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RISK FACTORS FOR IN-HOSPITAL MORTALITY AFTER SURGICAL TREATMENT OF INFECTIVE ENDOCARDITIS

Surgery

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ABSTRACT

INTRODUCTION: To study the clinical profile, effected heart valves and the organisms involved and prognostic factors in patients undergoing surgery for infective endocarditis.

MATERIALS AND METHODS: All patients who were admitted and operated for infective endocarditis from 2011 through 2017 in single unit of NIMS hospital were included in the study. The study protocol was approved by the Hospital Ethics committee.

RESULTS: A total of 30 patients with infective endocarditis were operated between 2011through 2017. 22 males and 8 females,mean age was 36.7.Out of 30 patients 29(96%) of the patients had native valve endocarditis (NVE) and only 1 patient had prosthetic valve endocarditis (PVE).The Mitral valve was involve in 12 (40%), Aortic valve 10 (33%) and both valves were effected in 6 patients. The most common indications for surgery were refractory heart failure and persistent infection, 9 and 5 respectively. Heart failure and sepsis were the major post-operative complications. Elevated liver aminotransferases had significant association with in-hospital mortality (p value AST-0.024; ALT-0.004). There were 9 deaths during study period.

CONCLUSIONS: Surgery for infective endocarditis still carries a high mortality rate. Elevated liver aminotransferases are helpful in predicting mortality rates.

KEYWORDS

INTRODUCTION:

Infective endocarditis has a high mortality and mortality with a reported incidence of 1.5 to 11.5 per 100,000 population[1]. A very important factor in the outcome of surgery is the timing, as early surgical intervention has been shown to reduce systemic embolization and mortality[2]. However, surgery in infective endocarditis is technically challenging with a reported in-hospital mortality of 20-30% and 5-year mortality at 40% [1]. There has been a changing trend in the global scenario of the disease with respect to the spectrum of patients, antimicrobial resistance, diagnostic modalities and perioperative care. We aimed to study the outcomes and trends in patients undergoing surgery for infective endocarditis.

AIMS AND OBJECTIVES:

To study the clinical profile, effected heart valves and the organisms involved in patients presenting with infective endocarditis. To assess the morbidity and mortality in patients who have undergone surgery and the prognostic factors affecting outcomes.

MATERIALS AND METHODS:

Data of patients who were admitted and operated for infective endocarditis from 2011 through 2017 was collected from database. Infective endocarditis was diagnosed as per modified Duke's criteria. The study protocol was approved by the Hospital Ethics committee. Demographic details, co-morbidities, involved pathogens and preoperative subsystem status were analysed. Morbidity and mortality related to the surgery were studied and compared with Indian and international studies. EuroSCORE II was used to calculate predicted mortality. The primary end-point was in-hospital mortality.

RESULTS:

Out of 30 patients operated for infective endocarditis, 22(73.3%) were male and 8 were female (26.7%) with a mean age of 36.7 years. Blood culture was positive in 23(76%) patients. Although there were 7 deaths in positive culture group and only 2 death in negative culture group, no statistically significant association was found. Staphylococcus was isolated in 8(26.6%) patients and streptococcus in 5(16.6%). Enterococcus fecalis and Klebsiella pneumoniae were found in 3 patients each. M.tuberculosis and Brucella species were isolated in one each and Burkholderia pseudomallei was isolated in 2 patients. Native valve endocarditis (NVE) occured in 29(96%) patients and only 1 patient had prosthetic valve endocarditis (PVE). Mitral valve was the commonest valve affected seen in 12(40%) patient followed by aortic valve, 10 (33%), both aortic and mitral valve in 6 (20%) patients. Only tricuspid valve was involved in one patient and pulmonary valve in one patient. The associated comorbidities included diabetes mellitus in 15(50%),raised bilirubin in 13(43%) ,elevated liver enzymes in 17(56%), elevated creatinine in14(46%)patients. The patients with elevated liver aminotranferases showed a statistically significant association with mortality (p value: AST- 0.024, ALT-0.004). Other laboratory parameters did not show any statistically significant association with mortality. 17(56%) patients had prior history of rheumatic heart disease as risk factor and 2 patients had congenital VSD. Emergency surgery was required in 8 (27%) patients, urgent surgery in 17 (56%) and 5(16%) patients underwent elective surgery. Refractory heart failure was the most common indications for surgery, present in 10 (33%), followed by persistent infection 9(30%), mitral regurgitation 5(117%), mitral and aortic regurgitation 2(6.6%). One each of the patients had aortic regurgitation, paravalvular abscess, VSD patch dehiscence and prosthetic valve endocarditis. 30 patients underwent 29 valve replacements, 24 mechanical and 5 bioprosthetic and one patient underwent tricuspid valve repair along with ventricular septal defect repair. Mitral valve was replaced in 12(40%),out of which 2 were bioprosthetic, aortic valve was replaced in 11(36.7%),out of which 2 were bioprosthetic, both mitral and aortic valves were replaced in 5(16.7%) and in one patient pulmonary valve replacement with bioprosthetic valve was done along with pulmonary artery mycotic aneurysm repair. 2 patients underwent valve repair (one tricuspid and one mitral valve in a aortic valve replaced patient). Some of these patients also underwent additional procedures such as dacron graft replacement of ascending aorta (2 patients), intracardiac repair in 2 patients, descending aortic pseudoaneurysm repair with dacron patch in 2 patients, and ventricular pseudoaneurysm repair in one patient. The mean post-operative hospital stay was 9.8+/-5.1 days. The major post-operative complications were sepsis 8(27%), heart failure 6(20%), sternal infection 5(17%) and bleeding 5(16.7%). 3 patients had temporary complete heart block which recovered. The in-hospital mortality was 30% (9patients). The causes were heart failure in 4(44%)patients, sepsis in 4(44%) patients and fulminant pneumonia in one. Predicted mortality was calculated using EuroSCORE II.

According to the score 15 patients were in the high risk category,out of which 9 patients died. There was no mortality in the low (8 patients) or medium (7) risk category.

Table: 1, Statistical results of Demographics and Laboratory parameters

Parameters	Survivors N=number of cases (Mean±SD) or (N%)	In-hospital mortality N=number of cases (Mean±SD) or (N%)	P value
Age	N = 21/30 36.6 ± 11.6	N =9/30 37.8± 11.1	0.795
Sex M:F 20:10	N =21/30 M:F=13:8(62%:38%)	N=9/30 M:F=7:2(78:22)	
Weight	N=21/30 52.76±13	N=9/30 49.56±8.9	0.515
Postoperative stay	N=21/30 9.05±3.7	N=9/30 11.67±7.3	0.205
Creatinine (Elevated:Normal) (14:16)	Elevated(N=8/14)	Elevated(N=6/14)	0.177
	Normal(N=13/16)	Normal(3/16)	
Blood cultures (Positive:Negative) (23:7)	Positive (N=16/23)	Positive(N=7/23)	0.657
	Negative(N=5/7)	Negative(N=2/7)	
Bilirubin (Elevated:Normal) (13:17)	Elevated(N=7/13)	Elevated(N=5/13)	0.294
	Normal(N=13/17)	Normal(4/17)	
Aspartate Aminotransferase (AST) (Elevated:Normal) (17:13)	Elevated(N=9/17)	Elevated(N=8/17)	0.024
	Normal(N=12/13)	Normal(1/13)	
Alanine Aminotranferase (ALT) (Elevated:Normal) (14:16)	Elevated(N=5/14)	Elevated(N=9/14)	0.004
	Normal(N=15/16)	Normal(2/16)	

Table 2: EuroScore II risk assessment.

Predicted mortality		
(EuroSCORE II)	No. of patients (% of sample)	Actual deaths(% of sample)
Low (0-2)	8 (26.6%)	0
Medium (3-5)	7 (23.3%)	9 (30%)
High (>6)	15 (50%)	9 (30%)

DISCUSSION

Infective endocarditis is a disease with high morbidity and mortality. The profile of infective endocarditis has been changing across the world, including India. This study attempts to compare the results obtained with other Indian and international studies.

The mean age of patients in our study was 36.7 years which was similar to most Indian studies [5,17,18] but was in contrast to most western studies,where the mean age was in the 5th and 6th decades [4,9]. The younger age group in our study can be attributed to higher prevalence of rheumatic heart disease in our part of the world, which was 56% in our study. However, there are reports from India which are showing an increasing trend in the age of affected patients[19,20]similar to the western population. The contributing factors being the general increase in the age of population and longitivity of patients with rheumatic heart disease and congenital heart diseases due to better early treatment. 73% of our study population was males which is consistent with other studies in India[5,17,19,21] as well as from the western hemisphere[9,16]. The increased prevalence of infective endocarditis in the male sex could not be explained. The most common predisposing factors for infective endocarditis are rheumatic heart disease and congenital heart disease[7].17 (56%) patients in our study had prior history of rheumatic heart disease. Most of the Indian studies have also reported the same[5,19,22]. In contrast, in the western population.[15,23] congenital heart disease was reported to be the major risk factor[24],with the highest being in patients with cyanotic heart disease followed by endocardial cushion defects. In our study we had 2 patients with VSD but none with cyanotic heart disease. Also, in contrast to western data, we encountered only 1 (3%) patient with mitral valve prolapse.Similar low occurence of mitral valve prolapse has been seen in other indian studies[5].

Although, Streptococcus was reported to be the leading cause of infective endocarditis [3,6,26], a change in this trend seems to be occuring across many regions of the world with Staphylococcal infection being reported more commonly. Our study had a culture positivity of 70%. Of this, 26.6% isolated were staphylococci, 16.6% were streptococci. Many Indian studies have reflected this change in profile of the organism[22,25]. In our study we identified some rare pathogens such as Mycobacteria(1), Brucella(1), Burkholderia(2). In our patient with Mycobacterial endocarditis there was a delay in diagnosis which resulted in prolonged morbidity. Yuan Shi-min and others in their study have recommended a high degree of suspicion for diagnosis. [26,,27 28]. One patient in our series was diagnosed with with Brucella endocarditis,involving aortic valve,which was similar to other case report[29,30]. He underwent underwent aortic valve replacement with recommended antimicrobial regimen.2 patients had Melioidosis caused by Burkholderia pseudomallei presenting aortic regurgitation and multiple pseudoaneurysms of the descending thoracic aorta. Apart from a few case reports[31,32,33]no series have been reported. Both patients underwent aortic valve replacements with mechanical valve prosthesis and repair of pseudoaneurysm. One patient died in the post-operative period.

Infective endocarditis, being a systemic disease, causes sepsis and end-organ damage. Leucocytosis, raised creatinine and hyperbilirubinemia are markers of end-organ dysfunction [(20)] . Garg et al[5] and Wallace et al[8] in their study found raised creatinine levels, to be independant predictor of poor prognosis. In contrast, Netzer et al.[33] in their review of 212 patients did not find renal insufficiency to be predictive of mortality. In our study, although 14 (46%) patients had raised creatinine levels, but statistically no significance could be established in relation with mortality.

The studies found impaired liver parameters such as raised bilirubin and aminotransferases to be independent predictors of early post-operative mortality. We found that raised liver parameters were predictive of mortality. Out of 17 patients with elevated AST 8 died (47%), which was statistically significant(p=0.024).Of the 17 patients with elevated AST,14 also had elevated ALT. Of the 14 patients 9 died (64%), which was statistically more significant(P=0.004) than AST.13 patients have raised bilirubin, out of which 5 died, which was statistically insignificant (p=0.294).

The most common indication for surgery in infective endocarditis is heart failure[14], followed by persistent infection and embolization[6,7]. In our study,heart failure (33.3%)was found to be the most common indication for surgery followed by persistent infection(30%).Preoperative heart failure has been found in most of the studies to be an independant marker for mortality[8,34]. In our study there was 70% mortality in patients operated for refractory heart failure. which is higher than other studies, Hasbun et al. (26%), Roder et al. (42%)[8,35]. Such a high incidence of mortality in our study can be attributed to the fact that ours being a tertiary referral centre,most of the times the patients are referred late in the course of disease to our centre. Persistent infection is caused commonly by perivalvular extention. The European Society of Cardiology guideline suggests early surgery in cases of uncontrolled infection[7.] to reduce mortality. Many studies[36,37,38]have suggested the same. In our study we operated on 9 cases for persistent infection of which only one had paravalvular abscess along with native aortic valve involvement. In our study, 25 patients (83.3%) underwent early surgery (emergent and urgent) and of these, 9 patients (36%) died. Reasons attributed for higher mortality than international studies might be the small sample size, poor general condition of patients at presentation.

The valve affected most frequently by this disease is the mitral valve (40-50%), followed by aortic valve (35-39%), tricuspid valve (19%) and pulmonary valve (1.5%-2%). In our study a similar frequency distribution of valves involvement by infective endocarditis was observed. Mitral valve in 40%cases, followed by aortic (36.7%). Both aortic and mitral valves were affected in 16.7% cases. One case each of tricuspid and pulmonary valve involvement was seen. Only one case of

prosthetic valve involvement was seen and the rest were native valve endocarditis (96.6%).

Society of Thoracic Surgeons (STS) guidelines (2011) suggests using either a mechanical or stented tissue valve in the aortic position if the infection is limited to the native aortic valve or to the annulus (Class IIa, level of evidence B). In our study 11(36.7%) patients received isolated aortic valve replacement (mechanical valve in 9 and bioprosthetic valve in 2). 5 more cases had mechanical aortic valves as part of double valve replacement. In case of native mitral valve endocarditis, although STS guidelines recommend repair rather than replacement (Class I, Level of Evidence B)[11,12] in our series, we found only one valve feasible for repair. In most of our cases, extensive disease and moribund preoperative status of the patient did not leave any scope for considering repairs. A total of 17 mitral valve replacements were done(15 mechanical, 2 bioprosthetic). There was only one patient with tricuspid valve involvement, who had dehiscence of VSD patch along with vegetations, which were extending into the right ventricle causing severe tricuspid regurgitation and heart failure. He underwent vegetetectomy, VSD closure, and repair of tricuspid valve by Teflon ring annuloplasty.in accordance with STS guidelines (Class I, Level of evidence B) [11]. Infective endocarditis involving pulmonary valve alone is rare[39] and is reported in about 1.5-2% of hospital admissions for infective endocarditis. Our study had only one patient with pulmonary valve pathology along with aneurysm of the pulmonary artery. The predisposing factor was subaortic VSD.

Post-operative continuing sepsis in spite of adequate cardiac surgery is an important risk factor for in-hospital mortality. In most of the patients the source of sepsis is not the heart. Peripheral mycotic aneurysms can be a potential source of sepsis [3].8 patients had sepsis in our study out of which 4(50%) died. Post-operative 2D-echocardiogram did not show any residual vegetation in the heart. Blood cultures were negative for infective endocarditis. The incidence of permanent pacemaker implantation for atrioventricular block following surgery was reported to be 12% to 15% by Delay and colleagues[39] and to be 24% by Jassal et al[40]. They observed that this was more so the case in patients requiring extensive debridement. In our series we had only 3 patients with heart block. All 3 were put on temporary pacing. 1 patient reverted to sinus rhythm while 2 died of other causes. The in-hospital mortality of infective endocarditis is estimated to vary between 4% and 30%. Most of the western [3,6,9,13] and indian [17,18,19,20]literature report similar in-hospital mortality rates. but the sample size is smaller in Indian studies. The most important adverse prognostic factors reported are old age, prosthetic valve endocarditis, heart failure, paravalvular complication, stroke, and infection with staphylococcus aureus, multiple valve involement, raised bilirubin, aminotransferases, creatinine and leukocytes. Our study had higher in-hospital mortality rate(30%) than that reported in both Indian and western literature. Heart failure and sepsis were the common causes of death in our series. All the non-survivors (30%) in our series had native valve endocarditis.had abnormal liver function test.

Since patients with infective endocarditis have a high risk of mortality, prediction models help in decision making and quality assurance. Mestres et al.[41]. Mokhles et al.[42] in their study of 181 and 138 cases respectively, concluded that both the additive EuroSCORE (European System for Cardiac Operative Risk Evaluation) model and the logistic EuroSCORE model were able to accurately predict the risk of in-hospital mortality in infective endocarditis patients who undergo operative procedures. However, they also observed that the predictive ability of the additive EuroSCORE was better than the predictive ability of the logistic EuroSCORE. In our study, according to EuroSCORE II,15 patients were in the high risk category, out of which 9 patients died. There was no mortality in the low (8 patients) or medium (7) risk category.

CONCLUSIONS:

Chronic rheumatic heart disease is still the major risk factor for infective endocarditis in our country. Staphylococci and streptococci are the predominant microorganisms causing endocarditis. The slightly higher proportion of staphylococcal infection and infective endocarditis due to unusual organisms may point towards a changing profile of infective endocarditis in this region, similar to rest of the world. Preoperative renal failure and deranged liver functions increase the in-hospital mortality apart from higher age and emergent surgery. Valve replacement rather than repair is the procedure of choice due to extensive destruction of the tissue and use of mechanical valve prosthesis is more common than biological prosthesis.Surgery for infective endocarditis still carries a high mortality rate.There is a significant association between elevated liver aminotransferases and mortality. The predictive ability of the additive EuroSCORE is better than the logistic EuroSCORE . Early diagnosis and early surgery, high degree of suspicion for presence of newer organisms, could reduce mortality due to infective endocarditis.

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