

1    **A Case of Fever with Diagnostic Dilemma**

2

3    **Introduction**

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5    Infective endocarditis (IE) is a potentially life-threatening microbial infection  
6    involving the endocardial surface of the heart, most commonly affecting the  
7    cardiac valves, but occasionally involving the mural endocardium or implanted  
8    intracardiac devices (1). Despite significant  
9    advances in diagnostic techniques, antimicrobial therapy, and surgical management,  
10   IE continues to be associated with high morbidity and mortality worldwide,  
11   with reported in-hospital mortality ranging from 15–30% (1). The disease  
12   represents a complex interaction between host factors, microbial virulence, and  
13   hemodynamic conditions within the heart.

14   The pathogenesis of IE involves transient or sustained bacteremia or fungemia,  
15   allowing microorganisms to adhere to damaged endocardial surfaces or  
16   prosthetic material (1,2). Endothelial injury leads to deposition of platelets and  
17   fibrin, forming sterile  
18   thrombotic vegetations that provide an nidus for microbial colonization and needs  
19   prolonged duration antibiotic therapy. Subsequent proliferation  
20   of organisms within these vegetations results in persistent  
21   infection, embolization, and immune-  
22   mediated phenomena (1). A wide variety of microorganisms can cause IE, including  
23   bacteria and fungi; however, streptococci, staphylococci, and enterococci  
24   remain the most common causative agents (2,3).

25   Clinically, infective endocarditis exhibits a highly variable spectrum, ranging  
26   from an indolent subacute illness characterized by low-grade fever, malaise,  
27   and weight loss, to a rapidly  
28   progressive acute disease with severe sepsis and cardiovascular collapse (1,3). Common  
29   clinical manifestations include fever, cardiac murmurs, signs of heart  
30   failure, embolic events, and immunologic phenomena such as  
31   glomerulonephritis and vasculitis (1). The diagnosis of IE is often challenging  
32   due to its protean manifestations and relies on an integrated approach  
33   incorporating clinical findings, blood culture results, and echocardiographic  
34   evidence, as  
35   outlined in the modified Duke's criteria (4).

36   The epidemiology of infective endocarditis varies significantly between  
37   developed and developing countries. In high-income nations, IE is increasingly  
38   associated with degenerative  
39   valvedisease, prosthetic valves, intracardiac devices, and healthcare-

40 associated infections (3,5). In contrast, developing countries like India continue  
41 to report a high burden of IE related to rheumatic heart disease (RHD), younger  
42 patient populations, delayed presentation, and limited access to advanced  
43 healthcare facilities (5,6). Additionally, widespread empirical antibiotic use  
44 before hospital admission contributes to a high incidence of culture-  
45 negative endocarditis, complicating diagnosis and management (6).  
46 Given the changing epidemiological patterns, microbiological profile, and  
47 persistent high complication rates, infective endocarditis remains a major clinical challenge in the Indian  
48 setting. Case reports continue to play an important role in highlighting unusual  
49 presentations, diagnostic difficulties, and management strategies, thereby  
50 contributing to improved understanding and outcomes of this complex disease.  
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### 52

### 53 **Case Presentation**

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### 55 **Patient Information**

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58 A 70 year old female patient presented to ER with complaints of Dyspnea and  
59 palpitation associated with generalized weakness for the last 4 days. It was  
60 also associated with a history of one week intermittent high grade fever  
61 associated with chills and malaise. The reported dyspnea was progressive on  
62 exertion (NYHA II). It was insidious in onset and gradually progressive and  
63 had no relieving factor. There was no associated chest pain and any history  
64 of syncopal attacks. It was not associated with any seasonal or diurnal variation. There  
65 was no history of chest pain, palpitations, PND.

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67

68 She was a known case of CKD Stage 5D on MHD (3/week), hypertension and  
69 hypothyroidism and on regular medication. She underwent a dental extraction  
70 four weeks prior to symptoms without antibiotic prophylaxis. There was no  
71 history of intravenous drug use.

### 72 **Clinical Findings on Examination:**

73

74 On Examination:

75 Patient was alert, conscious, co-  
76 operative well oriented to time,  
77 place and person. Temperature:  
78 102 degree F  
79 Pulse: 108/mi  
80 n, regular. BP:  
81 106/70  
82 mmHg.

83  
84  
85 In General Survey, there was conjunctival congestion present without itching or  
86 watering of eyes.  
87

88 Respiratory examination revealed tachypnoea and  
89 cardiovascular examination revealed a  
90 high pitched pansystolic murmur  
91 best heard at the apex, radiating  
92 to the axilla with bibasal  
93 crepitations denoting heart  
94 failure.  
95 There was no focal neurological deficit. Examination of other systems were  
96 unremarkable.  
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99 Later, by the ophthalmoscopic examination, Roth's Spot with conjunctival haemorrhages were confirmed by the Ophthalmologist .  
100

101 Treatment was started immediately after admission of the patient, initially with  
102 moist O<sub>2</sub> and  
103 Nebulization with Salbutamol. Foley's catheterization and i.v. cannulation  
104 was done. Inj Ceftriaxone - 1 gm in twice daily (APST) was administered with  
105 intravenous injection paracetamol, i.v. fluid 0.9%, Normal Saline, Injection PPI  
106 and ondansetron. ABG was done. Blood  
107 Culture send with three sets of sample and as per IE protocol.  
108

109  
110  
111 Other blood investigations were sent for:  
112 Complete Blood Count, Random Blood  
113 Sugar, urea, creatinine, Sodium, Potassium, LFT, CRP, Procalcitonin. Fever profile  
114

115 was also sent with MP Slide and dual Antigen, NS1 antigen,Typhi Dot  
116 M,Urine for RE/CS.

117

118 InRadiologicalinvestigation,Chest-x-raydoneinPAview revealing cardiomegaly  
119 with hilar congestion,Echocardiogram-2Ddone,ECGwas done.Laboratory  
120 Investigation showed:

121 Haemoglobin

122 -9.0g/dl TLC

123 - 18600/mm<sup>3</sup>

124 CRP-Elevatedmarkedly.

125

126 Bloodcultureswerenegative.

127

128 Patientwaspreviouslyadmittedinanotherhospitalfortwodaysbeforecoming to  
129 this hospital.

130 Inechocardiography,therewas‘Alargemovablemass(26x14mm)attachedtoposte  
131 rior mitral annulus in LA side’.with moderate MR, mild TR and Pulmonary  
132 arterial hypertension with normal ejection fraction.(**Fig 1**)

133 TransoesophagealEchocardiography(TEE)couldnotbeperformedduetosomelimit  
134 edresources and financial issues.

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137 **Diagnosticcriteria:**

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139 Major criteria: Echo cardiograph’s evidence

140 of vegetation. Minor criteria: Fever, vascular

141 and immunological phenomenon.

142 **Therapeutic Intervention:**

143 The patient was diagnosed as IE and started with Injection Ceftriaxone(1g) iv  
144 twice daily (APST), Injection Gentamicin(80 mg ) once in every 48  
145 hours(APST). She was also given Injection vancomycin (500mg.) post-  
146 Haemodialysis.(All antibiotics were given after renal dose  
147 adjustment)Supportive care included antipyreticsand close monitoring. A  
148 multidisciplinary Endocarditis team, including cardiologist and  
149 cardiothoracic surgeon evaluated the patient. Surgical intervention was not  
150 indicated due to clinical improvement, ,controlled infection and lack of  
151 embolic events.Patient started to respond with diuretics, oxygen and  
152 antibiotics with gradual normalization of Total leukocyte count and  
153 Procalcitonin. The patient was referred to higher Centre for TEE after three  
154 days in a clinically and hemodynamically stable condition.All the reports of  
155 fever profile were negative, including blood culture due to prior antibiotics  
156 use.USG whole abdomen revealed no abnormality.

157

158 **Discussion:**

159 The clinical profile of infective endocarditis in India differs significantly from  
160 that observed in Western countries. Several Indian studies have demonstrated  
161 that native valve endocarditis accounts for the majority of cases, with  
162 rheumatic heart disease being the most common  
163 underlyingcardiac abnormality(5–  
164 7).The mitral valve is most frequently involved,followed by the aortic valve,  
165 reflecting the high prevalence of rheumatic valvular lesions (5,7).  
166 Prolonged fever remains the most common presenting symptom, while heart failure is  
167 the most frequent and serious complication, often determining prognosis (7,8).  
168 Embolic complications involving the central nervous system, spleen, and  
169 kidneys are also commonly reported, particularly in patients with large  
170 vegetations and delayed diagnosis (6,8). These findings underscore the  
171 importance of early recognition and intervention.  
172 Blood culture remains the cornerstone of etiological diagnosis; however,  
173 Indian studies report culture positivity rates of only 50–60%, with culture-  
174 negative endocarditis occurring in up to 40%of cases(6,8). Prior antibiotic

175 exposure is the most important factor contributing to culture negativity. Recent  
176 Indian data suggest a shift in microbiological trends, with *Staphylococcus*  
177 *aureus* emerging as the most common causative organism, replacing *viridans* group  
178 *streptococci*, and reflecting an increase in healthcare-associated infections (9).  
179 Echocardiography is indispensable in the diagnosis and management of IE.  
180 While transthoracic  
181 echocardiography is widely available and serves as the initial imaging modality, trans  
182 esophageal echocardiography offers superior sensitivity for detecting  
183 vegetations, abscesses, and prosthetic valve involvement (10). Management  
184 requires prolonged intravenous antimicrobial therapy tailored to  
185 microbiological findings whenever possible. Early surgical intervention in  
186 patients with heart failure, uncontrolled infection, or high embolic risk has  
187 been shown to significantly improve outcomes in Indian studies (7,8).

## 188 **Conclusion:**

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190 Infective endocarditis remains a serious and potentially fatal disease in India, characterized  
191 by native valve involvement, a high prevalence of rheumatic heart  
192 disease, frequent culture-  
193 negative cases, and significant complication rates. Early diagnosis using modified Duke's  
194 criteria, prompt echocardiographic evaluation, appropriate antimicrobial  
195 therapy, and timely surgical intervention are crucial in reducing morbidity and  
196 mortality. Awareness of  
197 evolving microbiological trends is essential for guiding empirical therapy and improving  
198 patient outcomes.

## 200 **References:**

- 202 1) Sexton DJ, Chu VH. Infective endocarditis. In: Goldman L, Schafer A  
203 I, editors. Cecil Textbook of Medicine. 26th ed. Philadelphia:  
204 Elsevier; 2020. p. 1898–1912.
- 205 2) Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's  
206 Principles and Practice of Infectious Diseases. 9th ed. Philadelphia:  
207 Elsevier; 2020. p. 1025–1059.
- 208 3) Fauci AS, Braunwald E, Kasper DL, et  
209 al., editors. Harrison's Principles of Internal Medicine. 21st ed.  
210 New York: McGraw-Hill; 2022. p. 945–956.
- 211 4) Li JS, Sexton DJ, Mick N, et al. Proposed modifications to  
212 the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis.  
213 2000;30(4):633–638.
- 214 5) Garg N, Kandpal B, Tewari S, et al. Characteristics of infective endocarditis in a  
215 developing country. Indian Heart J. 2017;69(3):301–306.
- 216 6) Senthilkumar S, Menon T, Subramanian G. Epidemiology of infective endo

217 rditis in India. Indian J Med Res. 2010;132:124–130.

218 7) Math  
219 RS, Sharma G, Kothari SS, et al. Prospective study of infective endocarditis  
220 from a developing country. J Assoc Physicians India. 2011;59:3–8.

221 8) Balakrishnan KG, Tharakan J, Titus T, et al. Infective endocarditis in India  
222 : a changing profile. Indian Heart J. 1995;47(2):121–126.

223 9) Khalid IA, Khan KA, Shahid M, et al. Changing trends in the microbiolog  
224 ical profile of infective endocarditis. Indian Heart J. 2018;70(Suppl  
225 3):S353–S357.

226 10) Bansal M, Kasliwal RR. Echocardiography in infective endocarditis. I  
227 ndian Heart J. 2013;65(3):299–307.

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UNDER PEER REVIEW IN IJAR



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233 Fig 1: Mitral valve vegetation on Echocardiography

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