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Scientific Research

Clinical Spectrum of Infective Endocarditis in a Tertiary Care Centre in Western India: A Prospective Study

Sharad R. Jain[1], Jayesh S. Prajapati[1], Manjunath A. Phasalkar[1], Bhavesh H. Roy[1], Ashwal A. Jayram[1], Shaurinkumar R. Shah[1], Tarandeep Singh[1], Ashok S. Thakkar[2]

[1]Department of Cardiology, U. N. Mehta Institute of Cardiology and Research Centre, Ahmedabad, India
[2]Department of Clinical Trials, Sahajanand Medical Tech. Pvt. Ltd., Surat, India
Email: drsharadrjain@gmail.com

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Abstract

OBJECTIVES: We examined the microbiological spectrum, clinical profile, echocardiographic features and in-hospital outcomes of patients with definitive IE. METHODS: A total of 75 consecutive cases of definitive infective endocarditis (IE), admitted between January 2011 and January 2013, were included in the study. This was a prospective study enrolling all the consecutive definitive cases of IE admitted at U. N. Mehta Institute of Cardiology and Research Centre (UNMICRC), Ahmedabad, India. Only the patients who met the modified Duke's definitive criteria for IE were included in the study. We compared enrolled patients clinicoepidemiologic features and outcomes to subjects in the west. RESULTS: The mean age was 27.46 ± 17.11 years with a male preponderance (2.26:1). The rheumatic heart disease (41.3%) was the commonest underlying disease followed by coronary heart disease (34.7%). The blood culture was positive in 40% of episodes with commonest organisms being staphylococci (16%) and streptococci (12%). Complications were cardiovascular in 40 (53.3%) cases (congestive heart failure in 42.7%, atrioventricular block in 6.7%), septic shock in 20 (26.7%), neurological in 23 (30.7%) (cerebrovascular stroke in 20%, central nervous system hemorrhage in 5.3%, encephalopathy in 5.3%) and renal failure in 20 (26.7%) of cases respectively. Only 12 (16%) patients underwent surgery for IE. The total in hospital mortality rate was 22 (29.3%). On multivariate analysis, congestive heart failure, renal failure, neurological abnormalities, age < 20 years and septic shock were independent predictors of mortality. CONCLUSIONS: The spectrum of infective endocarditis is different in Indian population compared to the west and carries a substantial morbidity and mortality. The rheumatic heart disease is still the commonest underlying heart disease in our population. The culture positivity rates and surgery for infective endocarditis are unacceptably low. Early cardiac surgery may help to improve the outcomes of these patients.

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Keywords

Infective Endocarditis; Rheumatic Heart Disease; Echocardiography

1. Introduction

Despite the availability of improved diagnostic and treatment amenities, infective endocarditis (IE) continues to have a high morbidity and mortality in the developing world [1] [2]. Several data from the developed world have emphasized regarding the changing spectrum of infective endocarditis [3]-[6]. However, in the face of this changing trend, the incidence and mortality have not declined significantly [7]. In spite of the high incidence of rheumatic heart disease and unrepaired congenital heart defects in India and other developing countries, there are relatively scant data on the profile of IE. In fact, most of these studies have been retrospective in nature [8]-[11]. There are very few prospective studies of IE from the developing world [12] [13]. In the face of globalization and rapid urbanization, we need to answer whether the changing scenario of IE observed in the west also applies to our population. Hence, we undertook a prospective study of IE focusing on the epidemiological trend, clinical, and microbiological profile and in-hospital outcomes of patients admitted to our institute.

2. Materials and Methods

This is a prospective study enrolling all the consecutive definitive cases of IE admitted at U. N. Mehta Institute of Cardiology and Research Centre (UNMICRC), Ahmedabad, India from January 2011 to January 2013. Only the patients who met the modified Duke's definitive criteria for IE were included in the study. The data regarding the clinical presentation, predisposing factors, precipitating cause, investigative work up and outcome were recorded prospectively. At least three blood culture samples (aerobic and anaerobic) were obtained from three different vein puncture sites at least one hour apart before initiation of antibiotic therapy. Fungal culture was done if the clinical situation deemed necessary. All patients underwent transthoracic echocardiography (TTE) on admission and thereafter, if there was a change in the clinical status. The transesophageal echocardiography (TEE) was done in patients with high clinical suspicion but non-diagnostic TTE, in all patients with prosthetic valve endocarditis (PVE), and in patients with complications of IE (perivalvular abscess, valve perforation/rupture, worsening regurgitation). A serial follow up of all the patients was done at weekly intervals.

All the collected data were entered into IBM SPSS Version 20 for data analyses. Data were expressed as mean ± SD. While comparing culture positive and culture negative cases, paired "t" test was used for continuous variables and test of significance of proportion was used for categorical variables. Stepwise logistic regression analysis was done to determine the independent predictors of mortality and surgery. A p value < 0.05 was considered as significant.

3. Results

A total of 75 definitive cases of IE were admitted to our institute between January 2011 and January 2013. The male to female ratio was 2.26:1. The mean age of the patients was 27.46 ± 17.11 years (range, 7 months to 80 years). About 58 (77.3%) patients were younger than 40 years, with 30 (40%) patients under 20 years of age. Majority of cases (n = 64, 85.3%) fulfilled 1 major (echocardiographic) and 3 minor criteria. The rest 11 (14.7%) patients satisfied 2 major criteria (echocardiographic and blood/valve culture proven). Probable source of infection was present in 7 (9%) patients. The probable sources of infection were permanent pacemaker insertion, wound infection, dental manipulation, pyelonephritis, recent lower segment caesarean section with wound infection, maxillary sinusitis and pneumonia each being present in one patient respectively. Five patients had dental caries. None of our patients were intravenous drug abusers.

3.1. Underlying Heart Disease

Rheumatic heart disease (RHD) was the most frequent underlying heart disease. RHD was present in 31 (41.3%) patients (**Table 1**).

Table 1. Underlying heart disease in 75 patients of infective endocarditis.

Underlying heart disease	n = 75 patients
Rheumatic heart disease, n (%)	31 (41.3%)
Mitral valve disease, n (%)	28 (37.3%)
Aortic valve disease, n (%)	17 (22.7%)
Mixed valvular heart disease, n (%)	14 (18.7%)
Congenital heart disease, n (%)	26 (34.7%)
Post tetrology of fallot ICR[1], n (%)	7 (9.3%)
Post ICR with RV to PA conduit, n (%)	1 (1.3%)
Post ICR with PPI[2], n (%)	1 (1.3%)
Tetrology of fallot, n (%)	1 (1.3%)
Ventricular septal defect, n (%)	4 (5.3%)
Bicuspid aortic valve, n (%)	4 (5.3%)
Patent ductucs arteriosus, n (%)	2 (2.7%)
Subaortic membrane, n (%)	2 (2.7%)
RSOV[3] with VSD, n (%)	1 (1.3%)
Post truncus arteriosus reapir, n (%)	1 (1.3%)
Post Patent ductucs arteriosus ligation, n (%)	1 (1.3%)
Tetrology of fallot with post BT[4] shunt, n (%)	1 (1.3%)
Prosthetic valves endocarditis, n (%)	7 (9.3%)
Mitral valve prolapsed, n (%)	5 (6.7%)
Degenerative valve disease, n (%)	2 (2.7%)
No previous known heart disease, n (%)	8 (10.7%)

[1]Intracardiac repair; [2]Permanent pacemaker implantation; [3]Rupture of sinus of valsalva; [4]Blalock taussig shunt.

Among these, the most common lesion was mitral regurgitation in 28 (37.3%) cases followed by aortic regurgitation in 17 (22.7%) cases and combined mitral and aortic valve disease in 14 (18.7%) cases. None of these patients had isolated mitral stenosis or aortic stenosis. Congenital heart disease (CHD) represented the second most common underlying heart disease being present in 26 (34.7%) patients. Of these, 14 (18.7%) cases were uncorrected CHD'S and 12 (16%) cases were operated cases of CHD. Among the patients with uncorrected CHD, the most common disease was ventricular septal defect in 4 (5.3%) cases and bicuspid aortic valve in 4 (5.3%) cases. The most common corrected CHD predisposing to IE was intra-cardiac repair for tetralogy of fallot (TOF) in 8 (10.7%) patients (including one patient with right ventricle to pulmonary artery conduit). Prosthetic valve endocarditis (PVE) accounted for 7 **(**9.3%) cases. Mitral valve prolapse (MVP) and degenerative heart disease were observed in 5 (6.7%) and 2 (2.7%) patients respectively. In 8 (10.7%) patients, no structural heart disease could be identified.

3.2. Clinical and Laboratory Profile

The most common presenting feature in the patient was fever 69 (92%) followed by congestive heart failure 32 (42.7%). The most frequent peripheral signs were pallor 69 (92%) followed by clubbing 36 (48%) and splenomegaly 35 (46.7%) (**Table 2**).

The most common abnormal laboratory parameters were anemia 72 (96%) and raised erythrocyte sedimentation rate (ESR) 72 (96%). The most frequent complications were cardiac 40 (53.3%) followed by neurological 23 (30.7%), renal failure 20 (26.7%) and septic shock 20 (26.7%). Among the cardiac complications, the most common was congestive heart failure (CHF) 32 (42.7%). Five patients had conduction abnormalities, among which 3 (4%) had complete hearts block (CHB) and 2 (2.7%) had first degree atrioventricular block. Five (6.7%) patients with conduction abnormalities had aortic valve endocarditis. The other patient had CHB following intracardiac repair of TOF. 3 (4%) patients developed pericardial effusion among which one patient had tamponade that required tapping. Among neurological complications, the most frequent were cerebrovascular (CV) stroke 15 (20%) followed by Central nervous system (CNS) hemorrhage 4 (5.3%) and encephalopathy 4 (5.3%).

Table 2. Clinical and laboratory findings of 75 episodes in 75 patients of infective endocarditis.

Variables	n = 75 patients
Age, yrs (mean ± SD)	27.46 ± 17.11 (range 7 months to 80 yrs)
Sex (male/female)	2.26/1.0
Fever, n (%)	69 (92.0%)
Peripheral signs	
Splenomegaly, n (%)	35 (46.7%)
Clubbing, n (%)	36 (48.0%)
Osler's node, n (%)	5 (6.7%)
Roths spots, n (%)	7 (9.3%)
Splinter haemorrhage, n (%)	7 (9.3%)
Petechial haemorrhage, n (%)	6 (8.0%)
Janeway lesion, n (%)	3 (4.0%)
Complications	
Cardiac complications	
Congestive heart failure (CHF), n (%)	32 (42.7%)
Conduction abnormalities (CHB, AV block), n (%)	5 (6.7%)
Pericardial effusion, n (%)	3 (4.0%)
Neurological complications	
CV stroke, n (%)	15 (20.0%)
CNS haemorrhage, n (%)	4 (5.3%)
Mycotic aneurysm, n (%)	2 (2.7%)
Encephalopathy, n (%)	4 (5.3%)
Renal failure, n (%)	20 (26.7%)
Hepatic dysfunction, n (%)	17 (22.7%)
Embolism	
Brain (CV stroke), n (%)	15 (20.0%)
Extremities (digital infarcts), n (%)	3 (4.0%)
Septic pulmonary infarct, n (%)	1 (1.3%)
Splenic infarct, n (%)	1 (1.3%)
Renal infarct, n (%)	1 (1.3%)
Septicaemia, n (%)	20 (26.7%)
Laboratory parameters	
Hemoglobin (<12 gm %), n (%)	72 (96.0%)
ESR (≥20 mm), n (%)	72 (96.0%)
Leucocytosis (>11,000/mm^3), n (%)	53 (70.7%)
Leucopenia (<4000/mm^3), n (%)	2 (2.7%)
Thrombocytopenia, n (%)	21 (28.0%)
Microscopic haematuria, n (%)	31 (41.3%)
Elevated CRP, n (%)	70 (93.3%)
Positive RA factor, n (%)	9 (12.0%)

Mycotic aneurysms were detected in 2 (2.7%) patients. Embolic complications occurred in 21 (28%) episodes among which, the most common were CV stroke in 15 (20%) followed by digital infarcts in 3 (4%) episodes respectively. Pulmonary infarct, splenic infarct and renal infarct occurred in 1 patient each. The pulmonary infarct was a consequence of tricuspid valve endocarditis secondary to intracardiac repair for TOF with implanted permanent pacemaker. Renal function was deranged in 20 (26.7%) and hepatic dysfunction occurred in 17 (22.7%) patients.

3.3. Echocardiography

The TTE was performed in all 75 patients while, TEE was done in 17 (22.7%) patients only (**Table 3**).

TTE was diagnostic in a total of 67 (89.3%) cases and in the rest, TEE was diagnostic. Multiple vegetations (≥2) were more common than single vegetation (65.3% vs. 34.7% episodes respectively). Vegetations of <10 mm and ≥10 mm were nearly equally distributed (49.3% vs. 50.7% episodes respectively). The most common site of vegetation was mitral valve in 37 (49.3%) episodes followed by aortic valve in 29 (38.7%) episodes. Ten (13.3%) patients had vegetations in extravalvular location among which 8 patients were postoperative cases of CHD (right ventricle to pulmonary artery conduit in 3 patients, ventricular septal defect patch (VSD) in 3, right ventricular outflow tract (RVOT) in 2 patients) followed by 2 patients with unrepaired CHD (patent ductus arteriosus (PDA) insertion and pulmonary artery in 1 patient each). Nine (12%) patients had increase in size of vegetations on serial echocardiography. Seven (9.3%) patients had PVE among which one patient had partial dehiscence of prosthesis and four patients had moderate paravalvular leak. Three patients had aortic root abscess and two patients had aortic cuspal perforation causing severe regurgitation.

3.4. Microbiological Profile

Blood cultures were positive in 30 (40%) patients only. Among these, staphylococci were the most frequent isolate in 12 (16%) cases followed by streptococci in 9 (12%) cases (**Table 4**). However, among all the above culture positive cases, only 11 (14.7%) patients satisfied the duke's major criteria for culture positivity and in the rest of cases only single culture was positive. In patients with culture negative endocarditis who underwent surgery, tissue culture was negative in all except one patient in which the isolate was pseudomonas.

There were no significant differences in sex ratio, complications, need for early surgery, vegetation characteristics and mortality between culture positive and culture negative group (**Table 5**). There was significant higher proportion of patients with positive blood culture who had CHD as the underlying heart disease (50.0% vs. 24.4%, p = 0.04) and consequently culture positivity was more in younger age group as compared to older age group (p = 0.027). Also, a higher proportion of patients with negative cultures had prior antibiotic usage in comparison to culture positive patients (68.9% vs. 30.0%, p = 0.002).

Table 3. Echocardiographic profile in 75 episodes of infective endocarditis.

Echocardiographic features	Number of patients (%)
Vegetation	75 (100.0%)
Location	
Mitral valve	37 (49.3%)
Aortic valve	29 (38.7%)
Mitral and aortic valve	11 (14.7%)
Tricuspid valve	6 (8.0%)
Pulmonary valve	4 (5.3%)
Other sites of vegetations	10 (13.3%)
Size	
<10 mm	37 (49.3%)
>10 mm	38 (50.7%)
Number	
Single	26 (34.7%)
Multiple	49 (65.3%)
New/worsening regurgitation (changing murmur)	13 (17.3%)
Cardiac abscess	
Aortic root abscess	3 (4.0%)
Cuspal perforation	2 (2.7%)
Pericardial effusion	3 (4.0%)
Prosthetic valve dysfunction	
Dehiscence	1 (1.3%)
Paravalvular leak	4 (5.3%)

Table 4. Blood cultures in 75 episodes of infective endocarditis.

Microorganism	Number of episodes (%)
Streptococci viridians, n (%)	9 (12.0%)
Enterococci, n (%)	2 (2.7%)
Staphylococci	
MRSA[1], n (%)	9 (12.0%)
MSSA[2], n (%)	1 (1.3%)
CONS[3], n (%)	2 (2.7%)
Gram negative bacilli	
Pseudomonas aeruginosa, n (%)	2 (2.7%)
Klebsiella, n (%)	2 (2.7%)
Fungal (CANDIDA), n (%)	3 (4.0%)
Culture negative, n (%)	45 (60.0%)

[1]Methicillin resistant staphylococcus aureus; [2]Methicillin resistant staphylococcus aureus; [3]Coagulase negative staphylococci.

3.5. Clinical Course and Outcome

The antibiotics were used according to the underlying heart disease, clinical situation, offending organism and complications. The mean duration of antibiotic therapy was 26.61 ± 12.78 days (range 1 - 45 days). Most commonly, patients received two antibiotics 42 (56%). In successfully treated patients the mean duration of antibiotic treatment was 30.89 ± 10.3 days. The most commonly used antibiotic combination was cephalosporin and aminoglycoside 24 (32%). This was followed by cephalosporin, aminoglycoside and vancomycin 23 (30.7%); and crystalline penicillin with aminoglycoside in 12 (16%) of patients. The other antibiotics used were fluoroquinolones, teicoplanin and linezolid. Patients with either proven/suspected fungal IE were treated with fluconazole or amphotericin.

Only 12 (16%) patients underwent surgery for IE. The most common underlying heart disease was CHD (n = 5) followed by RHD (n = 3), no structural heart disease (n = 2), degenerative valve disease (n = 1) and MVP (n = 1). The reasons for surgery during active IE were uncontrolled CHF in 7 (58.3%) and persistent infection despite adequate antibiotic use in 5 (41.6%). The most common surgery done was mitral valve replacement 3 (25%) followed by double valve replacement (mitral and aortic) in 2 (16.7%) patients. The other surgeries done were VSD closure, VSD closure with aortic valve replacement, PDA ligation, conduit replacement, mitral valve repair, rupture of sinus of valsalva repair and left pulmonary artery plasty in one patient each. The total in hospital mortality of patients who underwent surgery was 8.3% (1 out of 12 patients).

The total in hospital mortality in patients with IE was 22 (29.3%). The RHD and CHD in 9 patients remained the most common underlying heart diseases followed by PVE in 3 patients. The refractory heart failure was the most common cause of death in 7 (31.8%) patients. The other causes of death were sepsis in 6 (27.3%), cerebral embolism in 6 (27.3%) and CNS hemorrhage in 3 (13.6%) patients respectively.

4. Discussion

Though there have been many prospective studies in the developed world [5], these data are not representative of the developing world. The spectrum of IE is different in India as compared to the west with respect to the predisposing factor's, underlying heart disease, microbiology and outcome [14]. The rapid urbanization, indiscriminate use of antibiotics, increasing geriatric population, use of prosthetic devices and increasing nosocomial infections has changed the clinical scenario of IE.

Age: The mean age of our patients was 27.46 ± 17.11 years with 77.3% of patients younger than 40 years which is very similar to the previous Indian studies [8] [9] [13]. This is in contrast to the west, were the majority of patients were older than fourth decade with a mean age of 56 ± 17 years [2] [3] [5]. This difference may be attributable to the fact that, this study also included the pediatric population in contrast to the studies from the west which included only the adult patients. Also, RHD which continues to be a rampant problem in the underprivileged population in India predominantly affects younger age group. In addition, the proportion of CHD patients

Table 5. Comparison of blood culture positive and negative episodes of infective endocarditis.

Variables	Culture positive(n = 30)	Culture negative (n = 45)	p value
Age yrs (mean ± SD)	22.49 ± 13.02	30.78 ± 18.7	0.027
Sex (male/female), n	20/10	32/13	0.683
Underlying heart disease			
RHD	11 (36.7%)	20 (44.4%)	0.660
CHD	15 (50.0%)	11 (24.4%)	0.04
Prosthetic valve	3 (10.0%)	4 (8.9%)	0.80
No structural heart disease	6 (20.0%)	2 (4.4%)	0.07
Degenerative heart disease	0 (0.0%)	2 (4.4%)	0.66
Prior antibiotic therapy	9 (30.0%)	31 (68.9%)	0.002
Vegetation Size			
<10 mm (small)	15 (50.0%)	22 (48.9%)	0.88
>10 mm (large)	15 (50.0%)	23 (51.1%)	0.88
Complications			
Congestive heart failure (CCF)	15 (50.0%)	17 (37.8%)	0.209
Neurological abnormalities	11 (36.7%)	8 (17.7%)	0.11
Renal failure	8 (26.7%)	12 (26.7%)	0.79
Embolism (digital infarcts, CV stroke, splenic infarcts)	8 (26.7%)	10 (22.2%)	0.86
Abscess			
Renal abscess	0 (0.0%)	3 (6.7%)	0.39
Aortic root abscess	2 (6.7%)	1 (2.2%)	0.72
Splenic abscess	0 (0.0%)	2 (4.4%)	0.66
Surgery	2 (6.7%)	10 (22.2%)	0.14
Death	12 (40.0%)	10 (22.2%)	0.16
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Surgery	2 (6.7%)	10 (22.2%)	0.14
Death	12 (40.0%)	10 (22.2%)	0.16

is our study was higher in contrast to the western studies [7]. The higher age group in the west is due to increasing geriatric population, increased incidence of degenerative valvular diseases and reduced frequency of RHD [4]-[7] [15] [16].

Underlying Heart Disease: RHD was the most common underlying heart disease in this study which accounted for 41.3% of all cases. This is similar to other studies from the developing world in which RHD accounted for 42% to 76% of cases of IE [8]-[11]. This is in contrast to the developed world in view of decreased incidence of rheumatic fever in west [4] [5] [7]. CHD also accounted for significant cohort (34.7%) of IE cases in our study similar to other Indian studies by Choudhary *et al.* (33%) and Math *et al.* (39.4%) [8] [13]. This high incidence of CHD in our study is in contrast to a large multi-centric study by Murdoch *et al.* in which CHD constituted 12% of IE cases [7]. This difference may be due to a large number of uncorrected CHD in Indian population as compared to the west. Out of all patients in CHD group, 12 (46.15%) patients were postoperative patients among which the most common surgery done was intracardiac repair for TOF (n = 8). This may be due to the reason that, our institute is a high volume tertiary referral cardiac surgical centre with active pediatric cardiology and cardiac surgery department. In contrast to the western data in which MVP was reported to be a common underlying heart lesion, this group constituted a very small fraction of patients 5 (6.7%) in our study similar to other Indian studies [8] [9] [13] [17]. In our study, PVE constituted 7 (9.3%) cases of IE which is very similar to other western studies but higher than some previous Indian studies [8] [18] [19]. The incidence of PVE has increased in India from 1% in 1980's to 10% in 1990's [9]. This increase may be attributable to the reason that an increasing number of patients are undergoing surgical treatment for valvular heart disease. None of our patients were intravenous drug abusers. Although it is traditionally believed that IE does not affect normal valves, recent large series have reported no underlying structural heart disease in about a third of patients [17]. While in our study 8 (10.7%) of patients had no structurally heart disease.

Blood Culture: In this study about 30 (40%) of blood cultures were positive in 75 episodes of IE. This is similar to most Indian series which have shown blood culture positivity rate ranging from 21% - 47% [8] [13] [20]. However blood culture positivity rates in western series is 90% as noted in the Murdoch *et al*. series [7]. A major factor for this disparity as compared to west may be related to the higher proportion of prior antibiotic therapy in culture negative patients before admission to hospital in our study (68.9% vs. 30.0%, p = 0.002). Another factor could be related to the underutilization of specialized culture media and various serological tests for fastidious organisms. The low culture positivity rate noted in our study is extremely worrisome, as the optimal therapy of IE depends on the organism isolated on culture and their sensitivity patterns. It is very difficult to draw any conclusion in view of the low culture positivity noted in our study.

Recent data from the western series have shown a shift in the microbiological spectrum with staphylococci being the commonest isolate [3] [7] [21]. This was very similar to our study in which the most common isolate is staphylococci followed by streptococci. This observation is similar to other Indian studies [8] [13]. However, the previous Indian study by Garg *et al.* has shown streptococci as the most common isolate [9]. The increasing emergence of staphylococcus in west is accounted by an increasing geriatric population, rising drug abuse, increasing nosocomial infections and use of prosthetic devices. However this doesn't apply to Indian patients as RHD and CHD continue to be the most common underlying heart disease in Indian population. In view of a large culture negative group in our study, it is difficult to draw any inference with respect to the commonest organism. Also, in view of our institute being a tertiary referral centre, our study group represents a skewed population of sick referred patients and may not be representative of the population in general.

Echocardiography: Echocardiography has proved as the most important tool in establishing diagnosis of IE in our study. This was especially due to the low culture positivity rates. Vegetations were detected by TTE of episodes in 67 (89.3%) and in all the remaining patients, TEE was diagnostic. This finding is higher than a study by Taams *et al*. (86%) and various other studies [9] [22].

The reason for this disparity may be due to the more young population in our study group and the lean built of the Indian patients thereby facilitating good echo windows. The stepwise approach consisting initial use of TTE followed by TEE in patients with non-diagnostic TTE like PVE and patients with poor echo windows explains the higher incidence of vegetations in our study. This underscores the importance of echocardiography in diagnosis of IE in culture negative cases. The most common site of vegetations in our study was mitral valve followed by aortic valve which is similar to a study by Garg *et al.* and other Indian studies [8] [9].

Outcome: In our study, the in-hospital mortality was 22 (29.3%) which is much higher than that reported in the recent western series (12.6% - 17.7%) [6] [7]. This higher figure in comparison to the west is attributable to

the differences in study population. This may be due to the relatively sicker, complicated and refractory cases referred to our centre; and relatively late presentation of patients in developing countries. Another important factor is CHF, which is the leading cause of death was present in 32 (42.7%) of episodes of IE. Also the high culture negative rates and lower rates of surgery 12 (16%) may be contributory. A higher proportion 32 (42.7%) of patients with PVE experienced death compared to the NVE that signifies the morbid nature of PVE. This may again be due to lower rates of surgery in this group as a part of reluctance on the cardiologist and cardiac surgeon in operating such morbid patients with PVE. Although the incidence of re-infection of the newly implanted valves is higher in PVE (6% - 15%) [23], the benefit of redo surgery far outweighs the risk of re-infection. Also, a very high proportion of patients with IE in corrected CHD group died (7 out of 12 cases) as compared to uncorrected CHD group (2 out of 14 cases) due to lesser rates of surgery in the corrected CHD group. Hence, we need to overcome these barriers by employing aggressive surgical strategy in IE affecting prosthetic valves and operated CHD cases.

The predictors for mortality on univariate analysis were age < 20 years; thrombocytopenia, hematuria, hepatic dysfunction, septic shock, neurological abnormalities, CV stroke, CNS hemorrhage, CHF, renal failure and AV block (**Table 6**).

But on multivariate analysis; the independent predictors for mortality were age (p = 0.030), CHF (p = 0.003), renal failure (p = 0.037) and neurological abnormalities (p = 0.046). Septic shock was of borderline significance (p = 0.062). Garg *et al*. and Siddiq *et al*. reported CHF, renal failure and prosthetic valve dysfunction as independent predictors of mortality. Choudhary *et al*. reported a significantly higher mortality in patients with neurological manifestations [8] [9] [21]. On multivariate analysis, Math *et al*. reported underlying heart disease other than NVD and septic shock to be independent predictors of mortality [13].

Surgery: Several studies have shown that surgery is potentially lifesaving and is required in 25% - 50% of cases during active infection [7] [23]. In our series, surgery was performed in only 16% of patients, with major indications being refractory CHF and persistent infection despite adequate antibiotic therapy. This is similar to other Indian studies by Math *et al*. (15%). This is in contrast to the recent data from developed countries where surgery was performed in 49% - 52% of cases [6] [7]. The major reason for this disparity is the lack of availability and affordability for cardiac surgery and reluctance on the part of cardiologist/cardiac surgeon in undertaking surgery in active endocarditis.

In our study, the most common complication leading to death was CHF 24 (31.8%). On stepwise logistic analysis for predictors of surgery, duration of illness < 45 days and culture positivity were predictors of cardiac surgery on univariate analysis (**Table 7**).

Table 6. Results of stepwise logistic regression analysis for predictors of lethality of active infective endocarditis.

	Univariate *p* value	Multivariate analysis			95% CI[1]
		p value	*β*	Exp *β*	
Age	0.055	0.030	−0.090	0.914	0.843 - 0.991
Thrombocytopenia	0.034	NS			
Haematuria	0.003	NS			
Hepatic impairment	<0.001	NS			
Septic shock	<0.001	0.062	2.131	8.419	0.902 - 78.619
Neurological abnormalities	0.010	0.046	2.071	7.930	1.041 - 60.400
CV[2] Stroke	0.028	NS[3]			
CNS[4] haemorrhage	0.076	NS			
CHF	<0.001	0.003	3.557	35.051	3.462 - 354.841
Renal failure	<0.001	0.037	2.472	11.843	1.164 - 120.493
AV block	0.033	NS			
Constant			−2.876	0.056	

[1]Confidence interval; [2]Cardiovasular; [3]Not significant; [4]Central nervous system.

Table 7. Results of stepwise logistic regression analysis for predictors of surgery in active infective endocarditis.

	Univariate *p* value	Multivariate analysis			95% CI
		p value	*β*	Exp *β*	
Duration of illness < 45 days	0.042	0.037	1.494	4.455	1.097 - 18.091
Culture positivity	0.072	NS			

But on multivariate analysis, only duration of illness <45 days was independent predictor of cardiac surgery ($p = 0.037$). Despite CHF being the commonest indication for surgery, the presence of CHF was not predictive of cardiac surgery on univariate analysis. In a similar study done by Garg *et al*., CHF and cardiac abscess were independent predictors of cardiac surgery [9]. In our study, the mortality rate in patients who underwent surgery was 6 (8.3%). The chance of re-infection of the newly implanted valve is 2% - 3% [1]. This may be far lower than the mortality rate in patients of IE with heart failure managed only medically (56% - 86%) [23]. Despite cardiac surgery, the most common cause of death in our study was CHF thereby, emphasizing the need for early surgery in these patients.

5. Conclusion

This prospective study emphasizes that the spectrum of infective endocarditis is different in Indian population compared to the west and carries a substantial morbidity and mortality. Infective endocarditis occurs at a relatively younger population than the west. Rheumatic heart disease followed by coronary heart disease still continues to be the most common underlying heart disease in our population. The lower culture positivity rate and lower rates of surgery are worrisome in Indian patients. Strategies need to be designed to improve the culture positivity by employing specialized culture media and other ancillary tests. Congestive heart failure, renal failure, neurological complications, age and sepsis were independent predictors of mortality. Also, prosthetic valve endocarditis and infective endocarditis affecting operated cases of coronary heart disease carry a high mortality risk. Hence, aggressive surgical strategy needs to be adopted to improve the outcome of the high risk patients.

Limitations of the Study

Firstly, the true microbiological spectrum of the patients could not be determined due to prior antibiotic therapy, lack of specialized culture media, serological tests and polymerase chain reaction for fastidious organisms thereby leading to high proportion of culture negative cases. Secondly, our institute being a tertiary referral centre; the data may be skewed to sick, complicated and refractory cases and may not be representative of general population at community level. Thirdly, our study included only duke's definitive cases thereby excluding the probable cases of IE. Also, the long-term follow-up of patients is not available.

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