

INFECTIVE ENDOCARDITIS ITS COURSE, COMPLICATIONS AND TREATMENT

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ABSTRACT:

BACKGROUND:

To combat infective endocarditis, we must have an adequate knowledge about the common causative organisms, the predisposing factors, complications, and outcome of the disease. Moreover does the rheumatic prophylaxis by penicillin confer protection against the commonly causative organism of endocarditis? Keeping these in view we planned the study in our population.

AIMS & OBJECTIVE:

To find out the common causative organisms, complications and outcome of endocarditis in our population. To find out the role of rheumatic prophylaxis in prevention of endocarditis.

MATERIAL & METHODS:

This observational prospective study was conducted at Punjab Institute of Cardiology, Lahore and Wazirabad Institute of Cardiology, Wazirabad between January 2019 and January 2020. Fifty patients of infective endocarditis were enrolled. Patients were followed throughout their hospital stay. Complications and outcome were recorded. Patients of adult age group who had either vegetation and/or blood culture positive were enrolled whereas patients who were suspected for endocarditis but lack major criteria were excluded. Vegetations were detected either on transthoracic Echo or trans-esophageal Echo or both.

RESULTS:

Between January 2019 to January 2020, we studied 50 patients of infective endocarditis, 29 of them were males and 21 were females. The age of patients ranged from 14 -69 years (27.5±9.9years). Fourteen patients were culture positive and most common organism isolated was Staphylococcus aureus. Methicillin resistant Staphylococcus (MRSA) aureus had the worst outcome. Our patients had a very high complications rate i.e. 72%. The most common complication was embolism (32%) to the limbs, lung and brain, and acute renal dysfunction (32%). Most of the patients who required the rheumatic fever prophylaxis were not taking prophylaxis (3 patients as opposed to 32 patients) p value < 0.001. The three patients who were taking rheumatic prophylaxis were culture negative and not by the organisms commonly infecting the heart. The mortality was also very high, nine patients (18%) died during their course of illness within their hospital stay. But there was significant difference in complication management medically or surgically. In medically managed patients 8 died as opposed to 0 in surgically managed patients (30.8% vs 0%).

CONCLUSION:

Infective endocarditis carries a very high mortality and complications rate. Surgically managed patients have better outcome. Patients infected with MRSA have the worst outcome. Rheumatic heart disease is the leading underlying structural cardiac problem. The patients taking rheumatic prophylaxis may have some protection against infective endocarditis at least to commonly offending microorganisms. This needs to be studied in a larger cohort.

KEY WORDS:

Infective endocarditis, rheumatic heart disease, complication, management.

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INTRODUCTION

Infective endocarditis is one of the most difficult infection of the heart to treat. It carries a very high mortality and morbidity that is upto 24%.¹ The mortality rate increases to 27.7%² if patient has prosthetic valve. In our population mortality reported is 19%³. The underlying cardiac condition can be rheumatic, congenital or an implanted prosthesis. Sometimes the underlying heart is normal but still endocarditis can occur, as is seen in intravenous drug abusers and nosocomial infections. In a study⁴ congenital heart disease was most commonly seen in 37%, followed by mitral valve prolapse 16%, IV drug abuser around 13%, prosthetic valves in 11%, and rheumatic heart diseases (RHD) in just 8%. In South east Asia rheumatic heart disease is very much prevalent⁵ and majority of cases of infective endocarditis have underlying RHD. Penicillin is used for secondary prophylaxis, but unfortunately majority of our patients do not use it and they are at risk of rheumatic recurrence. Penicillin is effective against Streptococcus and Staphylococcus the most common offending agents of endocarditis⁶. Endocarditis has also a very high complication rate including mechanical, embolic and metabolic derangements. To combat this deadly disease, we must have an adequate knowledge about the common causative organisms, the predisposing factors, complications, and outcome of the disease. Moreover does the rheumatic prophylaxis by penicillin confer protection against endocarditis by commonest organisms? Keeping these in view we planned the study in our population.

MATERIAL & METHODS:

An observational prospective study was conducted at Punjab Institute of Cardiology and Wazirabad Institute of cardiology. Fifty patients of infective endocarditis were enrolled between January 2019 and January 2020. Patients were followed throughout their hospital stay. Complications and

outcomes were recorded.

Patients of adult age group who had either vegetation and/or blood culture positive were enrolled whereas patients who were suspected for endocarditis but lack major criteria were excluded.

Vegetations were detected either on transthoracic echo or transesophageal echo or both.

Complications were defined as follows

- i) Renal Dysfunction - When serum creatinine is more than normal range and increases more than 50% of baseline
- ii) Deranged liver function tests - Bilirubin more than 1 mg/dl, alanine transaminase more than 40 mg/dl
- iii) Hematological - INR more than 1.5 (patients who are not on anticoagulants), Platelets less than 150000/ml³, Hemoglobin less than 12 g/dl

DATA ANALYSIS:

SPSS 23 was used to analyze the data. Categorical variables were expressed in percentages and continuous variables in mean \pm SD. Chi square and Fisher's exact test were used to determine the association of outcome variable with categorical variables. A p value \leq 0.05 was taken as significant.

RESULTS:

We studied 50 patients of infective endocarditis, 29 of them were males and 21 were females. The age of patients ranged from 14 -69 years (27.5 \pm 9.9 years) table 1. Forty seven patients had vegetations detected either on transthoracic (TTE) and or transesophageal echo (TEE). Most of the patients had large vegetations more than 10 mm. Fourteen patients were culture positive while remaining had negative blood cultures. The most common micro organism isolated was Staphylococcus aureus (7 patients) three of them were methicillin resistant, followed by enterococcus in 4 patients while pseudomonas and klebsiella

Table-1: Demographic data		
	Mean \pm SD	Range
Age (years)	27.5 \pm 9.9	14 – 69
Gender	Frequency	Percentage
Male	29	58.0
Female	21	42.0
Underlying structured heart disease		
Native valve	34	68
Prosthetic valve	4	8.0
Permanent pacemaker	1	2.0
Congenital heart	6	12.0
Native + congenital heart	5	10.0
TTE		
Vegetation not detected	3	6.0
Yes	47	94.0
Size		
Large > 10mm	30	60.0
Small < 10mm	17	34.0
TEE		
Not done/Not detected	32	64.0
Yes	18	36.0
Size		
Large > 10mm	12	66.7
Small < 10mm	6	33.3
Culture		
Positive	14	28.0
Negative	36	72.0
Organism		
Entrococcus	4	28.6
Kalbsilla	1	7.1
Staphylococcus aureus	4	28.6
MRSA	3	21.4
Pseudomonas	1	7.1
Coccobacillus unspecified	1	7.1
Outcome		
Recovered	41	82.0
Expired	9	18.0
Complication		
No	14	28.0
Yes	36	72.0

were positive in 1 patient each, one patient had unspecified coccobacillus. Methicillin resistant Staphylococcus (MRSA) aureus had worst outcome, two of the three patients died and one had three

relapses managed surgically with prolonged antibiotic cover for three months. All other culture positive patients recovered (table 2). Different antibiotics were given to culture negative patients

Table 2 - Outcome of patients depending upon organism			
Organism	Recovered	Expired	P value
Enterococcus	4 (100%)	0 (0%)	0.533
Klebsiella	1 (100%)	0 (0%)	
Staphylococcus aureus	4(100%)	0 (0%)	
MRSA	3 (60%)	2 (40%)	
Pseudomonas	1 (100%)	0 (0%)	
Coccobacillus unspecified	1 (100%)	0 (0%)	
Fisher's exact test			

Table 3 - Complications of patients	
Complications	Number of patients n=50
Acute Renal dysfunction	16
Deranged LFTs	02
<u>Mechanical complications</u>	11
Ruptured Chordae	02
Valve perforation	05
Ruptured sinus of valsalva	01
Pseudoaneurysm	01
Fistula	01
Periprosthetic leak	01
Embolism	16
<u>Hematological abnormalities</u>	07
Pancytopenia	02
Bicytopenia	02
Thrombocytopenia	01
Prolonged INR	02
Abcess	02
Intracerebral bleed	01
Relapse	01

but most of the patients responded to vancomycin or ceftriaxone combined with gentamicin. Native valve was involved in 34 cases, 11 cases were congenital, 4 patients had prosthetic valve and 1 patient had infected permanent pacemaker leading to tricuspid valve endocarditis. Most common site was mitral valve 18 (36%) out of which 15 were rheumatic, 2 were prosthetic and 1 was congenital, followed by aortic 18 (36%) 13 rheumatic 4

congenital and 1 prosthetic, tricuspid 6 all non rheumatic, pulmonic 2 both in congenital cases and , combined mitral and aortic in 2 patient. A congenital case had both aortic and pulmonic involvement due to patent ductus arteriosus. One patient had vegetation on RVOT due to congenital RVOT obstruction. Our patients had a very high complications rate that is 72%. The most common complication was

Table 4 - Valve involved and embolism	
Valve involved	Embolism
Aortic valve	5/18(27.7%)
Mitral valve	5/18 (27.7%)
Tricuspid valve	3/6 (50%)
Pulmonary valve	1/2 (50%)
Aortic and mitral	2/2 (100%)

Table 5 - Rheumatic prophylaxis taking patients			
Was patient on rheumatic fever prophylaxis			p-value
	observed	expected	
Yes	3	32	< 0.001
No	29	0	

Table 6 - Outcome of the patients depending upon management of complications				
Complication management	Outcome		Total	p-value
	Recovered	Expired		
Medical	18 (69.2%)	8 (30.8%)	26 (100%)	0.076
Surgical	10 (100%)	0 (0%)	10 (100%)	
	28 (77.8%)	8 (22.2%)	36(100%)	

Table 7 - Predisposing conditions in patients	
Predisposing condition	Number of cases n=50
IV drug abuser	3
Dental procedure	2
D&C	2
Cesarean section	1
Septic abortion	1
Nosocomial	1
Caries teeth	1
Intrauterine death	1

embolism (32%) to the limbs, lung and brain and acute renal dysfunction (32%) table 3. Mechanical complications were seen in 11(22%) patients and hematological complications in 7 (14%) patients. Embolism was most commonly observed percentagewise when both aortic and mitral valves were involved (2/2patients) table 4, followed by right sided endocarditis then mitral and then aortic. Peripheral embolism was seen in 6/17(35.3%) patients with small vegetation and 10/30(33.3%) patients with large vegetation. A very important finding observed in the study was that most of the patients who required the rheumatic fever

prophylaxis were not taking prophylaxis (3 patients as opposed to 32 patients) p value < 0.001 table 5. The three patients who were taking rheumatic prophylaxis were culture negative and infected with organisms not commonly infecting the heart. The mortality was also very high, nine patients (18%) died during their course of illness within their hospital stay. There was no difference in mortality with respect to culture positive or negative and complicated or uncomplicated. But there was significant difference in complication management medically or surgically. In medically managed patients 8 died as opposed to 0 in surgically

managed patients (30.8% vs 0%) table 6. Predisposing conditions were seen in 12 patients, out of which IV drug abuser 3 patients, Dental procedure 2 patients, D&C 2 patients, nosocomial 1 patient, Cesarean section 1, septic abortion 1, Intrauterine death 1 patient and caries teeth in 1 patient. (table 7)

DISCUSSION:

In this study males were more as compared to the females 58% vs 42%. Elamragy⁷ et al and Crestiet al¹ also showed the similar results having infective endocarditis more common in males. Gynaecological procedures puts females at increased risk whereas IV drug abuse is common amongst males.

As far as age distribution is concerned, patients in our study were younger with mean age of 27.5 years whereas in a study by Joffre et al⁸ patients were elderly 65 ± 16 years. Because we have rheumatic heart disease quite prevalent and our children and young adults have diseased valves which makes them quite predisposed to infective endocarditis at a relatively younger age. A study conducted by Shahid³ et al also showed similar results that patients with infective endocarditis presenting at an early age mean age around 35 years.

Vegetations were detected in almost all patients (94%) and most of them being large. In a study by Leitman⁹ et al vegetations were not detected in 8% of patients and too small to be measured in 22.6% patients and large vegetation was seen in 31.5% whereas in our study 60% patients had large vegetation. Very high number of vegetation positive patients in our study was simply because we selected the patients who were either having vegetation or culture positive or both.

Underlying structural heart disease was rheumatic in 64% of cases. Sunil et al¹⁰ also demonstrated RHD as most common cardiac condition (42%) Watt et al¹¹ in his study compared developing country where RHD was 31% as compared to developed country (4%). This is simply because rheumatic heart disease is quite prevalent in our part of world and not a major disease now in the west. Most of the patients who required the rheumatic fever prophylaxis were not taking prophylaxis (3 patients as opposed to 32 patients) in our study. The three patients who were taking rheumatic prophylaxis were culture negative and so at least not by the organisms commonly infecting the heart. It might be possible that rheumatic fever prophylaxis confers

protection against commonly offending organism causing infective endocarditis. This thing needs to be studied in a larger cohort.

Complication rate was very high in our study 72% where acute renal dysfunction and peripheral embolism were the commonest complications followed by mechanical problems and hematological derangements. Embolic events are seen in 20 to 50% of patients with endocarditis¹² as is seen in our study. Ren et al¹³ showed renal insufficiency in 8.9 % and embolism in 26 % of cases, a study conducted in China suggesting major complications of endocarditis. Abscess, pseudoaneurysm, fistulae, periprosthetic leak, perforation and valve aneurysm are cardiac complications of infective endocarditis¹⁴. Our patients had significant mechanical cardiac complications (20%), valve perforation (10%) being the most common requiring surgical intervention. Oliveira et al reported a surgical mortality of 17% in active infective endocarditis patients within one month. Surgical management showed good results in our study, and medical management of complicated patients showed increased mortality. This is because medically managed patients were too sick to undergo surgery, However surgical management remains the gold standard for at least mechanical cardiac complications.

Mortality^{1,2,16} of endocarditis is very high 8.1 to 27.7% and even higher in some studies. The mortality depends upon age of the patient, prosthetic material, co morbidities and microorganism. MRSA had the worst outcome. We had overall mortality of 18 % in our study, which is quite comparable to other studies. Relatively better outcome was due to younger age of the patients and no major co morbidities.

CONCLUSION:

Infective endocarditis carries a very high mortality and complications rate. Surgically managed patients have better outcome. MRSA had the worst outcome. Rheumatic heart disease is the leading underlying structural cardiac problem. The patients taking rheumatic prophylaxis may have some protection against infective endocarditis at least to commonly offending microorganisms. This needs to be studied in a larger cohort.

STUDY LIMITATIONS:

1. Small sample size
2. Some of the patients already had used antibiotics so increasing the number of culture negative cases.

DISCLOSURE: Nothing to disclose

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