, resistance, *Staphylococcus aureus.*

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a global threat and causes both colonization, resulting in carriage in healthy individuals, and infection in susceptible patients.[1] This leads to difficulties in treatment and higher mortality rates. Recently, the trend of MRSA infections has declined in several countries, coinciding with a greater focus on infection prevention control in healthcare facilities. Nevertheless, the decline occurs in both healthcare-associated (HA) and community-associated (CA) settings, suggesting the involvement of other factors such as the regional evolution of MRSA clones.[2] The SENTRY antimicrobial surveillance program gathered nearly 200,000 *S. aureus* isolates from patients of all ages in America, Europe, and Asia–Pacific between 1997 and 2016. The program highlighted that the proportion of MRSA infections was primarily HA and increased from 33.1% in 1997–2000 to the highest peak of 44.2% in 2005-2008 before dropping to 42.3%

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Received: February 1, 2024
Revised: March 27, 2024
Accepted: April 2, 2024

in 2009-2012 and 39.0% in 2013-2016.[2] Similarly, the China Antimicrobial Surveillance Network (CHINET) reported a decrease in MRSA rates from 69.0% in 2005 to 44.6% in 2014 among 25,000 *S. aureus* isolates obtained from patients of all ages in 19 Chinese hospitals.[3] According to the National antimicrobial resistant surveillance center (NARST), the proportion of MRSA isolates retrieved from 83 Thai hospitals decreased significantly from 28.0% in 2006 to 14.2% in 2016. The decrease was less marked from 2017 to 2021, with the proportion fluctuating between 6.5% and 9.6%. Despite limited reports on the clinical epidemiology of MRSA in Thailand, data are available from some tertiary hospitals. In northern Thailand, a hospital reported an increase in MRSA prevalence among *S. aureus* bloodstream infections (BSIs) from 23.0% in 2007 to 43.0% in 2011 in 179 patients of all ages,[4] whereas another equivalent hospital later reported a decrease in the prevalence of MRSA BSIs from 33.0% in 2013 to 15% in 2017 in 84 adult patients.[5] In central Thailand, a hospital observed a decline in HA-MRSA infections among 502 *S. aureus* isolates collected from clinical wards, dropping from 57.0% in 2012 to 38.0% in 2015,[6] and another larger hospital reported a lower MRSA prevalence at 17.0% among 890 *S. aureus* infections in 2017, and no difference was observed between pediatric and adult patients.[7] However, a large-scale study across all hospitals in two Thai rural provinces showed that 10.0% of 911 *S. aureus* BSIs in 2006-2014 were MRSA infections. This included a higher proportion of HA-MRSA infections than of CA-MRSA infections, with no clear chronological trends in incidence.[8]

MRSA is resistant to nearly all beta-lactam antibiotics. According to well-established guidelines for treating MRSA infections,[9, 10] antibiotic regimens are recommended based on the infection site. For invasive and high-inoculum MRSA infections, intravenous vancomycin therapy is the first-line agent. However, newer antibiotics have been introduced.[2, 9, 10] For example, linezolid is the primary alternative for treating invasive infections. Tigecycline and ceftaroline are approved for skin and soft tissue infections (SSTIs). In some cases, older antibiotics are still recommended. [2, 9, 10] Topical mupirocin or fusidic acid therapy can be used for mild skin infections. Oral trimethoprim–sulfamethoxazole (TMP/SMX), tetracycline, or clindamycin therapy are warranted for SSTIs, bone and joint infections (BJIs), or as step-down therapy. However, the retained activity of antibiotics against MRSA infections is crucial for successful treatment. To ensure the administration of appropriate initial anti-MRSA therapy, access to updated data on MRSA susceptibility profiles in each region is crucial.

In our hospital, inappropriate antibiotic prescription has been a significant problem. Despite a decreasing MRSA prevalence, the prescribing rate of vancomycin remains high, particularly for empirical therapy in pediatric inpatients.[11, 12] Overuse of vancomycin can lead to the emergence of vancomycin-resistant enterococci, which is becoming a national concern. To address this issue, this study aimed to examine the current burden of pediatric MRSA infections in our hospital that may promote judicious use of vancomycin. Specifically, the primary objective was to describe updated trends in the prevalence of MRSA infections among pediatric patients in a Thai tertiary-care hospital. The secondary objective was to describe the clinical spectra of pediatric MRSA infections and their antibiotic susceptibility profiles.

Materials and methods

Study population

This retrospective study was conducted at a tertiary-care hospital in central Bangkok, Thailand. The hospital has 1,500 beds in total, of which 200 are for pediatric care. All patients aged <15 years with positive culture for *S. aureus* between January 2016 and October 2022 were identified by searching through the database of the Department of Microbiology. For patients with more than one positive culture, relevant clinical data such as infection sites, therapeutic interventions, completion of antibiotic courses, and achievement of clinical resolution were collected to determine whether an isolate belonged to the same or a subsequent episode. If an isolate was associated with a different episode, it was counted as a new infection. Cases with *S. aureus* colonization, defined as not having symptoms and signs of illness or receiving medical attention, were excluded. Demographic data, underlying diseases, diagnosis, associated factors, microbiological laboratory results, and antibiotic therapy were extracted from the medical records.

This study was approved by the Institutional Review Board, Faculty of Medicine, Chulalongkorn University (IRB no. 717/64). Patients' anonymity and confidentiality were ensured during the study.

Definitions

Patients and their first MRSA isolates were classified into HA-MRSA or CA-MRSA.[13] An infection episode was considered caused by HA-MRSA when (1) an isolate was derived from a specimen collected after 48 h of admission, or (2) a patient had at least one of the following risk factors: chronic illness requiring repeated hospital visits, a history of hospitalization or surgery within the past year, or the presence of central venous catheters (CVCs) or an endotracheal, tracheostomy, or gastrostomy feeding tube at the culture date. An infection was caused by CA-MRSA if the isolate was obtained from a patient without the above-mentioned risk factors at the outpatient clinic or within 48 h of hospitalization.

Infection types were defined according to the surveillance definitions of the U.S. Centers for Disease Control and Prevention (CDC).[14] SSTIs were caused by MRSA identified from tissue or drainage in patients who have suppurative lesions or at least two of the following findings: tenderness, swelling, erythema, or heat. [14] BSIs were classified as central line-associated BSI (CLABSI) or primary bacteremia. CLABSI was considered when at least one positive blood culture was (1) obtained from a patient with CVC in place for >2 days or within the day of CVC removal and (2) not related to another infection site.[15] Primary bacteremia was defined if infectious foci at other body sites were ruled out. Ventilator-associated respiratory tract infections (RTIs) were defined as tracheitis or pneumonia in patients on a mechanical ventilator for >2 consecutive days.[16] Superficial incisional wound infections referred to surgical site infections (SSIs) when occurring within 30 days after an operative procedure.[17] A joint tissue infection surrounding a prosthesis with a communicating sinus tract was defined as a periprosthetic joint infection.[14] Among complications of MRSA infections, toxic shock syndrome (TSS) was identified based on the clinical and laboratory criteria of the CDC, and septic shock was defined as sepsis accompanied by hypotension requiring vasopressors.[18]

Microbiological studies

MRSA infections were considered when the cefoxitin screen showed positive or the oxacillin minimal inhibitory concentration (MIC) was ≥4 μg/mL. Only the first MRSA isolate obtained from each infectious episode was included. The susceptibility patterns to antibiotics were tested using the VITEK 2XL automated system (bioMérieux, Durham, NC, USA) in conjunction with the disk diffusion (Kirby–Bauer) method. The antibiotics for testing were selected based on their availability at a particular time in the laboratory. Vancomycin MICs were determined using the Etest (bioMérieux, Durham) only upon the primary physician's request, of which isolates with < 2 μg/mL were considered vancomycin-susceptible.[19] Most susceptibility results were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) documents. Given the lack of CLSI-defined breakpoints for fosfomycin, fusidic acid, and tigecycline, the interpretive criteria of the European Committee on Antimicrobial Susceptibility Testing were applied instead.

Statistical analysis

Categorical and continuous data were presented as percentages and median with interquartile range (IQR), respectively. The annual numbers of MRSA, HA-MRSA, and CA-MRSA infections among patients with *S. aureus* infections were estimated along with their exact 95% confidence intervals (CI). Trends in the prevalence of these infections were assessed using the Chi-square test for departure from the trend line. The characteristics of patients and antibiotic susceptibility rates were compared between HA-MRSA and CA-MRSA groups using Fisher's exact test or the Chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous ones. MIC_{50} and MIC_{90} represent the MIC required to inhibit MRSA growth in 50.0% and 90.0% of all tested isolates, respectively. A $P < 0.05$ was considered statistically significant. Statistical analysis was performed using Stata Statistical Software17 (StataCorp LLC., College Station, TX).

Results

During the 7-year study period, 1,059 children with *S. aureus* infections were identified, 82 of whom had MRSA infections. The prevalence of MRSA infections was 7.7% (95% CI 6.2–9.6). HA-MRSA and CA-MRSA infections were found in 65 (79.0%) and 17 patients, respectively. The overall prevalence of MRSA infections exhibited a significant downward trend ($P = 0$ .003) **(Table 1, Figure 1).** A reduction over time was more notable in HA-MRSA prevalence from 14 (10.1%; 95% CI 5.6-16.3) in 2016 to 5 cases in 2022 (4.1%; 95% CI 1.4-9.4). The number of CA-MRSA infections remained within the range of 1–3 cases per year, except for the peak in 2019.

Table 1. Prevalence of HA-MRSA and CA-MRSA among pediatric patients with *S. aureus* infections, sorted by year from 2016 to 2022.

Year	2016	2017	2018	2019	2020	2021	2022
Total patients with *S. aureus* infections	139	159	169	189	160	122	121
Total patients with MRSA infections	17	17	15	12	8	7	6
Prevalence of MRSA infections, % (95% CI)	12.2 (7.3 - 18.9)	10.7 (6.4 - 16.6)	8.9 (5.1 - 14.2)	6.3 (3.3 - 10.8)	5.0 (2.2 - 9.6)	5.7 (2.3 - 11.5)	4.9 (1.2 - 10.5)
				***P* for trend = 0.003**			
Total patients with HA-MRSA infections	14	15	12	6	8	5	5
Prevalence of HA-MRSA infections, % (95% CI)	10.1 (5.6 - 16.3)	9.4 (5.4 - 15.1)	7.1 (3.7 - 12.1)	3.2 (1.2 - 6.8)	5.0 (2.2 - 9.6)	4.1 (1.3 - 9.3)	4.1 (1.4 - 9.4)
				***P* for trend = 0.004**			
Total patients with CA-MRSA infections	3	2	3	6	0	2	1
Prevalence of CA-MRSA infections, % (95% CI)	2.1 (0.4 - 6.2)	1.3 (0.2 - 4.5)	1.8 (0.4 - 5.1)	3.2 (1.2 - 6.8)	0 (0.0 - 2.3)	1.6 (0.2 - 5.8)	0.8 (0.0 - 4.5)
				***P* for trend = 0.38**			

MRSA, methicillin-resistant *Staphylococcus aureus*; HA-MRSA, healthcare-associated MRSA; CA-MRSA, community-associated MRSA; CI, confidence interval.

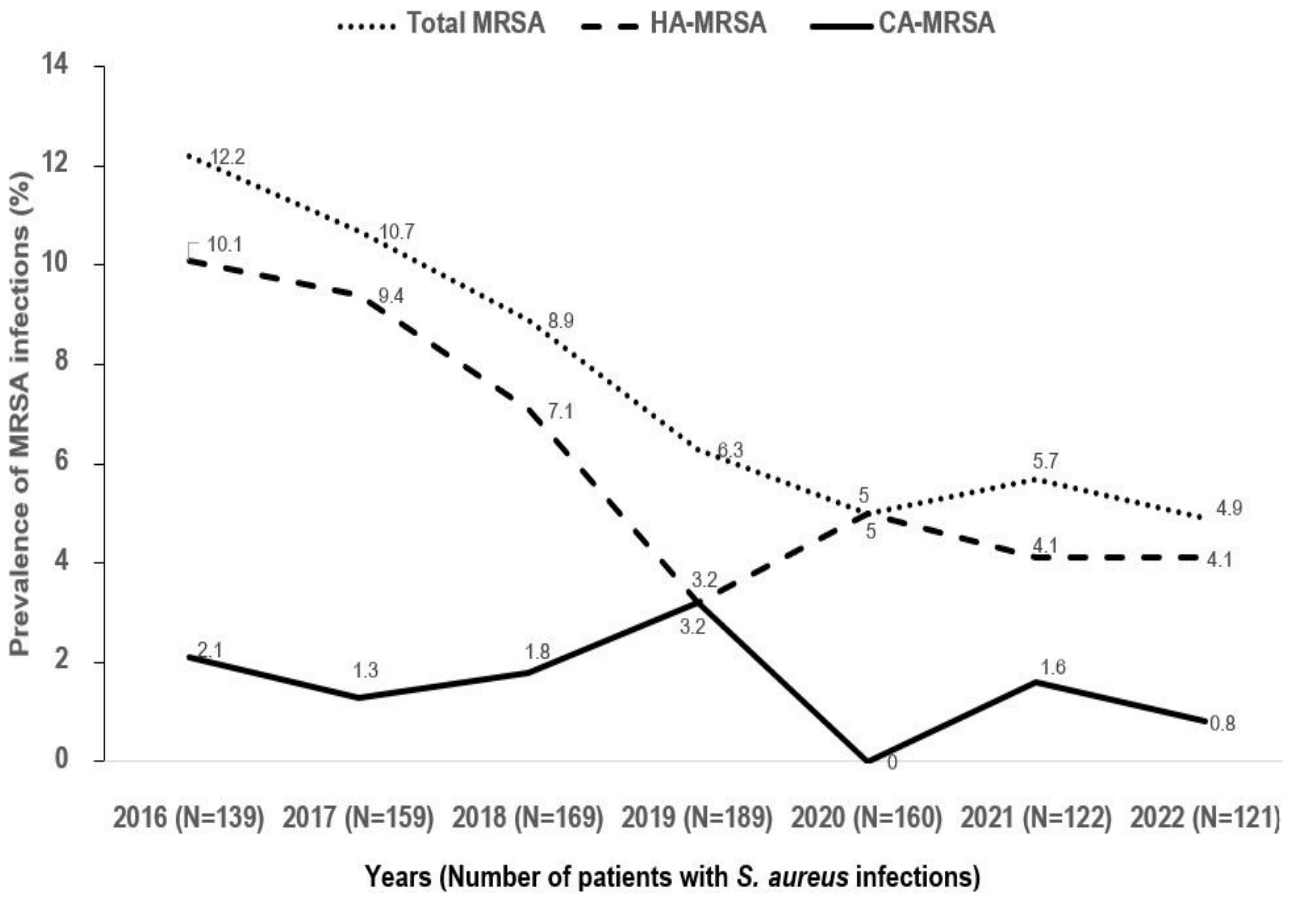

Figure 1. Prevalence of HA-MRSA and CA-MRSA among pediatric patients with *S. aureus* infections, sorted by year from 2016 to 2022.

Clinical characteristics

The majority of the patients (60.0%) were male and hospitalized (83.0%). Patients aged <5 years accounted for the majority in both HA-MRSA (53/65, 82.0%) and CA-MRSA (13/17, 76.0%) groups, of which 26 (49.0%) and 4 (31.0%) patients were infants, respectively. The HA-MRSA group had different distributions compared with the CA-MRSA group in terms of hospitalization (91.0% *vs.* 53.0%, $P < 0.001$), intensive care unit admission (61.0% *vs.* 11.0%, $P = 0.005$), and median length of stay (71 *vs.* 4 days, $P = 0.001$). Patients with an underlying medical condition were more common in the HA-MRSA group than in the CA-MRSA group (86.0% *vs.* 24%, $P < 0.001$) **(Table 2).**

The median duration of hospitalization before HA-MRSA infection was 24 (IQR 4–75) days. HA-MRSA most commonly caused SSTIs (35/65, 54.0%). The most frequent presentation was abscess formation requiring incisional drainage (11/35, 31.0%), followed by wound infections at peristomal gastrotomy or vascular access sites (10/35, 29.0%). HA-MRSA BSIs were found in 13 patients, which included 11 (85.0%) with CLABSI and 2 with primary bacteremia. Ventilator-associated RTIs accounted for the majority (9/10, 90.0%) of HA-MRSA RTIs. SSIs occurred in six patients who had undergone abdominal (n = 3), thoracic (n = 1), neck (n = 1), or limb amputation (n = 1) surgeries. One patient who underwent prior tumor resection and knee arthroplasty contracted a periprosthetic joint infection. Two patients with SSTIs

Table 2. Baseline and clinical characteristics of pediatric patients with MRSA infections.

Characteristics, n (%)	**All MRSA (n = 82)**	**HA-MRSA (n = 65)**	**CA-MRSA (n = 17)**	**HA vs. CA *P* - value**
Male	49 (60)	39 (60)	10 (59)	0.93
Median age at diagnosis, years (IQR)	2.1 (0.7 - 3.7)	1.8 (0.7 - 3.7)	2.9 (1.5 - 3.7)	0.21
Sites of MRSA infections				
Skin and soft tissue infections	48 (59)	35 (54)	13 (76)	0.09
Bloodstream infections	14 (17)	13 (20)	1 (6)	0.17
Respiratory tract infections	13 (16)	10 (15)	3 (18)	0.82
Surgical site infections	6 (7)	6 (9)	0 (0)	0.19
Periprosthetic joint infection	1 (1)	1 (2)	0 (0)	0.61
Underlying medical conditions, n = 60	60 (73)	56 (86)	4 (24)	< 0.001*
Congenital/genetic diseases	17 (28)	16 (29)	1 (25)	
Gastrointestinal/hepatobiliary diseases	17 (28)	16 (29)	1 (25)	
Neurological diseases	9 (15)	8 (14)	1 (25)	
Immunodeficiency or malignancy	8 (13)	8 (14)	0 (0)	
Respiratory diseases	5 (8)	5 (9)	0 (0)	
Renal or endocrine diseases	4 (7)	3 (5)	1 (25)	
Initial therapy with anti-MRSA agents				
Systemic agents	48 (59)	44 (68)	4 (24)	< 0.001*
Vancomycin	38 (79)	36 (82)	2 (50)	
TMP/SMX	6 (13)	5 (11)	1 (25)	
Quinolones[a]	4 (8)	3 (7)	1 (25)	
Topical agents[b]	19 (23)	13 (20)	6 (35)	0.18
None of anti-MRSA agents	15 (18)	8 (12)	8 (47)	0.006*
Hospitalization, n = 68	68 (83)	59 (91)	9 (53)	< 0.001*
Referral from other hospitals	22 (32)	17 (29)	5 (56)	0.11
ICU admission	37 (54)	36 (61)	1 (11)	0.005*
Median length of stay, days (IQR)	62 (14 - 131)	71 (21 - 136)	4 (3 - 18)	0.001*

*$P < 0.05$, considered statistically significant.

a, including ciprofloxacin and levofloxacin.

b, including mupirocin, fusidic acid, oxytetracycline, and ofloxacin.

MRSA, methicillin-resistant *Staphylococcus aureus*; HA-MRSA, healthcare-associated MRSA; CA-MRSA, community-associated MRSA; IQR, interquartile range; TMP/SMX, trimethoprim/sulfamethoxazole; ICU, intensive care unit.

exhibited TSS, whereas septic shock occurred in 4 patients with CLABSIs and 3 with SSTIs.

Among patients with CA-MRSA infections, SSTIs accounted for the majority (13/17, 76.0%), with 7 (54.0%) presenting with abscesses. Three CA-MRSA RTIs were identified: chronic rhinosinusitis, chronic otitis media, and necrotizing pneumonia consequent to influenza. TSS developed in one patient with SSTI, whereas the other had primary CA-MRSA bacteremia with septic shock. Co-existing skin disorders were found in 16/65 (25.0%) patients with HA-MRSA infections and 5/17 (29.0%) with CA-MRSA infections, including atopic dermatitis (n = 6), eczema related to underlying immunodeficiencies (n = 5), inherited or autoimmune skin disorders (n = 5), contact dermatitis (n = 3), and burn wound (n = 2).

Antibiotic susceptibility profiles

A total of 82 MRSA isolates were analyzed. MRSA isolates showed 100.0% susceptibility to newer antibiotics – vancomycin, teicoplanin, linezolid, and tigecycline. Vancomycin MICs were available for 18 HA-MRSA and one CA-MRSA isolate. Vancomycin's MIC_{50}, MIC_{90}, and MIC range were 1, 2, and 0.38–2.0 µg/mL, respectively. No vancomycin MIC creep was detected. Strains demonstrated varying susceptibility levels to older antibiotics, with higher to rifampicin, fusidic acid, and fosfomycin (>90.0%) and lower susceptibilities to TMP/SMX (77.0%), gentamicin (63.0%), tetracycline (48.0%), and ciprofloxacin (43.0%). Isolates were least susceptible to clindamycin (18.0%) and erythromycin (15.0%). CA-MRSA infections were significantly more susceptible than HA-MRSA infections to fusidic acid (100.0% *vs.* 80.0%), ciprofloxacin (65.0% *vs.* 37.0%), and clindamycin (41.0% *vs.* 12.0%) **(Table 3, Figure 2).** When comparing older antibiotic susceptibility rates in 2016-2019 with that in 2020–2022, the isolates susceptible to ciprofloxacin (30.0% *vs.* 81.0%) and erythromycin (8.0% *vs.* 33.0%) increased statistically significantly, whereas the susceptibility rates to the rest of the antibiotics increased but insignificant **(Table 4, Figure 3)**.

Table 3. Antibiotic susceptibility rates of HA-MRSA and CA-MRSA isolates obtained from pediatric patients from 2016 to 2022.

Antibiotics	n (%) susceptible			HA *vs.* CA
	All MRSA (n = 82)	HA-MRSA (n = 65)	CA-MRSA (n = 17)	*P* - value
Newer antibiotics				
Vancomycin	76/76 (100)	61/61 (100)	15/15 (100)	-
Teicoplanin	72/72 (100)	57/57 (100)	15/15 (100)	-
Linezolid	72/72 (100)	57/57 (100)	15/15 (100)	-
Tigecycline	36/36 (100)	27/27 (100)	9/9 (100)	-
Older antibiotics				
Rifampicin	71/72 (99)	56/57 (98)	15/15 (100)	0.61
Fusidic acid	35/37 (95)	27/27 (100)	8/10 (80)	0.02*
Fosfomycin	20/22 (91)	17/18 (94)	3/4 (75)	0.22
TMP/SMX	63/82 (77)	51/65 (79)	12/17 (71)	0.49
Gentamicin	47/75 (63)	34/59 (58)	13/16 (81)	0.08
Tetracycline	39/82 (48)	31/65 (48)	8/17 (47)	0.96
Ciprofloxacin	35/82 (43)	24/65 (37)	11/17 (65)	0.04*
Clindamycin	15/82 (18)	8/65 (12)	7/17 (41)	0.006*
Erythromycin	12/82 (15)	7/65 (11)	5/17 (29)	0.05

* $P < 0.05$, considered statistically significant.

This study included 82 MRSA isolates in total. However, the denominator for isolates tested with certain antibiotics may be lower than 82 due to limited availability at a particular time in the lab.

MRSA, methicillin-resistant *Staphylococcus aureus*; HA-MRSA, healthcare-associated MRSA; CA-MRSA, community-associated MRSA; TMP/SMX, trimethoprim/ sulfamethoxazole.

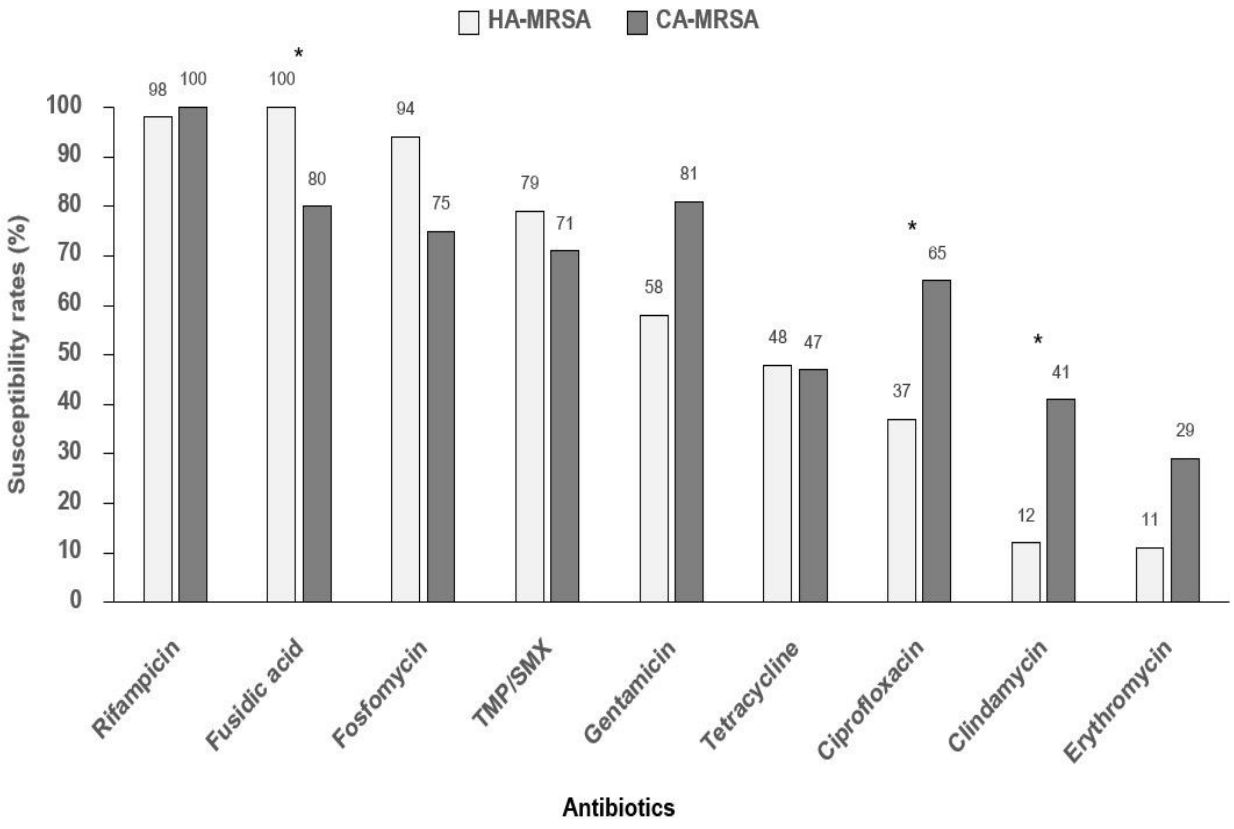

Figure 2. Susceptibility rates of HA-MRSA and CA-MRSA isolates to older antibiotics from 2016 to 2022.

Table 4. Antibiotic susceptibility rates of MRSA isolates obtained from pediatric patients, sorted by year of collection from 2016 to 2022.

Year	Isolate number (n = 82)	RIF	FUS	FOS	TMP/ SMX	GEN	TET	CIP	CLI	ERY
2016 - 2019	61	50/51 (98)	14/16 (88)	6/7 (86)	46/61 (75)	30/54 (56)	27/61 (44)	18/61 (30)	10/61 (16)	5/61 (8)
2020 - 2022	21	21/21 (100)	21/21 (100)	14/15 (93)	17/21 (81)	17/21 (81)	12/21 (57)	17/21 (81)	5/21 (24)	7/21 (33)
P* - value*		0.52	0.18	0.56	0.60	0.06	0.31	< 0.001*	0.45	0.005*

This study included 82 MRSA isolates in total. However, the denominator for isolates tested with certain antibiotics may be lower than 82 due to limited availability at a particular time in the lab. RIF, rifampicin; FUS, fusidic acid; FOS, fosfomycin; TMP/SMX, trimethoprim/sulfamethoxazole; GEN, gentamicin; TET, tetracycline; CIP, ciprofloxacin; CLI, clindamycin; ERY, erythromycin.

*$P < 0.05$, considered statistically significant.

** Denotes statistical tests for difference between 2016-2019 and 2020-2022.

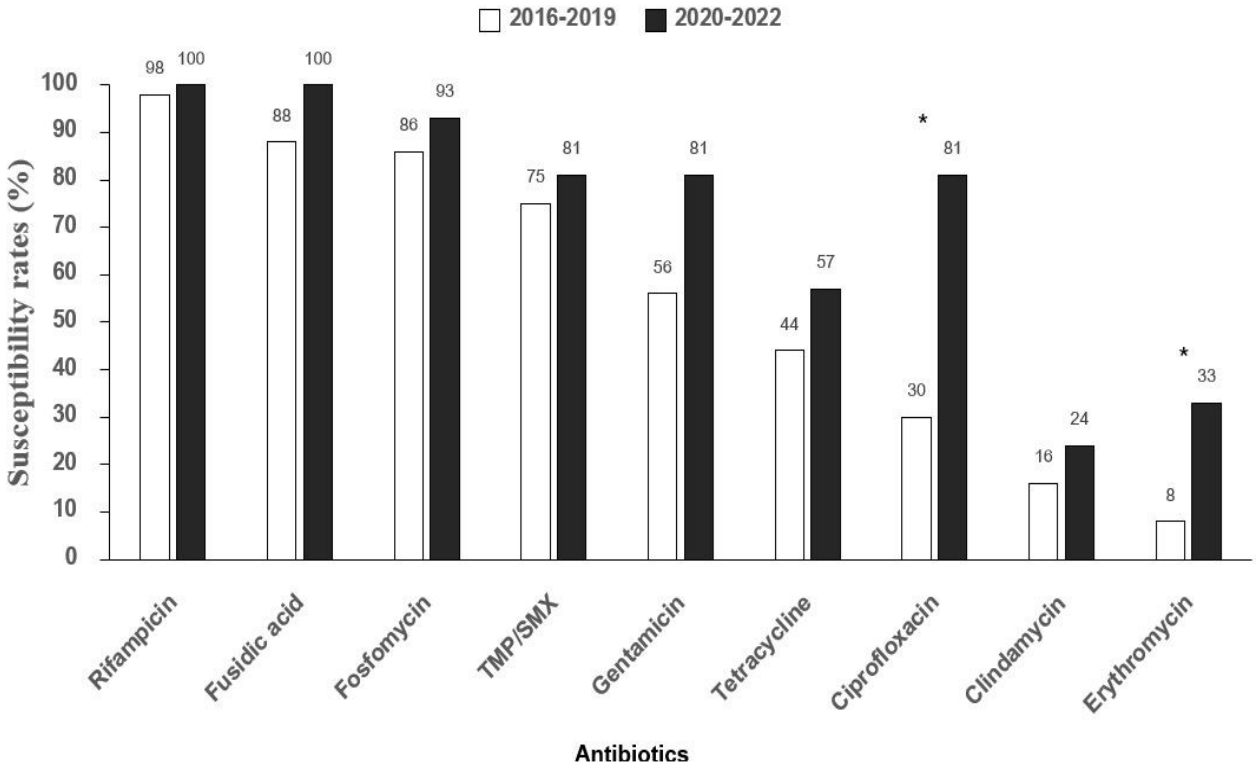

Figure 3. Susceptibility rates of HA-MRSA and CA-MRSA isolates to older antibiotics, compared between 2016-2019 and 2020-2022.

Antibiotic treatment regimens

In this study, 67 (82.0%) patients received anti-MRSA agents. Systemic agents were initially given to 44 (68.0%) patients with HA-MRSA infections compared with 4 (24.0%) patients with CA-MRSA infections ($P < 0.001$). Intravenous vancomycin therapy was most commonly prescribed in both HA-MRSA and CA-MRSA groups. Among patients receiving vancomycin, clindamycin was added to three patients with TSS to inhibit toxin synthesis, and one patient with periprosthetic joint infection was prescribed adjunctive rifampicin. For oral switch therapy, vancomycin was switched to TMP/SMX in three patients with SSTIs and was changed to linezolid in a patient with tracheitis.

Topical anti-MRSA therapy exclusively treated 13 patients with HA-MRSA infections and 6 with CA-MRSA infections. Mupirocin and fusidic acid were most frequently prescribed for 12 SSTIs and 2 SSIs. Oxytetracycline ophthalmic ointment was given to three patients with purulent conjunctivitis. Ofloxacin otic solution was administered to treat otitis externa in one patient and chronic otitis media in another.

No anti-MRSA medications were given to children with CA-MRSA infections (7/17, 41.0%) compared with children with HA-MRSA (8/65, 12.0%) infections ($P = 0.006$). Beta-lactams were initially given to 10 (67.0%) patients. Incision and drainage were performed in nine patients with cutaneous abscesses. Five patients with superficial wound infection received local wound care. Digital autoamputation occurred in one patient with dry gangrene.

Discussion

In our hospital, the prevalence of MRSA in children with *S. aureus* infections was low and decreased significantly. HA-MRSA infections were predominant, and SSTIs were the most common. All isolates were susceptible to newer antibiotics, including vancomycin – the most commonly prescribed antibiotic against MRSA. Isolates showed varied susceptibility rates to older antibiotics. Rifampicin, fusidic acid, and fosfomycin showed the highest susceptibility rates, whereas clindamycin and erythromycin had the lowest.

Our low and downward trend in MRSA infections was consistent with the change in MRSA proportion reported by NARST. Our data supported

the results of previous studies from other Thai tertiary-care hospitals, showing the continuous decline in MRSA trends.[5, 6] From 2016 to 2021, Malaysia (from 18.0% to 7.0%),[20] the Philippines (from 61.5% to 46.9%),[21] and Taiwan (from 66.8% to 52.3%)[22] also had decreased trends but relatively higher MRSA rates according to their national surveillance programs. Likewise, the European antimicrobial resistance surveillance network reported a significant decrease in MRSA isolates across 31 countries, from 18.4% in 2017 to 15.8% in 2021.[23] These decreasing rates may result from the widespread adoption of infection prevention and control (IPC) measures. Evidence-based IPC guidelines promote hand hygiene, patient screening for MRSA, and decolonization or isolation for positive cases.[24, 25] In our hospital, MRSA is monitored as a high-alert multidrug-resistant organism. Our patients with MRSA infections receive routine isolation and strict contact precautions. Despite the availability of IPC guidelines, the prevalence of multidrug-resistant Gram-negative bacteria remains unchanged and appears to be increasing.[20-23] Another explanation for MRSA reductions is the evolutionary changes in *S. aureus* clones in each geographic area, wherein less-fit MRSA clones have been replaced by successful MSSA clones.[26, 27]

In this study, CA-MRSA infections accounted for 1.6% of all infections, four times less common than HA-MRSA infections, aligning with the results of Asia-Pacific studies (0.7%–10.4%).[28] Contrarily, a US study reported CA-MRSA infections at 45.4%, which was 12 times more prevalent than pediatric HA-MRSA infections.[29] The emergence of the USA300 clone (or ST8) since the early 2000s is currently responsible for most CA-MRSA infections in the USA. This strain appears well-adapted and easily transmitted, leading to the increasing number of cases.[26, 30] Meanwhile, CA-MRSA infections outside the USA are caused by different predominant clones with lower transmission capacity, such as ST80 in Europe and ST59, ST72, ST30, and ST22 in Asia.[30, 31]

This study demonstrated 100.0% MRSA susceptibility to newer antibiotics. However, increased vancomycin use because of the global expansion of MRSA has led to the emergence of vancomycin intermediate-resistant *S. aureus* (MIC 3–8 μg/mL).[32] Fortunately, this is not a concern in this study because none of the patients receiving vancomycin experienced treatment failure. This positive outcome may result from the implementation of the antimicrobial stewardship program in our pediatric inpatient wards since July 2017.[11] Our hospital's low MRSA prevalence justifies our policy of not using vancomycin as empirical anti-MRSA therapy in patients without MRSA infection risk factors.

Among older antibiotics, fosfomycin and fusidic acid show promise in combating MRSA infections. Fosfomycin, classified as a "critically important" antibiotic by the World Health Organization (WHO), is effective for children with invasive infections caused by multidrug-resistant bacteria.[33] Fusidic acid is mainly used for anti-staphylococcal therapy, topically for superficial SSTIs and systemically in combination with other agents for BJIs.[34] A high susceptibility rate to rifampicin was also noted; however, it should be used in combination with another active agent for device-related BJIs to prevent resistance development.[9] In our hospital, we do not recommend TMP/SMX, tetracycline, or clindamycin as empirical therapy for suspected MRSA infections because of inadequate susceptibility.

Historically, CA-MRSA strains are more susceptible to older antibiotics than HA-MRSA.[35] However, our data reveal that compared with HA-MRSA isolates, CA-MRSA demonstrated significantly greater susceptibility to ciprofloxacin, clindamycin, and erythromycin. Both MRSA groups showed equal susceptibility to TMP/SMX and tetracycline. In addition, we observed a recent increase in MRSA susceptibility to ciprofloxacin and erythromycin, consistent with global studies.[2, 3] This change could be attributed to the replacement of *S. aureus* clones lacking specific resistance genes and reduced antibiotic usage.[2, 36] Although the favorable trend may provide prospects for recycling these antibiotics, the current level of susceptibility, particularly to erythromycin, remains inadequate for MRSA treatment.[9, 10]

This study had several strengths. First, we confirm a low declining burden of MRSA in pediatric patients in our analysis of a complete dataset from our hospital's electronic database, ensuring no missed cases. Second, this study presents contemporary MRSA susceptibility profiles for newer and older antibiotics, endorsing vancomycin as the optimal first-line treatment for severe MRSA infections. This study recommends judicious use of newer antibiotics to preserve their efficacy, while acknowledging the effectiveness of selected older antibiotics against MRSA.

Nevertheless, this study had limitations. Our data may not reflect MRSA trends in other Thai regions because of the single-center design. Given the lack of stored isolates, molecular studies to detect the *mecA* gene or staphylococcal cassette chromosome *mec* (SCC*mec*) to definitively confirm *S. aureus* resistance to methicillin were not possible.[19] Furthermore, identifying circulating MRSA clones using multilocus sequence typing could not be performed, hindering our ability to explain the MRSA downtrend in our hospital. This study might have included borderline oxacillin-resistant *S. aureus* (BORSA), characterized by beta-lactamase hyperproduction conferring low-level methicillin resistance. A defining criterion for BORSA is an oxacillin MIC of >2 μg/mL but susceptible to cefoxitin without the presence of *mecA*.[37] In this study, 47 out of the 82 oxacillin-resistant isolates were confirmed to be resistant to cefoxitin, thus likely excluding BORSA phenotypes. The remaining isolates were not tested for cefoxitin susceptibility. To analyze changing susceptibility to vancomycin, only 19/82 (23.0%) MRSA isolates had their vancomycin MICs obtained, preventing temporal analysis of MIC creep. Finally, livestock-associated MRSA (LA-MRSA) is a subset of MRSA infections in the community linked to livestock exposure. Differing from CA-MRSA in genomic traits, it was first reported in 2011 in Thailand from pigs as ST9-SCC*mec*IX, raising awareness of its potential spread from animals to humans and its role in severe infections in patients with immunocompromised status.[38, 39] Unfortunately, this study could not classify LA-MRSA due to a lack of molecular testing.

Conclusion

MRSA infections in our pediatric patients showed a low and declining prevalence, mainly by HA-MRSA. Newer antibiotics, including vancomycin, remain effective for MRSA treatment. MRSA displayed varying susceptibility levels to older antibiotics. Thus, ongoing MRSA studies are crucial for updated guidance on antibiotic treatment and effective control measures.

Acknowledgements

This work was partly supported by grants for the development of new faculty staff, Ratchadaphiseksomphot Fund, Chulalongkorn University [grant number DNS 65_005_30_002_1]. The funder had no role in this study.

Conflicts of interest statement

All authors have completed and submitted the International Committee of Medical Journal Editors Uniform Disclosure Form for Potential Conflicts of Interest. None of the authors disclose any conflict of interest.

Data sharing statement

All data generated or analyzed during this study are included in this published article and cited here. Further details, opinions, and interpretations are available from the corresponding author upon reasonable request.

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