Profile of exudative pleural effusion in the region of Bhuj people

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ABSTRACT

Background: Exudative pleural effusions are a common diagnostic problem in clinical practice, as the list of causes is quite exhaustive, although sometimes they can be inferred from the clinical picture. In the West the most common cause is Para pneumatic effusions followed by malignancy, while in India it is tubercular effusion followed by malignant effusion. Despite the availability of various tests, there is a need for defining the best diagnostic and cost-effective approach to quickly diagnose and treat exudative pleural effusions. The objectives are to conduct a clinical and etiological study of exudative pleural effusion, to evaluate biochemical profile, cytological profile and radiological profiles of exudative pleural effusion.

Methods: Prospective study of 100 patients with exudative pleural effusions. The demographic data was expressed as mean±standard deviation. Comparison between groups was done by Chi-Square test and Fischer exact test for categorical variables and Kruskar-Wallis and Mann-Whitney tests for continuous variables.

Results: There were 67 males and 33 females. The mean age was 41.6±15.74. The majority were tubercular in origin (67%), 13%, 8%,3% and 6% were malignant effusions, Syrnpneumonic effusion, pancreatic effusions and empyema respectively. Diagnosis was not established in 3% of effusions. Massive effusions were seen in 53.8% of malignant effusions and 33.3% of empyemas. Most effusions had a total cell count between 1000 to 5000 cells /mm3.Lymphocyte predominant effusions were seen in 84.6% and 89.6% of malignant and tubercular effusions. 61.5% of malignant effusions had a positive cytology. Tubercular effusion had a pleural fluid ADA more than 40 IU/L. 92.3% of malignant effusion had pleural fluid ADA less than 30IU.

Conclusions: Pleural effusion is a commonly encountered in medical practice and in our country, the commonest cause is tuberculosis, as is evidenced from the present study. The initial step in evaluating case of pleural effusion is to establish the cause of pleural effusion which is done by a detailed history, clinical examination and investigations like a chest radiology and pleural fluid analysis. Even in the advanced diagnostic approaches, still detailed clinical history and examination of the patient of the patient is important to make a clinical diagnosis. All suspected cases of pleural effusion should undergo Sonography of the thorax along with routine chest x-ray. Fluid cytology should be done to confirm tuberculosis or to rule out malignancy, which guides the physician for further evaluation of the patient if required.

Keywords: Empyema, Pleural effusion, Tuberculosis

INTRODUCTION

Exudative pleural effusions are a common diagnostic problem in clinical practice, as the list of cause's is quite exhaustive, although sometimes they can be inferred from the clinical picture.¹ The etiological distribution of pleural effusions in various series depends on the geographical area, patient's age, and advances in the diagnostic methods and treatment of the underlying causes. The difficulty in determining the cause of pleural effusion is shown by the fact that in many series unknown etiology constitutes nearly 15%.² Exudative
effusions require to be separated into infectious causes, noninfectious causes and malignancy. The most common causes in most series are infections and malignancy. In the West the most common cause is parapneumonic effusions followed by malignancy, while in India it is tubercular effusion followed by malignant effusion and a very few due to parapneumonic effusion.\textsuperscript{1,3}

India has the highest prevalence of tuberculosis in the world with 2/3rds of all TB patients being in India.\textsuperscript{4} Tuberculosis is the most common cause of effusion in India when compared to the West where malignancy and parapneumonic effusions are more common.\textsuperscript{3} Pleural tuberculosis is second in frequency after TB lymphadenitis.\textsuperscript{3} The clinical, biochemical and cytological parameters of tubercular effusion are shared by malignancy, both being exudates and predominantly lymphocytic effusions. This can pose a significant diagnostic dilemma. Adenosine deaminase enzyme activity, gamma interferon, polymerase chain reaction, lysozyme measurement pleural fluid tuberculosis protein antibodies and various tumor markers like CA15-3, squamous cell carcinoma antigen, etc have been used to differentiate TB from non TB.\textsuperscript{5} Other diagnostic tests including flow cytometry, chromosomal analysis of malignant cells, LDH isoenzymes assay, and tumor marker assays, immunohistochemical tests, and carcino embryonic antigen (CEA), are used to differentiate between benign and malignant effusions.\textsuperscript{5} Despite the availability of all tests, it might be necessary to avail of more invasive diagnostic tools like pleural biopsy or thoracoscopy to establish a diagnosis. Adenosine deaminase although shown to be promising in the West to differentiate tubercular from non-tubercular effusion, in Asian countries was not found to be of much diagnostic value and has shown mixed results.\textsuperscript{6,7} There is hence a need for defining the best diagnostic and cost-effective approach to quickly diagnose exudative pleural effusions.

METHODS

This is prospective study of 100 patients with exudative pleural effusions attending Department of pulmonary medicine, Government general hospital, Siddhartha medical college, Vijayawada from February 2017 to January 2018. A detailed clinical history and general physical examination was done on all the patients. A chest radiograph postero anterior view was done and the size of the effusion was estimated. The following investigations were done: routine base line investigations like complete hemogram, ESR, LFT/RFT, sputum for AFB, sputum for CBNAAT, chest X-ray-P/A view, USG chest, diagnostic pleurocentesis was performed on all patients after taking informed consent and pleural fluid sent for these investigations: Biochemical Study: Protein, Sugar, Chloride, LDH, ADA, Cholesterol; Cytological Study: Cell type, Cell count, Smear for malignant cells; Microbiological Study: Gram stain, AFB, Culture and sensitivity. CT Chest and Pleural biopsy done whenever appropriate.

### Inclusion criteria
- Both male and female patients with age more than 18 years
- Patients with exudative pleural effusion.

### Exclusion criteria
- Patients with other serious co-morbid conditions and those who are not able to co-operate for the study.
- Patients who are found to have transudative pleural effusion after initial screening.
- Patients who are immunocompromised (HIV Positive, long term usage of immunosuppressant drugs, steroids). Positive patients less than 18 years of age.

### Statistical analysis

The demographic data was expressed as mean±standard deviation. Comparison between groups was done by Chi-Square test and Fischer exact test for categorical variables and Kruskar-Wallis and Mann-Whitney tests for continuous variables.

### RESULTS

One hundred patients with pleural effusions were studied from February 2017 to January 2018. There were 67 males and 33 females. The mean age was 41.6±15.74. The mean age among men was 41.25±15.25 and in women was 41.85±15.39, as shown in (Table1).

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<td>Mean ± SD</td>
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**Figure 1: Gender distribution.**
Majority of the patients were in the age group of 21-40 years and 41-60 years. The male to female ratio was 2:1. In this study authors classified patients as tubercular effusion in patients who were sputum positive for AFB or who had demonstrated acid fast bacilli in the pleural fluid or those who had a lymphocyte predominant effusion therapeutic response to tuberculosis.

with tubercular effusion presented with fever as the predominant symptom (66.7%) followed by cough (56.7%) and breathlessness (43.3%). In those with malignant effusion it was breathlessness (61.5%) followed by cough (46.2%). In Synpneumonic effusion fever (100%) and cough (50%) were the major symptoms.

Figure 2: Etiology.

The majority were tubercular in origin (67%). There were 13% malignant effusions. Synpneumonic effusion and empyema were seen in 8% and 6% of patients respectively. Others causes included 3% of pancreatic effusions. Diagnosis was not established in 3% of effusions. Patients with tubercular effusion were much younger than those with malignant effusions (mean age 36.5±12.91 Vs 52.43±13.49).

Figure 3: Gender and etiology.

All pancreatic effusions were seen in males (4.5%). Tubercular effusions more common among both females (72.7%) and males (64.2%) whereas Empyemas were seen in both sexes in equal percentages (6%). Patients

Figure 4: Site of effusion in different etiologies.

All pancreatic effusions were present on left side. Tubercular, Malignant, Synpneumonic effusions and empyemas were more common on right side. Massive effusions (defined as pleural effusion occupying greater than 2/3rds of hemithorax on chest X-ray) were seen in 53.8% of malignant effusions and 33.3% of empyemas whereas moderate effusions are common in tubercular effusions (55.2%). In all other causes they were more commonly mild to moderate in size.

Figure 5: Appearance of pleural effusion with different etiologies.
Majority of the effusions were straw colored (81%). Hemorrhagic effusions were seen commonly in pancreatic fluid LDH to serum LDH was in the range of 1.84±0.71 in tubercular effusions. Patients with tubercular and malignant effusions had ratios greater than 2 in 46.2% and 38.4% of patients respectively. Pleural LDH to serum LDH ratio was greater than 2 in all of empyemas (100%).

Figure 6: Association of differential counts with different etiologies.

Empyemas had low glucose levels with mean of 49.17. All pancreatic effusions had high glucose levels with mean of 113.25% of synpneumonic effusion, 10% of Tubercular and 7% of malignant effusion also had pleural fluid glucose less than 40mg. Pleural fluid cytology was performed in all the patients with exudative effusions. No abnormal cell or AFB was seen in any of the tubercular effusions.

Figure 7: Pleural fluid glucose and etiologies.

61.5% of malignant effusions had a positive cytology. The yield increased with the number of samples examined, but the numbers were too small to draw a definite conclusion. Pleural fluid ADA was done in 94 patients out of whom 67 were tubercular effusion, 13 patients with malignancy and 3 unknown etiology and 8 patients with parapneumonic effusion. 31 patients with tubercular effusion had a pleural fluid ADA more than 40 IU/L. 92.3% of malignant effusion had pleural fluid ADA less than 30IU. 20.5% of tuberculosis had ADA between 30 and 40 IU/L. In patients in whom the diagnosis was not established, the pleural fluid ADA was less than 30 IU/L. In 28 patients with tubercular effusion, ADA was more than 70 IU/L.

DISCUSSION

100 patients with pleural effusion were studied of which 67% were cases of tuberculous effusion and 33% were cases of non-tuberculous effusion. The present study is particularly relevant in our country, as it has a high prevalence of tuberculosis.

Etiology of pleural effusion

Out of the 100 cases of pleural effusion, which were studied, 67 cases were of tuberculous effusion. This was reflective of the high prevalence of tuberculosis in the area being studied. The remaining 66 cases were of malignant effusion (13 cases), synpneumonic effusion (8 cases) and 3 cases of empyema, 3 cases of pancreatic effusion, 3 cases of unknown etiology. In comparison, the distributions in some of the previous studies are: Prabhuj Desai- tubercular effusion comprises 64% of infective cause and 8% were of empyema. In patients of age more than 40 years, malignant effusion was more common; Al Quatrain- common diagnosis was tubercular (37%) followed by neoplasm (8%), parapneumonic (14%). KZ Mamum also showed tubercular and malignancy were the major causes of pleural effusion.

Sex distribution

There were a greater number of male patients than female patients in this study with 67 males and 33 females. In
comparison, the sex distributions in some of the previous studies are: Subhakar K-77.5% males and 22.5% females; Burgess LJ-58% males and 42 % females; Al Quorain[9] -Of 101 cases 45 were males and 56 females; Valdes L-56.6% males and 43.3% females.9,11,13

**Age distribution**

The present study comprised of patients aged from 18 years to 80 years (mean age: 41.85±15.39 years). The mean age in case of tuberculous effusion was 39 years, with the maximum number of patients between 20-60. The mean ages in case of malignant, synpneumonic effusions were 63 years, 33 years respectively. In comparison, the age distributions in some of the previous studies are: Burgess LJ- the ages of the patients ranged from 6 months to 98 years with a mean age of 49±20.72 years; Subhakar K- the age of the patients ranged from 5 to 80 years with the mean ages in the various groups being: tuberculous 30.7±13.82 years, malignant 51.15±11.56 years and transudative effusion 48.15±6.92 years.11,12

The patients with TB were younger than the patients with malignancy. Their mean age was 39 years, consistent with Valdes L et al (34 years) and Sharma SK et al (33 years).14,15 Earlier studies done in United States by Epstein et al and Aho K et al showed a mean age of 54 and 28 years respectively.16,17

Malignant effusions in this study were seen in older age group (64yrs). This is older than that reported by Sharma et al (mean age 47 years), but consistent with reports from the West (65 years).18,19 Male to female ratio was 2:1in this study. Majority of the patients were in the age group of 21-40 years and 41-60 years irrespective of etiology.

**Presenting complaints**

The following were the presenting complaints among the patients, on admission. The commonest symptoms were cough (55%) and breathlessness (42%), followed by fever 57%, weight loss 25%, chest pain 6%, and hemoptysis 5%. Most of the patients with synpneumonic effusion, had complaints of a short duration with an acute onset, whereas those with tuberculous effusion and malignancy had complaints of a longer duration.

In comparison to other studies; Follader-main complaints were fever (41/44), chest pain (41/44) and weight loss (34/44).20 These findings are also compatible with the studies done earlier by Moudgil et al and Berger HW et al.21,22

Patients with malignant effusion had dyspnoea as a common symptom (61%) similar to that seen in a study by Chernov B et al though cough (42%) was the other predominant symptom.23 Patients with synpneumonic effusion had clinical symptoms suggestive of pneumonic illness.

**Clinical findings**

Out of the 100 patients with pleural effusion 61 patients had a right sided effusion and 35 patients had a left sided and 4 cases of empyema were on right side.

In comparison to other studies: Al Quarain-pleural effusion was more common in right side (55%) than on the left (32%); In Follander-both right and left side effusion were of equal distribution.9,20

**Investigations**

**Sputum for AFB**

In this study, out of the 67 cases of tuberculous effusion, in 7 cases acid fast bacilli could be demonstrated in the sputum by Ziehl Nielson's staining (16 %). The detection of AFB in the sputum in the tuberculous depends upon the associated lung parenchymal lesion. In comparison to other study: Subhakar K-7 of the 62 patients with tuberculous pleural effusion showed sputum positivity for AFB (i.e. 11%).11

**Radiology**

Chest X-ray showed the presence of fluid in all the patients and was diagnostic of pleural effusion. 28 of the patients also had associated pulmonary lesions. In radiological estimation of pleural fluid volume majority of tuberculosis (37 cases) had moderate effusion. (53.8%) cases of malignant effusion had massive effusion but synpneumonic mild effusion. Majority of malignant effusion had massive effusion and synpneumonic had minimal effusion. In present study authors demonstrated that massive effusion was most commonly seen in malignant effusion group (53.8%) similar to that observed, by Maher et al (55%).24 Large effusions were less commonly seen in the other observed etiologies. Although the majority of effusions were straw colored, hemorrhagic effusions were encountered predominantly in malignant effusions and pancreatic effusions. This is a well-established fact.5 In Follander study of radiological had shown parenchymal lesions in 23% of cases.20 Bowen in his study in quantitative study of pleural effusion, divided pleural effusion into mild (250-600) and massive (>1500) pleural effusion.25

**Pleural fluid analysis**

**Pleural fluid cytology**

The cell count in the pleural fluid ranged from 360 to 13000 cells/mm³. The average cell counts in tubercular, malignant, synpneumonic and empyema was 3814, 4618, 6093, and 5800 respectively.
Polymorphonuclear leucocytes were predominately seen in synpneumonic effusions and lymphocytes were predominantly seen in tuberculous effusion. Lymphocytes were also seen in the some of the cases of malignant effusions. Malignant cells could be demonstrated in 8 (61.5 %) cases of malignant effusion. The majority of effusions had total leukocyte count from 1000 to 5,000 mm³. Understandably the majority of empyemas had cell counts greater than 10,000 mm³ (50%) consistent with Light's observation et al 89.6 % of TB effusions and 84% of malignant effusions had lymphocyte predominance. Present result was similar to the study done by Valdes L et al where they have encountered neutrophil predominant tuberculous effusion in only 6.7% of patients and only one malignant effusion had neutrophil predominant effusion (3%). Among tuberculous effusions no acid-fast bacilli was seen. Among malignant effusion only 61.5% of the effusion showed malignant cells on cytological examination. In other studies, the percentage demonstrating malignant cells ranged from 40% to 87%. In the literature cytology has been a more sensitive test to diagnose malignancy when compared to biopsy. However, in present study of pleural fluid cytology, if only one sample is sent, the yield was 60%. The yield increases with the number of samples examined and reaches a maximum with 3 samples. While this is consistent with observed literature, the numbers are too small to draw a definite conclusion.

In comparison to other studies: Follander-demonstrated predominance of lymphocytes and scarcity of mesothelial cells in tubercular effusion; Nance KV-cytology for malignancy was diagnostic in 71%; Light RW large number of neutrophils indicate the presence of bacterial pneumonia. Lymphocytes predominant in tubercular pleural effusion. Cytology for malignant cells was positive in 33-87%; Light demonstrated predominantly polymorphs in bacterial pneumonia.

**Proteins**

The amount of proteins in the pleural fluid ranged from 3.2 gm/dl to 6 gm/dl. The mean protein level in tuberculous effusion was 4.19 gm/dl, in malignant effusion was 3.8 gm/dl, in synpneumonic effusion was 4 gm/dl, in empyema it was 3.8 gm/dl. In study by Light RW pleural protein was more than 3gm%. 

**Glucose**

The glucose level in the pleural fluid ranged from 18 to 147mg%. Low glucose levels were associated with tuberculous effusions, synpneumonic, empyema. In present study, the mean values of pleural fluid glucose were: tuberculous effusion 75.5 mg %, malignant effusion 84 mg%, synpneumonic effusion 57 mg %, empyema - 49 mg%. Low pleural fluid glucose was seen predominantly in patients with synpneumonic effusion and empyemas. The majority of pleural fluid glucose levels were between 40-100 mg/dl in tubercular effusions, consistent with the earlier observation by Light 108. 46% of present patients with malignant effusion had pleural fluid glucose level less than 40mg/dl, similar to that observed by Rodriguez-Panadero et al (20%). Presence of low pleural fluid glucose in malignant effusion indicates a poor prognosis, as it reflects a greater tumor burden. In comparison to other studies: Seaton A showed glucose level <60mg% in synpneumonic, empyema, tubercular and malignancy and >60mg% in transudates; Light RW pleural fluid glucose level below 40mg% in synpneumonic and empyema; Carr DT in his study of glucose in pleural effusion concluded that low value is seen in exudative pleural effusion and normal in cases of transudative effusion.

**Adenosine Deaminase levels**

The mean levels of Adenosine Deaminase in the pleural fluid in the various groups of effusions were estimated. In tuberculous effusions the mean ADA level was 66 IU/L, in malignant effusion the mean ADA level was 22 IU/L. In the present study, the pleural fluid ADA values were increased in all types of effusion but the ADA values were significantly higher in tuberculous effusions (p<0.001). According to the literature pleural fluid adenosine deaminase (ADA) has got a good discriminative value in differentiating tuberculous effusions from malignant effusion. Although a pleural fluid ADA above 70IU/L is diagnostic of tuberculosis it has to be considered if the pleural fluid ADA is between 40 IU/L and 70 IU/L. An ADA level less than 40IU/L rules out pleural tuberculosis. But different authors have used different cut off levels for pleural fluid ADA ranging between 33 IU/L to 50 IU/L. In present study out of 67 patients with tubercular pleural fluid, ADA was done in all of them and 33 (49%) of them had a level more than 40IU/L but 22 % showed a level of less than 30IU/L. Though studies done in the West demonstrate pleural fluid ADA more than 70 IU/L (Valdes et al and Burgess et al), present study showed a mean of 66 IU/L. But a significant percent of patients had a pleural fluid ADA less than 30IU/L. The mean ADA were high in the 2 Indian studies done by Prasad R et al, and Gilhotra et al with the mean ADA level ranging between76.8 IU (±23.8) to 95.8 (±57.5). In comparison to other studies: Burgess LJ, Baganha MF and Chopra RK. Values >45 IU/L is a sensitive method to differentiate tuberculous from non-tuberculous effusion.

**Lactate dehydrogenase**

The average LDH value in tuberculous effusion 251, malignant-346, synpneumonic-513 and empyema - 1244. The mean LDH in exudate effusion was higher. In comparison to other studies: Lakhotia-pleural fluid LDH >200 U/L and pleural fluid to serum ratio >0.6 helps to classify the effusion as transudates. The same view was held by Costa M.
CONCLUSION

Thus, the first step in the evaluation of a pleural effusion is to identify the cause of the effusion. This is achieved by a detailed history, clinical examination, relevant blood tests, radiological features and analysis of the pleural fluid for cytology, bacteriology and biochemical parameters like protein, glucose, LDH and ADA. This is important because in case of transudates, therapy is directed towards the underlying disease like congestive cardiac failure, nephrotic syndrome, liver cirrhosis or hypoproteinemia and usually therapeutic measures directed at the pleura are not necessary. But in case with exudate effusion, a definitive diagnosis has to be established, specific therapy for the pleural disease must be instituted.

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REFERENCES


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