

Native Valve Endocarditis in Cardiac Patients Admitted to Cardiovascular Department of Shaheed Madani Hospital, Tabriz

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Abstract

Background - Infective endocarditis is a disease caused by the microbial infection of the endothelium, which covers the inner layer of the heart. Different studies in advanced countries have reported the incidence of the disease from 1.6 to 6 in 100,000 patients.

Methods - This retrospective analysis was conducted at Shaheed Madani Hospital of Tabriz between 1995 and 1999. The patients who lacked diagnostic symptoms of endocarditis, and those who were diagnosed on the basis of clinical signs were excluded from the study, and 20 patients who had endocarditis of the native valves were studied. The information was collected through a questionnaire including demographic information, blood samplings, pathologic results, reports of echocardiography and radiology, feverish syndromes, records of antibiotic use, and the signs of disease. Information was analyzed using the statistical program of SPSS WIN.

Results - Twenty patients at an average age of 34 years with native valve endocarditis were selected for the study. 65% of these patients were male and 35% were female, and 17 patients had complete results of their blood culture test. *Staphylococcus aureus* was obtained in 11.67% of the cases, and two cases were positive for beta-hemolytic *streptococcus* (11.72%). In the analysis of cardiac complications, none of the patients had myocardial infarction and angina, 6 cases had embolism, 10% had no arrhythmias, and another 10% had heart block. Three of the patients had neurologic lesions, and radiological findings in 9 cases were abnormal. Eleven patients underwent open-heart surgery. The minimum duration of hospitalization was 6 days and the maximum 94 days. 80% of the patients recovered, while 20% died. Three patients had *Brucella* endocarditis, which was diagnosed via the Wright test. The most common site of infection was the aortic valve.

Conclusion - Rheumatic fever is a universal disease, the outbreak of which is very high in the countries which have poor economic conditions, are overpopulated, and have substandard living conditions. These conditions cause the rapid transmission of rheumatogenic streptococcus. Improving these conditions and proper and timely antimicrobial treatment can decrease the prevalence of rheumatic fever as well as endocarditis (*Iranian Heart Journal 2008; 9 (1): 22-28*).

Key words: cardiac patients ■ endocarditis ■ heart valve

The exact prevalence of infective endocarditis has not yet been clarified. Several studies in advanced countries have reported the prevalence of this disease from 1.6 to 6 cases per 100,000 patients.¹

The overall prevalence of infective endocarditis in the general population is about 1.7 to 4 cases per 100,000 persons. In children, the incidence is lower and is associated with rheumatic and underlying congenital heart diseases.²

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Native human heart valve endocarditis more often occurs in men and after the age of 50 years, and is rare in children. About 60 to 80 percent of patients have predisposing cardiac lesions, and 25% of these lesions are the result of rheumatic heart disease. The mitral valve, followed by the aortic valve, is the most common site of involvement. The tricuspid valve is rarely affected, but the involvement of the aortic valve has the poorest prognosis. 10-30% of the underlying conditions for this illness are related to mitral valve prolapse.^{3,4} Although most bacteria can cause endocarditis, among them *streptococcus*, *enterococcus* and *staphylococcus* are the most common causes. As we know, rheumatic fever is a worldwide disease with maximum prevalence in poor economic conditions, crowded populations, and substandard living conditions. Thus, we can prevent this illness by improving economic and living conditions.

Methods

The present investigation is a statistical study of native heart valve endocarditis in Tabriz Shaheed Madani Hospital between the years 1995 and 1999. To that end, we investigated the archived records of patients admitted within this time frame. The files of patients with infective endocarditis were extracted, and patients without the diagnostic criteria of endocarditis and those who had been diagnosed based only on clinical symptoms were set aside, and 20 cases with a definite diagnosis of native valve endocarditis were investigated. Our study criteria for establishing a diagnosis of infective endocarditis included pathologic and clinical criteria. The pathologic criteria for infective endocarditis included microorganisms isolated by culture or histologic studies of vegetations and pathologic lesions in the form of vegetations or cardiac abscess, cytology of which had shown active endocarditis. Clinical criteria consisted of two major or one major plus two minor or five minor criteria.

The major criteria comprised positive blood culture and positive echocardiography, and the minor criteria consisted of suitable cardiac background, febrile syndromes $> 38^{\circ} \text{C}$, vascular accidents such as arterial embolism, pulmonary infarction, mycotic aneurysms, intracerebral and conjunctival hemorrhage and Janeway lesions, echocardiographic findings not meeting the major criteria, immunologic phenomena, and positive serology. These patients were studied for age, sex, occupation, rheumatic fever history, underlying cardiac disease, recent predisposing surgical history, antibiotic usage, symptoms of disease including fever, chills, weakness, fatigue, headache, lethargy, delirium, anorexia, weight loss, back pain, arthralgia, myalgia, dyspnea, chest pain, cardiac infarction, abdominal pain, coldness and tremors in the extremities, arteritis, heart murmurs, splenomegaly, petechiae, Janeway lesions, clubbing of fingers, uremia and neurologic symptoms, extremities and visceral embolism, chest X-ray changes, echocardiographic positive findings, complications of endocarditis, laboratory tests of blood and urine, rheumatic factors, blood culture, VDRL, culture of specimens from vegetations, catheterization, cardiac surgery, prophylaxis, and mortality ratio.

Results

Sixty-five percent of the patients were female and 35% were male. 45% of the patients were in the age group of 10-29 years old, 40% 30-49, and 15% 50-69 years old. From 20 patients, 3 had a history of using antibiotics before hospitalization and blood culture and 4 patients were given monthly prophylactic penicillin and their cultures were negative. In 17 patients, from 20 patients with infective endocarditis, blood cultures were done with 4 positive and 13 negative results. Surgery was performed in 2 patients and PTMC in one case. Ninety percent of the patients had previous heart disease history. The most common clinical symptoms were fever,

weakness, dyspnea, chills, anorexia, and weight loss (Table I).

Table I. Clinical symptoms

	Symptom	Number	Percent
Evidence of systemic infection	Fever	15	75
	Chills	14	70
	Perspiration	8	40
	Weakness and fatigue	15	75
	Headache	11	55
	Lethargy	1	5
	Delirium	1	5
	Anorexia	12	60
	Weight loss	12	60
	Back pain	2	10
	Arthralgia	7	35
	Myalgia	3	15
	Dyspnea	15	75
	Evidence of vascular lesion	Chest pain	4
Infarction		3	15
abdominal pain		8	40
Coldness and pain in extremities		3	15
Evidence of immunologic lesion	Arthralgia	7	35
	Myalgia	3	15

Table II depicts positive physical findings. Cardiac complications such as myocardial infarction and angina were not seen. From 20 cases, 6 patients had embolic complications, with the most common site being the extremities.

Ten percent had atrial fibrillation, 5% had first-degree atrio-ventricular block, and 5% of aortic valve endocarditis had second-degree (Wenkebach) block.

Three patients from the total of 20 cases had neurologic complications.

Twelve patients had chest X-ray; in three cases they were normal and in 9 cases abnormalities were reported. The most common antibiotic regimen in the patients with unknown organisms was ampicillin/gentamycin.

Table II. Positive physical findings in 20 patients

Physical findings	Number	Percent
Fever	16	80
Arthralgia	7	35
Myalgia	3	15
Arteritis	1	5
Heart murmurs	20	100
Splenomegaly	9	45
Petechiae (skin, eye, mucosa)	3	15
Osler's nodules	1	5
Janeway lesion	1	5
Clubbing of fingers	8	40
Symptom of uremia	1	5
Symptom of embolization	3	15

Table III. Laboratory findings in 20 patients

No. of patients	Positive findings	Positive	Percent
17	Anemia	14	82/35
20	Leukocytosis	5	20
18	Proteinuria	9	50
18	Microscopic hematuria	10	55
20	High ESR	14	70
16	Rheumatoid factor	4	25
7	VDRL	1	14.28
3	Hypocomplementemia	1	33.3

In 11 cases from the 20 patients, surgery was performed. The minimum time of hospitalization was 6 days and maximum time was 94 days; 80% percent of the patients recovered and 20% died.

Discussion

According to previous studies, the age limit of patients with infective endocarditis is 45 to 60 years², and the disease more often occurs after the age of 50 years;³ whereas in this study the maximum prevalence was between the ages of 20 to 29 years and only 3 patients were more than 50 years of age. The mean age of the patients was 34 years. Perhaps the high mean age of patients is related to different conditions in Western countries.

Previous studies also show that men are at a higher risk for endocarditis^{2,3} and male-to-female ratio is reported at 1.2–3 : 1. In our study, however, 13 cases were female and 7 cases were male. Therefore, the present study shows that the male sex is not a risk factor for endocarditis. As regards underlying diseases, nearly 60-80% of patients have predisposing underlying heart lesions and rheumatic heart disease is the reason in 25% of them.³ A study done in America shows that 10% of children of age between 2 and 15 years with endocarditis have rheumatic fever history, and 10-15% of patients with endocarditis between the ages of 15 and 50 years and more than 50 years have rheumatic disease.¹ Previous studies also show that congenital heart disease except for mitral valve prolapse (MVP) are predisposing factors in 10-20% of patients with endocarditis, and MVP is the predisposing factor in 10-33% of cases. In 20-40% of patients with infective endocarditis, an underlying cause is never found. In another investigation in America, a study of patients with endocarditis demonstrated that 30-50 percent of children under the age of 2 years, 70-80 percent between ages 3 to 15 years, and 5 to 50 percent between 15 and 50 years had congenital heart disease. There was also a history of previous endocarditis in 5-10 percent of patients 15-50 years old and over. Ten to 20 percent of patients between 15 and 50 years of age and over had a history of cardiac surgery and about 10-20 percent of patients had no known heart disease, and the most common underlying disease was congenital heart disease.

In the present study, about 75% of the patients had predisposing cardiac lesions, which is almost compatible with previous studies. Among all our patients, 50% had rheumatic fever history, 15% had previous endocarditis history, 50% had PDA history, and 5% had bicuspid aortic valve (BAV) history. 25% of the patients did not have any predisposing heart lesion, which is also compatible with previous studies. One patient had a history of

cardiac surgery. Our investigation shows that cardiac rheumatic fever is the most common underlying reason for endocarditis. In our study, the other predisposing factors were a history of previous endocarditis in 3 cases, congenital heart disease in 2 cases, and recent surgical history in 2 cases. In previous studies, the mitral valve and the aortic valve in order of frequency are the most common sites of involvement. The tricuspid valve is rarely affected. In other studies in patients with endocarditis who had brain complications, the aortic valve was involved in 55.5%, mitral valve in 49.8%, and tricuspid valve in 1.3%.

From the prognostic point of view, aortic involvement has the poorest prognosis. In contrast with previous studies, in our investigation the most commonly affected valve was the aortic valve. Existence of a single vegetation on the aortic valve was seen in 45%, and multiple vegetations were seen in 10%. The second site of involvement in the present study was the mitral valve. A single vegetation on both sides of the valve was seen in 30%, and multiple vegetations were detected in 5% of the cases.

Table IV. Differences between the present and previous studies

Parameter	Previous study	Present study
Fever	>95%	80%
Arthralgia / myalgia	25-54%	55%
Heart murmur	>85%	100%
Splenomegaly	20-60%	45%
Petechiae	20-40%	15%
Osler nodules	10-25%	5%
Clubbing of fingers	10-20%	40%
Neurologic symptoms	20-40%	15%
Symptoms of embolism	25-45%	25%

The most common symptoms in this study were fever, weakness, fatigue, dyspnea, chills, anorexia, and weight loss (Table IV), which

are compatible with symptoms cited in textbooks.

In previous studies, fever is one of the most common symptoms and anorexia, fatigue, and weakness are definitive symptoms of the disease. With respect to physical findings, in comparison with previous studies, we found the most common physical finding to be heart murmur: 100% of our patients had a murmur. But in previous studies, as mentioned in textbooks, fever is the most common and cardiac murmur is the second most common finding. In our study, 4 patients had no fever at all. At admission, one case had renal failure, 2 cases had accelerated heart failure, and one case had both heart failure and old age. As was mentioned above, positive blood culture is one of two major criteria for the diagnosis of endocarditis. In studies accomplished by Hook, Kaye, Cobbs, and Werner, blood culture was reported positive in 93% of patients¹, and in other studies this ratio was 68% and 70%.¹⁻⁵ Several studies in other references have reported positive blood cultures in 99%, on the condition that the patient had not been given antibiotics. In this study, for 17 cases from the 20 patients with endocarditis, blood culture was done: 4 cases had positive (23.52%) and 13 cases had negative blood cultures. From among those who were given antibiotics before blood culture, 3 cases had *brucella* endocarditis, which was proved by the Wright test. The blood cultures of these patients also were negative. Reasons for negative blood cultures in the rest of the cases are probably factors such as insufficient equipment and fungal endocarditis. Blood culture in infection due to *Haemophilus parainfluenzae* may be negative. 50 percent of patients with *candida* endocarditis and almost all *aspergillus*, *histoplasma* or *C. burnetti* endocarditis have negative blood cultures. Other reasons for negative blood cultures are usage of antibiotics before blood culture, poor bacteriologic equipment, organisms which need specific growth requirements such as *brucella*, anaerobic bacteria and discarding of

medium and not protecting them for a long period.^{3,4}

It is reported that 20 to 30 percent of patients with endocarditis have cerebrovascular complications.⁶ Previous studies show from 55 patients with neurologic complications of endocarditis, 70% suffer from infarction and 25% from hemorrhage. Studies about embolism by Pelletier and Petersdorf in 125 patients reported 8 cases in the spleen and 8 cases in the extremities. Previous studies also show mycotic aneurysms, which spread in 3 to 15 percent of patients with infective endocarditis and can rupture or show symptoms of expanding mass. Common sites are the Valsalva sinuses 25%, visceral arteries 24%, extremities 22%, and brain arteries 15%.¹ In our study from the total of 20 patients, 3 cases had neurologic complications. With respect to CT-scan and clinical symptoms from these 3 patients, 2 cases had probability of hemorrhage and one case had infarction due to septic embolism. Six cases of the 20 patients had embolism and 20% were in the extremities, 5% in the brain, and 5% in the spleen. The extremities were the most common sites for embolism. In this study in 2 cases, suspicion of mycotic aneurysm in cerebral arteries had been reported. Previous studies show that bacterial endocarditis of cardiac valves is often treated by antibiotics; characteristics of involving microorganisms and sites of affected valves are two factors which define the prognosis of antibiotic therapy. Empiric therapy must be done when the responsible microorganism has not been isolated. In our study in cases with unknown responsible microorganisms, the majority of therapy was ampicillin in conjunction with gentamicin. The response of *Staphylococcus aureus* endocarditis to therapy is variable. Some patients, especially young intravenous drug abusers, often are cured in two weeks but in some patients fever remains for 10 to 14 days due to complications such as abscess or other extracardiac manifestations of *Staphylococcus aureus* and often treatment for 4 weeks is

sufficient. But this subject must not be taken as a general rule, because some patients have *Staphylococcus aureus* endocarditis and the period of treatment is six weeks or longer. In the present study, there were two cases of staphylococcal endocarditis and one of them had cardiac arrest on the 6th day of admission and died. The second case was treated by cefazolin and gentamicin for 94 days and was discharged in good general condition. Previous studies show one third of patients with infective endocarditis need surgery.¹ In the present study, 11 cases from 20 patients with infective endocarditis underwent surgery. Surgery in active endocarditis treatment (NVE) has increasingly obtained importance in recent years. According to existing findings in records, two cases had severe heart failure due to valvular dysfunction and 2 cases according to echocardiography had large vegetations associated with perivalvular abscess. In one of them also there was stage I heart block and the perivalvular abscess was significant during surgery and another case underwent surgery due to the existence of numerous vegetations and no response to therapy. Six patients underwent surgery due to having large vegetations. Mortality rate in cardiac surgery after (NVE) has been less than 10%.⁵ From these 11 patients in whom surgery was done, 2 cases died after surgery. One of these patients was a 70-year-old lady who had fever after surgery and also had tachycardia, diminished respiratory sounds and in chest radiography there was parapneumonic effusion in the left hemithorax. Tap of fluid was accomplished and in blood cultures after surgery, gram negative bacilli *Pseudomonas aeruginosa* was reported and she died on the 17th day after surgery due to septicemia and surgical complications. The second case was a 47-year-old patient with hemodynamic disorder due to renal failure and was in deep coma after surgery. In neurologic consultation, anesthetic drug overdose or emobilization during surgery were reported and cardiac arrest happened 7 days after

surgery. In our study, also from 11 patients undergoing surgery, 7 cases had specimens obtained from vegetations during surgery. Six of these cases had negative cultures and in one of them gram positive cocci of *Streptococcus* was reported, blood culture in this patient also revealed *Streptococcus*.

Conclusion

Studies of patients' records show that 75% of patients have predisposing cardiac lesions and that cardiac rheumatic fever is the most common underlying reason for endocarditis. Rheumatic fever is a worldwide disease with maximum prevalence in poor economic conditions, crowded populations, and substandard living conditions. Such conditions cause propagation and transmission of rheumatogenic streptococcus; therefore, prevention of rheumatic fever can be accelerated by improving economic conditions and decreasing crowding, which is an essential environmental factor dependent on disease induction and usage of antibiotic therapy. Given that a suitable assessment can be obtained by surgery and that timing is essential for surgery in endocarditis, surgery must be accomplished in patients with heart failure or no response to drug therapy. To prevent disease complications and also since infective diseases such as brucella are common in Iran and cause endocarditis in significant numbers of people, we must prevent disease through the immunization of animals and boiling or pasteurization of milk products and generally by controlling of infective sources. In addition, because patients with negative culture endocarditis are probably exposed to invading brucella infection due to environmental contact, physicians must warn bacteriologic laboratories to keep blood cultures for longer periods, to culture in specific media, and to consider biological dangers. Given the high percentage of negative cultures, which is one of major criteria in the diagnosis of the

disease, it is necessary to exploit advanced laboratory equipment with precision.

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