

# Infective Endocarditis: A Long Term Experience

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## SUMMARY:

Infective endocarditis is common in our experience and remains unchecked as far as prevention is concerned. The mortality is significant and is due to greater incidence of gram negative organisms in both surgical and non surgical patients. Similar to other preventable general infections, infective endocarditis shall continue to pose a serious challenge to the survival of cardiac patients for the near future.

## INTRODUCTION:

Infective endocarditis usually occurs on the abnormal cardiac surfaces. The areas in the heart which are specially affected by the infective vegetative processes are the damaged surfaces affected by the trauma of the haemodynamic jets created between chambers and great vessels as in ventricular septal defect and semilunar valve stenosis. Rheumatic endocarditis also predisposes to infective endocarditis. Since both conditions are commonly encountered in Pakistan, the infective endocarditis is expected to be a common problem. There is virtually no mechanism in place in Pakistan which would ensure prevention of infective endocarditis from occurring on congenital or rheumatic cardiac lesions. This factor adds to the expected increased incidence of infective endocarditis in Pakistan.

We analysed our hospital experience of infective endocarditis during 1980-1988 period with a view to study the incidence, clinical profile, diagnostic capability and infecting organism profile over an extended period of observation.

## MATERIAL AND METHODS:

The patients with infective endocarditis included in the study were searched, retrospectively, from amongst all of the patients who visited the NICVD paediatric cardiology department at the National Institute of Cardiovascular Diseases between 1980-1988. This included patients who were seen in the out-patients department as well as those who were admitted in the paediatric ward. Two thousand seven hundred

and forty-three children were under 12 years of age were admitted in the children ward during the period of 1980-1988. A total of 10,679 new cases under 12 years age attended the paediatric clinic during this time. There were 63 children under 18 years of age who were proven to have infective endocarditis and 54 children were under 12 years age.

The mean age of 63 infective endocarditis patients was  $9.8 \pm 3.0$  years. The diagnosis of infective endocarditis was made on clinical grounds in 21 of 63 (33 per cent), on the basis of imaging the infective vegetations by 2-D echocardiography in 28 of 63 (44 per cent) and by positive blood culture growth of organisms in 24 of 63 (38 per cent) Table I.

TABLE I

### MODE OF DIAGNOSIS IN 63 IE PATIENTS

	No.	%
Clinical	21	33
Echo Positive	28	44
Culture Positive	24	38

The clinical criteria of diagnosis of infective endocarditis were a prolonged (more than 1 week) fever due to no obvious cause and with the exclusion of malaria and typhoid fever by blood smear examination, blood

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culture and widal test. Clinically presence of clubbing, anaemia, splenomegaly and microscopic haematuria were considered strongly suggestive of infective endocarditis. The patients were all admitted and treated with specific antibiotics after blood culture report was available. In cases of negative blood culture the initial drugs were penicillin and streptomycin. If response was not obtained with these drugs then combination of antibiotics against gram negative and gram positive organisms was given. Routine investigations included full blood count, erythrocyte sedimentation rate, throat swab culture, urine and stool examination, search for malarial parasites and widal test. In-patients who, previous to admission at the NICVD, had been given antibiotics blood cultures were obtained after 72 hours of discontinuation of the antibiotics. In acutely sick children antibiotics were started immediately after taking blood culture samples otherwise selection of antibiotics was made according to the sensitivity of the cultured organisms. Treatment of streptococcal infective endocarditis was extended for 4 weeks period of intravenous therapy and for six weeks period for gram negative organisms and coagulase positive staphylococci or when organisms could not be cultured. Patients in the recent years underwent echocardiography, 12 lead electrocardiography and chest x-ray examination.

## RESULTS:

The mean age of 63 patients with infective endocarditis was  $9.8 \pm 3.0$  years, range 3-18 years. The incidence of infective endocarditis was 19.7 per 1,000 for admissions to the children's ward and 5 per 1,000 patients for out-patients in children under 12 years of age. The overall incidence of infective endocarditis was 4 per 1,000 in children under 12-year age Table II.

TABLE II

### HOSPITAL INCIDENCE IE (1981-1989)

	No.	IE No.	Incidence Per 1,000
In-Patients	2,743	54	19.7
Out-Patients	10,679	54	5.0

The duration of symptoms, that is the time lapse between presentation at our hospital and the onset of symptoms was  $50 \pm 45$  days (range 3 days 210 days). In majority of patients there was no definite history of preceding episodes of infection, or dental extraction or non cardiac operative procedures. One patient had boil on the skin. There were 7 patients (11 per cent) who had previous surgery for rheumatic or congenital cardiac lesions. Congenital heart lesions constituted the largest group 35 of 63 (56 per cent) on which infective endocarditis occurred. Chronic rheumatic carditis was the underlying cause in 27 of 63 patients (43 per cent) and one patient had prolapse mitral valve as the underlying lesion Table III.

TABLE III

### INFECTIVE ENDOCARDITIS 1980-1988

Lesions	No.	%
Congenital Heart Disease	35	56
Rheumatic Heart Disease	27	43
Mitral Valve Prolapse	1	2
Total:	63	

Amongst the congenital cardiac lesions, tetralogy of Fallot constituted the largest group, 12 of 38 patients (34 per cent). Seven of these had previous surgery; complete correction in 2 and shunt operation in 5. Five patients with tetralogy of Fallot had no previous surgery and three of these were admitted with severe tricuspid regurgitation and signs of gross right sided failure such as marked hepatomegaly ascitis and peripheral pitting oedema. In two tetralogy of Fallot patients, large vegetations were detected on the tricuspid valve, pulmonic valve, the main and branch pulmonary arteries. These 2 patients developed repeated episodes of pulmonary embolisms. Eight patients had obstruction of the left ventricular outflow tract, four due to aortic valve stenosis and 4 due to subaortic fibromuscular stenosis. Ventricular septal defect was present in 7 patients one of whom had complete surgical closure few days prior to developing infective endocarditis. Patent ductus arteriosus was present in

six, coarctation of aorta in one and complicated cyanotic heart disease in one Table IV.

TABLE IV

## CONGENITAL HEART LESIONS WITH IE

Lesions	No.	%
Tetralogy of Fallot	12	34
Aortic Stenosis	8	23
Ventricular Septal Defect	7	20
Patient Ductus Arteriosus	6	17
Coarctation of Aorta	1	3
Complicated	1	3
Total:	35	

Rheumatic heart lesions were the second most common underlying cardiac defects. Mitral regurgitation was noted in 9 patients (33 per cent), aortic regurgitation in six, and combined mitral regurgitation/aortic regurgitation/mitral stenosis in 10 patients Table V.

TABLE V

## RHEUMATIC HEART LESIONS WITH IE

Lesion	No.	%
Mitral Regurgitation (MR)	9	33
Aortic Regurgitation (AR)	6	22
MR/AR	5	19
MR/Mitral Stenosis (MS)	4	15
Prosthetic MV	2	7
MS	1	4
Total:	27	

Two patients had mitral valve prosthesis since 2 years and one year previously. Fever was the most common symptom and was present in all 63 patients (100 per cent) Table VI.

TABLE VI

## SYMPTOMS IN 63 PATIENTS WITH IE

	No.	%
Fever	63	100
Arthralgia	8	13
Headache	6	10
Shortness of Breath	7	11
Chest Pains	5	8
Sweating	3	5
Abdominal Pain	2	3
Vomiting	2	3

Arthralgia was noted in 8 patients, headache in six, shortness of breath in 7 and chest pain in 5. Sweating, abdominal pain and vomiting were noted in the remaining patients. Amongst the signs, splenomegaly was present in 30 of 63 patients (48 per cent), pallor in 30 of 63 (48 per cent) and clubbing was noted in 17 of 63 patients (27 per cent) Table VII.

TABLE VII

## PHYSICAL SIGNS IN 63 IE PATIENTS

	No.	%
Splenomegaly	30	48
Pallor	30	48
Clubbing	17	27
Peripheral Embolism	6	10
Petichae	2	3
Pericarditis	1	2

Peripheral embolisms, petichae and pericarditis was noted in descending order of frequency. The combination of splenomegaly, pallor and clubbing was noted in 13 of 63 patients (21 per cent) anaemia and clubbing was present in 15 of 63 (24 per cent) and anaemia and splenomegaly in 23 of 63 (37 per cent). Laboratory investigations showed that the mean haemoglobin was  $9.7 \pm 1.6$  G% in 52 of 63 patients. In 11 of 63 patients who had cyanotic heart disease the average haemoglobin was  $12.5 \pm 2.0$  G%. Thus relative anaemia was present in this group as well. Erythrocyte sedimentation rate in 51 acyanotic children was elevated and mean was  $74 \pm 30$  mm (westergren). Cyanotic children were excluded since erythrocyte sedimentation rate was often normal in these Table VIII.

TABLE VIII

LABORATORY INVESTIGATIONS  
IN 63 PATIENTS

Haemaglobin acyanotic	$9.7 \pm 1.55$ n=52
cyanotic	$12.5 \pm 2.0$ n=11
ESR	$74 \pm 30$ n=51
WBC	$13,243 \pm 6,203$ n=63
Microscopic Haematuria	n=35 (56%)

Microscopic haematuria was present in 35 of 63 (56 per cent) patients. Macroscopic haematuria was present in 7 of 63 patients (11 per cent).

Two Dimensional echocardiography was done in 46 of 63 patients (73 per cent). Twentyeight of 46 patients (61 per cent) showed presence of vegetations and 18 of 46 patients (39 per cent) showed no vegetations. Mitral valve was the site of vegetations in 16 patients (57 per cent), aortic valve in six (21 per cent), tricuspid valve in 4 and pulmonic valve in 2 patients.

Sixteen patients died, the largest group of six patients died following peripheral embolization to the central nervous system Table IX.

TABLE IX

CAUSES OF 16 DEATHS FOLLOWING IE

	No.	%
CNS Complications	6	38
Congestive Heart Failure	5	31
Surgery	3	19
Disseminated Intravascular Coagulopathy	1	6
Ventricular Fibrillation	1	6

Total: 16

Convulsions with localised loss of limbs function was the common symptom heralding the onset of embolization to the brain. The embolic episodes often occurred when patient was responding to the antibiotic treatment. One patient with acute infective endocarditis due to staph. aureus had complete blockage of left branchial artery with gangrene of the left hand at presentation. Five patients died due to congestive cardiac failure. In three patients surgery proceeded death, one of these patients had tetralogy of Fallot and massive vegetations on the tricuspid valve, in the right ventricular outflow tract and in the main pulmonary arteries and had multiple episodes of pulmonary infarction during the antibiotic treatment. She underwent total correction but died with hyperpyrexia in the post operative period. One patient, after surgical closure of ventricular septal defect, developed infective endocarditis immediately in the post operative period. Third patient was operated upon and died for large vegetations in the left ventricular outflow tract involving the anterior leaflet of mitral and aortic valves. Disseminated intravascular coagulopathy in one patient and ventricular fibrillation in one patient accounted for the other deaths. Convulsions occurred in

six patients and large vegetations were visualised in 3 patients in whom echocardiography was done. Three others did not undergo echocardiographic examination. Of the 16 patients who died, five patients had ventricular septal defect, 4 had mitral regurgitation, 3 tetralogy of Fallot, 2 aortic stenosis, coarctation of aorta and aortic stenosis was noted in one each. Nine patients who died had vegetations visualised on Two Dimensional echocardiography and 2 failed to show vegetations while echocardiography was not done in the remaining five patients.

Twentyfour of 63 patients (38 per cent) had positive blood culture Table X.

TABLE X

ORGANISM CULTURED FROM 24 PATIENTS WITH IE

	No.	%
Staph. aureus	10	42
Str. viridans	4	17
Pseudomonas	3	13
Micrococci	2	8
E. Coli	1	4
Klebsiella	1	4
Str. Pepto	1	4
Str. Haemolyticus	1	4
Str. Pyogenes	1	4
Total:	24	

Majority of patients, 10 of 24 (42 per cent), grew staph. aureus on blood culture and four patients (17 per cent) had str. viridans. Gram negative organisms such as pseudomonas occurred in three (13 per cent), Klebsiella and E. Coli in one each. Micrococci were cultured in 2, str. pepto occurred in one and str. Haemolyticus in one and str. pyogenes in two patients.

Four patients had prior surgery and three of these developed staph. aureus endocarditis while one had pseudomonas on blood culture. Of the 20 patients without prior surgery 7 patients had staph. aureus, 2 had pseudomonas, one Klebsiella and one E. Coli. Str. viridans, haemolyticus, str. pepto and micrococci accounted for the rest (table). Thus both gram negative and gram positive organisms were grown from patients who had had no prior surgery.

Five patients with positive blood cultures died and 19 with positive blood cultures survived. While 11 patients with negative blood culture died and 28 survived. Of the 4 patients with gram negative organism two died. All 6 patients with streptococcal organisms survived and one of 10 patients with staph. aureus died. Twelve of 24 patients with positive blood cultures also had vegetations detected by the Two Dimensional echocardiography.

## DISCUSSION:

Our data shows that compared to the incidence reported the literature<sup>1,2</sup> a much higher incidence i.e., 20 per 1,000 Hospital admissions of infective endocarditis was noted in the children under 12 years of age at the National Institute of Cardiovascular Diseases, Karachi. This may be explainable in various ways. Firstly our data is from the National Institute which is a purely cardiac hospital as opposed to the data generated in the literature which was either based on population studies or generated in a general hospital where cardiac and non-cardiac patients were seen. The high incidence of infective endocarditis noted among our patients imposes a severe financial burden on the Institute and demands extra allocation of beds. On the average 4-6 week antibiotic treatment cost for one patient is expected to be approximately 50-60,000 rupees. Added to it is the management cost by medical or surgical means which may be required for the deterioration of haemodynamic state of the patient. Infective endocarditis is a preventable disease and recommendations for its prevention are well worked out both for surgical as well as congenital and rheumatic heart patients. In Pakistan mechanisms for prevention of infective endocarditis are non-existent and the situation is similar to that observed for other preventable

conditions such as diarrhoea and infective fever. Systematic structuring of health delivery system is required so that effective prevention for conditions including infective endocarditis can be achieved. The clinical spectrum of infective endocarditis observed in our study suggested that patients came to the hospital when florid clinical picture had developed<sup>2,3,4,5</sup>. This is because in our communities patients seek medical advice only when symptoms get worst. The other reason is that the medical practitioners manage fever in children with preexisting congenital or rheumatic lesions in a similar fashion to the practised for dealing with fever in children who have normal hearts. It is suggested that pyrexia of unknown origin for more than one week, in a patient with preexisting heart disease should be suspected to be due to infective endocarditis and no antibiotics should be administered unless definite cause of the fever is found. Once a patient is known to have rheumatic or congenital cardiac lesion he must be instructed on prevention of infective endocarditis. We at the National Institute have a card made out which outlines these recommendations. This card is given to all our patients with instructions as to how to implement these recommendations.

In our study were able to isolated infective organisms in 38 per cent of our cases. The reason for this low yield seems to be prior use of low dose antibiotics either in the medical practitioners office or in the general hospitals.<sup>1,6</sup> If one adopts the policy of not using antibiotics in cardiac patients without a firm diagnosis then culture yield would improve. The management of infective endocarditis is more likely to be successful when infective organism and their sensitivity is known. Our data showed that gram negative organisms were as common as gram positive organisms in patients who had no previous cardiac or other surgery. We suggest that the abnormal pattern of infecting organisms in our cases was due to the indiscriminate use of antibiotics by the medical personnel at large.

Echocardiography has provided a powerful tool for the diagnosis and management of infective endocarditis<sup>7,8</sup>. We had noted that the visualization of

vegetations on echocardiography conferred greater mortality on patients with infective endocarditis than when no vegetations were detected. Some of this increased mortality was clearly due to embolization from these vegetations and some of it was due to the haemodynamic deterioration of a long duration endocarditis. Partly it was due to ineffective clearance of infecting organisms which were trapped in these large vegetations. Our present policy is to advise surgery on patients in whom large or multiple vegetations are detected. In our study the surgery was undertaken after a week of antibiotic cover when temperature had settled and splenomegaly had regressed. We also considered surgery if vegetations were on the left side since these are likely to embolize in the systemic circulation. This policy was based on our observation of death due to embolization in children in whom infection was being effectively controlled.

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