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# Pathogen Distribution and Antimicrobial Resistance Analysis in Pediatric Acute Hematogenous Osteomyelitis: A Dual-Center Retrospective Study

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## Abstract

**Objective:** To analyze the distribution and antibiotic resistance of pathogenic bacteria in children with acute hematogenous osteomyelitis (AHO), and to provide evidence for rational antibiotic use in clinical

practice.

**Methods:** Clinical data of 204 pediatric AHO patients admitted to the Shanghai Children's Medical Center Guizhou Hospital and the Affiliated Hospital of Zunyi Medical University between January 2012 and December 2023 were retrospectively analyzed. The spectrum of pathogenic bacteria and their antibiotic susceptibility were examined. The distribution of pathogenic bacteria and changes in antimicrobial resistance across different genders, age groups, and onset time periods were compared.

**Results:** Among the 204 children, 127 were male and 77 were female, with a median age at presentation of 9.7 years (IQR: 7.0, 12.2). Five bacterial species were isolated. The predominant pathogen was *Staphylococcus aureus* (SA) (199 cases, 97.5%), which included 84 cases (42.2%) of methicillin-resistant *Staphylococcus aureus* (MRSA) and 115 cases (57.8%) of methicillin-susceptible *Staphylococcus aureus* (MSSA). The resistance rate of SA to penicillin was 96.5% (192/199). Resistance rates to clindamycin, cefoxitin, erythromycin, oxacillin, and tetracycline were 73.4% (146/199), 58.8% (117/199), 55.3% (110/199), 49.2% (98/199), and 47.7% (95/199), respectively, showing an increasing trend over time. No statistically significant differences in the MRSA detection rate were found between different genders or age groups. However, the MRSA detection rates varied significantly across different time periods, and exhibited a

significant increasing trend over time.

**Conclusion:** The MRSA detection rate did not differ significantly by gender or age group among children with AHO. However, both the MRSA detection rate and the resistance rates of SA to clindamycin, cefoxitin, erythromycin, oxacillin, and tetracycline demonstrated an increasing trend over time. It is crucial to promote the rational and standardized use of antibiotics in clinical settings. Antibiotic selection should be guided by antimicrobial susceptibility testing results to enhance treatment efficacy and reduce the development and spread of resistant strains.

**Key words:** Acute hematogenous osteomyelitis; Child; *Staphylococcus aureus;* Methicillin-resistant *Staphylococcus aureus;* Antibiotic resistance

## 1 Introduction

Acute hematogenous osteomyelitis (AHO) is an inflammation of the bone marrow and destruction of bone structure caused by bacteria invading the bone trabeculae via the bloodstream. It commonly occurs in the metaphyses of long tubular bones in children under 5 years of age, with an incidence of 2–10 per 100,000 individuals [1–2]. The underlying reasons are as follows: the metaphyses of long tubular bones lack a reticuloendothelial system, resulting in poor anti-infective capacity; in addition, they have abundant blood supply and slow blood flow in the vascular loops, which facilitates bacterial colonization [3]. *Staphylococcus*

*aureus* (SA) is the main pathogenic bacterium of AHO in China. With the overuse of antimicrobial agents, the incidence of methicillin-resistant Staphylococcus aureus (MRSA)-associated osteomyelitis has been increasing year by year, which poses severe challenges to the treatment of pediatric hematogenous osteomyelitis. The early administration of active antimicrobial agents is critical for improving patient outcomes. Conversely, inappropriate selection of antimicrobial agents for AHO can lead to failure to effectively control the infection, and consequently result in adverse outcomes such as bone and joint deformities and ischemic osteonecrosis [4]. Currently, there are limited reports on the types of pathogenic bacteria and their antimicrobial resistance in AHO, which may exhibit significant geographic variations. This study analyzed and summarized the pathogenic bacteria spectrum and their antimicrobial resistance in pediatric AHO patients admitted to the Department of Pediatric Orthopedics, Shanghai Children's Medical Center Guizhou Hospital and the Department of Pediatric Surgery, Affiliated Hospital of Zunyi Medical University between January 2012 and December 2023, aiming to provide references for the early use of antimicrobial agents in children with AHO.

## 2 Patients and Methods

### 2.1 Patients

A total of 204 pediatric patients with AHO hospitalized in the Department of Pediatric Orthopedics at Shanghai Children's Medical Center Guizhou

Hospital and the Department of Pediatric Surgery, Affiliated Hospital of Zunyi Medical University between January 2012 and December 2023were enrolled in this study.

The inclusion criteria were as follows: (1) age < 15 years; (2) disease duration < 14 days; (3) definitive diagnosis of AHO established by magnetic resonance imaging (MRI) or aspiration/surgical findings; (4) Children residing in Guizhou Province.

Exclusion criteria included: (1) infection secondary to trauma, surgery, or other iatrogenic procedures; (2) infection caused by *Mycobacterium tuberculosis*; (3) no bacterial growth detected in blood or pus cultures; (4) use of immunosuppressive medications.

### 2.2 Data Collection

Clinical data of children who met the criteria for AHO was retrieved from the hospital medical record system. Demographic characteristics (gender, age), time of onset, laboratory findings, pathogenic bacteria profiles, and their susceptibility to antibiotics were collected.

### 2.3 Grouping

The children were grouped according to age, which were divided into four stages: Infant stage (0 – ≤ 3 years), Preschool stage (> 3 and ≤ 7 years), School-age stage (> 7 and ≤ 12 years), and Adolescent stage (> 12 and < 15 years). The differences in MRSA detection rate among children with

AHO in different age groups were compared. Furthermore, the children were grouped according to the time of disease onset to analyze the changes in the distribution of pathogenic bacteria and their antimicrobial resistance across different time periods (2012–2014, 2015–2017, 2018–2020, 2021–2023).

### 2.4 Statistical Analysis

Statistical analysis was performed using SPSS software (version 22.0). Non-normally distributed data were expressed as median with interquartile range (IQR) [*M (Q1, Q3)*]. Categorical data were described as numbers and percentages [n (%)]. *The chi-square test* or *Fisher's exact test* was used for comparisons between groups. The *Linear-by-Linear Association test* was employed to assess whether a linear correlation existed between the resistance rates of SA to various antibiotics and the different time periods. The strength and direction of the correlation were evaluated using *Pearson's correlation test*. A *P-value* of less than 0.05 was considered statistically significant.

## 3 Results

### 3.1 Distribution of Pathogenic Bacteria

Among the 204 children with AHO, there were 127 males and 77 females, with a median at admission of 9.7 (7.0, 12.2) years. A total of 204 pus cultures and 63 blood cultures were obtained. Five distinct bacterial pathogens were isolated, all of which were monomicrobial infections.

Specifically, *Staphylococcus aureus* (SA) was detected in 199 cases (97.5%), *Streptococcus pyogenes* (SP) in 2 cases (1.0%), *Citrobacter freundii* (CF) in 1 case (0.5%), *Acinetobacter baumannii* (AB) in 1 case (0.5%), and *Salmonella stanley* (SS) in 1 case (0.5%). The distribution of the identified pathogens is illustrated in Figure 1.

### 3.2 Antibiotic Susceptibility of the Primary Pathogen

Of the 199 *Staphylococcus aureus* (SA) isolates, 84 (42.2%) were methicillin-resistant *Staphylococcus aureus* (MRSA) and 115 (57.8%) were methicillin-susceptible *Staphylococcus aureus* (MSSA). The resistance rate of SA to penicillin was 96.5% (192/199). Resistance rates to clindamycin, cefoxitin, erythromycin, oxacillin, and tetracycline were 73.4% (146/199), 58.8% (117/199), 55.3% (110/199), 49.2% (98/199), and 47.7% (95/199), respectively. Resistance to gentamicin, trimethoprim-sulfamethoxazole, and rifampin was low, at only 7.5% (15/199), 4.0% (8/199), and 3.0% (6/199), respectively. No resistant strains were found for levofloxacin, moxifloxacin, linezolid, teicoplanin, vancomycin, tigecycline, ciprofloxacin, or nitrofurantoin, as shown in Figure 2.

### 3.3 MRSA detection rates of different genders, ages, and different time periods

The MRSA detection rate was 39.4% (50/127) in male patients and 44.2% (34/77) in female patients, with no statistically significant difference

observed ($P$=0.501).For different age groups, the MRSA detection rates were 57.1% (4/7) in the 0 to ≤3 years group, 51.1% (24/47) in the >3 to ≤7 years group, 38.1% (37/97) in the >7 to ≤12 years group, and 35.8% (19/53) in the >12 to <15 years group. The differences in detection rates across these age groups were not statistically significant ($P$=0.296).A significant increasing trend in MRSA detection was observed over time: the rates were 11.1% (2/18) for 2012-2014, 24.4% (11/45) for 2015-2017, 47.4% (27/57) for 2018-2020, and 52.4% (44/84) for 2021-2023. This temporal trend was statistically significant ($P$=0.001). For detailed data, please refer to Table 1 and Figure 3.

### 3.4 Trends in Antimicrobial Resistance of SA

Significant differences in resistance rates of SA to clindamycin, cefoxitin, erythromycin, oxacillin, and tetracycline were observed across time periods ($P$<0.001), with a significantly increasing trend in resistance rates over time ($P$<0.001). Detailed data are presented in Table 2 and Figure 4.

## 4 Discussion

AHO is a common and serious infectious disease in pediatric orthopedics. Its occurrence is associated with factors such as hygiene conditions, nutritional status, socioeconomic status, and immune function in children [5]. There are significant geographic variations in the spectrum of pathogenic bacteria and their antibiotic resistance profiles. The current

primary treatment approach involves comprehensive management, including surgical drainage, antibiotic therapy, and nutritional support. Rational use of antibiotics based on the specific types of pathogenic bacteria and their drug susceptibility is crucial for controlling AHO infections. It can not only halt the progression of infection and accelerate healing but also reduces reduce the development of chronic osteomyelitis.

With the widespread and inappropriate use of antibiotics, drug-resistant strains are increasingly emerging, and the types of pathogenic bacteria causing AHO worldwide are also changing. SA remains one of the primary pathogens causing bone and joint infections in children worldwide. This predominance is likely attributable to its biological characteristics, which include strong adhesive capabilities and the production of various virulence factors that facilitate colonization in bone tissue and the initiation of infection [6].

In the United States, SA accounted for 87.6% of pathogenic bacteria in children with AHO [7]. In Italy, SA was also the most dominant pathogen of AHO, with a proportion of 66.15% [8]. In France, SA represented 64% of pathogenic bacteria, followed by coagulase-negative staphylococci (CNS) at 11% [9]. In Australia, the main pathogenic bacteria of AHO were SA (30.4%) and *Streptococcus pyogenes* (17.4%) [10]. In South America, the predominant pathogenic bacteria of AHO were SA (87%) and *Streptococcus pyogenes* (11%) [11]. In Asia, SA was the leading

196 pathogenic bacterium of AHO in Japan, India, Cambodia, and
197 Singapore[12-15]. In contrast, Switzerland reports a distinct
198 epidemiological profile, with *Kingella kingaeas* the leading pathogen (32%)
199 and SA accounting for only 20.7% of cases [16]. These studies collectively
200 indicate substantial geographic disparity in the distribution of AHO
201 pathogens, particularly regarding the relative prevalence of SA and other
202 bacteria. In the present study, SA was identified in 97.5% of cases, a
203 prevalence notably higher than that reported in most other regional and
204 international studies. Conversely, the proportions of *S. pyogenesand*
205 *Salmonellawere* only 1% and 0.5%, respectively, and no cases of *K. kingae*
206 infection were identified. These findings strongly suggest a distinct
207 regional pattern in the etiology of pediatric AHO in our patient population.

208 Recent studies have generally shown that the resistance rate
209 of *Staphylococcus aureus* (SA) strains to penicillin exceeds 90%. The
210 resistance rates to commonly used drugs such as cefoxitin, erythromycin,
211 oxacillin, and tetracycline are also on the rise [17]. ln contrast, resistance
212 to gentamicin and rifampin remains relatively low. No cases resistant to
213 linezolid, moxifloxacin, or nitrofurantoin have been reported [18]. The
214 results of this study are consistent with these findings.

215 Notably, the resistance rate of SA to clindamycin observed in our study was
216 significantly high at 73.4%, whereas reported rates in other countries are
217 considerably lower, ranging from 6.6% to 13.9% [7,19]. This may be

attributed to the previous lack of hierarchical management of antibiotics in China, which led to the overuse of clindamycin in primary hospitals. Additionally, clindamycin was once permitted to be used as a growth promoter and for the treatment of animal infections in China's animal husbandry industry. Additionally, clindamycin was once permitted to be used as a growth promoter and for the treatment of animal infections in China's animal husbandry industry. This results in animal-derived SA being transmitted to humans through environmental exposure (e.g., fecal contamination) or the food chain (e.g., meat products). These strains carry drug-resistant genes and colonize the human body, indirectly increasing the proportion of clindamycin-resistant strains in China.

Furthermore, this study analyzed the trends in resistance rates of SA to five common antimicrobial agents (clindamycin, cefoxitin, erythromycin, oxacillin, and tetracycline) over different years. The results showed that SA resistance rates to all five of these antibiotics demonstrated a year-on-year increasing trend. Although the absolute values of the *Pearson Correlation Coefficients (r)* between the resistance rates of each antibiotic and the different time periods were not very high, the resistance rates of SA to each drug showed statistically significant differences across the study years ($P< 0.001$), statistically significant differences in the resistance rates of SA to each drug were observed across different years ($P< 0.001$). These findings further confirm the serious challenge of continuously

increasing bacterial resistance and highlight the urgency and necessity of curbing antibiotic misuse.

MRSA is the most common drug-resistant strain of SA. Studies have shown that its detection rate exhibits significant geographical and age-related variations [20]. The prevalence of MRSA remains very low across Europe, Africa, and South America [8, 9-11]. In contrast, the MRSA detection rate in the United States has risen to as high as 50% [7]. A similar increasing trend is observed in Australia, where the rate has reached 40% [10], while in Japan, it is reported to be 29.2% [12]. In our study, the overall MRSA detection rate was 41.7%. Notably, this rate increased markedly from 11.1% during the 2012-2014 to 52.4% during the 2021-2023. This trend is consistent with the patterns observed in the United States and Australia but differs from the low prevalence reported in European, African, and South American countries. This discrepancy may be associated with the geographical distribution of patients and the misuse of antibiotics. Quinolone antibiotics should be avoided in the treatment of MRSA-induced pediatric AHO due to their potential adverse effects on cartilage development. At present, vancomycin is the current first-line therapeutic agent. Although no vancomycin-resistant Staphylococcus aureus (VRSA) strains have been detected in China, there have been numerous reports of vancomycin-resistant Staphylococcus aureus strains overseas [21-25].

## 5 Limitations and Future Perspectives

This study has several limitations. First, it was conducted at only two hospitals in Guizhou Province, which may limit the generalizability of our findings to other regions. Second, the sample size was relatively small (n=204), and the distribution of cases across different years and age groups might be uneven, which may affect the generalizability of the conclusions.

Future multi-center studies with larger sample sizes are warranted to evaluate the pathogen spectrum and antibiotic resistance profiles of AHO across China. Meanwhile, if experimental studies can be carried out to further investigate the molecular mechanisms of MRSA resistance, it could provide new insights for the development of new antimicrobial agents and treatment strategies, as well as a basis for formulating effective prevention strategies, thereby reducing the MRSA infection rate in children with AHO.

## 6 Conclusion

This study demonstrates that SA remains the predominant pathogenic bacterium causing pediatric AHO in Guizhou Province. No significant differences were observed in the MRSA detection rates among AHO patients of different genders and age groups. However, the MRSA detection rate and the resistance rates of SA to clindamycin, cefoxitin, erythromycin, oxacillin, and tetracycline all exhibited an increasing trend year by year.

Clinically, rational and standardized use of antibiotics is imperative. It is

essential to strengthen the monitoring and management of SA resistance, and select effective antibiotics based on drug susceptibility test results. This approach will improve treatment efficacy and reduce the emergence and spread of drug-resistant strains.

## Ethics statement

The retrospective study was conducted in accordance with theDeclaration of Helsinki. It was approved by the Medical EthicsCommittee of Shanghai Children's Medical Center GuizhouHospital, Shanghai Jiao Tong University School of Medicine(Approval No. 2025 (XJS) -064). The requirements for informedconsent were waived because of the retrospective use of anonymousrecords. In accordance with the ethics approval, we analyzed all dataanonymously and reported only aggregate data.

## Author Contributions

Conceptualization, Yanhong Ma and Yongqiao Gan; Data curation, Yanhong Ma and Yongqiao Gan; Formal analysis, Yanhong Ma; Funding acquisition, Yanhong Ma; Investigation, Yanhong Ma and Yongqiao Gan; Methodology, Yanhong Ma and Yongqiao Gan; Project administration, Yongqiao Gan; Resources, Yongqiao Gan; Software, Yanhong Ma; Supervision, Yongqiao Gan; Validation, Yanhong Ma and Yongqiao Gan; Visualization, Yanhong Ma; Writing – original draft, Yanhong Ma and

Yongqiao Gan; Writing – review & editing, Yanhong Ma and Yongqiao Gan.

## Institutional Review Board Statement

The study was approved by the Medical Ethics Committee of Shanghai Children's Medical Center GuiZhou Hospital, Shanghai Jiao Tong University School of Medicine (Approval Number: 2025-064). The study was conducted in accordance with the local legislation and institutional requirements.

## Data Availability Statement

The data presented in this study are available on request from the corresponding author.

## Conflicts of Interest

The authors declare no conflict of interest.


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## Tables and Figures

**Table 1. MRSA detection rates of different genders, ages, and different time periods**

| Variable | Group | Number of Cases n | MRSA n (%) | Non-MRSA n (%) | *P*-value |
|---|---|---|---|---|---|
| **Gender** | Male | 127 | 50(39.4) | 77(60.6) | 0.501 |
| | Female | 77 | 34(44.2) | 43(55.8) | |
| **Age Group (years)** | 0~≤3 | 7 | 4(57.1) | 3(42.9) | 0.296* |
| | > 3 and ≤7 | 47 | 24(51.1) | 23(48.9) | |
| | > 7 and≤12 | 97 | 37(38.1) | 60(61.9) | |
| | > 12 | 53 | 19(35.8) | 34(64.2) | |
| **Time** | 2012- | 18 | 2(11.1) | 16(88.9) | 0.001 |

| | | | | |
|---|---|---|---|---|
| **Period (year)** | 2014 | | | |
| | 2015-2017 | 45 | 11(24.4) | 34(75.6) |
| | 2018-2020 | 57 | 27(47.4) | 30(52.6) |
| | 2021-2023 | 84 | 44(52.4) | 40(47.6) |

428 **Fisher's precision probability test* was used.

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433

434 **Table 2. Resistance rates of SA to different antibiotics in different**

435 **time periods**

| **Time Period** (year) | **Different Antibiotics** %(resistant cases/total cases) | | | | |
|---|---|---|---|---|---|
| | Clindamycin | Cefoxitin | Erythromycin | Oxacillin | Tetracycline |
| 2012–2014 | 22.2(4/18) | 16.7(3/18) | 27.8(5/18) | 16.7(3/18) | 11.1(2/18) |
| 2015–2017 | 51.1(23/45) | 42.2(19/45) | 24.4(11/45) | 24.4(11/45) | 26.7(12/45) |
| 2018–2020 | 83.9(47/56) | 67.9(38/56) | 51.8(29/56) | 51.8(29/56) | 53.6(30/56) |
| 2021–2023 | 90.0(72/80) | 71.3(57/80) | 81.3(65/80) | 68.8(55/80) | 63.8(51/80) |
| ***P*-Value | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| #*P*-Value | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| *r* | 0.477 | 0.334 | 0.453 | 0.389 | 0.359 |

436 * *The *P*-value for *the chi-square test*.

# The *P*-value for *the Linear-by-Linear Association test*.

*r Pearson correlation coefficient*

Figure 1. Pathogen distribution among AHO children

Legend: Pie chart illustrating the proportion of isolated bacterial pathogens from 204 pediatric acute hematogenous osteomyelitis (AHO) patients. Staphylococcus aureus (SA) was the predominant pathogen, while other bacterial species accounted for a small proportion. SA: Staphylococcus aureus; SP: Streptococcus pyogenes; CF: Citrobacter freundii; AB: Acinetobacter baumannii; SS: Salmonella stanley.

Figure 2. Antibiotic-resistance rates of SA isolates

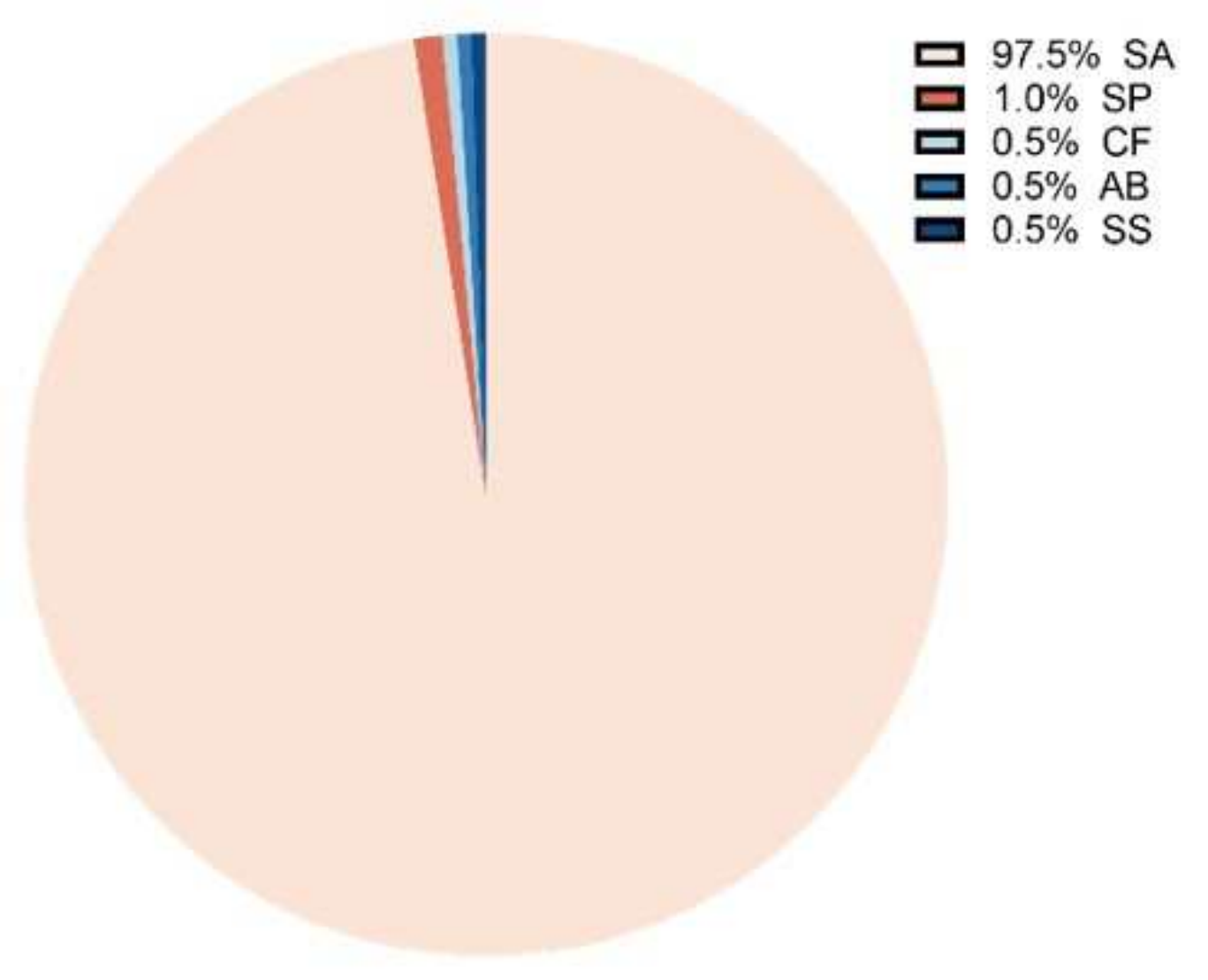
Legend: Bar chart showing antimicrobial-resistance percentages of Staphylococcus aureus against different antibiotics. PEN: Penicillin; CLI: Clindamycin; FOX: Cefoxitin; ERY: Erythromycin; OXA: Oxacillin; TET: Tetracycline; GEN: Gentamycin; SMZco: Trimethoprim-sulfamethoxazole; RIF: Rifampicin.

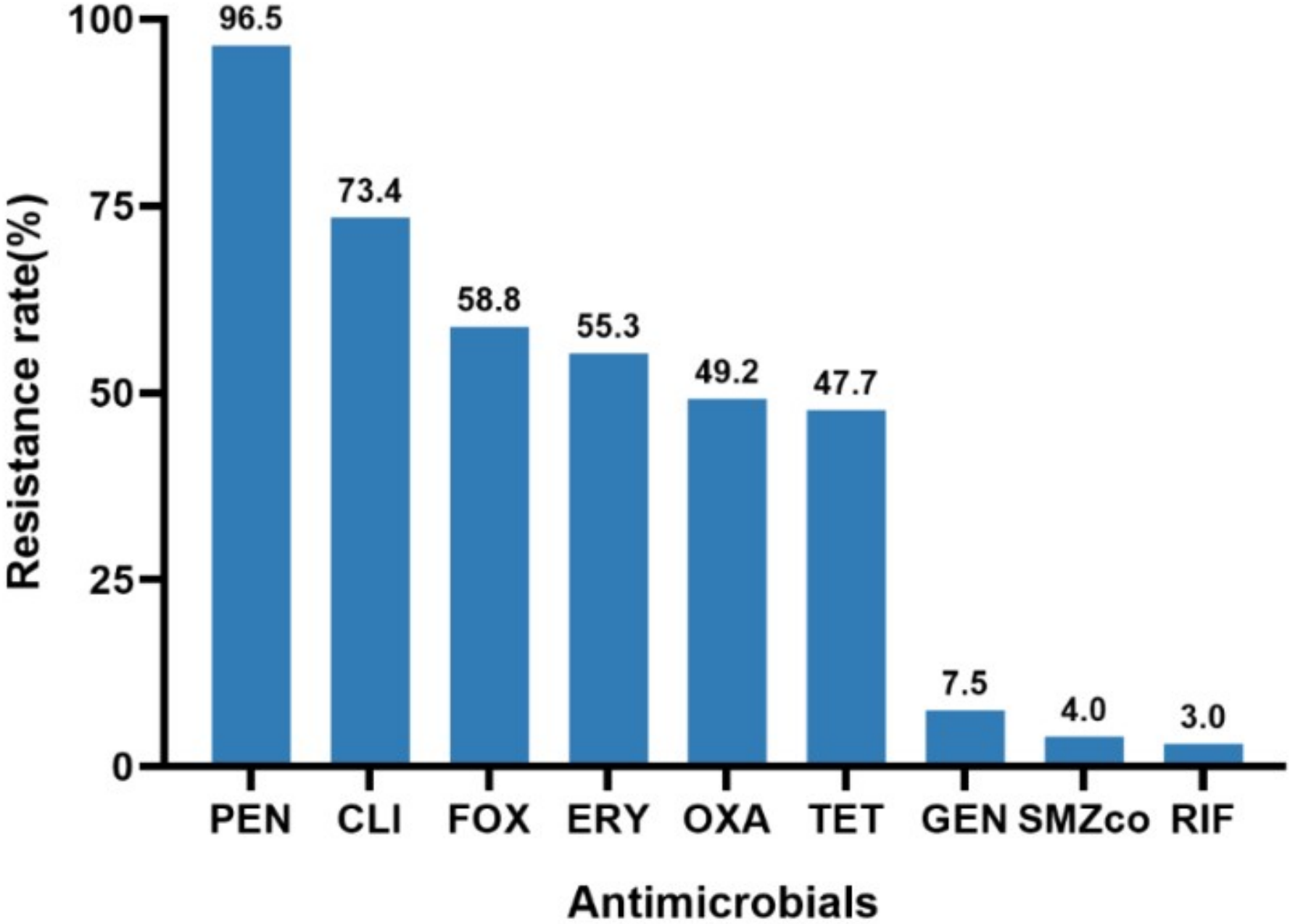
Figure 3. Temporal changes in MRSA detection

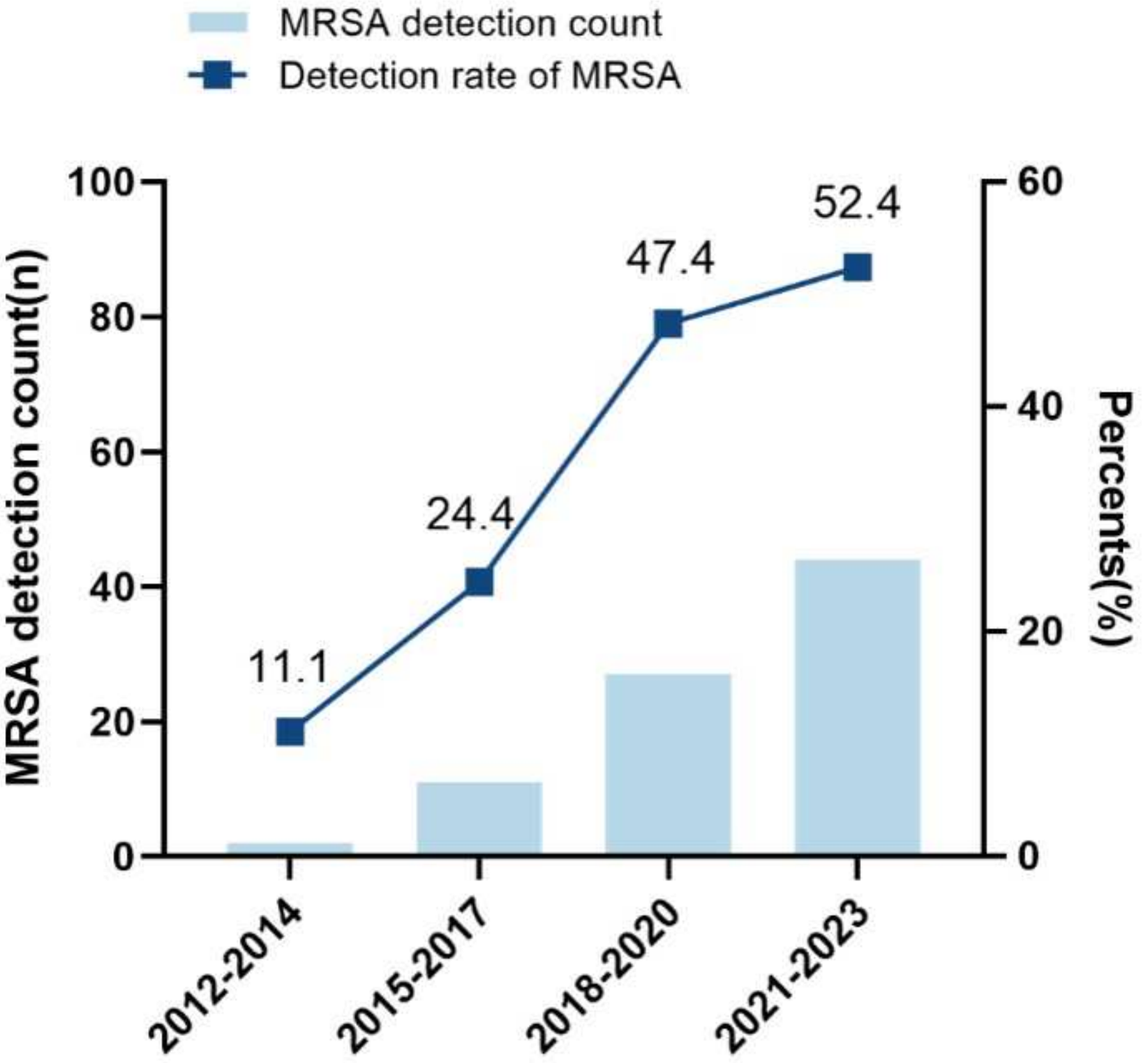
Legend: Combined bar-line graph presenting MRSA case counts (light-blue bars) and MRSA detection rates (dark-blue line) across four time periods (2012-2014, 2015-2017, 2018-2020, 2021-2023) in pediatric AHO isolates.

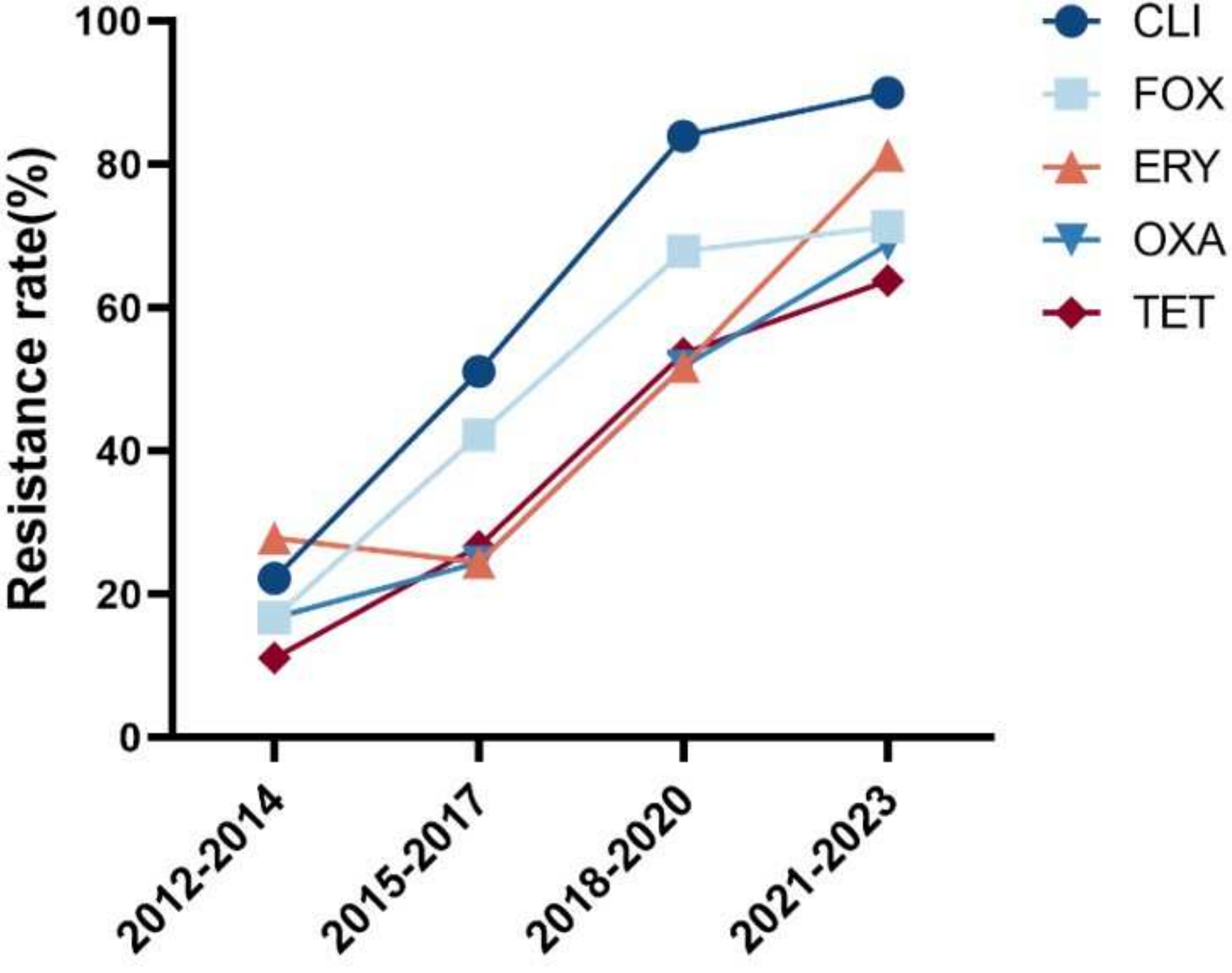
Figure 4. SA antibiotic-resistance trends over time

Legend: Multi-line plot showing changing resistance rates of Staphylococcus aureus for five key antibiotics across four study periods. CLI: Clindamycin; FOX: Cefoxitin; ERY: Erythromycin; OXA: Oxacillin; TET: Tetracycline.


97.5% SA
1.0% SP
0.5% CF
0.5% AB
0.5% SS


100
75
50
25
0
Resistance rate(%)
96.5
73.4
58.8
55.3
49.2
47.7
7.5
4.0
3.0
PEN
CLI
FOX
ERY
OXA
TET
GEN
SMZco
RIF
Antimicrobials


MRSA detection count
Detection rate of MRSA
MRSA detection count(n)
Percents(%)
100
80
60
40
20
0
60
40
20
0
11.1
24.4
47.4
52.4
2012-2014
2015-2017
2018-2020
2021-2023


100
80
60
40
20
0
Resistance rate(%)
2012-2014
2015-2017
2018-2020
2021-2023
CLI
FOX
ERY
OXA
TET