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Original article

Clinical – microbiological characterization and risk factors of mortality in infective endocarditis from a tertiary care academic hospital in Southern India

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ABSTRACT

Aims: To dissect the clinical-microbiological profile of Infective endocarditis (IE) population and to determine the risk factors for IE related mortality
Methods: A cohort study was conducted using relevant data from clinical records of patients (≥12 years) with definite/possible IE from December 2007 to December 2013 and was analyzed using appropriate statistical tests.
Results: In the cohort of 139 IE patients, mean age was 47.9 ± 15.8 years, with male preponderance (68.3%). Rheumatic heart disease was the commonest (30.9%) underlying cardiac lesion followed by mitral valve prolapse with mitral regurgitation (23.7%), degenerative valvular disease (23%), congenital heart disease (15.8%) and prosthetic valves (3.6%). Vegetations were detected in 94.2% cases. Blood cultures were positive in 69.8% cases, commonest organism isolated was *α – hemolytic streptococci* (30.9%) followed by *Enterococcus* (12.9%) and methicillin sensitive *Staphylococcus aureus* (10.8%). Complications observed were congestive cardiac failure (31.2%), acute kidney injury (25.9%), stroke (21.6%), septic shock (16.5%), embolic phenomenon non-stroke (8.6%), atrial fibrillation (5%) and ring abscess (2.9%). Mortality rate was 17.3%. Congestive cardiac failure, increase in the peak leucocyte count and stroke were the independent predictors of mortality.
Conclusions: This study reiterates the persistent dominance of rheumatic heart disease in the population studied and α – haemolytic Streptococci as the commonest responsible microorganism.

1. Introduction

Infective endocarditis (IE) is a life threatening disease with high mortality (up to 30%) [1,2] and morbidity.[3,4] From India, mortality rate in completely treated patients of IE has been reported to be over 29%.[5] Mortality in IE is associated with the microorganisms involved,[6] the heart valve infected (native/prosthetic)[7] and other underlying conditions. Despite excellent improvements in the diagnostic and treatment modalities, IE persists with high incidence and mortality. This is reasoned to be due to gradual transformation in epidemiology and risk factors for infective endocarditis such as intravenous drug use, intracardiac devices and health-care associated bacteremia.[2]

Rheumatic heart disease (RHD) as such, is deemed to be a disposing risk factor for IE in developing countries primarily[8] but infrequently in industrialized and developed countries.[2] India alone contributes about 25–50% of global burden of RHD[9]. While IE with underlying chronic RHD previously a hallmark disease in children and young adults, now IE is frequently being observed in new risk groups of industrialized urban world, including intravenous (IV) drug users of older age (>40 years)[10], patients with prosthetic valves & intravenous catheters, patients undergoing hemodialysis, and elderly people (>65 years) with degenerative valve lesions.[2] Although *Staphylococci* and *Streptococci* account for majority of the cases, there have been reports of rise in staphylococcal dermal commensal causing iatrogenic nosocomial infection, *Staphylococcus aureus* affecting intravenous drug users,

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and *Streptococcus bovis* (*Streptococcus gallolyticus*) in the elderly, often associated with underlying gastrointestinal neoplasia.[4] Furthermore, previously undetected pathogens are now being identified with the disease,[6,11] and multidrug resistant bacteria are challenging conventional antibiotics.[6]

In view of changing face of infective endocarditis across the world, a renewed evaluation of this mediaeval illness is compulsory. This study was aimed to dissect the clinico-microbiological profile of IE population served by the Kasturba Hospital, Manipal, India and to determine the risk factors for IE related mortality.

2. Methods

2.1. Study design and population

We conducted a hospital based retrospective cohort study among patients diagnosed with definite/possible IE as per the modified Duke's criteria,[12] aged ≥12 years admitted to the Kasturba Hospital, Manipal, Karnataka, India from December 2007 to December 2013. In order to estimate the mortality rate at 30% with an absolute precision of 8% and drop out of 5%, a minimum of 138 IE patients were to be enrolled in the cohort.

2.2. Ethics statement

Ethical approval (IEC 88/2014) for the study was obtained from the Kasturba Hospital and Kasturba Medical College, Manipal ethics committee prior to commencing the study. Retrospective study design deemed patients' consent redundant. Nonetheless, all patients' identifications were turned incognito during data abstraction and database configuration.

2.3. Patients' screening, blood culture and echocardiography

Relevant data on in-depth history assessment, clinical examination and necessary laboratory investigations were extracted from the hospital records. Results of blood culture were captured form the hospital records. Venous blood sample (Three sets of blood culture with 10 ml/bottle from three different sites at 1 h interval prior to administration of empiric broad spectrum antibiotics) collection was done in BacT/Alert, Biomerieux Diagnostic's blood culture bottles in sterile condition. Blood culture was done using BacT-ALERT 3D automated microbial detection system (bioMérieux, Marcy l'Etoile, France), and growth of *S. aureus* was identified according to standard laboratory procedures. Antimicrobial susceptibility was tested in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines by Kirby–Bauer disk diffusion method.[13] Transthoracic and trans-esophageal echocardiography (TTE & TEE) were done by VINGMED System V, Wipro GE Medical Systems echocardiography machine in the Department of Cardiology, Kasturba Medical College, Manipal University, Manipal, India.

2.4. Treatments

Provisionally on presentation, majority of patients were administered empiric broad-spectrum antibiotics. Later on patients were switched over to suitable antibiotics in accordance with their antibiotic susceptibility reports and as per standard recommendation.[14]

2.5. Statistical analyses

Categorical variables were summarized as frequency with proportion and compared using chi-square test. Continuous variables were tested for normality by Kolmogorov-Smirnov test. Normally distributed variables were summarized as mean with standard deviation and compared by either independent *t*-test or one way ANOVA. Skewed variables were summarized as median with interquartile range and compared by either Mann Whitney *U* test or Kruskal-Wallis H test. Univariate logistic regression analysis was performed for determining the odds of factors associated with mortality. Variables having p-value < 0.20 in univariate logistic regression was analyzed through multivariate logistic regression using forward Wald method. All tests of significance were two sided and the level of significance was set at 95%. All analysis was done using Statistical Package for the Social Sciences (SPSS v15.0) Bangalore, India.

3. Results

3.1. Demographics

A total of 139 IE cases comprising of 95 (68.4%) definite IE and 44 (31.6%) possible IE were included in the study. Mean age of the study population was 47.9 ± 15.8 years. The population comprised of 35.2% (47) young (≤40 years), 51.1% (71) middle aged (41–64 years) and 13.7% (19) elderly (≥65 years). Male to female ratio was found to be 2.2: 1 (95 male: 44 female).

3.2. Predisposing cardiac lesions

RHDs were the most frequent predisposing lesions followed by mitral valve prolapses with mitral regurgitations, degenerative valvular diseases, congenital heart diseases and prosthetic valves involvement (Table 1).

3.3. Clinical features and echocardiographic findings

Fever (axillary temperature >37.5 °C) was most frequent followed by murmur, pallor, dyspnea, splenomegaly, history of weight loss, neurologic deficit, clubbing, complaint of chest pain, splinter hemorrhage, purpura, Roth's spot and Janeway lesions (Table 2). While all patients had undergone TTE, TEE was done in 23% (32/139) patients. These included one case of aortic mechanical prosthetic valve, and patients in whom TTE was inconclusive. Of 94.2% patients with vegetations, those attached with mitral valve was most common followed by aortic, both aortic & mitral, tricuspid, and pulmonary valves. Prosthetic valve vegetations were recorded with 3.05% (4/131) patients. Majority of vegetations were gauged between 5 and 10 mm (47.3%, 62/131) and over 10 mm (35.1%, 46/131). There was no association between vegetation sizes and organisms isolated from blood culture ($\chi^2 = 10$, df = 9, p = 0.24).

3.4. Complications

Most frequent complications noted were congestive cardiac failure followed by acute kidney injury, stroke, septic shock, embolic phenomenon-non stroke, atrial fibrillation and ring abscess (Table 2). Atrial fibrillation was noted in 58.3% (7/12) patients with embolic phenomenon. Of total 3 cases with embolic phenomenon among atrial fibrillation cases, both stroke and embolic phenomenon (multiple splenic infarcts) occurred in one patient, whereas in another two cases, one presented with stroke alone and another with embolic phenomenon (septic embolism to spleen). The embolic phenomena included 8 patients with cerebrovascular accident, 2 patients with lower limb arterial occlusion, 1 patient with splenic infarct and 1 with amaurosis fugax. One patient with pulmonic valve endocarditis had bilateral bronchopneumonia. Embolic phenomena were noted among 50%

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