ORIGINAL ARTICLE

Group A Streptococcal Bacteremia: Ten Years' Experience from a Tertiary Care Center in South India

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Abstract

Background: Bacteremia is an uncommon complication of group A streptococcal (GAS) infections. The data on GAS bacteremia is scarce from developing nations such as India.

Patients and methods: We performed a retrospective analysis of patients diagnosed with GAS bacteremia in a tertiary care hospital in Kerala, India over a 10-year period (2012–2021) by review of the electronic medical records (EMRs).

Results: A total of 58 cases of GAS bacteremia were identified in the study period. Skin/soft tissue infection was the most common source of bacteremia. A total of 34.4% of the patients required ICU admission and the in-hospital mortality was 22.4%. All the GAS isolates were sensitive to penicillin, ampicillin, and ceftriaxone. Erythromycin and clindamycin resistance was seen in 39.7% and 24.1% isolates, respectively.

Conclusion: This study shows that despite advancement in medical sciences, GAS bacteremia remains as a disease with high morbidity and mortality. A higher rate of clindamycin resistance was observed compared to previous Indian studies.

Keywords: Bacteremia, Group A *Streptococcus*, *Streptococcus pyogenes*.

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Highlights

- In this EMR-based retrospective analysis of GAS bacteremia over 10 years, mortality was 22.4%. Despite the advances in medical sciences mortality remains high in this clinical syndrome.
- Contrary to the previous Indian studies on invasive GAS infections, a high prevalence of clindamycin resistance was observed in this study.

Introduction

Bacteremia due to GAS (*Streptococcus pyogenes*) occurs usually as a complication of infection at a primary site, most common source being skin and soft tissue infection.[1,2] Although considered as an uncommon complication of GAS infection, bacteremia is associated with significant mortality.[1,3] Most GAS infections are community acquired although nosocomial outbreaks have also been reported.[4,5] Data on invasive GAS infections, particularly bacteremia, is scarce from the developing countries such as India. We retrospectively analyzed the clinical and microbiological profile of patients of GAS bacteremia admitted to a tertiary care hospital in South India.

Materials and Methods

The EMRs review of all the patients whose blood culture yielded GAS during a 10-year period (January 2012 to August 2021) at Kerala Institute of Medical Sciences/KIMSHEALTH (a tertiary care hospital in Kerala, India) was done. For the detection of bacterial growth, BacT/AlLERT 3D instrument was used. Identification and antibiotic susceptibility were done by the VITEK-2 system.

Demographic and clinical details were retrieved from EMRs. The clinical details collected included comorbidities, sources of bacteremia, complications, antibiotics used and use of intravenous immune globulin (IVIG), and surgical procedures and outcomes. Comparison of demographic and clinical parameters between patients who died in hospital (non-survivors) and those who were discharged after treatment (survivors) were done to assess the risk factors of mortality. Details of infectious diseases (ID) consultation and its effects on antibiotic de-escalation and mortality was also assessed.

The categorical variables were compared using Chi-squared test. The continuous variables were expressed as median [interquartile range (IQR)] and compared between survivors and non-survivors using Mann–Whitney *U test*. The variables that were found to be significant risk factors for mortality on univariate analysis ($p < 0.05$) were subjected to multivariate analysis to identify the independent risk factors for mortality.

Results

A total of 58 cases of bacteremia due to GAS were identified in the study period. A total of 44 (75.9%) were males and the median age

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Table 1: Focus of infection associated with *Streptococcus pyogenes* bacteremia

Focus of infection	*Number of patients (%)*
Skin/soft tissue infection	**42 (72.4)**
• Cellulitis	24 (41.4)
• Necrotizing fasciitis	11 (18.9)
• Secondary infection of chronic skin conditions	3 (5.1)
• Superficial wound infections	2 (3.4)
• Bursitis	1 (1.7)
• Septic arthritis	1 (1.7)
Pharyngitis	**2 (3.4)**
No focus identified (primary bacteremia)	**12 (20.6)**

was 65 years (IQR: 55–72.25). Five patients (8.62%) belonged to the pediatric age-group (≤18 years).

Diabetes mellitus was the most common comorbidity, which was present in 37 patients (63.8%). A total of 19 patients (32.8%) had chronic kidney disease (CKD), 14 (24.1%) had chronic liver disease (CLD), 5 (8.6%) had underlying malignancy, and 5 (8.6%) were on immunosuppressive medicines.

Skin/soft tissue infection was identified as the focus of infection in 42 (72.4%) patients while it was pharyngitis in two (Table 1). No focus could be identified in 12 patients (primary bacteremia). Among the patients with skin/soft tissue infections, 24 patients had cellulitis, while 11 patients had necrotizing fasciitis. Both patients who had pharyngitis as the source of infection belonged to the pediatric age-group (aged 10 and 7 years). The complications included septic shock (24.1%), renal impairment (50%), abscess formation (5.2%), and pneumonia (8.6%). One patient was diagnosed to have streptococcal toxic shock syndrome (TSS).

All the isolates were sensitive to penicillin, ampicillin, and ceftriaxone. Erythromycin resistance was seen in 23 isolates (39.7%) and clindamycin resistance in 14 isolates (24.1%). The antibiotics used prior the identification of organism in blood culture included clindamycin (43% of patients), carbapenems (37.9%), teicoplanin (36.2%), cefoperazone-sulbactam (29.3%), piperacillin–tazobactam (17.2%), doxycycline (10.3%), azithromycin (8.6%), ceftriaxone (6.8%), linezolid (6.8%), and amoxycillin-clavulanate (5.1%) in various combinations. The antibiotics used after identification of the organism as GAS included ceftriaxone (32.7%), clindamycin (31%), piperacillin-tazobactam (15.5%), teicoplanin (5.1%), carbapenem (5.1%), amoxycillin–clavulanate (5.1%), benzyl penicillin (1.7%), ampicillin (1.7%), and cefoperazone–sulbactam (1.7%) in various combinations. Intravenous immune globulin was given only in one patient. The surgical procedure for source reduction was done for 9 patients (15.5%). Antibiotic de-escalation was done for 31 patients (53.4%) after the blood culture reports.

An ID consultation was done in 26 patients (44.8%). Antibiotic de-escalation was done in 21 (80.8%) patients among the 26 patients for whom an ID consultation was done while it was done in 10 (31.3%) among the 32 patients for whom an ID consultation was not done. The difference was statistically significant (p <0.01).

The median duration of hospital stay was 5 days (IQR: 2–9). A total of 20 patients (34.4%) required ICU admission. In-hospital mortality was 22.4% (13 patients). Table 2 lists the potential risk factors of mortality associated with GAS bacteremia. On univariate analysis septic shock, renal impairment, necrotizing fasciitis, non-de-escalation of antibiotics after blood culture reports, higher serum values of creatinine, potassium, alanine aminotransferase, and aspartate aminotransferase were statistically significant risk factors of mortality. However, on multivariate analysis none of these variables were found to be independent predictors of mortality.

Discussion

We observed that GAS bacteremia was associated with a high mortality of 22.4%. Despite the advances in medical sciences, GAS bacteremia remains as a condition with high mortality. Burkert et al. observed a mortality of 24% in patients with GAS bacteremia admitted to a community teaching hospital in Ohio, United States between 1980 and 1989.[1] In a 27-years study from a London-based teaching hospital between 1970 and 1997, the mortality was reported to be 19%.[6] Morales et al., in their study during a period from 1994 to 2003 in a teaching hospital in Spain, observed a mortality of 28.6%.[3] The advanced age of presentation and the high prevalence of comorbidities may be contributing to the high mortality.

The skin/soft tissue infections were identified as the most common source of bacteremia, most of them being cellulitis. No focus of bacteremia could be found in 20.6% of the patients. The percentage of patients with primary bacteremia ranged from 0 to 41% in previous studies.[2,3,6]

All the isolated of GAS were uniformly sensitive to penicillin and ceftriaxone. However, the rate of clindamycin resistance is alarming as a combination therapy of a β-lactam agent and clindamycin is advocated in severe GAS infection, especially TSS. This is contrary to the previous Indian studies, where the isolates showed uniform susceptibility to clindamycin.[7,8] On the other hand, the previous studies from different parts of the world have shown an increasing resistance of GAS isolates to clindamycin.[9,10]

Conclusion

In conclusion, in this-single center retrospective study from South India, GAS bacteremia was associated with a mortality of 22.4%. While all the isolates of GAS were susceptible to penicillin and ceftriaxone, clindamycin resistance was high.

Table 2: Comparison of clinical and laboratory parameters between survivors and non-survivors

	Survivors (n = 45)	*Non-survivors (n = 13)*	*p-value*
Clinical parameters [number (%)]			
Age >65	25 (55.6%)	6 (46.2%)	0.75
Male gender	33 (73.3%)	11 (84.6%)	0.49
Diabetes mellitus	27 (60.0%)	10 (76.9%)	0.34
CKD	15 (33.3%)	4 (21.1%)	1.00
CLD	12 (26.7%)	2 (15.4%)	0.49
Malignancy	3 (6.7%)	2 (15.4%)	0.31
Immunosuppressive drugs	3 (6.7%)	2 (15.4%)	0.31
Septic shock	4 (8.9%)	10 (76.9%)	<0.01
Renal impairment	18 (40%)	11 (84.6%)	0.01
Pneumonia	3 (6.7%)	2 (15.4%)	0.31
Abscess formation	3 (6.7%)	0 (0%)	1.00
Necrotizing fasciitis	4 (8.9%)	7 (53.8%)	<0.01
ID consultation	22 (48.9%)	4 (30.8%)	0.24
Antibiotic de-escalation following culture reports	28 (62.2%)	3 (23.1%)	0.01
Laboratory investigations [median (IQR)]			
Total leukocyte count (/µL)	13,300 (9,250–17,600)	15,900 (7,800–19,850)	0.51
Hb (gm/dL)	11.4 (9.5–13.0)	11.6 (8.3–13.2)	0.69
Platelet count (1,000/µL)	169.0 (111.5–223.0)	164.0 (105.5–207.0)	0.73
C-reactive protein (mg/L)	98.6 (17.9–240.1)	289.0 (34.3–336.2)	0.12
Creatinine (mg/dL)	1.6 (0.9–3.1)	3.2 (1.5–4.8)	0.03
Sodium (mEq/L)	134.0 (130.5–137)	136.0 (131–141)	0.22
Potassium (mEq/L)	4.3 (3.8–4.5)	5.4 (4.5–6.0)	<0.01
Bilirubin (mg/dL)	0.7 (0.5–1.6)	0.9 (0.7–2.5)	0.34
Alanine aminotransferase (U/L)	27.0 (17.5–49.5)	100.0 (35.7–535.5)	<0.01
Aspartate aminotransferase (U/L)	26.0 (15.5–44.0)	65.5 (35.7–299.2)	<0.01
Alkaline phosphatase (U/L)	83.5 (62.7–132.5)	94.0 (65.5–173.7)	0.46

CKD, chronic kidney disease; CLD, chronic liver disease; IQR, interquartile range

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