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# Original Article Tricuspid valve endocarditis in non-drug abusers: A case series from India

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ARTICLE INFO	A B S T R A C T
Article history: Received 18 May 2016 Accepted 15 September 2017 Available online 20 September 2017	<i>Objective:</i> The etiology of tricuspid valve endocarditis (TVE) seems to be different in our country as intravenous (IV) drug abuse is not known to be a major health hazard. The objective of this communication is to study the risk factors, clinical profile, follow-up data of TVE patients and focus on the difficulties in diagnosis and variations encountered.
<i>Keywords:</i> Endocarditis Non-drug abusers Tricuspid valve endocarditis	<ul> <li>Methods: A retrospective analysis of data of 10 patients of TVE managed in a tertiary care center during January 1992 to June 2015 was done.</li> <li>Results: TVE was encountered in a diverse subset of patients with cardiac implantable electronic device (CIED) (group I; 3 patients), immunocompromised state with indwelling central venous catheter (CVC) (group II; 2 patients), congenital heart disease (CHD) (group II; 3 patients) and in apparently healthy individuals (group IV; 2 patients). Blood cultures were negative in half the patients. In group I early surgical extraction of leads, device and vegetation provided excellent results. Prognosis was poor with 100% mortality in immunocompromised patients. Patients in group II did well on medical management. The overall mortality was high (30% in hospital and additional 20% within one year).</li> <li>Conclusions: TVE is rare and can occur in different clinical scenarios. Indiscriminate use of antibiotics modifies the clinical picture causing delay in diagnosis and referral to speciality care. Echocardiography remains the main modality and should be used serially to facilitate early diagnosis. The prognosis is guarded. Early surgery is recommended in pacemaker lead, fungal endocarditis, persistent sepsis or hemodynamic instability for favorable prognosis.</li> <li>© 2017 Published by Elsevier B.V. on behalf of Cardiological Society of India. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).</li> </ul>

# 1. Introduction

Tricuspid valve endocarditis (TVE) is rare and mainly reported in intravenous (IV) drug abusers in the western literature. Endocarditis due to IV drug abuse is virtually unreported in India.<sup>1.2</sup> TVE in non-drug abusers can occur in a variety of conditions including congenital heart disease (CHD), intra-cardiac devices, central venous catheters, immunocompromised patients and community acquired infections.<sup>3,4</sup>

There are case reports of TVE and right sided endocarditis in Indian literature.<sup>1,2,5–8</sup> The aim of this communication is to report clinical, investigative, management and outcome data in 10 patients of TVE seen in our unit during the last 23 years.

# 2. Methods

The material for this study is obtained from records of academically interesting patients maintained by the author in a tertiary care referral postgraduate teaching institute. During 1992 to 2015, 10 cases of TVE were diagnosed, treated and followed up. The records of these cases form the material for this analysis.

The diagnosis of TVE was entertained on the basis of modified Dukes criteria.<sup>9</sup> There was no history of IV drug abuse in any of the patients. Patients were categorized in four groups based on predisposing factors.

Group I: Cardiac implantable electronic device (CIED)

Group II: Immunocompromised state with indwelling central venous catheter (CVC)

Group III: Congenital cardiac malformation

Group IV: Unknown etiology

Clinical data, management details and follow-up information was analyzed. Detailed laboratory workup including complete blood count, erythrocyte sedimentation rate (ESR), renal and liver function test and blood cultures were studied. Electrocardiogram





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(ECG), X-ray chest, echocardiography, computed tomography (CT) of chest (three patients) and surgical details (four patients) along with culture from excised material was available (three patients).

### 3. Results

**Group I** includes three patients with prior single (2) or dual chamber (1) pacemaker (PM) implantation. Table 1 shows relevant clinical data. Cases 1 and 3 underwent pulse generator re-implantation due to pocket infection. Prior to referral to our center all had febrile illness, multiple hospitalization and had received several courses of antibiotics. Transesophageal echocardiography (TEE) image from case 1 is shown in Fig. 1A.

Antibiotic therapy as per culture sensitivity (case 1 and 3) and empirical (case 2) was administered for six weeks. Case 1 underwent surgical removal of endocardial leads and vegetation from tricuspid leaflet along with epicardial lead placement. Patient improved rapidly and had an uneventful course during the next 14 years. Case 2 and 3 refused surgery and died of intractable heart failure within one year.

**Group II** data is shown in Table 2 and includes patients with immunocompromised state and indwelling CVC.

Case 4 with chronic kidney disease (CKD) on maintenance dialysis through hemodialysis (HD) catheter was referred with febrile illness of three weeks, hemoptysis and tachypnea. ECG revealed sinus tachycardia, S1Q3T3 pattern and skigram chest showed multiple areas of consolidation consistent with pulmonary embolism. Despite antimicrobial therapy as per culture sensitivity he had rapid deterioration and death within a week due to multiorgan failure.

Case 5 had received cyclophosphamide and adriamycin chemotherapy for non-Hodgkins lymphoma through Hickman catheter. There was leucopenia and thrombocytopenia after chemotherapy with high grade fever and right heart failure. Skigram chest showed Hickman catheter port and multiple areas of consolidation. Transthoracic echocardiography (TTE) image is shown in Fig. 1B. Despite IV amphotericin B, oral itraconazole, multiple platelet transfusions, surgical excision of tricuspid valve vegetation and removal of Hickmans port, patient expired as a sequel to immunocompromised state. Fig. 1C shows echocardiogram performed after surgery.

**Group III** data is summarized in Table 3. All patients had underlying perimembranous ventricular septal defect (VSD) with left to right shunt. The VSD was restrictive and measured between 4 and 6 mm. Clinical presentation was dominated by febrile illness of 2–6 months with anemia, leucocytosis and elevated ESR. The referral diagnosis was pneumonia in case 6 and 7, which was unresponsive to multiple short courses of antibiotics. Fig. 1D shows vegetation in case 7.

Case 8 had fever, hemoptysis and was on empirical anti tubercular treatment prior to cardiology referral. CT of chest revealed large irregular area of consolidation in anterior segment

Table 1	
Clinical data in group I.	

Case (year of presentation)	1 (1996)	2 (1998)	3 (2001)
Age, sex	68, M	60, F	65, F
Risk factors	PM (1992), Reimplant (1993, 1996)	PM (1998)	PM (1997), Reimplant (2000)
Echocardiography	$1.5 \times 1 \text{ cm}$ vegetation on TV (TEE)	$1 \times 1$ cm vegetation on TV, $2/4$ TR (TEE)	$2 \times 1$ cm vegetation on TV, $3/4$ TR, (TTE)
Blood/PM lead culture	Acinetobacter anitratus (lead culture- Pseudomonas)	Negative	Pseudomonas
Treatment	Surgical <sup>a</sup>	Antibiotics	Antibiotics
Outcome and FU	Excellent for 14 years	Death after 1 year	Death after 9 months

Abbreviations;: M- male, F- female, FU- follow-up. Rest abbreviations as in text.

<sup>a</sup> Removal of endocardial leads and vegetation from septal leaflet along with epicardial lead implant.

of right upper lobe with multiple small nodular opacities in bilateral lung fields interpreted as pulmonary emboli and its sequel (Fig. 2A). Culture guided antibiotic therapy for six weeks resulted in clinical remission, negative blood cultures and disappearance of vegetation on TTE (Fig. 2B and C). Dental, ear, throat and other relevant check-up did not reveal any focus of infection.

The relevant data of **Group 4** is summarized in Table 4. Clinical presentation was marked by fever, pulmonary emboli (pneumonia) and right heart failure. The underlying risk factor for infective endocarditis was unclear in both the cases.

Case 10 was referred with diagnosis of pneumonia. There was right heart failure and tricuspid regurgitation (TR) with no clinical improvement despite antibiotics, decongestive and supportive medication. Excision of vegetation along with tricuspid valve (TV) replacement using 29 mm Sorin Biomed Biocarbon metallic valve was performed. Histopathology of excised valve tissue showed markedly thickened valve with fibro-collagenous tissue infiltrated with neutrophils, mononuclear cells, histocytes and multinucleate giant cells. Surface of the valve was covered with necrotic slough containing fungal hyphae. IV amphotericin B was administered for eight weeks followed by oral fluconazole 200 mg daily indefinitely. At 15 years follow up, patient is asymptomatic with normal functioning tricuspid valve. International normalized ratio is maintained around 3.

#### 3.1. Summary of results

CIED (30%), CHD (30%) and CVC (20%) were common predisposing factors. Majority (70%) of the patients were male aged 7–68 years (average 35). Chest X-ray suggested features of pneumonia/ pulmonary infarction in 7 (70%) patients. Blood cultures were negative in 50%. TTE provided diagnostic information in 8 (80%) patients and TEE was superior in CIED group. The overall in hospital mortality was 30% with invariably fatal outcome in immunocompromised patients.

#### 4. Discussion

TVE in western world is predominantly reported in IV drug abusers. In earlier series from India, right sided endocarditis was seen in CHD or in patients with puerperal sepsis and septic abortion.<sup>1,2</sup> Compared to earlier series, TVE was encountered in a diverse subset of patients. There were several underlying risk factors which led to endocarditis. In young individuals, it was usually due to underlying CHD, whereas pacemaker lead related TVE occurred in elderly population. In patients with CVC and immune compromised state, TVE was seen in a child and an adult. Surprisingly, TVE occurred in two apparently healthy individuals without any obvious cause. Despite advances in diagnosis, the recognition of TVE remains difficult. Indiscriminate use of antibiotics modifies the clinical picture causing delay in diagnosis and

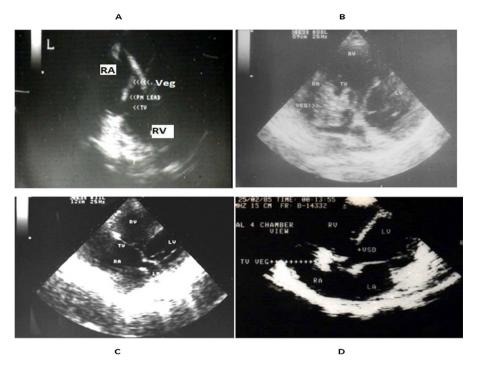


Fig. 1. TEE in four chamber view shows vegetation (veg) and pacemaker lead in case 1 (panel A). TTE in apical four chamber view showing a large 2 × 1.5 cm vegetation over TV occupying the RA (panel B) and no vegetation after surgery (panel C) in case 4. Panel D demonstrates TTE in apical four chamber view showing VSD and vegetation on TV (case 7).

Abbreviations: RA- right atrium, RV- right ventricle, LA- left atrium, LV- left ventricle. Rest abbreviations as in text.

#### Table 2

Clinical data in group II.

Case (year of presentation)	4 (2001)	5 (1996)
Age, sex	30, M	9, M
Risk factors	HD catheter, immunosuppression	Hickman catheter, immunosuppression
Echocardiography	$2 \times 1$ cm vegetation on TV, grade $\frac{3}{4}$ TR	$2 \times 1.5$ cm vegetation on TV, grade $2/4$ TR
Blood culture	Pseudomonas aeurogenosa	Aspergillus fumigates
Treatment	Antibiotics	Surgical excision of vegetation and port removal
Outcome and FU	Death, multi-organ failure	Death, multi-organ failure

M- male, FU- follow-up. Rest abbreviations as in text

#### Table 3

Clinical data in group III.

Case (year of presentation)	6 (1992)	7 (1993)	8 (2015)
Age (years), sex	18, M	22, M	7, F
Echocardiography	0.5  imes 0.5 cm vegetation on TV	$1 \times 0.5$ cm vegetation on TV	0.8  imes 0.5 cm vegetation on TV
Blood culture	Negative	Staphylococcus aureus	Streptococcus viridians
Management	VSD closure with excision of vegetation	Medical	Medical
Outcome and FU	Excellent at 20 years	Lost to follow up after 5 years	Doing well at 6 months

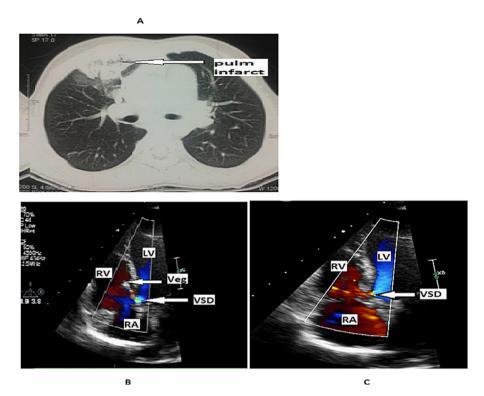
M- male, F- female, FU- follow-up. Rest abbreviations as in text

referral to speciality care.<sup>10</sup> TVE was encountered in four distinct groups as described earlier.

#### 4.1. Group I

CIED related endocarditis is infrequent but needs awareness due to increasing proportion of PM, defibrillator and cardiac resynchronization therapy device implantation.<sup>11</sup> It refers to presence of infective material in relation to the CIED in veins leading up to the heart, or right sided chambers and valves. Pathogenesis of CIED infections is associated with biofilm formation on device surfaces described as a 'structured community of bacterial cells enclosed in a self produced polymeric matrix'. In a large cohort of pacemaker recipients, estimated incidence was 1.82/1000 device-years.<sup>12</sup> The recognition is challenging and delay in the diagnosis and management can prove fatal.<sup>13</sup> Symptoms usually begin with pulse generator site infection leading to multiple courses of antibiotics, change of pulse generator and a relapsing febrile illness. Ultimately, the lingering infection results in TV vegetations, TR and secondary pulmonary embolism.<sup>14</sup> Accurate diagnosis in all patients was delayed for months to years despite multiple medical consultations.

CIED related TVE should be considered in patients with chronic fever, recurrent respiratory and implant site infections.<sup>10</sup> CIED lead



**Fig. 2.** CT chest with contrast showing pulmonary (pulm) infarct (white arrow) in case 8 (panel A). TTE with Doppler in apical four chamber view demonstrating VSD jet and vegetation (veg) on TV (panel B) and disappearance of vegetation after 6 weeks of antimicrobial therapy in case 8 (panel C). Abbreviations: RA- right atrium, RV- right ventricle, LV- left ventricle. Rest abbreviations as in text.

Та	b	le	4	

Clinical	data	in	group IV.	
			8	

Case (year of presentation)	9 (1993)	10 (2001)
Age (years), sex	40, M	38, M
Echocardiography	$0.5 \times 0.5$ cm vegetation on TV, 3/4 TR	$2.6 \times 1.5$ cm mobile vegetation on TV, 2/4 TR
CT chest	Multiple pulmonary infarcts	Bilateral pulmonary infarcts
Blood/valve culture	Negative	Negative,
		(Valve culture- Aspergillus fumigatus and penicillium)
Treatment	Medical	Excision of vegetation and TVR (29 mm Sorin Biomed Bicarbon)
Outcome and FU	Death, multi-organ failure	Doing well for 14 years

M- male, FU- follow-up. Rest abbreviations as in text.

infection can spread to TV at the contact point. Anterior tricuspid leaflet affection was encountered and is related to the anterior curvature of PM lead.<sup>15</sup> Echocardiography plays an important role in device related endocarditis. The overall sensitivity of TTE is poor due to difficulty in distinguishing between abnormal masses, TV and the lead itself. Additional difficulties can occur due to lead reverberations and poor window. Images should be recorded in multiple views (right ventricular inflow, parasternal short axis at the level of aortic valve, apical four chamber and subcostal views). TTE was disappointing in our experience and could diagnose TVE in only one case. TEE improves the quality of exploration and is able to visualize the entire intracardiac route of the leads from the superior vena cava to the right ventricular apex and facilitated diagnosis in case 1 and 2. The sensitivity of TTE is 22-30% while that of TEE is 92–96%.<sup>10,13</sup> Advent of real time transthoracic three dimensional echocardiography should improve the diagnostic yield. The diagnosis of septic emboli in this group can be facilitated by use of 18-fluorodeoxyglucose (FDG), positron emission tomography (PET)/CT scanning.<sup>16</sup>

Infection occurring within first month after PM implantation is caused by *staphylococcus aureus* whereas *staphylococcus* 

*epidermidis*, pseudomonas or other organisms are seen in late infections.<sup>14</sup> The yield of blood cultures is variable depending on technique and prior antibiotic use. Pseudomonas was the commonest organism and was isolated in two (lead in case 1 and blood culture in case 3). Bacteria in biofilms on surface of leads are protected from killing by host defences and antimicrobial agents. Hence, antibiotic therapy is insufficient to eradicate the adherent bacteria.<sup>10,13</sup> Early surgical correction is life saving and involves extraction of leads, device, vegetation with or without valve replacement.<sup>10,13</sup> The prognosis is poor on conservative treatment. Both cases who refused surgery succumbed to heart failure. Conservative treatment without explantation of the devices resulted in 100% mortality compared to 12.5% in combined surgical and antibiotic therapy.<sup>17</sup>

#### 4.2. Group II

CVC related endocarditis is a lethal condition and is diagnosed with increasing frequency. This trend parallels the increasing use of CVC that have become an integral part of modern day care.<sup>18–20</sup> Both patients in this group had significant co-morbid conditions with chronic indwelling venous lines. Case 4 had CKD and was on dialysis. HD catheters have been reported to have high rate of systemic infection either by bacterial contamination via the hub of the line or via the catheter tract. The vegetation formation may result from presumed damage to the endocardial surface by the catheter itself.<sup>18,20</sup> Pseudomonas endocarditis resulted in septic complications, fulminant course and death due to multi-organ failure. *Staphylococcus aureus*, coagulase negative staphylococci and candida have commonly been reported.<sup>18,21</sup> Case 5 had aspergillus fumigatus endocarditis, which is extremely rare and carries a poor prognosis. Invasive aspergillosis occurs in immuno-compromised patients and large vegetation on echocardiography provides a clue to fungal etiology.<sup>22</sup> The combined medical and surgical approach involving amphotericin B, vegetation removal and valvulectomy did not alter the course of his underlying illness.

#### 4.3. Group III

This group of patients had underlying small sized VSD and were initially treated as pneumonia or tuberculosis. Serial echocardiography in such patients can facilitate early diagnosis. TTE or TEE will detect vegetation, diagnose VSD and quantitate TR, if any. CT chest with contrast or CT pulmonary angiography is useful to diagnose pulmonary embolism and lung infarcts which can mimic consolidation or tuberculosis on x-ray and plain CT. In small VSDs, the high velocity jet traumatizes the endothelium and vegetation tends to form in the area immediately down-stream. The vegetations usually occur on the RV side of the defect or on TV<sup>23</sup> (Table 3). Staphylococcus aureus (case 8) and streptococcus viridans (case 7) grew in blood cultures and responded well to appropriate antimicrobial therapy. These organisms are reported in most series.<sup>23</sup> Case 6 had culture negative endocarditis and required surgery in view of persistent infection despite prolonged antibiotic therapy. Patient did extremely well during next 20 years following removal of vegetation and closure of VSD. Prognosis is usually good on medical management and surgery is indicated for congestive cardiac failure or persistent sepsis.<sup>23,2</sup>

# 4.4. Group IV

TVE in this group is perplexing. Both patients had fever and pneumonia without underlying risk factor like CHD, intra-cardiac devices, CVC, CKD, diabetes, immunosuppression or drug abuse. It is possible that the infection is community acquired. Persistent fever associated with pulmonary events, anemia, and microscopic hematuria the so-called "tricuspid syndrome", should alert a clinician to search for TVE.<sup>4,15,23,24</sup> Echocardiography, bacterial and fungal blood cultures, HRCT chest/CT pulmonary angiography should be promptly considered as the delay in diagnosis can compromise favorable outcome.<sup>23,25</sup> Aspergillus TVE is a rare entity and virtually unknown in young healthy individuals without history of IV drug abuse. Case 10 presented with picture of infective pulmonary emboli and had large mobile vegetation raising the possibility of fungal endocarditis. Fungal blood cultures were negative and should not exclude the diagnosis as negative cultures are frequent in Aspergillus endocarditis.<sup>22,26</sup> Medical therapy alone is invariably fatal. Early surgery involving removal of vegetation and TV replacement resulted in excellent early and long term result.<sup>20,26</sup> The diagnosis of aspergillus endocarditis was confirmed on culture and histopathology of excised valve. Amphotericin B was administered for eight weeks followed by oral fluconazole 200 mg daily indefinitely. Voriconazole, caspofungin are newer antifungal agents currently in use.<sup>7</sup>

There are several important observations from this series and include:

- 1) Occurrence of TVE in a wide range of patients without history of IV drug abuse.
- 2) Invariably delay in referral to speciality care
- 3) High incidence of pseudomonas (30%) and fungal (20%) endocarditis
- 4) Overall high mortality (30% in hospital) and additional 20% within one year.

These findings should enable clinicians in our country to make a rapid diagnosis and consider an early surgical intervention when necessary.

#### 5. Conclusions

TVE is rare and occurs in a wide range of underlying conditions like implantable electronic devices, indwelling catheters, CHD and immunocompromised state. Surprisingly, it can occur in individuals without known risk factors. A high degree of suspicion is required and early echocardiography is recommended in patients with unexplained fever and pulmonary events. Blood cultures were negative in half the patients. Pseudomonas and *aspergillus fumigatus* were responsible for endocarditis in 50% of the cases. Early surgery is recommended in pacemaker lead and fungal endocarditis for favorable prognosis. Patients with CHD usually do well on medical management.

## Limitations

This is a retrospective study. TVE is rare in non-drug addicts and small number of patients in each group made a statistical analysis difficult.

### **Conflicts of interest**

The authors declare that there are no conflicts of interest.

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perforation and exteriorisation following failed percutaneous extraction, superior vena cava obstruction, tricuspid valve endocarditis, pulmonary embolism and prosthetic tricuspid valve thrombosis. *J Cardiothorac Surg.* 2009:4:12.

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