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Research article

Mortality patterns in patients with Staphylococcus aureus bacteremia during the COVID-19 pandemic: Predictors and insights

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ABSTRACT

Objectives: This paper aims to determine the *Staphylococcus aureus* bacteremia (SAB) in-hospital mortality rate and its associated risk factors during the COVID-19 pandemic.
Methods: A total of 167 SAB samples were collected between March 2020 and March 2022 at a teaching hospital in Tehran, Iran. The patient's baseline data and antibiograms were collected. The outcome of the study was in-hospital mortality.
Results: The overall in-hospital mortality rate was 41.9 %, with higher mortality observed in patients over 60 years old (P = 0.032), those with community-acquired *Staphylococcus aureus* bacteremia (P = 0.010), and those admitted to the ICU (P = 0.016). Antibiotic resistance profiles indicated a higher mortality in resistant S.aureus strains but only significant for ciprofloxacin (P = 0.001), methicillin (P = 0.047), and sulfamethoxazole (P = 0.023). Multivariate analysis identified age, sex, ICU admission, and the source of bacteremia as independent predictors of mortality, while COVID-19 coinfection and resistance to antibiotics were not found to be significant predictors.
Conclusion: SAB remains a challenging infection that is amplified by the pandemic. Older age and ICU admission are significant mortality predictors. In settings with a high prevalence of MRSA, factors like age, sex, and quality of care outweigh pathogen-related factors such as antibiotic resistance.

1. Background

Staphylococcus aureus holds the top position in mortalities due to antibiotic resistance [1], and *Staphylococcus aureus* bacteremia (SAB) contributes to the greatest number of fatalities due to bloodstream infections [2]. The World Health Organization regards S. aureus as a high-priority bacteria for which new antibiotics are urgently needed [3]. Although the global mortality rate for SAB appears to be on the decline [4], a meta-analysis in 2022 revealed that approximately one patient out of every four patients diagnosed with SAB would die in the hospital [5]. In low- and middle-income countries, the mortality rate worsens to one in every three patients [6]. In

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addition, since the emergence of COVID-19, there has been a tendency to overlook cases of SAB, ultimately leading to an elevated mortality rate during the pandemic [7].

Mortality is influenced by multiple factors, encompassing host-related aspects, interactions between the pathogen and host, and specific attributes of the pathogen itself [8]. In elderly individuals, the higher prevalence of multiple comorbidities, presentation of atypical symptoms for bacteremia, and other age-related changes [8] contribute to vulnerability against SAB. While old age and Intensive care unit (ICU) admission have been recognized as well-known risk factors for mortality of SAB [9,10], the evidence about the impact of sex remains controversial [11–13]. In terms of pathogen-related aspects, some studies recommend higher mortality in methicillin-resistant S.aureus (MRSA) [6], while others challenge the effect of antibiotic resistance [14].

Data concerning this severe condition are generally heterogeneous, and identifying the most influential risk factors is beneficial for clinical decision-making. To provide insight and add to the literature about the predictors of SAB mortality, the study's objective is to ascertain the in-hospital mortality rate during the first two years of the COVID-19 pandemic and strive to identify potential predictors of mortality in patients with SAB.

2. Methods

2.1. Aim

The current study aimed to determine SAB-related in-hospital mortality and associated risk factors during the COVID-19 pandemic.

2.2. Study design

This retrospective cohort study aimed to investigate the in-hospital mortality of patients positive for SAB. The study was conducted in a teaching hospital in Tehran, Iran, from March 1st, 2020, to March 1st, 2022.

2.3. Data collection

One-hundred-sixty-seven SAB samples were collected from patients admitted during the study period. Patients were identified by review of the WHONET microbiology laboratory database software. The samples were collected using standard aseptic techniques and transported to the microbiology laboratory for further processing. All adult patients (18 years or older) diagnosed with *S. aureus* bacteremia during the study period were included. Patients with incomplete medical records or missing data on any of the variables of interest were excluded from the study. The following data were collected from the patient's records: age, sex, diabetes mellitus, prior antibiotic consumption, COVID-19 PCR result, ICU admission during the hospital stay, length of hospital stay, bedside device implementation, surgery, complete blood counts (CBCs), antibiograms and outcome (in-hospital mortality).

2.4. Variables and measures

Staphylococcus aureus bacteremia was described as having at least one blood culture with proven S.aureus growth. Prior antibiotic consumption was defined as any antibiotic administration during the previous seven days before hospitalization. COVID-19 infection was diagnosed based on pulmonary CT-scan and/or RT-PCR tests. Intensive care unit (ICU) admission was positive if the samples were sent to the laboratory from ICU wards. Bedside device implementations were considered procedures performed by the patient's bedside without general anesthesia, such as central venous line implementation, ascitic tap, pleuritic fluid tap, chest tube insertion, and bone marrow aspiration. Surgeries were undertaken in the operating room using anesthesia. CBC was recorded on the same date the blood cultures were positive using a hematology analyzer (Siemens, Germany). Leukocytosis was considered present when the white blood cell count (WBC) surpassed $11 \times 10\hat{}9$ cells per liter, while leukopenia was defined as a WBC falling below $4.5 \times 10\hat{}9$ cells per liter. Thrombocytopenia was identified when the platelet count (PLT) fell below $150 \times 10\hat{}9$ per liter. Anemia was characterized by a hemoglobin level lower than 10 g per deciliter (g/dL).

2.5. Antibiotic susceptibility testing

Our study utilized the disc diffusion method for antibiotic susceptibility testing due to its simplicity, availability, and cost-effectiveness. This method, while qualitative and having certain limitations, offers reasonably accurate results and is recommended by the Clinical and Laboratory Standards Institute (CLSI) in their 30th edition guidelines. We selected this approach for testing antibiotics such as Penicillin G, Ciprofloxacin, Clindamycin, Erythromycin, and Sulfamethoxazole.

The procedure involved applying standard disks to Mueller-Hinton agar plates inoculated with *S. aureus*, followed by incubation. Post-incubation, the results were interpreted as susceptible, intermediate, or resistant, based on CLSI breakpoints. For Methicillin resistance, a 30-μg Cefoxitin disk was used in accordance with CLSI recommendations, with an incubation time of 16–18 h. An *S. aureus* isolate was classified as Methicillin-resistant (MRSA) if the inhibitory zone around the disk measured $\leq$21 mm.

Given the disc diffusion method's limitations for Vancomycin, we determined the minimum inhibitory concentration (MIC) using E test strips (BioMerieux, France). These strips were placed on Mueller-Hinton agar plates with *S. aureus* isolates and incubated for 24 h at 35 °C. The MICs were then evaluated, and results categorized as susceptible, intermediate, or resistant according to CLSI standards.

2.6. Statistical analysis

Descriptive statistics were used to summarize patient characteristics. Continuous variables were reported as the means ± standard deviations or medians with interquartile ranges (IQRs), depending on their distribution. Categorical variables were reported as frequencies and percentages. The chi-square test was used to compare categorical variables between groups. Student's t-test or the Mann-Whitney *U* test was used to compare continuous variables between groups. We performed multivariable analysis using a logistic regression model, selecting variables for inclusion based on a significance level of $P < 0.2$. The level of significance was considered at 0.05. During our analysis, we encountered a few intermediately resistant samples. Due to their scarcity and to maintain statistical robustness, these were grouped with resistant samples for p-value calculations. This decision ensured a more robust statistical analysis by addressing the limited occurrence of intermediate samples and allowed for a clearer interpretation of antibiotic susceptibility patterns.

2.7. Ethical considerations

This study was approved by the ethics committee of Iran University of Medical Sciences (IUMS) (IR.IUMS.REC.1397.1155). Informed consent was waived due to the retrospective nature of the study.

3. Results

3.1. Baseline characteristics

Table 1 displays the baseline characteristics of the study population. The median age of the patients was 63 years (IQR: 51–74), and 42.5 % were over 60 years old. The majority of the patients (61.1 %) were male. Sixty-seven patients were diagnosed with COVID-19 during their hospital stay (40.1 %). The median length of hospitalization was 13 days (IQR: 7–22), and more than half of the patients (53.3 %) were admitted to the ICU. Fifteen patients (9 %) had community-acquired SAB (Table 1).

3.2. Bivariate analysis

As described in Table 2, the overall mortality was 41.9 %. Patients over 60 had a significantly higher mortality rate (49 % vs. 32.4 %, $P = 0.032$). The median age for the dead patients was 68 (23–98) and 60 (18–84) for the surviving patients. Females had a higher mortality rate than males (49.2 % vs. 37.5 %), but the difference was insignificant ($P = 0.137$). Although patients diagnosed with concomitant COVID-19 had a higher mortality rate (49.3 % vs. 37.0 %), the difference was negligible. Patients with community-acquired SAB (CA-SAB) infections had a higher mortality rate (73.3 %) than those with hospital-acquired infections (HA-SAB) (38.8 %) ($P = 0.01$). Patients admitted to the ICU had a significantly higher mortality rate (50.6 vs. 32.1 %, $P = 0.016$) (Table 2).

Table 1
Baseline characteristics of the patients with S.aureus bacteremia (n = 167).

Variables		
Age (Years)		63 [51–74][b]
Age group	<60	71 (42.5)[a]
	≥60	96 (57.5)[a]
Male		102 (61.1)[a]
Medical history	DM	53 (31.7)[a]
	Prior antibiotic consumption	14 (8.4)[a]
COVID-19		67 (40.1)[a]
Mean Hospitalization (Days)		13 (7–22)[b]
In-hospital intervention	Surgery	58 (34.7)[a]
	Bedside device implementation	99 (59.3)[a]
ICU admission		89 (53.3)[a]
Labs	White blood cell, (× 10^9/L)	9.9 [6.6–14.1][b]
	Hemoglobin, (g/dL)	11.7 [9.7–13.5][b]
	Platelet count, (× 10^9/L)	175 [115–268][b]
Infection source	Community acquired	15 (9)[a]
	Hospital acquired	152(91)[a]
Leukocytosis		73 (43.7)[a]
Leukopenia		21 (12.6)[a]
Thrombocytopenia		66 (39.5)[a]
Anemia		72 (43.1)[a]

DM: Diabetes mellitus, ICU: Intensive-care unit.
[a] Frequency (%).
[b] median [IQR].

Table 2
Mortality proportion of patients with S.aureus bacteremia based on measured variables.

Variables		Frequency of Deaths (%)	P-value
Overall		70 (41.9)	
Sex	Male	38 (37.2)	0.126
	Female	32 (49.2)	
Age group	<60	23 (32.4)	**0.032**
	≥60	47 (49.0)	
COVID-19	Positive	33 (49.3)	0.116
	Negative	37 (37.0)	
Infection source	Community acquired	11 (73.3)	**0.010**
	Hospital acquired	59 (38.8)	
DM	Yes	25 (47.2)	0.348
	No	45 (39.5)	
Leukopenia	Yes	8 (38.1)	0.704
	No	62 (42.5)	
Leukocytosis	Yes	34 (46.6)	0.282
	No	36 (38.3)	
Thrombocytopenia	Yes	27 (40.9)	0.831
	No	43 (42.6)	
Anemia	Yes	33 (45.8)	0.372
	No	37 (38.9)	
Prior antibiotic consumption	Yes	6 (42.9)	0.957
	No	64 (42.1)	
Surgery	Yes	23 (39.7)	0.666
	No	47 (43.1)	
Bedside device implementation	Yes	43 (43.4)	0.631
	No	27 (39.7)	
ICU admission	Yes	45 (50.6)	**0.016**
	No	25 (32.1)	

DM: Diabetes mellitus, ICU: Intensive-care unit.

3.3. Antibiotic resistance

Table 3 presents the antibiotic resistance profiles of the study population. Methicillin-resistant *Staphylococcus aureus* (MRSA) was detected in 71.9 % of patients. The majority of the isolates were resistant to Penicillin G (95.8 %), Erythromycin (80.8 %), Clindamycin (77.2 %), and Ciprofloxacin (69.5 %). Resistance to sulfamethoxazole was 21.0 %, and all the specimens were susceptible to vancomycin.

Complete or intermediate resistance to ciprofloxacin (P = 0.001), methicillin (P = 0.047), and sulfamethoxazole (P = 0.023) were associated with significantly higher mortality, while resistance to other antibiotics did not show a significant correlation with mortality.

Table 3
Frequency distribution of Antibiotic resistance and attributed mortality in patients with S.aureus bacteremia.

Antibiotic		Overall (n = 167) Frequency (%)	Deaths (n = 70) Frequency (%)	P-value[a]
Penicillin G	Resistant	160 (95.8)	68 (42.8)	0.465
	Sensitive	7 (4.2)	2 (25.0)	
Methicillin	Resistant	120 (71.9)	56 (46.7)	**0.047**
	Sensitive	47 (28.1)	14 (29.8)	
Ciprofloxacin	Resistant	116 (69.5)	59 (50.9)	**0.001**
	intermediate	4 (2.4)	1 (25.0)	
	Sensitive	47 (28.1)	10 (21.3)	
Clindamycin	Resistant	129 (77.2)	59 (45.7)	0.131
	intermediate	5 (3.0)	1 (20.0)	
	Sensitive	33 (19.8)	10 (30.3)	
Erythromycin	Resistant	135 (80.8)	61 (45.2)	0.210
	intermediate	6 (3.6)	1 (16.7)	
	Sensitive	26 (15.6)	8 (30.8)	
Sulfamethoxazole	Resistant	35 (21.0)	20 (57.1)	**0.023**
	intermediate	3 (1.8)	2 (66.7)	
	Sensitive	129 (77.2)	48 (37.2)	
Vancomycin	Resistant	0 (0)	0 (0)	1
	intermediate	0 (0)	0 (0)	
	Sensitive	160 (100)	70 (41.9)	

[a] Intermediate and resistant strains were merged and compared as a combined group against susceptible strains.

3.4. Multivariate analysis

A logistic regression model was developed using age, sex, COVID-19 coinfection, source of bacteremia, ICU admission, and resistance to Clindamycin, Sulfamethoxazole, Ciprofloxacin, and Methicillin as predictors of mortality. The findings of the multivariable analysis are summarized in Table 4. The R-squared value for our logistic regression model is 0.285. While age, sex, ICU admission, and the source of bacteremia were statistically independent predictors, COVID-19 coinfection and resistance to antibiotics were not found to be independent factors.

4. Discussion

Staphylococcus aureus remains a prominent pathogen responsible for bacteremia, with a notable impact on mortality among hospitalized individuals. A comprehensive understanding of the prevalence and risk factors associated with a worse prognosis can equip physicians with valuable knowledge for effectively managing this formidable infection. The key outcome of the study was an overall in-hospital mortality rate of 41.9 % during the COVID-19 pandemic. Additionally, the multivariate analysis identified several significant predictors of mortality, including age, sex, ICU admission, and community-acquired infection ($P < 0.05$).

4.1. Overall in-hospital mortality

Staphylococcus aureus bacteremia (SAB) is a critical health concern with significant mortality rates. A comparative analysis of pre- and post-pandemic mortality rates reveals insightful trends. Before the COVID-19 pandemic, the mortality rate of SAB was notably high, with a study by Tong et al. (2015) reporting a 30-day mortality rate of approximately 20 % [15]. This high mortality rate was attributed to factors like the increasing prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) and comorbid conditions in patients. During the pandemic, the landscape of SAB mortality experienced a shift. According to a research by Rawson et al. (2020), there was an observed increase in the incidence of SAB, potentially due to enhanced healthcare-associated transmissions during the pandemic [16]. Furthermore, a study by Stevens et al. (2021) indicated a noticeable uptick in the 30-day mortality rate, reaching up to 25 %, possibly exacerbated by the strain on healthcare systems and delayed treatments during the pandemic [17]. The starting point of this retrospective study was the beginning of the COVID-19 outbreak in Iran. In comparison to other reports from Iran, the mortality rate reported by Heydari et al. just before the pandemic in 2019 (38.2 %) was lower than what we observed during the pandemic (41.9 %) [18]. These findings underscore the heightened risk and severity of SAB in the context of a global health crisis.

In the management of *Staphylococcus aureus* bacteremia (SAB), consultations with infectious diseases (ID) specialists are crucial. They provide expert guidance on antibiotic selection, appropriate treatment durations, and the identification of potential complications. Such consultations have been associated with reduced mortality rates in SAB patients [10]. However, the COVID-19 pandemic placed unprecedented demands on ID departments in hospitals, primarily focusing their efforts on managing COVID-19 cases. This shift in focus led to a decrease in ID consultations for patients with SAB, which, in turn, may have contributed to a diminished quality of care for these patients. Consequently, studies suggest that the mortality rate for SAB patients has increased during the pandemic due to these healthcare system strains [7].

4.2. Age

Another factor contributing to this relatively elevated mortality could be the advanced median age of 63 years (with a range of 51–74) within the population under study. Our results align with Hal et al. and indicate that age is an independent and robust predictor of mortality [8]. Big et al. suggested that the elevated mortality rates could be ascribed to variations in the management and detection of SAB cases in the elderly population due to atypical and minimized symptoms in this population [19]. Nonetheless, in a case-control

Table 4
Logistic regression model for risk factors of mortality in patients with S.aureus bacteremia.

Variables		OR (95%CI)	P-value
Age		1.029 (1.007–1.052)	0.009
Sex	male	reference	0.033
	female	2.260 (1.067–4.788)	
COVID-19	Negative	reference	0.436
	Positive	1.344 (0.639–2.828)	
Source	Hospital-acquired	reference	**0.015**
	Community-acquired	5.281 (1.389–20.080)	
ICU admission	Negative	reference	**0.025**
	Positive	2.406 (1.118–5.177)	
Resistance to Clindamycin		0.939 (0.633–1.392)	0.755
Resistance to Sulfamethoxazole		1.211 (0.901–1.628)	0.204
Resistance to Ciprofloxacin		1.450 (0.983–2.139)	0.061
Resistance to Methicillin		0.992 (0.728–1.352)	0.960

ICU: Intensive-care unit.

study by Tacconelli et al., age was a significant factor in predicting mortality, even when elderly patients had comparable baseline characteristics and received similar SAB management [20]. Hence, the higher mortality rates attributed to SAB in older people are directly linked to age-related changes within the host [8].

4.3. Sex

In the current literature, there is a debate on the association between sex and death. Although there was no significant difference between genders in the bivariate analysis (P = 0.126), after adjustments in multivariate analysis, we found that female sex is a predictor of mortality (OR = 2.260, 95 % CI = [1.067–4.788]). Similar to our results, studies from Denmark (2638 patients) [21] and Israel (1293 patients) [11] suggest higher mortality in females. Nevertheless, studies from the United States (3384 patients) [13] and South Korea (1974 patients) [22] suggest the same mortality risk for males and females. Due to the heterogeneity of the evidence and the absence of any proposed etiology, systematic reviews and meta-analyses are recommended to shed light on the difference in mortality between genders.

4.4. Comorbidities

Although mortality in patients with DM was higher than in normal patients (47.2 % vs. 39.5 %), the difference was insignificant (P = 0.384). Similarly, Kaasch et al. conducted a pooled multicenter study of 3395 patients (856 diabetics) from Germany, Spain, the United Kingdom, and the United States. They found that DM was not associated with 7-, 14-, 30-, or 90-day mortality in bivariate analysis or multivariate analysis [23]. However, in the most extensive study on this topic in 2017, Hansen et al. mentioned that the risk of SAB was highest within the first year of diabetes diagnosis and gradually decreased over time [24]. This observation suggests that there could be a significant number of undiagnosed diabetes cases among patients with SAB. In other words, individuals who have not yet been diagnosed with diabetes may be more prevalent among those who develop SAB. This underscores the importance of early detection and diagnosis of diabetes to better manage the condition and potentially reduce the risk of SAB. Additionally, Hansen et al. found that DM with or without complications significantly increases the risk of 30-day mortality (P = 0.0001) [24]. Undiagnosed DM among patients could introduce confounding bias and influence the observed differences.

In a study by Vaart et al., in 2022 with 166 CA-SABs and 161 HA-SABs, they witnessed lower 90-day all-cause mortality in CA cases, while in multivariate analysis, the difference between CA and HA was insignificant (OR = 0.59, 95 % CI = [0.34–1.19]) [25]. Similarly, Østergaard et al. mentioned that the mortality rate was not different between CA- and HA- SAB even though patients with CA-SAB had an increased chance of developing *S. aureus* infective endocarditis (SAIE) [26]. Although the abundance of samples in the CA group was inadequate, a significant proportion of deaths (73.3 %) can be attributed to their underlying medical conditions. Among the 15 CA patients, eight had documented cancer cases, four were intravenous drug users, two had bedsores, and one was under routine dialysis with a catheter infection. Considering the outcomes observed in our study, it can be deduced that patients with community-acquired SAB were more susceptible to bacteremia and demonstrated decreased resilience to the infection.

4.5. Antibiotic resistance

The most recent systematic review and meta-analysis on SAB mortality conducted in 2022 by Bai et al. indicates that, however, the distinction remains significant, with MRSA associated with a higher number of fatalities, the mortality gap between MRSA and MSSA bloodstream infections has reached its minimum level [6]. As SAB is a high-risk condition, timely suspicion and antimicrobial treatment are necessary. Vancomycin is widely accepted for empiric therapy of SAB in countries with a high prevalence of MRSA. In the bivariate analysis, resistant strains caused higher mortality than susceptible strains, with significance observed only for Methicillin, Sulfamethoxazole, and Ciprofloxacin. However, in the multivariate analysis with adjusted data, antibiotic resistance did not independently predict mortality. Thus, we can conclude that pathogen-related factors like antibiotic resistance do not significantly impact mortality rates in settings with a low prevalence of vancomycin resistance.

In contrast, host-related factors such as age, sex, and comorbidities appear more influential. Fortunately, there were no reported cases of vancomycin-intermediate *Staphylococcus aureus* (VISA) or vancomycin-resistant *Staphylococcus aureus* (VRSA) at our center. As Shariati et al. report, resistance to vancomycin is on the rise yearly, although this rise is significant for bacteria intermediately resistant to vancomycin [27]. Possible explanations for the increase in the emergence and detection of resistant strains in recent years encompass several factors: high utilization of vancomycin for treating MRSA infections, improved diagnostic practices, insufficient monitoring of drug-resistant strains, and a potential alteration in the vancomycin-resistance thresholds since 2006 [27,28]. As reported by Tiri et al., the antibiotic resistance of *S. aureus* has been on the rise since the beginning of the COVID-19 pandemic [29]; therefore, it is essential to establish more effective antibiotic stewardship programs.

4.6. Other predictors

Similar to age, ICU is a well-established risk factor for mortality due to bloodstream infections SAB [9,10,30,31]. Yilmaz and colleagues conducted a study identifying ICU admission and age as independent risk factors for mortality [32]. They also noted a significant link between prior antibiotic consumption (at least three days within the last 30 days) and mortality within 28 days (P = 0.002); however, upon constructing a Cox proportional hazard model (unlike age and ICU admission), the association became insignificant (P = 0.181) [32]. Patients in the ICUs are more vulnerable and often present with more severe conditions compared to

those in general wards. Therefore, in ICU settings, there should be a heightened level of suspicion for bacteremia, and preventive measures should be initiated promptly.

Gafter-Gvili et al. suggested that thrombocytopenia could serve as a predictor for SAB mortality [33]. However, our findings were more consistent with those of Yilmaz and colleagues, as they did not observe a significant association between thrombocytopenia or any other CBC measures and mortality [32].

4.7. Limitations

This is study has many strengths and addressable limitations. Its strengths lie in its comprehensive analysis of SAB mortality, significant sample size of 167 cases, effective identification of key predictors like age, sex, ICU admission, and bacteremia source, and its relevance to the COVID-19 pandemic context. These aspects provide critical insights and data for understanding and managing SAB in a pandemic scenario.

Regarding its limitations, the study faces challenges like lack of past medical history and drug history of the patients, antibiotic resistance data (eg. for rifampin and cephalotin), lack of long-term follow-up, and its retrospective nature. However, these are mitigated by focusing on the most impactful comorbidities, including major antibiotics relevant to SAB treatment, providing valuable insights into mortality risks during hospitalization, and using real-world data to reflect actual clinical scenarios. These rebuttals highlight the study's practical applicability and relevance despite its constraints.

4.8. Recommendations

We recommend conducting a study with clearly defined population characteristics that include detailed information on specific comorbidities, hospital interventions, and treatments. A comparison of the quality of care through an analysis of Infectious Disease (ID) consultation frequency, antibiotic selection, and the quality of nursing care could provide valuable insights. Further comprehensive research into the differential impact of sex on *Staphylococcus aureus* bacteremia (SAB) outcomes is warranted. Investigating the prevalence of complications, such as infective endocarditis among SAB patients, would also be beneficial. We advise including data on both short- and long-term mortality rates, as well as post-discharge complications, in follow-up studies. Additionally, for the methods of antibiotic susceptibility testing, the use of quantitative approaches for all antibiotics—methods that provide exact Minimum Inhibitory Concentrations (MIC), such as the Broth Dilution Test or E Test—is recommended to obtain more accurate results.

5. Conclusion

In conclusion, this study provides valuable insights into SAB mortality during the initial two years of the COVID-19 pandemic and its predictors. With an in-hospital mortality rate of 41.9 %, SAB remains a challenging infection amplified by the pandemic. The study underscores the vulnerability of older individuals to SAB, highlighting the need for tailored care for this age group. While sex appears to predict mortality, further research is required for confirmation. Other key mortality predictors include ICU admission and community-acquired infections, emphasizing the importance of timely interventions and adaptable treatment strategies. Furthermore, in settings with high empiric therapy administration and high MRSA prevalence, host-related factors like age, sex, and quality of care are more important than pathogen-related factors such as antibiotic resistance. Further explorations concerning initial symptoms, precise patient characteristics, and long-term complications could yield more profound insights.

Ethics approval and consent to participate

This study was approved by the ethics committee of the Iran University of Medical Sciences (IUMS) (IR.IUMS.REC.1397.1155). Informed consent was waived due to the retrospective nature of the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author upon request.

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CRediT authorship contribution statement

Arash Abdollahi: Writing - review & editing, Writing - original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Marzieh Nojomi:** Writing - review & editing, Supervision, Methodology, Formal analysis. **Yeganeh Karimi:** Writing - original draft, Formal analysis, Data curation. **Mitra Ranjbar:** Writing - review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

List of abbreviations

SAB	*Staphylococcus aureus* bacteremia
DM	Diabetes Mellitus
CA-SAB	community-acquired *Staphylococcus aureus* bacteremia
HA-SAB	hospital-acquired *Staphylococcus aureus* bacteremia
ID	infectious disease
SAIE	*Staphylococcus aureus* infective endocarditis
ICU	Intensive care unit
AB	Antibiotic
MSSA	Methicillin-sensitive staphylococcus aureus
MRSA	Methicillin-resistant staphylococcus aureus
CSSA	Ciprofloxacin-sensitive staphylococcus aureus
CRSA	Ciprofloxacin-resistant staphylococcus aureus
VISA	Vancomycin-intermediately-resistant *Staphylococcus aureus*
VRSA	Vancomycin-resistant *Staphylococcus aureus*

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