Indian Heart Journal 74 (2022) 163–169

Contents lists available at ScienceDirect

Indian Heart Journal

journal homepage: www.elsevier.com/locate/ihj

Original Article

# Clinical profile and one-year outcomes of patients with mural infective endocarditis: – A tertiary care centre study based on data from a seven-year registry

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ARTICLE INFO

*Article history:*
Received 18 January 2022
Received in revised form
23 April 2022
Accepted 8 May 2022
Available online 10 May 2022

*Keywords:*
Infective endocarditis
Mural vegetations
Embolism

ABSTRACT

*Background:* Infective endocarditis patients present very rarely with vegetations on the mural endocardium. Only very few studies are available comparing Mural infective endocarditis with commoner valvular or device related infective endocarditis.
*Aim:* To analyse the clinical features, microbiological profile and clinical course of mural endocarditis in comparison to valvular endocarditis.
*Methods:* This was a retrospective analysis of data from a registry of infective endocarditis. Patients enrolled between April 2012 and April 2019 were included. Patients who were reported to have vegetations on the mural endocardial surface were taken as a group and compared with rest of the patients. Clinical profile, laboratory parameters including culture and outcomes were compared between the two groups.
*Results:* Out of 278 patients in the study, 15 (5.38%) had vegetations on the mural endocardium. Of them, only 4 patients had structural heart diseases. All the patients with mural endocarditis were NYHA class II or below at presentation. Ventricles were the commonest sites of vegetations. Inflammatory markers like ESR and CRP were low in mural endocarditis compared to rest. Culture positivity was high in mural endocarditis and Staphylococcus Aureus was the commonest organism. Mural endocarditis patients had similar in hospital mortality to rest of the patients. Cardiac complications were not reported in mural endocarditis, but they had similar incidence of embolic complications including neurological events.
*Conclusion:* Mural endocarditis is a rare clinical entity with similar morbidity and mortality to that of endocarditis with valvular vegetation.


## 1. Introduction

Infective endocarditis (IE) is defined as an infection of a native or prosthetic heart valve, the endocardial surface, or an indwelling cardiac device. Mural infective endocarditis (MIE) may be clinically defined as infective endocarditis with visible vegetations on the endocardial surfaces of cardiac chambers with or without vegetations elsewhere. Compared to the valvular endocarditis, this is an extremely uncommon and easily overlooked entity. Conditions which predispose the vegetations to localise on to mural endocardium are variable[1] This may be endocardial injury resulting from high velocity jets of regurgitation lesions or of intracardiac shunts. It can also be structural changes like aneurysms or pseudoaneurysms or contact with infected leads. Another common source of infection in MIE is indwelling catheters. Rarely, it may be a consequence of generalised immunosuppression without any cardiac damage. Mural vegetations can be solitary or multiple[2] and are more difficult to be distinguished from other masses like thrombi or tumours. The annual incidence of infective endocarditis is 3–10 per 100000 people[1] and the true incidence of mural endocarditis is unknown. Most of the literature associated with mural endocarditis are case reports or small case series. Recently, a study using the data

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https://doi.org/10.1016/j.ihj.2022.05.003

from the GAMES registry, which is a large multicentre registry of infective endocarditis from Spain analysed MIE and compared with valvular infective endocarditis (VIE) and device related infective endocarditis (DIE).[3] More number of similar studies are needed for the proper understanding of this entity and forming guidelines for the management.

## 2. Aim of study

To analyse the clinical features, microbiological profile and clinical course of mural endocarditis and to compare them with those of valvular endocarditis.

## 3. Methods

This is a retrospective analysis of patients admitted between April 2012 and April 2019 from a prospectively maintained registry of adult patients with infective endocarditis at a tertiary cardiac care centre. Patients with mural endocarditis were grouped and compared with rest of the patients. Mural infective endocarditis was defined as vegetations attached to nonvalvular endocardial structures in patients fulfilling criteria for infective endocarditis by modified Duke criteria. All definite and possible cases of IE were included in the analysis. Paediatric cases were not included in the registry as such cases are managed in a separate Institute of Maternal and Child health. Data collected included demographic characteristics, clinical features, echocardiographic parameters and laboratory values. In hospital outcomes were analysed and patients were followed up to 6 months. Many of the patients were initially admitted at other hospitals and to other departments at our hospital and taken over after the diagnosis of endocarditis. A clear distinction in to nosocomial or community acquired endocarditis could not be made in many of these patients.

Transthoracic echocardiography (TTE) was performed as the initial screening test in all patients with suspected endocarditis. Patients who satisfy the modified Duke criteria after transthoracic echo were included in the registry. All these patients subsequently underwent Transoesophageal echocardiography (TEE). Patients who did not satisfy modified Duke criteria after the initial TTE and had no alternate diagnosis also underwent TEE for the exclusion of infective endocarditis.

Primary outcome measured was in hospital mortality. The other outcomes which were used for analysis are:

1. Cardiac complications which are defined as refractory heart failure, aortic root abscess, high grade AV block, hemodynamically unstable tachyarrhythmias or pericardial tamponade.
2. Clinically manifested embolic events, of which neurological events were assessed individually also.
3. Acute kidney injury defined as 50% fall from estimated GFR at presentation. Suspected drug induced renal dysfunction which promptly recovered on stopping the drugs was not considered.

Patients were treated as per the protocol which was in practice at the particular time and modifications were done at the discretion of treating physician. Almost all of the patients completed the whole course of antibiotic therapy from this hospital itself. The patients, either treated medically or underwent surgery were followed up at intervals of 1 month, 3 months and 6 months after discharge by outpatient visits. Follow up TTE was done routinely at 1 month and thereafter as clinically indicated.6-month mortality also was estimated.

## 4. Statistical analysis

Categorical and quantitative variables were expressed as frequency (percentage) and mean ± SD respectively. Independent *t* test was used to compare quantitative parameters between categories. Chi-square test was used to find association between categorical variables. Mann–Whitney *U* Test was used to compare ordinal parameters between groups. For all statistical interpretations, $p < 0.05$ was considered the threshold for statistical significance. Statistical analysis was performed by using a statistical software package SPSS, version 20.0.

## 5. Results

The study flow chart is given in the Fig. 1. Out of 278 patients diagnosed with infective endocarditis during the study period, 18 patients had vegetations on native endocardial surfaces other than cardiac valves and were diagnosed as MIE. The other 260 patients had vegetations on native or prosthetic valves or on indwelling cardiac leads and were considered as non-mural endocarditis. Of the 18 patients with mural endocarditis, 3 patients had vegetation on the valves also and they were excluded from the study. So finally, 15 patients (5.4%) were included in the MIE group for analysis Fig. 2).

The details of structural heart diseases and pre disposing conditions if any among patients with MIE are given in Table 1. In the case of four patients with structural heart disease, two had mild to moderate valvular regurgitation (one mitral and one aortic) with vegetations at a possible site of impingement of regurgitant jet. Third one was a small ventricular septal defect with vegetation on the RV side of septum. Fourth patient was a case of coronary artery disease with LV apical aneurysm with a thrombus on follow up. He presented with prolonged fever and echo showed a long mobile vegetation attached to thrombus. The very next day, a large part of it embolised to produce a massive stroke.

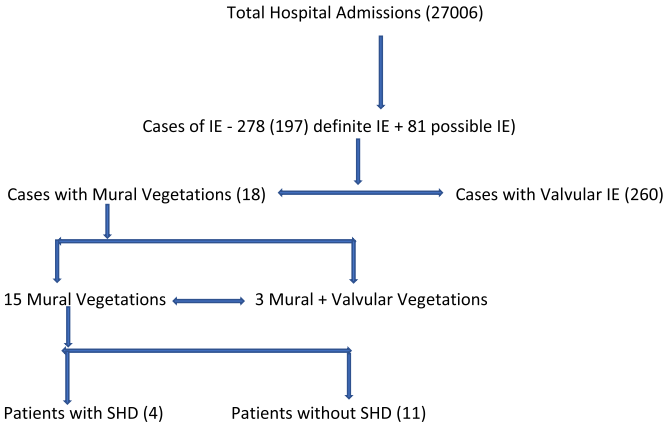


**Fig. 1.** Study flow chart.

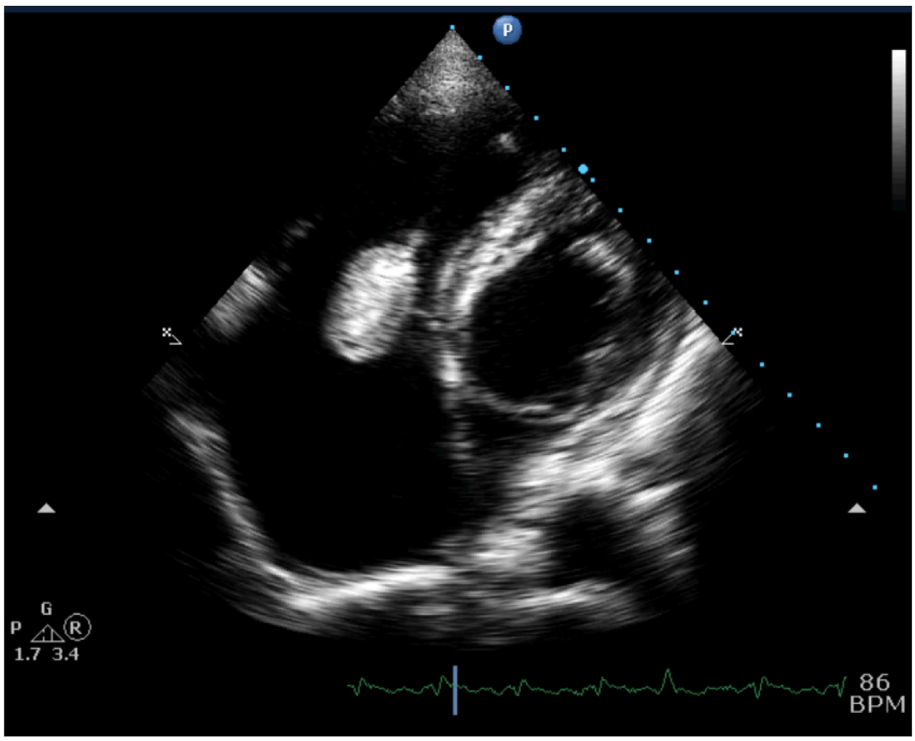


**Fig. 2.** Large freely mobile vegetation in RV attached by a thin stalk to RVOT.

**Table 1**
Predisposing conditions in mural endocarditis.

| Predisposing condition | Number |
|---|---|
| Structural heart disease | 4 |
| Central vein cannulation | 1 |
| Disseminated TB | 1 |
| Nocardiosis | 1 |
| Cirrhosis | 1 |
| Chronic kidney disease | 1 |
| Post-partum period | 1 |
| DM | 2 |
| None | 3 |

11 patients had no structural heart disease at the time of diagnosis of mural endocardial vegetations. One patient had prolonged use of central vein catheter and had vegetation at RA roof near SVC orifice and might be causally related to central vein cannulation. Two patients had disseminated infections, nocardiosis (Fig. 5) in one and tuberculosis in the other. Five patients had co morbid conditions which might have reduced their immune status and/or predisposed them to exposure to invasive procedures. Two had diabetes, one each had cirrhosis and chronic kidney disease and one patient developed the disease in post-partum period. Three patients had no co morbid conditions.

The demographic, clinical and laboratory features of patients are given in the Table 2. Patients with mural endocarditis were less sick at the time of presentation and had lower levels of inflammatory

**Table 2**
Baseline clinical and laboratory parameters.

| | Mural Endocarditis | Valvular endocarditis | P value |
|---|---|---|---|
| Age | 38.2 (14.2) | 41.5 (15.1) | 0.237 |
| Male | 9 (60%) | 151 (58%) | |
| NYHA class at presentation | 5 (33.3%) | 25 (9.6%) | <0.01 |
| NYHA I | 10 (66.6%) | 98 (37.7%) | |
| NYHA II | 0 | 111 (42.7%) | |
| NYHA III | 0 | 26 (10%) | |
| NYHA IV | | | |
| ESR mm/hr | 74.2 (14.7) | 93.4 (20.7%) | <0.01 |
| CRP above 40 mg/L | 2 (13.3%) | 111 (42.7%) | 0.025 |
| Large Vegetation (10 mm or more) | 12 (80.3%) | 113 (44.5%) | 0.007 |
| Culture Positive | 13 (86.7%) | 175 (67.3%) | 0.117 |
| Staphylococcus Aureus N | 10 (66.7%) | 88 (33.8%) | 0.01 |

ESR, Erythrocyte sedimentation rate; CRP, C reactive protein.
Data expressed as Number (percentage) or Mean (standard deviation).

markers like ESR and CRP. None of the patients with mural endocarditis had ESR greater than 100 mm/h. The number of patients with larger vegetations (more than 10 mm) was higher in the MIE group (80.3% v/s 44.5%). Culture positivity was high among patients with mural endocarditis, only two patients remaining culture negative. Staphylococcus aureus was the commonest pathogen both in mural and valvular endocarditis, more so in the mural endocarditis (66.7% v/s 33.8% p value 0.01). Streptococcus, Candida and Nocardia were the other three organisms isolated from one each of culture positive patients.

**Table 3**
Location of vegetations in mural endocarditis.

| Chamber | Number (%) | Sites |
|---|---|---|
| Right Ventricle | 4 (26.6) | 1.RVOT:2<br>2.IVS:1<br>3.Free wall:1 |
| Left Ventricle | 6 (33) | 1.Lateral wall:2<br>2.Apex: 2<br>3.LVOT:1<br>4.IVS:1 |
| Right Atrium | 2 (13.3) | 1.Roof: 1<br>2.Eustachian valve: 1 |
| Left Atrium | 2 (11) | 1.Torus aorticus:1<br>2.Posterior wall: 1 |
| More than one chamber | 1(6.6) | RVOT and LV lateral wall |

RVOT, Right Ventricular Outflow Tract; LVOT, Left Ventricular Outflow Tract; IVS, Interventricular Septum, LV, Left Ventricle.

Regarding the site of vegetations, ventricles predominated with more patients with vegetations in LV (Figs. 2 and 4) than in RV (Fig. 3). One patient had vegetations in both RV and LV. The number and distributions of vegetations are shown in the Table 3.

Comparison of outcomes between MIE and valvular endocarditis is given in the Table 4. The in hospital and 6 months mortality did not differ between the two groups. The incidence of neurological complications as well as overall embolic phenomena also did not differ between the two groups. One patient with right sided mural endocarditis had paradoxical embolism and anterior spinal artery occlusion. In this patient, we could demonstrate transient right to left shunt through patent foramen ovale during Valsalva in TEE. Out of the 7 patients who had right sided vegetations in the MIE group, two patients developed septic embolization in to lungs. None of the patients with MIE developed complications like refractory heart failure, complete heart blocks and abscess formation. None of the patients underwent surgery in the MIE group. In the MIE group, 5 patients had a stormy course with multiorgan dysfunction. One of them was the patient with systemic tuberculosis and another one was Candida endocarditis. All the other three patients had Staphylococcus aureus endocarditis. All of them were managed medically and patient with Candida endocarditis, tuberculosis and one patient with staphylococcus aureus had in hospital mortality. Another patient with CKD and Staphylococcus aureus endocarditis had a relatively stable hospital course, but had sudden death at home the cause of which and any association with endocarditis could not be established.

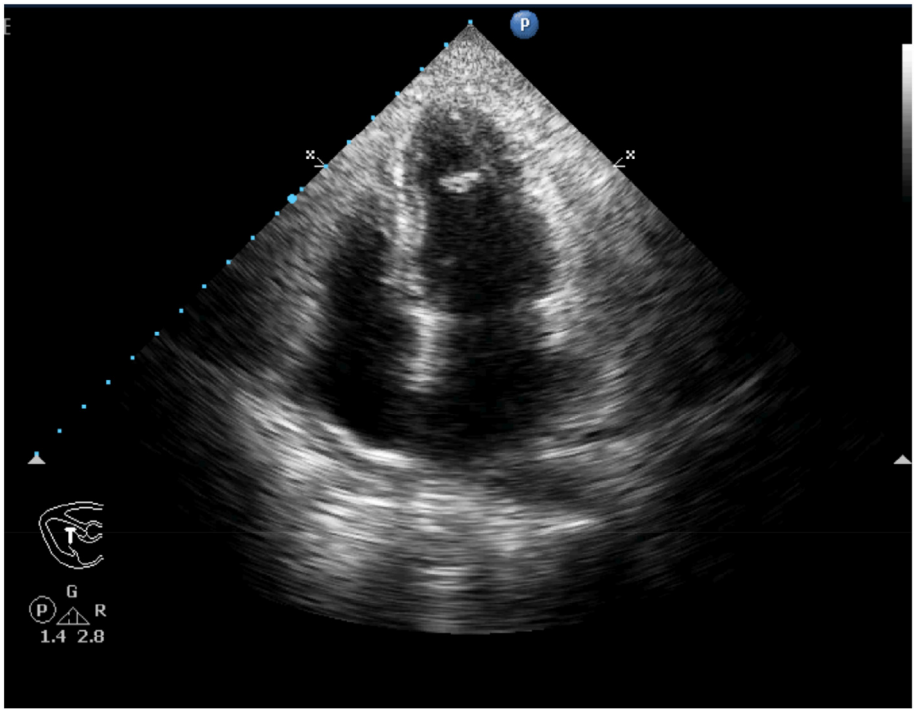


**Fig. 3.** Vegetation attached to anterolateral wall of LV close to apex.

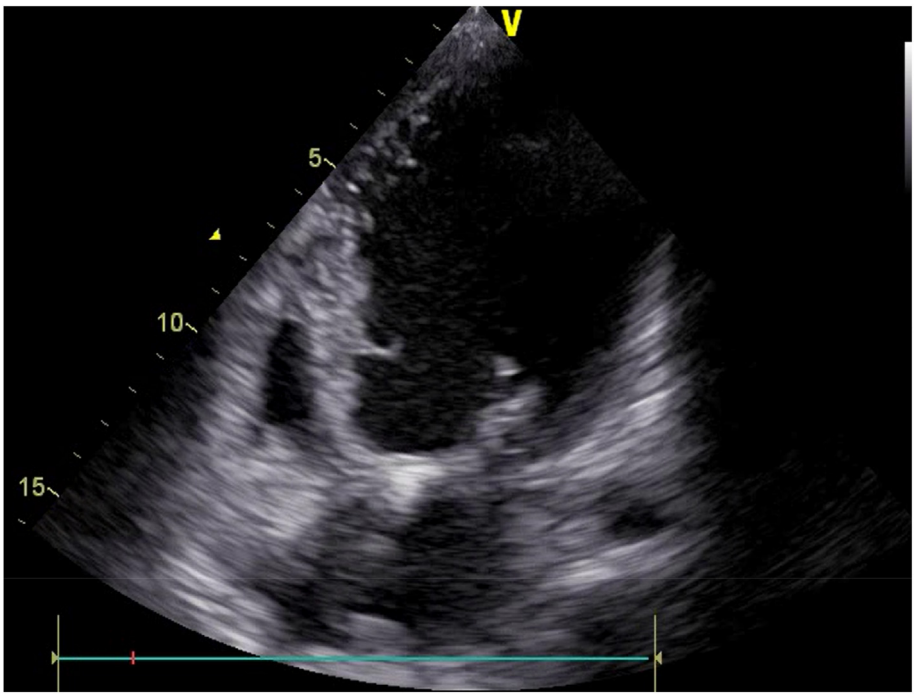


**Fig. 4.** Small linear vegetation attached to LV side of IVS. This patient had Aortic regurgitation and the vegetationwas at the site of impingement of AR jet.

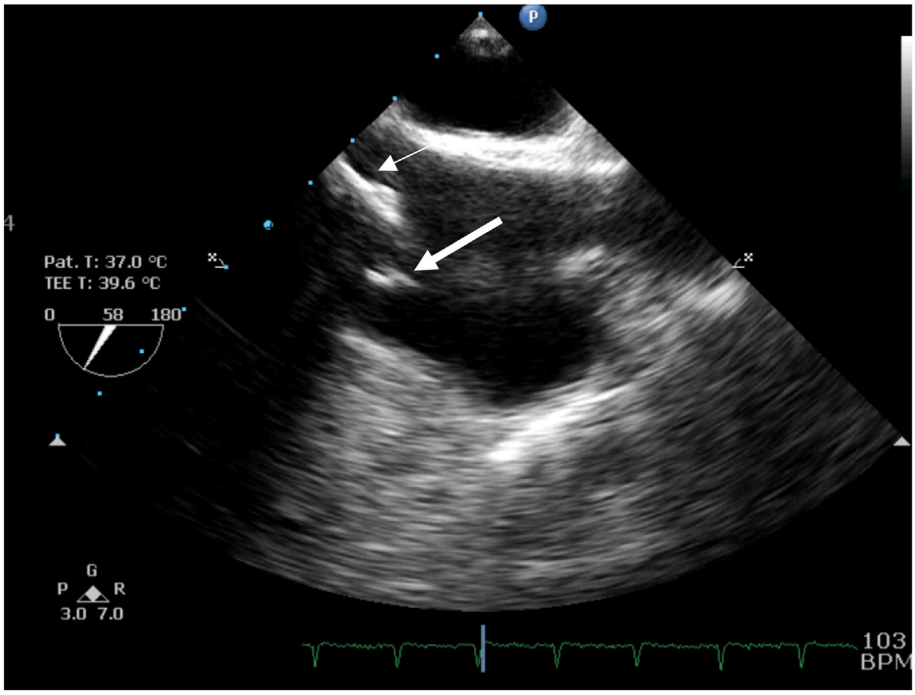


**Fig. 5.** TEE image from patient with systemic Nocardiosis with a vegetation (thick arrow) attached to a prominent Eustachian valve (thin arrow).

There are three patients in the series who had no structural cardiac damage other than vegetations and no conditions predisposing them for compromised immune status or multiple hospitalisations. All of them were below 40 years of age. All the three had left ventricle as the site of vegetation and culture positivity with Staphylococcus aureus. Two patients had renal dysfunction during the course of illness and the third patient had multiorgan dysfunction and in hospital mortality.

**Table 4**
Comparison of outcomes between mural and valvular endocarditis.

| | Mural endocarditis | Valvular endocarditis | P value |
|---|---|---|---|
| Cardiac complications | 0 | 85 (32.7%) | 0.004 |
| Neurological events | 3 (20%) | 56 (21.5%) | 0.888 |
| Composite embolic phenomena | 8 (53.3%) | 93 (35.8%) | 0.17 |
| Renal failure | 4 (26.7%) | 68 (26.3%) | 0.972 |
| Need for emergency surgery | 0 | 53 (20.4%) | 0.02 |
| In hospital mortality | 3 (20%) | 54 (20.8%) | 0.95 |
| 6 months mortality | 1 (10.7%) | 14 (9.1%) | 0.86 |

Data expressed as Number (percentage).

## 6. Discussion

Mural infective endocarditis is a very rare condition and its incidence is not known. Apart from a study by Villanueva et al,[3] based on the large GAMES registry data, most of the published literature consist of case reports and few case series. This study consists of two sets of patients with MIE. One set consists of patients prospectively recruited in the GAMES registry and the other set formed from patients reported in the literature case reports and case series. In the GAMES registry, MIE cases represented 0.07% of the total infective endocarditis. This was a multicentre study involving 35 centres forming a comprehensive database of infective endocarditis. In our series, the proportion of MIE was relatively high (5.34%). Such a disproportionate increase may be explained by the strong referral bias inherent to any single centre study being conducted in a tertiary care centre. Usual cases of valvular endocarditis would have been managed by peripheral hospitals and presence of vegetations at unusual sites prompt reference to higher centre. Hence the higher prevalence of MIE in our series may not be reflecting the true state of affairs. In the GAMES series, 63% cases were hospital acquired while in the literature series reported in the same study only 14% were hospital acquired.[3] In our series, the data was not sufficient enough to clearly separate hospital acquired and community acquired infections.

Patients with endocarditis and vegetations on heart valves usually have structural damage to the valve which may or may not be known to them. It will be difficult to estimate how much of that damage was contributed by infection and how much was pre-existing. In the case of MIE, one should look for structural heart diseases with high velocity jets, which may not be hemodynamically significant but can cause endocardial injury at the site of impingement predisposing to MIE. In our series, there were three such patients. In the study by Villanueva at al,[3] there were three patients with congenital heart diseases but no specific mention to the possibility of a jet related endocardial injury. In that study, there was a significant proportion of patients with history of organ transplantation, I.V drug abuse and maintenance haemodialysis. But in our series, none of the patients had these conditions, may be due to smaller size of the series. In our series, there were three patients who did not have any structural heart disease or any co morbidities prior to presentation with MIE. All these three patients had a stormy clinical course with multi-organ dysfunction and one had mortality. Probably, these patients had systemic sepsis due to some unexplained condition and cardiac vegetation may be a small part of it as in the case of two patients with tuberculosis and Nocardiosis in our series.

In suspected native valve endocarditis, transthoracic echocardiography (TTE) is moderately sensitive (75%) and specific (more than 90%) for detection of a vegetation.[4] But in the case of MIE, being in an unusual location, one may expect these vegetations to escape detection during initial echocardiographic examination. But surprisingly, in all of our patients with mural vegetations, they were seen in the first transthoracic examination itself. This may be due to their relatively larger size at presentation. This may also be due to their locations being the areas well visualised transthoracially. For apical endocardial masses, TTE is regarded to be superior to transoesophageal echocardiography (TEE). This is because apical regions of both ventricles are often foreshortened on TEE.[2] Nonetheless, all these patients require TEE for comprehensive assessment of the spread of infection.

Staphylococcus aureus is one of the most common organisms to affect the cardiac tissue, especially in settings in which patients are exposed to health care–related procedures. Virulent staphylococci have eclipsed penicillin-sensitive streptococci as the most common cause in many high-income countries.[5] Staph aureus contributed only to 14% cases of MIE in the GAMES registry but in the literature series reported in the same study, 50% had Staph aureus as the aetiology.[3] In our series also, Staph. aureus was the commonest pathogen both in mural and valvular endocarditis, more so in the mural endocarditis. Staph. aureus positivity is consistently an independent risk factor for in-hospital death. In the current series also most of the patients with staphylococcus positivity had a stormy post operative course. The study by Villanueva et al[3] reported a high prevalence of fungal endocarditis reaching up to 25%. But our study had only a single case of fungal endocarditis. This is probably due to the difference in patient population.

Mural vegetations are less likely to produce hemodynamic compromise and hence cardiac symptoms in the early phase of illness. None of the patients with MIE developed cardiac complications defined in the methodology section. Same findings are observed in the GAMES registry series also.[3] Mural vegetations were larger at the time of detection compared to non-mural endocarditis. Same finding was seen in GAMES registry series.[3]

The most frequent complication of MIE is peripheral embolization, especially neurological.[2] In our series, mural vegetations were equally likely to produce embolic manifestations compared to valvular vegetations. Neurological events and renal failure were similar. Same findings were observed in the GAMES registry series except for a slightly lower incidence of neurological events in the MIE group than in valvular endocarditis.[3]

Inflammatory markers were consistently lower in MIE as shown in the Table 2. In an earlier study involving the patients from a part

of same registry (between 2012 and 2015) showed a CRP level above 40 mg/L at presentation to be a strong predictor of mortality.[6] The same cut off was used in the present study and was found that significantly lower proportion of patients with mural endocarditis had this value at presentation (Table 2.) But the sample is too small to permit a subgroup analysis of effects of CRP on mortality between mural and valvular endocarditis. The reason for lower degree of inflammation in mural endocarditis patients is not clear.

A 1994 review of non-valvular cardiovascular infections, including mural endocarditis, by Kearney et al highlighted the paucity of data to guide treatment and management strategies.[2] An established guideline for managing valvular endocarditis recommends early surgical intervention when the infection is associated with a large vegetation, major valvular complications, and peripheral embolism. It is not yet clear whether this approach is appropriate for mural endocarditis. Culture directed antibiotic treatment was the initial approach for all our mural endocarditis patients. Majority of our patients responded well to medical management. Patients who had embolic episodes were also continued on medical treatment as they were otherwise responding clinically. Mortality was comparable to that of valvular endocarditis (Table 4). Our mortality data is similar to that of the GAMES registry and the associated literature series reported in the study by Villanueva et al except for a slightly higher in hospital mortality among patients with valvular endocarditis in the GAMES registry series[3]

## 7. Limitations

All retrospective data analysis has its own limitations as some data may be missing from the registry. We could not ascertain all patients definitely in to hospital acquired, health care related or catheter related endocarditis, such analysis was not attempted. Some laboratory parameters which are important in a prognostic point of view like plasma d Dimer, Rheumatoid factor and procalcitonin were not measured in our patients. Neurological imaging was done only in patients who had clinical manifestations of nervous system involvement. Referral bias is another limitation as the series belong to a tertiary care referral centre. We excluded paediatric cases of IE as such cases are managed in separate hospital away from our hospital.

## 8. Conclusion

Mural infective endocarditis is a rare but significant type of intracardiac infection which produces less hemodynamic disturbances but similar morbidity and mortality to that of valvular infective endocarditis. Larger prospective studies are needed for proper understanding of this disease and for developing management strategies.

## 9. Key questions of the study

1. What is already known on this subject?

Infective endocarditis with vegetations on the mural endocardium is a rare entity. There are only very few studies analysing Clinical and microbiological profile as well as prognosis of mural endocarditis as a separate entity in comparison with valvular endocarditis.

2. What does this study add?

Patients with Mural infective endocarditis are likely to have larger vegetations, to be less symptomatic and to be hemodynamically stable at presentation. But they do have an equal probability for an embolic episode with possibly equal morbidity and mortality.

3. How might this impact on clinical practice?

Findings of this study implicate the need for larger prospective studies for establishing the guidelines for management including the surgical intervention for this entity which is currently being managed on same guidelines of valvular endocarditis.

## Declaration of competing interest

None of the authors have any conflicts of interest to declare. The study has received no financial support.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2022.05.003.

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