

General Features of Infective Endocarditis in the South-Eastern and Eastern Anatolia: A Retrospective, Multicenter Study

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The present study aimed to evaluate general features of infective endocarditis (IE) in multiple tertiary university hospital. The study included 44 patients (23 women, 21 men; mean age 44 ± 19 years; range 15 to 85 years) who were diagnosed as having definite IE, according to the modified Duke criteria, between June 2007 and June 2011. Data were reviewed on age, sex, underlying heart disease, echocardiographic and microbiological findings, treatment, complications, and mortality. Infective endocarditis developed on a native valve in 30 (72.7%), a mechanical prosthetic valve in 12 (27.3%). Prosthetic valves 12 (27.3%) were the most common preexisting valvular abnormality. The mitral valve was the most commonly affected valve in both native valves (50%) and prosthetic valves (66.6%). The most frequent symptom was fever ($n=27$, 61.4%). Electrocardiography showed abnormal findings in 22 cases (50%). Transthoracic and/or transesophageal echocardiography showed a vegetation in 41 cases (93.2%), and abscess 3 cases (6.8%). Staphylococci (29.6%) and streptococci (25%) were the most common causative agents, and Brucella were 15.9%. Cultures were negative in 7 cases (15.9%). Nine patients (20.4%) underwent surgical treatment. Embolic events ($n=6$, 35.3%) were the major complications. In-hospital mortality occurred in 6 cases (13.6%). The data reflect epidemiological, clinical, and microbiological profile of IE in multiple tertiary hospital located in the South-eastern and Eastern Anatolia.

Key Words: Infective endocarditis; Heart valves; Staphylococcal infections; Streptococcal infections.

Infective endocarditis (IE) is an endovascular microbial infection of cardiovascular structures and a life-threatening serious disease¹. Its incidence is estimated at between 1.9 and 6.2 infections per 100 000 general population^{2,4}. Despite advances in treatment, establishment of preventative strategies and earlier detection of complications, in-hospital mortality remains high, at about 20%^{5,6}.

In this study, we aimed to evaluate epidemiological, clinical, and microbiological profile of IE in hospital outcomes in multiple tertiary center during June 2007 to June 2011. Additionally, we compared our findings with reported in previous series in Turkey^{7,10}.

MATERIALS AND METHODS

Study design; Medical Center of Dicle University, Ataturk University and Harran University are tertiary referral center. The records of all patients admitted with a definite diagnosis of endocarditis from June 2007 to June 2011 were retrospectively reviewed after obtaining approval

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of the institutional ethics committee. Inclusion criteria were definite IE according to the modified Duke criteria. A total of 44 patients were admitted with the diagnosis of IE; of these, leaving 44 patients (23 women, 21 men; mean age 44 ± 19 years; range 15 to 85 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 \pm 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 13.0 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 30 cases (72.7%), a mechanical prosthetic valve in 12 cases (27.3%). Three 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 (50%) and prosthetic valves (66.6%).

All symptoms and signs were nonspecific and occurred in a significant number of patients:

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

	n	%
Gender (Male/Female)	21/23	47.7/52.3
Valves involved (Nativ/Prosthetic)	32/12	72.7/27.3
Nativ valves		
Mitral	16	50
Aortic	14	43.7
Tricuspid	2	6.3
Prosthetic valves		
Mitral	8	66.6
Aortic	4	33.4
Complications		
None	27	61.4
Embolic phenomenon	6	15.5
Abscess (lung or splenic)	3	6.9
Cerebrovascular accidents	2	4.6
Acute renal failure	2	4.6
Congestive heart failure	1	2.3
Acute aortic insufficiency	1	2.3
Chordae rupture	1	2.3
Acute coronary syndrome	1	2.3
Echocardiographic manifestation		
Vegetation	41	93.2
Abscess	3	6.8
Treatment		
Medical	35	79.5
Surgery	3	6.8
Combined	6	13.6

Table 2. Distribution of causative microorganisms

Microorganism	n	%
<i>Staphylococcus aureus</i>	9	20.5
<i>Viridans streptococci</i>	9	20.5
<i>Brucella</i>	7	15.9
<i>Enterococcus faecalis</i>	4	9.1
<i>Staphylococcus epidermidis</i>	3	6.8
<i>Streptococcus pyogenes</i>	2	4.5
<i>Staphylococcus hominis</i>	1	2.3
Other	2	4.5
Culture-negative	7	15.9

Table 3. Cardiac risk factors for infective endocarditis and underlying conditions

Cardiac risk factors	n	%
Rheumatological valvular disease	10	22.7
Degenerative heart valve	9	20.5
Artificial heart valves	12	27.3
Venous catheters	2	4.5
None	11	25

Table 4. Comparison of the characteristics of infective endocarditis (IE) in patients of the present study

	Present study (n:44)	Sucu <i>et al.</i> (n:72)	Tugcu <i>et al.</i> (n:68)	Leblebicioglu <i>et al.</i> (n:112)	Cetinkaya <i>et al.</i> (n:228)
Age (years)				45	
Patients with native valve IE	45	48	46	?	34
Patients with prosthetic valve IE	43	39	54	?	38
Gender (%)					
Male	47.7	56.9	58.8	50	55
Female	52.3	43.1	41.2	50	45
Valves involved (%)					
Native	72.7	65.3	41.2	83	80
Prosthetic	27.3	29.2	55.8	17	20
Native valves (%)					
Mitral	50	65.9	46.4	62.5	41
Aortic	43.7	21.2	35.7	42	32
Tricuspid	6.3	10.6	3.6	13.4	-
Multipl	-	2.1	14.3	-	23
Prosthetic valves (%)					
Mitral	66.6	47.6	47.3	?	?
Aortic	33.4	38.1	39.4	?	?
Tricuspid	-	14.3	-	?	?
Multipl	-	-	13.1	?	?
Complications (%)					
None	61.4	52.7	32.3	43.9	?
Embolic phenomenon	15.5	1.4	4.5	33	7
Abscess (lung or splenic)	6.9	-	-	?	?
Cerebrovascular accidents	4.6	13.9	9	?	26
Acute renal failure	4.6	-	11.7	?	?
Congestive heart failure	2.3	31.9	11.1	?	?
Acute aortic insufficiency	2.3	-	-	?	?
Chordae rupture	2.3	-	3.6	?	?
Acute coronary syndrome	2.3	-	-	?	?
Septic shock	-	-	7.2	?	?
Treatment (%)					
Medical	79.5	61.1	39.7	86.6	76
Surgery	20.5	38.9	60.3	13.4	24
In-hospital mortality (%)	13.6	15.3	25	28.6	23
Microorganism (%)					
Staphylococcus aureus	20.5	16.7	28	35.1	11.8
Viridans streptococci	20.5	16.7	13.2	28.7	7.5
Coagulase-negative staphylococci	9.1	9.7	13.2	14.9	5.8
Other streptococci	4.5	5.6	11.8	-	6
Brucella	15.9	4.2	-	-	5.7
Enterococcus faecalis	9.1	4.2	1.5	16	5.7
Candida albicans	-	2.8	-	-	0.4
HACEK	-	-	5.9	-	-
Other	4.5	2.8	5.9	5.3	7.1
Culture-negative	15.9	36.1	20.6	16.1	50

fever (n=27, 61.4%), dyspnea (n=15, 34.1%), fatigue (n=10, 22.7%), sweating (n=7, 15.9%), nausea and vomiting (n=7, 15.9%), chills and shivering (n= 5, 11.4%), chest pain (n=5, 11.4%), myalgia/arthralgia (n=5, 11.4%), impaired general condition (n:4, 9.1%), cough (n=2, 4.6%), loss of appetite (n=1, 2.3%),

syncope (n:1, 2.3%) and splenomegaly (n=2, 4.6%). Cardiac symptoms or signs (new or altered cardiac murmur, heart failure) were documented in 5 patients (11.4%). Six patients (13.6%) exhibited neurological signs. The majority of patients developed anemia (n=32, 72.8%). Anemia occurred more often in patients with vegetations. Congestive heart failure was observed in 2 patients (0.45%).

Electrocardiography; Electrocardiography showed abnormal findings in 22 cases (50%), including sinus tachycardia (n=22, 50%), atrial fibrillation (n=7, 31.8%), complete or incomplete right or left bundle branch block (n=2, 4.6%), and ST depression or T inversion (n=2, 4.6%).

Echocardiography; Transthoracic and/or transesophageal echocardiography showed a vegetation in 41 cases (93.2%), abscess in 3 cases (6.8%), moderate or severe mitral regurgitation in 1 case (0.23%), aortic regurgitation in 1 case (0.23%).

Microbiology; Causative microorganisms isolated from cultures of blood, tissue or device are listed in Table 2. Staphylococci (29.6%) and streptococci (25%) were the most commonly isolated causative agents of IE, accounting for a total of 54.6% of all the isolated microorganisms. Cultures remained negative in 7 cases (15.9%).

Risk factors and underlying conditions; The factors predisposing to bacteremia are listed in Table 3. Prosthetic valves (27.3%) 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 9 cases (20.4%) (Table 1). In-hospital mortality occurred in 6 cases (13.6%).

DISCUSSION

This observational retrospective study provided data on general features of IE at tertiary care multicenter in Turkey. In our study, the mean age of our patients was 44 ± 19 years. Compared to other reports from Turkey, our patient population was similar. But, in a recent study by Cetinkaya *et al.*⁹ the mean age for IE was 36 years. Artificial heart valves was the sole predisposing factor in 27.3% of episodes which is significantly higher

than the figures reported in most recent series^{7,10}. In the studies performed, most cases of IE involved native valves, aortic and mitral valves being the most commonly affected^{11,13}. In our study, native valve involvement was seen in 72.7% and mitral valve involvement (native and prosthetic) accounted for 58.3%.

Staphylococci were the most frequent causative microorganisms in IE. However, staphylococcus aureus and streptococcus viridans were similar in the incidence (20.5 and 20.5, respectively). Recent series also found staphylococcus aureus as the main pathogenic agent in IE^{8,10}. In Sucu *et al.*⁷ study, staphylococcus aureus and streptococcus viridans were the prevailing etiological agents, and it was similar at our findings. The rate of enterococci was higher in the present study compared to Sucu *et al.*⁷, Tugcu *et al.*¹⁰, and Cetinkaya *et al.*⁹ study but, lower according to Leblebicioglu *et al.*⁸ study.

The rate of Brucella was very high in our study population (15.9%) when compared with these studies (0-5.7%)^{7,10}. In our study, this finding was the most important difference from the others. In the studies performed, Brucella endocarditis incidence varies widely and ranges from 0.7 to 10.9%^{14,15}. In a study by Aygen *et al.*¹⁶, a total of 480 cases were reviewed, and the rates of endocarditis after Brucella infection was found in 0.4%. But the incidence Brucellosis is high (5.4% with standard tube agglutination test, 11.9% with Rose-Bengal test) in the eastern and southeastern anatolia region¹⁷, therefore Brucella was high rate in our study population.

In our study, cultures were negative in 15.9%. The rate of culture-negative endocarditis is lower (n=7, 15.9%) compared with rates reported in previous series^{7,9,10}. However, it is similar at Leblebicioglu *et al.*⁸ study (15.9 to 16.1). 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. Recent observational series reported the frequencies of culture-negative endocarditis between 9% to 25%^{9,18,22}.

Fever was the most prevalent symptom (61.4%) among our patients, lower according to other studies^{7,10}. In our study, 20.5% of the patients underwent surgery, which was intermediate rate

according to reported in previous studies^{7,10}.

A wide variety of risk factors have been reported for mortality in IE. Those found as independent risk factors of mortality are as follows: heart failure^{23,25}, neurological abnormality^{26,27}, staphylococcal IE^{9,26,28,29}, renal failure^{9,30}, noncardiac shock²⁷, septic shock³¹, cerebral emboli³¹, systemic embolism²⁹, immunosuppression³¹, cardiac surgery³¹, nosocomial IE¹⁹, prosthetic valve¹⁹, comorbidity²⁵, medical treatment alone^{25,29}, and echocardiographic evidence for paravalvular abscess^{29,32}. In our study, there were many risk factors. However, number of risk factors were little. Therefore in-hospital mortality occurred in 13.6% of our cases. This rate is lower than the reported rates in the studies performed in Turkey^{7,10}. It was another reason that the antibiotic treatment after the diagnosis of IE was effective in most cases.

The main limitations of this study are its retrospective design and limited sample size. The latter restricts to draw conclusions for some specific subgroups. In addition, the fact that it reports from a referral tertiary care center might have caused a selection bias towards more severe or complicated cases.

In conclusion, the diagnosis and treatment of infective endocarditis should be planned different according to reported epidemiological and clinical data in regions.

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