J Cardiovasc Disease Res., 2017; 8(2):56-60
A Multifaceted Peer Reviewed Journal in the field of Cardiology
www.jcdronline.org | www.journalonweb.com/jcdr

Original Article

Changing Trends of Infective Endocarditis in India: A South Indian Experience

Kundavaram Paul Prabhakar Abhilash[1], Shalom Patole[1], Mohan Jambugulam[1], Sowmya Sathyendra[1], Shubhanker Mitra[1], Grace Rebekah[2], Bijesh Yadav[2], Balaji Veeraraghavan[3], Ooriapadickal C. Abraham[4]

[1]Department of General Medicine, Christian Medical College, Vellore, Tamil Nadu, INDIA.
[2]Department of Biostatistics, Christian Medical College, Vellore, Tamil Nadu, INDIA.
[3]Department of Microbiology, Christian Medical College Vellore, Tamil Nadu, INDIA.
[4]Department of Medicine, Christian Medical College Vellore, Tamil Nadu, INDIA.

ABSTRACT

Background: Infective endocarditis (IE) is an important cause of morbidity and mortality. The pattern of the disease in terms of the host, agent and the environment appears to be changing globally. **Methods:** Patients admitted to a tertiary care center in South India between 2005 and 2015 with definite IE, as confirmed by the modified Duke's criteria were included in this retrospective analysis. We analyzed the demographic, microbiological and survival data and compared our results with similar studies done in India over the last 3 decades to assess the changing pattern of IE. **Results:** 172 patients were diagnosed to have definite IE based on modified Duke's criteria. The mean age of the patients was 41.8 ± 14.2 years, and there was a male predominance (78.4%). Culture positive endocarditis was seen in 83.7 %. Streptococcus species was the predominant etiological agent (44.7%) followed by staphylococcal species (16.8%), enterococcus (9.8%) and gram negative bacteria (9.3%). Native valve endocarditis was seen in 87.8% of patients while prosthetic valve and pacemaker endocarditis was seen in 10.4% and 1.7% respectively. Mitral valve was the most commonly affected valve (52.9%), followed by the aortic valve (23.2%). Multiple valves were involved in 9.3% of patients. Vegetations on the valves were seen in 88.9% of patients. The in-hospital mortality rate was 23.8%. Infection with staphylococcal species, complications of congestive cardiac failure and septic shock were associated with a poor outcome in terms of survival. **Conclusion:** The disease profile of patients has undergone a change with an increase in mean age and a higher percentage of streptococcal endocarditis. The yield of blood culture has almost doubled over the last three decades. Despite significant advances in medical technology over the last 3 decades, mortality rate remains the same.

Key words: Infective endocarditis, India, Changing trends, Native valve endocarditis.

Correspondence
Dr. Kundavaram Paul Prabhakar Abhilash,
Assistant Professor, Department of GeneralMedicine, Christian Medical College, Vellore 632 004, Tamil Nadu, INDIA.
Mobile No: 91-9994924743
E-mail address: kppabhilash@gmail.com

Submission Date: 05-12-2016;
Revision Date: 26-12-2016;
Accepted Date: 26-01-2017.
DOI : 10.5530/jcdr.2017.2.13

INTRODUCTION

Infective endocarditis (IE) is an infection of the endothelial surface of the heart or intravascular and intra- cardiac devices like prosthetic valves and pacemaker cables. IE can be classified according to location of endocarditis, the presence or absence of intra-cardiac devices or prosthetic valves and mode of IE acquisition (nosocomial, community-acquired or intravenous drug use related). There are wide geographic variations in the risk factors and etiology of IE. In industrialized countries, more than 50% with IE have normal heart valves, while less than 10% have rheumatic heart disease.[1-3] Three previous studies from India have shown rheumatic heart disease (RHD) to be the most common underlying cardiac condition for IE in the developing world (40-45%).[4-6] However, the prevalence of RHD in India has decreased significantly over the past few decades.[7, 8] With the decrease in prevalence of the most common risk factor for IE, we expected the clinical presentation, microbiological profile and clinical outcome to have changed over the last few decades. The rate of culture positivity is higher in industrialized countries (60-80%) compared to developing countries (40-60%) like India.[1,4] With globalization and improvement in healthcare and per capita income, access to healthcare has improved, and with the advent of better diagnostic techniques like transesophageal echo (TEE) and improved culture methods, the risk factors and microbiological etiology of IE is likely to have changed. We therefore studied the profile and outcome of IE patients presenting to our hospital over a eleven year period and compared our results with studies done over the last three decades.

METHODOLOGY

This study was done in Christian Medical College, Vellore, a 2700-bed tertiary care referral hospital between January 2005 and December 2015. The records of all adult patients (age >16 years) admitted with a definite diagnosis of IE according to the modified Duke criteria during the study period were retrospectively reviewed after obtaining approval of the institutional review board. Baseline demographic data on age, sex, underlying heart disease and predisposing conditions for bacteremia (e.g: infections, central venous catheters, surgeries, invasive procedures) were collected and the echocardiographic and microbiological findings, complications, treatment and outcome were noted. All blood cultures done for diagnosis of IE were processed by standard methods to identify bacterial and fungal species and antimicrobial susceptibility profiles. For all the patients in this study, blood (5-8 ml per bottle) was collected in adult blood culture bottles (BacT®/Alert) using standard precautions and processed by semi-automated blood culture system (BacT®/Alert; BioMérieux, Marcyl' Etoile, France). Identification of the causative organisms was performed by standard microbiological methods. Transthoracic and/or transesophageal echocardiography were performed to determine location of vegetation, type of valve infected, and cardiac complications.

Statistical methods

The data were entered into a pre-designed clinical research proforma, and then transferred in to the Microsoft excel (version 17). It was analysed using Statistical Package for Social Sciences software for Windows (SPSS Inc. Released 2007, version 16.0. Chicago). Continuous vari-

ables are presented as mean (standard deviation) or as median (range) depending upon the distribution of the data. Categorical and nominal variables are presented as percentages. Chi-square test or Fisher exact test was used to compare dichotomous variables and T-test or Mann-Whitney test was used for continuous variables as appropriate. The association of clinical and laboratory features to the outcome were analysed by univariate analysis and a two-sided p value < 0.05 was considered statistically significant.

This study was approved by the Institutional Review Board of Christian Medical College, Vellore (IRB Min No:8325 dated 01.06.2013) and patient confidentiality was maintained using unique identifiers.

RESULTS

The study cohort contained 172 cases of definite Duke's IE admitted during the study period. The mean age of the patients was 41.8 ± 14.2 years and there was a male predominance (78.4%). The median duration of fever prior to presentation was 60 days (Interquartile range (IQR)20,120). Only 16.8 % of patients had a definite source or focus identified for the bacteremia. Native valve endocarditis was seen in 87.8% of patients while prosthetic valve and pacemaker endocarditis was seen in 10.4% and 1.7% respectively. Only 23.2% (40/172) were aware of an underlying RHD while 44.1% (76/172) of patients had a previously undiagnosed cardiac condition at presentation. After evaluation, 30 of them were determined to have RHD. Overall, RHD was the predisposing cardiac condition in 40.6% (70/172) of patients, while 13.9% had congenital heart disease and 2.9% had a mitral valve prolapse. Most of the patients (83.1%) had left sided endocarditis. The baseline characteristics are shown in Table 1.

Mitral valve was the most commonly affected valve (52.9%), followed by the aortic valve (23.2%). Multiple valves were involved in 9.3% of patients. Vegetations on the valves were seen in 88.9% (153/172) of patients. Transthoracic echocardiography (TTE) identified vegetations in 69.7% of patients. TEE was done in 51 patients and vegetations were seen in 94.1% of them. Among the 18 patients with PVE, the diagnostic rate of a TTE was only 50% and the rest required a TEE for demonstration of vegetations.

Blood cultures were positive in 83.7% of the patients. The number of blood cultures taken ranged from 3-16. An average of 4 blood cultures were taken per patient. Common organisms were *Streptococcus* species (44.7%), *Staphylococcus* species (16.8 %), *Enterococcus species* (9.8%) and gram negative bacteria [GNB] (9.3%). Infection due to methicillin resistant *staphylococcus* comprised 52% of the *staphylococcal* isolates. (Table 2) Among those with PVE, 37.5% (6/16) were due to GNB infections. We found GNB IE to be significantly associated with prosthetic valves (Odds ratio: 7.2; 95% CI: 2.2-23.2).

The in-hospital mortality rate was 23.8% (41/172). This included 4 patients who left against medical advice due to poor prognosis and deteriorating medical condition. Embolic phenomenon were seen in 38.3%, splenic abscess in 10.4%, congestive cardiac failure(CCF) in 21.5% and septic shock in 11% of patients. The cause of death was thought to be CCF in 58.5% and septic shock in 46.3%. Surgical intervention was done in only 27 patients (15.7%) though most of the patients were advised surgery. The predictors of mortality were explored using univariate analysis. Significant factors associated with mortality were infection with staphylococcal species, complications of congestive cardiac failure and septic shock. (Table 3) We compared our study with studies done in similar tertiary care hospitals the past 3 decades in India. (Table 4)

Table 1: Baseline characteristics (N=172)

Variable	Number (N=172)
Age (years)	41.8 ± 14.2
Male sex (%)	135 (78.4)
Median duration of illness (days)	60 (IQR: 20, 120)
Co-morbidities	Number **(%)**
Diabetes mellitus	31 (18)
Hypertension	24 (14)
Chronic renal failure	10 (5.8)
HIV infection	4 (2.3)
Pregnancy	6 (3.4)
Underlying cardiac condition	Number **(%)**
Known RHD	40 (23.2)
Previously undiagnosed cardiac condition	76 (44.1)
Congenital heart disease	24 (13.9)
Prosthetic valve	18 (10.4)
Pace maker	3 (1.7)
Side of the heart involved (%)	Number **(%)**
Left sided endocarditis	143 (83.1)
Right sided endocarditis	15 (8.7)
Bilateral and others	14 (8.1)
Culture positivity (%)	144 (83.7)

Table 2: Microbiological etiology of IE

Organism	Number (%)
Streptococcus species	**77 (44.7)**
Alpha haemolytic streptococcus	47
Non haemolytic streptococci	11
Nutritionally variant streptococci	9
Beta haemolytic streptococci	4
Non identifiable streptococci	6
Staphylococcus species	**29 (16.8)**
Methycillin sensitive staphylococcus aureus (MSSA)	8
Methycillin resistant staphylococcus aureus (MRSA)	15
Coagulase negative staphylococci	6
Enterococcus species	**17 (9.8)**
Gram negative bacilli	**16 (9.3)**
Pseudomonas aeruginosa	4
Other NFGNB	4
Escherichia coli	3
Citrobacter freundii	1
Burkholderia cepacia	1
Klebsiella	1
Salmonella group D	1
Hemophilus parainfluenzae	1
Others	**7 (4)**
Candida species	4
Diphtheroids	1
Aspergillus species	1
Culture negative endocarditis	**28 (16.3)**

Table 3: Risk factor analysis for mortality

Risk Factors (Univariate analysis)	Alive n=131	Dead n=41	p value
Mean age (years)	41.37 ± 14.0	43.22 ± 15.1	0.47
Age > 50 years	39 (29.7%)	18 (43.9%)	0.09
Male sex	102 (77.8%)	33 (80.4%)	0.72
Congenital heart disease	21 (16%)	3 (7.3%)	0.16
Prosthetic valve endocarditis	11 (8.4%)	7 (17%)	0.11
Culture positive endocarditis	23 (17.5%)	5 (12.2%)	0.41
Peripheral emboli	46 (35.1%)	20 (48.7%	0.12
Congestive cardiac failure	13 (9.9%)	24 (58.5%)	< 0.001
Septic shock	0	19 (100%)	
Staphylococcal species	17 (12.9%)	12 (29.2%)	0.02
Streptococcus species	68 (51.9%)	9 (21.9%)	0.001
Left side endocarditis	109 (83.2%)	34 (82.9%)	0.96

Table 4 : Infective endocarditis across the decades: A comparison between 3 studies done in each decade since 1981 in India

Characteristic	Choudhury *et al*[6]	Garg *et al*[5]	Math *et al*[4]	Our study
Time period	1981-1991	1992-2001	2004-2006	2005-2015
Place	Chandigarh	Lucknow	New Delhi	Vellore
Episodes of IE	190	198	104	172
Sex (Males %)	71.5%	73.4%	71.1%	78.4%
Mean age (years)	25 ± 12	27.6 ± 12.7	23.5	41.8 ± 14.2
Portal of entry	15%	16.6%	18.2%	16.8%
RHD endocarditis (%)	42%	46.9%	NA	40.6%
Congenital Heart disease (%)	33%	28.6%	39.4%	13.9 %
Prosthetic valve endocarditis (%)	1%	10.4%	20%	10.4%
Normal Valve (%)	9%	NA	7.7%	28.4%
Culture positive (%)	47%	67.6%	41%	83.7 %
ECHO positive (%)	64%	89.8%	90.3%	88.9 %
Streptococcus species	18.2%	23.2%	22.8%	44.7 %
Staphylococcus species	19.8%	19.7%	20%	16.8 %
Surgical management	1%	23%	15%	15.7 %
In hospital mortality (%)	25%	21%	26%	23.8%

DISCUSSION

The purpose of the study was to study the profile and outcome of IE in our hospital and to compare our results with studies done in India over the last 3 decades. During this period, literature published in India on IE showed a definite change in profile. The clinical presentation of IE started showing features more commonly seen in the developed countries: a higher mean age at presentation and an increase in prosthetic valve endocarditis.[1-3] *Streptococcal* species remain the commonest causative organisms.

The increase in age by a decade at presentation of IE is an important positive finding of this study. This trend is confirmed by another Indian study (Gupta *et al*) done among adults which showed a higher mean age at presentation (49.3 ± 13.7 years).[9] However, Senthilkumar S *et al* reported a mean age of 29.9 ± 14.2 years among patients with IE.[10] The factors that may have contributed to the higher age group among our patients are a general increase in age of the population as a whole and the possibility that patients with RHD and congenital heart diseases are living longer.

More than half (55.9%) the patients had a diagnosed cardiac condition prior to the onset of fever. Most of the remainder probably had underlying asymptomatic RHD or MVP and were diagnosed during the current episode of IE. An Indian Council of Medical Research (ICMR) based school survey showed the prevalence of RHD to be 5.3/1000 in 1972-75, 2.97/1000 in 1992-95 and 0.9/1000 in 2002-2005.[7,8] RHD was earlier a common cause of IE in India with the valvular lesions predisposing to vegetation formation on the leaflet. However with the decline in RHD, the incidence of endocarditis in those with no known or demonstrable underlying valvular disease has increased relatively and is starting to resemble the profile of IE in the West.[1,11,12] Another contemporary study done between 2005-2010 in India also reported RHD to be the underlying cardiac condition in only 37.7% of patients with IE. (9) Since our study included only adults >16 years, the percentage of CHD

was lesser than in some other studies and this perhaps contributed to a falsely higher percentage of RHD among all IE cases. The rate of PVE in our study (13%) and in the study by Math *et al*. (20%) is a significant increase compared to earlier studies.[4,6] We did not have any case of either peri-partum or peri-abortal sepsis predisposing to IE. Studies by Chaudury et al and Khanal *et al* had reported a small but significant number (3.1% and 8.7% respectively) of cases of IE related to peri-partum or peri-abortal sepsis.[6,13] This may be due to the improved antenatal screening and follow up and also due to a reduction in number of abortions or deliveries performed by untrained midwives in our country. We were able to identify a portal of entry in only a small percentage (15.5%) of patients. This result however, is comparable with studies done in the past.[4-6]

The sensitivity of TTE varies from 40-63%, and for TEE between 90-100%, while the specificity for both is greater than 95%.[14-16] The diagnostic yield of echocardiography reported by Chaudhury *et al* (64%) was lower, probably due to lack of TEE at that time.[6] The culture positivity of 83.8% of IE in our study is higher than that reported by Math (41%), Chaudhury *et al* (47%) and Garg *et al* (67.6%).[4-6] As these studies were done earlier, the possible reasons for this remarkable improvement could be a) institutional policy that discourages empirical antibiotic therapy unless patient is in sepsis, b) more stringent rules regarding blood culture techniques, and c) improved microbiological equipment for isolation of bacteria-esp. fastidious organisms d) A minimum requirement of 3 cultures were mandatory for every patient and e) use of BacTec culture bottles.

Despite advances in antibiotics, diagnostic techniques and surgical interventions, the mortality rate of 23.8% in our study is similar to the mortality rates reported in studies over the last 3 decades (21% and 26% according to Garg *et al* and Math *et al* respectively).[4-6] Gupta *et al*. reported prosthetic valve involvement, combined mitral and aortic valve involvement, male gender, and leukocytosis to be independent predictors of mortality.[17] We found septic shock, CCF and staphylococcal endocarditis to be associated with higher risk of mortality. This finding is also consistent with studies done in India, Western and Middle Eastern populations.[4,5,12,18,19]

There exists a need to improve accessibility of imaging facilities and microbiological laboratories across the country for early and accurate diagnosis. Studies from the West have shown early surgical intervention to be associated with reduced mortality.[20-22] More aggressive and early surgical intervention as has been advocated in many reviews may have improved the outcome and this change in clinical practice is perhaps the need of the hour in developing countries.

Our study has certain limitations. As it was conducted at a single medical center, the patient population may be biased by patient selection and referral pattern. The retrospective nature of the study resulted in some missing data. Certain tests like polymerase chain reaction were not done routinely for cases of culture negative endocarditis. Nonetheless, the study provides relatively rare information about the changing trends of IE in India over the past 3 decades.

CONCLUSION

The profile of IE in India has undergone substantial changes in the last 3 decades, mirroring the improvements in the country's general health care. The underlying disease profile of patients has shifted from young patients with RHD towards an increasing proportion of patients with prosthetic valves or those without known or demonstrable underlying valvular disease. The yield of blood cultures has almost doubled over the last two decades with the commonest organisms still being *Streptococcus* and *Staphylococcus* species. Despite significant advances in medical technology over the last 3 decades, mortality rate remains the same. Our study provides ample evidence for developing countries to introspect and initiate early surgical intervention that should lead to better outcomes.

ACKNOWLEDGEMENT

None

CONFLICTS OF INTEREST

None

ABBREVIATION USED

IE: Infective endocarditis; RHD: Rheumatic heart disease; TEE: Transesophageal echo; TTE: Trans-thoracic echo; IQR: Inter-quartile range; CCF: Congestive cardiac failure; CHD: Congenital heart disease; MVP: Mitral valve prolapse.

REFERENCES

1. Bruno H, Xavier D. Infective Endocarditis. N Engl J Med. 2013;368:1425-33.
2. Tornos P, Iung B, Permanyer-Miralda G, Baron G, Delahaye F, Gohlke-Bärwolf Ch, *et al*. Infective endocarditis in Europe: lessons from the Euro Heart Survey. Heart. 2005;91(5):571-5.
3. Prendergast BD. The changing face of infective endocarditis. Heart. 2006;92(7):879-85.
4. Math RS, Sharma G, Kothari SS, Kalaivani M, Saxena A, Kumar AS, *et al*. Prospective study of infective endocarditis from a developing country. Am Heart J. 2011;162(4):633-8.
5. Garg N, Kandpal B, Garg N, Tewari S, Kapoor A, Goel P, *et al*. Characteristics of infective endocarditis in a developing country-clinical profile and outcome in 192 Indian patients1992-2001. Int J Cardiol. 2005;98(2):253-60.
6. Choudhury R, Grover A, Varma J, Khattri HN, Anand IS, Bidwai PS, *et al*. Active infective endocarditis observed in an Indian hospital 1981-1991. Am J Cardiol. 1992;70(18):1453-8.
7. Prevalence of rheumatic fever and rheumatic heart disease in school children: Multicentre study. Annual report. New Delhi: Indian Council of Medical Research; 1977:108.
8. Ramakrishnan S, Kothari SS, Juneja R, Bhargava B, Saxena A, Bahl VK. Prevalence of rheumatic heart disease: has it declined in India?. Natl Med J India. 2009;22(2):72-4.
9. Gupta A, Gupta A, Kaul U, Varma A. Infective endocarditis in an Indian setup: Are we entering the 'modern' era? Indian J Crit Care Med. 2013;17(3):140-7.
10. Senthilkumar S, Menon T, Subramanian G. Epidemiology of infective endocarditis in Chennai, South India. Indian J Med Sci. 2010;64(4):187-91.
11. Sy RW, Kritharides L. Health care exposure and age in infective endocarditis: results of a contemporary population-based profile of 1536 patients in Australia. Eur Heart J. 2010;31:1890-7.
12. Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler VG Jr, Bayer AS, *et al*. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis-Prospective Cohort Study. Arch Intern Med. 2009;169(5):463-73
13. Khanal B, Harish BN, Sethuraman KR, Srinivasan S. Infective endocarditis: report of a prospective study in an Indian hospital. Trop Doct. 2002;32(2):83-5.
14. Shapiro SM, Young E, De Guzman S, Ward J, Chiu CY, Ginzton LE, *et al*. Transesophageal echocardiography in diagnosis of infective endocarditis. Chest. 1994;105(2):377-82.
15. Erbel R, Rohmann S, Drexler M, Mohr-Kahaly S, Gerharz CD, Iversen S, *et al*. Improved diagnostic value of echocardiography in patients with infective endocarditis by transoesophageal approach. A prospective study. Eur Heart J. 1988;9(1):43-53.
16. Shively BK, Gurule FT, Roldan CA, Leggett JH, Schiller NB. Diagnostic value of transesophageal compared with transthoracic echocardiography in infective endocarditis. J Am Coll Cardiol. 1991;18(2):391–7
17. Gupta K, Jagadeesan N, Agrawal N, Bhat P, Nanjappa MC. Clinical, echocardiographic and microbiological study and analysis of outcomes of infective endocarditis in tropical countries: a prospective analysis from India. J Heart Valve Dis. 2014;23(5):624-32.
18. Kiwan YA, Hayat N, Vijayaraghavan DG, Das Chugh T, Khan N, Mualla F. Infective endocarditis: a prospective study of 60 consecutive cases. Med Pol. 1990;22(3):173-5.
19. Benito N, Miro JM, de Lazzari E, Cabell CH, del Río A, Altclas J, *et al*. Health care-associated native valve endocarditis: importance of non-nosocomial acquisition. Ann Intern Med. 2009;150:586-94.
20. Beynon RP, Bahl VK, Prendergast BD. Infective endocarditis. BMJ. 2006;333:334-9.

21. Vikram HR, Buenconsejo J, Hasbun R, Quagliarello VJ. Impact of valve surgery on 6-month mortality in adults with complicated, left-sided native valve endocarditis. A propensity analysis. JAMA. 2003;290(24):3207-14.

22. Tornos P, Iung B, Permanyer-Miralda G, Baron G, Delahaye F, Gohlke-Bärwolf Ch, *et al.* Infective endocarditis in Europe: Lessons from the Euro heart survey. Heart. 2005;91(5):571-5.

Cite this article: Abhilash KPP, Patole S, Jambugulam M, Sathyendra S, Mitra S, Rebekah G, Yadav B, Veeraraghavan B, Abraham OC. Changing trends of Infective endocarditis in India: A South Indian experience. Journal of Cardiovascular Disease Research. 2017;8(2)56-60.