

## Epidemiological, clinical and microbiological profile of infective endocarditis in a tertiary hospital in the South-East Anatolia Region

Güneydoğu Anadolu Bölgesi'nde üçüncü basamak bir hastanede enfektif endokarditin epidemiyolojik, klinik ve mikrobiyolojik özellikleri

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**Objectives:** We aimed to evaluate epidemiological, clinical, and microbiological features of infective endocarditis (IE) in a tertiary university hospital.

**Study design:** The study included 72 patients (31 women, 41 men; mean age 45±16 years; range 18 to 80 years) who were diagnosed as having definite IE, according to the modified Duke criteria, between 2004 and 2007. Data were reviewed on age, sex, underlying heart disease, predisposing conditions for bacteremia, echocardiographic and microbiological findings, treatment, complications, and mortality.

**Results:** Infective endocarditis developed on a native valve in 47 (65.3%), a mechanical prosthetic valve in 21 (29.2%), and a pacemaker in two cases. The location of IE could not be determined in two cases (2.8%). Rheumatic heart disease (36.1%) was the most common preexisting valvular abnormality. The mitral valve was the most commonly affected valve in both native valves (43.1%) and prosthetic valves (13.9%). The most frequent symptom was fever (n=60, 83.3%). Electrocardiography showed abnormal findings in 24 cases (33.3%). Transthoracic and/or transesophageal echocardiography showed a vegetation in 63 cases (87.5%), moderate or severe mitral regurgitation in 41 cases (56.9%), aortic regurgitation in 21 cases (29.2%), and tricuspid regurgitation in 29 cases (40.3%). Staphylococci (26.4%) and streptococci (22.2%) were the most common causative agents. Cultures were negative in 26 cases (36.1%). Twenty patients (27.8%) underwent surgical treatment. Congestive heart failure (n=23, 31.9%) and cerebrovascular accidents (n=10, 13.9%) were the major complications. In-hospital mortality occurred in 11 cases (15.3%).

**Conclusion:** Our data reflect epidemiological, clinical, and microbiological profile of IE in a tertiary hospital located in the Southeastern Anatolia.

**Key words:** Echocardiography; endocarditis, bacterial/epidemiology; heart valve diseases; heart valve prosthesis; prosthesis-related Infections; Turkey/epidemiology.

**Amaç:** Üçüncü basamak üniversite hastanemizde enfektif endokarditin (EE) epidemiyolojik, klinik ve mikrobiyolojik özelliklerinin belirlenmesi amaçlandı.

**Çalışma planı:** Çalışmada, 2004-2007 yılları arasında, modifiye Duke ölçütlerine göre kesin EE tanısı konan 72 hasta (31 kadın, 41 erkek; ort. yaş 45±16; dağılım 18-80) incelendi. Hastaların, yaş, cinsiyet, altta yatan kalp hastalığı, bakteremiye zemin hazırlayan etkenler, ekokardiyografik ve mikrobiyolojik bulgular, tedavi, komplikasyon ve mortalite ile ilgili bilgileri değerlendirildi.

**Bulgular:** Enfektif endokardit 47 hastada (%65.3) doğal kapakta, 21 hastada (%29.2) mekanik protez kapakta, iki hastada (%2.8) kalp pili üzerinde saptandı. İki hastada (%2.8) enfeksiyonun yeri belirlenemedi. Romatizmal kalp hastalığı (%36.1) en yaygın kapak patolojisiydi. Hem doğal kapaklarda (%43.1) hem de prostatik kapaklarda (%13.9) en sık etkilenen kapak mitral kapak idi. En yaygın semptom ateş (n=60, %83.3) idi. Yirmi dört hastanın (%33.3) elektrokardiyografisinde anormal bulguya rastlandı. Transtorasik ve/veya transözofageal ekokardiyografide 63 olguda (%87.5) vejetasyon, 41 olguda (%56.9) orta-ciddi derecede mitral yetersizliği, 21 olguda (%29.2) aort yetersizliği, 29 olguda (%40.3) triküspit yetersizliği saptandı. Kültürlerde etken mikroorganizma olarak en sık stafilokok (%26.4) ve streptokok (%22.2) üredi; 26 olgunun kültürlerinde (%36.1) üreme olmadı. Yirmi hastaya (%27.8) cerrahi tedavi uygulandı. Ana komplikasyon olarak en sık konjestif kalp yetersizliği (n=23, %31.9) ve serebrovasküler olay (n=10, %13.9) görüldü. Hastane içi ölüm 11 olguda (%15.3) meydana geldi.

**Sonuç:** Bulgularımız Güneydoğu Anadolu Bölgesi'nde üçüncü basamak bir hastanede EE'nin epidemiyolojik, klinik ve mikrobiyolojik özelliklerini yansıtmaktadır.

**Anahtar sözcükler:** Ekokardiyografi; endokardit, bakteriyel/epidemioloji; kalp kapağı hastalığı; kalp kapağı protezi; protezli ilişkili enfeksiyon; Türkiye/epidemioloji.

Received: February 27, 2009 Accepted: October 22, 2009

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Infective endocarditis (IE) is an infection of the cardiac valves or mural endocardium caused by bacteria, fungi and, less commonly, rickettsiae, chlamydiae, mycoplasmas and possibly viruses. The Duke diagnostic criteria have been used for case definition as definite or possible IE.<sup>[1]</sup> Despite great medical progress, IE remains a serious infection, with a stable incidence of *Streptococcus* spp. being the main causative microorganisms. However, recently, other pathogens have gained importance.<sup>[2]</sup> Culture-negative IE is also recognized as an important clinical entity.<sup>[3]</sup> In this study, we aimed to evaluate epidemiological, clinical, and microbiological profile of IE in hospital outcomes in a tertiary hospital during 2004 to 2007. Additionally, we compared our findings with those of the Euro Heart Survey recently published.<sup>[4]</sup>

## PATIENTS AND METHODS

**Study design.** Medical Center of Gaziantep University is a tertiary referral center. The records of all patients admitted with a definite diagnosis of endocarditis from 2004 to 2007 were retrospectively reviewed after obtaining approval of the institutional ethics committee. Inclusion criteria were definite IE according to the modified Duke criteria.

A total of 82 patients were admitted with the diagnosis of IE; of these, 10 patients were excluded because they did not fulfill the Duke criteria, leaving 72 patients (31 women, 41 men; mean age 45±16 years; range 18 to 80 years) with a definite diagnosis of endocarditis.

**Baseline demographics.** Data were collected on the following: age, sex, underlying heart disease, predisposing conditions for bacteremia, complications, echocardiographic and microbiological findings, treatment and outcome.

**Microbiological data.** All blood cultures used to evaluate IE were obtained by the Microbiology Laboratory of the University Hospital and processed by standard methods to identify bacterial and fungal species and antimicrobial susceptibility profiles. For blood cultures, conventional manual systems (BacT/ALERT 3D, BioMérieux, Durham, NC, USA) were used with at least three aerobic and anaerobic bottles inoculated with blood for at least 14 days. The Wright seroagglutination test was used for brucella microorganisms.

**Echocardiographic data.** Transthoracic and/or transesophageal echocardiography were performed to determine location of vegetation, type of valve infected, and cardiac complications.

**Statistical analysis.** Data were expressed as mean±standard deviation and analyzed statistically using the Student's t-test for continuous variables and the chi-square test for discrete variables. All analyses were made using the SPSS 15.0 statistical package.

## RESULTS

**Clinical features.** Table 1 summarizes data on valve (or other intracardiac structure) involvement, clinical characteristics, complications, and treatment in patients with IE. Infective endocarditis developed on a native valve in 47 cases (65.3%), a mechanical prosthetic valve in 21 cases (29.2%), and a pacemaker in two cases (2.8%). The location of the infection could not be determined in two cases (2.8%). Four patients with a prosthetic valve had early-onset endocarditis (infection that developed within 60 days of cardiac surgery). The mitral valve was the most affected valve in our series, in both native valves (43.1%) and prosthetic valves (13.9%).

**Table 1. Valve involvement, clinical characteristics, complications, and treatment in patients with infective endocarditis**

	n	%
Sex		
Male	41	56.9
Female	31	43.1
Valves involved		
Native	47	65.3
Prosthetic	21	29.2
Non-valve		
Pacemaker	2	2.8
Unidentified	2	2.8
Native valves		
Mitral	31	43.1
Aortic	10	13.9
Tricuspid	5	6.9
Multiple	1	1.4
Prosthetic valves		
Mitral	10	13.9
Aortic	8	11.1
Bioprosthetic tricuspid	3	4.2
Complications		
Congestive heart failure	23	31.9
Cerebrovascular accidents	10	13.9
Embolic phenomenon	1	1.4
Echocardiographic manifestation		
Vegetation	63	87.5
Abscess	9	12.5
Treatment		
Surgery	20	27.8
Medical	44	61.1
Combined	8	11.1

All symptoms and signs were nonspecific and occurred in a significant number of patients: fever (n=60, 83.3%), fatigue (n=55, 76.4%), loss of appetite (n=52, 72.2%), dyspnea (n=36, 50%), cough (n=32, 44.4%), sweating (n=19, 26.4%), weight loss (n=25, 34.7%), myalgia/arthralgia (n=25, 34.7%), back pain (n=6, 8.3%), vascular phenomena (n=14, 19.4%), and splenomegaly (n=14, 19.4%). Cardiac symptoms or signs (new or altered cardiac murmur, heart failure) were documented in 23 patients (31.9%). Ten patients (13.9%) exhibited neurological signs. One patient (1.4%) had intracranial hemorrhage. The majority of patients developed anemia (n=53, 73.6%). Anemia occurred more often in patients with vegetations compared to those having an abscess (87.5% vs. 73.6%;  $p<0.05$ ). Congestive heart failure was observed in 23 patients (31.9%).

**Electrocardiography.** Electrocardiography showed abnormal findings in 24 cases (33.3%), including atrial fibrillation (n=12, 16.7%), right or left bundle branch block (n=3, 4.2%), sinus tachycardia (n=13, 18.1%), and ventricular tachycardia (n=3, 4.2%).

**Echocardiography.** Transthoracic and/or transesophageal echocardiography showed a vegetation in 63 cases (87.5%), moderate or severe mitral regurgitation in 41 cases (56.9%), aortic regurgitation in 21 cases (29.2%), and tricuspid regurgitation in 29 cases (40.3%).

**Microbiology.** Causative microorganisms isolated from cultures of blood, tissue or device are listed in Table 2. Staphylococci (26.4%) and streptococci (22.2%) were the most commonly isolated causative agents of IE, accounting for a total of 48.6% of all the isolated microorganisms. Cultures remained negative in 26 cases (36.1%).

**Risk factors and underlying conditions.** The factors predisposing to bacteremia are listed in Table 3.

**Table 3. Risk factors for infective endocarditis and underlying conditions**

	n	%
Cardiac risk factors		
Preexisting valvular heart disease (rheumatological)	26	36.1
Congenital heart disease	3	4.2
Artificial heart valve	17	23.6
Degenerative heart valve	6	8.3
Non-cardiac risk factors and conditions		
Renal insufficiency	2	2.8
Diabetes mellitus	8	11.1
Dental procedure	1	1.4
Unknown	8	11.1

**Table 2. Distribution of causative microorganisms**

Microorganism	n	%
Viridans streptococci	12	16.7
<i>Streptococcus bovis</i>	4	5.6
<i>Enterococcus faecalis</i>	3	4.2
<i>Salmonella typhi</i>	1	1.4
<i>Candida albicans</i>	2	2.8
Brucella	3	4.2
<i>Staphylococcus aureus</i>	12	16.7
<i>Staphylococcus epidermidis</i>	7	9.7
Culture-negative	26	36.1
Other	1	1.4

Cardiac risk factors were more frequent in men than in women (56.9% vs. 43.1%;  $p<0.05$ ). Rheumatic heart disease (36.1%) was the most common preexisting valvular abnormality.

All patients received at least two intravenous antibiotics. The choice of antimicrobial agents was made on the basis of culture results or, in the case of culture-negative endocarditis, on an empirical basis.

Surgical treatment of IE was performed in 20 cases (27.8%), two of which (2.8%) underwent surgical removal of pacemaker (Table 1). In-hospital mortality occurred in 11 cases (15.3%).

## DISCUSSION

In our study, 72 patients who fulfilled the Duke criteria for definite IE were reviewed. The mean age of patients with IE varies from 36 to 69 years, with an increasing incidence in parallel with age.<sup>[5]</sup> In our study, the mean age of our patients was 45±16 years, which lies between the mean ages reported from Greece (54.4±17.1 years) and Tunisia (32.4±16.8 years).<sup>[6,7]</sup> However, over the last decades, an important shift to older ages has been observed in studies performed in western countries, mainly being attributed to decreased incidence of acute rheumatic disease.<sup>[7,8]</sup> In the studies performed, most cases of IE involved native valves (58.4% to 84%), aortic and mitral valves being the most commonly affected.<sup>[7,9,10]</sup> In our study, native valve involvement was seen in 65.3% and mitral valve involvement (native and prosthetic) accounted for 57%.

Fever was the most prevalent symptom (83.3%) among our patients, similar to other studies.<sup>[10-12]</sup> However, its absence in the remaining patients suggests that patients without fever may still have IE.<sup>[6]</sup> The role of echocardiography has been established in

**Table 4. Comparison of the characteristics of infective endocarditis (IE) in patients of the present study and the Euro Heart Survey**

	This study (n=72)			Euro Heart Survey (n=159)		
	n	%	Mean±SD	n	%	Mean±SD
Age (years)						
Patients with native valve IE			48±17			56 ±17
Patients with prosthetic valve IE			39±12			61 ±13
Sex						
Male	41	56.9		111	69.8	
Female	31	43.1		48	30.2	
Valves involved						
Native	47	65.3		118	74.2	
Prosthetic	21	29.2		41	25.8	
Native valves						
Mitral	31	43.1		35	22.0	
Aortic	10	13.9		56	35.2	
Tricuspid	5	6.9		4	2.5	
Multiple	1	1.4		15	9.4	
Prosthetic valves						
Mitral	10	13.9		6	14.6	
Aortic	8	11.1		23	56.1	
Bioprosthetic tricuspid	3	4.2		–		
Multiple	–			10	24.4	
Not mentioned	–			2	4.9	
Non-valve						
Pacemaker	2	2.8		4	2.5	
Unidentified	2	2.8		6	3.8	
Complications						
Congestive heart failure	23	31.9		92	57.9	
Cerebrovascular accidents	10	13.9		18	11.3	
Embolic phenomena	1	1.4		43	27.0	
Treatment						
Surgery	20	27.8		82	51.6	
Medical	44	61.1		77	48.4	
In-hospital mortality	11	15.3		24	15.1	
Microorganisms						
Viridans streptococci	12	16.7		14	8.1	
Staphylococcus aureus	12	16.7		34	21.4	
Enterococcus faecalis	3	4.2		15	9.4	
Culture-negative	26	36.1		15	9.4	
Other	1	1.4		10	6.3	

the diagnosis of IE, with specificity rates as high as 98% to 100%.<sup>[13]</sup> Echocardiography was the mainstay of diagnosis in our series.

In this study, positive blood cultures showed staphylococci and streptococci as the most commonly isolated causative agents of IE (26.4% and 22.2%, respectively). Two studies reported staphylococcal organisms in 11% and 38.9%, and streptococcal organisms in 7.5% and 24.1% as etiological agents of native valve endocarditis, respectively.<sup>[14,15]</sup> It seems that, in the last decade, staphylococcal species have exceeded streptococcal organisms in causing endo-

carditis, with a parallel decrease in the frequency of viridans streptococcal infections.<sup>[6,10,11,13,16,17]</sup>

Culture-negative endocarditis accounts for 30% to 45% of all cases of IE.<sup>[17,18]</sup> In our study, cultures were negative in 36.1%. Antibiotic treatment before the diagnosis of IE did not influence the rate of negative blood cultures in our study because antibiotic treatment was started only when the diagnosis of IE was suspected. Antibiotic treatment after the diagnosis of IE was effective in most cases. Culture-negative endocarditis may be due to several reasons including previous antibiotic therapy, lack of optimal conventional

culture techniques, and lack of systematic investigation for rare microorganisms. A study on blood culture-negative endocarditis found that most of the cases (48%) were associated with *Coxiella burnetii*, and 78% were associated with intracellular bacteria.<sup>[3]</sup>

The prognosis of IE is significantly complicated by congestive heart failure and cerebrovascular accidents.<sup>[4,19]</sup> These were also the major complications observed in our population (31.9% and 13.9%, respectively). In-hospital mortality occurred in 15.3% of our cases. In a recent study from Turkey, the incidence of congestive heart failure was reported as 55.9% and in-hospital mortality was reported as 25%.<sup>[20]</sup>

The Euro Heart Survey on valvular heart disease included 5001 patients from 92 centers in 25 European countries.<sup>[4]</sup> Acute endocarditis was found in 159 patients (3.2%), occurring on a native valve in 118 patients (74.2%) and on a heart valve prosthesis in 41 patients (25.8%). Compared to the findings of the Euro Heart Survey, the incidence of IE on aortic valves was lower, and on mitral valves was higher in our study (Table 4).

In conclusion, despite advances in both diagnosis and treatment, IE is still associated with high morbidity and mortality rates. This study confirms the protean nature of infective endocarditis.

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