Prosthetic Valve Infective Endocarditis: Clinical Findings and Hospital Management of Twenty-Nine Patients

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Twenty-nine consecutive patients with prosthetic valve endocarditis were studied during five-year period. Patients were divided into early (<60 days) and late (>60 days) cases. Mean age was 27 years, 23 male and 6 females. Majority of the valve (24) was metallic with equal proportions of mitral and aortic prosthesis. Fever was present in more than 95% of cases, while breathlessness was more common in early cases. Cardiac murmurs were absent in 30-40% of cases. Clinical splenomegaly was noted more commonly in late presenters while aortic root abscess and pericardial effusion were more common in early cases (P. NS). Majority of the patients, especially early cases, had already received antibiotic therapy. Overall culture positivity was 55%; it was 40% in early cases. Streptococcus viridans was the main isolate in late presenters. Transthoracic echocardiography provided valuable diagnostic clues in 70% cases. Intractable heart failure, uncontrolled infection, aortic root abscess and recurrent emboli were main complications. However emergency cardiac surgery carried a high mortality (66%). Overall mortality was 52%.
Key words: prosthesis, infective endocarditis, vegetation, heart failure, valve dehiscence. Trans-thoracic echocardiography.

Prosthetic valve endocarditis (PVE) is an infectious disorder of valves and surrounding cardiac tissue occurring after valve replacement. It is estimated that as many as 1% to 4% of these devices will become infected sometime during the life span of the prosthesis [1]. Its management requires prolonged hospital stay, expensive diagnostic workup, costly medical treatment and frequent need for surgical intervention. Complication rate and mortality associated with this disease is disheartening, more so when one considers the high initial costs of valve replacement and subsequent endocarditis management. Frequently, appropriate antimicrobials and surgical expertise needed are not available even at the best cardiac centers in Pakistan.

Clinical pattern of this disease, complications, mortality rate and risk factors related to prognosis are some of the issues, which are not previously studied in Pakistan. Neither we know about the impact of various modern therapeutic and diagnostic (Echocardiography) modalities on its management.

This study was carried out at Punjab Institute of Cardiology, Lahore between 1991 to 1996. Main objective was to analyze the clinical characteristics and outcome of admitted patients with prosthetic valve endocarditis.

Materials and Methods

Site: Punjab Institute of Cardiology, Lahore is a cardiac tertiary unit which serves as a referral center for adult and pediatric population from Punjab and other provinces.

Study Population: To establish uniformity in patient's selection, Duke's Criteria [2] were used. Twenty-nine patients of prosthetic valve endocarditis were thus identified during five years of study period. Adult patients of both sexes were included. Infective endocarditis was categorized as 'early', if infection occurred within 60 days of cardiac surgery; and 'late' if infection occurred more than 60 days after surgery.

Diagnostic studies: Routine tests of blood, urine, serum electrolytes, BUN and serum creatinine were done for evidence of infection and to help in subsequent management. Three venous blood samples of 10 cc. each were collected, one hour apart, at the time of admission. If initial cultures were negative, further two samples were collected. All the blood samples were incubated aerobically in Brain Heart infusion Broth with added SPS. For anaerobic cultures, fluid thioglycolate medium with SPS (sodium polyanethol sulfonate) was used. Routine subcultures were performed at 24, 48 hours, at seven days and after two weeks if cultures still remain negative. Sensitivity of streptococci was checked by disc diffusion method, utilizing blood agar. Muller Hinton agar was used for staphylococci.

A real time trans-thoracic echocardiogram was performed by standard techniques using 2.5 or 3.5 MHz phased array transducer, in all the patients. Trans-esophageal echocardiography was available in the latter part of the study.
Abdominal ultrasound and lung perfusion scans were done as needed for specific indications.

Statistical analysis: Percentage and mean calculations were performed to assess the relative frequency of different findings. Between-the groups analysis was done by unpaired student's- *t* test. Fisher exact test was used where a cell count was less than 5. P-value of <.05 was chosen as significance level.

Results

Base line characteristics are described in table1. A total of 29 patients were diagnosed as cases of prosthetic valve endocarditis; 23 were males and 06 were females, giving a male:female ratio of 4:1. Age range was 18 to 54 years with a mean of 27 years. 19(65.5%) patients were categorized as 'late' prosthetic valve endocarditis and 10 (34.5%) presented 'early' after cardiac surgery. Metallic

valves were implanted in 24 patients (Starr-Edward's in 22, St. Jude's in 2) while 5 patients had received stented porcine xenografts. 14 of the prosthesis were at aortic position and 13 at mitral position; while two patients had double valve replacement.

Clinical findings at the time of admission are given in Table 2. Fever>100.4 ^{0}F was present almost all of the patients. Hectic fever of acute Infective endocarditis was not seen in 'early' cases. Breathlessness was significantly (P<.05) more common in 'early' cases than in 'late' presenters. Prosthetic valvular sounds were equally diminished in both 'late' and 'early' cases. Other features which were more commonly observed in 'late' cases were splenomegaly and splenic abscesses (PNS), while murmurs were inconspicuous in almost 40% of 'early' cases.

Table.1 Base line characteristics of the patients

Description	n
Total cases	29
Males	23
Females	6
Age	
Range	18-54 Y
Mean	27Y
Prosthesis type	
Metallic	24
Tissue	5
Valve site	
Aortic	14
Mitral	13
Aortic+Mitral	2
Early cases (<60 days)	
Late cases (>60 days)	
Early	
Metallic valves	10
Tissue valves	0
Late	
Metallic valves	14
Tissue valves	5

Table 2. Clinical manifestations of PVE

Symptoms/signs	Early(%)	late(%)
Fever	90	95
Weight loss	60	72
Fatigue/ malaise	40	42
Breathlessness	70	33(P<0.05)
Joint pains	20	26
Cardiac murmers	60	72
Pallor	60	52
Splenomeglay	10	42(P.NS)
Gross emboli	50	42(P.NS)
Vascular Phenomena	20	20
Pericardial effusions	30	10(P.NS)
Abnormal valve sounds	70	78

Majority of our patients had already received antibiotic therapy, as shown in Table 3. Similarly in the majority, portal of entry was not definitely established. However it

was considered to be peri-operative in majority of 'early' cases. Only three 'late' presenters gave definite history of dental work-up in recent past. Positive cultures of blood were found in 55% of cases. No Significant difference was noted in culture positivity rate of 'late' vs. 'early' cases (Table 4). Streptococcus viridans was the commonest isolate (all 'late' presenters); Isolation of Staphylococcal species was not significantly different between the two groups.

Table 3. Previous antibioci therapy and origin of sepsis.

	Early(%)	Late(%)
Antibiotic therapy	100	78
Origin of sepsis		
• Not known	30	78
• Perioperative	70	00
• Dental workup	00	15
• Skin abscess	00	05

Table 4. Microbiology of PVE.

	Early(%)	Late(%)
Culture positivity (55%)		
Positive	40	63
Negative	60	37
Organisms isolated	n.	N
Staph.aureus	2	3
Staph. Epidermidis	1	1
Strept. Viridans	0	7
Pseudomonas	1	0
Serratia mercenens	0	1

Trans-thoracic echocardiography yielded finding of diagnostic importance in 68% of cases (Table 5). Vegetations were noted with equal frequency in both groups but the yield was low. However valve dehiscence, aortic root abscess and pericardial effusion were more common in 'early' presenters but the difference was not significant. Valvular and para-valvular regurgitation was an important finding of dysfunctional prosthesis.

Table 5 Trans-thoracic echocardiography

	Early(%)	Late(%)
Vegetations	30	26
Valve dehiscence	40	10(P..NS)
Valvular regurgitation	20	31
Pericardial effusion	40	10(P.NS)
Aortic root abscess	40	10(P.NS)

ECG was helpful as an early pointer for aortic root abscess. Out of six patients with such abscess, prolonged PR interval was noted in 3 patients, these patients subsequently progressed to complete heart block; remaining three patients presented with complete heart block.

Twelve patients were referred for emergency cardiac surgery (Table 6). Uncontrolled infection, (defined as failure of fever to respond with in 10 days) para-valvular infection, progressive cardiac failure and recurrent emboli

were the main reasons. Table 6 also shows outcome after emergency cardiac surgery; 8 patients out of 12 died peri-operatively.

Table 6. Emergency cardiac surgery (n=12)

Indications	n.
Intractable heart failure	6
Uncontrolled infection	5
Recurrent emboli	2
Multiple causes	1
Cured	4
Died	8

Drug induced phlebitis was the chief but 'easy to treat' complication in our patient population. Intractable heart failure, aortic root abscess, recurrent emboli and pericarditis with effusion were of more sinister significance (Table 7).

Table 7.Complications during hospital course

Complications	n.
Phlebitis	10
Intractable heart failure	8
Aortic root abscess	6
Dehiscence/paravalvular leak	6
Pericardial effusion	4
Systemic Emboli	4

Table 8 summarizes overall outcome in these 29 patients, 15 expired while 14 were cured, giving a mortality of about 52%. Causes of death are given in Table 8.

Table. 8 Overall outcome and causes of death

	Early(%)	Late(%)
Cured	3	11
Died	7	8
Group mortality	70	42((P.NS)
Overall mortality	52	
Cause of mortality		
Aortic root abscess	5	
Severe CCF	8	
CNS	2	

Aortic root abscess, progressive heart failure (valvular/ para-valvular regurgitation especially aortic) recurrent peripheral emboli (especially to central nervous system) were the main underlying causes of mortality.

Discussion

In this largest prospective study of prosthetic valve endocarditis in Pakistan , we have presented data of 29 patients . Strict inclusion criteria were applied to collect data.

Prosthetic valve endocarditis is a serious disorder with an annual incidence of 0.32 to 1.2%[3]; our study showed predominant young male population, probably because two principles underlying pathological states *i.e.* rheumatic heart disease and bicuspid aortic valve presently necessitate valvular surgery in younger age group. All the early cases occurred in patients with metallic prosthesis. This finding is in keeping with several observations [4] that soon after surgery mechanical valves appear to be more susceptible to infection; while later, bioprosthetic valves may be more likely to be infected. However as very few bioprosthetic valves are currently used in Pakistan , no meaningful analysis can be done from the data presented ; however we did not see any differential susceptibility of aortic vs mitral prosthesis - as suggested in the study by Watanakunkron C [5] .

Fever(>100.4°F) was noted in about 95%of cases in both groups and infection was a very important pointer to the diagnosis; persistent fever on antibiotic therapy suggested extension of infection beyond the valve, metastatic abscess or micro-organisms not susceptible to antimicrobial agent.

Breathlessness was significantly more common in early presenters. These patients were sick with cardiac failure , infection, anemia, and were usually in immediate post-operative period .

There should not be any cardiac murmur related to prosthetic valve so presence of a regurgitant murmur was a very important pointer towards malfunctioning prosthetic valve. However it was not a sensitive indicator as many as 30- 40 % patients of each group did not have any audible murmur, thus underscoring the importance of echocardiography in the diagnosis of prosthetic dysfunction. Pallor was noted in the majority. Diminished prosthetic valve sounds were in both early and late cases in the majority, most probably due to vegetations interfering with valve mechanics

Majority of patients had already received antibiotic therapy. This was especially true of early cases who presented soon after operation and were sicker of the lot. This prior antibiotic therapy had an important bearing on dismal culture results, especially in acute cases. Overall culture positivity rate was thus 55%, in contrast to 95% rate cited in western studies [4], while rate is definitely better than other studies from Pakistan [6,7]. Of the organisms isolated, Streptococcal species were mainly isolated in 'late' cases while staphylococcal organisms were equally distributed in both groups. Without doubt, with better culture facilities and with holding antibiotics till blood cultures are sent, apparent culture negative cases can be decreased. It is important, because many organisms associated with prosthetic valve endocarditis have inherent resistance to antibiotics and proper selection of these antimicrobials requires sensitivity pattern of organism. Proper techniques of sample acquisition and handling, using proper culture media, and educating doctors and public against indiscriminate use of antibiotics, can go a long way to improve the culture positivity rate in this serious disease.

TTE was done in all the cases. In the presence of low culture positivity rate, detection of vegetations, valve dehiscence, valvular or para-valvular regurgitation and aortic root abscesses is of great help in the diagnosis.

Owing to high acoustic impedance of metallic prosthetic valves however, TTE is not a suitable tool for interrogating these valves. In future given the much better sensitivity and specificity of TEE [8], it would be of great help in this group of patients. TTE however provided important information in assessment of left ventricular size and function. Gradual increase in end-diastolic size and premature closure of mitral valve in patients with aortic regurgitation imply worsening or severe heart failure[9]. Given the high surgical mortality rate in patients with clinically apparent severe heart failure, either of these Echo findings may pickup a case in an early stage of deterioration and thus help improve surgical results.

In patients with prosthetic valve infective endocarditis some complications require early operative management; These include moderate to severe heart failure, persistent bacteremia, invasive infection and an unstable prosthesis. Prognosis in these patients is much improved by combined medical and surgical approach [10]. It is doubtful if replacing prosthetic valve can reduce incidence of embolization and mortality. However one CNS embolic episode or two peripheral episodes were our threshold point for referring these patients to surgery, provided the patient remained clinically stable with no large neurologic deficit. Emergency cardiac surgery in these patients, however carried high mortality (70%).

Total mortality was 51%, a figure within range of that described by Douglas JL et al[4]. 'Early' cases and emergency cardiac surgery in those with complications contributed heavily in this high mortality. Majority of those with chronic 'late' disease were cured of their illness (58%).

Summary

Prosthetic valve endocarditis is a serious disease with high unacceptable mortality. Certain subsets fare worse than other, namely those with aortic valve involvement, severe heart failure, persistent infection and aortic root abscesses. On the diagnostic side, laboratory culture techniques have shown some improvement but echocardiography has provided the major stimulus. Routine use of Trans-esophageal echocardiography in future will further increase the diagnostic yield. Emergency cardiac surgery itself needs to be improved if the mortality has to be decreased in the groups where surgery has most to offer. Early selection of patients with deteriorating left ventricular function by echocardiography will be helpful in this regard.

Limitations: Our study contained too few subjects in some categories to draw any meaningful conclusion. A much larger population is needed to get detailed picture of prosthetic valve endocarditis.

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