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Original Article

Clinical and microbiological findings of infective endocarditis

Nur Cancan Gursul[1], İlknur Vardar[2], Tuna Demirdal[2], Erdal Gursul[3], Serap Ural[2], Murat Yesil[4]

[1] *Infectious Disease Department, Biga State Hospital, Canakkale, Turkey*
[2] *Infectious Disease Department, Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey*
[3] *Cardiology Department, Biga State Hospital, Canakkale, Turkey*
[4] *Cardiology Department, Katip Celebi University Ataturk Training and Research Hospital, Izmir, Turkey*

Abstract

Introduction: Infective endocarditis (IE) is an infection that develops on the endothelial surface of the heart. Endocarditis is a major problem for the clinicians despite of the developments in diagnostic, surgical, and medical treatment methods. In this study, we aimed to evaluate symptoms, laboratory findings, treatment options, and clinical endpoint of the patients who were diagnosed with IE in a tertiary healthcare organization according to the literature data.

Methodology: Between January 2006 and March 2013, 80 IE patients who were diagnosed and treated in accordance with modified Duke criteria were enrolled in the study. Demographic features, symptoms, and laboratory and echocardiographic findings were recorded after reviewing the patient files.

Results: The mean age of the patients was 51.3 ± 16.0, and IE was more common in men (n = 56; 70%). Of 41 patients who had positive blood cultures, 20 patients had *Staphylococcus* spp. (48.7%) and 8 patients had *Streptococcus* spp. (19.5%). *Brucella* spp. was isolated from 5 patients (12.2%). While 48.7% (n = 39) of the patients had cardiac complications, 22 patients (27.5%) had embolic complication. Hospital mortality was observed in 20 patients (15%).

Conclusions: In our patients, endocarditis was seen at a young age, and staphylococci were the most frequently isolated microorganism from blood culture. There were more patients with *Brucella* endocarditis compared to the general population. Complications are frequently seen in the course of endocarditis, and they cause problems for the clinicians during follow ups due to the high mortality rate of IE.

Key words: infective endocarditis; Duke criteria; Brucella endocarditis.

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Introduction

Infective endocarditis (IE) is an infection that develops on the endothelial surface of the heart. IE incidence has been determined to be 1.9–6.2/100,000 population annually, especially in studies from Western countries [1-3]. IE was monitored more in men, and the male/female ratio has been determined to be 2.3 [2,3]. While the disease affected young patients with rheumatic or congenital heart disease in the past, it now develops in mostly older patients, depending on degenerative valve diseases or the procedures associated with healthcare as a result of the decrease in the frequency of rheumatic fever [4,5]. IE is diagnosed by evaluating clinical, laboratory, and echocardiography findings together. The most frequent symptom in patients is fever. Systemic symptoms such as anorexia and weight loss are seen along with fever [6]. Anemia, leukocytosis, increase in C-reactive protein (CRP) and erythrocyte sedimentation rate (ESH) are non-specific laboratory findings that help the diagnosis. The most important steps in diagnosis are the detection of vegetation in echocardiographic investigation and the detection of the pathogen with culture and serologic methods. Criteria used for IE diagnosis were standardized by Duke *et al*. in 1994 and modified in 1996 [7,8].

IE is still a major problem for clinicians in spite of the developments in diagnosis and surgical and medical treatment options; the 15–20% mortality rate reveals the severity of the disease [4,9,10].

In our study, we aimed to evaluate the symptoms, examination and laboratory findings, treatment options, and clinical endpoints of the patients followed up for IE diagnosis according to the literature data in our hospital, a tertiary healthcare organization.

Methodology

Patient characteristics

In this study, patients who were hospitalized and followed by the infectious disease clinic in our hospital,

a tertiary healthcare organization, were enrolled in the study. The study was planned retrospectively. Eighty patients who met the Duke criteria were included in the study. For each patient, age, gender, predisposing heart disease and interventions, coexistent disease, localization of infection, type of endocarditis, existing valve disease, echocardiographic findings, laboratory findings, cardiac or non-cardiac complications, antibiotic treatment and treatment duration, surgical procedures applied and mortality data were obtained by analyzing the patient files and computer records. Obtained data were recorded on the forms that were provided individually for each patient. Patients who were diagnosed with IE but failed to meet Duke criteria were excluded from the study.

Echocardiography

Echocardiography procedure was done using VIVID S3 (General Electric, New York, USA) equipped with a transthoracic echocardiography (TTE) 2.5–3.5 MHz band transducer. Left ventricle ejection fraction (EF) was calculated using the M-mode method on the parasternal long axis guided by 2D display. Patients who were within the indication underwent transesophageal echocardiography (TEE) with VIVID S3 (General Electric, New York, USA) equipped with a 5 MHz band transducer. In patients with mild valve insufficiency or above and mild valve obstruction or above were considered to have valvular disease. Also, the presence of vegetation, abscess, dehiscence, and chorda rupture were evaluated in patients. The highest vegetation diameter measured with echocardiography was recorded as the vegetation size in the study.

Laboratory findings

The patients' leukocyte and thrombocyte counts, hemoglobin, hematocrit, urea, creatine, CRP levels, and ESR were analyzed. The leukocyte threshold value for leukocytosis was taken as 11,000/mm³; the hemoglobin threshold value for anemia was taken as 13.0 g/dL in men and 12.0 g/dL in women. The thrombocyte threshold value for thrombocytopenia was set at 150,000/mm³ [11-13]. Patients in whom the serum creatinine concentration was calculated to have increased by 0.5 mg/dL or higher than the starting point, and in whom there was a 50% decrease in the creatinine clearance value, were considered to have developed acute renal failure [14]. In the evaluation of the erythrocyte sedimentation rate, the upper border values accepted to be normal in males and females according to the age were taken as the basis, and values exceeding the upper border levels were evaluated to be high ESR levels [15]. Serum albumin values lower than 3.5 gr/dL were evaluated as hypoalbuminemia.

Microbiological analysis

At least three blood cultures from each patient were taken and the samples were analyzed in the microbiology laboratory. Blood culture positivity was determined using the BACTEC 9240 (Becton Dickinson Instrument System, Sparks, USA) automatized blood culture system. For identifying the microorganism the macroscopic appearances of the colonies, Gram staining characteristics, conventional methods, and the fully automatized bacterial description and the ID description kit of the antibiogram apparatus were used. The antibiotic sensitivity of the grown microorganism was specified; using the disk-diffusion method (according to the Clinical Laboratory Standard Institute criteria) and the automatized system Phoenix 100 (Becton Dickinson Instrument System, Sparks, USA), the minimum inhibitory concentration (MIC) values were determined.

The patients in whose blood cultures microorganisms had grown were evaluated in the presence of the criteria indicated by the Duke standards, and when consistent with the criteria, the microorganism was accepted as an IE cause. For the serological diagnosis of *Brucellosis*, a titer of 1/160 and higher in the standard tube agglutination test was accepted as positive [16].

Statistical analysis

SPSS for Windows version 15.0 (SPPS Inc., Chicago, USA) was used for the statistical analysis. Descriptive statistics such as age, leukocyte and thrombocyte counts, hemoglobin level, duration of antibiotic use, EF value, average size of the vegetation, duration of hospital stay, and length of time between hospitalization and mortality were given as average ± standard deviation (SD). Categorical variables, such as gender, symptoms and physical examination findings, predisposing diseases, anemia, leukocytosis, thrombocytopenia, high CRP and ESR, hypoalbuminemia, distribution of isolated causes, choices of antibiotics used for treatment, the applied surgical procedures, complications, and causes of mortality were given as numbers and percentages.

Results

Eighty patients with the diagnosis of IE were included in the study. Seventy percent (n = 56) of the patients were male, and 30% (n = 24) were female, and

the mean age was calculated as 51.3 ± 16.0 (19–83) years.

The most frequent complaint upon admission to the hospital was fever, at a rate of 83.7%, and the most frequent examination finding was cardiac murmur (n = 37;, 46.2%). The other symptoms and physical examination findings of the patients are presented in Table 1.

When the patients were evaluated with regard to having chronic diseases, 20 (25%) patients had hypertension (HT), 19 (23.7%) patients had diabetes mellitus (DM), and 6 (7.5%) patients had chronic renal failure (CRF) (Table 1). No narcotic drug addiction was encountered.

When considering cardiac diseases causing a tendency towards IE, while existing aortic and mitral valve diseases were observed as the most frequent (n = 35; 43.7%), isolated mitral valve disease was encountered more frequently than was isolated aortic valve disease (n = 25; 31.2% and n = 7; 8.7%, respectively). Among the congenital heart diseases, there was a ventricular septal defect (VSD) in 1 patient and a history of having undergone an operation due to an Ebstein anomaly in another patient. A bicuspid aortic valve was found in 1 patient. Dilated cardiomyopathy (CMP) was observed in 1 patient and hypertrophic cardiomyopathy was seen in another patient (Table 1). Tricuspid valve disease was determined in 29 (36.2%) patients included in the study. In 6 patients, there was a

Table 1. The symptoms, physical examination and laboratory findings of the patients.

Variables	Patients n (%) (N = 80)
Symptoms	
Fever	67 (83.7)
Weakness	49 (61.2)
Dyspnea	24 (30.0)
Weight loss	24 (30.0)
Chest pain	9 (11.25)
Examination findings	
Cardiac murmur	37 (46.2)
Hepatomegaly	16 (20.0)
Splenomegaly	16 (20.0)
Janeway lesions	2 (2.5)
Splinter hemorrhages	2 (2.5)
Left cardiac diseases	
Aortic and mitral valve diseases	35 (43.7)
Mitral valve diseases	25 (31.2)
Aortic valve diseases	7 (8.7)
Congenital heart diseases	3 (3.7)
Cardiomyopathy	2 (2.5)
Right heart diseases	
Tricuspid valve disease	29 (36.2)
Device/catheter	24 (30)
Valve replacement	
MVR	3 (3.7)
AVR	5 (6.2)
AVR + MVR	1 (1.2)
Other chronic diseases	
Hypertension	20 (25)
Diabetes mellitus	19 (23.7)
Chronic renal failure	6 (7.5)
Laboratory findings	
Anemia	61 (76.2)
Leukocytosis	32 (40)
Thrombocytopenia	11 (13.7)
High CRP values (n = 76)	67 (88.1)
High ESR values (n = 76)	62 (81.5)

MVR: mitral valve replacement; AVR: aortic valve replacement; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate;Continuous data are expressed as mean ± standard deviation; categorical data are expressed as n (%).

dialysis catheter extending to the right atrium and the presence of a pacemaker lead was observed in 18 patients (Table 2). The presence of a metallic prosthetic valve was determined in 5 (6.2%) patients secondary to aortic valve replacement, in 3 (3.7%) patients secondary to mitral valve replacement, and in 1 (1.2%) patient secondary to aortic and mitral valve replacements, resulting in a total of 9 (11.5%) patients (Table 1).

Based on the history in the patients' files, in the pre-presentation period, there were histories of tooth extraction in 8 patients, bronchoscopy in 1 patient, and a urethral intervention in 1 patient.

While the average hemoglobin level at the time of admission in patients included in the study was observed to be 11.2 ± 2.1 g/dL, anemia was determined in 61 (76.2%) patients. Leukocytosis and thrombocytopenia were determined in 32 (40%) and 11 (13.7%) patients, respectively. High CRP levels were determined in 67 of 76 (88.1%) patients, and high ESR values were determined in 62 of 76 (81.5%) patients. The laboratory findings of the patients are presented in Table 1.

A total of 33 (40.7%) patients had used antibiotics for any reason prior to presenting to the hospital. In 39 (48.7%) of the patients included in the study, no microorganism that may have caused IE was observed. Staphylococci were the most frequent microorganisms causing IE in our study and were isolated in 20 (48.7%) of 41 patients whose blood cultures were positive. *Staphylococcus aureus* was isolated in 11 (26.8%) patients; 9 (21.9%) of these were methicillin sensitive (MSSA), and 2 (4.8%) were methicillin resistant (MRSA). Coagulase negative staphylococci (CNS) was isolated in 9 (22%) patients, and 6 (14.6%) of these were determined to be methicillin resistant (Table 2).

In 7 of 8 patients in whom streptococci had grown, viridans streptococci were isolated and 3 of them were identified as species: *S. mitis* in 2 cultures and *S. sanguinis* in 1 culture. In 1 pregnant patient, there was culture growth of *S. porcinus*, and in another patient, there was culture growth of *Gemella morbillorum* (Table 2).

Enterococci were isolated in the blood cultures of 7 patients, comprising *Enterococcus faecalis* in 5 patients and *Enterococcus faecium* in 2 patients (Table 2). While penicillin resistance was determined in 3 of the grown enterococcal species, no resistance to vancomycin was encountered. A high level of gentamicin resistance was determined in 3 isolates.

Brucella spp. were isolated in 5 of 10 patients with a diagnosis of *Brucella* endocarditis who had received treatment; however, in the remaining 5 patients, the diagnosis was made through serological investigations (Table 2).

The mean duration of antibiotic use in the patients was determined to be 44.6 ± 23.8 (4–108) days. In 39 of the 41 patients (95.1%), the empirical antibiotic treatment that had been started was observed to be effective on the microorganism isolated in the blood culture. While the most frequently preferred empirical treatments were the combination of ceftriaxone and gentamicin and the combination of crystallized penicillin G and gentamicin (n = 11; 13.7% and n =11;

Table 2. The distribution of patients with infective endocarditis according to microbiological findings.

Microorganisms	Positive blood culture n (%) (N = 41)
Staphylococcus	**20 (48.7)**
Stafilococcus aureus	***11 (26.8)***
MSSA	9 (21.9)
MRSA	2 (4.8)
Coagulase-negative staphylococci	**9 (21.9)**
MRCNS	6 (14.6)
MSCNS	3 (7.3)
Streptococcus	**8 (19.5)**
Viridans streptococci	7 (17.0)
Streptoccus porcinus	1 (2.4)
Enterococcus	**7 (17.0)**
Enterococcus faecalis	5 (12.1)
Enterococcus faecium	2 (4.8)
Others	**6 (14.6)**
Brucella spp.	5 (12.1)
Gemella morbillorum	1 (2.4)

MSSA: methicillin-sensitive Staphylococcus aureus; MRSA: methicillin-resistant Staphylococcus aureus; MRCNS: methicillin-resistant coagulase-negative staphylococci; MSCNS: methicillin-sensitive coagulase-negative staphylococci

13.7%, respectively), the combination of vancomycin and gentamicin was preferred in 8 patients (10%), and the combination of vancomycin and ceftriaxone was preferred in empirical treatment in 6 patients (7.5%) The combination of ceftriaxone and teicoplanin was used in 7 patients. While the combination of doxycycline, rifampicin, and ceftriaxone was preferred in the treatment of *Brucella* endocarditis in 6 patients, 3 patients were treated with the combination of doxycyclin, rifampicin, and streptomycin, and 1 patient was treated with the combination of doxycycline, ceftriaxone, and ciprofloxacin.

In the echocardiography investigation of the patients, the mean EF value was determined to be 55.4% ± 9.4%. Vegetations were determined in all of the patients who had been diagnosed as having IE via TTE and/or TEE. Among the patients, native valve endocarditis was observed in 55 (68.7%) patients, device-related IE was observed in 20 (25.0%) patients, and prosthetic valve endocarditis was observed in 5 (6.2%) patients. In 4 of the 5 patients with prosthetic valve endocarditis, the endocarditis was determined to be late prosthetic valve endocarditis (Table 3).

The vegetations over the normal valves were observed to be mostly over the mitral valve (n = 34; 42.5%) (Table 3). The mean of the largest vegetation size measured through TTE or TEE that could be observed in the patients was 15.0 ± 5.3 mm. Additional findings included chorda rupture in 3 patients, periannular abscess in 2 patients, abscess and valve dehiscence in 1 patient, leaflet perforation in 2 patients, valve aneurysm and leaflet perforation in 2 patients, and fistula in 1 patient (Table 3).

The mean duration of hospitalization of the patients was 43 ± 23.5 (4–108) days. The follow-up of 35 patients was made with medical treatment alone, and a surgical procedure had been performed in addition to the medical treatment in 45 (56.2%) patients. While valve replacement had been performed on 31 patients (38.7%), 14 patients required removal of the pacemaker leads (17.5%). Removal of leads had been performed through a surgical procedure in 9 patients and through the percutaneous method in 5 patients (Table 4). The mean duration of time between the time of hospitalization and the application of the surgical procedure was found to be 35 ± 23.0 (3–94) days.

At least one complication was determined in 71% (n = 56) of the patients included in the study. While the most frequently observed complications were cardiac complications, renal failure was the second-most frequently observed complication (n = 39; 48.7% and n = 21; 26.2%, respectively). Among the cardiac complications, heart failure was observed to be the most frequent (n = 26; 32.5%). While renal failure as a result of antibiotic nephrotoxicity developed in 10 patients, opaque nephropathy developed in 1 patient, hypotension as a result of heart failure had developed in

Table 3. Echocardiographic findings of patients diagnosed with infective endocarditis.

Echocardiographic findings	**Patients (N = 80)**
Ejection fraction % ± standard deviation (SD)	55.4 ± 9.4
Average size of vegetation mm ± SD	15.0 ± 5.3
Location of vegetation	**n (%)**
Natural valve	55 (68.7)
Mitral	34 (42.5)
Aortic	18 (22.5)
Tricuspid	2 (2.5)
Aortic + mitral	1 (1.2)
Prosthetic valve	5 (6.2)
MVR	3 (3.7)
AVR	2 (2.5)
Device	20 (25.0)
Lead	20 (25.0)
Valve complications	
Chord rupture	3 (3.7)
Leaflet perforation	2 (2.5)
Abscess	2 (2.5)
Valve disease	1 (1.2)
Valve aneurysm and perforation	1 (2.5)
Fistula	1 (1.2)

Continuous data are expressed as mean ± SD; categorical data are expressed as n (%). MVR: mitral valve replacement; AVR: aortic valve replacement.

3 patients, and renal failure as a result of sepsis developed in 1 patient.

Embolic complications, including ischaemic stroke, were observed in a total of 22 patients (27.5%). Neurological complications were observed in 12 patients. Among the neurological complications, while ischemic stroke was encountered most frequently (n = 11; 13.7%), brain abscess was determined in 1 patient. Splenic infarct was determined in 5 patients; a splenic abscess was found in 1 patient, and a liver abscess was found in another patient. Septic pulmonary embolism was determined in 3 patients and a lung abscess was determined in 1 patient. Peripheral arterial embolism was determined in 3 patients and spondylodiscitis was observed in 2 patients.

In-hospital death was seen to have developed in 12 patients included in the study. The most frequent cause of death was heart failure (n = 5; 6.2%). A total of 4 (5%) patients died due to cerebrovascular events, 2 (2.5%) patients died due to septic shock, and 1 patient with a diagnosis of gastric cancer died due to gastrointestinal bleeding. The mean duration of hospitalization in patients with mortality, from the time of admission until the time of death, was calculated to be 34 ± 29.0 (5–108) days. The complications and the causes of mortality are shown in Table 4.

Discussion

IE is a disease that develops through infection of the endothelial surface of the heart. IE is rarely seen, and in prospective studies carried out in Western populations, the annual incidence of the disease has been determined to be 1.9–6.2/100,000 population [1-3]. The male/female ratio is between 1.5 and 2.5 [2,3]. Consistent with the information in the literature, in our study, IE was observed more frequently in men, and the male/female ratio was found to be 2.3. In Netzer *et al*.'s study [17], the age at which IE is seen was 53 ± 16 years; in Habib *et al*.'s study [18], the age was 60 ± 16 years. Similar to the studies [19,20] carried out in Turkey, in our study, the average age at which the disease was observed was 51.3 ± 16.0 years. The reason for the lower patient age in Turkey may have arisen from factors such as poor oral hygiene and valvular insufficiencies due to acute rheumatoid arthritis, which is more frequently seen in Turkey than in developed countries.

In up to 90% of the patients with IE, there is the complaint of fever, and systemic symptoms such as chills, loss of appetite, and loss of weight often accompany the fever [6]. The most frequently determined symptoms in our patients, similar to the information in the literature, was fever (83.7%). After fever, weakness and dyspnea are the most frequently

Table 4. Complications, performed surgery, and mortality reasons of patients.

Variables	Patients n (%) (N = 80)
Complications	**74 (92.5)**
Cardiac	39 (48.7)
Acute renal failure	21 (26.2)
Neurological	12 (15.0)
Spleen-liver abscess	9 (11.2)
Pulmonary embolism	4 (5.0)
Peripheral embolism	3 (3.75)
Spondylodiscitis	2 (2.5)
Operations	**45 (56.2)**
Cardiac valve surgery	31 (38.7)
MVR	14 (17.5)
AVR	12 (15.0)
MVR + AVR	5 (6.2)
Lead extraction	14 (17.5)
Open-heart surgery	9 (11.2)
Percutaneous	5 (6.2)
Mortality reasons	**12 (15.0)**
Heart failure	5 (6.2)
Cerebrovascular events	4 (5.0)
Sepsis	2 (2.5)
Gastrointestinal bleeding	1 (1.2)
Mean duration of time between hospitalization and mortality, days ± SD	**34 ± 29.0**

MVR: mitral valve replacement; AVR: aortic valve replacement; Continuous data are expressed as mean ± standard deviation; categorical data are expressed as n (%).

observed symptoms. Similar to the classical information and the rates reported in the literature, splenomegaly was determined in 20% of our patients [6,19]. In our study, Janeway lesion was determined in 2 patients (2.5%) and splinter hemorrhages were encountered in 2 patients (2.5%). The skin findings of IE are encountered less frequently this in the past; the reason for this has been considered to be the diagnosis, which is made over a shorter duration of time [6].

Microbiological diagnosis is the most important step in managing the treatment of IE. In 2.5%–1% of all IE cases, there were no microorganisms isolated in blood cultures; this situation leads to delaying diagnosis and treatment of IE and leads to a significant effect on the clinical outcome [21]. The most frequently encountered cause of negative blood culture IE is previous antibiotic use. Infections with microorganisms which are difficult to isolate with conventional culture methods are gradually being encountered more often [22]. No microorganism that may have caused IE could be isolated in the blood cultures of 39 (48.7%) of the patients included in this study. The high rate of antibiotic use in our patients at the time of diagnosis (48%) and the insufficient use of serological methods apart from the *Brucella* agglutination test may be the reasons for the rate of blood culture-negative IE being higher in our study than in previous studies.

The most frequent microorganisms causing IE are Gram-positive cocci. In the literature, the most frequent cause of IE has been reported to be viridans streptococci, and *S. aureus* has been reported to be the second-most frequent cause [6]. Today, in many published studies, staphylococci are at the first rank in microorganisms causing IE [23-25]. The most probable reason for this increase in the observation of staphylococcal IE is the increased risk of IE secondary to bacteremia developing as a result of prolonged medical treatment of the patient at the hospital and the increased number of invasive interventions as a result of augmentation of health services [6].

In Cabell *et al*.'s study [23] on 329 patient diagnosed with IE, the authors reported an increase in the development of IE secondary to *S. aureus* in recent years, and in contrast, they reported a decrease in the number of IE caused by viridans streptococci. In the meta-analysis comprising 40 studies on IE carried out by Head *et al*. [24] evaluating 11,348 patients, the rate of *S. aureus* infection was reported to be 21%, and the rate of viridans streptococci infection has been reported to be 20%. In Murdoch *et al*.'s study [25] performed in 58 centers, prospectively evaluating 2,781 patients, these rates were reported as 31% and 17% for *S. aureus* and viridans streptococci, respectively. In a study performed on 58 patients in Turkey [26], culture growth was determined in 36 patients; among the isolated agents, staphylococci were reported to be in the first rank, at a rate of 58%, and streptococci were the second-most frequent causative agent, at a rate of 25%. Culture growth occurred in 41 patients in our study, and staphylococci grew in 51% of these, streptococci in 19%, and enterococci in 17%; consistent with the literature [5], the most frequent causative microorganism were staphylococci. Methicillin resistance was determined in 2 isolates in which *S. aureus* had grown.

Device-related IE was encountered in 9% of the IE cases, and staphylococci were the most frequent causative agent in device-related IE [27,28]. In a recently published study carried out in Turkey on IE related to cardiac devices, the causative microorganisms in 60% of the patients were found to be staphylococci [29]. In our study, the rate of device-related endocarditis was observed to be higher (20%) than the rates reported in patients with endocarditis; this condition could potentially explain why staphylococci were the most commonly seen etiologic agents in our study.

Similar to the fidings encountered in the literature, the most frequently isolated agent in the blood cultures in streptococcal IE was viridans streptococci (n = 7; 17%) [5]. Interestingly, among streptococcal IE, growth of *S. porcinus* was found in a pregnant patient. In a previous study, this agent was found to be able to cause infection in pregnancy and in the postpartum period, but no reports regarding this agent being the causative agent in endocarditis in humans were found. In swine, *S. porcinus* has been observed to cause lymphadenitis, endocarditis, and abortion [30,31].

In the literature, a large majority of enterococcal IE developed due to *E. faecalis* [5,6]. In our study, enterococcal IE was determined in 17% of the patients whose blood cultures were positive, and in most cases, *E. faecalis* (12%) was isolated. In enterococcal bacteremia, vancomycin resistance was reported in 20% of *E. faecium* isolates and in 3% of *E. faecalis* isolates [4,5]. In our study, vancomycin resistance was not encountered in any of the *Enterococcus* species. In 3 isolates (42%), a high degree of gentamicin resistance was determined; this finding is consistent with that of previous studies in the literature [6,32]. In the presence of a high degree of gentamicin resistance, vancomycin, linezolid, or teicoplanin have been preferred in the treatment of these diseases due to the inability to attain a synergistic effect with β-lactam antibiotics.

Endocarditis is a rarely observed complication of brucellosis (0.3%–0.6%) [20,21]. In Aygen *et al.*'s study [33], in which brucellosis was evaluated in 480 patients, the frequency of *Brucella* endocarditis was reported to be 0.4%. However, in another study evaluating brucellosis in 75 patients, endocarditis was determined in 4 patients [34]. In our study, endocarditis due to *Brucella* spp. was observed in 10 patients (11%). In Turkey, the predisposing condition to *Brucella* endocarditis was the higher frequency of rheumatic heart disease compared with that in developed countries; in addition, brucellosis is endemic around the Mediterranean, rendering the *Brucella* endocarditis rates in our study higher than those reported in the literature. *Brucella* spp. were isolated from the blood cultures of 5 of the 10 patients with *Brucella* endocarditis, and in the remaining 5 patients, the diagnosis of *Brucella* endocarditis was made through serological analyses. For this reason, in culture-negative IE patients, brucellosis should be considered as the etiologic agent, and performing serological analyses is important. While 2 of 10 patients with *Brucella* IE were followed up with medical treatment, medical treatment together with surgical treatment were administered to the remaining 8 patients. Due to the fact that success with only medical treatment of *Brucella* IE is achieved in a small portion of patients, and due to the high mortality rate in recent years, medical treatment together with surgical treatment has been recommended [16]. In our study, the surgical treatment of *Brucella* IE was preferred over only medical treatment.

Due to the frequent and fatal complications of IE, the necessity for surgery for patients with IE has been reported in the literatüre [9]. Heart failure is the most frequently observed complication of IE, and it is the most widely used indication for a surgical intervention in IE [9]. In other studies, heart failure was reported to have developed in 32%–34% of the patients [24,25]. Similarly, in our patients, heart failure was observed to be the most frequently encountered complication.

Removing the device in device-related IE cases is recommended in literature [35,36]. In our study, in there were 20 cases with device-related IE. The devices were removed through a surgical method in 9 patients, and the percutaneous removal method was used in 5 patients. The device removal procedure was planned for 6 patients appropriately according to the recommendations of the guidelines [35]; however, due to the fact that consent could not be obtained from the patients, the procedure could not be performed.

Embolic complications are the most important complications observed in IE patients. In a study evaluating the systemic embolism risk factors, systemic embolism was observed to have developed in 33.2% of the IE patients, and in 56% of these, there were neurological complications [37]. In our study, embolic complication was observed in 22 patients (27.5%), and 54.5% of these embolic complications were neurological complications. In the literature, it was reported that neurological complications occur in 20%–40% of all patients with IE, and that this is mainly the result of vegetation embolism [38,39]. In our study, the rate of neurological complications was 15%, and consistent with the literature, 91.6% of the neurological complications developed secondary to vegetation embolism.

In our study, 4 pulmonary embolisms developed in 22 right-heart endocarditis cases, and 18 embolic complications (peripheral embolism and ischaemic stroke) developed in 58 left-heart endocarditis cases. While mortality was observed secondary to cerebral embolism, mortality secondary to pulmonary embolism was not observed. In cases with left-heart IE, death was recorded secondary to ischaemic embolism in 4 patients. Though embolic complications of IE are important causes of mortality and morbidity, the most frequent cause of death in these patients is heart failure [40]. The mortality rate of IE patients at hospitals is between 9.6% and 26%. Similarly, in our study, the mortality rate at the hospital was observed to be 15%, and consistent with the literature, the most frequent cause of mortality was heart failure (41.6%).

Conclusions

There have been recent changes in the epidemiological and microbiological profile of IE. The gradually increasing widespread use of intra-cardiac devices has caused an increase in the number of IE due to staphylococci. In IE, which has high rates of mortality and morbidity, early diagnosis, correct choice of antibiotic, and appropriate surgery timing are very important.

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Corresponding author

Erdal Gursul, MD
Biga State Hospital
Kıbrıs Sehitleri Street
Canakkale, Turkey
Postal code: 17200
Phone: +90 (286) 316 10 06
Fax: +90 (286) 316 10 06
Email: erdalgrsul@yahoo.com.tr

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