

# Characteristics of Patients with Tuberculous Pleural Effusion in Rural Nepal

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## ABSTRACT:

**Introduction:** Tuberculosis (TB) is a major cause of mortality and morbidity in developing countries. Tubercular Pleural effusion is the second most common form of extra pulmonary tuberculosis (EPTB), superseded in Prevalence only by lymph node tuberculosis. Pleural effusion occurs in approximately 5% of patients with TB. The purpose of this study was to assess the demographic characteristics of patients presenting with pleural effusion in rural Nepal. **Methods:** A retrospective study was conducted with all the cases diagnosed and admitted with pleural effusion at Lumbini Medical College And Teaching Hospital from April 2011 to March 2013 of all the cases diagnosed and admitted with pleural effusion were included in the study. Hundred cases diagnosed with pleural effusion by clinical Examination or chest X-ray or ultrasonography's (USG) of the chest were included in the studied. The following parameters patients demographic profile, causes of pleural effusion, location (unilateral/bilateral), hemoglobin and complete blood count, sputum stain and culture sensitivity, Montoux test, chest X-ray and USG findings and Pleural fluid analysis (biochemical, hematological, microbiological and cytological) were analyzed by using SPSS 21. **Results:** Out of 100 cases, the cause of pleural effusion in 59 patients was tuberculosis, 14 by malignancy, next 14 by Para pneumonic Effusion, 12 by congestive cardiac failure and three cases by alcoholic liver disease. Patients with tuberculous pleural effusion were younger, predominantly males, had unilateral effusion, lower blood hemoglobin, lower Pleural fluid neutrophils, higher pleural fluid Adenosine Deaminase (ADA) levels and higher level of pleural fluid to serum protein ratio as compared to the patients with non-tuberculous effusion. **Conclusion:** Tuberculosis is the most common cause of pleural effusion in patients of rural Nepal.

**Keywords:** adenosine • deaminase • extrapulmonary • exudative • malignancy

## INTRODUCTION:

Tuberculosis (TB) is a major cause of mortality and morbidity in developing countries. Tuberculous pleural effusion is the second most common form of extrapulmonary tuberculosis (EPTB), superseded in

prevalence only by lymph node tuberculosis. Pleural effusion occurs in approximately 5% of patients with TB.<sup>1</sup> The incidence of EPTB is rising with the rise in pandemic of human immunodeficiency virus (HIV). The diagnosis of tuberculous pleural effusion is difficult as extrapulmonary specimens have very few bacilli and consequently are associated with low sensitivity of acid fast bacillus (AFB) smear and culture. Pleural effusions are classified into transudative or exudative.<sup>2,3</sup> Exudative pleural effusions require further evaluation to differentiate among tuberculosis, malignancy and para pneumonic effusion which are the major causes in patients.<sup>4,6</sup>

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## METHODS:

This retrospective study was carried out

in patients over the age of 14 years, admitted to the medical ward at Lumbini Medical College and Teaching Hospital (LMCTH), Palpa, from April 2011 to March 2013. All patients who were admitted with a diagnosis of pleural effusion were included. The study was approved by the Institutional Review Committee. Data was retrieved from the medical record section. Information on regarding the diagnosis, comorbidities and results of biochemical analysis of blood and pleural fluid was noted. Patients were classified as having effusion due to tuberculosis, malignancy, pneumonia, congestive cardiac failure or liver disease. Rests of the causes were classified as others. Data were also obtained regarding sputum examination and pleural fluid cytology in all patients. Results were analyzed using Statistical Package for Social Sciences (SPSS 21). Continuous data were expressed as mean, standard deviation (SD), median and interquartile range (IQR), and a categorical variable as number (%). In case of continuous variables, t-test/Mann-Whitney test was applied as appropriate to see the difference in average between the groups. Similarly, Chi square analysis was performed to test differences in proportions of categorical variables between two or more groups. The cut-off value for significance was considered to be  $p < 0.05$ .

## RESULTS:

One hundred patients were included in the study. Fifty nine patients were diagnosed as tuberculous pleural effusion, 14 had malignant pleural effusion, 14 had parapneumonic effusion, 10 had effusion due to congestive cardiac failure and three had liver disease. The patients were divided into two groups. More than 50% of cases were diagnosed as tuberculous pleural effusion ( $n=59$ ) whereas 41 cases were under non-tuberculous pleural effusion.

Table 1 shows that the patients with tuberculous effusion were younger than the patients with non-tuberculous pleural effusion ( $p=0.03$ ). Patients with tuberculous pleural effusion were more commonly males ( $p=0.04$ ), had lower levels of hemoglobin ( $p=0.01$ ) and the effusion was more commonly unilateral (0.001) as compared to the patients with non-tuberculous pleural effusion. Pleural fluid analysis was also significantly different between the two groups with patients with tuberculous pleural effusion having higher pleural fluid level of adenosine deaminase (ADA) ( $p=0.001$ ), higher differential lymphocyte count ( $p=0.04$ ), lower differential neutrophil count ( $p=0.02$ ), higher pleural fluid lymphocytes to neutrophils ratio ( $p=0.02$ ) and higher pleural fluid to serum protein ratio ( $p=0.006$ ).

Table 1: Comparison between tuberculous and non-tuberculous pleural effusion

Characteristics	Tuberculous pleural effusion (n=59)	Non-tuberculous pleural effusion (n=41)	p-value
Age (years)	57.2±15.94	64.7±16.32	0.03
Gender	Male=46(77.9%) Female=13(22.0%)	Male=24 (58.5%) Female=17(41.4%)	0.04
Duration of illness (days)	18.9±14.09	19.5±18.54	0.41
Laterality of effusion	Unilateral=57(96.6%) Bilateral=2(3.3%)	Unilateral=30(73.1%) Bilateral=11(26.8%)	0.001
Hemoglobin (g/dl)	10.8±1.60	11.5±1.65	0.01
Blood glucose (mg/dl)	113±40.46	129.6±160.9	0.28
AST (U/L)	54.6±29.63	51.1±71.41	0.64
ALT (U/L)	50.5±29.63	62.1±67.39	0.10
Serum protein (g/dl)	6.6±0.51	6.7±0.46	0.26
Creatinine (mg/dl)	0.9±0.21	0.9±0.17	0.48
Pleural fluid TLC ( /cu.mm)	1220±2419	907±1223	0.31
Pleural fluid neutrophils (%)	22.0±26.54	34.4±34.10	0.02
Pleural fluid lymphocytes (%)	76.5±27.44	65.6±33.72	0.04
Pleural fluid lymphocytes/ neutrophil ratio	16.4±23.00	8.5±11.12	0.02
Pleural fluid glucose (mg/dl)	82.5±36.69	92.2±35.8	0.19
Pleural fluid ADA (U/L)	53.9±22.52	15.0±7.72	0.0001
Pleural fluid/serum protein	0.6±0.12	0.5±0.20	0.006

AST=Aspartate amino transferase, ALT=Alanine amino transferase, TLC=total leukocyte count, ADA= adenosine deaminase

The most common symptoms presented in patients with tuberculous pleural effusion were cough (54.2%), fever (50.1%) and shortness of breath (38.9%). In patients with malignant pleural effusion, most common symptom was weight loss (100%) whereas cough was most common symptom in patients with parapneumonic effusion (Table 2). Only four (6.7%) patients with tuberculous pleural effusion had sputum positive for acid fast bacillus (AFB) and none had AFB stain positive in the pleural fluid. Twenty eight percent of patients with tuberculous pleural effusion had chronic obstructive pulmonary disease (COPD) and 16.9 % had diabetes mellitus (DM). While, 42.8% of patients with malignancy had underlying COPD and 21.4 % had DM (Table 3).

## DISCUSSION:

This is a retrospective study evaluating the etiology of pleural effusion in patients of rural Nepal. Tuberculosis was identified as the most common cause of pleural effusion and it resulted most commonly into a unilateral pleural effusion. As compared to the patients with non tuberculous effusion, patients with tuberculous effusion were younger, more commonly males, had higher levels of lymphocytes, lower levels of neutrophils, higher level of lymphocyte to neutrophil ratio and higher levels of ADA in pleural fluid. The ratio of pleural

fluid to serum protein was higher in patients with tubercular effusion. Coughs, fever, shortness of breath and chest pain were the major presenting complains of patient with tubercular effusion. COPD and DM were the major comorbidities in this group of patients. Only four patients with tuberculous pleural effusion had sputum positive pulmonary tuberculosis.

Of all the causes of pleural effusion, tuberculosis is identified as the most common cause in many studies.<sup>7,8,10,11</sup> In a retrospective study from Malaysia, the most common cause of pleural effusion was tuberculosis and 70.4% of patients in this study were males.<sup>9</sup> Tuberculosis is also more common in younger patients and malignancy is the important cause of pleural effusion in older patients.<sup>9-11</sup> These results are similar to that observed in this study.

Increased level of lymphocytes was seen in tubercular pleural effusion in various studies.<sup>12,13</sup> Adenosine deaminase (ADA) level >36U/l is seen in patients with tuberculosis and level >100U/l is not seen in other causes of pleural effusion.<sup>14</sup> A combined use of pleural fluid ADA level of 50U/L with lymphocyte/neutrophil ratio of 0.75 or greater has been shown to have increased specificity for diagnosis of tubercular pleurisy.<sup>15</sup> Our patients with tubercular pleural effusion had mean ADA level of 53.9U/L and mean lymphocyte to neutrophil ratio of 16. In 1972, pleural fluid to serum protein ratio of

Table 2: Symptoms at presentation in patients with pleural effusion (N=100)

Diagnosis	Cough f(%)	Shortness of breath f(%)	Chest pain f(%)	Fever f(%)	Weight loss f(%)	Edema f(%)	Others f(%)
Tuberculosis	32 (54.2)	23 (38.9)	20 (33.8)	29 (50.1)	13 (22.0)	2 (3.3)	2 (3.3)
Malignancy	13 (92.8)	0	0	3 (21.4)	14 (100)	0	1 (7.1)
Pneumonia	12 (85.7)	5 (35.7)	3 (21.4)	10 (71.4)	1 (7.1)	3 (21.4)	0
Congestive cardiac failure	1 (10)	4 (40)	0	0	1 (10)	7 (70)	4 (40)
Liver disease	0	0	0	0	0	3 (100)	2 (66.6)

Table 3: Comorbidities in patients with pleural effusion (N=100)

Diagnosis	COPD f(%)	DM f(%)	HTN f(%)	IHD f(%)	Others f(%)
Tuberculosis	17 (28.8)	10 (16.9)	2 (3.3)	3 (5.0)	2 (3.3)
Malignancy	6 (42.8)	3 (21.4)	0	0	0
Pneumonia	6 (42.8)	1 (7.1)	1 (7.1)	3 (21.4)	3 (21.4)
Congestive cardiac failure	1 (10)	2 (20)	0	9 (90)	4 (40)
Liver disease	0	0	0	0	3 (100)

COPD=chronic obstructive pulmonary disease, DM=diabetes mellitus, HTN = hypertension, IHD= ischemic heart disease



>0.5 was described as one of the criteria for diagnosis of exudative pleural effusion.<sup>16</sup> We identified that mean level of pleural fluid to serum protein ratio was higher in patients with tubercular effusion as compared to non-tubercular effusion.

Most tubercular pleural effusions, unlike pulmonary tuberculosis present as an acute illness. Cough (93.8%), temperature above 100°F (85.7%) and chest pain (77.5%) are the three major presenting complaints in patient with tuberculous pleurisy.<sup>17</sup> In patients with human immunodeficiency virus (HIV) infection there is increased incidence of development of tuberculous pleural effusion as compared to the immune competent individuals.<sup>18,19</sup> Presence of DM also increases the risk of active tuberculosis.<sup>20</sup> Similarly, COPD patients have a threefold increased hazard ratio of developing active tuberculosis that is mainly dependent on an increased risk of pulmonary TB.<sup>21</sup> We identified the presence of COPD in 28.8% and DM in 16.9% of patients with tubercular pleural effusion. None of the patients in our study had HIV infection. A prospective study in 2006 has identified the presence of pulmonary tuberculosis in 31% of patients with tuberculous pleuritis by analysis of

sputum and bronchial washings.<sup>22</sup> We found that only 4 (6.7%) patients of tubercular pleural effusion were sputum positive for tuberculosis.

This study has a few limitations. This is a single center retrospective study in limited number of patients and an analysis of the serum and pleural fluid lactate dehydrogenase were not performed.

## CONCLUSION:

This retrospective study provides data on the causes of pleural effusion in patients of rural Nepal. It emphasizes that tuberculosis is the most important cause of pleural effusion in this area and should be considered in any adult patient with unilateral pleural effusion.

## Abbreviation:

- AST = Aspartate amino transferase
- ALT = Alanine amino transferase
- TLC = total leukocyte count
- ADA = adenosine deaminase
- COPD = chronic obstructive pulmonary disease
- DM = diabetes mellitus
- HTN = hypertension
- IHD = ischemic heart disease

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