

Original Research Article

A study of clinical and etiological profile of infective endocarditis and its correlation with echocardiography in patients of rheumatic heart disease

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ABSTRACT

Background: This observational study was to determine the offending microorganisms and clinical profile of infective endocarditis in rheumatic heart disease patients in local population of Jharkhand, the response of disease to medical treatment and to evaluate the prognosis of the cases.

Methods: 25 cases of Rheumatic heart disease, fulfilling the diagnostic criteria for infective endocarditis were studied prospectively with baseline investigations, blood culture and echocardiography and were treated with appropriate antibiotics.

Results: In this study, the mean age observed was 26 year and male patient to female patient ratio was 3.16:1. Aortic valve was the commonest valve to be involved. Cardiac murmurs were present in all patients, splenomegaly was present in 56% of patients but peripheral signs of infective endocarditis were rare. Blood culture was positive in 28% of cases and staphylococcus aureus was the main organism isolated. 23 cases out of 25 cases studied showed vegetations on echocardiography mostly on aortic or mitral valve. In majority of patients (80%) injection Penicillin G and Gentamicin were started in standard recommended dose first on empirical basis but later on suitable antibiotics were started according to sensitivity pattern. Mortality was significantly high (20%).

Conclusions: Fever and constitutional symptoms were the most common presentation. Mild to moderate anemia, leucocytosis, high ESR were very common but, peripheral signs were rarely observed in our study. Staphylococcus was the predominant etiological agent and treatment of endocarditis was more successful when suitable antibiotics were started after culture and sensitivity.

Keywords: Echocardiography, Infective endocarditis, Rheumatic heart disease

INTRODUCTION

Infective endocarditis is a disease caused by microbial infection of the endothelial surface of the heart. Infective endocarditis is often called acute or subacute. Acute infective endocarditis is caused typically by

staphylococcus aureus. It presents with marked toxicity and progresses during days to several weeks to valvular destruction and metastatic infection. Subacute infective endocarditis, usually caused by viridians streptococci, enterococci, coagulase negative staphylococci, or gram-negative coccobacilli, evolves during weeks to months

with only modest toxicity and rarely cause metastatic infection.¹ It is a very serious complication of rheumatic valvular heart disease.

Several studies from developed countries have shown changing spectrum of infective endocarditis which are attributed to better diagnostic facility, greater longevity of patients with congenital and acquired valvular disease, aggressive surgical approach, emergence of new risk group for infective endocarditis (intravenous drug abuse, prosthetic heart valves, nosocomial bacteremia, degenerative heart disease), declining incidence of rheumatic heart disease.^{2,3} Echocardiography has added a great deal to the ability to confirm or reject the diagnosis of infective endocarditis.⁴ First of all vegetative lesions can be detected. Echocardiography also plays a major role in the recognition of complication of endocarditis as perivalvular abscesses, aneurysm, fistulas, rupture of valvular leaflets, chordae and papillary muscles or interventricular septum.

Very few Indian studies are available regarding infective endocarditis. That too, most of works have been done on pediatric age group. The data from Indian studies differ from that of most of the western countries in several aspects like, population at risk for infective endocarditis, incidence of rheumatic heart disease, availability of transesophageal echocardiography and other diagnostic facility, emergency facility for surgical correction, etc. Therefore, infective endocarditis in India requires further studies.

METHODS

All patients attending Cardiology, Medicine or Pediatric O.P.D. or Emergency in Rajendra Institute of Medical Sciences, from October 2011 to October 2012, clinically suspected of having infective endocarditis were thoroughly investigated. Those cases of rheumatic heart disease, labeled as having infective endocarditis has been taken for further study. The study was done on 25 selected patients of Rheumatic heart disease, fulfilling the diagnostic criteria for infective endocarditis. Diagnostic criteria proposed by DUKE university was applied for the study.⁵

A complete clinical history and physical examination along with special attention to predisposing factors and complication were taken according to the points as per Performa. A complete hemogram, urinalysis especially for microscopic hematuria, chest X-ray and EGG was undertaken routinely. Before initiation of therapy blood cultures were taken. A detailed M mode and 2 D echocardiographic study was performed in all suspected cases, and doubtful cases underwent TEE. Further investigations were done to document and confirm complications wherever it was indicated. Informed consents were taken from all the patients and the ethics committee approval was obtained prior to study initiation.

RESULTS

Study have selected 25 cases of Rheumatic heart disease, fulfilling the diagnostic criteria for infective endocarditis. Age of the patients studied varied from 10 to 50 years with maximum number of patients were in the age group of 10-20 years (11 patients = 44%). Male to female patients' ratio was 3.16:1. Maximum number of patients had combined mitral and aortic valve lesion (48%). Commonest combined lesions in our patients were mitral and aortic regurgitation (24%). Source of infection was detected in only 5 patients (20%) in our study.

Table 1: Relative incidences of different clinical features and complications in patients presenting with infective endocarditis.

Symptoms	No. of patients	Percentage
Fever	25	100
Malaise	19	76
Weight loss	10	40
Anorexia	20	80
Oedema	8	32
Arthralgia	8	32
Myalgia	4	16
Altered sensorium/ neurological deficit	7	28
Oliguria/ anuria	5	20
Breathlessness	12	48
Signs		
Fever	25	100
Altered sensorium	5	20
Pallor	25	100
Clubbing	9	36
Pedal edema	6	24
Lymphadenopathy	4	16
JVP (raised)	11	44
Murmurs	25	100
Splenomegaly	14	56
Petechiae	1	4
Osler's node	-	-
Janeway lesions	-	-
Splinter hemorrhage	-	-
Roth's spot	-	-
Peripheral emboli	5	20
Fundus exam	N	-
Complications		
Refractory heart failure	7	28
Cerebro vascular accidents	4	16
Acute renal failure	5	20
Peripheral arterial embolism	5	20
Septicemia	3	12
Upper GI bleeding	1	4

All patients in our study had mild to moderate grade fever (100%). On examination, almost all patients had pallor. 5

patients were in altered sensorium with or without focal neurological deficit. Cardiac murmur was auscultated in all patients. Eleven patients (44%) were in congestive heart failure. Among peripheral signs of infective endocarditis clubbing was present in nine patients (36%). Other signs like oslers node, Janeway lesion and roth's spots were not seen in any of the patients. One patient had petechial hemorrhage. Among the study group, spleen was enlarged in 14 patients (Table 1).

Table 2: Results of different investigations in patients presenting with infective endocarditis.

Hb% (mg/dl)	No. of patients	Percentage
Normal >14	0	0
Mild Anaemia 11-14	10	40
Moderate anaemia 7-10	12	48
Severe anaemia <7	3	12
Total leucocyte count		
<10,000 cells/mm ³	12	48
Blood culture positivity		
Positive (+ve)	7	28
Negative (-ve)	18	72
Vegetations on echocardiography		
Aortic	15	60
RCC	11	44
NCC	2	8
Both RCC and NCC	2	8
Mitral	7	28
AML	6	24
PML	1	4
Both AML and PML	-	-
Both aortic and mitral	1	4

Haemoglobin level was less than normal in all 25 studied cases (100%), while 3 patients were severely anaemic with haemoglobin level less than 7gm/dl. Thirteen patients of the study group had leukocyte count more than 10,000 cells per cubic millimeter at the time of admission (Table 2). Almost all patients in study group had raised ESR [23 patients (92%)]. Only four patients (16%) showed feature of microscopic haematuria. Blood culture was positive in seven out of all twenty-five patients (28%) while in 18 patients blood culture was negative despite repeated collection of sample and incubation for seven day (Table 2). *Staphylococcus aureus* was the commonest organism to be grown and was seen in 3 of 25 patient's blood sample (12%). It was sensitive to vancomycin in all 3 cases. *Staphylococcus aureus* was sensitive to aminoglycosides in two but resistant in one sample. *Staphylococcus aureus* was resistant to penicillin G in all 3 patients. In one patient culture showed growth of coagulase negative *staphylococci*. It was sensitive to ciprofloxacin, Oxacillin and Vancomycin. *Streptococcus viridans* was grown in 2 patient's blood culture (8%). It was sensitive to penicillin G and aminoglycosides. One patient showed growth of acinobacter. In 23 out of 25 patients vegetations were

documented on echocardiography (92%). Most commonly involved valve was aortic (in 15 patients (60%). Mitral valve was involved in 7 patients (28%). Of these most patients have vegetations on AML. In one patient vegetation was present in both mitral and aortic valve.

Treatment was started on empirical basis in all patients after sending 3 blood samples for blood culture. Empirically treatment was started with injections of Penicillin G in 12 to 18 million IU in 6 divided doses with injection of gentamicin in 3 to 5mg/kg/day in 3 divided doses in 20 patients (80%). 4 of these patients expired during the course of treatment. 11 patients responded to treatment and become afebrile in 8 days and treatment was given for only 2 weeks. Five of these patients became afebrile after 10 days of treatment and injection penicillin G was continued for additional 2 weeks with total duration of treatment given was 4 weeks (Table 3). Injection ceftriaxone 2gm IV OD was started in 5 patients (20%), One of these patients expired on third day due to poor general condition. Rest of the patients completed the 4 weeks course successfully.

Table 3: Treatments of patients presenting with infective endocarditis with different regimens of antibiotics and mortality outcomes in those patients.

Regimen with duration	No. of patients (%)	Mortality
Penicillin G (12-18 million IU) IV in 6 divided doses -for 2 weeks Plus Gentamicin - for 2 weeks (1mg/kg IV 8 hours)	15 (60%)	4
Penicillin G (12-18 million IU) IV in 6 divided doses for 4 weeks Plus Gentamicin -for 2 weeks (1mg/kg IV 8 hr)	5 (20%)	-
Ceftriaxone (2gm) IV OD -for 4 weeks.	4	1

Mortality was significantly high (20%) and the cause of death was attributed to septicemia (8%), refractory heart failure (4%), acute renal failure (4%) and arrhythmia/sudden death (4%).

DISCUSSION

Most of the western studies where there is upward shift in mean age from 30 to about 50 years in past 3 decades.⁶ In India mean age has remained more or less the same with majority of Indian patients still being under 40 years of age. Important factors include low life expectancy and high incidence of rheumatic heart disease.⁷ In our study age group varied from 11 to 43 years with maximum number of patients in the age group of 10 to 20 years age

group (11 patients = 44%) and the mean age observed was 26.00 years. In our study, total number of male patients was 19 and that of female patients was 6. Male to female ratio was 3.16:1. This figure is in accordance with other Indian studies.⁷

Lone aortic valve involvement was noted in 32% of cases and combined involvement of both aortic and mitral valve was noted in 48% of cases in present study. Isolated mitral valve lesion was seen in 20% of cases. These findings are in consistent with Indian and western studies. Tricuspid valve involvement is rare as noted by various studies and same is with pulmonary valve. In our study tricuspid valve was involved in 4% of the cases, and that too in association with mitral valve lesion. Isolated tricuspid valve involvement was not observed in our study.

In this study, source of infection was detected in only 20% of cases; similar observations were made by others.⁸ In our study 11 patients (44%) were already diagnosed case of rheumatic heart disease and only 5 patients (20%) were taking long acting penicillin prophylaxis. This suggests poor compliance among our patients.

Fever is one of the cardinal manifestation of infective endocarditis. In our study, all patients had mild to moderate grade fever (100%). Fever varied from 41.2 to 100% in other series. A moderate normocytic normochromic anaemia is a common finding in infective endocarditis. In our study, all patients had pallor (100%). This is in accordance with various Indian studies. However, the incidence of anaemia in western series varied from 34-91%. This high incidence of anaemia among Indians may be explained mainly by poor nutritional status and long duration of illness before presentation. In present study spleen was enlarged in 14 patients (56%). It has been recorded to occur in 36-60% of Indian patients. Among peripheral signs of IE, clubbing was noted in 9 patients (36%). Incidence of clubbing in Indian studies varies from 32-80%. In west presently clubbing is identified in only 10-20% of cases. High incidence of clubbing in Indian studies is because of late presentation of these patients. One patient has petechial haemorrhage (4%) in our study. In spite of thorough search in our cases we failed to identify other signs like splinter hemorrhage Osler's node and Janeway lesions even in single case. Various studies have shown that these are uncommon finding of IE.^{9,10} In our study 28% of patients developed congestive heart failure. Incidence of heart failure varied from 21 to 75% in various studies. Indian workers have reported a higher incidence of congestive heart failure in their study. In present study 16% of patients developed hemiplegia/hemiparesis. It commonly results from embolism of middle cerebral artery by friable vegetations. This is in accordance to findings reported in various studies.^{11,12}

In present study, Haemoglobin was low in all patients 88% of them had mild to moderate anaemia. This finding is in accordance with the finding of various Indian studies. Incidence of leucocytosis varies from 39-58% in various studies.¹³ In our study in 52% of patients leucocytosis was seen. Most of them were case of acute IE with history of less than 4 weeks. In present study 92% of patients has raised ESR. In various studies, the percentage of patients showing raised ESR ranges from 72% to 100%.² In present study microscopic hematuria was detected in 16% of patients. Similar incidence has been seen in different Indian series. A higher incidence has been reported from the west.

In this study blood culture was positive in 28% of cases, in Indian studies blood culture positivity varies from 21% to 97%. While as in western series culture positivity varies from 73 to 97%. In present study *staphylococcus aureus* was the main organism isolated in 12% of cases. *Streptococcus viridans* was isolated in 8% cases and coagulase negative staphylococcus and acinobacter were isolated from one cases each (4%). Results in these studies are different from results of various western studies but matching with some of Indian studies.¹⁴

The sensitivity of TTE for the detection of vegetations, even with the use of harmonic imaging and other modern techniques, in patients with NVE is approximately 45% to 65%, whereas that of TEE in these patients is 85% to 95%. The likelihood of a false-negative study can be reduced to 5% to 10% if TEE is repeated.¹⁵ TEE is the preferred approach in patients in whom TTE is technically suboptimal and is the procedure of choice for imaging of the pulmonary valve and patients with suspected PVE.^{13,15} In present study vegetations were demonstrated in 92% of cases. In present study vegetations were mainly confined to aortic and mitral valves. Aortic valve was involved in 60% of cases and mitral valve in 28% cases. In one patient, vegetation was seen on both mitral and aortic valve. Similar results have been shown in various. Indian studies.^{7,10} However, in western studies mitral valve is more commonly involved as compared to Indian study. This may be because of high incidence of mitral valve prolapse or prosthetic valve as predisposing cardiac lesion in patients with IE.

Out of 25 patients 5 patients expired during hospital study in our study (20%). Of these patients culture was positive in four patients and three had staphylococcal infection. This figure of mortality is comparable to other Indian reports of 21-54%.^{7,9,10} More recent series suggest that mortality can be reduced to 10-13% by timely surgical interventions. In our study mortality was high with staphylococcal infective endocarditis. The factors contributing to mortality include non-availability of surgical facilities and poor economic status of our patients who could not afford the high cost of cardiac surgery which could be life-saving in patients of refractory heart failure and uncontrolled sepsis.

CONCLUSION

Mean age of our patients is still lower than western part of world. Fever and constitutional symptoms are the most common presentation. Mild to moderate anemia, leucocytosis, high ESR are very common. Peripheral signs of infective endocarditis were scanty in this series as - petechial haemorrhage was noted in only 1 patient and Osler's node, splinter hemorrhage, Janeway's lesion and Roth's spot were not observed in our study. Staphylococcus was the predominant etiological agent in our study. Treatment of endocarditis was more successful when suitable antibiotics were started after culture and sensitivity rather than the empirical treatment. To conclude, we have reached at a point that infective endocarditis is not so uncommon manifestation seen in the Department of Medicine and Cardiology because of higher incidence of rheumatic heart disease in our society. We must take into account the gravity of the illness and to start an early treatment in order to salvage these cases without which the mortality would be higher as discussed.

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