



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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ARTICLE INFO

Article history:

Received 1 June 2017

Accepted 10 August 2017

Available online 16 August 2017

Keywords:

Infective endocarditis

α – Hemolytic streptococci

Rheumatic heart disease

Mitral regurgitation

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 – hemolytic *Streptococci* as the commonest responsible microorganism.

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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 IE 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 primarily⁸ but infrequently in industrialized and developed countries.² India alone contributes about 25–50% of global burden of RHD⁹. 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 and 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 IE across the world, a renewed evaluation of this medieval 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 from 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 transesophageal 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 $p < 0.20$ 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 $>37.5^\circ\text{C}$) 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 and 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%

Table 1

Predisposing cardiac lesions of the study cohort (N = 139).

Predisposing cardiac lesions	No. of patients (%)
Rheumatic heart disease (RHD)	
• Mitral and aortic regurgitation – 15	43 (30.9)
• Mitral regurgitation alone – 17	
• Aortic regurgitation alone – 3	
• Mitral stenosis – 6	
• Aortic stenosis – 1	
• Mitral/aortic stenosis – 1	
Mitral valve prolapse with mitral regurgitation	33 (23.7)
Degenerative valvular diseases	
• Sclerotic aortic valve – 8	32 (23.0)
• Aortic and mitral valve regurgitation – 11	
• Degenerative aortic regurgitation – 6	
• Degenerative mitral regurgitation – 7	
Congenital heart disease	
• Bicuspid aortic valve – 11	22 (15.8)
• Ventricular septal defect – 4	
• Patent ductus arteriosus – 2	
• Atrial septal defect – 1	
• Aortic regurgitation – 4	
Prosthetic valve	5 (3.6)
No predisposing cardiac lesion	4 (2.9)

(6/12) subjects with vegetation sizes between 5 and 10 mm. The risk of embolism among patients with vegetation size over 10 mm was estimated to have 1.1 relative risk (RR), 95% confidence interval (CI) = 0.49, 2.51, whereas for size between 5 and 10 mm RR was 0.99, 95% CI = 0.56, 1.74. The organism type had no association with the occurrence of embolism ($\chi^2 = 5.8$, $df = 3$, $p = 0.18$).

3.5. Disease outcomes (Table 2)

Mortality was noted among 17.3% (24/139) patients. Death occurred due to various complications viz. septic shock, cardiogenic shock, and acute respiratory distress syndrome with multiorgan dysfunction, aspiration pneumonia, congestive cardiac

Table 2

Clinical features of the study cohort (N = 139).

Clinical features	No. of patients (%)
Fever	112 (80.6)
Murmur	104 (74.8)
Pallor	97 (69.8)
Dyspnea	55 (39.6)
Splenomegaly	48 (34.8)
Weight loss	35 (25.2)
Neurological deficit	30 (21.6)
Clubbing	26 (18.7)
Chest pain	12 (8.6)
Splinter hemorrhages	5 (3.6)
Purpura	4 (2.9)
Roth's Spots	2 (1.4)
Janeway Lesions	2 (1.4)
Complications	
Congestive cardiac failure	43 (31.2)
Acute kidney injury (Serum creatinine >1.6 mg/dL)	36 (25.9)
Stroke	30 (21.6)
Septic shock	23 (16.5)
Embolic phenomenon, non – stroke	12 (8.6)
Atrial fibrillation	7 (5.0)
Ring abscess	4 (2.9)
Echocardiographic findings	
Vegetations	131 (94.2)
Vegetation site	Mitral (80), Aortic (27), Aortic & Mitral (9), Pulmonary (3), Tricuspid (8) and Prosthetic (4)
Vegetation size	<5 mm (7), 5–10 mm (62), >10 mm (46), not recorded (16)
Outcomes	
Survival	98 (70.5)
Mortality	24 (17.3)
Discharge against medical advice (DAMA)	17 (12.2)

failure and pulmonary oedema. *Enterococcus*, methicillin sensitive *Staphylococcus aureus*, α – hemolytic streptococci, *Acinetobacter* species, *Brucella*, β -hemolytic streptococci, and *E. coli* were isolated among 4 (16.7%), 3 (12.5%), 2 (8.3%), 2 (8.3%), 1 (4.2%), 1 (4.2%), and 1 (4.2%) deceased cases, respectively.

3.6. Comorbidities

Premorbidity profile included diabetes mellitus, hypertension, ischemic heart diseases, chronic kidney diseases, tuberculosis, and HIV, rheumatoid arthritis, Marfan's syndrome, bronchial asthma, carcinoma and seizure disorder. One patient with Marfan's syndrome had undergone tricuspid and mitral valve annuloplasty 12 years prior to admission for mitral and tricuspid regurgitation and presented with endocarditis involving the mitral valve. Another patient with predisposing cardiac condition had remnant of a pacemaker lead implanted into the right ventricular endocardium. No history of invasive procedures including dental procedures or invasive diagnostic techniques involving genitourinary tract or gastrointestinal tract was obtained in any of the cases. No septic foci which could potentially be the source of the infecting organism were identified in any of the patients. Notably, no case of intravenous drug abuse leading to endocarditis was found.

3.7. Etiological organism and time to initial presentation

Organisms were isolated from 69.8% of cases. α – hemolytic streptococcus was the commonest organism isolated followed by *Enterococcus*, methicillin sensitive *S. aureus* and others (Table 3). Majority of patients (62.6%, 87/139) presented within one month of initiation of symptoms. Methicillin sensitive *S. aureus* resulted in significantly ($p=0.02$) prolonged presentation than α – hemolytic streptococci. (Table 4)

3.8. Blood culture positive and negative cohort's comparison

There was no difference in predisposing cardiac lesions, clinico-laboratory findings, vegetation characteristics, complications and mortality between blood culture positive and negative groups of endocarditis. However, mean age of positive blood culture group was significantly ($p=0.03$) high.

3.9. Treatments

All patients received pharmacological treatments as per the clinical judgement of clinicians and antimicrobial susceptibility profiles of respective patients. Additionally, 3.6% (5/139) patients

Table 3
Blood culture and antibiotic susceptibility profile of 139 IE patients.

Organisms isolated →	SV	ES	MSSA	CONS	PA	SS	AS	EC	NVS	BHS	LS	GM	ML	SG	MRSA
No. of isolates (%) →	43 (30.9)	18 (12.9)	15 (10.8)	3 (2.2)	2 (1.4)	2 (1.4)	2 (1.4)	2 (1.4)	2 (1.4)	1 (0.7)	1 (0.7)	1 (0.7)	1 (0.7)	1 (0.7)	1 (0.7)
↓ Antibiotics tested and their susceptibility (n/N, where n is number of 'susceptible' isolates out of N i.e. total number of isolates tested)															
Chloramphenicol	12/12	6/6	–	–	0/1	–	–	–	1/1	–	–	–	–	0/1	–
Penicillin	7/7	3/3	0/1	–	–	1/1	–	–	1/1	–	–	–	–	1/1	–
Amoxicillin	12/12	8/11	3/7	0/1	0/1	1/1	0/1	0/2	1/1	1/1	1/1	–	1/1	1/1	1/1
Ampicillin	7/8	1/1	0/4	–	0/1	1/1	–	–	–	–	–	–	1/1	–	–
Amoxiclav	1/1	–	3/3	–	–	–	–	–	–	–	–	–	–	–	0/1
Cloxacilin	1/1	0/1	6/6	0/1	0/1	–	–	–	–	–	–	–	–	–	–
Cefuroxime	–	1/1	–	–	–	–	–	0/1	–	–	–	–	1/1	–	–
Cefotaxime	4/5	–	–	–	–	2/2	1/2	–	–	–	–	–	1/1	–	–
Ceftriaxone	5/6	–	–	–	–	1/1	1/2	–	1/1	–	–	–	–	–	–
Cefazoline	8/8	–	8/8	0/1	–	1/1	–	0/1	–	–	0/1	–	1/1	1/1	0/1
Ceftazidime	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–
Cefepime	–	–	–	–	–	–	0/1	0/2	–	–	–	–	–	–	–
Cefadroxil	5/5	–	1/1	–	–	–	–	0/1	–	–	–	–	–	–	0/1
Cefaperazone-sulbactam	1/1	0/1	2/2	–	0/1	1/1	0/1	1/1	–	–	–	–	–	–	–
Piperacillin-Tazobactam	1/1	0/1	1/1	–	0/1	–	0/1	2/2	–	–	–	–	–	–	–
Trimethoprim-Sulfamethoxazole	3/5	0/4	8/8	1/1	–	1/1	0/1	1/2	–	–	–	–	1/1	–	1/1
Amikacin	1/1	–	4/4	–	0/1	–	1/1	–	–	–	–	–	1/1	–	1/1
Gentamycin	11/15	10/12	7/8	0/1	0/1	2/2	1/2	1/2	1/1	1/1	1/1	–	1/1	1/1	1/1
Doxycycline	19/21	3/11	7/7	1/1	–	2/2	–	1/1	1/1	1/1	1/1	–	–	0/1	1/1
Ciprofloxacin	12/15	3/10	2/7	1/1	0/1	2/2	0/1	0/2	1/1	1/1	1/1	–	1/1	1/1	0/1
Levofloxacin	–	–	–	–	0/1	–	–	–	–	–	–	–	–	–	–
Clindamycin	2/3	–	5/5	1/1	–	–	–	–	–	–	–	–	–	–	–
Vancomycin	5/5	5/5	3/3	1/1	–	–	–	–	–	–	0/1	1/1	–	–	1/1
Teicoplanin	1/1	4/4	1/1	1/1	–	–	–	–	–	–	0/1	–	–	–	–
Linzolid	1/1	5/5	1/1	1/1	–	–	–	–	–	–	–	1/1	–	–	–
Netilmycin	–	0/2	–	–	0/1	–	1/2	1/2	–	–	–	–	1/1	–	–
Erythromycin	16/17	1/7	3/5	0/1	–	1/1	–	–	1/1	–	1/1	–	–	0/1	–
Tetracycline	2/2	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Colistin	–	–	–	–	1/1	–	1/1	–	–	–	–	–	–	–	–
Imipenem	1/1	–	–	–	0/1	–	0/1	–	–	–	–	–	–	–	–
Aztreonam	–	–	–	–	–	–	0/1	–	–	–	–	–	–	–	–
Rifampicin	–	–	1/1	1/1	–	–	–	–	–	–	–	–	–	–	1/1

Note: Number of isolates having either partially or full resistant to respective antibiotics are shown in bold-italic face.

SV-*Streptococcus viridans*, MSSA-Methicillin sensitive *Staphylococcus aureus*, ES- *Enterococcus species*, BS-*Brucella species*, PA-*Pseudomonas aeruginosa*, CONS-Coagulase negative *Staphylococcus aureus*, SS- *Streptococcus sanguis*, BHS- β -hemolytic *Streptococci*, LS-*Lactobacillus species*, GM-*Gamella morbillorum*, ML-*Moraxella lacunata*, AS-*Acinetobacter species*, EC-*Escherichia coli*, SG-*Streptococcus gordonii*, NVS-Nutritionally variant *Streptococcus*, CS-*Candida species*, MRSA-Methicillin resistant *Staphylococcus aureus*.

Table 4

Comparison between etiologic organism and time to initial presentation.

Organism	Time to initial presentation. (Median Days)	Interquartile range (IQR)	p value*
α – Hemolytic streptococci	15.0	(9.8, 22.5)	–
<i>Enterococcus</i>	15.0	(14, 39)	1.00
Methicillin Sensitive <i>Staphylococcus aureus</i> (MSSA)	60.0	(21.3, 75.0)	0.02
Others	25.0	(11.0, 60.0)	0.31

* As compared to α – Hemolytic streptococci (Significant p-value i.e. <0.05 is shown in bold face).

had to undergo surgical intervention (mitral valve replacement). Underlying complications which mandated surgical interventions included one patient with congestive cardiac failure, another one with embolic phenomenon-non stroke, another with both congestive cardiac failure and stroke, another one with congestive cardiac failure, atrial fibrillation, septic shock and acute kidney injury and one more patient with atrial fibrillation and embolic phenomenon non-stroke. Microbiologically each one of those five patients was having endocarditis due to methicillin sensitive *S. aureus*, *Enterococcus species*, *Pseudomonas aeruginosa*, *E. coli* and sterile endocarditis. The length of treatment in the hospital varied depending on the organism and the course of events during the hospital stay. Ceftriaxone (33.1%, 46/139) and gentamicin (30.2%, 42/139) were the most frequently used antibiotics for duration of 2–6 weeks. α – hemolytic streptococci cases were most frequently treated with ceftriaxone (69%, 29/42) and gentamicin (71.4%, 30/42). *Enterococcus species* were most frequently treated with gentamicin (72.2%, 13/18) and ampicillin (55.6%, 10/18). Methicillin sensitive *S. aureus* were treated variably with various antibiotics viz. teicoplanin, cloxacillin, vancomycin, doxycycline, meropenem etc. Additionally, clinically reserved antimicrobials viz. vancomycin, linezolid, piperacillin-tazobactam, meropenem, teicoplanin and colistin were administered among 17.3% (24/139) cases. Two cases of brucellosis were successfully treated with doxycycline (6 months) and gentamicin (3 weeks). Repeat echo after 2 weeks was done in all patients and showed decrease in the size of vegetations or increased echogenicity suggesting healing.

3.10. Risk factors of mortality

On univariate logistic regression analysis, degenerative aortic regurgitation, increase in the peak leucocyte count, congestive cardiac failure, stroke and septic shock were found to result in higher odds of mortality. Increasing age turned out to have reverse relation showing lesser odds of mortality. Organisms other than α -hemolytic streptococci, methicillin sensitive *S. aureus* and *Enterococcus species* were shown to result in higher odds [odds ratio 7.71, 95% CI (1.32–45.00)] of mortality with respect to α -hemolytic streptococci. Vegetations at both aortic and mitral valve had significantly higher odds [5.63 (1.02–30.90)] of mortality

than vegetations at aortic valve alone. Other site vegetations were not associated with mortality. Multivariate logistic regression analysis brought out the independent associations of increase in the peak leucocyte count, congestive cardiac failure and stroke with mortality by significantly higher odds. (Table 5)

4. Discussion

Under the impression of changing clinico-microbial epidemiology of endocarditis,^{4,9,15,16} the preponderant clinico-microbiologic features and risk factors of mortality in IE patients admitted at the Kasturba Hospital, Manipal were determined.

The IE cohort of the present study was contrastingly younger than those of previous studies from outside India.^{17,18} Nonetheless, recent studies from both northern^{5,19,20} and southern India²¹ had remarkably younger (by about two decade) adults than current study in their study population. Furthermore, the proportion of elderly patients (>65 years) among our study group was found to be 13.7%, whereas it was reported to be about 50% in other series.^{3,17,22} Increase in mean age of IE patients may be due to either rise in elderly proportion among general population or due to decline in RHD as risk factor.²³ However, relatively younger age of our cohort may be due to the predominance of RHD as the underlying etiology of IE in the current study. In agreement with current study, RHD as the most commonly occurring cardiac lesion has been reported by other recent Indian studies as well.^{5,20,21} Prevalence of RHD in India has not been assessed all over the country uniformly and is reported to be on decline in few parts of country while in majority of India it continues to predominate.^{9,21}

Median duration of presentation to the hospital was 15 days with 62.6% (87/139) patients presenting in ≤ 30 days, which is very similar as Murdoch et al.¹⁷ Socioeconomic factors are likely to be responsible for the delay in presentation. Also, since the present study was conducted in a tertiary care center, in most cases this would not have been the first point of care for the patients. In this study occurrence of majority of native valve, community acquired IE cases without any intravenous drug user and nosocomial IE may have translated into: a high proportion of streptococci and a relatively low proportion of staphylococci. Fever was the commonest symptom on presentation, which is also in agreement with

Table 5

Univariate and multivariate logistic regression analysis for factors associated with mortality (N = 24).

Variables	Frequency (%)	Odds ratio (95% CI)	p-value	Adjusted odds ratio (95% CI)	p-value
Age (years)	41 \pm 16.7 ^a	0.96 (0.93–0.99)	0.01	0.96 (0.92–1.00)	0.05
Mitral valve prolapse with mitral regurgitation	2 (8.3)	0.24 (0.05–1.09)	0.06	Went out of equation	
Aortic regurgitation alone	2 (8.3)	8.81 (0.77–101.65)	0.08	Went out of equation	
Degenerative aortic regurgitation	3 (12.5)	6.86 (1.08–43.63)	0.04	Went out of equation	
Fever duration (days)	7.5 (3.8,15)	0.98 (0.95–1.00)	0.08	Went out of equation	
Peak leucocyte count/1000 (cells/mm ³)	19400 (13200,24000) ^a	1.20 (1.10–1.31)	<0.001	1.17 (1.04–1.31)	0.01
Congestive cardiac failure	17 (70.8)	7.92 (2.92–21.45)	<0.001	7.35 (1.84–29.30)	0.01
Stroke	9 (37.5)	3.08 (1.15–8.23)	0.03	4.34 (1.10–17.11)	0.04
Septic shock	9 (37.5)	3.98 (1.47–10.78)	0.01	Went out of equation	
Acute kidney injury	9 (37.5)	1.96 (0.76–5.06)	0.17		

*Confidence intervals which do not overlap the null value of odds ratio i.e. 1 are shown in bold face and respective p-value < 0.05 are shown in bold face.

^aContinuous variable are summarized as either mean \pm standard deviation or median (interquartile range).

other series.^{20,21} Murmur was found to be the most common sign on examination in 74.8% of our study patients, but 64% by Murdoch et al.¹⁷ and 72.3% by Nashmi et al.²⁴ Congestive cardiac failure was the most frequent complication in the present study as previously reported by Jain et al.⁵

Proportion of vegetations detected by TTE in present study was fairly higher (94.2%) than another recent report (70%) from India [21]. Mitral and aortic valves are the most commonly affected valves as evident from the current study and reports from other parts of India.^{17,21}

Positive blood culture yield in the present study (69.8%) was lower than the rate of over 88% reported by Hill et al.³ but similar to Garg et al.²⁰ and Nashmi et al.²⁴ Proportion of culture yield is exceptionally higher than other recent series from India.^{5,21} Like several reports from developing countries present study also shows an increased proportion of streptococcal endocarditis.^{15,25} The high positive blood culture yield in the present study can be attributed to the high index of suspicion for diagnosis of IE along with prompt collection and transfer of blood samples. Use of current generation high throughput automated analyzer is one of the contributing factors for such good blood culture yield in this study. Further, in contrast to several reports from developed countries which showed a predominance of staphylococcal endocarditis^{3,7}; current cohort had lower proportion of staphylococcal endocarditis. Two cases of Brucella endocarditis were found in middle-aged farmers (1 male and 1 female) with exposure to cattle, which is typical of the demographic profile associated with etiologic organism. Both patients were successfully treated by medication alone (doxycycline with gentamicin), and were asymptomatic at 6 month follow up with echocardiogram showing healed vegetations. Very few cases of Brucella endocarditis have been reported to be treated successfully by medication alone and majority required surgical intervention in addition to medication. Brucella endocarditis generally involves aortic valve,²⁶ but in patients of the current study one had mitral valve and other had tricuspid valve involvement. *Pseudomonas aeruginosa* is a rare cause of infective endocarditis,²⁷ mostly occurs in intravenous drug abusers.²⁸ The single case of *Pseudomonas aeruginosa* endocarditis was noted in a female patient with a foreign body embedded in the right ventricular endocardium after incomplete removal of a temporary pacemaker. This patient was referred to another center for the necessary surgical intervention and removal of this foreign body. She was subsequently lost to follow up. Failure to obtain a positive blood culture in IE setting often results due to prior antibiotics consumption by patients, or due to presence of nonculturable organisms.¹¹ A few unusual and nonculturable etiologic agents of endocarditis have been brought into light from across the globe.^{11,29} As the unsought goes undetected, it might be possible that unusual organisms within the study population would have been missed out due to retrospective design of the current study. Future studies should perform both molecular and serological investigations to dissect the more appropriate microbial epidemiology in IE.

Similar to current study, congestive cardiac failure has been found to be the most common risk factor for mortality in other studies as well.^{5,19,30} Septic shock was the only independent risk factor of mortality as reported by Math et al.¹⁹ Although septic shock was significant on univariate analysis along with peak leucocyte count in the current study, multivariate analysis brought out peak leucocyte count to be independently associated with mortality which is an evidence of severity of inflammation and underlying sepsis. In addition to congestive cardiac failure, renal failure, neurological complications, age <20 years and sepsis were independent predictors of mortality as reported by Jain et al.⁵ The current study reinforces independent association of stroke with mortality.

Strengths of this study include robust statistical analysis, comparably higher sample size than recent studies^{5,19,21} and remarkably high blood culture yields. Retrospective study design poses its characteristic limitations on this study. Single center tertiary care setting renders the study cohort less representative of the general community. Future studies must try to overcome the aforesaid limitations.

To conclude, RHDs, mitral valve prolapses with mitral regurgitations, degenerative valvular diseases and congenital heart diseases are the frequently occurring predisposing cardiac lesions among IE patients. α – *hemolytic streptococci* are the commonest etiologic microorganisms. Morbidity and mortality remain high. Peak leucocyte count, congestive cardiac failure and stroke were the independent predictors of mortality.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

KS, JVM and AK conception and design, JVM, SP and GM acquisition of data, KS, JVM and AK analysis and interpretation of data, KS, JVM, SP, RS and GM drafting the manuscript, KS revising it critically for important intellectual content. All authors have given final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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