



## SURGICAL OUTCOMES IN NATIVE VALVE ENDOCARDITIS RETROSPECTIVE ANALYSIS OVER A PERIOD OF FOUR YEARS

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### KEYWORDS :

#### INTRODUCTION

Infective endocarditis is a well established cause of valvular heart disease. It carries a diagnostic and therapeutic challenge that is associated with high patient morbidity and mortality.<sup>1</sup> Despite the use of preventative measures such as antibiotic prophylaxis in patients with valvular heart disease undergoing bacteremia causing procedures, the overall incidence of infective endocarditis continues to rise. Infective endocarditis affects primarily the left-sided valves with a higher incidence of aortic versus mitral valve involvement.<sup>2</sup> The therapeutic approach is based on epidemiology, clinical, microbiological and echocardiographic diagnosis and the combined medical and surgical therapy. The optimal therapy for infective endocarditis includes the use of culture-directed parenteral antibiotics over a prolonged period, for effective eradication of the causative pathogen. However, in certain clinical situations, surgical intervention remains an indispensable adjunct to the management of endocarditis.<sup>3</sup> The appropriate timing of surgical intervention remains a subject of intense debate, as it depends upon the cardiac and systemic complications of the infection, the virulence of the organism, and the patient's response to antimicrobial therapy.<sup>4,5</sup> The indications for surgery in infective endocarditis was reviewed in 2004 by the Canadian Cardiovascular Society Consensus Conference on the Surgical Management of Valvular Heart Disease.<sup>6</sup>

#### AIMS AND OBJECTIVES

**PLACE OF STUDY :** Dept of Cardiothoracic Surgery, Tamilnadu Govt MultiSuper Speciality Hospital, Chennai.

1. The aim of the study was to evaluate the surgical management of individuals with native valve endocarditis in a tertiary level hospital over a period of five years.
2. The objectives of the study were to evaluate the epidemiological profile, clinical characteristics, diagnostic investigations required, indications for surgery, operative procedure undertaken and to assess postoperative morbidity and mortality.
3. Finally, to determine the early outcomes following surgery.

#### MATERIALS AND METHODS

The study was conducted for a period of four years from January 2015 to December 2018. During this period, forty eight patients who underwent surgery for native valve endocarditis only in our institution were included in the study. The patients from prosthetic valve endocarditis and pacemaker endocarditis were excluded from the study.

It was a retrospective study and data were obtained through an extensive chart review process. The patient's information were then entered in an Excel spreadsheet (Microsoft Corporation, Redmond, WA). Preoperative variables those were analysed included: epidemiological factors, presenting symptoms, NYHA class, risk factors for infective endocarditis, causative microorganism, echocardiographic findings, antibiotic treatment, the type of endocarditis and the indications for surgery. Intraoperative variables of great interest included: which valve was infected,

intraoperative pathological findings, the surgical procedure performed. The postoperative variables of importance included: in-hospital mortality rate, the risk factors for hospital mortality, duration of ventilation, the length of intensive care stay, amount of intercostal drainage, requirement of transfusion of blood and blood products, duration of antibiotic treatment. Postoperative morbidities like reexploration for bleeding, arrhythmias, conduction abnormalities, permanent pacemaker implantation, pericardiostomy rate, wound infection, stroke, dialysis, gastrointestinal bleeding were also analysed.

The epidemiological factors like age, sex distribution and state of origin were analysed. The predominant presenting symptoms include fever, dyspnoea, palpitation, embolism and acute renal failure. New York Heart Association classification of cardiac symptoms was used to categorize the patients into functional class I, II, III or IV.

The predisposing factors that would have contributed to the development of endocarditis assessed in the study include rheumatic heart disease, congenital heart disease, long standing central catheters, intravenous drug abuse, cellulitis and bad oral hygiene. In general examination, it was looked for pallor, jaundice, cyanosis, clubbing, pedal edema, elevated jugular venous pulse and oral hygiene. Cardiac examination was done to look for cardiomegaly, regurgitant murmurs and features of underlying heart disease if any. Investigations that were utilised in diagnosis of infective endocarditis were blood tests and radiological investigations. Blood tests done include haemoglobin, total count, differential count, erythrocyte sedimentation rate, C reactive protein, electrolytes, blood urea nitrogen, serum creatinine, liver function test, coagulation parameters (prothrombin time, activated partial thromboplastin time, platelet count).

The diagnosis of infective endocarditis was made as per modified Dukes criteria using blood culture results, echocardiographic findings and typical clinical findings. Transthoracic echocardiography was done in all patients to detect the vegetations, to assess the valvular lesions and complications of infective endocarditis. Transoesophageal echocardiography was done in selected patients with doubtful findings in transthoracic echocardiography. Electrocardiography was done to assess rhythm, chamber enlargement or hypertrophy, arrhythmias, conduction abnormalities and ischemic changes. Computed tomography of the brain was done in patients with neurological complications. Colour Doppler study of the lower limb was done in patients with peripheral arterial embolism.

Antibiotics, given intravenously, were the main stay of treatment before surgery. Initially, blood cultures were taken and started on empirical antibiotic with penicillin and gentamicin in subacute cases and with vancomycin and gentamicin in acute cases. In patients who were already on antibiotics, blood cultures were taken 48 hours after stopping the antibiotics. Based on the sensitivity results, the antibiotic regimen were altered, if required.

Surgery was mainly done on an elective basis after administering appropriate antibiotics for a minimum period of four weeks. But urgent surgery was done in two patients.

With regard to surgical technique, the following principles were utilised. All patients underwent surgery through median sternotomy approach. Routine aorto bicaval cardiopulmonary bypass was utilised in 45 patients. Femorofemoral bypass was required in 2 patients who had previous cardiac surgery. Aortofemoral bypass was utilised in 1 patient who was suspected to have pedunculated vegetation in right atrium – inferior vena caval junction. Myocardial protection was achieved with antegrade cold blood cardioplegia. While going on bypass, minimal handling of the heart was followed to avoid dislodging infected thrombotic material or vegetations. In patients with aortic valve endocarditis, the mitral valve and its apparatus was inspected to rule out drop lesions. After resection of the valve tissue, care was taken to examine the annulus and adjacent structures to detect possible extension of infective process. All infected or necrotic structures were adequately resected before valve replacement. Surgical instruments were changed after debridement of the infected tissue. The choice in selecting either the mechanical or biological prosthesis depended on patient's age, surgeon preference. The prosthetic valve was soaked with antibiotic solution before implantation. Specimens of vegetations and valvular debris were sent for bacterial and fungal cultures and histopathological examination.

The intraoperative pathological findings assessed include presence of vegetations, abscess, leaflet perforation and chordal rupture. Valve replacement was the main stay of surgical procedure in majority of the patients. Mitral valve repair was performed in one patient while tricuspid valve repair was undertaken in patients with tricuspid endocarditis. Concomitant coronary artery bypass surgery was done in patients with coronary artery disease.

With regard to immediate postoperative management, the same protocols as utilised in any valve replacement procedures were followed. The antibiotic regimen followed preoperatively was followed postoperatively, given mostly intravenously for a minimum period of four weeks. The antibiotic regimen was changed if required based on the culture and sensitivity of the excised valve. Postoperatively, acute phase reactants like total count, differential count, erythrocyte sedimentation rate, C reactive protein were done once weekly to assess the resolution of infective process. Serum potassium and creatinine were done twice weekly to assess renal toxicity. Permanent pacemaker implantation was done in patients who develop complete heart block postoperatively. Pericardiostomy was done in patients with moderate to massive pericardial effusion.

Finally, followup of the patients were carried out at the end of six months, two years and five years. The followup data were collected through medical records, telephonic contact and letters. During followup, it was assessed for NYHA class, echocardiographic findings, prosthetic valve related complications, recurrence of endocarditis, need for reoperation, late mortality.

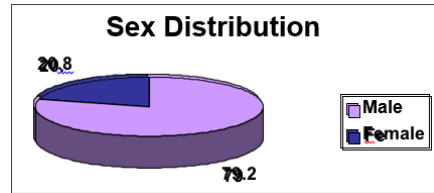
**Statistical analysis:**

Data analysis was done with SPSS 16.1 software (SPSS Inc, Chicago, IL). The continuous variables were summarized as mean and standard deviation. The categorical variables were analyzed as number (percentage).

**RESULTS**

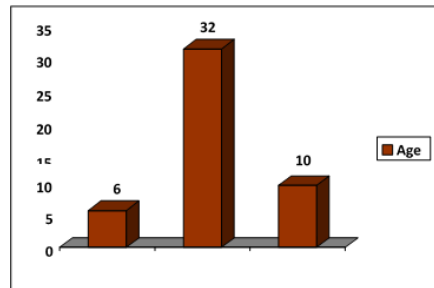
A total of forty eight patients were found to satisfy the inclusion criteria during the study period of five years from January 2003 to December 2007.

There were 38 men (79.2%) and 10 women (30.8%).



The patient's age varied from six years to sixty seven years with a mean of 37.5 years. Thirty two patients were in the middle age group of 21 to 50 years. above the age of fifty years. There were six patients below the age of twenty and there were 10 patients above the age of fifty.

**Age Distribution**



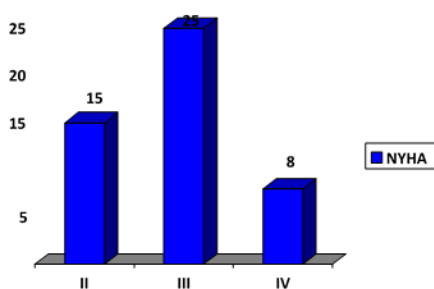
With regard to demographic data, thirty eight patients were from states of North East India, eight from the states of South India and one each came from Bhutan and Bangladesh.

| Place of origin  | N=48 |
|------------------|------|
| North East India | 38   |
| South India      | 08   |
| Bhutan           | 01   |
| Bangladesh       | 01   |

Fever was the most common presenting symptom found in 93.8% (n=45) of patients. It was followed by dyspnoea in 91.6% (n=44), palpitation in 70.8% (n=34), embolism in 29.16% (n=14) and acute renal failure in 8.33% (n=4) of patients.

With regard to New York Heart Association (NYHA) functional class, 33 patients were in functional class III (n=25) or class IV (n=8). The remaining fifteen patients had class II symptoms.

**NYHA Functional Class**



Fourteen patients (29.16%) presented with embolic phenomena. Twelve patients had left sided embolism and only two patients had right sided embolism.

Out of the two patients with pulmonary embolism, one patient had right lower lobe infarction and the other had left middle zone infarct. Both the patients had congenital heart disease and suffering from tricuspid valve endocarditis.

Left-sided embolism included central and peripheral sites. Neurological complications were encountered in seven (12.5%) patients, which included stroke in 4 patients (8.33%), ruptured mycotic aneurysm with intracerebral hemorrhage in 2 patients (4.16%), multiple cerebral infarct with dementia in one (2.08%). In

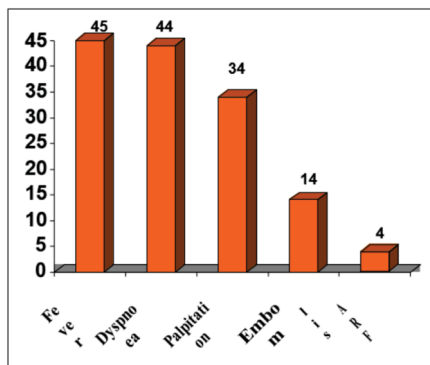
four patients with stroke, two had right sided stroke and two had left sided stroke. One patient with left hemiplegia had transient blindness which recovered fully. The patient with rupture of mycotic aneurysm involving right temporoparietal region with intracranial hematoma presented with severe headache without localising neurological symptoms. One patient presented with dementia with memory loss due to multiple brain infarct. Syncope was noticed in one patient who had subarachnoid hemorrhage and required aneurysmal clipping. This patient also developed subdural hematoma which was successfully evacuated. Valve replacement surgery was deferred by three months in two patients who had hemorrhage. Both the patients survived after surgery.

The peripheral embolism manifested in five patients which include left common iliac artery (n=1), left common femoral artery (n=1), right superficial femoral artery (n=2) and right popliteal artery (n=1). The patient with left common iliac artery occlusion who presented to us six months after the episode had adequate collateral supply on Doppler screening and was not surgically intervened. Emergency left femoral embolectomy was done in patient with left common femoral artery embolism and the pathological examination of the embolectomy specimen revealed it to be an embolised vegetation. The patients who had embolism of right superficial femoral artery and right popliteal artery had good distal blood supply and were treated conservatively.

Two patients (4.16%) had splenic abscess. Splenectomy was done in one patient with massive splenic abscess and three weeks later had successful valve replacement. The other patient had multiple small splenic abscesses which resolved with antibiotics alone.

Four patients had acute renal failure and two patients required hemodialysis and the other two were treated conservatively.

**CLINICAL PRESENTATION**



While analysing the predisposing factors, the following results were obtained. Fourteen patients had rheumatic heart disease and on regular medical treatment. Four patients had congenital heart disease which includes ventricular septal defect (n=1), ventricular septal defect with pulmonary stenosis (n=2), Tetralogy of Fallot (n=1). Two patients with history of long standing jugular central catheters were in renal failure requiring hemodialysis. Two patients gave history of chronic intravenous drug abuse and incidentally both were found to be government employed doctors who had easy access to narcotic drugs. One had multiple large bilateral lower limb ulcers which required debridement and split skin graft cover in stages before valve replacement. Two patients suffered from Streptococcal cellulitis of leg with positive blood culture in one and negative in the other.

The other incidental comorbidities found during the study includes congenital right blindness with bilateral nystagmus (n=1), acromegaly (n=1), marfanoid features (n=2).

Two patients with associated coronary artery disease were found to be diabetic, hypertensive and smokers. Clubbing was noticed in ten

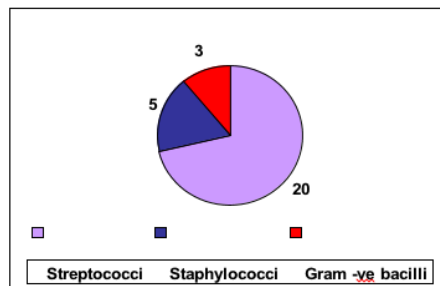
patients. The oral hygiene was poor in twelve patients. Hepatomegaly was noticed in 22 patients and splenomegaly in 10 patients. Mild splenomegaly was found in seven patients while two had moderate splenomegaly and massive in one patient who had large splenic abscess.

Anaemia was present in 32 patients (66.6%) with elevated erythrocyte sedimentation rate in 31 patients (64.5%). Leukocytosis was present in 28 patients (58.3%). Elevated C reactive protein was seen in 28 patients. Thrombocytopenia was seen in 8 patients (16.6%). Serum creatinine was elevated in seven patients and were grossly elevated in five patients.

Preoperatively, 45 patients were in sinus rhythm while three patients were in atrial fibrillation. One patient had first degree heart block and complete heart block in the other. Old inferior wall infarct changes were noticed in two patients and both of them had triple vessel disease.

Positive blood cultures were obtained in 28 patients (58.3%) and cultures were negative in 20 patients (41.7%). Gram positive cocci was the predominant organism isolated in 71.4% (n=20) which includes streptococcal viridians (n=18, 64.3%), non-hemolytic Streptococci (n=1, 3.57%), nutritionally deficient Streptococci (n=1, 3.57%). Staphylococcus represented 17.8% (n=5) of positive cultures which includes Staphylococcus aureus (n=3, 10.7%) and Staphylococcus epidermidis (n=2, 7.14%). Gram negative bacilli was the second common isolated group (n=3, 10.7%) which includes Enterococcus (n=2) and Salmonella typhi (n=1).

**Micro Organism grown in Blood culture**



| MICROORGANISM                        | N=28 |
|--------------------------------------|------|
| Streptococcal viridians              | 18   |
| Non haemolytic Streptococci          | 01   |
| Nutritionally deficient Streptococci | 01   |
| Staphylococcus aureus                | 03   |
| Staphylococcus epidermidis           | 02   |
| Enterococcus                         | 02   |
| Salmonella                           | 01   |

Transthoracic echocardiography was performed in all 48 patients. Vegetations were detected in 42 patients (87.5%) with their size varying from 2mm to 27mm. Multiple vegetations were found in 14 patients (29.2%) and pedunculated, mobile vegetations were detected in 5 patients (10.4%). Perforation of anterior mitral leaflet, posterior mitral leaflet, rupture of anterior mitral chordae and posterior mitral chordae were detected in one patient each. It detected abscesses in two patients, one each of aortic root abscess and anterior mitral annular abscess.

Trans oesophageal echocardiography was done in fourteen patients. It detected vegetations in all patients, abscesses in four patients which includes three aortic root abscess and one anterior mitral annular abscess.

Computed tomography of brain was done in seven patients with neurological complications which showed right middle cerebral artery territory infarct (n=2), left middle cerebral artery territory infarct (n=2), multiple cerebral infarct (n=1), ruptured mycotic

aneurysm of right temporoparietal region with intracerebral hematoma (n=1) and post aneurismal clip status (n=1).

In 28 patients with positive blood cultures, appropriate antibiotics were given intravenously. In 20 patients in whom, no organism could be cultured, were treated with empirical crystalline penicillin and gentamicin. The duration of antibiotics ranged from one week to six weeks with a mean duration of four weeks. One patient did not receive antibiotics preoperatively, as it was diagnosed postoperatively. Allergy to penicillin and vancomycin developed in one patient each and alternate antibiotics started. Drug induced renal toxicity was noticed in seven patients and renal adjusted doses were administered.

Four patients required inotropic support before surgery and one of them in addition required ventilation and GIK (glucose-insulin-potassium) infusion. Preoperative dialysis was required in three patients.

The indications for surgery in 25 patients with active endocarditis were congestive heart failure (n=24), large aortic root abscess (n=1). In 23 patients with healed endocarditis, the hemodynamic severity of the valvular lesion was the primary indication for surgery.

The surgery was done on an elective basis in 46 patients (96%) whereas it was urgent in two cases (4%). The indication for urgent surgery was frank aortic abscess in one and worsening heart failure with progressive renal failure and embolism in the other patient.

The aortic valve and mitral valves were equally affected with endocarditis. Aortic and mitral valve alone in fifteen patients each and both aortic and mitral valves in fourteen patients. Four patients had tricuspid valve endocarditis and all of them had an underlying congenital heart disease. In two patients with intravenous drug abuse, aortic valve was found to be affected.

| Location of endocarditis                  | N=48 |
|---|------|
| Aortic valve endocarditis                 | 15   |
| Mitral valve endocarditis                 | 15   |
| Both aortic and mitral valve endocarditis | 14   |
| Tricuspid valve endocarditis              | 04   |

Assessment of the intraoperative pathological findings revealed the following. Vegetations were detected in 41 patients (85.4%). Abscess were detected in 12 patients (25%) which includes aortic abscess (n=11) and mitral annular abscess (n=1). Leaflet perforation was seen in 8 patients involving aortic valve leaflets (n=3), anterior mitral leaflet (n=4), posterior mitral leaflet (n=1). Chordal rupture was found in 7 patients involving anterior mitral chordae in 4 patients, posterior mitral chordae in 2 patients, both chordae in 1 patient.

| Intraoperative characteristic       | N  |
|-------------------------------------|----|
| Vegetations                         | 41 |
| Abscess                             | 12 |
| Aortic abscess                      | 11 |
| Mitral annular abscess              | 01 |
| Leaflet perforation                 | 08 |
| Aortic leaflet perforation          | 03 |
| Anterior mitral leaflet perforation | 04 |
| Posterior leaflet perforation       | 01 |
| Chordal rupture                     | 07 |
| Anterior mitral chordae             | 04 |
| Posterior mitral chordae            | 02 |
| Both mitral chordae                 | 01 |

The surgical procedure performed includes valve replacement (n=43, 89.6%), mitral valve repair (n=1, 2%), tricuspid valve repair (n=4, 8.3%).

Mechanical prosthesis was implanted in 38 patients while bioprosthetic valves were utilised in 5 patients. Aortic root replacement was done in one patient with large aortic root abscess

utilising a mechanical prosthesis sutured to Dacron tube graft conduit.

Mitral valve repair was undertaken in one patient with small anterior mitral leaflet perforation and prolapse of P2 area of posterior mitral leaflet for whom direct closure of perforation with quadrangular resection of posterior mitral leaflet with ring annuloplasty was done. Tricuspid valve repair was done in 4 patients with correction of the underlying congenital heart disease.

| SURGERY PERFORMED  | N=48 |
|--|------|
| Aortic valve replacement Mechanical (11), biological (2) | 14   |
| Mitral valve replacement Mechanical (11), biological (3) | 14   |
| Double valve replacement                                 | 14   |
| Aortic root replacement                                  | 01   |
| Mitral valve repair                                      | 01   |
| Tricuspid valve repair                                   | 04   |

Concomitant procedures performed include coronary artery bypass surgery (n=2), septal myectomy (n=1) and repair of ruptured sinus of Valsalva (n=1).

Intraoperative transoesophageal echocardiography was utilised in two patients. In one patient who underwent mitral valve repair, it was useful to assess the quality of repair while in the other patient who underwent septal myectomy, it was useful to assess the left ventricular outflow gradient.

Postoperative ventilation time varied from 8 hours to 90 hours with an average of 24 hours. Prolonged ventilation of more than 24 hours was required in seven patients. The amount of intercostal drainage varied from 120ml to 3100ml on an average of 590ml per patient. Most of the patients (n=35) had drainage less than 500ml and only three had drainage between 1500ml to 3100ml. The blood transfusion requirement per patient on an average was 2.42 units. Reexploration for bleeding was done in three patients (6.25%) who had massive drainage.

The valve cultures were positive in seven patients which includes coagulase negative staphylococcus (n=3), methicillin resistant Staphylococcus aureus (n=1) and yeast like organisms (n=3). The duration of postoperative antibiotics ranged from 2 weeks to 6 weeks with an average of 4 weeks. Three patients whose valve culture grew fungal organisms had negative blood cultures preoperatively, were treated with amphotericin for 4 weeks followed by oral fluconazole for 3 months. Antibiotic related renal toxicity developed in five patients while one patient in addition had ototoxicity. Conduction abnormalities developed in four patients (8.3%). Two patients had first degree atrioventricular block and the other two had complete heart block. Complete heart block developed in 2 patients who required extensive valve debridement before aortic valve replacement. They were treated with steroids for five days and planned for permanent pacemaker implantation. One patient underwent pacemaker implantation successfully, but the other patient expired while awaiting pacemaker implantation.

One patient had ventricular tachycardia and cardiac arrest and was resuscitated successfully. It was found to be due to drug interaction between fluconazole and hypokalemia.

Pericardial effusion was noticed in 15 patients. It was mild in 11 patients. The remaining four patients had moderate to massive effusion and underwent pericardiostomy.

The hospital mortality was 6.25% (3 patients). One patient who underwent aortic root replacement for aortic root abscess had fungal endocarditis based on valve culture developed intractable congestive cardiac failure and expired after four weeks. The second patient who underwent double valve replacement died at the end of two weeks due to severe cardiac failure. The third patient had aortic valve replacement for calcific aortic stenosis, subaortic membrane, root abscess, progressive renal failure and cardiac failure developed complete heart block postoperatively. She died



before permanent pacemaker implantation.

Neurological complications occurred in three patients. One patient had right sided stroke, while the other two had transient psychiatric disorders. Massive upper gastrointestinal bleeding requiring therapeutic endoscopy and blood transfusion was seen in one patient.

Five patients had wound infection and were treated with dressings and antibiotics. One patient had sternal dehiscence in the second week which required sternal rewiring.

Postoperative fever was noticed in five patients. Four patients had post cardiomy syndrome and was treated with a course of indocid. One patient had malaria and was treated with antimalarials. Postoperative dialysis was required in one patient.

The length of the hospital stay ranged from 11 days to a maximum of 102 days with a mean of 43 days. Recurrence of endocarditis was seen in one patient three years after the operation. Initially, the patient had mitral valve replacement for staphylococcal aureus endocarditis. Later, he developed again Staphylococcal aureus endocarditis of prosthetic mitral valve with partial dehiscence and native aortic valve. He was treated with antibiotics but had resistant cardiac failure and underwent uneventful double valve replacement using bioprostheses. This patient also had acromegaly due to pituitary microadenoma and was advised surgical resection of tumor keeping in mind the cardiovascular effects of growth hormone but patient refused for the same.

#### LIMITATION OF THE STUDY

The primary limitations of the study includes

- Small sample size
- Retrospective nature of the study
- Short term followup
- Incomplete followup
- Inability to assess out-of-hospital mortality.

#### CONCLUSION

In this study, men were most commonly affected than women and majority of them were in the adult age group between twenty to fifty. Fever was the predominant clinical symptom and majority of them were in congestive cardiac failure. Congestive cardiac failure, embolism and acute renal failure were the major complications noted in the study. They had significant importance in the surgical morbidity and mortality. Positive blood cultures and echocardiographic findings were the major diagnostic tools in the establishment of diagnosis of infective endocarditis.

Transoesophageal echocardiography was found to be more sensitive in detecting vegetations and abscess cavities. Being a referral centre, some of the cases were referred on antibiotic treatment and found to be culture negative on admission which accounted for one third of the cases. Some of the cases have been taken for valve replacement on emergency basis if not responding to medical treatment. The choice of the valve replacement depended on the age of the patient and the operating surgeon. The incidence of mitral valve repair was very rare and done for cases of healed infective endocarditis with complications. The repair was attempted mainly in tricuspid valve.

In stable cases and if appropriate antibiotics were given for a minimum period of six weeks preoperatively, the surgical morbidity and mortality were low. Antibiotic cover was given for another four weeks postoperatively to prevent reinfection. Antibiotics were always intravenously both preoperatively and postoperatively.

If heart block occurs, it has to be managed by permanent pacemaker implantation.

Finally, early diagnosis, appropriate and adequate antibiotic treatment and timely surgical intervention would give good

surgical results in infective endocarditis patients.

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