Research Article

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Streptococcus Mitis Group Infections: Epidemiology, Antibiotic Susceptibility Profile And Risk Factors Evaluation

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1. Abstract

1.1. Aims:
To assess the epidemiological, clinical characteristics of Streptococcus mitis group (SMG) infections, their drug resistance profile, and their relative risk and prevalence for yielding clinical diseases in recent years, we conducted a retrospective cohort study on SMG infected patients in a tertiary hospital of China.

1.2. Methods:
A total of 167 patients with SMG infection were recruited from May 2022 to March 2024 in Anhui. These SMG isolates were identified with MALDI-TOF mass spectrometry. The susceptibility to antibiotics was measured by minimal inhibitory concentrations and Kirby-Bauer disk diffusion methods. The results were grouped and compared based on species.

1.3. Results:
Our results showed that SMG specimen can be isolated from diverse clinical sources including blood, urine, body fluid, et al., with a high resistance rate to erythromycin and clindamycin. Anaemia, hypoproteinemia, elevated C-reactive protein and procalcitonin were the common hematological changes in patients with SMG bloodstream infections. In SMG bacteremia, Streptococcus gordonii (S. gordonii), Streptococcus sanguinis (S. sanguinis) and Streptococcus orals/mitis (S. oralis/ mitis) were the leading group causing infective endocarditis. Patients with risk factor for myocardial disease should be particularly mindful. S. oralis/ mitis bacteremia more occurred in patients with renal transplants progressing to pulmonary infection.

1.4. Conclusion:
In Anhui, β- lactam antibiotics are best superiority in effect on SMG due to low penicillin, ampicillin, ceftriaxone-resistance. Early prevention and diagnosis of bacteremia caused by SMGs are necessary due to their different prevalence for clinical diseases. Overall, this work can provides a reference for clinical diagnosis, treatment and effective infectious diseases control.

2. Keywords:
Streptococcus mitis group; epidemiology; drug resistance; bacteremia; risk factors

3. Introduction

Based on the 16S ribosomal RNA gene sequences, streptococci can be classified into six major groups [1,2]. The well-known Streptococcus mitis group (SMG) is a Gram-positive, alpha-hemolytic species of bacteria that inhabit the oral cavity, colonizes dental plaque and nasopharynx, as well as in the skin, gastrointestinal tract and female reproductive tract. In recent years, SMGs have become important pathogens which are still under investigation concerning epidemiology and clinical characteristics. Streptococci are the most common cause of infective endocarditis (IE), with SMG species being the most common, responsible for 20% of the IE burden [3,4]. SMG consists of a variety of distinct streptococcus species, with characteristics established includingStreptococcus oralis(S. oralis), Streptococcus mitis(S. mitis), and Streptococcus pneumonia(S. pneumoniae), Streptococcus gordonii(S. gordonii), Streptococcussanguinis(S. sanguinis), and Streptococcus parasanguinis(S. parasanguinis) [5]. Most of these members are often

regarded as commensals, presenting a nonvirulent behaviour, yet the alteration of SMG composition and antimicrobial resistance poses a pathogenic potential to cause infectious diseases, and threaten the public health. Some SMG bacteria are commonly found in the heart valves/ endocardium and blood cultures and are recognized as pathogenic organisms in case of infective endocarditis and bacteremia [6-8]. S.mitis and S.oralis inhabit the oropharynx and can cause severe pneumonia, bacteremia, or infective endocarditis in immunodeficient patients who have experienced tissue transplants and cancer [5]. S. pneumoniae, the closest relative to S. oralis /S. mitis, colonizes in the human nasopharynx, causing local infections and entering the bloodstream to cause severe infective septicaemia, endocarditis, meningitis and pneumonia [9].

S. sanguinis and S. gordonii colonize oral biofilms on tooth surfaces and can be released and enter the bloodstream, resulting in systemic and severe infection that includes infective endocarditis and potentially fatal complications. A similar genomic pattern of clinical infective endocarditis and oral isolates was found both in S. sanguinis and S. gordonii, which show different species-specific virulence mechanisms [10]. S. parasanguinisrarely migrates to the bloodstream and results in infective endocarditis [11]. It yet reported a unique S. parasanguinis sepsis case in neonatal endocarditis [12]. To date, few studies have examined the clinical importance of SMG infection. Thus, the association of individual species with disease must be reassessed to recognize important pathogenic traits. Due to genetic recombination and horizontal gene transfer among SMG members, it is often difficult to classify mitis group species [13]. In the clinical diagnosis, through matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) identification, it is possible to distinguish between SMG, except for S. mitis and S. oralisdifferentiation. It is crucial to differentiate SMG species in the laboratory, since misidentification can impact diagnosis and infection treatment. To better understand characteristics of SMG infection, in this retrospective study, we aim to investigate the distribution characteristics, drug resistance, and the association of SMG species with clinical diseases in recent years, which may provide a reference for clinical treatment and effective control of infectious diseases.

4. Materials and Methods

4.1. Strains and data collection

A total of 167 strains were collected from patients with SMG infection (84 S. orali/mitis, 52 S. pneumoniae, 11S. gordonii, 10 S. sanguinis, and 10 S. parasanguinis) at the First Affiliated Hospital of Anhui Medical University in a tertiary hospital of China from 2022.5 to 2024.3. The same isolate of SMG that appeared in cultures from the same patients was excluded. Among the 167 strains, 48 were cases of SMG bloodstream infection. SMG infection was diagnosed by combining clinical presentation and laboratory identification isolated from patients, including blood, other normal sterile foci, and sputum. All patients' clinical information (age, basic diseases and comorbidities, complications, hospitalzation time, laboratory test results, et al.) was retrieved from the hospital's electronic medical system. This study was approved by the Ethics Committee of the First Affiliated Hospital of Anhui Medial University in accordance with the declaration of Helsinki (Reference number: Quick-PJ 2024-01-60). The written informed consent was obtained from patients or legal guardian of patients under 18 years of age.

4.2. Microorganism Identification and drug resistance

Specimens were obtained from blood and normal sterile body fluids, including urine, catheter and drainage fluid, ascites, pleural fluid, bronchoalveolar lavage (BAL), secretion, and non-sterile sputum of SMG - infected patients. The specimens were inoculated onto Columbia blood Agar plates for culture at 35°C for 24h. The blood samples were tested on an automatic microbial identification system (BacT/ALERT 3D, bioMérieux, Marcy l'Étoile, France). SMG bacteremia were determined by more than two blood cultures positive or combined only one blood positive with obvious clinical symptoms. The quality control strain used included S. pneumoniae (ATCC49619). All the bacteria were identified by Matrix-Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI- TOF MS, BioMérieux, France). Antibiotic susceptibility tests were performed by automatic microbial identification and drug sensitivity analysis system using DL-120STREP kit (DL-96A, China) for the minimal inhibitory concentrations (MICs) and performed by Kirby-Bauer disk diffusion. The interpretative criteria for susceptibility and breakpoints for antibiotic drugs were referenced by the Clinical and Laboratory Standards Institute M100 with microdilution and KB method.

4.3 Statistical Analysis

The data were analyzed using the SPSS software version 26.0(SPSS, Chicago, Il, USA). The continuous variables assumed normal distribution were presented as mean ± standard deviation (SD) and compared by Student's t-test and chi-square tests. Data without a normal distribution was described as medians (interquartile range) and examined by the Mann-Whitney U-tests. A comparison of five groups or every two groups used the one-way ANOVA or the Kruskal-Wallis H-test followed by the post-doc Bonferroni correction. The categorical data were compared using chi-square tests or presented as frequency. Statistical significance was determined by two-tailed tests and defined as $p<0.05$.

5. Results

5.1. Clinical distribution characteristics of SMG infection

During the period of two years, a total of 167 patients were admitted and diagnosed with mitis group streptococci infection. Among them, 84 (50.30%),52(31.14%), 11(6.59%), 10 (5.99%), and 10 (5.99%) patients were infected, respectively, with S. oralis/ mitis, S. pneumoniae, S.gordonii, S. sanguinis, and S. parasanguinis, which were identified using MALDI-TOF-MS (Figure 1A).The clinical sources of these bacteria were diverse. As shown in Figure 1B, the S. oralis/ mitis was the predominant species with the highest detection rate (50.30%), coming from different sources, including blood (31%), urine (20%), and puncture fluid (6%) samples. The overwhelming majority (82%) ofS. pneumoniaewas isolated from thoracic airways (including Sputum,BALF,Tracheal),and then from blood (10%).Although found in a small amount, S. gordonii, S. sanguinis

involved in bacteremia infection, were isolated from blood samples in 64% and 80% proportions, respectively. Similarly, S. oralis/ mitis, and S. parasanguinwere isolated from a broad range of sources, including blood, puncture fluid and ascites, in each accounting for 20%.

5.2. Antimicrobial susceptibilities of the mitis group streptococci

According to CLSI and EUCAST guiding criteria, Table 1 presents the in vitro susceptibility of SMG isolates from patients to common antimicrobial agents. Specifically, no resistance of these 5 common SMG bacteria (S. oralis/ mitis, S. pneumoniae, S. gordonii, S. parasanguin and S. parasanguinis) to vancomycin and linezolid was observed, except one S. oralis/ mitis strain, which showed moderate resistance to linezolid. The resistance analysis of S. oralis/ mitis showed that the resistance rate to erythromycin and clindamycin, levofloxacin, and ceftriaxone was relatively variating form high to moderate, with 78.3%, 53.1%, 39.5% and 38.1% resistance, respectively. However, their resistance rates to penicillin and ampicillin were relatively low, with 29.6% and 34.4% resistance, respectively. Regarding the isolated S. pneumoniaes, the high resistance rates were observed against erythromycin, clindamycin and cotrimoxazole, with 92.2%, 82.4% and 64.0% resistance, followed by 47.1%, 47.1%, and 23.8% resistance to penicillin, ampicillin and chloramphenicol. In contrast, no resistance was observed when tested against moxifloxacin.S. gordonii, S. sanguinis were susceptible to almost all tested antibiotics, except erythromycin, which showed 45.5% and 40.0% resistance rates, respectively. Moreover, S. gordoniiwas non-susceptible to clindamycin with 72.7% intermediate resistance, while the resistance rate of S. sanguinis to clindamycin was 40%. The resistance rate of S. parasanguinisto erythromycin (80%), clindamycin (60%), levofloxacin (60%) and ceftriaxone (50%) exceeds 50%, presenting high and multiple drug resistance. To penicillin and ampicillin, S. parasanguinis exhibited medium resistance.

Table 1. Susceptibility of SMG species to antimicrobial agents

Antimicrobial agent	S. Oral/mitis			S.pneumoniae			S.gordonii			S. sanguinis			S.parasanguinis			total		
	N	R%	S%	N	R%	S%	N	R%	S%	N	R%	S%	N	R%	S%	N	R%	S%
Erthromycin	83	78.3	10.8	51	92.2	7.8	11	45.5	45.5	10	40	60	10	80	0	165	78.1	14.5
Clindamycin	81	53.1	39.5	51	82.4	13.7	11	9.1	18.2	10	40	60	10	60	40	163	58.9	31.3
Levofloxacin	81	39.5	50.6	49	4.1	93.9	11	18.2	81.8	10	10	90	10	60	40	161	26.7	67.7
Penicillin G	27	29.6	25.9	51	47.1	51	8	0	37.5	2	0	100	3	33.3	0	91	36.3	41.8
Ampicillin	32	34.4	25	51	47.1	51	8	0	62.5	2	0	100	3	0	0	96	36.5	42.7
Ceftriaxone	84	38.1	60.7	20	0	95.2	11	0	90.9	10	0	90	10	50	50	135	27.4	69.6
Vancomycin	84	0	100	51	0	100	11	0	100	10	0	100	10	0	100	166	0	100
Linezolid	84	0	98.8	51	0	100	11	0	100	10	0	100	10	0	100	166	0	99.4
Chloramphenicol				21	23.8	76.2										21	23.8	76.2
Cotrimoxazole				50	64	18										50	64	18
Moxifloxacin				26	0	96.15										26	0	96.2

Note: Nindicates number of patients.R indicates resistant rate and S indicates susceptible rate.

5.3. Clinical characteristics of bloodstream infection caused by SMG

The oral SMGs are commensals, but may invade the blood and cause invasive infections such as bacteremia and infective endocarditis, which area leading cause of threaten human health. Data of 48 patients with bloodstream infection by SMG were collected and further analyzed to investigate the clinical importance of SMG bacteremia.

5.3.1. Laboratory results

Anaemia (43/48, 90%) and hypoproteinemia (43/48, 90%) were the common haematological changes caused by SMG bacteriain patients with bloodstream infections (Table 2). Significant pathological difference was observed, including reduced albumin (ALB) among patients with SMG bacteremia (P=0.003) and changes in aspartate aminotransferase (ALT) in S.gordonii and S. sanguinis infected patients (P=0.015). As shown in Table 2, there were 42/48 (87.5%) patients with an elevated C-reactive protein (CRP) and 22/48 (48.9%) patients with increased procalcitonin (PCT), although these laboratory results did not show significant differences (P>0.05) among 5 common SMG bacteremia. The significant difference in ALT was observed among SMG bacteremia, with higher ALT in S. gordonii infected patients (P=0.045). An epidemiological feature of patients with S. pneumoniae bacteremia was that S. pneumoniae bloodstream infection mainly occurred in children under 5 years oldwith significant difference of P=0.000 (Table 3). For patients with S. pneumoniae bloodstream infection, white blood cell (WBC) count was significantly elevated, compared with other S. oralis/ mitis (P=0.027), S. gordonii(P=0.025), S. sanguinis (P=0.044), and S. parasanguinis(P=0.019). Although the results of RBC and PLT were within the normal range, there were statistically significant differences among patients with 5 common SMG bacteremia (P=0.021 and P=0.001).

Table 2: Laboratory results of bacteremic patients infected by Streptococcus mitis group

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	Streptococcus oral/mitis	Streptococcus pneumoniae	Streptococcus gordonii	Streptococcus sanguinis	Streptococcus parasanguinis	P
	(N=26)	(N=5)	(N=7)	(N=8)	(N=2)	
Elevated WBC (>9.5x109/L)	6 (23.1)	5 (100.0)	2 (28.6)	4 (50.0)	0 (0.0)	0.008
WBC	6.73±4.43	23.39±11.02	6.58±3.25	9.20±2.51	4.75±1.10	0.004
(x109/L)						
RBC	3.45±0.65	4.44±0.82	3.07±1.03	3.31±0.63	4.07±0.33	0.021
(x1012 /L)						
Reduced Hb	22(84.6)	4 (80.0)	7 (100.0)	8 (100.0)	2 (100.0)	0.617
(Anemia)						
Hb	100.84±20.84	112.2±17.34	85.00±26.60	88.5±26.55	88.5±17.23	0.078
(g/L)						
PLT	146.00±85.26	368.4±100.03	163.85±138.74	181.13±78.09	216.00±83.44	0.001
(x109 /L)						
TP	59.23±6.75	71.08±11.23	61.70±9.78	58.06±10.65	66.20±14.57	0.066
(g/L)						
Reduced ALB	24 (92.3)	3 (60.0)	7 (100.0)	8 (100.0)	1 (50.0)	0.05
(hypoproteinemia						
ALB	33.00±4.71	39.96±6.16	31.56±2.78	29.83±5.72	41.45±8.56	0.003
(g/L)						
GLO(g/L)	25.85±5.66	31.12±6.37	30.14±8.05	28.24±9.08	24.75±6.01	0.361
TBIL	12.55(8.45-17.05)	10.76±2.92	10.70(9.00-20.60)	11.69±4.82	8.05±0.07	0.539
(μmol/L)						
Elevated ALT	9 (34.6)	1 (20.0)	4 (57.1)	1 (12.5)	0 (0.0)	0.377
ALT	26.50(15.50-46.75)	18.00(11.00-76.00)	83.57±67.82	19.00(9.00-19.00)	10.50±2.12	0.045
(U/L)						
Elevated AST	13 (50.0)	2 (40.0)	3 (42.9)	1 (12.5)	1 (50.0)	0.436
AST	39.00(21.00-57.25)	61.60±53.30	33.00(16.00-147.00)	22.00(17.00-27.50)	33.00±19.80	0.312
(U/L)						
Urea	10.98±7.23	3.60±0.77	5.24(3.84-12.56)	6.64±5.09	5.48±2.22	0.074
(mmol/L)						
Elevated CRP	21 (80.8)	5 (100.0)	7 (100.0)	8 (100.0)	1 (50.0)	0.201
(>10 mg/L)						
CRP	35.11(12.93-111.93)	87.24±83.21	69.28±40.05	63.58±43.49	42.74±60.37	0.654
(mg/L)						
Elevated PCT	15 (60.0)	2 (50.0)	3 (42.9)	2 (28.6)	0 (0.0)	0.371
(>0.5ng/mL)						
PCT	1.54(0.20-10.05)	2.25±2.65	0.34(0.25-0.96)	0.17(0.10-0.81)	0.11±0.08	0.189
(ng/mL)						

Notes: Data are expressed as mean ± standard deviation (SD), and number (%) of patients. Elevated ALT: male >50 U/L and female > 40 U/L; Elevated AST: male > 40 U/L and female > 35 U/L; Elevated CRP: >10mg/L; Elevated PCT: > 0.5ng/mL; Elevated WBC (>9.5x109/L); Reduced Hb: male <130 g/L and female< 115g/L;Reduced ALB: <40g/L. Range of normal values: Hb, male (130–175) g/L and female (115–150) g/L; WBC, (3.5–9.5)×109/L; RBC, male (4.0–5.5) and female (3.5-5.0)×1012 /L;PLT, (125–350)×109/L; CRP, (0.00–10.00) mg/L; PCT, (0.00–0.50) ng/mL; ALT, male (9–50) U/L and female (7–40) U/L; AST, male (15–40) U/L and female (13–35) U/L; TP, (65.0–85.0)g/L; ALB, (40.0–55.0) g/L; GLO, (20.0–40.0) g/L; TBIL, (0.0–23.0) μmol/L; Urea, male (3.10–8.00) mmol/L and female (2.60–7.50) mmol/L.

Abbreviations: Hb, hemoglobin; WBC, white blood cell; RBC, red blood

cell; PLT, platelet; PCT, procalcitonin; ALT, aspartate aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; TP, Total Protein; ALB, albumin; GLO, globulin; TBIL, total bilirubin.

5.3.2. Infective endocarditis

According to Kim et al. [7], 70% of streptococcal IE is attributed to SMG. Moreover, a previous study reported that the most common SMG causing IE were S. gordonii, S. sanguinis and S. oralis/ mitis, with a high prevalence of 44.2%, 34.6% and 19.4%, respectively. Besides, S. pneumoniae was with a low but considerable prevalence of 1.2% [8]. Consistent with previous studies, we found that among the five common SMG studied here, S. gordonii (57.14%, 4/7), S. sanguinis (37.5%, 3/8) and S.oralis/mitis (3.85%, 1/26) were the main invasive SMG bacteria causing IE (P=0.002). A pairwise comparison confirmed that the classification of pathogenicity to cause IE:S.gordonii was more epidemic than S. oralis/ mitis (P=0.004), while S. sanguinis epidemicity was higher than that of S. oralis/ mitis (P=0.033). As shown in table 3, underlying diseases such as diabetes, myocardial disease, and kidney transplant were shown to be associated factors in five SMG bloodstream infection. For instance, risk factors of myocardial disease showed significant differences in pathogenicity between S. gordonii and S. oralis/ mitis (P=0.042), and between S. sanguinis and S. oralis/ mitis (P=0.040). When compared patients with bacteremia infected by five SMG, the outcomes of those did not show significant differences (P>0.05).

5.3.3. SMG infection characteristics in renal transplant progression to pulmonary infection patients

Here, we investigated the clinical presentations and epidemiology of bloodstream infections by SMG in renal transplant progression to pulmonary infection patients. Our results showed that the potential for each of the five SMG species to cause SMG bacteremia in renal transplant progression to pulmonary infection patients was remarkably and significantly variable (P=0.008) (Table 3). S. oralis/ mitis (46.15%, 12/26) was the most predominant cause of bacteremia in renal transplant progression to pulmonary infection patients, and this pathogenicity was significantly difference compared with that of S. gordonii(P=0.032).

Table 3: Baseline demographic and epidemiological characteristics of bloodstream infected patients by Streptococcus mitis group (N = 48).

Clinical characteristics	Streptococcus oral/ mitis (N=26)	Streptococcus pneumoniae (N=5)	Streptococcus gordonii(N=7)	Streptococcus sanguinis (N=8)	Streptococcus parasanguinis (N=2)	P
Gender						
Male	17	3	5	7	2	0.732
Female	9	2	2	1	0	0.732
Age						
0-11 years	1	4	0	0	0	0
12-45 years	14	0	1	5	2	0.022
>45 years	11	1	6	3	0	0.101
Mean hospitalization time (day)						
≤7 days	1	2	1	2	0	0.084
7-14 days	2	1	1	1	2	0.036
>14 days	23	2	5	5	0	0.011
Risk factors						
Invasive intervention/procedure	9	1	5	3	0	0.326
Catheter intubation	4	1	2	2	0	0.863
Surgery	7	1	3	4	0	0.502
Hemodialysis/Peritioneal dialysis	5	0	0	0	0	
Immunosuppressive state	10	0	1	1	0	0.341
Underlying disease						
Diabetes	1	0	1	2	2	0.01
Cancer	5	1	1	3	0	0.879
Myocardial disease	4	0	4	4	0	0.017
Hepatobiliary disease	4	0	5	2	0	0.064
Nephropathy (kidney disease)	9	0	4	2	2	0.132
Cerebral vascular disease	3	0	0	2	0	
Chronic respiratory disease	15	4	3	3	2	0.506
leukemia	1	0	1	0	0	0.507

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Kidney transplant	12 (46.15%)	0	0	1(12.5%)	2 (100%)	0.008
Concomitant other bacterial infection	7	0	0	0	1	
Infective endocarditis	1(3.85%)	0	4 (57.14%)	3 (37.5%)	0	0.004
Outcome						
Improvement	21	5	5	8	2	0.649
Deterioration	2	0	2	0	0	0.679
Death	3	0	0	0	0	

Note: Data are expressed as number and number (%) of patients.

6. Discussion

Although SMG's virulence is generally considered low, it can still cause severe infections in infants, the elderly patients, and immunocompromised patients. In particular, oral streptococci often cause severe disease when the organisms migrate from the oral cavity into the bloodstream. Infection with SMG is a complex event, generally associated with the host's weak immune state. Isolating and characterizing a typical SMG organism makes it easy to prevent the eventual occurrence of severe infection and treat associated diseases. Hence, we isolated five main SMGs and investigated their antimicrobial susceptibilities, prevalence, and risk of causing relative diseases in SMG bloodstream infection. First, in our study, the total resistance rates of all SMG to erythromycin and clindamycin were 78.1% and 58.9%, respectively. This result is basically consistent with other previous studies [14,15]. Moreover, our results align with that of Basaranogluet al., where they observed that S.mitis/oralis strains were susceptible to linezolid and vancomycin according to CLSI guidelines and EUCAST guidelines [16] However, in that same study [16], they found that the S. mitis/ oralisresistance rate to penicillin was 45.2%, which was higher than that in our study (29.6%). Furthermore, our results are inconsistent with those of Suzuk et al. [17] and Chun et al. [18], which showed a higher resistance rate of S. mitis/ oralisto penicillin, ampicillin, and erythromycin, especially found above 50% resistance.

The United Arab Emirates reported that the resistance rate of S. pneumoniae to β-lactam antibiotics decreased, while that to levofloxacin, trimethoprim/ sulfamethoxazole, moxifloxacin and erythromycin increased [19]. Inconsistent with this result, our study showed high resistance rates of S. pneumoniae to erythromycin (92.2%), clindamycin (82.4%) and sulfamethoxazole (64%), and increased resistance rates to penicillin (47.1%), ampicillin (47.1%).Our data suggested levofloxacin, moxifloxacin and ceftriaxone with high sensitive rate, are the most effective antibiotics for treatment of S. pneumoniae infection. In our study, S. gordonii and S. sanguinis showed increased resistance rates to erythromycin and clindamycin. It was inconsistent with that of Smith A et al., where they observed that S. sanguinis is sensitive to erythromycin and clindamycinin a hospital in Glasgow, England [20], but similar to another study showing that the insensitive rates of S. sanguinis to clindamycin and erythromycin were 16.3% and 36.5%, respectively [18]. Different drug resistance rates of SMG in various regions, may be due to the empirical use of antibiotics and epidemic drug-resistant strains in each region. Thus, in Anhui province, SMG strains were highly resistant to erythromycin and clindamycin, while sensitive to vancomycin, linezolid and β- lactam antibiotics. In cases of treatment of β- lactam sensitive SMG infection, β- lactams implies superiority in effect than vancomycin. Secondly, blood culture or valve culture is typically the first step to detect microorganismsinIE diagnosis.The results of our study align with those from a previous report [8] showing that S. sanguis, S.gordonii and S. orals/ mitis were the three most common strains to cause IE, but some different from the data of epidemiological characteristics of species prevalence in Spain [21]. In our study, the higher risk of causing IE was associated with S. gordonii (57.14%) and S. sanguis (37.5%), while the lowest risk of developing IE was associated with S. orals/ mitis (3.85%). However, there was no IE prevalence with S. pneumoniae and S. parasanfuinis bacteremia. S. gordonii and S. sanguis proved to be the numerically dominant species, which confirms that they are the most important of the oral streptococci associated with IE in Anhui. Differently, S. orals/ mitis induced IE was uncommon. It was speculated that there may be regional differences in the prevalence and pathogenicity of SMG isolates. Because these S. gordonii, S. sanguis and S. orals/ mitis are isolated from the blood culture of infective endocarditis patients, carrying pathogenic features particularly relevant to IE. More research in the future focus on the pathogenic mechanisms of these SMG. Infective endocarditis can be treated with parenteral sensitive antibiotics. In addition to targeted antimicrobial therapy, early surgical intervention has been shown to reduce mortality and embolic events with large vegetation.

Thirdly, compared with other SMG bacteria, S. oralis/ mitisshowed a higher predilection for bacteremia in renal transplant progression to pulmonary infection patients. Our finding suggests that more attention should be paid to the S. oralis/ mitisbacteremia in renal transplant patient, especially those with pulmonary infections, since the exact pathogenesis and connection are unclear. The origin of S. oralis/ mitis bacteremia might from the kidney and urinary tract. A review highlighted that Gram-positive cocci were the predominant bacteria in our oral cavity with S. oralis/ mitis accounting for 87.3% [22]. The oral cavity is a site where many important species causing bloodstream infection, so S. oralis/ mitishas greater opportunities and advantages entering the bloodstream to cause bacteremia in immunodeficient patients. In addition, in our study, almost 50% of patients suffer from pulmonary infections among each type of SMG bacteremia, except S. pneumoniaebacteremia with higher (80%) pulmonary infection. Pulmonary infections are the leading cause

of morbidity and mortality in renal transplant recipients [23,24]. The S. oralis/ mitisas a concurrent bacterial infection may be associated with pulmonary infection. Moreover, the interaction mechanism between the host immune system and S. oralis/ mitis is of great importance and needs further investigation . A little report showed S. parasanguinis invading the bloodstream, and it was a common cause of bacterial subacute endocarditis when access to the bloodstream [25]. However, in our analysis, two S. parasanguinisbacteremia were observed in renal transplant patients with complications including pulmonary infection and diabetes. Due to the small number of samples, it was not statistically significant. In the future, more cases of S. parasanguinis bacteremia must be collected to identify clinical outcomes. Fifty percent of severe pneumonia is due to S. pneumoniae infection, non-invasiveS. pneumoniae is the leading cause of pneumococcal disease [26]. Similarly, in our analysis, ~80% of specimens of pneumonia patients were from thoracic (sputum, BALF, tracheal cannula). Pneumococcal disease caused by invasive S. pneumoniae resulted in high case fatality rates of 5% to 20% for bacteremia[27]. Although there were limited cases of only 5 Streptococcus pneumoniae bacteremia, a trend that S. pneumoniae bacteremia often occurred in hospitalized children under five years of age was also found in our study. Our study about bacteremia in hospitalized children is limited by incomplete culture or the use of antibiotics before culture. More blood culture data are needed to assess bacteremia's prevalence and clinical characteristics in children. Due to certain limitations with a relatively small number of patients, our study can not draw a causal relation between species and disease as the risk factor, it should provide a reference for clinical diagnosis and treatment.

7. Conclusion

In summary, in the last two years, this study reported the distribution and antimicrobial susceptibilities of SMG. Streptococcus mitis group species with closely related phylogenetically showed different prevalence and risk of clinical disease in bloodstream infection patients in Anhui, China.Anaemia, hypoproteinemia, elevated C-reactive protein and procalcitonin were the common hematological changes in patients with SMG bloodstream infections. S. gordonii and S. sanguinis epidemicity to cause IE were higher than that of S. oralis/ mitis. Compared with S.oralis/mitis, the common risk factors of S. gordonii and S. sanguinis infection in IE patients in Anhui is myocardial disease. Patients with myocardial disease should be mindful of S. gordonii and S. sanguinis infection, which develops into IE. In addition, S. oralis/ mitis bacteremia occurred more frequently in renal transplant progression to pulmonary infection patients, compared with S. gordonii. Thus, in renal transplant patients, early prevention and diagnosis of bacteremia caused by S. oralis/ mitis are necessary. At last, our data suggested that β- lactam antibiotics are best superiority in effect on SMG due to low penicillin, ampicillin, ceftriaxone-resistance in Anhui, while macrolides (erythromycin) and lincoamides (clindamycin) are likely to be inferior. This work provides a reference for improving strategies for prevention, diagnosis and treatment of SMG infection in other places.

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