

# Clinical Profile and Etiology of Patients with Pericardial Effusion

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## ABSTRACT

**Background:** Pericardial effusion are one of the common cardiac problems in our part of the world and is associated with high risk of morbidity and mortality if not diagnosed and treated. The aim of this study was to determine etiological spectrum and clinical presentation of moderate to large pericardial effusion. **Methods:** A descriptive cross-sectional study was conducted from February 2023 to July 2023 at Department of Cardiology, NMC-TH. Fifty patients were included in the study who visited to NMC-TH; OPD, ward and emergency department. Apart from routine investigations, ECG, chest X-ray and echocardiography were performed in all patients. Pericardiocentesis was done in 37 patients (74%). Specific investigations for the suspected etiological diagnosis were done. **Results:** A total of 50 patients (30 Male, 20 Female) were included in the study with age ranging from 11 to 76 years. The most common clinical presentations were dry cough (86%) followed by shortness of breath (70%) and fever (66%). In this study, the most common etiology of pericardial effusion was tuberculosis (n=22; 44%) followed by malignancy 6(12%), idiopathic 6(12%), and Hypothyroidism 4(8%). Among malignancies, carcinoma of lung was the commonest 3(50%). Tuberculosis was the most common cause in patients presenting with tamponade 8(61.5%) followed by malignancy 2(15.3%). **Conclusion:** This study shows tuberculosis is the most common cause of pericardial effusion followed by malignancy.

**Keywords:** pericardial effusion; cardiac tamponade; tuberculosis.

## INTRODUCTION

Pericardial effusion is an abnormal accumulation of fluid in the pericardial cavity.<sup>1</sup> A pericardial effusion with enough pressure to adversely affect heart function is called cardiac tamponade.<sup>2</sup> Pericardial effusion may be caused by a wide variety of infectious or noninfectious processes.<sup>3</sup> The common causes of pericardial effusion vary depending on geography and the population. Echocardiography confirms the diagnosis of pericardial effusion and allows to assess for the signs of hemodynamic. The pericardiocentesis is indicated when the effusion is symptomatic and accompanied by tamponade or the causes is of questionable.<sup>5</sup> In Developed Countries Malignant pericardial effusion is seen in around 50-60% of patients<sup>6,7</sup>. In Developing Countries study done by Jamal Uddin et al.<sup>10</sup> the common etiology of pericardial effusion was tuberculosis followed by Idiopathic, uremic, and Malignancy. The purpose of this study is

to determine the etiology and clinical profile of Tarai region patients who present with pericardial effusion.

## METHODS

All the patients who presented to National Medical College and Teaching hospital and who met the inclusion criteria were included in the study from February 2023 to July 2023. Inclusion criteria includes patients age >10 years, patients with moderate to large pericardial effusion and patients with moderate to large pericardial effusion with cardiac tamponade. Whereas exclusion criteria were patients with Mild pericardial effusion <10mm in absence of cardiac tamponade and iatrogenic such as cardiac surgery, catheterization and posttraumatic cases. ECG, Echocardiography, X-ray chest along with baseline blood investigations were sent for confirmation of pericardial effusion, cardiac tamponade and constrictive pericarditis. By 2-D echocardiography, a pericardial effusion is semi-

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quantitatively described on the basis of the size of the echo-free space seen between the parietal and visceral pericardium at end-diastole small effusion(10mm) moderate effusion (10–20 mm), large effusion (>20 mm) or very large (>25 mm). Cardiac tamponade with a moderate or large pericardial effusion, showing the effects of the cardiac compression and reduced filling. Early diastolic collapse of the right ventricular free wall, late diastolic collapse of the right atrium. An important 2D sign of cardiac tamponade is IVC dilatation (>2.1 cm) with <50% collapsing during inspiration. For peak mitral E inflow, the maximal drop occurs with the first beat of inspiration and the first beat of expiration and usually exceeds >30% respiratory variation. For peak tricuspid E inflow, the maximal drop is on the first beat in expiration at the same time as the hepatic vein atrial reversal and usually exceeds >40% respiratory variation. Chronic constrictive pericarditis was confirmed by CECT chest showing thickened and calcified pericardium. Ethical and Research Committee of National Medical College-Teaching Hospital has discussed and approved the proposal and has given clearance for this study (Ref. F-NMC/624/079-080).

## RESULTS

A total of 50 patients were included in the study with age ranging from 11 to 76 years. 30 patients (60%) were male and 20 (40%) were female. The most common clinical presentation was dry cough (86%) followed by shortness of breath (70%) and fever (66%). The least common clinical presentation was bradycardia (6%). Among 50 patients, large pericardial effusion was present in 34 patients (68%), whereas 16 patients (32%) had moderate pericardial effusion. Out of which 13 patients (26%) had echocardiographic as well as clinical evidence of cardiac tamponade. There were no patients with mild or loculated effusion. The baseline clinical characteristics are shown in Table 1. In the study the most common etiology of pericardial effusion was found as tuberculosis 22(44%) followed by malignancy 6(12%), acute idiopathic/viral 6(12%), and Hypothyroidism 4(8%). The information of etiological profile of pericardial effusion is listed in

**Table 1. Demographic, Clinical and Laboratory characteristics. (n=50)**

Clinical/laboratory characteristics	Frequency (%)
<b>Age (years)</b>	
Mean $\pm$ SD	45.6 $\pm$ 17.6
Range	11-76
<b>Gender</b>	
Male	30(60)
Female	20(40)
<b>Symptoms</b>	
Cough	43(86)
Breathlessness	35(70)
Fever	33(66)
Palpitation	17(34)
Chest pain	14(28)
Other associated symptoms	11(22)
<b>Signs</b>	
Tachycardia	16(32)
Hypotension	16(32)
Muffled Heart sounds	16(32)
Raised JVP	14(28)
Pulsus paradoxus	4(8)
Bradycardia	3(6)
Electrical Alternans (ECG)	11(22)
Cardiomegaly (CXR)	37(92)
<b>Echocardiography</b>	
Moderate PE	16(32)
Large PE	34(68)
Tamponade	13(26)

**Table 2. Etiological Profile of Pericardial Effusion. (n=50)**

Diagnosis	Frequency (%)
Tuberculosis	22(44)
Malignant	6(12)
Idiopathic/Viral	6(12)
CKD (Uremia)	3(6)
CKD with TB	2(4)
PCKD with TB	1(2)
Hypothyroidism	4(8)
Pyogenic	3(6)
Post MI	1(2)
SLE	2(4)
HIV	0

(Table2).

Most of the idiopathic effusion was considered to be of viral origin. Among malignancies, carcinoma of

lungs was the most common 3(6%) (Table 3).

**Table 3. Malignancies associated with Pericardial Effusion (n=6).**

Malignancy	Frequency (%)
Carcinoma Lung	3(50)
Carcinoma Breast	1(16.6)
Thyroid Papillary Carcinoma	1(16.6)
Carcinoma Ovary	1(16.6)

**Table 4. Patients presenting in Cardiac Tamponade and Etiological groups. (n=13)**

Etiology	Number (%)
Tuberculosis	8(61.5)
Malignancy	2(2)
SLE	1(7.6)
Uremic	1(7.6)
Pyogenic	1(7.6)

**Table 5. Etiology versus echo characteristics of the effusion.**

Etiology	Thickened Pericardium (n=7)	Thickened Fluid (n=10)	Fibrin Strands (n=18)	Shaggy Pericardium (n=2)	Hemorrhagic Appearance
Tuberculosis	6(66.6)	7(70)	9(50)	1(50)	-
Pyogenic	-	-	3(16.6)	-	-
Malignancy	-	2(20)	2(11)	1(50)	-
Idiopathic	-	-	1(5.5)	-	-
SLE	-	1(10)	1(5.5)	-	-
Uremic	1(33.3)	-	1(5.5)	-	-
Hypothyroidism	-	-	1(5.5)	-	-

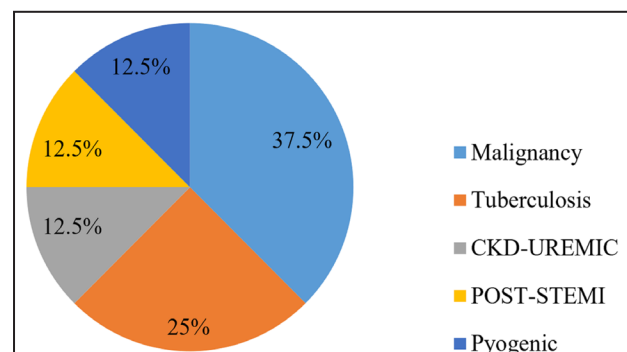
**Table 6. Relationship between the etiology and the Echo features of the effusion.**

Echo feature	Tuberculous (22)	Malignant (6)	Idiopathic (6)
Fibrin strands	9(40.9)	2(33.3)	1(16.6)
Thickened pericardium	6(27.2)	-	-
Thickened fluid	6(27.2)	2(33.3)	-
Shaggy Pericardium	1(4.5)	1(16.6)	-

Tuberculosis was the most common cause in patients presenting with tamponade (n=8; 61.5%) followed by malignancy (n=2; 15.3%); in (Table 4).

One patient (2%) had large pericardial effusion of more than 3 months duration in which no etiology could be established after extensive evaluation and was labeled as chronic idiopathic effusion. The etiology of pericardial effusion was evident clinically or by specific investigations. Also, 43 patients (86%) had the correct diagnosis of pericardial effusion and

37 patients had the diagnosis on first visit while remaining patients on subsequent visit. The arrhythmia associated with pericardial effusion was present in 9 patients (18%) and the most common arrhythmia was frequent VPCs (n=4; 44.4%) followed by AF (n=3; 33.3%). Pericardiocentesis was done by sub-xiphoid approach in 37 patients (74%). The procedure related complications were in 2 patients (5.4%), one patient had vasovagal response with hypotension and another had supraventricular tachycardia. There was no death as a consequence of the procedure. Macroscopically, the fluid was hemorrhagic in 19 patients (51%), serous in 15 patients (40%), and purulent in 3 patients (8.1%). However, one patient among 3 patients with purulent effusion was sent to another center for



**Figure 1. Mortality on the basis of Etiology in patients with Pericardial Effusion.**

pericardiectomy. Cytology for malignant cells was positive in 2 patients (50%) out of 4 patients who underwent pericardiocentesis of malignant etiology. The total mortality was 8 (16%). Among 8 patients who died, 6 patients (75%) had cardiac tamponade and had undergone pericardiocentesis. The underlying etiology of these patients is shown in (Figure 1).

The echocardiography characteristics in relation to the etiology showed tuberculosis to be the commonest cause of effusion and thickened fluid appearance. Fibrin strands were found mainly with tuberculosis (50%). The shaggy pericardium was associated with tuberculous and malignancy etiologies as listed in Table 5. The echocardiography characteristics of the pericardial effusion were helpful to differentiate between the tuberculous, malignant and idiopathic etiologies as mentioned in (Table 6).

The diagnosis of tubercular pericardial effusion was done based on clinical and specific investigations. Among 22 tubercular patients, 15 (68%) had the correct diagnosis based on pericardial fluid analysis for ADA which accounts for 30% of the total patients and 7 patients (32%) were treated empirically with ATT who responded on it. Out of 7 patients who were empirically treated with ATT, 1 patient diagnosed as malignancy in other visit when presented with recollection and in Tamponade. In 93% of tuberculosis patients who underwent pericardiocentesis had ADA activity  $\geq 40$  U/L and 7% with ADA activity  $\geq 30$  U/L. Two patients with non-tubercular effusion had ADA activity  $\geq 30$  U/L and 2 patients with non-tubercular effusion had ADA activity  $\geq 40$  U/. These included patients with malignancy and chronic kidney diseases. The total mortality was 8 (16%), out of which 4 patients (8%) had in-hospital mortality and 4 patients (8%) had out-hospital mortality confirmed by phone call. Patients were followed up after 1 and 3 months for reassessing the pericardial effusion and complications. In our study, 29 patients (58%) came for follow up at 1 months, 22 patients (44%) came for follow up for 3 to 6 months and 9 patients (18%) didn't come for follow up. There were 4 out-hospital mortality, 2 patients (4%) had died in first month and 2 patients (4%) died

in 3 to 6 months which was confirmed on phone call. During the follow up period, symptomatic persistent pericardial effusion was found in 1 patient with known malignancy (Ca. Papillary Carcinoma), 1 patient with tuberculosis, and 1 patient with hypothyroidism.

## DISCUSSION

Pericardial effusion can be a result of wide variety of conditions and can occur at any age. In our study majority of patients were 35 to 65 years of age with mean age of  $45.6 \pm 17.6$  SD. The common symptoms and signs were cough (86%), shortness of breath (70%), fever (66%), chest pain (28%), tachycardia (32%). However, pericardial effusion with bradycardia (6%) may be found in patients with hypothyroidism and uremia. Thirty-two percentages of our patients had clinical hemodynamic significance of cardiac tamponade. In our study, we found the most common causes of pericardial effusion were tuberculosis (44%) followed by malignancies (12%) and idiopathic (12%). Among malignancies the most common was carcinoma lung (50%). In developed countries the most frequent etiologies of pericardial effusion are viral, idiopathic, neoplastic, uremic and iatrogenic, where as in developing countries tuberculous pericardial effusion is the leading cause.<sup>9</sup> In our study we found tuberculosis as the commonest cause of large effusion and cardiac tamponade followed by malignancy. In the study conducted by Alkhalifa et al.<sup>13</sup> of 51 Sudanese patients with follow up of 1 year, tuberculosis (29.4%) was the most common etiology followed by malignancy (17.6%). Similarly in the study conducted by Jamal Uddin et al.<sup>10</sup> in India, of total 66 patients in 1 year period, most common etiology was tuberculosis (27.27%) followed by idiopathic (19.69%) then Uremia (16.66%), and Malignancy (13.63%). The high frequency of tuberculosis from the above studies reflects the high incidence of tuberculosis in the developing countries like Nepal and India. Among malignant patients in our study the most common malignancy was carcinoma lung (50%), papillary thyroid carcinoma (16.6%), carcinoma ovary (16.6%) and carcinoma breast (16.6%). In

the study conducted by Irfan Yaqoob et al.<sup>11</sup> among malignancies, carcinoma lung was the most common followed by breast carcinoma and lymphoma. Acute idiopathic effusion is mostly of viral origin and performing specific investigation for viral diagnosis is not routinely done in Nepal because of cost benefit ratio, low yield, unavailability of tests and less impact on management. In the study conducted by Alkhalifa et al.<sup>13</sup> there was a strong positive correlation between the thickened appearance of the fluid and tuberculous etiology (93%) [ $p < 0.001$ ] but it was also seen in 55% of the malignant cases. A strong negative correlation (0%) [ $p < 0.001$ ] between the thickened appearance of the fluid and idiopathic etiology was also noted in their study. In our study correlation between thickened fluid/exudates and tuberculosis showed 27% sensitivity and 86% specificity and was also seen in other cases which makes this feature not highly specific. In our study features of fibrin strands and thickened pericardium was strongly correlated with tuberculosis (41% sensitivity, 68% specificity) and (5% sensitivity, 93% specificity) respectively and was more specific for tuberculosis, as it was not much seen in other cases. In the study conducted by Alkhalifa et al.<sup>13</sup> the shaggy pericardium correlated with the idiopathic (50%) ( $p < 0.05$ ) and tuberculous (33%) etiologies and was negative for malignancy. From the results of different studies, tuberculous effusion was found to be associated with exudates coating, thickened pericardium and the inflammatory signs of fibrin strands and shaggy pericardium, while thickened fluid without the inflammatory signs makes malignancy a presumptive diagnosis. The accurate diagnosis of tuberculous effusion is important because without specific treatment there is high chances of developing CCP early or late and the mean survival rate is low in these patients. The pericardial biopsy specimens taken from tuberculosis patients in our

study demonstrated nonspecific findings (chronic inflammatory lesion) in most of the patients. The diagnostic sensitivity for tuberculosis by pericardial biopsy ranged from 10% to 64% as per different studies.<sup>16 17</sup> Therefore, a normal pericardial biopsy specimen does not exclude tuberculous pericarditis.

In our study pericardial fluid ADA was significantly elevated in tuberculous pericardial effusion. The diagnostic results were obtained at cut off value of ADA  $\geq 40$  U/L (64% sensitivity and 93% specificity) and ADA  $\geq 30$  U/L (5% sensitivity and 93% specificity). In the study conducted by Burgess LJ et al.<sup>14</sup> in the Western Cape Province of South Africa involving 110 patients (of whom 64 had tuberculous pericarditis), pericardial ADA levels  $\geq 30$  U/L had sensitivity and specificity of 94% and 68% respectively and with ADA  $\geq 35$  U/L had a sensitivity and specificity of 90% and 74%, respectively, for the diagnosis of tuberculous pericarditis. Pericardiocentesis is not always feasible and non-invasive tests that are indicative of tuberculosis are very useful. These include chest radiography, CT chest, tuberculin skin test and serum globulin level. Hypothyroidism may present with large pericardial effusion and even in cardiac tamponade. In our study 4 patients (8%) were diagnosed as hypothyroidism presented with moderate to large pericardial effusion.

## CONCLUSIONS

The study showed tuberculosis as the most common cause of pericardial effusion followed by malignancy in patient presented in our center.

**Limitations:** There is lack of improved techniques for recovery of M. tuberculosis such as PCR technology, pericardial IFN-g, biopsy and culture. The present study did not determine the direct evidence for diagnosis of viral pericardial effusion.

**Conflict of interest:** None.

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