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Evaluation of Infective Endocarditis Agents

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Abstract

Endocarditis is an inflammation or microbial infection of the heart valves and the endocardium of the heart. Bacteria that enter the blood due to various reasons can multiply in the endocardial layer of the heart and cause infection. In addition, these infections can be carried to different parts of the body through the bloodstream. This study aims to evaluate the distribution of microorganisms grown in blood cultures taken from patients diagnosed with endocarditis. The distribution of microorganisms grown in blood culture samples sent from patients diagnosed with endocarditis to our Ondokuz Mayıs University Medical Microbiology Laboratory between 2018-2021 was retrospectively examined. The distributions of the most frequently isolated bacteria from 63 strains obtained from blood samples are as follows; 61.90% Staphylococcus spp., 11.11% Streptococcus spp., 9.52% Enterococcus spp., 3.17% Escherichia coli, 1.58% Enterobacter cloacae, 6.34% Klebsiella pneumoniae, 1.58% Acinetobacter baumannii, 1.58% Stenotrophonomonas maltophilia, 1.58% Corynebacterium stratum, 1 1.58% Micrococcus spp. Oxacillin resistance was detected as 44.44% in S. aureus isolates. Carbapenem resistance was not detected in Enterobactarales bacteria. Vancomycin resistance was not detected in enterococcus isolates. Despite significant developments in the diagnosis and treatment of infective endocarditis, there has been no decrease in its incidence and mortality. Similar to many articles in the literature, it has been determined that the most frequently isolated pathogen is S. aureus. Knowing the distribution of infective endocarditis agents is important in guiding clinicians in both prophylactic and empirical treatment selection.

Keywords: infective endocarditis, diagnosis, therapy, prevention and control

1. Introduction

Infective endocarditis (IE) is defined as infection of the endocardial surface of the heart; it usually refers to infection of one or more heart valves or infection of an intracardiac device (1).

A variety of microorganisms can cause infective endocarditis (IE), The three most common causes of IE worldwide are staphylococci, streptococci, and enterococci. In the United States and most developed countries, *Staphylococcus aureus* is the most common cause of IE (2); Staphylococcal IE is a common cause of health care-associated IE (3); streptococcal IE is a common cause of community-acquired IE (4).

In a large cohort study involving 2,781 patients diagnosed with infective endocarditis (IE), the distribution of causative microorganisms was as follows: Staphylococcus aureus was the most frequently identified pathogen (31%), particularly associated with right-sided IE. This was followed by Viridans group streptococci (17%), enterococci (11%), coagulase-negative staphylococci (11%), and Streptococcus bovis (7%). Other streptococcal species, including nutritionally variant streptococci, accounted for 5% of cases. Non-HACEK (Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella, Kingella) gram-negative bacilli and fungal pathogens were each detected in 2% of cases. The HACEK group, comprising fastidious gram-negative bacilli such as Haemophilus aphrophilus (currently classified as Aggregatibacter aphrophilus and A. paraphrophilus), Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, and Kingella kingae, was also responsible for 2% of cases. The remaining patients were diagnosed with culture-negative endocarditis (8%), polymicrobial infections (1%), or infections caused by various other rare pathogens (3%) (5, 6). Gram-negative bacterial species, such as *Escherichia coli* and *Klebsiella pneumoniae*, exhibit a lower affinity for adherence to cardiac valves when compared to gram-positive organisms (7). *Brucella* is an important cause of IE in endemic regions (8). Patients with ulcerative lesions of the colon due to carcinoma or inflammatory bowel disease have a predilection to develop IE due to *S. bovis* (9, 10). *Candida* spp. (11, 12) and *Aspergillus* spp. (13, 14) are the major causes of fungal IE.

Symptoms: The most common symptom of infective endocarditis (IE) is fever. Systemic symptoms such as fatigue, headache, muscle and joint pain, night sweats, abdominal pain and dyspnea are also common.

Diagnostic (modified Duke) criteria: The modified Duke criteria, which are widely used in the diagnosis, categorise patients into three groups: ‘definite IE’, ‘probable IE’ and ‘excluded IE’. These criteria were developed mainly for the evaluation of infections involving native left heart valves; however, their diagnostic sensitivity is lower in prosthetic

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valves, right heart involvement or pacemaker infections (15).

The diagnosis of infective endocarditis (IE) is based on the modified Duke criteria, which include major and minor clinical findings. Major clinical criteria consist of the identification of typical microorganisms associated with IE in two separate blood cultures, or persistently positive blood cultures. A single positive blood culture for Coxiella burnetii or a phase I immunoglobulin G (IgG) antibody titer greater than 1:800 is also considered a major criterion. Evidence of endocardial involvement demonstrated by echocardiography—such as vegetation, abscess, or partial dehiscence of a prosthetic valve—or the presence of new valvular regurgitation also fulfills the major criteria. (16)

Evidence of endocardial involvement includes at least one of the following major findings: a positive echocardiographic result indicating infective endocarditis, such as valvular vegetation, abscess formation, or partial detachment of a prosthetic valve; or the presence of newly developed valvular regurgitation. Minor criteria include the presence of risk factors (such as intravenous drug use or underlying structural heart disease), fever equal to or exceeding 38.0°C, vascular phenomena (e.g., arterial emboli or Janeway lesions), immunologic manifestations (e.g., glomerulonephritis or Osler nodes), and microbiological evidence that does not meet the major criterion threshold. The modified Duke criteria have been validated in several studies and remain a widely accepted tool for the clinical diagnosis of infective endocarditis (17, 18).

Blood cultures − At least three sets of blood cultures should be obtained from separate venous vessels prior to initiation of antibiotic therapy.

The diagnosis of infective endocarditis heavily relies on the importance of blood culture and the identification of grown microorganisms. Therefore, the objective of this article is to evaluate the distribution of microorganisms grown in blood cultures among patients diagnosed with endocarditis. As a summary in this comprehensive analysis of microorganism distribution in infective endocarditis, our goal is to gain a holistic understanding of the microbial landscape in the challenging condition. By integrating research findings and leveraging technological advancements, our aim is to enhance patient outcomes and alleviate the burden of this devastating infection. The aim of this study is to evaluate the distribution of microorganisms grown in blood cultures taken from patients diagnosed with endocarditis.

2. Materials and Methods

The distribution of microorganisms isolated from blood culture samples sent by patients diagnosed with endocarditis between the years 2018-2021 was retrospectively examined in our Ondokuz Mayis University medical microbiology laboratory.

The blood culture bottle samples sent to the laboratory were incubated in the fully automated Bact/ALERT 3D instrument (Biomerieux,France). The blood culture bottles showing growth signals were incubated onto 5% sheep blood agar and EMB agar media. The isolated bacteria was identified using the Vitex MS instrument (Biomerieux,France), and their antimicrobial sensitivity was determined using the Viteks2 compact automated system (Biomerieux,France).

3. Results

The distributions of the most frequently isolated bacteria from 63 strains obtained from blood samples are as follows; 61.90% (n=39) *Staphylococcus spp*., 11.11% (n=7) *Streptococcus spp*., 9.52% (n=6) *Enterococcus spp*., 6.34% (n=4) *Klebsiella pneumoniae*, 3.17% (n=2) *Escherichia coli*, 1.58% (n=1) *Enterobacter cloacae*, 1.58% (n=1) *Acinetobacter baumannii*, 1.58% (n=1) *Stenotrophonomonas maltophilia*, 1.58% (n=1) *Corynebacterium stratum*, 1.58% (n=1) *Micrococcus spp.* Among Staphylococcus aureus isolates, resistance to oxacillin, indicating methicillin resistance, was detected in 44.44% of the strains. In the Enterobacterales group, resistance to carbapenem antibiotics (e.g. imipenem, meropenem or ertapenem) was not observed. No vancomycin resistance was found among Enterococcus species isolates (Table 1). The gender distribution of the patients with isolated strains was 23.87% female and 76.11% male.

Table 1. Distribution of microorganisms grown in blood culture

Microorganism name	Total number of isolates	Antibiotic resistance
		Oxacillin (R)
Staphylococcus	**39**	**25**
S.aureus	18	8
S.hominis	8	6
S.epidermidis	16	11
S.capitis	2	1
S.haemolyticus	6	5
S.lugdunensis	1	0
Streptococcus	**7**	
S.sangius	2	
S.pneumoniae	1	
S.dysgalactiae	1	
S.mitis/oralis	1	
S.galiolyticus	1	
S.gordonii	1	
		Imipenem/ Meropenem (R)
Enterobacterales	**7**	**0**

Escherichia coli	2	0
Enterobacter cloacae	1	0
Klebsiella pneumoniae	4	0
		Vancomycin (R)
Enterococcus	**6**	0
***E**.faecalis*	3	0
***E**.faecium*	2	0
***E**.avium*	1	0
Acinetobacter baumannii	**1**	
Stenotrophonomonas maltophilia	**1**	
Cornybacterium stratum	**1**	
Micrococcus spp.	**1**	

The distribution of isolated microorganisms according to clinical departments is presented below. Among all departments, Staphylococcus species were the most frequently isolated microorganisms with a total of 39 isolates. These were most frequently detected in cardiology (n = 10), infection (n = 6) and coronary intensive care unit (n = 6) departments. Streptococcus species were isolated in 7 cases, the majority of which were in cardiology (n=3), infection (n=2) and coronary intensive care unit (n=2). Enterococcus species were isolated in 6 cases and were found in cardiology (n=3), infection (n=1), general surgery (n=1) and haematology (n=1). Among Gram-negative bacteria, Klebsiella spp. were isolated in four samples originating from the cardiology, nephrology, general surgery and coronary intensive care units (n=1 each). Escherichia coli was detected in two samples, both from the cardiology department. Enterobacter spp. was isolated from a single sample from the infection unit and Acinetobacter baumannii from a patient in the neurology department. Less frequently isolated organisms included Stenotrophomonas maltophilia (n=(n=1, coronary intensive care), Corynebacterium striatum (n=1, cardiology) and Micrococcus spp. (n=1, urology).

4. Discussion

The incidence of infective endocarditis (IE), which varies greatly from country to country, ranges between 3 and 10 per 100000 (19). The infection is usually associated with heart valves (native or prosthetic) or implanted cardiac devices (20). Despite all medical advances in the last 30 years, significant advances in the diagnosis and treatment of infective endocarditis, the incidence and mortality have not decreased (19; 21).

Blood cultures are the most important diagnostic method in IE. Patients have a low level of persistent bacteremia. Therefore, blood cultures taken at any time can show the etiologic agent. In patients who have not received antibiotics before, the chance of two blood cultures taken on admission being positive is around 90%. Therefore, 10 mL of venous blood from different veins at different times within the first 24 hours should be taken for three separate blood cultures. The most common microorganisms causing infective endocarditis are streptococci, staphylococci and enterococci (22; 23). It is estimated that staphylococci, streptococci, and enterococci collectively account for approximately 70–80% of all infective endocarditis cases. Among these, staphylococci—primarily Staphylococcus aureus—represent around 40–45%, viridans group streptococci contribute to 35–40%, and enterococci are responsible for roughly 10% (24; 25). Recent studies have shown that the frequency of staphylococci has increased in recent years (19; 26). In most cases of native-valve infective endocarditis, the causative agents are bacterial in origin. The most commonly isolated organisms include Staphylococcus aureus (accounting for approximately 35–40% of cases), followed by streptococcal species such as viridans group streptococci (~20%) and Streptococcus gallolyticus (formerly known as S. bovis, ~15%). Additionally, enterococci are identified in around 10% of patients (27).

Pehlivan et al. (1998); in their case reports, it was determined that infective endocarditis was detected in 7 (11.2%) of 62 patients who were hospitalized and followed up in their clinics between 1994-1997 and diagnosed with infective endocarditis using Duke criteria and the cases were examined prospectively. Four of these patients were female and three were male. *Staphylococcus aureus* was the causative agent in three of the patients, *Streptococcus viridans* in one, and *Staphylococcus epidermidis* in the other, while no growth was detected in two (28%) (28).

Çaylan et al. (2001), between 1997-2001, 32 endocarditis attacks in 30 cases were treated in our department. 22 (73.33%) of the patients were male and 8 (26.66%) were female. Blood cultures grew in 78.1% (25/32) of the attacks; *Staphylococcus spp.* (12), *Streptococcus spp.* (6), *Enterococcus spp.* (3), *Stenotrophomonas maltophilia* (2), *Pseudomonas aeruginosa* (1) and *Listeria spp.* (1) were the pathogens grown (29).

Şırlak et al. (2003): Patients operated on for infective valvular endocarditis in the Cardiovascular Surgery Clinic of Ankara University Medical Faculty between January 1990 and July 2001 were evaluated. During this period, 18 patients were operated for infective valve endocarditis. The ratio of patients operated on for infective valve endocarditis to the total number of patients operated on during this period was 0.231%. Eight of the patients were female (44.4%) and 10 were male (55.5%). Staphylococcus (22.2%), streptococcus (22.2%) and brucella (11.1%) were the causes of infective valve endocarditis in 4, 4 and 2 patients, respectively. However, in 8 patients (44.4%) the microorganism could not be detected (30).

Irdem et al. (2012), the microbiology and blood culture results of 36 patients diagnosed with definite and probable infective endocarditis were analyzed. The responsible agent was isolated in 14 (38.9%) of the cases by blood culture. The most frequently isolated agents were *S. viridans* 5 (13.88%), *S. aureus* 4 (11.11%), *S. epidermidis* 3 (8.33%) (21).

Lindberg et al. (2022), hospitalised adult patients with Gram-positive bacteraemia during 2017-2019 were evaluated retrospectively through medical records and the Swedish Death Registry. 480 patients with bacteraemia were included and definite endocarditis was diagnosed in 20 (7.5%), 10 (6.6 %), and 2 (3.2 %) patients with *S. aureus*, non-β-hemolytic streptococci and *E. faecalis*, respectively (31).

Despite the global data on infective endocarditis, comprehensive epidemiological studies focusing on Asian populations remain limited. In one investigation conducted within a Chinese cohort, Staphylococcus aureus was identified as the most common causative agent (23.4%), followed closely by streptococcal species (21.9%) (32).

Acet et al. (2024), blood cultures were positive in 75.5% of the cases (175 patients). The predominant causative organisms identified were: Streptococcus viridans (26.08%), Staphylococcus aureus (18.6%), Enterococcus faecalis (10.8%) (33).

Infective endocarditis was more frequently isolated from male study isolates in parallel with the general literature data on gender distribution (19; 34).

Blood culture-negative infective endocarditis is most frequently associated with prior antibiotic exposure, which can lead to sterilization of blood cultures. Retrospective analyses have reported that such cases may account for approximately 35% to 74% of all culture-negative endocarditis occurrences (35). Thanks to effective antibiotherapy and improved surgical techniques, IE is a disease with great advances in its treatment. The conventional management of infective endocarditis typically requires 4 to 6 weeks of intravenous antibiotic administration. Therefore, the overall treatment cost is significantly influenced by the prolonged duration of hospitalization and the expenses associated with intravenous therapy. However, despite all these advances, it remains a disease with high mortality and morbidity (36; 37; 38). Identification of the microorganisms causing IE is crucial for the diagnosis of the disease and determination of appropriate antimicrobial therapy (39).

IE remains a condition associated with considerable morbidity and mortality. To reduce adverse outcomes, more effective strategies and timely interventions are required. The incidence of healthcare-associated IE has been rising, with *Staphylococcus aureus* emerging as the predominant causative agent across various geographical regions. In this context, outpatient parenteral antimicrobial therapy and oral step-down approaches have gained attention as potential alternatives to prolonged hospitalization.

Conflict of interest

The authors declared no conflict of interest.

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None to declare.

Authors' contributions

Concept: Y.T.Ç., Design: Y.T.Ç., Data Collection or Processing: İ.B., M.C., Analysis or Interpretation: M.C., İ.B., Literature Search: Y.T.Ç., İ.B., M.C., Writing: Y.T.Ç., A.B., İ.B., M.C.

Ethical Statement

This study was approved by the Clinical Research Ethics Committee of Ondokuz Mayıs University (Date: 19.12.2024, Decision No: OMU KAEK 2024/462).

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