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Clinical Characteristics and Microbial Profiles of Paediatric Patients with Methicillin-Resistant *Staphylococcus aureus* Pneumonia in China

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Abstract

Background: *Staphylococcus aureus* can cause fatal pneumonia. The evolution of bacteria and the overuse of antibiotics have enhanced the drug resistance of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *Staphylococcus aureus* (MSSA).

Objectives: This study aimed to recapitulate the microbiological profile and clinical characteristics of paediatric patients with MRSA.

Methods: This retrospective study was conducted to investigate 1372 paediatric patients with *S. aureus* pneumonia from January 2017 to December 2021. Sputum specimens were collected and processed for performing bacterial culture and drug sensitivity tests. Medical records of patients were reviewed for clinical characteristics and laboratory examination results.

Results: The MRSA and MSSA pneumonia mainly occurred in infants; however, comparisons of sex, age, and sampling time between patients with MRSA and MSSA pneumonia showed no significant differences ($P > 0.05$). The results of drug sensitivity in sputum culture revealed that all MRSA and MSSA isolates were susceptible to vancomycin, tigecycline, linezolid, teicoplanin, and ceftaroline. Methicillin-sensitive *Staphylococcus aureus* was completely sensitive to rifampicin and oxacillin. Methicillin-resistant *Staphylococcus aureus* was completely resistant to penicillin and oxacillin, while MSSA was less sensitive to penicillin. Methicillin-resistant *Staphylococcus aureus* and MSSA both maintained high sensitivity rates to gentamicin, sulfamethoxazole-trimethoprim, levofloxacin, and moxifloxacin, with the exception of clindamycin and erythromycin. According to our results, moreover, the sensitivity of MRSA to gentamicin and sulfamethoxazole-trimethoprim was significantly higher than that of MSSA ($P < 0.05$). The common symptoms of patients with *S. aureus* pneumonia were fever, cough, and wheezing. patients with MRSA pneumonia had significantly higher counts of white blood cells (WBCs), C-reactive protein (CRP), and procalcitonin (PCT) than patients with MSSA pneumonia ($P < 0.05$).

Conclusions: The results of antimicrobial sensitivity test in sputum culture of MRSA and MSSA isolates can reflect the sensitivity of antibiotics and guide the use of clinical antibiotics. Infectious biomarkers can reflect the severity of infection and guide prognosis.

Keywords: Methicillin-Resistant *Staphylococcus aureus*, Microbial Sensitivity Test, Pneumonia, *S. aureus*

1. Background

Community-acquired pneumonia (CAP) is a leading cause of morbidity and mortality worldwide and a major public health hazard for Chinese children (1). According to the China's mortality monitoring system, under-five mortality rate is 153.2 deaths per 100,000 live births (2). Rigorous estimation of disease severity is critical to clinical decision-making. *Staphylococcus aureus* can cause many different infectious diseases, including fatal pneumonia (3). *Staphylococcus aureus* can be classified into methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *Staphylococcus aureus* (MSSA) based on the sensitivity to antibiotics. The evolution of bacteria and the overuse of antibiotics have enhanced drug resistance of MRSA and incremental infection trends, making clinical anti-infection therapy more formidable (4).

At present, sputum culture is the most economical method to detect pathogens in patients with CAP and evaluate their drug resistance to antibacterial drugs (5). Research from the China antimicrobial resistance surveillance system indicated that sputum was the main specimen of hospitalized patients who participated in respiratory departments in China (6). Despite the proliferation of antibiotic resistance, rigorous administration of appropri-

ate therapeutic drugs can significantly reduce mortality associated with the disease (7). Biomarkers in pneumonia may be indicators of inflammation or be specific markers released after lung injury due to infection (8). Therefore, it is critical to acquire the microbial spectrum and biomarkers of patients with MRSA pneumonia in order for guiding timely and appropriate empirical treatment of MRSA pneumonia.

2. Objectives

This retrospective study aimed to examine the clinical manifestations and microbial spectrum of MRSA pneumonia, as well as to determine drug sensitivity and direct timely and appropriate empiric therapy.

3. Methods

3.1. Study Design and Population

Community-acquired pneumonia was diagnosed according to the clinical practice guidelines of the Paediatric Infectious Diseases Society of America (9). A total of 1372 children with *S. aureus* pneumonia and hospitalized between January 2017 and December 2021 in the Department of Paediatrics of Linyi People's Hospital and respiratory department of Children's Hospital of Soochow University were included in this study. Community-acquired pneumonia was diagnosed based on the presence of fever, cough, dyspnoea, and other signs of respiratory distress combined with new pulmonary infiltrates on chest X-ray (9). Exclusion criteria were as follows: Patients who were under antimicrobial treatment within the last 14 days during data collection and had incomplete medical records, as well as patients with comorbidities at the time of admission (e.g., immunosuppression, congenital heart defect, pulmonary developmental malformation, etc.). It should be noted that Linyi People's Hospital is a tertiary general hospital, and Children's Hospital of Soochow University is a provincial children's hospital accommodating 4082 and 1306 beds, respectively.

3.2. Specimen Preparation

All specimens were sent for examination within two hours, and strains isolated from the same patient several times were not recounted. All cultured specimens were evaluated by Gram staining before culture analysis. Thus, sputum specimens with at least 25 polymorph-nuclear leukocytes and less than 10 epithelial cells per low power field, and more than 10 bacteria per high-powered field were processed for culture (10, 11). The bacteria were cultured for 24~ 48 hours at 37°C in a completely humidified atmosphere with 5% CO_2.

3.3. Detection of Antimicrobial Susceptibility Analysis

The experiment was conducted by using the dilution method (Biotechnology Companies, Merrier, French) and Kirby-Bauer disk diffusion test (K-B method) (Oxoid, Hampshire, UK) in accordance with the regulatory guidelines and standards published by the Clinical and Laboratory Standards Institute (CLSI) (12).

3.4. Laboratory Quality Control

Staphylococcus aureus ATCC29213 and ATCC25923 were selected as positive and negative controls, respectively. Sensitivity to antimicrobial agents was judged according to the antimicrobial chemosensitivity standards of the American Society of Antimicrobial Chemotherapy (13).

3.5. β-Lactamase Detection

To this end, 30 μL of cefdinalothiophene was added to a clean glass plate or a microporous plate, and a ring of fresh moss was added to the plate. The results were observed after 30 minutes. A lack of colour change indicated a negative result, while a colour change to red indicated a positive result (14).

3.6. Data Analysis

Statistical analyses were performed using SPSS 23.0 (IBM, SPSS, Chicago, IL, USA). Demographic and clinical information of cases were expressed by the means of frequencies, percentages, and proportions. Descriptive continuous outcome variables were shown as the medians (25% to 75%). To compare the data about patients with MRSA and MSSA pneumonia, the χ^2 test was applied to categorical variables, Fisher's exact test for small sample sizes ($n < 5$), and the non-parametric test (Mann-Whitney U test) for continuous variables; $P < 0.05$ was considered significant.

4. Results

4.1. Demographic Characteristics

Out of 1372 patients with *S. aureus* pneumonia, 608 (44.31%) were MRSA and 764 (55.69%) were MSSA. The results form comparison of sex, age, and sampling time of the patients with MRSA and MSSA pneumonia are shown in Table 1. However, the percentages of males to females, age, and sampling time revealed no significant differences (P-values 0.718, 0.110, and 0.614, respectively) (Table 1). The ratios of male to female patients with MRSA and MSSA pneumonia were 2.45 and 2.35, respectively ($P > 0.05$), and the median age was three and four months, respectively (range, 1 month to 10 years, $P > 0.05$) (Table 1). As for the age, patients with MRSA and MSSA pneumonia were categorized

into the infancy group (1 m - 1 y, 58.55%, 356 versus 62.83%, 480), toddler group (1 - 3 y, 18.42%, 112 versus 18.06%, 138), preschool group (3 - 6 y, 15.63%, 95 versus 11.26%, 86), and school group (6 - 14 y, 7.40%, 45 versus 7.85%, 60). There were no significant differences among four groups regarding age ($P > 0.05$) (Table 1). Patients with MRSA and MSSA were divided into four groups based on sampling times: Spring (24.01%, 146 versus 25.13%, 192), summer (18.76%, 114 versus 16.24%, 124), autumn (14.47%, 88 versus 13.87%, 106), and winter (42.76%, 260 versus 44.76%, 342). No significant differences were detected between two groups in terms of sampling times ($P > 0.05$) (Table 1).

4.2. Antimicrobial Sensitivity Tests

The distributions of the drug sensitivity tests of MRSA and MSSA in the previous five years are presented in Tables 2 and 3. The results revealed that all MRSA and MSSA isolates were susceptible to vancomycin, tigecycline, linezolid, teicoplanin, and ceftaroline. MSSA was also found to be completely sensitive to oxacillin. The sensitivity rate of MRSA to rifampicin was 95.74% in 2020, and that of MSSA to rifampicin was 92.45% in 2021; and they were completely sensitive in the remaining four years (Tables 2 and 3). It was also discovered that MRSA was completely resistant to penicillin and oxacillin, while MSSA was less sensitive to penicillin (Tables 2 and 3). The resistance rate of MSSA to penicillin was 100% in the first three years and decreased to the lowest level (94.44%) in the last two years (Tables 2 and 3). MRSA and MSSA both showed high sensitivity rates to gentamicin, sulfamethoxazole-trimethoprim, levofloxacin, and moxifloxacin, with the exception of clindamycin and erythromycin (Tables 2 and 3). The sensitivities of MRSA and MSSA to moxifloxacin and levofloxacin were higher than 91.67%, and those of MRSA and MSSA to sulfamethoxazole-trimethoprim were unstable, ranging from 92% to 95.74% and 69.70% to 81.13%, respectively (Tables 2 and 3).

The overall sensitivity of MRSA to gentamicin has declined from 100% to 92% over the last five years, and it is still higher than that of MSSA (Tables 2 and 3). The sensitivity of MRSA to moxifloxacin and levofloxacin has fluctuated and decreased to the lowest level (92.31%) in the last two years, while the sensitivity of MSSA to these two drugs initially declined and, then increased to more than 98% in 2021 (Tables 2 and 3). The results further demonstrated that the sensitivity of MRSA to gentamicin and sulfamethoxazole-trimethoprim was significantly higher than that of MSSA ($P < 0.05$) (Table 4). The sensitivity rate of MRSA was significantly lower than that of MSSA to levofloxacin, moxifloxacin, rifampicin, clindamycin, and erythromycin ($P > 0.05$) (Table 4).

4.3. Clinical Symptoms and Laboratory Examination of Pneumonia Children with Methicillin-Resistant Staphylococcus aureus and Methicillin-Sensitive Staphylococcus aureus

Children with MRSA pneumonia had a longer median hospital stay than children with MSSA pneumonia (9.00 days versus 8.00 days, $P < 0.05$) (Table 5). No significant differences were found between two groups in terms of the median duration of symptoms before admission (5.00 days versus 6.00 days, $P > 0.05$) (Table 5). The common symptoms of children with *S. aureus* pneumonia are fever, cough, and wheezing. Children with MRSA pneumonia had more fever, while the symptoms of cough and wheezing were lower than those of children with MSSA pneumonia. There was no significant difference between two groups regarding these three symptoms (47.37% versus 43.98%, 83.55% versus 84.29% and 61.84% versus 63.09%), respectively (all $P > 0.05$) (Table 5).

Children with MRSA pneumonia had significantly higher white blood cells (WBCs), C-reactive protein (CRP), and procalcitonin (PCT) than children with MSSA pneumonia [9.16×10^9/L (6.77, 12.58) versus 8.84×10^9/L (6.78, 11.25), 5.20 mg/L (2.30, 10.00) versus 3.40 mg/L (2.60, 8.28), and 0.38 ng/mL (0.18, 1.12) versus 0.34 ng/mL (0.17, 0.63)], respectively (all $P < 0.05$) (Table 5). There was no significant difference between two groups regarding other laboratory findings. No significant differences were also revealed between two groups in terms of the imaging manifestations of single lateral infiltration and bilateral infiltration (16.12% versus 18.32% and 83.88% versus 81.68%, $P > 0.05$) (Table 5).

5. Discussion

Staphylococcus aureus pneumonia has become increasingly frequent, and is associated with significant morbidity and mortality (15). A considerable cohort of community-associated *S. aureus* cases hospitalized in two hospitals in the previous five years was retrospectively reviewed in our study. There were more male patients than female patients in the two groups. Most of our patients were young infants, and the median ages were three and four months, which was in accordance with the documentation by Doudoulakakis et al., who reported a median age of 4.3 months among patients with *S. aureus* pneumonia (16). Age differentiation is considered to be associated with the immature immune function of infants. *Staphylococcus aureus* pneumonia mostly occurred in winter and less in spring; however, comparing two groups in terms of sex, age, and sampling time showed no significant differences.

The evolution of bacteria and the overuse of antibiotics have enhanced drug resistance of MRSA and MSSA, making clinical anti-infective treatment more formidable

Table 1. Characteristics of 1372 Included Paediatric Patients with *Staphylococcus aureus* Pneumonia [a]

Characteristics	MRSA (n = 608)	MSSA (n = 764)	χ^2	P-Value
Sex			0.131	0.718
Male	432 (71.05)	536 (70.16)		
Female	176 (28.95)	228 (29.84)		
Age			6.027	0.110
1 m - 1 y (infancy group)	356 (58.55)	480 (62.83)		
1 - 3 y (toddler group)	112 (18.42)	138 (18.06)		
3 - 6 y (preschool group)	95 (15.63)	86 (11.26)		
6 - 14 y (school group)	45 (7.40)	60 (7.85)		
Sampling time			1.806	0.614
Spring (from March to May)	146 (24.01)	192 (25.13)		
Summer (from June to August)	114 (18.76)	124 (16.24)		
Autumn (from September to November)	88 (14.47)	106 (13.87)		
Winter (from December to February)	260 (42.76)	342 (44.76)		

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.
[a] Values are expressed as No. (%) unless otherwise indicated.

Table 2. The Number and Susceptibility of Methicillin-Resistant *Staphylococcus aureus* to Antibiotics from 2017 to 2021 [a]

Antimicrobial Agents	2017	2018	2019	2020	2021
	MRSA (n = 64)	MRSA (n = 100)	MRSA (n = 100)	MRSA (n = 188)	MRSA (n = 156)
Ceftaroline	64 (100.00)	100 (100)	100 (100)	188 (100.00)	156 (100.00)
Clindamycin	12 (18.75)	28 (28)	4 (4)	44 (23.40)	44 (28.21)
Erythromycin	12 (18.75)	20 (20)	4 (4)	36 (19.15)	44 (28.21)
Gentamicin	64 (100.00)	100 (100)	92 (92)	176 (93.62)	148 (94.87)
Levofloxacin	60 (93.75)	96 (96)	100 (100)	180 (95.74)	144 (92.31)
Linezolid	64 (100.00)	100 (100)	100 (100)	188 (100.00)	156 (100.00)
Moxifloxacin	64 (100.00)	96 (96)	100 (100)	180 (95.74)	144 (92.31)
Oxacillin	0	0	0	0	0
Penicillin	0	0	0	0	0
Rifampicin	64 (100.00)	100 (100)	100 (100)	170 (90.43)	156 (100.00)
Sulfamethoxazole-trimethoprim	60 (93.75)	92 (92)	92 (92)	180 (95.74)	148 (94.87)
Teicoplanin	64 (100.00)	100 (100)	100 (100)	188 (100.00)	156 (100.00)
Tigecycline	64 (100.00)	100 (100)	100 (100)	188 (100.00)	156 (100.00)
Vancomycin	64 (100.00)	100 (100)	100 (100)	188 (100.00)	156 (100.00)

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.
[a] Values are expressed as No. (%).

(4). When community-associated MRSA (CA-MRSA) infections are under suspicion, primary empiric antimicrobial therapy, including vancomycin or clindamycin, is put into practice (17). Recent research has demonstrated that *S. aureus* is more susceptible to linezolid and vancomycin. The results of the antimicrobial susceptibility test indicated that linezolid and vancomycin were suitable drugs for treating CA-MRSA pneumonia in children (18, 19). Our results were consistent with those reported in the literature suggesting that all MRSA and MSSA isolates were susceptible to vancomycin, tigecycline, linezolid, teicoplanin, and ceftaroline. Our study also revealed that MSSA was completely sensitive to rifampicin and oxacillin. As for CAP caused by MSSA, the first-line treatment is usually ce-

Table 3. The Number and Susceptibility of Methicillin-Sensitive *Staphylococcus aureus* to Antibiotics from 2017 to 2021 [a]

Antimicrobial Agents	2017	2018	2019	2020	2021
	MSSA (n = 132)	MSSA (n = 168)	MSSA (n = 108)	MSSA (n = 144)	MSSA (n = 212)
Ceftaroline	132 (100.00)	168 (100.00)	108 (100.00)	144 (100.00)	212 (100.00)
Clindamycin	24 (18.18)	40 (23.81)	32 (29.63)	48 (33.33)	48 (22.64)
Erythromycin	6 (18.18)	36 (21.43)	28 (25.93)	52 (36.11)	32 (15.09)
Gentamicin	104 (78.79)	132 (78.57)	92 (85.19)	124 (86.11)	192 (90.57)
Levofloxacin	132 (100.00)	164 (97.62)	100 (92.59)	132 (91.67)	208 (98.11)
Linezolid	132 (100.00)	168 (100.00)	108 (100.00)	144 (100.00)	212 (100.00)
Moxifloxacin	132 (100.00)	164 (97.62)	104 (96.30)	132 (91.67)	212 (100.00)
Oxacillin	132 (100.00)	168 (100.00)	108 (100.00)	144 (100.00)	212 (100.00)
Penicillin	0	0	0	8 (5.56)	8 (3.77)
Rifampicin	132 (100.00)	168 (100.00)	108 (100.00)	144 (100.00)	196 (92.45)
Sulfamethoxazole-trimethoprim	92 (69.70)	120 (71.43)	84 (77.78)	104 (72.22)	172 (81.13)
Teicoplanin	132 (100.00)	168 (100.00)	108 (100.00)	144 (100.00)	212 (100.00)
Tigecycline	132 (100.00)	168 (100.00)	108 (100.00)	144 (100.00)	212 (100.00)
Vancomycin	132 (100.00)	168 (100.00)	108 (100.00)	144 (100.00)	212 (100.00)

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.
[a] Values are expressed as No. (%).

Table 4. The Number and Susceptibility of Methicillin-Resistant *Staphylococcus aureus* and Methicillin-Sensitive *S. aureus* Isolated from Children with Pneumonia [a]

Antimicrobial Agents	MRSA (n = 608)	MSSA (n = 764)	χ^2	P-Value
Ceftaroline	608 (100.00)	764 (100.00)	-	-
Clindamycin	132 (21.71)	192 (25.13)	2.196	0.138
Erythromycin	116 (19.08)	172 (22.51)212	2.407	0.121
Gentamicin	580 (95.39)	644 (84.29)	43.359	0
Levofloxacin	580 (95.39)	736 (96.34)	0.765	0.382
Linezolid	608 (100.00)	764 (100.00)	-	-
Moxifloxacin	584 (96.05)	744 (97.38)	0.149	0.7
Oxacillin	0	764 (100.00)	-	0
Penicillin	0	16 (2.09)	-	0
Rifampicin	590 (97.04)	748 (97.91)	1.051	0.305
Sulfamethoxazole-trimethoprim	572 (94.08)	572 (74.87)	22.541	0
Teicoplanin	608 (100.00)	764 (100.00)	-	-
Tigecycline	608 (100.00)	764 (100.00)	-	-
Vancomycin	608 (100.00)	764 (100.00)	-	-

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.
[a] Values are expressed as No. (%) unless otherwise indicated.

fazolin, oxacillin, or ceftaroline (20). The reason that MRSA and MSSA isolates are susceptible to ceftaroline may be attributed to the rare application of this antimicrobial agent. Linezolid has been proposed for dealing with CA-MRSA pneumonia (21).

It is recommended that panton-valentine leukocidin (PVL)-positive MRSA patients should receive clindamycin or rifampicin under the premise of vancomycin or teicoplanin (22). The sensitivity rate of MRSA to rifampicin was 95.74% in 2020, and that of MSSA to rifampicin was

Table 5. Clinical Features of Pneumonia Children Hospitalized with Methicillin-Resistant *Staphylococcus aureus* and Methicillin-Sensitive *S. aureus* [M (P25, P75)] [a]

Clinical Features	MRSA (n = 608)	MSSA (n = 764)	χ^2/Z	P-Value
Personal history				
Length of stay (days)	9.00 (8.00, 12.00)	8.00 (7.00, 11.00)	-4.662	0.000
Symptom duration prior to admission (days)	5.00 (3.00, 7.00)	6.00 (4.00, 7.00)	-1.897	0.058
Clinic presentation				
Fever	288 (47.37)	336 (43.98)	1.569	0.210
Cough	508 (83.55)	644 (84.29)	0.138	0.710
Wheezing	376 (61.84)	482 (63.09)	0.225	0.635
Laboratory findings				
White blood cell count ($\times 10^9$/L)	9.16 (6.77, 12.58)	8.84 (6.78, 11.25)	-3.049	0.002
NE%	29.20 (19.90, 46.83)	29.40 (21.50, 46.50)	-0.611	0.541
LY%	56.90 (37.80, 68.90)	56.20 (39.90, 67.10)	-0.735	0.462
CRP (mg/L)	5.20 (2.30, 10.00)	3.40 (2.60, 8.28)	-2.434	0.015
PCT (ng/mL)	0.38 (0.18, 1.12)	0.34 (0.17, 0.63)	-2.389	0.017
PLT ($\times 10^9$/L)	351.00 (267.00, 418.00)	339.00 (245.00, 421.75)	-1.357	0.175
CKMB (ng/mL)	3.70 (2.19, 5.38)	3.56 (2.39, 5.09)	-1.480	0.139
ALT (U/L)	22.75 (15.60, 35.78)	23.10 (15.80, 32.60)	-0.606	0.545
Imaging manifestation			1.149	0.284
Single lateral infiltration	98 (16.12)	140 (18.32)		
Bilateral infiltration	510 (83.88)	624 (81.68)		

Abbreviations: NE%, neutrophil percentage; LY%, lymphocytes percentage; CRP, c-reactive protein; PCT, procalcitonin; PLT, platelet count; CKMB, creatine kinase myocardial band; ALT, alanine aminotransferase: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.
[a] Values are expressed as No. (%) unless otherwise indicated.

92.45% in 2021, and they were completely sensitive in the remaining four years. The study demonstrated that the above-mentioned antibiotics had good antibacterial activity against *S. aureus* and may have been used for its clinical treatment. Community-associated MRSA strains are resistant to β-lactams and cephalosporins but are mostly sensitive to several non-β-lactam antibiotics (18, 19). Our study results determined that MRSA was completely resistant to penicillin and oxacillin, while MSSA was less sensitive to penicillin. The results also suggested that the resistance of *S. aureus* to β-lactam antibiotics was extremely serious and may have been related to its universal application in the clinic. Resistance is usually generated by acquiring a non-native gene encoding a penicillin-binding protein (PBP2a), which has significantly lower affinity for β-lactams. This resistance allows cell-wall biosynthesis, the target of β-lactams, to continue even in the presence of typically inhibitory concentrations of antibiotics (23).

According to our study results, MRSA and MSSA both maintained high sensitivity rates to gentamicin, sulfamethoxazole-trimethoprim, levofloxacin, and moxifloxacin. Our results further demonstrated that the sensitivity of MRSA to gentamicin and sulfamethoxazole-trimethoprim was significantly higher than that of MSSA. These drugs cannot be suitable for the treatment of paediatric patients with *S. aureus* pneumonia due to their adverse side effects. However, our study revealed that MRSA and MSSA both showed low susceptibility to clindamycin and erythromycin from 4% to 28.21% over the last five years.

A study determined that MRSA and MSSA had low susceptibility to erythromycin (18.4%) and clindamycin (40.8%). Its results further indicated that clindamycin may not have been the optimal empirical medication for CA-MRSA and MSSA in Shanghai (24). Low susceptibility to erythromycin and clindamycin resistance (54.4% and 41.8%, respectively) was seen in isolates from the Nepal Medical College and Teaching Hospital (25). Erythromycin and clindamycin are two important antibiotics for clinicians. However, resistance to erythromycin induced by clindamycin may often occur during the application of the two antibiotics (26). This may be due to the non-standardized appli-

cation of antibiotics in our country, which has increased the drug-resistant strains.

Clinical presentations vary depending on the age and health status of the child, the responsible pathogen, and the severity of the disease. The clinical manifestations are non-specific in that no sole symptom or physical sign is characteristic of pneumonia (27, 28). Common symptoms are fever, cough, and dyspnoea (28). In this study, the main symptoms of *S. aureus* pneumonia were fever, cough, and wheezing, which may have been due to the immature development of the lung and the imperfect development of the surface mucosal system. Biomarkers are considered to be an important approach to detecting a patient's response to infection by predicting disease severity and therapeutic outcome (29). Biomarkers in pneumonia may be indicators of inflammation or be specific markers released after lung injury due to infection (8). In recent years, numerous investigations have demonstrated that WBCs, CRP, and other biomarkers are effective in the selection of bacterial pneumonia (30). Huang explored the relationship between WBC levels and positive bacterial sputum cultures (31).

The results indicated that a higher WBC count was associated with a greater possibility of acquiring a positive bacterial culture (31). C-reactive protein is a sophisticated biomarker for more complex acute phase features. The application of sole measurements of CRP for diagnosing CAP has not produced positive results constantly (32). However, continuous monitoring of CRP levels is potentially useful for the early prediction of CAP and response to antibiotics (33). In the circumstances of bacterial infection, procalcitonin is produced in large quantities by macrophages and monocytes throughout the body (34). Procalcitonin has been shown to significantly decrease the initiation and duration of antibiotic therapy in pneumonia (35). Additionally, PCT may be a superior diagnostic biomarker for detecting *S. aureus* pneumonia in paediatric patients and may contribute to early β-lactam therapy (36). In this research, children with MRSA pneumonia had significantly higher WBCs, CRP, and PCT levels than children with MSSA pneumonia.

These results suggested that children with MRSA pneumonia experienced more severe infections and, therefore, these indicators may have reflected the severity of the infection. The median hospital stay among children with MRSA pneumonia was higher than that among children with MSSA pneumonia. Our study results also indicated that MRSA cases required more medical resources, resulting in higher economic and social burdens.

Our study faced certain limitations. First, it was difficult to identify colonized bacteria in sputum culture in some cases. Therefore, whether the isolated strains of sputum specimens were colonized bacteria or infectious pathogens was not confirmed. Second, no outside antibiotic history associated with index diseases was obtained, which may also have influenced sputum culture for antimicrobial susceptibility testing.

5.1. Conclusions

Methicillin-resistant *S. aureus* and MSSA were found to mainly occur in infants. No significant differences were detected regarding sex, age and sampling time. The results of antimicrobial sensitivity test in sputum culture of MRSA and MSSA isolates may have shown the sensitivity of antibiotics and guided the application of clinical antibiotics. The common symptoms of children with *S. aureus* pneumonia were fever, cough, and wheezing. Infectious biomarkers, including WBCs, CRP, and PCT may have reflected the severity of infection and guided the prognosis.

Footnotes

Authors' Contribution: Study concept and design: Shu Li Wang, Jun Lin Wang and Yong Dong Yan; analysis and interpretation of data: Shu Hong Sun, Hua Tao, and Li Wang; drafting of the manuscript: Shu Li Wang; critical revision of the manuscript for important intellectual content: Yong Dong Yan, Jun Lin Wang and Ming Ying Han; statistical analysis: Xing Long Wu.

Conflict of Interests: This study was supported by the National Natural Science Foundation of China (81870006). The funders had no role in study design, data collection, analysis, decision to publish, or preparation of the manuscript. We declare that we have no employment, personal financial interest relationships, stocks or shares in companies, consultation fees, patents with other people or organizations that can inappropriately influence our work. There are no personal or professional relations with organizations and individuals (parents and children, wife and husband, family relationships, etc.), unpaid membership in a government or non-governmental organization that could be construed as influencing the position presented in, or the review of, the manuscript entitled. I am not one of the editorial board members or a reviewer of this journal.

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