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Hospital Based Microbiological Surveillance and Antibiotic Resistance of Infective Endocarditis in Fars Province

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Abstract

Background: Infective endocarditis (IE) is a severe cardiac infection involving microbial colonization of endocardial surfaces, primarily valves. Diagnosis is complex, requiring identification of the primary cardiac site and assessment of systemic complications.

Objectives: This study aims to identify, monitor, and characterize nosocomial pathogens causing IE to enhance therapeutic strategies.

Methods: This cross-sectional study was performed on 20 patients with IE in Namazi, Shahid Faqihi, and Qalb al-Zahra hospitals in Shiraz. Participants were Iranian adults (aged 18 - 80) presenting with initial symptoms of IE according to the modified Duke criteria. The study period was 18 months. All cases were evaluated by blood culture test. Then, by biochemical methods, known microorganisms were assessed. Finally, the genome of all known bacteria in IE was amplified by polymerase chain reaction (PCR) and then sequenced. GraphPad Prism 9.0 was used for statistical analysis. The chi-square and Fisher's exact tests were used to assess correlations (P-value < 0.05 considered significant).

Results: Blood culture analysis in this IE cohort revealed 85% positivity (17/20 cases). Among positive cultures, *Staphylococcus aureus* (25%), *Streptococcus* spp. (20%), and *S. epidermidis* (15%) were the most prevalent pathogens. Notably, staphylococci collectively accounted for 74% of all pathogenic isolates. The affected population was predominantly male (highest percentage) within the 41 -60 year age range. Furthermore, antimicrobial susceptibility testing indicated markedly elevated rates of antibiotic resistance among the identified microorganisms.

Conclusions: This study identifies *Staphylococcus* species, particularly *S. aureus*, as the predominant IE pathogens. The detection of fastidious organisms in culture-negative cases highlights the need to expand the etiological spectrum considered, especially in region-specific contexts. The high prevalence of antimicrobial resistance among isolates necessitates enhanced microbial surveillance and robust antibiotic stewardship. Rapid pathogen identification and molecular characterization remain critical for optimizing IE diagnostic and therapeutic management.

Keywords: Cardiovascular Diseases, Infective Endocarditis, Bacteria, Cardiac Valve, 16S rRNA

1. Background

Infective endocarditis (IE) is a mysterious disease that continues to puzzle scientists. After penetrating the bloodstream, bacteria are moved via the heart at a speed of nearly 60 km/h (1, 2). However, because of this whirling stream, some bacteria connect to one of the valves of the heart. There, they conscript fibrin and platelets in a growing endocarditis lesion called vegetation. This vegetation, which is at its core an infected blood clump dangling off one of the heart valves, protects the pathogens from the immune system's continuous attacks and allows them to grow uncontrolled and achieve higher bacterial densities than those in skin abscesses (1). If left untreated, the mortality rate of IE reaches almost 100%, and even with

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optimal therapy, one in three patients dies (3). Even though the high mortality rate of IE compared to other infectious and cardiovascular diseases has not changed in the past decades, and even though IE remains a rather rare illness, affecting yearly between 2 - 12 × 10^5 persons, it is estimated that the cause of death is above 10^5 persons around the world per year (4). The most common type of IE is mitral or aortic valve endocarditis (5, 6).

Different types of *Staphylococcus* are the most commonly involved bacteria (7, 8) and are correlated with high rates of morbidity and mortality because of their strong avidity for endothelial tissue, their ability to create an endovascular infection, and their aggressive nature (9-11). New treatments and prophylactic methods for this devastating disease are urgently required. Unfortunately, the IE pathogenesis is so complex and strange that up to now it is not clear how and why some bacteria like *Staphylococcus aureus*, *Streptococcus* spp., and *S. epidermidis*, flourish in places such as the cardiac valves. In this study, we explore the hospital microorganisms that lead to IE.

2. Objectives

This study aims to identify, monitor, and characterize nosocomial pathogens causing IE to enhance therapeutic strategies.

3. Methods

3.1. Study Subjects and Sampling

For this study, 20 IE patients (55% male and 45% female) over 18 months from September 2018 to February 2020 were selected from hospitalized patients in Namazi, Shahid Faqihi, and Qalb al-Zahra hospitals in Shiraz, Iran. All included cases were selected from Iranian adults (18 - 80 years old) who had the initial symptoms of IE. Written informed consent was obtained from all study participants. In addition, all protocols used complied with the medical guidelines of the Declaration of Helsinki. The sample size of 20 was specified by the number of confirmed IE cases presenting at the selected hospitals during the study period that met the inclusion criteria, reflecting the preliminary and descriptive nature of this study. Blood sampling of all participants after obtaining written consent was done in a final volume of 20 mL in a blood culture tube.

3.2. Blood Culture

The blood culture was performed in blood culture tubes. In the first step, the caps of blood culture tubes were sterilized, and then blood was added to the tubes. The blood culture tubes were incubated in a 37°C, CO_2 incubator for 48 hours. All of them were assessed periodically; hence, when the growth of bacteria was clear, the amount of blood was sub-cultured on an efficient culture medium such as blood agar, chocolate agar, and Eosin Methylene Blue agar (EMB) for a variable time between 7 - 21 days. After colony growth, to identify the gram-negative bacteria, the lysine decarboxylase, ornithine decarboxylase, phenylalanine decarboxylase, urease, Triple Sugar-Iron (TSI), Voges-Proskauer (VP), methyl red (MR), citrate, and sulfide indole motility (SIM) tests were performed. Also, to identify the gram-positive bacteria, standard biochemical tests were used.

3.3. Antibiotic Susceptibility Evaluation by Disk Diffusion Method

After bacteria isolation, an amount of each bacterial colony was added to sterile normal saline, and the concentration was confirmed compared to 0.5 McFarland solution. In the next step, the solution was cultured on a Mueller Hinton agar medium. In the third step, appropriate antibiogram discs for the type of studied bacteria were placed in a circular pattern with a 12 mm distance on the cultured medium. All discs were selected based on the Clinical and Laboratory Standards Institute (CLSI 2021) standards (12). After that, all plates were incubated in a 37°C, CO_2 incubator for 24 hours. At the end of 24 hours, zones of lack of growth were assessed in plates and compared to the company instruction (Padtanteb company, Iran) (https://padtanteb.ir/), and results were published in three different statuses: Sensitive, Intermediate, and Resistant. In this study, 20 antibiotics from 12 different antibiotic classes were used (Table 1).

3.4. Molecular Tests

3.4.1. Bacterial DNA Extraction

For specific bacterial DNA extraction, the studied individual's erythrocytes should be removed, so based on the company protocol, the MR buffer was used. Then,

Table 1. Antibiotic Classes and Agents Used in Microorganism Resistance Evaluation

No.	Antibiotic Classification	Antibiotic (µg)
1	Aminoglycoside	Gentamicin (10), amikacin (30)
2	Carbapenem	Imipenem (10)
3	First and second Cephalosporin	Cefalexin (30)
4	Third and fourth Cephalosporin	Cefotaxime (30), ceftazidime (30), cefixime (5)
5	Macrolide	Erythromycin (15), azithromycin (15), clindamycin (2), lincomycin (2)
6	Glycopeptide	Vancomycin (30)
7	Sulfonamide	Co-trimoxazole (10)
8	Fluroquinolone	Ciprofloxacin (5), ofloxacin (5)
9	Penicillin	Ampicillin (10), cloxacillin (10)
10	Phenicol	Chloramphenicol (30)
11	Polymyxin	Colistin (10)
12	Tetracycline	Tetracycline (30)

for gram-positive and gram-negative bacteria DNA extraction, all steps were done according to the DNA extraction kit company instruction (Bacteria DNA Extraction kit, Poya Gene azma, Iran). Extracted DNA samples' purity and concentration were determined using a Nanodrop spectrophotometer (Thermo Fisher Scientific, USA) by measuring the optical density at 260/280 nm.

3.4.2. Molecular Identification

To improve extracted DNA copies, a polymerase chain reaction (PCR) was performed by the listed primers in Table 2 (13). The amount of each required agent and the condition of PCR are shown in the following table. After the end of PCR, to evaluate the PCR products, electrophoresis was done. To investigate the final results, after the electrophoresis duration, the agarose gel was placed in an ultraviolet transillumination device, and the final picture appeared. All PCR products were sent to Macrogen, South Korea for sequencing, and the sequencing method was Sanger sequencing. The phylogenetic tree of 16S rRNA gene sequences was constructed using the neighbor-joining method with 100 bootstrap replicates in MEGA 10.

3.5. Statistical Analysis

GraphPad Prism 9.0 was used for statistical analysis (GraphPad Software, Inc., San Diego, CA, USA). The chi-square and Fisher tests evaluated the correlation among the investigated variables. P-values less than 0.05 were considered statistically significant.

4. Results

The most frequent persons with IE belonged to ages 41 - 60 years old (6 females and 5 males), and the lowest frequency belonged to ages 61 - 80 years old (2 males) (For more information see Table 3).

4.1. Antibiotic Susceptibility

In an investigation of *S. aureus* antibiotic susceptibility, it was found that the highest resistance of this microorganism is to clindamycin, erythromycin, and cloxacillin, which are respectively located in the macrolide and penicillin groups of antibiotics (Table 1). This microorganism's susceptibility to different antibiotics is listed in Table 4, which shows the pattern of *S. aureus* sensitivity. Following this, in the evaluation of *S. epidermidis*, we found that it is highly sensitive to vancomycin (glycopeptide group) and also showed a low-level resistance to lincomycin (macrolide group) and chloramphenicol from the phenicol group of antibiotics.

In the same investigation on *Streptococcus* spp., it was revealed that it has a high resistance to a member of the penicillin group, called ampicillin, and it has a high sensitivity to co-trimoxazole, lincomycin, and imipenem, which respectively belong to the sulfonamide, macrolide, and carbapenem groups of antibiotic classification. For *Enterococcus* spp., our results showed high sensitivity to ampicillin from the penicillin family. Also, the same tests for *Escherichia coli* showed high sensitivity to amikacin from the aminoglycoside family and colistin from the polymyxin family. In *Pseudomonas* spp., susceptibility tests revealed a high resistance against cefotaxime and

Table 2. The Primer Sequences and Polymerase Chain Reaction Conditions

Genes	Primer Sequence 5´ to 3´	PCR Condition	Reaction Mixture
16SF(a)	GCTCAGATTGAACGCTGG	1 cycle: 94◦C /5 min 35 cycles: Denaturation: 95◦C/60 s Annealing: 58◦C/60 s Extension: 72◦C/60 s Followed by 1 cycle: 72◦C/7min	5 µL of PCR buffer, 1.5 µL of $Mgcl_2$ solution, 0.5 µL of dNTP mix,1 µL of each forward primer a and b, and reverse primer (10 pm), 0.5 µL of Taq DNA polymerase, and 3µL of extracted DNA, Add water up to a total volume of 50 µL
16SF(b)	GCTCAGGACGAACGCTGG		
16SR	TACTGCTGCCTCCCGTA		

Abbreviation: PCR, polymerase chain reaction.

Table 3. Demographic and Descriptive Characteristics in Study Groups [a]

Factors	IE Cases
Number of participants	20
Gender of participants	
Female	9 (45)
Male	11 (55)
Age of participants (y)	
1 - 20	3 (15)
21 - 40	4 (20)
41 - 60	11 (55)
61 - 80	2 (10)
Underline disease	
Cardiac rheumatism	6 (30)
Congenital heart disease	4 (20)
Coronary heart disease	7 (35)
Other diseases	3 (15)
History of surgery	
Valve replacement or repair surgery	6 (30)
Gingiva surgery	4 (20)
Pacemaker implantation surgery	3 (15)
Other surgery	2 (10)
Without surgery	5 (25)

Abbreviation: IE, infective endocarditis

[a] Values are expressed as No. (%).

chloramphenicol, which belong to the phenicol and cephalosporin families.

4.2. Antimicrobial Susceptibility Patterns of Identified Pathogens

After the investigation of microorganisms' resistance to antibiotics, our studied microorganisms were classified into three different groups: Multi drug resistant (MDR), pandrug resistant (PDR), and extensively drug-resistant (XDR). Three (60%) of 5 cases of *S. aureus* were resistant to different antibiotics, and the remaining 2 patients were sensitive. So, 4 (80%) of those infected with *S. aureus* were non-MDR and 1 (20%) person was MDR. All infected cases with *S. epidermidis* [3 cases, (2, 66.67% MDR and 1, 33.33% PDR)], *Streptococcus* spp. [4 cases (3, 75% non-MDR and 1, 25% MDR)], *Enterococcus* spp. (2 cases were PDR), *E. coli* [2 cases (1, 50% XDR and 1, 50% MDR)], and *Pseudomonas* spp. (1 person MDR) were resistant to different types of antibiotics, and their classification is shown in Table 5.

4.3. Blood Culture Test

Based on blood culture, it was found that 17 [11 males (55%) and 6 females (30%)] IE cases were positive and 3 [all of them were female (15%)] were negative (Figure 1A). So, a significant relation was detected between the most

Table 4. Percentage of Resistant Antibiotic among Clinical Isolates from Infective Endocarditis Patients

Antibiotics	Susceptibility	*Staphylococcus aureus* (N = 5)	*S. epidermidis* (N = 3)	*Streptococcus* sp. (N = 4)	*Enterococcus* sp. (N = 2)	*Escherichia coli* (N = 2)	*Pseudomonas* sp. (N = 1)
Vancomycin	Resistant	1 (20)	0	1 (25)	2 (100)	-	-
Chloramphenicol	Resistant	1 (20)	1 (33.33)	2 (50)	2 (100)	1 (50)	1 (100)
Gentamicin	Resistant	2 (40)	3 (100)	-	-	1 (50)	0
Lincomycin	Resistant	1 (20)	1 (33.33)	0	2 (100)	-	-
Co-trimoxazole	Resistant	1 (20)	2 (66.67)	0	2 (100)	1 (50)	0
Ciprofloxacin	Resistant	1 (20)	3 (100)	1 (25)	2 (100)	2 (100)	1 (100)
Cloxacillin	Resistant	2 (40)	3 (100)	1 (25)	2 (100)	-	-
Cefalexin	Resistant	1 (20)	2 (66.67)	1 (25)	2 (100)	2 (100)	1 (100)
Erythromycin	Resistant	2 (40)	2 (66.67)	-	2 (100)	-	-
Clindamycin	Resistant	2 (40)	2 (66.67)	-	2 (100)	-	-
Ampicillin	Resistant	-	-	3 (75)	0	-	-
Imipenem	Resistant	-	-	0	2 (100)	2 (100)	0
Ofloxacin	Resistant	-	-	1 (25)	2 (100)	-	-
Azithromycin	Resistant	-	-	-	2 (100)	-	-
Amikacin	Resistant	-	-	-	-	0	0
Colistin	Resistant	-	-	-	-	0	0
Tetracycline	Resistant	-	-	-	-	2 (100)	1 (100)
Cefotaxime	Resistant	-	-	-	-	2 (100)	1 (100)
Cefixime	Resistant	-	-	-	-	2 (100)	0
Ceftazidime	Resistant	-	-	-	-	2 (100)	0

[a] Values are expressed as No. (%).

Table 5. Resistance Pattern of Isolated Bacteria from Infective Endocarditis Patients

Antibiotic Resistance Pattern	*Staphylococcus aureus* (N = 5)	*S. epidermidis* (N = 3)	*Streptococcus* spp. (N = 4)	*Enterococcus* spp. (N = 2)	*Escherichia coli* (N = 2)	*Pseudomonas* spp. (N = 1)
MDR	0	2	1	0	1	1
XDR	0	0	0	0	1	0
PDR	1	1	0	2	0	0
Non-MDR	4	0	3	0	0	0

Abbreviation: IE, infective endocarditis; MDR, multi drug resistant; PDR, pandrug resistant; XDR, extensively drug-resistant.

positive (N = 11) and negative (N = 0) blood culture in the male group ($P < 0.001$). The microorganisms of negative blood culture cases were sequenced and it was discovered that the genomes belonged to *S. sanguinis*, *S. mitis*, and *Brucella melitensis*. In the frequency distribution investigation of blood culture tests in different age groups, the analysis showed that the most positive blood culture frequency belonged to ages 41 - 60 (Figure 1B). Also, the most frequent microorganism in blood culture positive was *S. aureus* in males, with a percentage of 17.65% (Table 6).

4.4. Phylogenetic Trees of Blood Culture Negative Microorganisms

Phylogenetic trees of *S. sanguinis*, *S. mitis*, and *B. melitensis* are shown, respectively, in Figure 2.

5. Discussion

Infective endocarditis remains a significant clinical challenge and is currently recognized as the fourth leading cause of life-threatening infectious syndromes worldwide. Despite advances in antimicrobial therapy, diagnostic imaging, particularly echocardiography, and surgical interventions, the disease continues to carry considerable morbidity and mortality rates (14). The implementation of updated clinical diagnostic criteria, such as those outlined in the modified Duke criteria,

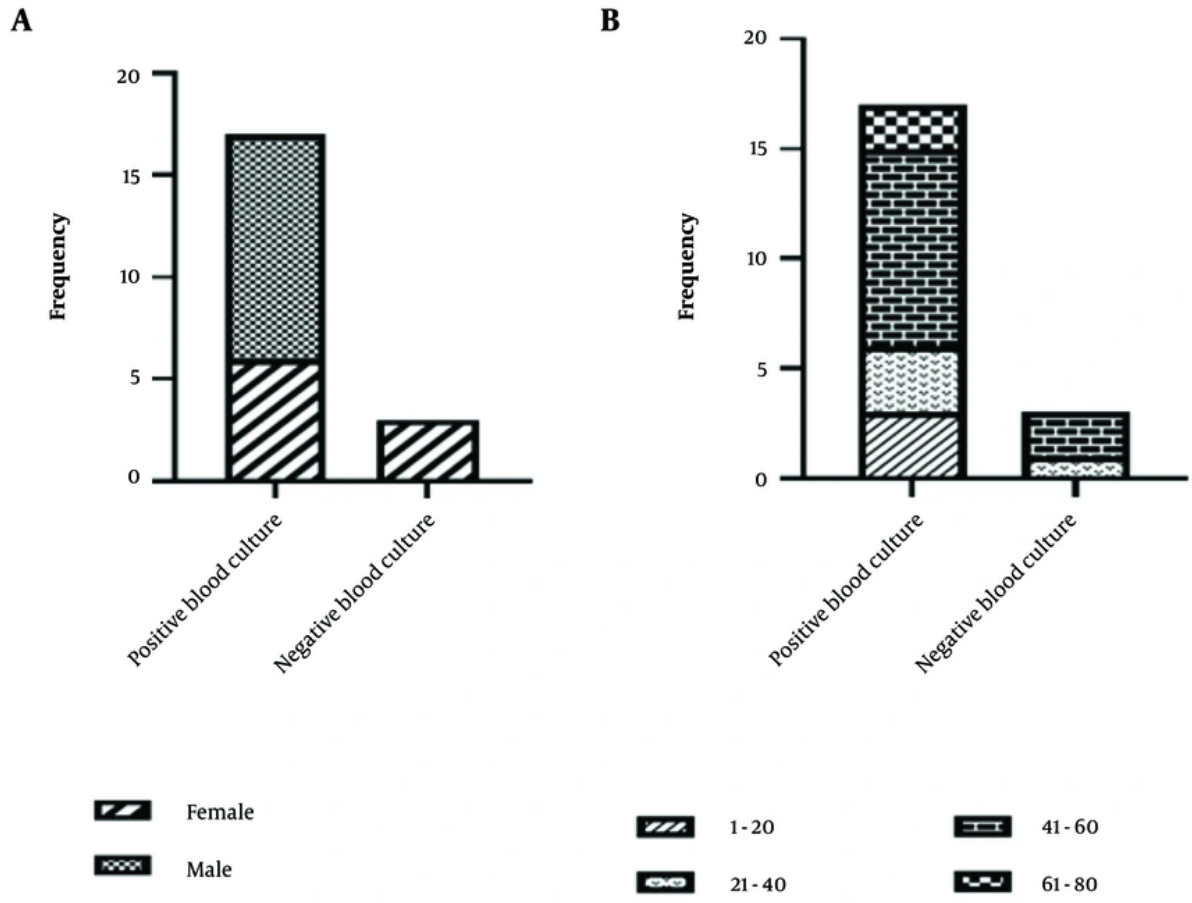

Figure 1. A, distribution of infective endocarditis (IE) patients by blood culture results stratified by gender; B, distribution of IE patients by blood culture results across different age groups

Table 6. The Frequency Distribution of the Study Population Based on the Genus and Bacteria [a]

Microorganism	Female	Male
***Pseudomonas* sp.**	0	1 (5.88)
Escherichia coli	1 (5.88)	1(5.88)
***Enterococcus* sp.**	0	2 (11.76)
***Streptococcus* sp.**	2 (11.76)	2 (11.76)
Staphylococcus epidermidis	1 (5.88)	2 (11.76)
S. aureus	2 (11.76)	3 (17.65)

[a] Values are expressed as No. (%).

alongside an emphasis on early and accurate echocardiographic assessment, has markedly improved diagnostic precision. Nonetheless, the evolving landscape of microbial resistance and shifts in patient demographics necessitate continual reassessment of

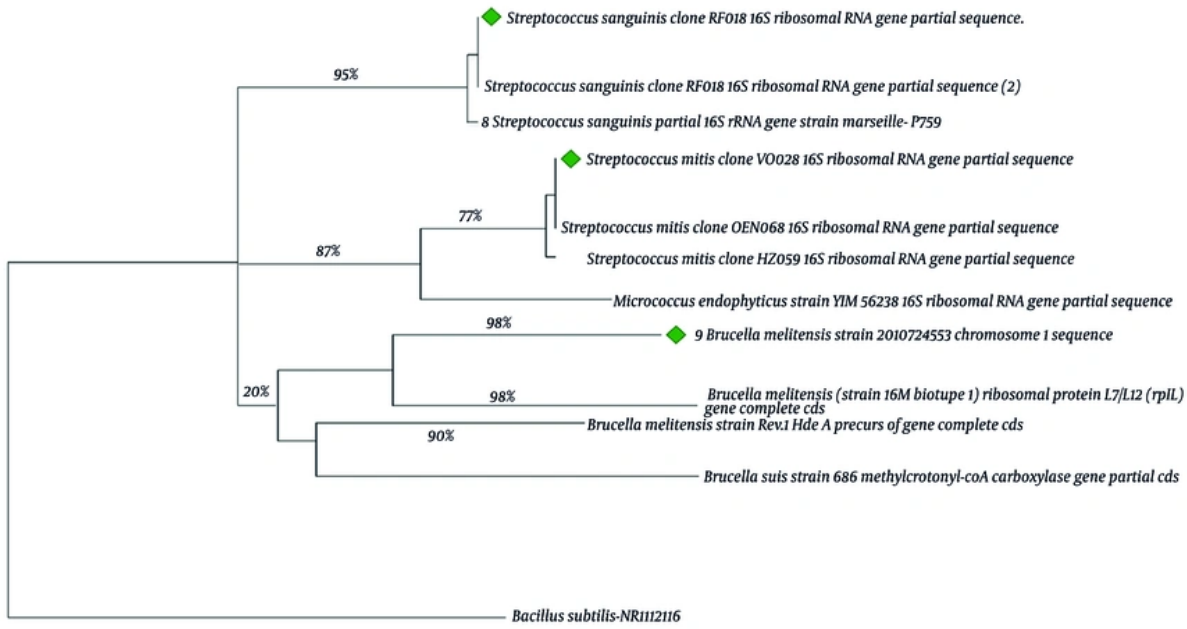

Figure 2. Phylogenetic tree using the neighbor-joining method with 100 bootstrap replicates. Bacillus subtilis has been selected as outgroup. Isolates are shown.

treatment protocols and prevention strategies (15).

This study underscores the critical importance of pathogen identification and antimicrobial susceptibility profiling in the management of IE. The increasing prevalence of IE in many regions, including Iran, highlights the urgent need to revisit and reinforce effective treatment strategies. Particularly concerning is the growing incidence of IE among men aged 41 - 60, a demographic that appears disproportionately affected, consistent with previous studies that have identified male sex and older age as risk factors for IE (16).

Antibiotic resistance is a pivotal matter in the infectious disease treatment process, and in recent years it has become a world concern; as a result, antibiotic resistance is a crisis. This resistance can increase the rate of disease transmission, disease duration (which may raise the costs of treatment), and mortality. Chirillo et al. reported that 73% of IE patients in their cohort were male, with a predominant age range of 34 - 60 years (17), findings echoed across multiple epidemiological investigations. In several studies, it was confirmed that most IE patients are men and their ages are higher than 35 years (18-21).

Comorbidities and predisposing factors continue to play a vital role in the pathogenesis of IE. In our study, the most prevalent underlying conditions among IE patients were coronary heart disease (35%) and cardiac rheumatism (30%). These findings align with prior reports indicating that structural heart diseases and previous cardiac surgeries are major contributors to IE susceptibility. For instance, Day et al. observed that among 1,588 IE patients, 662 had cardiac comorbidities, including congenital heart disease (81%), valve replacement or repair (80%), and cardiac rheumatism (5%) (22). Additional studies have reinforced the link between IE and prior cardiac surgery, gingival procedures, and rheumatic heart disease (17-20).

Microbiological evaluation remains a cornerstone in the diagnosis and management of IE. In our cohort, blood cultures were positive in 85% of patients. The predominant pathogens identified included *S. aureus* (25%), *Streptococcus* spp. (20%), *S. epidermidis* (15%), *Enterococcus* spp. (10%), *E. coli* (10%), and *Pseudomonas* spp. (5%). These findings are consistent with global data indicating that *Staphylococcus*, *Streptococcus*, and *Enterococcus* species are the leading causative agents in

IE (17, 19, 20). Notably, among patients with negative blood cultures (15%), the most frequently identified organisms were *Streptococcus* spp. (66.66%) and *Brucella* spp. (33.33%). This result reflects recent reports suggesting that fastidious organisms, such as Bartonella spp. and *Brucella* spp., are increasingly implicated in culture-negative endocarditis cases (18, 23, 24).

The challenge of antimicrobial resistance cannot be overstated. The widespread emergence of resistant strains significantly complicates IE management and contributes to prolonged disease courses, increased healthcare costs, and elevated mortality rates. The findings from Shiraz, Iran, are consistent with a broader national scoping review which highlighted antibiotic resistance as a major public health threat in Iran, underscoring the need for local antimicrobial stewardship programs (25). The resistance patterns observed in our study support the growing concern surrounding the efficacy of standard antibiotic regimens and underscore the necessity of tailoring therapy based on local microbiological data and resistance trends. These findings further reinforce the global call for antimicrobial stewardship and the rational use of antibiotics in clinical practice. Given the complexity of IE and the evolving epidemiological and microbiological profiles, adherence to updated international guidelines is essential.

Recommendations from authoritative bodies such as the European Society of Cardiology (ESC) and the American Heart Association (AHA) provide crucial direction for clinicians in diagnosing, managing, and preventing IE (26-28). These guidelines emphasize individualized patient assessment, early surgical intervention when indicated, and rigorous follow-up, all of which are pivotal in improving clinical outcomes.

5.1. Conclusions

This study highlights the epidemiological and microbiological characteristics of IE in our patient cohort, with a marked predominance among males aged 41 - 60. A significant proportion of IE cases (74%) with positive blood cultures were associated with *Staphylococcus* species, reaffirming their central role as primary pathogens in IE. Furthermore, antimicrobial susceptibility testing revealed a concerning level of resistance among the isolated microorganisms, underscoring the growing threat of antibiotic resistance in managing IE. These findings emphasize the urgent need for ongoing surveillance, routine antimicrobial resistance profiling, and adherence to updated clinical guidelines to optimize therapeutic outcomes. Future studies with larger sample sizes and molecular diagnostic approaches are recommended to further investigate resistance mechanisms and refine targeted treatment strategies.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: All authors contributed to the revision of the manuscript, read, and approved the submitted version. Study design: M. K. and A. Kh.; Data analysis: A. Kh.; Manuscript preparation: A. Kh., M. R. F., M. K., and L. H.

Conflict of Interests Statement: The authors declare no conflict of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Ethical Approval: The project and data collection were approved by the Ethics Committee of Islamic Azad University, Jahrom Branch (IR.IAU.SHIRAZ.REC.1402.251).

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Informed Consent: Written informed consent was obtained from the participants.

References

1. Liesenborghs L, Meyers S, Vanassche T, Verhamme P. Coagulation: At the heart of infective endocarditis. *J Thromb Haemost*. 2020;**18**(5):995-1008. [PubMed ID: 31925863]. https://doi.org/10.1111/jth.14736.
2. Xiong YQ, Van Wamel W, Nast CC, Yeaman MR, Cheung AL, Bayer AS. Activation and transcriptional interaction between agr RNAII and RNAIII in Staphylococcus aureus in vitro and in an experimental endocarditis model. *J Infect Dis*. 2002;**186**(5):668-77. [PubMed ID: 12195354]. https://doi.org/10.1086/342046.
3. Hill EE, Herijgers P, Claus P, Vanderschueren S, Herregods MC, Peetermans WE. Infective endocarditis: Changing epidemiology and predictors of 6-month mortality: A prospective cohort study. *Eur Heart J*. 2007;**28**(2):196-203. [PubMed ID: 17158121]. https://doi.org/10.1093/eurheartj/ehl427.

4. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;**380**(9859):2095-128. [PubMed ID: 23245604]. [PubMed Central ID: PMC10790329]. https://doi.org/10.1016/S0140-6736(12)61728-0.
5. Rajani R, Klein JL. Infective endocarditis: A contemporary update. *Clin Med (Lond)*. 2020;**20**(1):31-5. [PubMed ID: 31941729]. [PubMed Central ID: PMC6964163]. https://doi.org/10.7861/clinmed.cme.20.1.1.
6. Tran HM, Truong VT, Ngo TMN, Bui QPV, Nguyen HC, Le TTQ, et al. Microbiological profile and risk factors for in-hospital mortality of infective endocarditis in tertiary care hospitals of south Vietnam. *PLoS One*. 2017;**12**(12). e0189421. [PubMed ID: 29240776]. [PubMed Central ID: PMC5730146]. https://doi.org/10.1371/journal.pone.0189421.
7. Tleyjeh IM, Abdel-Latif A, Rahbi H, Scott CG, Bailey KR, Steckelberg JM, et al. A systematic review of population-based studies of infective endocarditis. *Chest*. 2007;**132**(3):1025-35. [PubMed ID: 17873196]. https://doi.org/10.1378/chest.06-2048.
8. Mostaghim AS, Lo HYA, Khardori N. A retrospective epidemiologic study to define risk factors, microbiology, and clinical outcomes of infective endocarditis in a large tertiary-care teaching hospital. *SAGE Open Med*. 2017;**5**:9. [PubMed ID: 29163950]. [PubMed Central ID: PMC5692128]. https://doi.org/10.1177/2050312117741772.
9. Gasch O, Camoez M, Dominguez MA, Padilla B, Pintado V, Almirante B, et al. Predictive factors for early mortality among patients with methicillin-resistant Staphylococcus aureus bacteraemia. *J Antimicrob Chemother*. 2013;**68**(6):1423-30. [PubMed ID: 23404193]. https://doi.org/10.1093/jac/dkt016.
10. Joo EJ, Park DA, Kang CI, Chung DR, Song JH, Lee SM, et al. Reevaluation of the impact of methicillin-resistance on outcomes in patients with Staphylococcus aureus bacteremia and endocarditis. *Korean J Intern Med*. 2019;**34**(6):1347-62. [PubMed ID: 29347812]. [PubMed Central ID: PMC6823568]. https://doi.org/10.3904/kjim.2017.098.
11. Hidalgo-Tenorio C, Galvez J, Martinez-Marcos FJ, Plata-Ciezar A, De La Torre-Lima J, Lopez-Cortes LE, et al. Clinical and prognostic differences between methicillin-resistant and methicillin-susceptible Staphylococcus aureus infective endocarditis. *BMC Infect Dis*. 2020;**20**(1):160. [PubMed ID: 32085732]. [PubMed Central ID: PMC7035751]. https://doi.org/10.1186/s12879-020-4895-1.
12. Farva K, Sattar H, Ullah H, Raziq A, Mehmood MD, Tareen AK, et al. Phenotypic analysis, molecular characterization, and antibiogram of caries-causing bacteria isolated from dental patients. *Microorganisms*. 2023;**11**(8):27. [PubMed ID: 37630520]. [PubMed Central ID: PMC10457851]. https://doi.org/10.3390/microorganisms11081952.
13. Harris KA, Hartley JC. Development of broad-range 16S rDNA PCR for use in the routine diagnostic clinical microbiology service. *J Med Microbiol*. 2003;**52**(Pt 8):685-91. [PubMed ID: 12867563]. https://doi.org/10.1099/jmm.0.05213-0.
14. Kamde SP, Anjankar A. Pathogenesis, diagnosis, antimicrobial therapy, and management of infective endocarditis, and its complications. *Cureus*. 2022;**14**(9). e29182. [PubMed ID: 36258995]. [PubMed Central ID: PMC9572932]. https://doi.org/10.7759/cureus.29182.
15. Lerche CJ, Schwartz F, Theut M, Fosbol EL, Iversen K, Bundgaard H, et al. Anti-biofilm approach in infective endocarditis exposes new treatment strategies for improved outcome. *Front Cell Dev Biol*. 2021;**9**:25. [PubMed ID: 34222225]. [PubMed Central ID: PMC8249808]. https://doi.org/10.3389/fcell.2021.643335.
16. Nappi F, Martuscelli G, Bellomo F, Avtaar Singh SS, Moon MR. Infective endocarditis in high-income countries. *Metabolites*. 2022;**12**(8):682. [PubMed ID: 35893249]. [PubMed Central ID: PMC9329978]. https://doi.org/10.3390/metabo12080682.
17. Chirillo F, Faggiano P, Cecconi M, Moreo A, Squeri A, Gaddi O, et al. Predisposing cardiac conditions, interventional procedures, and antibiotic prophylaxis among patients with infective endocarditis. *Am Heart J*. 2016;**179**:42-50. [PubMed ID: 27595678]. https://doi.org/10.1016/j.ahj.2016.03.028.
18. Fournier PE, Thuny F, Richet H, Lepidi H, Casalta JP, Arzouni JP, et al. Comprehensive diagnostic strategy for blood culture-negative endocarditis: A prospective study of 819 new cases. *Clin Infect Dis*. 2010;**51**(2):131-40. [PubMed ID: 20540619]. https://doi.org/10.1086/653675.
19. Li K, Zhang FE, Wang AP, Zhu GF. [The clinical feature and microbiological etiology of patients with infective endocarditis]. *Chinese J Intern Med*. 2016;**55**(10):774-8. ZH. [PubMed ID: 27686438]. https://doi.org/10.3760/cma.j.issn.0578-1426.2016.10.010.
20. Regueiro A, Linke A, Latib A, Ihlemann N, Urena M, Walther T, et al. Association between transcatheter aortic valve replacement and subsequent infective endocarditis and in-hospital death. *JAMA*. 2016;**316**(10):1083-92. [PubMed ID: 27623462]. https://doi.org/10.1001/jama.2016.12347.
21. Zaqout A, Mohammed S, Thapur M, Al-Soub H, Al-Maslamani MA, Al-Khal A, et al. Clinical characteristics, microbiology, and outcomes of infective endocarditis in Qatar. *Qatar Med J*. 2020;**2020**(2):24. [PubMed ID: 33282709]. [PubMed Central ID: PMC7684547]. https://doi.org/10.5339/qmj.2020.24.
22. Day MD, Gauvreau K, Shulman S, Newburger JW. Characteristics of children hospitalized with infective endocarditis. *Circulation*. 2009;**119**(6):865-70. [PubMed ID: 19188508]. https://doi.org/10.1161/CIRCULATIONAHA.108.798751.
23. Hoen B, Alla F, Selton-Suty C, Beguinot I, Bouvet A, Briancon S, et al. Changing profile of infective endocarditis: results of a 1-year survey in France. *JAMA*. 2002;**288**(1):75-81. [PubMed ID: 12090865]. https://doi.org/10.1001/jama.288.1.75.
24. Lamas CC, Eykyn SJ. Blood culture negative endocarditis: Analysis of 63 cases presenting over 25 years. *Heart*. 2003;**89**(3):258-62. [PubMed ID: 12591823]. [PubMed Central ID: PMC1767579]. https://doi.org/10.1136/heart.89.3.258.
25. Bonyani A, Mesgarpour B, Taheri F, Nasiri MJ, Soleimani F, Khorasani E, et al. Antibiotic resistance clinical research in Iran: A scoping review. *Arch Clin Infect Dis*. 2023;**18**(5). e137094. https://doi.org/10.5812/archcid-137094.
26. Horstkotte D, Follath F, Gutschik E, Lengyel M, Oto A, Pavie A, et al. Guidelines on prevention, diagnosis and treatment of infective endocarditis executive summary; the task force on infective endocarditis of the European society of cardiology. *Eur Heart J*. 2004;**25**(3):267-76. [PubMed ID: 14972429]. https://doi.org/10.1016/j.ehj.2003.11.008.
27. Nishimura RA, Carabello BA, Faxon DP, Freed MD, Lytle BW, O'Gara PT, et al. ACC/AHA 2008 Guideline update on valvular heart disease: Focused update on infective endocarditis: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol*.

2008;**52**(8):676-85. [PubMed ID: 18702976]. https://doi.org/10.1016/j.jacc.2008.05.008.

28. Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009): The Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). *Eur Heart J*. 2009;**30**(19):2369-413. [PubMed ID: 19713420]. https://doi.org/10.1093/eurheartj/ehp285.