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Infective Endocarditis in the Colombian Caribbean Region: Clinical Profile, Microbiological Insights, and Risk Factors for Mortality

Endocarditis Infecciosa en la Región Caribe Colombiana: Perfil Clínico, Conocimientos Microbiológicos y Factores de Riesgo de Mortalidad

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SUMMARY

Background: *Infective endocarditis (IE) is defined as the infectious and inflammatory process of the heart's internal structures. It can be caused by a broad group of bacteria and, rarely, fungi, with potentially life-threatening consequences.* **Objective***: To profile bacterial resistance and identify mortality risk factors in IE patients.* **Methods:** *This cross-sectional study included clinically diagnosed IE patients. Sociodemographic, comorbidity, clinical, and microbiological data were recorded. Descriptive analyses, Chi-Square/Fisher's exact tests, and Student's t-tests examined variables in relation to IE outcomes (survival vs. mortality). Multivariate logistic regression calculated odds ratios and confidence intervals.* **Results:** *We enrolled 39 patients (mean age 51 ± 19.5 years, 54 % male). Common comorbidities included acute kidney injury (AKI) (46 %), heart failure (26 %), and ischemic stroke (21 %). Deceased patients had higher rates of fatigue (p=0.03), lower limb edema (p=0.01), and AKI (p=0.01) than survivors. Fifteen (38 %) patients had positive cultures; Staphylococcus aureus predominated in survivors (13 %) and deceased (13 %) patients (p=0.06). Multi-drug-resistant bacteria were found in six (15 %) patients, and one (2.6 %) had Extensively Drug-Resistant bacteria. Multivariate Logistic Regression indicated that lower limb edema (OR 8.6, 95 % CI 1.5–49, p=0.01), and AKI (OR 7.8, 95 % CI 1.65–37.2, p=0.01) increased mortality risk in IE patients.* **Conclusion:** *In this study, lower limb edema and AKI were significant predictors of mortality in IE patients, emphasizing their clinical importance in IE progression and resolution. Further research should explore additional variables and risk factors to enhance our ability to predict and manage outcomes in this population.*

Keywords: *Infective endocarditis, outcome, antimicrobial resistance, heart failure.*

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RESUMEN

Antecedentes: *La endocarditis infecciosa (EI) se define como el proceso infeccioso e inflamatorio de las estructuras internas del corazón. Puede ser causada por un amplio grupo de bacterias y, rara vez, por hongos, con consecuencias potencialmente mortales.* **Objetivo:** *perfilar la resistencia bacteriana e identificar factores de riesgo de mortalidad en pacientes con EI.* **Métodos:** *Este estudio transversal incluyó pacientes con EI clínicamente diagnosticada. Se registraron datos sociodemográficos, de comorbilidad, clínicos y microbiológicos. Los análisis descriptivos, las pruebas de Chi-Cuadrado/exactas de Fisher y las pruebas t de Student examinaron las variables en relación con los resultados de IE (supervivencia versus mortalidad). La regresión logística multivariada calculó los Odds ratios y los intervalos de confianza.* **Resultados:** *Se incluyeron 39 pacientes (edad media 51 ± 19,5 años, 54 % hombres). Las comorbilidades comunes incluyeron lesión renal aguda (IRA) (46 %), insuficiencia cardíaca (26 %) y accidente cerebrovascular isquémico (21 %). Los pacientes fallecidos tuvieron tasas más altas de fatiga (p=0,03), edema de miembros inferiores (p=0,01) y IRA (p=0,01) que los supervivientes. Quince (38 %) pacientes tuvieron cultivos positivos; Staphylococcus aureus predominó en los pacientes sobrevivientes (13 %) y fallecidos (13 %) (p=0,06). Se encontraron bacterias multirresistentes en seis (15 %) pacientes y uno (2,6 %) tenía bacterias extremadamente resistentes a los medicamentos. La regresión logística multivariada indicó que el edema de las extremidades inferiores (OR 8,6, IC 95 % 1,5–49, p = 0,01) y la IRA (OR 7,8, IC 95 % 1,65–37,2, p = 0,01) aumentaron el riesgo de mortalidad en pacientes con EI.* **Conclusión:** *En este estudio, el edema de las extremidades inferiores y la IRA fueron predictores significativos de mortalidad en pacientes con EI, enfatizando su importancia clínica en la progresión y resolución de la EI. Investigaciones adicionales deberían explorar variables y factores de riesgo adicionales para mejorar nuestra capacidad de predecir y gestionar los resultados en esta población.*

Palabras clave: *Endocarditis infecciosa, resultado, resistencia antimicrobiana, insuficiencia cardíaca.*

INTRODUCTION

Infective endocarditis (IE) is a disease that primarily affects internal structures of the heart, such as the cardiac endothelium itself, as well as native or prosthetic valves, resulting from a bacterial or fungal infection. Its presentation can range from acute to subacute (1). It is closely associated with healthcare practices, with the placement of central venous catheters and dental procedures being among the leading risk factors for developing this cardiac infection. However, patients with intravenous drug use, congenital defects, degenerative heart diseases, among others, can also develop IE (2-4).

Complications arising from IE can be catastrophic and result in high morbidity and mortality, despite its diagnosis and management having been established in clinical practice guidelines for several years (5). Additionally, these complications impose significant costs on the healthcare system, as they lead to physical disabilities that can impact the employment status of those affected and their substantial socioeconomic burden on the population. Hospital-acquired infections follow a more severe and increasing pattern in terms of occurrence, mainly due to the frequent need for invasive procedures in complicated patients who require closer monitoring of their condition (6-8).

IE primarily affects middle-aged individuals, with an average age of 55 years, and the gender distribution is marked by 68 % in males and 32 % in females. At the time of diagnosis, up to 40 % of patients with IE have no comorbidities. However, up to 10% of patients diagnosed with congestive heart failure can have IE (8). This is likely due to valvular anatomy degeneration; nevertheless, the epidemiological profile of this disease is not yet clearly understood (9).

In Latin America, including Colombia, it was observed that IE predominantly affects males in up to 68.5 % of the cases. Valvulopathies were the most frequent risk factor (24.3 %). Regarding microbiological characteristics, the most prevalent isolated microorganisms were *Staphylococcus aureus* (27.3 %), followed by viridans group streptococci (VGS) in up to 26.7 % of the cases with IE (10).

In the Colombian Caribbean Region, especially in Barranquilla city, epidemiological reports of IE are outdated and scarce. This implies that establishing the infectious profile of a rare but necessary pathology can be complex. This study aimed to characterize the bacterial resistance profile in patients diagnosed with infective endocarditis at a hospital reference

center in Barranquilla and to identify risk factors associated with mortality in this population.

METHODS

A cross-sectional study was conducted, enrolling clinically diagnosed IE patients hospitalized at a reference hospital center in Barranquilla, Atlántico, Colombia between 2017 and 2022. Sociodemographic, comorbidity, and clinical characteristics were collected. A database was designed, incorporating admission data, and this information was cross-referenced with culture data.

Data distribution was assessed using the Shapiro-Wilk test, confirming the parametric nature of the data for subsequent analysis. Measures of central tendency (mean and standard deviation) were calculated for quantitative variables, while for categorical variables, absolute and relative frequencies were determined. Means obtained by patients were compared based on the outcome (Survivor vs. Deceased) using the Student's t-test. The Chi-Square test or Fisher's exact test was employed to analyze categorical variables, depending on the distribution compliance of the categories.

A multivariate logistic regression model was constructed to identify potential risk factors for mortality. The model was selected and adjusted using the Backward method, considering the minimum number of variables necessary. Adjusted Odds Ratios were reported along with 95 % confidence intervals. A p-value < 0.05 was considered statistically significant. The statistical software used in this study was R-CRAN VERSION 4.3.0 (11).

RESULTS

Thirty-nine patients with IE were enrolled in the study. The average age was 51 ± 19.5 years. The most common age group was adults (44 %) (27 - 59 years) (Table 1). In this study, 54 % of the patients were male, with a male-to-female ratio of 6 to 5. No significant difference was found between age and sex (p=0.8) (Figure 1). Acute kidney injury (AKI) (49 %) was the most common comorbidity, followed by heart failure (26 %) and ischemic stroke (21 %) (Table 1).

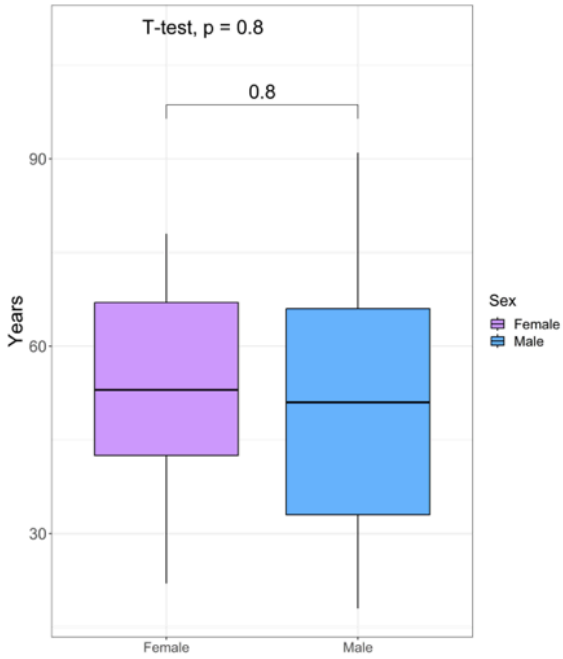

Figure 1. Distribution of the age (in years) of patients with IE by gender.

Comorbidities and Outcomes

In this study, we compared the frequency of comorbidities in patients with IE based on the outcome (Survivors *vs*. Deceased) (Table 1). No significant differences were identified in the frequency of ischemic stroke (p = 0.7), hemorrhagic stroke (p = 0.4), heart failure (p = 0.5), pulmonary embolism (p = 0.4), and splenomegaly (p = 0.4) between survivors and deceased cases. However, a notable association was observed between AKI and mortality, with a higher prevalence in deceased patients (73 % *vs*. 33 %, p = 0.02) (Figure 2) (Table 1).

Table 1

Sociodemographic Characteristics and Comorbidities in Survivor vs. Deceased Patients with Infective Endocarditis

Characteristic	**Overall (n=39)[1]**	**Deceased (n=15)[1]**	**Survivor (n=24)[1]**	**p-value**
Age	51 ± 19.5	54 ± 20.6	50 ± 17	0.6[2]
Sex				>0.9[3]
Female	18 (46 %)	7 (47 %)	11 (46 %)	
Male	21 (54 %)	8 (53 %)	13 (54 %)	
Age Group				0.6[4]
Adulthood	17 (44 %)	7 (47 %)	10 (42 %)	
Elderly	16 (41 %)	7 (47 %)	9 (38 %)	
Youth	6 (15 %)	1 (6.7 %)	5 (21 %)	
Comorbidities and clinical findings				
HF	10 (26 %)	5 (33 %)	5 (21 %)	0.5[4]
IS	8 (21 %)	4 (27 %)	4 (17 %)	0.7[4]
ICH	1 (2.6 %)	1 (6.7 %)	0 (0 %)	0.4[4]
Abscesses	1 (2.6 %)	0 (0 %)	1 (4.2 %)	>0.9[4]
Pulmonary Embolism	1 (2.6 %)	1 (6.7 %)	0 (0 %)	0.4[4]
AKI	19 (49 %)	11 (73 %)	8 (33 %)	0.015[3]
Splenomegaly	1 (2.6 %)	1 (6.7 %)	0 (0 %)	0.4[4]

HF: Heart failure, IS: Ischemic Stroke, ICH: Intracerebral Hemorrhage, AKI: Acute Kidney Injury
[1] Mean (SD); n (%)
[2] Welch Two Sample t-test
[3] Pearson's Chi-Squared test
[4] Fisher's exact test

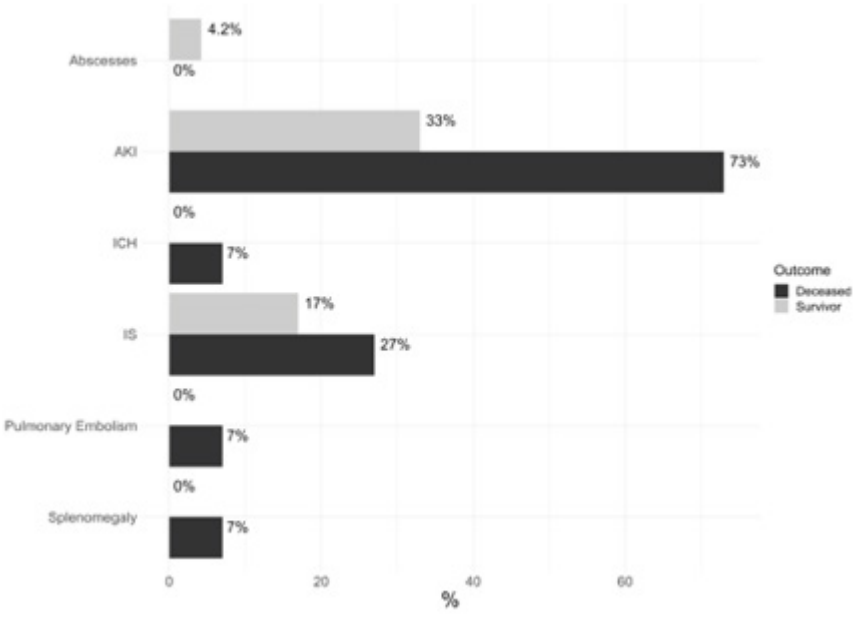

Figure 2. Comorbidities and clinical findings in patients with IE according to outcome

Clinical and Echocardiographic Manifestations

Table 3 presents a summary of the primary clinical and echocardiographic findings in patients with infective endocarditis, categorized by the outcome. In terms of clinical manifestations, a notably higher proportion of deceased patients exhibited fatigue (71 % *vs*. 100 %, p = 0.03) and lower limb edema (60 % *vs*. 21 %, p = 0.01) compared to survivors. However, no significant differences were detected in left ventricular ejection fraction between survivors and deceased patients (53.2 ± 10.3 vs. 52.1 ± 15.2, p = 0.8) (Figure 3). Similarly, there were no significant disparities in the affected heart valves, as the mitral, aortic, mitral, and tricuspid valves displayed similar frequencies across both groups (p > 0.05) (Table 2).

Microbiological Profile and Bacterial Resistance

Microbiological characterization of patients with IE is summarized in Table 4. There were no significant differences observed in culture positivity between survivors and deceased individuals (29 % *vs*. 53 %, p = 0.18) (Table 3) (Figure 4). *Staphylococcus aureus* (13 %) was the most frequently isolated microorganism in both groups. No significant differences were found in the distribution of isolated microorganisms between the groups. Regarding the resistance profile, there were no significant differences observed in sensitivity or resistance to antimicrobials (p > 0.05). Specifically for resistance, two cases of *methicillin-resistant Staphylococcus aureus* (MRSA) were identified in each group for MDR (Multidrug Resistance), along with one case of *methicillin-resistant Staphylococcus aureus* (MRSA) with the mecA gene in the deceased group. Furthermore, one case of extensively drug-resistant (XDR) bacteria was identified in the deceased group (Table 3).

Table 2

Clinical and Echocardiographic Manifestations in Surviving vs. Deceased Patients with Infective Endocarditis

	Characteristic	Overall (n=39)[1]	Deceased (n=15)[1]	Survivor (n=24)[1]	p-value
Clinical Manifestations	Arthralgia	8 (21 %)	4 (27 %)	4 (17 %)	0.7[2]
	Myalgia	4 (10 %)	2 (13 %)	2 (8.3 %)	0.6[2]
	Dyspnea	24 (62 %)	11 (73 %)	13 (54 %)	0.2[3]
	Fatigue	32 (82 %)	15 (100 %)	17 (71 %)	0.031[2]
	Edema	14 (36 %)	9 (60 %)	5 (21 %)	0.013[3]
	ACS	9 (23 %)	2 (13 %)	7 (29 %)	0.4[2]
	Chills	10 (26 %)	3 (20 %)	7 (29 %)	0.72
Echocardiography	EF	52 ± 12	52.1 ± 15.2	53.2 ± 10.3	0.8[4]
	EF Categories				0.9[3]
	HFpEF	24 (62 %)	9 (60 %)	15 (63 %)	
	HFrEF	15 (38 %)	6 (40 %)	9 (38 %)	
	Affected Heart Valve				>0.9[2]
	Aortic	3 (18 %)	1 (14 %)	2 (20 %)	
	Mitral	7 (41 %)	3 (43 %)	4 (40 %)	
	Mitral y Aortic	5 (29 %)	2 (29 %)	3 (30 %)	
	Tricuspid	2 (12 %)	1 (14 %)	1 (10 %)	

EF: Ejection Fraction, HFpEF: Heart failure with preserved ejection fraction, HFrEF: Heart failure with reduced ejection fraction, HFpEF: Heart failure with preserved ejection fraction

[1] n (%); Mean ± SD

[2] Fisher's exact test

[3] Pearson's Chi-Square test

[4] Welch Two Sample t-test

Table 3

Microbiological Characterization in Surviving vs. Deceased Patients with Bacterial Endocarditis

Characteristic	Overall (n=39)[1]	Deceased (n=15)[1]	Survivor (n=24)[1]	p-value
Culture				0.13[2]
Negative	24 (62 %)	7 (47 %)	17 (71 %)	
Positive	15 (38 %)	8 (53 %)	7 (29 %)	
Microbial Profile				0.06[3]
Enterobacter cloacae	1 (2.6 %)	1 (6.7 %)	0 (0 %)	
Enterococos faecalis	3 (7.7 %)	3 (20 %)	0 (0 %)	
Klebsiella pneumoniae	1 (2.6 %)	1 (6.7 %)	0 (0 %)	
Pseudomonas aeruginosa	1 (2.6 %)	0 (0 %)	1 (4.2 %)	
Staphylococcus aureus	5 (13 %)	2 (13 %)	3 (13 %)	
Staphylococcus lentus	1 (2.6 %)	0 (0 %)	1 (4.2 %)	
Staphylococcus saprophyticus	1 (2.6 %)	1 (6.7 %)	0 (0 %)	
Stenotrophomona maltophila	1 (2.6 %)	0 (0 %)	1 (4.2 %)	
Streptococcus bovis	1 (2.6 %)	0 (0 %)	1 (4.2 %)	
AMR				0.4[3]
MDR	6 (15 %)	3 (20 %)	3 (13 %)	
XDR	1 (2.6 %)	1 (6.7 %)	0 (0 %)	

AMR: Antimicrobial Resistance, MDR: Multi-Drug Resistant, XDR: Extensively Drug-Resistant
[1] n (%)
[2] Pearson's Chi-Square test
[3] Fisher's exact test

Risk Factors for Mortality

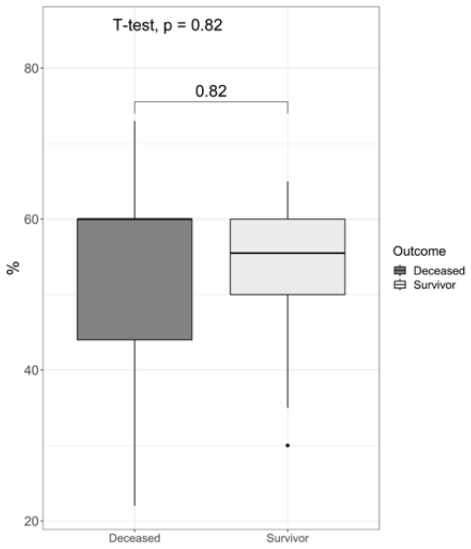

Figure 3. Left ventricular ejection fraction.

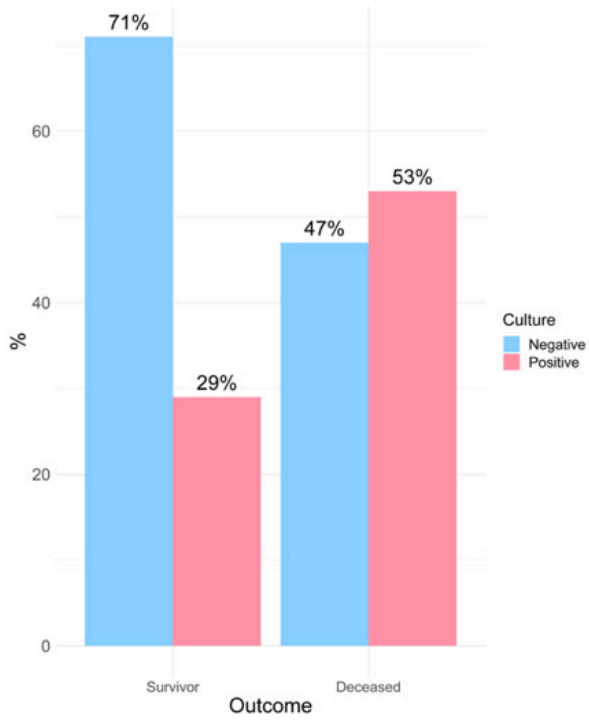

Figure 4. Culture positivity and negativity in survivors and deceased IE patients.

In the multivariate logistic regression analysis, we assessed several factors with mortality outcomes in patients with IE. Following model adjustments, our results revealed that edema (OR 8.6, 95 % CI 1.5 – 49, p = 0.01) and AKI (OR 7.8, 95 % CI 1.65 – 37.2, p = 0.01) significantly elevated the risk of mortality among IE patients (Table 4). No statistically significant associations were identified in variables related to microbiological, echocardiographic, or antimicrobial resistance factors.

Table 4

Results of the logistic regression multivariable model

Characteristic	n	OR1	95% CI1	p-value	Adjusted OR1*	95% CI1	p-value
Age	39	1.01	0.98, 1.05	0.5			
Sex	39						
Male		0.97	0.26, 3.59	>0.9			
Age Group	39						
Elderly		1.11	0.28, 4.50	0.9			
Youth		0.29	0.01, 2.32	0.3			
Edema	39						
Yes		5.70	1.43, 25.8	0.017	8.6	1.5, 49	0.01
AKI	39						
Yes		5.50	1.41, 25.4	0.019	7.8	1.65, 37.2	0.01
HF	39						
Yes		1.90	0.43, 8.44	0.4			
EF Category	39						
HFrEF		1.11	0.29, 4.19	0.9			
Affect Heart Valve	17						
Mitral		1.50	0.09, 42.1	0.8			
Mitral y Aortic		1.33	0.07, 41.6	0.9			
Tricuspid		2.00	0.04, 120	0.7			
Culture	39						
Positive		2.78	0.74, 11.1	0.14			

AKI: Acute kidney injury, EF: Ejection fraction, HF: Heart failure, HFrEF: Heart failure with reduced ejection fraction
* Adjusted by Backward method
1 OR = Odds Ratio, CI = Confidence Interval

DISCUSSION

Staphylococcus aureus was the most frequently isolated microorganism, and no differences were observed in culture positivity or the distribution of isolated microorganisms between the groups. Cases of methicillin resistance and MRSA were identified in the deceased group. Finally, in the multivariate logistic regression model, the presence of lower limb edema was found to increase the likelihood of mortality in patients with Bacterial Endocarditis. These findings underscore the significance of edema and AKI as risk factors in the outcome and mortality of patients with IE.

One of the key findings of this study is the sociodemographic and clinical profile of patients with infective endocarditis. With a sample of 39 patients, an average age of 51 years was identified, with the adult patient group (44 %) being the most frequent. These results support the notion that IE can affect a wide range of ages, although it appears to be more common in adults. The absence of significant differences in patient gender suggests that this disease does not exhibit a marked gender preference (12,13).

The comorbidities identified in the study population shed light on concurrent medical conditions in patients with IE. The most prevalent comorbidities included AKI, heart failure, and ischemic stroke. These findings are consistent with existing medical literature, highlighting how preexisting medical conditions can increase susceptibility to developing infective endocarditis and complicate its clinical management (14,15).

The results showed that there were no significant differences in the frequency of comorbidities between survivors and deceased individuals, except in the case of AKI. This suggests that the presence of AKI could serve as a predictive indicator of a worse prognosis in IE patients. This could have significant implications in the assessment and management of patients with this disease, allowing for early identification of cases at higher risk and more intensive medical care (9,16).

The significant association between lower limb edema and mortality is another notable finding. This observation underscores the existence of serious complications related to the cardiovascular or renal system in patients with IE who present lower limb edema. It indicates that the presence of lower limb edema could be linked to the progression of the disease or the development of severe complications, which could explain its association with mortality (9).

It is noteworthy that no significant differences were found in most clinical and echocardiographic manifestations between surviving and deceased patients. This finding might suggest that, in general, clinical, and echocardiographic features are not definitive predictors of mortality risk in patients with IE. However, one aspect to highlight is the identification of significant associations between specific symptoms and the fatal outcome. In particular, the significant relationship between fatigue and mortality raises the possibility that other factors may influence the deterioration of patients' conditions and their lack of response to treatment in these cases (14,15).

The predominant presence of *Staphylococcus aureus* as the most frequently isolated microorganism in both groups, survivors, and deceased, highlights the importance of this pathogen in the etiology of IE in the region. This finding supports existing literature, which also emphasizes the relevance of *Staphylococcus aureus* in cardiac infections (17-19). No significant differences were observed in culture positivity or the distribution of isolated microorganisms between the groups of survivors and deceased individuals, this could indicate that the presence of certain pathogens may not be a determining factor in the mortality associated with infective endocarditis. This raises the possibility that other clinical factors, such as the severity of the infection, the patient's immune response, and the effectiveness of treatment, may have a more direct impact on clinical outcomes (20).

The identification of cases of antibiotic resistance in the deceased patient group underscores a concerning trend in bacterial resistance and its association with worse clinical outcomes. These results suggest that antibiotic resistance could play a relevant role in the disease's progression and possibly in the mortality of patients with infective endocarditis. This highlights the ongoing need for monitoring and proper management of bacterial resistance in the clinical context to ensure that treatments are effective and can adequately control infections (21).

The fact that no significant differences were found in the sensitivity or resistance to antimicrobials based on the outcome is an important consideration. This could suggest that, in the context of this research, bacterial resistance was not directly related to the patient's outcomes. However, it is crucial to consider that clinical and therapeutic factors may be interrelated and may have influenced the observed relationship. It is possible that other elements, such as timely antimicrobial therapy and proper disease management, may have mitigated the impact of bacterial resistance in this population (1,22).

Risk factors for mortality in patients with IE are of great interest as they allow for the identification of critical elements that influence clinical outcomes. In this study, a significant result is highlighted through a multivariate logistic regression model: the presence of lower limb edema and AKI are significantly associated with an increased likelihood of mortality in patients with IE. This finding has important implications for clinical practice and the management of patients with infective endocarditis (23). It is

plausible that this clinical manifestation is related to the spread of the infection or the involvement of the cardiovascular system that leads to kidney injury, which could explain its association with increased mortality. These results underscore the need for a comprehensive and vigilant evaluation of patients with endocarditis, especially those presenting clinical signs such as lower limb edema (23,24).

This study highlights the clinical significance of lower limb edema and AKI as critical markers in the progression and resolution of IE. These findings underscore the importance of early detection and intervention in patients presenting with these symptoms, as they are associated with an increased risk of mortality. Additionally, the prevalence of *Staphylococcus aureus*, including multi-drug-resistant and extensively drug-resistant strains, emphasizes the need for vigilant monitoring of bacterial resistance in IE cases. Further research is warranted to explore additional variables and risk factors that may influence the mortality of IE patients, ultimately enhancing our ability to predict and manage adverse outcomes in this population.

Ethics approval and consent to participate

This study was approved by the ethics committee of the clinic where the research was conducted. All procedures were performed under the relevant guidelines and regulations. Written informed consent was obtained from the patients for their participation in this study.

Consent for publication

Written informed consent was obtained from the patients for publication. There are no identifying images or other personal or clinical details of the patient that compromise their anonymity in this manuscript.

Availability of data and materials

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

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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