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Original Article

Clinical and microbiological features of *Streptococcus anginosus* group infections: a 7-year retrospective study in Vietnam

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Abstract

Introduction: The *Streptococcus anginosus* group (SAG) is emerging as a significant cause of invasive infections, yet data from Vietnam remain scarce. This study characterized the clinical features and outcomes of SAG infections in Ho Chi Minh City.

Methodology: We retrospectively reviewed patients with culture-confirmed SAG infections at the Hospital for Tropical Diseases (January 2017–August 2023). Demographics, clinical, and microbiological data were analyzed.

Results: A total of 82 patients (mean age 50.6 ± 16.8 years; 64.6% male) with culture-confirmed SAG infections were included. Comorbidities were present in 56.1% of patients, with diabetes mellitus being the most common (23.2%). *S. anginosus* was the most frequently isolated species (43.9%), followed by *S. constellatus* (34.1%) and *S. intermedius* (22.0%). Bacteremia (35.4%) and intra-abdominal infections (31.7%, mainly hepatic abscesses) were the predominant clinical presentations. Polymicrobial infections occurred in 14.6% of cases, primarily among patients with bacteremia and skin or soft tissue infections. All isolates remained susceptible to ceftriaxone and vancomycin, and 94.3% to ampicillin, but susceptibilities were lower to penicillin (84.3%), erythromycin (65.7%), clindamycin (54.3%), and tetracycline (54.3%). Despite a 92.7% cure rate, 19.5% required drainage procedures, and the 28-day mortality rate was 6.1%.

Conclusions: In this cohort, SAG infection most often present as occult bacteremia or hepatobiliary abscess, frequently in patients with comorbidities, but not restricted to immunocompromised hosts. Empirical β-lactam therapy (ampicillin or ceftriaxone) remains appropriate, although rising penicillin and macrolide resistance and the 15% polymicrobial rate, may warrant broader initial coverage when deep soft-tissue foci are suspected.

Key words: abscesses; bacteremia; *Streptococcus anginosus* group; SAG.

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Introduction

The *Streptococcus anginosus* group (SAG), previously known as the *Streptococcus milleri* group, comprises three primary species: *Streptococcus anginosus*, *Streptococcus intermedius*, and *Streptococcus constellatus* [1]. Traditionally considered benign commensals of the human mucosa, these bacteria have emerged as significant pathogens capable of causing invasive pyogenic infections in various body sites, including the lungs, liver, brain, abdomen, and soft tissues [2,3]. SAG organisms are facultatively anaerobic, catalase-negative, Gram-positive cocci that exhibit variable hemolytic patterns on blood agar [4]. They are distinguished by their ability to produce abscesses and empyema [1]. Recent studies indicate that the incidence of SAG infections exceeds that of infections caused by *Streptococcus pyogenes* and *Streptococcus agalactiae* combined [5].

Despite the global recognition of SAG as important pathogens, there is a paucity of data on their clinical impact in Vietnam. Understanding the local epidemiology, clinical features, and antimicrobial susceptibility patterns is crucial for effective management. This study aims to fill this gap by investigating the clinical presentations, microbiological characteristics, treatment outcomes, and antimicrobial susceptibility profiles of SAG infections in patients admitted to a major infectious disease hospital in Ho Chi Minh City, Vietnam.

Methodology

Study design

We conducted a retrospective cohort study at the Hospital for Tropical Diseases, a 550-bed tertiary care center specializing in infectious diseases in Ho Chi Minh City, Vietnam. All consecutive patients with culture-confirmed SAG infection managed between January 2017 and August 2023 were eligible. Ethical approval was obtained from the Biomedical Research Ethics Council of the Hospital for Tropical Diseases (Approval No. 3811/QD-BVBNĐ). Due to the retrospective, observational nature of the study, the informed consent requirement was waived. Patient confidentiality was maintained throughout the study.

Patient selection

Patients were included if they met both the following criteria: (i) microbiological isolation of *Streptococcus anginosus* group (*S. anginosus*, *S. constellatus*, or *S. intermedius*) from sterile sites (blood, cerebrospinal fluid, peritoneal/pleural fluid, abscess aspirates) or non-sterile specimens (lower respiratory tract, urine); and (ii) compatible clinical presentation (e.g., fever, abscess formation, or organ-specific manifestations). Exclusion criteria comprised: (i) admission for unrelated conditions without SAG-suggestive symptoms, if the culture result was judged to be an incidental finding, or (ii) incomplete medical records.

Data collection

Data were extracted retrospectively from the hospital's electronic health records using a standardized collection form. The extracted information included: (1) demographic characteristics (age, gender, and comorbidities including diabetes mellitus, hypertension, chronic renal failure, cirrhosis, heart valve disease, and human immunodeficiency virus (HIV) infection status); (2) clinical presentation at admission (documented signs and symptoms); (3) laboratory findings upon presentation (complete blood counts, C-reactive protein levels (CRP)), and liver/renal function tests); (4) microbiological data, including microbial identification and antimicrobial susceptibility test results; and (5) clinical outcomes, namely clinical cure, 3-month recurrence, 28-day all-cause mortality, and the need for surgical or wound debridement. Clinical cure was defined as resolution of presenting signs and symptoms at discharge, supported, as applicable, by objective improvement (improvement or normalization of white blood cell or CRP; radiologic regression of abscesses; or radiographic improvement on chest X-ray for pneumonia). Follow-up for recurrence was conducted at 90 days via phone call or review of subsequent medical records. Recurrence was defined as the re-emergence of clinical or radiological evidence of infection within this 90-day period. Separately, 28-day all-cause mortality encompassed any death occurring within 28 days of treatment initiation.

Bacterial identification and antibiotic susceptibility

The patient's blood was inoculated into blood culture bottles of an automated system, including BD BACTEC™ (Becton Dickinson, Sparks, MD, USA) and the Bact/Alert Blood Culture System (bioMérieux, Marcy L'Étoile, France). When a bottle tested positive, the blood was cultured on blood agar and incubated at 35 °C in a 5% CO_2 incubator. Other samples were inoculated directly onto blood agar and incubated under the same conditions. Initial presumptive identification of the SAG was based on the morphology of Gram-positive, non-motile, non-spore-forming cocci that exhibit microaerophilic or anaerobic growth, produce minute colonies with alpha-, beta-, or no hemolysis, emit a distinctive caramel odor, and test negative for catalase. Any culture containing more than one organism was considered polymicrobial. Species-level identification was subsequently confirmed using the matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry system (Bruker Daltonics, Bremen, Germany). Antimicrobial susceptibility testing was performed using the automated VITEK 2 system (bioMérieux, Marcy L'Étoile, France) with the VITEK® 2 AST-ST03 testing. Antimicrobial susceptibility breakpoints were interpreted using the current Clinical and Laboratory Standards Institute (CLSI) M100-S24 guidelines for the *Streptococcus* spp. Viridans Group [6]

Statistical analyses

Analyses were conducted using SPSS v22.0 (IBM Corp., Armonk, NY, USA). Continuous variables are reported as mean ± standard deviation (SD) or median [interquartile range (IQR)] based on distribution; categorical variables as frequencies (%). Intergroup comparisons utilized Chi-square or Fisher's exact tests (categorical data), and Student's t-test or Mann-Whitney U test (continuous data). Associations were quantified via odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was defined as $p < 0.05$.

Results

Demographic and clinical characteristics

A total of 94 patient records with cultures positive for SAG were initially identified from the bacterial laboratory database. Of these, 12 records were excluded for specific reasons: 10 due to the absence of a compatible clinical syndrome and 2 due to incomplete medical records. Consequently, the final study cohort comprised 82 patients who met the eligibility criteria. The mean age was 50.6 ± 16.8 years (range 2–91 years), and 64.6% were male. Comorbidities were documented in 56.1% of patients, with diabetes mellitus being the most prevalent (23.2%), followed by hypertension (21.9%) and chronic renal disease (19.5%). A subset of patients (6.1%, 5/82) were HIV-positive with 4 having CD4 counts below 100 cells/μL and one having a CD4 count of 450 cells/μL. Additionally, 7.3% (6/82) of patients had documented dental caries and had undergone dental procedures within the preceding 3 months. Detailed demographic, comorbidity, and clinical data are presented in Table 1.

Patients infected with *Streptococcus anginosus* display a diverse range of clinical symptoms. Fever was observed in nearly all patients (97.6%), with a median duration of 6 days [IQR 3–8] and a maximum duration of 30 days. Laboratory evaluations revealed elevated inflammatory markers, including leukocytosis with neutrophilic predominance and CRP, as well as elevated liver enzymes (Table 1).

Sites of infection

The distribution of infection sites is summarized in Table 2. Occult bacteremia was the most common presentation, identified in 35.4% (29/82) of patients. Intra-abdominal infections were the second most common, accounting for 31.7% (26/82) of cases. Within the intra-abdominal group, hepatic abscesses predominated (20/26, 76.9%). All patients with hepatic abscesses presented with fever (100%), while 45% experienced abdominal pain, and 20% reported vomiting or diarrhea. Most hepatic abscesses were solitary (80%), predominantly located in the right lobe (75%), and had a median size of 59 [38–79] mm. Other intra-abdominal infections included peritonitis (n = 4), biliary tract infections (n = 1), and a splenic abscess (n = 1). Skin and soft tissue infections comprised 18.3% (15/82) of cases. Of these, 8 involved infections of the head, face, or neck; and 7 were furuncle cases affecting the arms, legs, and perianal regions. Multiple infection sources were identified in 3 cases (3.7%): one with a liver abscess and infective endocarditis, one with a soft tissue abscess accompanied by purulent meningitis, and one with an abscess at the mandibular angle accompanied by purulent meningitis.

Overall, 46 of 82 patients (56.1%) developed infections characterized by abscesses or empyema, underscoring the propensity of SAG to form localized collections.

Species distribution

The distribution of the three main pathogenic organisms is shown in Table 2. Overall, *S. anginosus*

Table 1. Demographic, clinical, and laboratory characteristics of patients with *Streptococcus anginosus* group infection (n = 82).

Characteristics	n (%)
Age (years), mean ± SD	50.6 ± 16.8
Male, n (%)	53 (64.6)
Comorbidities, n (%)	
No	36 (43.9)
Yes	46 (56.1)
Diabetes mellitus	19 (23.2)
Hypertension	18 (21.9)
Chronic renal failure	16 (19.5)
Cirrhosis	14 (17.1)
Heart valve disease	7 (8.5)
HIV/AIDS	5 (6.1)
Dental caries/undergone dental procedures , n (%)	6 (7.3)
Signs and symptoms at admission, n (%)	
Fever	80 (97.6)
Cutaneous soft tissue lesions	15 (18.3)
Digestive symptoms	10 (12.2)
Neurological symptoms	4 (4.9)
Urinary symptoms	4 (4.9)
Respiratory symptoms	3 (3.7)
Shock	2 (2.5)
Hypoxemia	2 (2.5)
Laboratory tests at admission, median [IQR]	
White blood cells (× 10^9 cells/L)	14.5 [12.1–16.7]
Neutrophils (× 10^9 cells/L)	12.2 [8.5–14.7]
Lymphocytes (× 10^9 cells/L)	1.04 [0.55–2.13]
Hemoglobin (g/dL)	11.6 [10.4–13.5]
AST (U/L)†	57.0 [39.0–101.0]
ALT (U/L) †	68.0 [41.0–120.0]
CRP (mg/L) ‡	75.4 [30.6–104.2]
Creatinine (μmol/L)	90.5 [78.1–122.5]
Outcomes, n (%)	
Required surgery or wound debridement	**16 (19.5)**
Clinical cure	76 (92.7)
3-month recurrence	1 (1.2)
28-day all-cause mortality	5 (6.1)

SD: standard deviation; IQR: interquartile range; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CRP: C-reactive protein; PaO_2: partial pressure of oxygen; SpO_2: peripheral capillary oxygen saturation; HIV/AIDS: human immunodeficiency virus/acquired immunodeficiency syndrome.

Gastrointestinal symptoms: nausea, vomiting, abdominal pain, diarrhea, or progressively increasing ascites (in cirrhotic patients). Respiratory symptoms: cough, shortness of breath, pleuritic chest pain or abnormal breath sounds. Urinary symptoms: dysuria, urinary urgency, urinary frequency, cloudy or foul-smelling urine, or hematuria. Neurological symptoms: headache, altered mental status, photophobia, seizures, weakness, or numbness. Shock: persisting hypotension requiring vasopressors to maintain a mean arterial pressure of ≥ 65 mmHg. Hypoxemia: either an SpO_2 level below 90% on ambient air or a PaO_2 level below 60 mmHg, as determined by arterial blood gas analysis. † AST and ALT values were available for n = 58 patients. ‡ CRP values were available for n = 62 patients.

Table 2. Distribution of infection sites among *Streptococcus anginosus* group isolates (n = 82).

Infection site	Total, n (%)	*S. anginosus* (n = 36)	*S. constellatus* (n = 28)	*S. intermedius* (n = 18)
Occult bacteremia	29 (35.4)	15	11	3
Intra-abdominal infection	26 (31.7)	8	6	12
Liver abscess	20 (24.4)	3	5	12
Spontaneous bacterial peritonitis	3 (3.7)	3	0	0
Spleen abscess	1 (1.2)	0	1	0
Biliary tract infection	1 (1.2)	1	0	0
Secondary bacterial peritonitis	1 (1.2)	1	0	0
Skin and soft tissue infection	15 (18.3)	4	9	2
Cervicofacial	8 (9.8)	0	8	0
Extremity and trunk	7 (8.5)	4	1	2
Purulent meningitis	4 (4.9)	1	3	0
Endocarditis (with vegetation)	4 (4.9)	3	1	0
Urinary	4 (4.9)	4	0	0
Pleuropulmonary	3 (3.7)	1	1	1
Pneumonia with empyema	2 (2.4)	0	1	1
Pneumonia	1 (1.2)	1	0	0

Three cases with more than 2 infection sites: 1 case of liver abscess with endocarditis, 1 case of cellulitis with meningitis, 1 case of head and neck abscess with meningitis.

was the most frequently isolated pathogen (43.9%), followed by *S. constellatus* (34.1%), and *S. intermedius* (22.0%). Statistically significant differences in the distribution of these organisms across various infection sites were observed. *S. intermedius* had a strong propensity for forming abscesses and deep tissue infections (15/18 cases).

Polymicrobial infections were identified in 12 patients (14.6%). These infections involved both normal flora, primarily Gram-positive anaerobes, and Gram-negative bacteria, including *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Table 3 details the clinical and microbiological characteristics of these patients, with skin and soft tissue infections (6 patients) and occult bacteremia (5 patients) being the predominant presentations, and one patient presenting with meningitis.

Table 3. Clinical and microbiological characteristics of patients with *Streptococcus anginosus* group (SAG) infections and co-infections (n = 12).

Patient	Age, gender	Comorbidities	Site of infection	SAG isolate grown	Co-infection		
					Gram-negative bacteria	Gram-positive bacteria	Anaerobic bacteria
1	20, M	-	Skin and soft tissue infection	*S. constellatus*	-	-	*Eikenella corrodens*
2	29, F	-	Skin and soft tissue infection	*S. constellatus*	*Klebsiella pneumonia*	-	-
3	41, M	-	Skin and soft tissue infection	*S. constellatus*	-	-	*Peptoniphilus harei*
4	55, M	Cirrhosis Diabetes mellitus	Skin and soft tissue infection	*S. intermedius*	-	*Streptococcus oralis*	-
5	63, M	Diabetes mellitus	Skin and soft tissue infection	*S. anginosus*	*Escherichia coli*	-	-
6	64, M	Cirrhosis	Skin and soft tissue infection	*S. anginosus*	*Escherichia coli*	-	-
7	35, M	HIV	Occult bacteremia	*S. anginosus*	*Pseudomonas aeruginosa*	*Staphylococcus argenteus*	-
8	52, M	Cirrhosis	Occult bacteremia	*S. anginosus*	-	*Streptococcus oralis* *Streptococcus salivarius*	-
9	57, M	-	Occult bacteremia	*S. anginosus*	*Escherichia coli* *Pseudomonas aeruginosa*	-	-
10	63, F	Cirrhosis	Occult bacteremia	*S. anginosus*	-	*Streptococcus cristatus*	-
11	59, M	Diabetes mellitus	Occult bacteremia	*S. constellatus*	-	-	*Pavimonas micra*
12	87, F	Diabetes mellitus	Meningitis	*S. anginosus*	*Escherichia coli*	-	*Actinomyces urogenitalis* *Bacteroides thetaiotaomicron* *Clostridium innocuum*

HIV: human immunodeficiency virus.

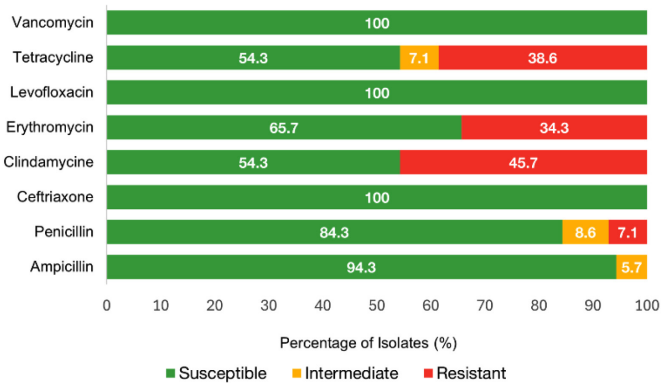
Antimicrobial susceptibility

Antimicrobial susceptibility testing was performed for 70 isolates. The bacteria exhibited high susceptibility to ceftriaxone and vancomycin (100% for both), and good susceptibility to ampicillin (94.3%). Lower susceptibility rates were observed to penicillin (68.6%), clindamycin (54.3%), erythromycin (65.7%), and tetracycline (54.3%) (Figure 1). No significant differences in susceptibility patterns were observed across species within the SAG.

Treatment and outcomes

A total of 19.5% of patients required surgical or interventional drainage/debridement. The overall prognosis was favorable, with a clinical cure rate of 92.7%. One patient (1.2%) experienced recurrence within 3 months, and the 28-day all-cause mortality was 6.1% (n = 5) (Supplementary Table 1). Among non-survivors (Table 4 and Supplementary Table 2), deaths in patients with spontaneous peritonitis were attributed to progression of underlying liver cirrhosis. Deaths in patients with meningitis resulted directly from infection-induced septic shock and organ failure.

Figure 1. Antibiotic susceptibility rate of *Streptococcus anginosus* group (SAG) isolates (n = 70).



Discussion

This study characterizes SAG infections in Vietnam, detailing their clinical spectrum, microbiology, and outcomes. While more than half of the patients in the cohort had chronic comorbidities, a considerable proportion of cases also occurred in hosts without apparent comorbidities, suggesting that impaired immunity may not be a prerequisite for SAG translocation. Polymicrobial infections were documented in 14.6% of cases, particularly in bacteremia and soft-tissue involvement. Although susceptibility to ceftriaxone, vancomycin, and ampicillin remained high, the rates were lower for penicillin, clindamycin, erythromycin, and tetracycline, particularly compared with earlier reports. Nevertheless, 19.5% of patients required surgical or image-guided drainage, highlighting the critical role of prompt source control in managing SAG-related abscesses.

SAG bacteria, while typically commensal inhabitants of the oropharynx, gastrointestinal tract, and urogenital tract [7], have increasingly been recognized as opportunistic pathogens capable of causing invasive disease under specific host conditions. Previous studies have linked immunocompromising conditions, such as diabetes mellitus, hypertension, chronic renal disease, and malignancy, to an increased risk of invasive SAG infections [8,9]. In this study, 56.1% of patients had underlying comorbidities, most commonly diabetes mellitus and hypertension, and a subset also had HIV coinfection, further highlighting the role of impaired host defenses in facilitating bacterial translocation and systemic dissemination. Notably, SAG infections also appeared in individuals without pre-existing immunocompromising conditions, from toddlers to the elderly, suggesting that factors beyond immunity may

Table 4. Characteristics of patients who died from *Streptococcus anginosus* group (SAG) infections.

Patient	Age, gender	Comorbidities	Site of infection	SAG isolate grown	Co-infection	Antibiotics used	Main cause of death
1	60, M	Cirrhosis	Spontaneous peritonitis	*S. anginosus*	-	Piperacillin-tazobactam	Progression of comorbidities
2	50, M	Cirrhosis	Spontaneous peritonitis	*S. anginosus*	-	Imipenem-cilastatin + Vancomycin	Progression of comorbidities
3	87, F	Diabetes mellitus	Meningitis	*S. anginosus*	*Escherichia coli, Actinomyces urogenitalis, Bacteroides thetaiotaomicron Clostridium innocuum*	Ceftriaxone + Vancomycin	Septic shock and organ failure due to SAG infection
4	45, M	None	Meningitis	*S. constellatus*	-	Ceftriaxone + Vancomycin	Septic shock and organ failure due to SAG infection
5	61, F	Diabetes Severe COVID-19	Pneumonia	*S. constellatus*	-	Piperacillin-tazobactam	Septic shock and organ failure due to SAG infection

COVID-19: coronavirus disease 2019.

facilitate invasion. Disruption of the mucosal barrier, especially in the oral cavity, may represent an important portal for bacteremia. Lockhart demonstrated that even minor gingival bleeding (e.g., from tooth brushing) can significantly elevate bacteremia risk [10], a finding that may help explain SAG bacteremia in otherwise healthy adults. In this cohort, 7.3% had recent dental interventions, consistent with prior findings implicating transient oral bacteremia. Nevertheless, additional mechanisms, such as synergistic interactions with other organisms [11] and specific bacterial virulence factors [12–14], also contribute to SAG invasiveness in heterogeneous populations and warrant deeper exploration. Regarding clinical presentation, bacteremia, often manifesting as fever as the sole symptom, appears to be a common presentation in this cohort, which seems to differ from some patterns reported in other regions. The data show that bacteremia was the most prevalent presentation, followed by intra-abdominal abscess formation, primarily in the liver. In contrast, previous studies have identified abdominal infections [8] or skin and soft tissue infections [15,16] as the most common manifestations. Demographic, clinical, and microbiological comparisons between the present study and published cohorts are detailed in Table 5. Of note, occult bacteremia accounted for 35.4% of cases, which may explain the comparatively low surgical-intervention rate (19.5%) versus the 39.6–90.0% reported elsewhere [8,15,17–19]. This high proportion is likely multifactorial. Our hospital is a tertiary infectious-diseases center that receives numerous referrals for fever of unknown origin, increasing the pool of patients without an initially identifiable source. Furthermore, the older age range of the cohort (mean age 50.6 years), in which classic signs of localized infection can be absent or blunted, may contribute to this finding.

In this study, 56.1% of cases resulted in abscess formation, showing a strong propensity for localized suppuration in these infections. Species-specific tropisms were evident: *S. intermedius* was

Table 5. Comparison of demographic, clinical and microbiological characteristics of *Streptococcus anginosus* group (SAG) infections in the present study and published cohorts.

	Present study (Vietnam, n = 82)	**Kim *et al.*,[a] (Korea, n = 84) [17]**	**Jiang *et al.*, (China, n = 463) [8]**	**Majid *et al.*, (Saudi Arabia, n = 105) [15]**	**Suzuki *et al.*,[a] (Japan, n = 78) [18]**	**Shaukat *et al.*, (Qatar, n = 101) [19]**
Study period	2017–2023	2010–2021	2014–2019	2015–2017	2005–2014	2006–2012
Male, %	64.6	65.5	66.1	52.4	65.4	75.0
Age (years)	50.6	69.5	35.0–54.0[b]	52.4	67.4	44.0
Species distribution, %						
S. anginosus	43.9	47.6	54.9	-	21.8	29.7
S. constellatus	34.1	36.9	37.4	-	34.6	40.6
S. intermedius	22.0	15.5	7.8	-	24.4	6.9
Not identified	-	-	-	-	19.2	22.8
Comorbidities, %						
Diabetes	23.3	31.0	15.1	34.3	18.0	25.0
Malignancy	-	29.8	14.9	15.2	33.3	4.0
Chronic kidney disease	19.5	7.1	4.3	12.4	3.9	2.0
Chronic respiratory disease	-	3.6	2.6	-	-	-
Primary infection site, %						
Occult bacteremia	35.4	16.7	5.6	14.3	9.0	22.7
Intra-abdominal[d]	31.7	45.2	28.9	23.8	43.6	24.8
Cervicofacial[e]	9.8	8.3	22.5	-	-	7.9
Extremity and trunk	8.5	3.6	11.9	55.2	7.7	28.7
Central nervous system infection	4.9	-	1.1	1.0	1.3	6.9
Chest infection	3.7	15.5	16.8	5.7	10.2	2.0
Endocarditis	4.9	3.6	0		3.8	2.0
Genitourinary	4.9	6.0		8.6	7.7	
Polymicrobial infection, %	14.6	22.6	-	45.7	35.9	43.6
Antibiotic susceptibility, %						
Penicillin	84.3	73.8	-	90.4	100	100.0
Clindamycin	54.3	-	-	-	94.6	95.0
Erythromycin	65.7	-	-	-	84.8	91.1
Ceftriaxone	100.0	98.5	-	-	-	100.0
Vancomycin	100.0	100.0	-	100.0	-	100.0
Outcomes, %						
Surgical/drainage intervention	19.5	52.4	26.1	90.0	52.6	39.6
Clinical cure	92.7	-	-	-	-	87.0
Mortality	6.1	6.0	2.2	5.7	14.1	9.9

[a] Study by Kim *et al.* and Suzuki *et al.*: comprised only patients with bacteremia (all with positive blood cultures). [b] Age presented as the most prevalent age range. [c] Includes solid tumors and hematological malignancies. [d] Intra-abdominal infection encompasses hepatobiliary and gastrointestinal sources. [e] Cervicofacial skin-and-soft-tissue infection combines oral-maxillofacial and ear-throat-nose/cervical sites.

predominantly associated with intra-abdominal abscesses and less frequently with bacteremia, consistent with its known tendency for deep tissue invasion [20]. In contrast, *S. anginosus* and *S. constellatus* were more common in bacteremia and soft tissue infections; with all head, face, and neck abscesses caused exclusively by *S. constellatus*. The occurrence of multi-organ infections in 3.7% of patients supports considering for systematic screening for distant infection foci.

Empiric broad-spectrum therapy was justified by local epidemiology from the institutional surveillance program. In this setting, severe infections, beyond the SAG, are frequently caused by *Klebsiella pneumoniae*, *Escherichia coli*, and *Staphylococcus aureus*. Therefore, a regimen active against these organisms was initiated while culture results were pending. Subsequent identification of SAG, which in the surveillance shows high in-vitro susceptibility to narrower-spectrum β-lactams (ceftriaxone 100% and ampicillin 94.3%), supported de-escalation to these agents as first-line therapy. These high susceptibility rates are consistent with international reports [17,19]. However, the reduced susceptibility to penicillin (84.3%) is a major concern. This finding, which is consistent with the trend seen in a recent Korean study [17] (73.8% susceptibility), is a notable contrast to older data that reported 100% susceptibility [18,19]. These findings may reflect temporal or regional variation in penicillin susceptibility, indicating that penicillin may be less reliable as a sole empirical therapy. Similarly, the low susceptibility rates for clindamycin (54.3%) and erythromycin (65.7%), especially compared to earlier data [18,19,21–25], highlight a steady upward trend in resistance, suggesting these agents may be less suitable for empirical coverage in this setting. Collectively, these findings underscore the importance of local antimicrobial-susceptibility surveillance and advocate for periodic guideline revision to preserve therapeutic efficacy against SAG pathogens.

A subset of patients presented with polymicrobial infections, frequently involving Gram-negative or anaerobic organisms, necessitating broader antimicrobial coverage. Nearly all such cases were associated with bacteremia or soft tissue infections. Co-pathogens, particularly in deep-seated infections, can contribute to treatment failure if not adequately targeted. This underscores the need for clinicians to consider broader-spectrum agents, such as beta-lactam/beta-lactamase inhibitors (e.g., amoxicillin-clavulanate), in patients failing initial SAG-directed therapy. Furthermore, the requirement for surgical intervention in nearly one-fifth of patients highlights the importance of a multidisciplinary approach integrating appropriate antimicrobial therapy with timely surgical consultation.

This study demonstrated a favorable prognosis, with a high cure rate (92.7%) and a 28-day all-cause mortality rate of 6.1%. This mortality rate was comparable to reports from South Korea (6.0%) [17] and Saudi Arabia (5.7%) [15]. This mortality rate was lower than those reported in Japan (14.1%) [18], and Qatar (9.9%) [19]. This difference might be related to the smaller proportion of patients with high-risk comorbidities, such as advanced-stage cancer, in the cohort. The present analysis found factors associated with mortality: meningitis ($p = 0.017$) and spontaneous peritonitis ($p = 0.009$). In the case of patients with spontaneous peritonitis, death was linked to the progression of underlying cirrhosis, which underscores that managing liver disease is as critical as antibiotic therapy. In stark contrast, meningitis fatalities were a direct consequence of the infection itself. Therefore, for these patients, the immediate priority is aggressive infection control to prevent the onset of fatal septic shock.

This study has several limitations. Its retrospective design and single-center setting may limit the generalizability of the findings. Additionally, while the hospital is equipped with advanced imaging modalities, all patients received chest X-rays and abdominal ultrasounds; however, only 9 patients proceeded to a computed tomography (CT) scan. The routine use of CT scans was limited to cases where a large lesion was identified on initial abdominal ultrasound, primarily to guide drainage procedures. The CT scanner available at the hospital is a 16-slice model. This selective use of advanced imaging may have led to an underestimation of abscess formation in patients with smaller lesions, contributing to the high observed rate of occult bacteremia. The sample size of 82 patients, while significant for a single-center study on this relatively uncommon pathogen, may limit the statistical power for certain subgroup analyses and the detection of less frequent clinical outcomes. Future multi-center studies would be beneficial to build a larger cohort and further validate these findings. The generalizability of the findings is also limited by the single-center, specialty-hospital setting, which resulted in the underrepresentation of certain patient groups. For instance, cancer patients, a population well-documented in prior studies as being susceptible to SAG infections and its severe sequelae, were underrepresented in this cohort.

Conclusions

This study provides insight into the clinical profile of SAG infections in Vietnam which primarily present as bacteremia and intra-abdominal abscesses. The SAG isolates generally showed good susceptibility to β-lactam antibiotics, although the presence of polymicrobial infections in some cases may warrant broader-spectrum antimicrobial coverage. Despite overall favorable outcomes, the observed variability in antibiotic susceptibility shows the need for continued surveillance and careful antimicrobial stewardship.

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Availability of data and material

The datasets of this study can be available from the corresponding author upon reasonable request.

Authors' contributions

LTKT, study conception, data curation; LTKT, HAV, formal analyses; LBC, LTKT, methodological framework; LTKT, HAV, QKTL, QMH, experimental investigations; LTKT, HAV, QKTL, original draft manuscript; LBC, LTKT, HAV, QKTL, QMH, manuscript review and editing.

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Conflict of interest

No conflict of interest is declared.

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Annex – Supplementary Items

Supplementary Table 1. Clinical and microbiological details of the patient with recurrent *S. anginosus* bacteremia.

Characteristic	First admission	Second admission (recurrence)
Profile		
Demographics	Male, 55 years old	
Comorbidities	Diabetes mellitus, neurofibromatosis	
Clinical presentation		
Onset	Fever on day 7	Fever on day 3
Interval between episodes		**26 days post-discharge**
Laboratory findings		
Hematology		
WBC Count (K/µL)	13.9	12.8
Neutrophil Count (K/µL)	11.0	10.6
Lymphocyte Count (K/µL)	2.4	2.2
Hemoglobin (g/dL)	13.2	12.9
Platelet Count (K/µL)	154	142
Biochemistry		
AST (U/L)	50	48
ALT (U/L)	60	55
Serum Creatinine (µmol/L)	80	79
CRP (mg/L)	252.9	
Diagnostic imaging		
Chest X-ray	Normal	Normal
Abdominal ultrasound	Normal	Normal
Microbiology and treatment		
Initial Antibiotic Therapy	Piperacillin/tazobactam	Ampicillin/sulbactam
Culture Specimen	Blood	Blood
Isolate	*S. anginosus*	*S. anginosus*
Antimicrobial Susceptibility		
Penicillin	Susceptible	Resistant
Ampicillin	Susceptible	Intermediate
Ceftriaxone	Susceptible	Susceptible
Vancomycin	Susceptible	Susceptible
Targeted Therapy (Post-AST)	Piperacillin/tazobactam (5 days)	Ceftriaxone (14 days)
Outcome		
Complications	None	None
Final Outcome	Recurrence	Clinical cure

WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CRP, C-reactive protein.

Supplementary Table 2. Study variables stratified by the outcome among patients with *Streptococcus anginosus* infections.

Study variables		Dead n (%)	Survived n (%)	*p* value*	OR (95% CI)
Age (years)	Above 60	3 (11.5)	23 (88.5)	0.255	3.52 (0.57–21.93)
	Below 60	2 (3.6)	54 (96.4)		
Gender	Male	3 (5.7)	50 (94.3)	1.0	0.81 (0.13–5.15)
	Female	2 (6.9)	27 (93.1)		
Comorbidities					
Diabetes	Yes	2 (10.5)	17 (89.5)	0.328	2.35 (0.36–15.24)
	No	3 (4.8)	60 (95.2)		
Cirrhosis	Yes	2 (14.3)	12 (85.7)	0.2	3.61 (0.54–23.96)
	No	3 (4.4)	65 (95.6)		
Site of infection					
Meningitis	Yes	2 (50.0)	2 (50.0)	0.017	25.0 (2.57–243.08)
	No	3 (3.8)	75 (96.2)		
Spontaneous peritonitis	Yes	2 (66.7)	1 (33.3)	0.009	50.67 (3.53–726.78)
	No	3 (3.8)	76 (96.2)		
Co-infection	Yes	1 (8.3)	11 (91.7)	0.556	1.5 (0.15–14.7)
	No	4 (5.7)	66 (94.3)		

OR: odds ratio; CI: confidence interval. **p* value is significant at < 0.05.