


# Cross-sectional Hospital-based Investigation on Clinical Characteristics of Pediatric *Staphylococcus aureus* Isolates in a Beijing Hospital from 2013 to 2022

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**Background:** *Staphylococcus aureus* (*S. aureus*) was a prevalent pathogenic bacterium among children. Due to the extensive use of antibiotics, the sensitivity of *S. aureus* to these drugs has gradually declined. Since the 1960s, methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged and spread worldwide, becoming a primary cause of both healthcare-associated (HA) and community-acquired (CA) infections. This retrospective study aimed to highlight the significance of *S. aureus* among bacteria isolated from children in Beijing, China, and to elucidate its antimicrobial resistance patterns.

**Methods:** Data on all *S. aureus* infections from 2013 to 2022 were collected from the microbiology department of Beijing Children's Hospital. Only the first isolate from the same kind of specimen was analyzed. Antimicrobial susceptibility tests were carried out by Vitek 2 automated system (bio Mérieux, France) or Kirby–Bauer disc diffusion method, according to the guidelines recommended by the Clinical and Laboratory Standards Institute (CLSI).

**Results:** During the decade-long research period, a total of 47,062 bacterial isolates were isolated from 433,081 submitted specimens, with 6477 of these isolates identified as *S. aureus*. The majority of patients with *S. aureus* infections belonged to the age group of infants under one-year-old, accounting for 37.9% of cases. *S. aureus* isolates were predominantly found in the Pneumology Department, and the most common source of these isolates was lower respiratory tract specimens, comprising 34.3% of the total. The resistance rates of *S. aureus* to penicillin and erythromycin were notably high, at 89.5% and 73.8%, respectively. In contrast, the resistance rates to linezolid, vancomycin, rifampicin, and moxifloxacin were remarkably low, at 0.0%, 0.0%, 1.3%, and 3.9%, respectively. The detection rate of MRSA was 27.8%. MRSA isolates were predominantly found in the newborn group, ICU, and sterile body fluids.

**Conclusion:** In our study, the most prevalent specimen type was derived from the lower respiratory tract, whereas the highest positive rate was observed in ear secretions. These findings underscored the pressing necessity for ongoing antimicrobial resistance (AMR) surveillance and the revision of treatment guidelines, particularly given the elevated detection of MRSA in ICU wards, sterile body fluids, and the neonatal age group. MRSA exhibited significant resistance to all  $\beta$ -lactam antibiotics, erythromycin, and ciprofloxacin. Therefore, future research endeavors should prioritize examining specific antimicrobial resistance populations and potential intervention strategies, as these were vital in mitigating the dissemination of antimicrobial-resistant isolates.

**Keywords:** *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus*, antimicrobial resistance, children

## Introduction

*S. aureus*, a common bacterial flora that colonizes the human skin and mucous membranes, can be found in both community and hospital settings. Additionally, it is one of the most prevalent pathogens in both community-acquired (CA) and

healthcare-associated (HA) infections, capable of causing a diverse range of infections, including pneumonia, sepsis, infective endocarditis, toxic shock syndrome, and necrotizing fasciitis. These severe and invasive infections, such as pneumonia and sepsis, can have fatal consequences.<sup>1</sup> The nasal carriage of *S. aureus* can be intermittent or persistent, potentially functioning as a source for self-infection and facilitating the spread of infection to others through cross-transmission.<sup>2-4</sup> The increase in the detection rate of MRSA, the emergence of vancomycin-resistant *S. aureus*, and the formation of biofilms on implanted medical devices have rendered infections associated with these microorganisms a significant public health concern.<sup>5</sup> MRSA infections are the second leading cause of deaths due to bacterial resistance and constitute an independent risk factor for increased mortality rates in *S. aureus* bloodstream infections.<sup>6</sup> The antimicrobial resistance (AMR) of *S. aureus* poses a significant threat to public health, particularly the emergence of MRSA,<sup>7</sup> which has been classified in the high-priority group of the World Health Organization's Bacterial Priority Pathogens List. MRSA has become a pressing global public health concern, especially in neonatal intensive care units. Recently, outbreaks of MRSA have been documented in pediatric wards across various countries, such as Iceland,<sup>8</sup> the Netherlands,<sup>9</sup> and Brazil.<sup>10</sup> Several specific isolates of both CA and HA MRSA have spread widely worldwide and exhibit a high level of cross-adaptability, resulting in increased incidence rates in both community and hospital settings.<sup>11</sup> The distribution of MRSA is indeed dynamic and exhibits specific regional characteristics.<sup>12</sup> According to recent data from the China Antimicrobial Surveillance Network (CHINET), there has been a notable decline in the prevalence of MRSA. Specifically, the prevalence of MRSA in adults has decreased significantly, from 69.0% in 2005 to 29.6% in 2023, as reported on the CHINET website (<https://www.chinets.com/Data/GermYear>). A study conducted in Turkey revealed that the incidence of MRSA among *S. aureus* isolates in central venous catheter-associated infections among pediatric patients diagnosed with hematological malignancies stood at 66.7%.<sup>13</sup> This trend highlights the importance of ongoing surveillance and the effectiveness of antimicrobial stewardship programs in reducing the incidence of MRSA infections. Conversely, the prevalence of MRSA in children does not mirror that of adults. Specifically, for children, the prevalence of MRSA has gradually risen from 18.0% in 2006 to 33.0% in 2014, before slowly declining to 29.8% in 2017.<sup>14</sup> CHINET is a highly influential drug resistance monitoring network in China, boasting 73 member units across 31 provinces, municipalities, and autonomous regions as of 2024. These member units consist of 53 comprehensive hospitals and 20 specialized children's hospitals. As the top pediatric hospital in China, Beijing Children's Hospital joined CHINET. Given that CHINET mainly focuses on adult data, it cannot represent the data situation of children's hospitals. The application of antibiotics is the main measure for treating *S. aureus* infections. However, with the updating and the indiscriminate use of antibiotics, *S. aureus* has developed resistance to antibiotics, especially with the emergence and spread of multidrug-resistant isolates (MDR) under increasing selection pressure.<sup>15</sup> AMR poses a significant threat to global public health, and its incidence varies according to time, geographical location, hospital wards, and other factors.<sup>16</sup> Internationally, numerous scholars have also focused on the issue of antibiotic resistance in MRSA. For instance, a general hospital in Vietnam conducted a study on the resistance patterns of *S. aureus* spanning from 2014 to 2021, featuring a lengthy time frame. However, this study was not specifically targeted at pediatric patients and had a relatively small specimen size.<sup>17</sup> Another report of 14-year period by Oren Gordon et al, focusing on *S. aureus* isolated from pediatric patients, similarly suffered from a limited specimen size.<sup>1</sup> Data from these studies indicated that the resistance patterns of MRSA varied across different regions. A study on *S. aureus* in pediatric patients in China collected data over 12 years for a meta-analysis but was limited to the colonization of *S. aureus* isolated in the upper respiratory tract.<sup>18</sup> The research by Xu et al included *S. aureus* isolated from clinical specimens at Beijing Children's Hospital over a two-year period, yet it lacked an analysis of trends in SA antibiotic resistance.<sup>5</sup> This study, targeting pediatric patients in Beijing, analyzed the resistance patterns of *S. aureus* in all specimen types over a decade, encompassing both pre- and post-COVID-19 pandemic periods. With its extensive time frame and large specimen size, specific to the Beijing region, this study holds significant importance for predicting antibiotic resistance trends, guiding clinical treatment, and formulating strategies to prevent resistance in this area. Given the scarcity of child prevalence data on *S. aureus* infections in Beijing based on hospital records, the aim of this study is to assess the impact of *S. aureus* among currently detectable bacteria and to evaluate the antibiotic resistance of *S. aureus* isolates in Beijing, China.

## Materials and Methods

### Study Setting and Design

This cross-sectional study was a retrospective analysis of all the *S. aureus* data collected from Beijing Children's Hospital, a large tertiary hospital in Beijing, China. Beijing Children's Hospital was the National Center for Children's Health, China, with more than 3 million outpatients and 80,000 inpatients per year. The clinical information and laboratory examination results of the patients were collected and analyzed from the electronic information system, from January 2013 to December 2022. The data included the patient's age, sex, collecting year, specimen type, hospital ward, and antimicrobial susceptibility testing result. To avoid bias in antibiotics sensitivity caused by multiple specimen submissions, only the first isolate from the same patient and the same site was included in our analysis. To ensure the accuracy of antimicrobial susceptibility testing, our laboratory conducted weekly quality control on the Vitek 2 automated system and the Kirby–Bauer disc diffusion method to guarantee the precision of our data. Additionally, quality control was also performed after each machine maintenance and new reagent batches arrived.

### Bacterial Culture and Identification

The microbial culture of specimens was promptly conducted in the microbiology laboratory within 2 hours of collection. Following the guidelines outlined in the National Guide to Clinical Laboratory Procedures, the specimens were inoculated onto Columbia blood agar plates and incubated for several hours under controlled conditions of 35°C and 5% CO<sub>2</sub>. Sterile specimens, including blood, cerebrospinal fluid, pleural fluid, synovial fluid, and ascitic fluid, were injected into blood culture bottles and incubated using the BD BACTEC FX blood culture instrument. In the event of a positive alert, the cultures were subsequently transferred to Columbia blood agar plates and further incubated under the same controlled conditions. Species identification of the isolated microorganisms was carried out using the MALDI-TOF MS (bioMérieux, France) instrument.

### Antimicrobial Susceptibility Testing

Antimicrobial susceptibility tests were carried out by Vitek 2 automated system (bio Mérieux, France) or Kirby–Bauer disc diffusion method, according to the guidelines recommended by the Clinical and Laboratory Standards Institute (CLSI). Antibiotic susceptibility testing results were interpreted according to the CLSI guidelines (M100 32th edition). *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 27853 were used as internal quality controls.

### Definitions

*S. aureus* isolates resistant to oxacillin or cefazolin were recognized as MRSA. *S. aureus* isolates susceptible to oxacillin and cefazolin were recognized as MSSA. The culture obtained within the first 48 hours of hospitalization was considered as a CA infection. The culture obtained after 48 hours of hospitalization was considered as a HA infection. This definition did not apply if the patient was a permanent resident of a chronic care institution, had been hospitalized in the year preceding the current one, or had a permanently indwelling central venous catheter.<sup>19</sup>

### Statistical Analysis

The data underwent processing and statistical analysis using WHONET 5.6 software. GraphPad Prism 6 (La Jolla, CA, USA) was used for additional statistical analysis. The chi-square test was utilized for data analysis. P-value <0.05 was considered as a significant difference.

## Results

### The Rank of *S. aureus* in the Isolated Bacteria Isolates

As shown in Table 1, from 2013 to 2022, a comprehensive total of 47,062 non-duplicate bacterial isolates were collected, amongst which 6477 were identified as *S. aureus*. Notably, the top three most prevalent isolates were *S. aureus*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*, constituting 13.8%, 10.1%, and 9.6% of the total isolates, respectively. From 2013 to 2017, the number of *S. aureus* isolates exhibited a discernible upward trend (Figures 1 and 2).

**Table 1** Distribution of Collecting Year/Season and Specimen Types of the Isolated Isolates

Parameters	Total No. of Specimens	<i>Staphylococcus aureus</i>		
		No. of isolates (n)	Percentage (%)	Positive Rate (%)
<b>Total</b>	433,081	6477	100.0	1.5
<b>Collecting year</b>				
2013	37,418	512	7.9	1.4
2014	37,747	581	9.0	1.5
2015	40,099	635	9.8	1.6
2016	48,589	693	10.7	1.4
2017	54,335	808	12.5	1.4
2018	56,656	766	11.8	1.4
2019	56,265	805	12.4	1.4
2020	33,955	555	8.6	1.6
2021	36,895	551	8.5	1.9
2022	31,122	571	8.8	1.8
<b>Collecting season</b>				
Spring	128,625	1418	21.9	1.1
Summer	73,626	1475	22.7	2.0
Autumn	72,324	1719	26.5	2.4
Winter	158,507	1865	28.8	1.2
<b>Specimen types</b>				
Lower respiratory tract	34,011	2222	34.3	6.5
Upper respiratory tract	53,330	1231	19.0	2.3
Skin and soft tissue secretions	10,958	993	15.3	9.1
Sterile body fluids	9955	548	8.5	5.5
Blood	231,839	485	7.4	0.2
Vulvar secretion	14,005	462	7.1	3.3
Ear secretion	813	194	3.0	23.9
Eye secretion	961	122	1.9	12.7
Bones or joints	4243	106	1.6	2.5
Urine	23,312	84	1.3	0.4
Cerebrospinal fluid	49,654	30	0.5	0.1

## Specimen Distribution and Positive Rate

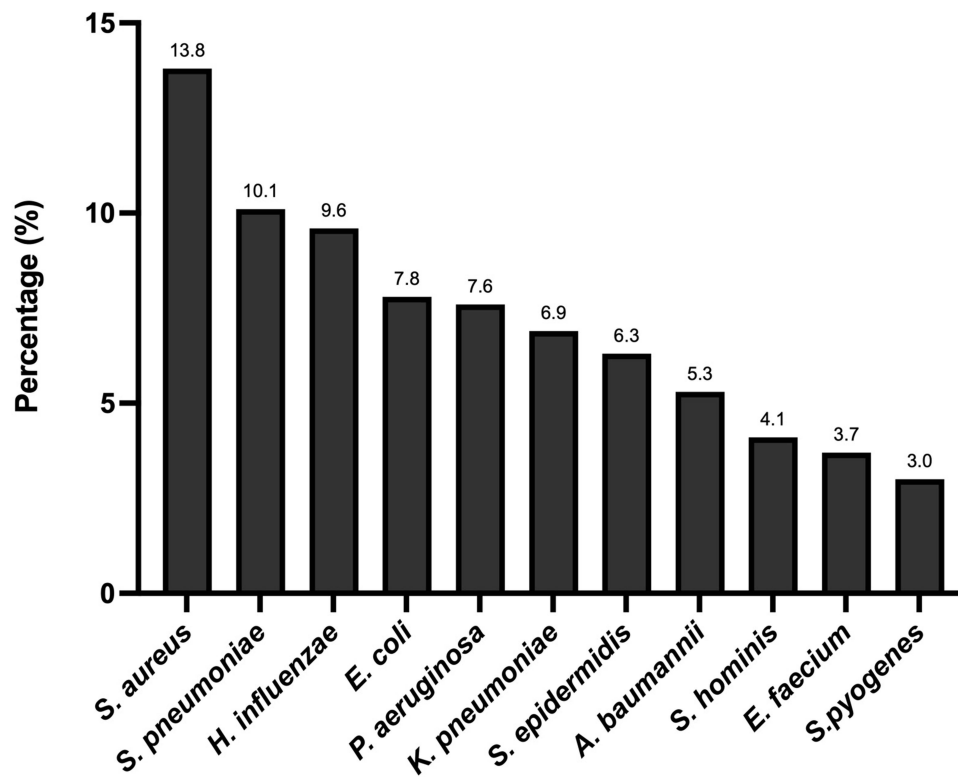
A total of 433,081 specimens were submitted to the microbiology laboratory for cultivation. Among these, blood specimens were the most frequent ( $n = 231,839$ , accounting for 53.5% of the total), followed by upper respiratory tract specimens ( $n = 53,330$ , 12.3%) and cerebrospinal fluid ( $n = 49,654$ , 11.5%). Six thousand four hundred seventy-seven isolates of *S. aureus* were collected and included into our study. The total positive rate was 1.5% (6477/433,081). Notably, ear secretions exhibited the highest positive rate at 23.9% ( $P < 0.05$ ), as shown in Table 1.

## Yearly and Seasonal Distribution

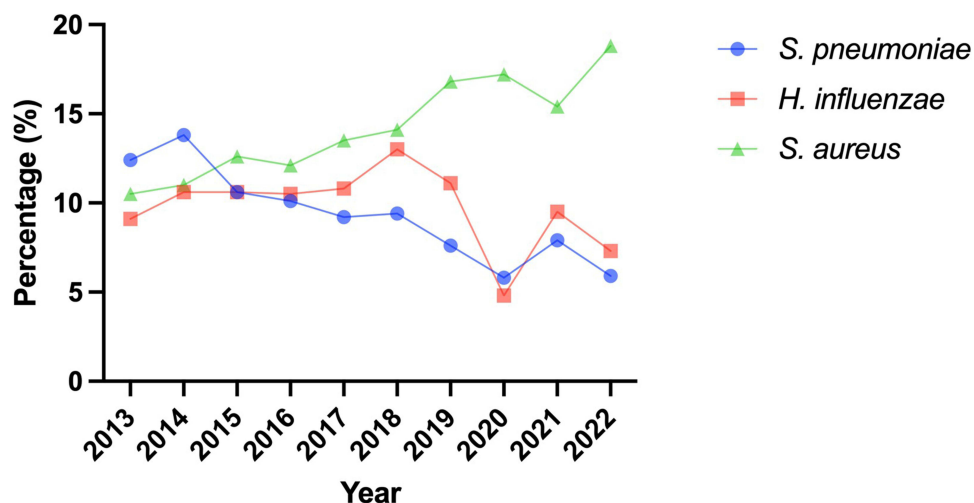
During the period of our study, the number of *S. aureus* isolates showed an upward trend from 2013 to 2019, and then decreased to 551 in 2021, as shown in Table 1.

## Demography of Patients with *S. aureus* Infection

Table 2 shows the demography of patients with *S. aureus* infection. Over 10 years, a total of 6477 patients were diagnosed with *S. aureus* infections, with a male-to-female ratio of 1.17 (3488/2989). The highest proportion of infections was in the infant group ( $n = 1528$ , 23.6%).



**Figure 1** Distribution of total bacterial isolates isolated from pediatric patients in Beijing from 2013 and 2022. A total of 47,062 unduplicated bacterial isolates were obtained, the top three isolates were *S. aureus*, (*S*) *pneumoniae*, and *H. influenzae*, accounting for 13.8%, 10.1%, and 9.6%, respectively.



**Figure 2** Distribution of top three bacterial isolates isolated from pediatric patients in Beijing from 2013 and 2022.

## Antimicrobial Susceptibility Testing of *S. aureus* Isolates

The resistance of *S. aureus* to the antibiotics tested is presented in Table 3. According to the CLSI breakpoints, all isolates exhibited sensitivity to vancomycin and linezolid. However, *S. aureus* displayed the highest resistance to penicillin (89.5%) and erythromycin (73.8%). The proportions of isolates resistant to clindamycin, oxacillin, and trimethoprim-sulfamethoxazole (SXT) were 40.8%, 27.8%, and 23.2%, respectively. The resistance rates of *S. aureus* to rifampicin, moxifloxacin, levofloxacin, and ciprofloxacin were relatively lower. From 2013 to 2022, the resistance rate

**Table 2** Demography of Patients with *S. Aureus* Infections

Parameters	No. of Isolates (n)	Ratio (%)
<b>Total</b>	6477	100.0
<b>Gender</b>		
Male	3488	53.9
Female	2989	46.1
<b>Age</b>		
Neonate (Newborn up to first 28 days)	929	14.3
Infant (28 days below 1 year)	1528	23.6
Toddlers (1 year-below 3 years)	914	14.1
Preschool (3 years below 6 years)	963	14.9
School		
≥6	342	5.3
≥7	320	4.9
≥8	316	4.9
≥9	277	4.3
≥10	211	3.3
≥11~18	645	10.0
<b>Hospital ward</b>		
Outpatient	1426	22.0
Hospitalized patient		
Pneumology Department	1684	26.0
Intensive Care Unit	970	15.0
Neonatal Medical Ward	700	10.8
Dermatological Department	341	5.3
Infectious Disease Department	217	3.4
Nephrology Department	208	3.2
Burn Unit	164	2.5
Orthopedics Department	157	2.4
Hematology Department	146	2.3
Otolaryngologist Department	99	1.5
Neurology Department	88	1.4
Gastroenterology Department	71	1.1
Endocrinology Department	46	0.7
<b>Strain type</b>		
HA	1852	28.6
CA	4625	71.4

**Abbreviations:** HA, healthcare-associated infection; CA, community-acquired infection.

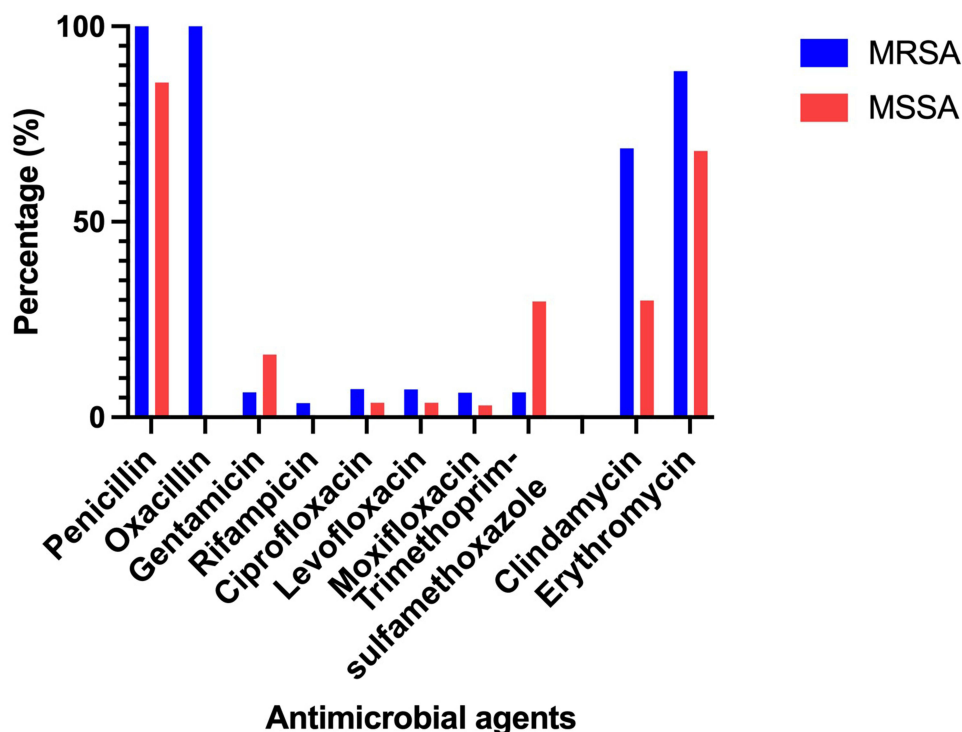
of *S. aureus* to penicillin showed downward trends from 93.4% in 2013 to 83.9% in 2022. The resistance rate of oxacillin increased from 25.1% in 2014 to 32.3% in 2018 and then decreased to the lowest level of 24.3% in 2022.

According to the resistance of *S. aureus* to oxacillin, all the isolates were divided into two groups: MRSA and MSSA. There was a difference in the resistance rate of the tested antibiotics between the two groups. The rate of MRSA resistance to gentamicin and SXT was lower than the MSSA group ( $P < 0.05$ ). Conversely, the rates of MRSA resistance to other antibiotics were lower than that in the MSSA group ( $P < 0.05$ ) (Figure 3). Among the age groups, the proportion of MRSA in the neonate and infant groups was higher than in the children's group since 2014 (Figure 4). According to the departments of the patients visited, they were divided into ICU, inpatient, and outpatient. The rate of MRSA in the ICU group was higher than that in the inpatient group and outpatient group, although the statistically significant difference in the isolation rate of MRSA between ICU and non-ICU wards was only observed in 2013 and 2015 ( $P = 0.0058$  in 2013,  $P = 0.0091$  in 2015). The proportion of MRSA in outpatient was higher than in inpatient groups throughout the study, except for 2013, and there was no statistically significant difference between the two groups ( $P > 0.05$ ). The changes in these two groups were almost synchronous (Figure 5). Among the types of different specimens, the

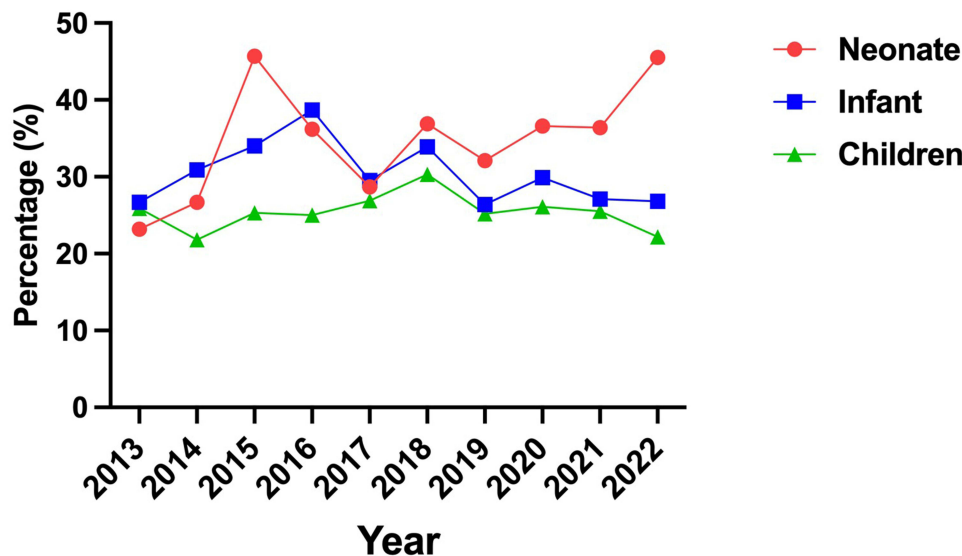
**Table 3** Resistance of *Staphylococcus aureus* Isolates to Antimicrobial Agents

Antibiotics	2013		2014		2015		2016		2017		2018		2019		2020		2021		2022		Total	
	N	R%	N	R%	N	R%	N	R%	N	R%	N	R%	N	R%	N	R%	N	R%	N	R%	N	R%
Penicillin	511	93.4	581	91.2	632	92.9	692	92.2	808	89.8	766	88.5	803	86.0	539	90.0	551	88.8	571	83.9	6454	89.5
Oxacillin	511	25.4	581	25.1	632	29.6	692	29.9	808	27.8	766	32.3	803	26.9	539	28.0	549	27.1	571	24.3	6454	27.8
Gentamicin	509	23.2	581	17.7	632	18.4	692	18.1	808	14.9	766	10.8	803	8.7	539	9.3	551	7.8	571	5.6	6452	13.3
Rifampicin	508	3.3	578	1.7	629	3.0	690	0.9	799	1.9	764	0.5	800	0.8	539	0.9	551	0.4	571	0.5	6429	1.3
Ciprofloxacin	511	6.7	580	5.2	632	6.3	692	2.9	808	5.1	766	4.0	799	4.3	539	4.6	549	4.0	42	2.4	5918	4.7
Levofloxacin	504	6.3	571	5.1	629	6.5	690	2.6	799	5.0	764	4.1	802	4.1	539	4.8	551	3.8	571	4.4	6420	4.6
Moxifloxacin	506	5.7	578	4.2	629	6.2	690	2.5	799	4.5	764	3.7	799	3.8	539	3.7	549	2.0	570	3.3	6423	3.9
Trimethoprim-Sulfamethoxazole	511	36.6	581	29.6	632	28.3	692	28.5	808	24.9	766	18.3	802	18.2	539	17.4	551	17.2	571	14.5	6453	23.2
Erythromycin	510	79.0	580	76.2	632	75.6	692	81.1	808	74.3	766	73.0	803	73.6	539	72.4	551	69.0	571	62.3	6452	73.8
Clindamycin	510	58.4	580	50.7	632	50.6	692	51.9	808	42.6	766	37.5	803	34.6	539	30.2	551	26.9	571	24.5	6452	40.8
Linezolid	511	0.0	579	0.0	632	0.0	691	0.0	808	0.0	766	0.0	803	0.0	539	0.0	551	0.0	570	0.0	6450	0.0
Vancomycin	510	0.0	581	0.0	632	0.0	692	0.0	808	0.0	766	0.0	803	0.0	539	0.0	551	0.0	571	0.0	6453	0.0

**Note:** N, number of *Staphylococcus aureus* isolates tested for specific antibiotics.



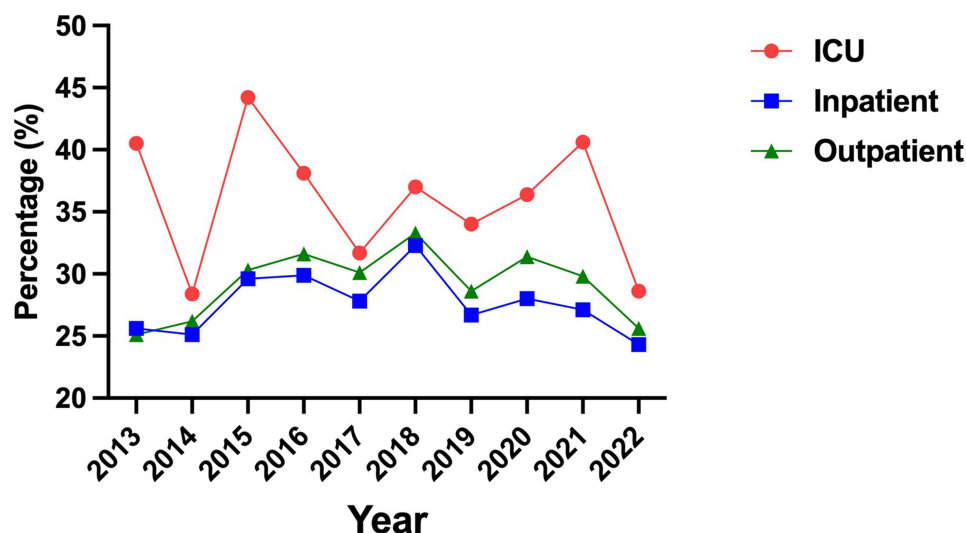
**Figure 3** Antibiotic resistance of MSSA and MRSA to the tested antimicrobial agents. The P values for the rates of the tested antibiotics between MRSA and MSSA were all <0.05. The differences were statistically significant.



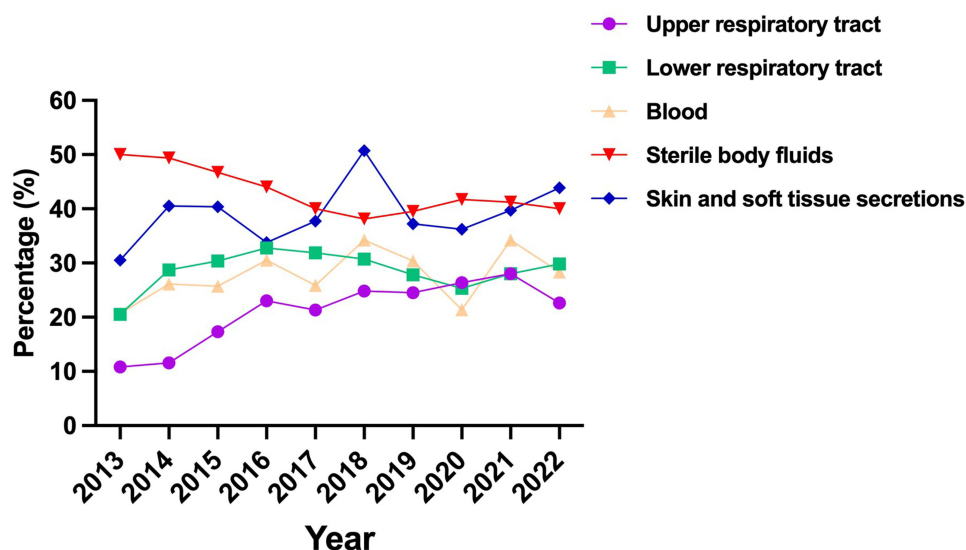
**Figure 4** The detection rate of MRSA in the neonatal group, infant group, and children group from 2013 to 2022.

annual MRSA rate of sterile body fluid specimens was the highest during the study period, except for 2018 and 2022. The annual isolation rate of MRSA from skin and soft tissue secretions was only lower than that of sterile body fluid specimens; however, 50.7% in 2018 and 43.9% in 2022 were both the highest rate for that year, and there was no statistically significant difference between the different specimens ( $P > 0.05$ ). (Figure 6).





**Figure 5** The proportion of MRSA in different hospital wards from 2013 to 2022. In both 2013 and 2015, there was a statistically significant difference observed in the detection rate of MRSA between ICU and non-ICU wards, the P value was 0.0058 and 0.0091, respectively.



**Figure 6** The proportion of MRSA in different specimen types from 2013 to 2022.

## Discussion

*S. aureus* was the main pathogenic bacterium that caused HA and CA infections.<sup>10,11,20</sup> Our ten-year retrospective study revealed that *S. aureus* ranked first among all the isolated isolates. *S. aureus* has been one of the most serious pathogens leading to infections in China,<sup>14</sup> Vietnam,<sup>17</sup> Japan,<sup>21</sup> and other countries. The report in 2019 pointed out that *S. aureus* was the second pathogen globally causing AMR-related deaths, bringing a heavy burden to the healthcare system. Our study showed that since 2015, the number of isolates of *S. aureus* has always been the highest. All these studies above demonstrated that *S. aureus* played an important role in bacterial isolates from adult and pediatric patients in China.

It was noteworthy that the annual count of *S. aureus* isolates observed between 2020 and 2022 was significantly lower compared to the period spanning from 2013 to 2019. Notably, the years from 2020 to 2022 coincided with the COVID-19 pandemic in China, which was marked by a high incidence of the disease. It was speculated that this decline could be attributed to the enforcement of national measures such as intermittent schooling for children, mandatory mask-wearing, and maintaining social distancing during the COVID-19 outbreak.<sup>22,23</sup> Physical interventions could interrupt or reduce

the transmission of pathogenic microorganisms, which might be one of the reasons for the decrease in the prevalence of *S. aureus* among children in our study during the COVID-19 pandemic.<sup>24,25</sup> Apart from our research, a study conducted in Henan Province, China, on *S. aureus* and MRSA among children also observed the similar trend.<sup>26</sup> These measures reduced the likelihood of CA infections caused by *S. aureus* significantly. At the same time, the other two bacteria of CA infections, *H. influenzae* and *S. pneumoniae*, also showed a significant decrease.

Our results indicated that the overall positive rate of *S. aureus* in the specimens was 1.5%, with significant variations observed among different specimen types. Specifically, ear secretions and eye secretions comprised 0.19% and 0.22% of the total specimens, respectively, yet these with the widespread exhibited significantly higher positive rates compared to other specimen types. Notably, despite ear secretions accounting for just 0.19% of the total specimens, they had the highest positive rate of 23.9%, aligning with findings from a meta-analysis conducted in sub-Saharan Africa, where the positive rate ranged between 15.0% and 39.0%.<sup>27</sup> A study conducted in Spain reported a lower positive rate of *S. aureus* in acute otitis media (AOM) of 10.5%.<sup>28</sup> These discrepancies highlighted the geographical and regional variations in the prevalence of *S. aureus*. *S. aureus* ranked as the second most prevalent causative agent in the pathology of chronic suppurative otitis media (CSOM).<sup>29</sup> Some of the mechanisms by which *S. aureus* contributes to CSOM include biofilm formation, the production of beta-lactamases, and its capacity to invade human middle ear epithelial cells via a cholesterol-dependent pathway.<sup>30</sup> Furthermore, we observed that the number of ear secretion specimens was relatively low compared to other types, with only 813 specimens collected over a decade. This could be attributed to the common practice of treating AOM infections in outpatient settings directly with antibiotics based on clinical experience, without conducting further bacterial cultures. This finding may suggest a lack of vigilance in outpatient diagnosis. Consequently, there was a need for greater emphasis on pathogen detection in pediatric outpatient patients, particularly given the high positivity rate of *S. aureus* in AOM cultures that has been recently identified. The research indicated that *S. aureus* was mainly isolated from respiratory specimens and skin and soft tissue secretions. Still, the study was inconsistent with a recent report from Romania, which reported a much higher proportion of *S. aureus* isolated from wound secretion (57.8%).<sup>31</sup> Some other reports from Vietnam<sup>17</sup> and China<sup>32</sup> also revealed that much more *S. aureus* was isolated from skin and soft tissue secretions other than respiratory specimens. The difference was mainly because a large proportion of patients with respiratory tract infections were admitted to our hospital. Moreover, as the National Children's Medical Center, Beijing Children's Hospital treated children with severe respiratory diseases from all over the country.

Among the antibiotics tested in this study, *S. aureus* demonstrated the highest level of resistance to macrolide antibiotics. This finding aligned with the results reported by a researcher from Vietnam, who conducted a survey on AMR between 2014 and 2021.<sup>17</sup> Simultaneously, the resistance rate of *S. aureus* to SXT exceeded the findings (9.3%) reported by the ISPED program, which conducted a survey across eleven tertiary care pediatric hospitals in China spanning from 2016 to 2020.<sup>32</sup> Compared to the monitoring data from ISPD, the higher SXT resistance rate observed in our study may be attributed to the following factors: differences in antimicrobial prescribing practices, antimicrobial use policies, and medical resources. Furthermore, variations in the underlying health status of the population and differences in the prevalence of SXT-resistant isolates may also contribute to these discrepancies. Our study found no instances of *S. aureus* resistant to either linezolid or vancomycin, confirming the monitoring data reported by CHINET in 2018.<sup>33</sup> Vancomycin was the most important antibiotic for empiric and definitive treatment of MRSA infections. In recent years, there have been reports of reduced sensitivity of MRSA to vancomycin worldwide.<sup>34–36</sup> The literature reported that during the treatment of *S. aureus* infection with vancomycin, vancomycin-sensitive *S. aureus* could convert to vancomycin-intermediate *S. aureus*.<sup>37,38</sup> Although vancomycin-resistant *Staphylococcus aureus* (VRSA) has not been detected in China, much more attention should be paid to the patients who were treated with vancomycin for the long term. In this study, MSSA maintained high sensitivity to all antibiotics except penicillin, erythromycin, and clindamycin. In contrast, MRSA showed high resistance to all  $\beta$ -lactam antibiotics, erythromycin, and ciprofloxacin. These results were consistent with previous studies on populations from China.<sup>33</sup>

A study conducted in Canada revealed a decline in the prevalence of MRSA from 26.1% to 16.9% between 2006 and 2017.<sup>39</sup> In contrast, the detection rate in MRSA in northern Taiwan during the period from 2004 to 2012 was notably high, reaching 63.6%.<sup>40</sup> In China, the surge in MRSA cases has rendered *S. aureus*-related infections a particularly formidable challenge.<sup>41</sup> Fortunately, according to the CHINET, the prevalence of MRSA in Chinese hospitals decreased

gradually from 69.0% in 2005 to 35.3% in 2017. However, for children under the age of 18, the prevalence of MRSA exhibited an opposite trend, increasing from 18.0% in 2005 to 29.8% in 2017.<sup>33</sup> Our research showed that after a slight increase, the detection rate of MRSA returned to the level of 2013 in 2022. Our detection rate of MRSA was consistent with a previous study in China, which showed that the average proportion of MRSA was 32.8%.<sup>42</sup> Our data indicated that, among the various hospital wards, the ICU had the highest proportion of MRSA during the study period. This was likely due to the fact that patients admitted to the ICU typically suffer from severe illnesses, immune dysfunction, and underlying conditions. Furthermore, the use of medical equipment such as ventilators, central venous catheters, and other catheters in the treatment of these patients may contribute to the spread of MRSA.<sup>43</sup> Since 2017, the neonate age group has exhibited the highest proportion of *S. aureus* infections, followed closely by the infant and children age groups. Notably, in recent years, there has been an upward trend in the proportion of MRSA infections among neonates, whereas the detection rate of MRSA in the other two age groups has been decreasing annually. Various studies have reported outbreaks of MRSA in neonatal wards globally, emphasizing the significance of screening for MRSA, particularly in high-risk environments such as neonatal intensive care units. Consequently, early screening has proven to be an effective strategy for the early detection and containment of MRSA transmission.<sup>10</sup> Our research showed that among the specimen types, the sterile body fluids had the highest proportion of MRSA, followed by skin and soft tissue secretions. These findings were not the same as a previous study, which showed a higher proportion of MRSA isolates from the lower respiratory tract than sterile body fluids.<sup>44</sup> Previous literature reported that the high detection rate of MRSA in lower respiratory tract specimens was related to the formation of biofilm,<sup>45</sup> but the relevant conclusions could not support our research.

A crucial evolution of *S. aureus* occurred in the early 1960s when several MDR (resistant to antibiotics such as penicillin, streptomycin, tetracycline, and erythromycin),<sup>46</sup> independently acquired the SCC*mec* complex, thereby conferring resistance to the majority of  $\beta$ -lactam antibiotics on *S. aureus*.<sup>47</sup> Certain mutant types of the *mec*, such as types I, II and III are associated with HA infections, while others like types IV and V are linked to CA infections.<sup>48</sup> Internationally, the prevalence of MRSA in Europe and America has declined in recent years.<sup>49,50</sup> This decline can be partly attributed to changes in the organism itself, with a loss in survival fitness leading to shifts in the circulating clones.<sup>51,52</sup> Another contributing factor may be the implementation of a multifaceted prevention strategy,<sup>53</sup> encompassing stringent hand hygiene protocols, proactive surveillance,<sup>54</sup> reinforced contact precautions, and effective isolation practices.<sup>55</sup>

This phenomenon aligned with the observed decline in MRSA prevalence during the pandemic in our study. The management approaches for MRSA vary across different geographical regions, specifically tailored to the local prevalence of MRSA and the availability of antimicrobial agents, particularly novel drugs. Decolonization was a highly effective strategy that can aid in controlling MRSA by reducing the risk of transmission and infection.<sup>56</sup> All these approaches may result in unique patterns of antibiotic resistance in each region. By exploring these local factors, we can not only refine the interpretation of the results but also provide valuable insights for tailored interventions and strategies to effectively address antibiotic resistance issues within our healthcare system.

## Conclusion

In summary, our study reported on the distribution and antibiotic resistance profiles of *S. aureus* in Beijing from 2013 to 2022. We found that *S. aureus* infections were prevalent among infants and young children under 6 years old, with the most common specimen types being lower respiratory tract, followed by upper respiratory tract, skin and soft tissue secretions, and sterile body fluids. The average positive rate among specimens was 1.50%, with the highest positive rate observed in ear secretions (23.9%). Our findings revealed that the ICU, sterile body fluids, and the neonate age group had the highest proportions of MRSA. MSSA maintained high sensitivity to all antibiotics except penicillin, erythromycin, and clindamycin, whereas MRSA exhibited high resistance to all  $\beta$ -lactam antibiotics, erythromycin, and ciprofloxacin. Therefore, it is crucial to closely monitor antibiotic resistance and use antibacterial agents judiciously.

## Ethical Information

The *S. aureus* isolates analyzed in this study were collected from clinical laboratories. Our study was a retrospective study based on the clinical specimens, which were part of the routine hospital laboratory procedures. This study was reviewed and approved by the Ethics Committee of Beijing Children's Hospital. The ethics committee waived the need for participants' informed consent because the study was retrospective. The study was conducted following the principle of the Declaration of Helsinki.

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