Research Article

Etiology and clinical profile of pleural effusion

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Received: January 06, 2018; **Accepted:** January 31, 2018

ABSTRACT

Background: Pleural effusion is an excessive or abnormal collection of fluid in pleural space. Etiological study of pleural effusions is challenging to the physician as it differs depending on the region where the study is being carried out and the population involved. **Objective:** In this study, we aimed to identify the common etiologies causing pleural effusion and their clinical profile in a teaching institution. **Materials and Methods:** It was a prospective evaluation of 250 consecutive cases of pleural effusion. Detailed history and physical examination, pleurocentesis and pleural fluid analysis were done in all cases and closed pleural biopsy, computed tomography (CT), fiber-optic bronchoscopy, and other relevant examination in selected cases. **Results:** The most common cause pleural effusion in this study was tuberculosis (68.8%), followed by malignancy (14%), empyema (6%), and transudative effusion (2.8%). Pleural effusion was commonly seen in male (66%). The occurrence of tubercular pleural effusion was maximum in the age group 21–30 years, but malignant pleural effusion was more common above 60 years of age. Right-sided effusions were more common. Estimation of pleural fluid adenosine deaminase plays a significant role in the diagnosis of tubercular pleural effusion. Pleural fluid cytology and closed pleural biopsy can diagnose most of the cases of pleural effusion due to malignancy. **Conclusion:** The etiological diagnosis of pleural effusion remains unchanged even after few decades in our country. Even after thorough investigations with the help of closed pleural biopsy, fiber optic bronchoscopy, CT scan and CT guided fine needle aspiration cytology and others, 5.2% of cases could not be diagnosed. It has been also observed in another study where 15% cases remain undiagnosed. Thoracoscopic pleural biopsy may narrow down this gap.

KEY WORDS: Pleural Effusion; Tubercular Pleural Effusion; Pleural Biopsy

INTRODUCTION

Pleural effusion is an excess fluid that accumulates between the two pleural layers.[1] It is not a disease entity but is either a manifestation or a complication of pulmonary or non-pulmonary diseases and can leads to grave consequences if not managed timely. List of causes of pleural effusion is quite exhaustive.[2] They are classified broadly into exudative and transudative effusion based on light's criteria.[2] Congestive cardiac failure (CCF) is the most common cause of transudative pleural effusion worldwide.[2] Among exudative pleural effusions, in the west the most common causes are malignancy and pneumonia, but in India, it is tubercular effusion followed by malignant effusion and a very few due to parapneumonic effusion (PPE).[2,3]

When pleural effusion is detected, an effort should be made to determine the etiology, and it is a challenge to the physician. Diagnosis of transudative pleural effusions is fairly easy as the underlying causes is clearly evident through history, clinical examination, and few common laboratory investigations. On the other hand, most exudative pleural effusions are difficult to diagnose and need initial thoracentesis followed by a series of biochemical, cytological and microbiological

Access this article online	
Website: http://www.ijmsph.com	**Quick** Response code
DOI: 10.5455/ijmsph.2018.0101931012018	

investigations and in some cases, it requires use of special diagnostic techniques such as computed tomography (CT) scan of thorax, pleural biopsy, bronchoscopy, and thoracoscopy.

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. There is still a gap in the knowledge of etiological diagnosis and clinical profile of pleural effusion as there is a limited study in different geographical location. We aimed this study to know the etiology and clinical profile of patients with pleural effusion presenting to teaching hospitals mostly from eastern part of India. We also wanted to check the performance and complication of different diagnostic tests to reach the etiological diagnosis of pleural effusion because knowledge of this should be evolved more to choose an appropriate diagnostic tool in an actual scenario. The difficulty in determining the cause of pleural effusion is shown by the fact that in many series "unknown etiology" constitutes nearly 15%.[3]

Objective

This study had been carried to find out the clinical profile and various etiological causes of pleural effusion in a teaching hospital located in Eastern part of India.

Our specific objective was
1. To study the clinical profile of patients of pleural effusion.
2. To determine the etiology of all pleural effusions by the conventional diagnostic method.
3. To evaluate the yield of different diagnostic procedures.
4. To observe complications arising out of different interventions.

MATERIALS AND METHODS

Study Design

This was a prospective, observational, and cross-sectional study over a period of 1 year, carried out in the Department of Pulmonary Medicine of a tertiary level teaching institution of eastern India.

Study Population

A total of 250 consecutive adult cases of pleural effusion of both gender attended to the department of pulmonary medicine during the study period were included after confirming to the inclusion and exclusion criteria.

Inclusion Criteria

1. Patients of both gender of more than 10 years of age with clinical, radiological features of pleural effusion and ultimately confirmed by pleurocentesis presented to outpatient department (OPD) and Indoor Department of Pulmonary Medicine.
2. Patients who had given valid consent.

Exclusion Criteria

1. Patient already undergone pleurocentesis and on treatment for that.
2. Non aspirable pleural effusion (after image guided).
3. Hemothorax and chylothorax.
4. Hemodynamically unstable patients.
5. Patients are unwilling to give valid consent.

Study Protocol

Approval of the Institutional Ethics Committee was taken before initiation of this study. Every patient enrolled after obtaining written consent (both for study and diagnostic interventions) from them.

A total of 250 cases had been selected in this study. All of them were subjected to detail history taking, physical examination (including general, respiratory, and other systemic examination) and findings were recorded in a predesigned pro forma. All patients were undergone chest radiography posteroanterior view (lateral and decubitus view in selected cases). Diagnostic pleurocentesis (with or without image-guided) was done in all cases. After observing the physical appearance of the fluid it was sent for cytological (including detection of malignant cell), microbiological (Gram staining, acid-fast bacilli [AFB] staining, and culture in selected cases) and biochemical tests (glucose, protein, and lactate dehydrogenase [LDH]) including estimation of adenosine deaminase (ADA) where physical appearance of the fluid not seems to be of transudate. In selected cases, pleural biopsy (for histopathology and mycobacterial culture) with Abram's needle was done. At the same time blood was examined for complete hemogram, plasma glucose and LDH estimation, renal and liver function tests for each patient. Examination of sputum for AFB staining was done in all cases but the mycobacterial culture in selected cases. Sputum examination for Gram stain and pyogenic culture was performed in selective relevant cases. Human immunodeficiency virus (HIV) status was also tested for every patient. Fine needle aspiration cytology (FNAC)/biopsy of lymph node/swelling was done wherever these were detected in a few cases. Estimation of serum/pleural fluid amylase and lipase was performed in selected cases. Collagen profile in blood and pleural fluid was undertaken in relevant cases. CT scan and ultrasonography of thorax/abdomen had been done in a number of cases where necessary. In some cases to reach etiological diagnosis, image-guided (CT) FNAC, fiber optic bronchoscopy (FOB), and biopsy were done. Electrocardiography and echocardiography were done in some relevant cases. Even after extensive investigation, those

patient remained undiagnosed were referred to another center for thoracoscopic evaluation.

Criteria for Different Etiology

Tubercular pleural effusion (any of the following):

1. Presence of AFB in sputum.
2. Pleural biopsy or lymph node FNAC/biopsy shows well-formed granulomatous lesion composed of epithelioid and giant cells associated with caseation necrosis.
3. Chest radiography shows features suggestive of tubercular infiltration and/or cavitations.
4. Exudative pleural effusion containing predominately lymphocytes and pleural fluid ADA ≥40 U/L.

Malignant pleural effusion/pleural effusion with malignancy (any of the following):

1. Pleural fluid cytology showing the presence of malignant cell.
2. Pleural biopsy showing classical histopathological features of malignant infiltration.
3. FNAC/biopsy from lymph node/lung mass showing malignancy.

PPE

PPE is an acute febrile illness with purulent sputum and pulmonary infiltrate or disease-causing exudates with high leukocytic count with predominant neutrophils, low glucose, and high LDH in the absence of malignancy.

Empyema

Empyema is a collection of pus in pleural space, predominantly polymorphs, and it is positive on Gram stain/Ziehl-Neelsen stain and low glucose.

CCF

Pleural fluid is not fulfilling any of the Light's criteria, increased cardiothoracic ratio, pulmonary venous congestion, pulmonary edema on chest radiography, response to diuretics, and absence of malignancy or pulmonary infiltrate.

RESULTS

A total of 250 consecutive cases of pleural effusion had been included in this study. Exudative pleural effusions were more common than transudative pleural effusions.

Among all cases (n −250) the most common cause of pleural effusion was tubercular (68.8%, 172 cases) followed by malignancy (14%, 35 cases), empyema (6%,15 cases), and parapneumonic (2.4%,6 cases) effusion. Among transudative group CCF (5 among 7) was the most common cause. After extensive evaluation in 13 cases (5.2% of 250) etiology of pleural effusion remained unknown.

Table 1 showing different etiology of all 250 cases of pleural effusion.

Among 250 patients 165 (66%) were male and 85 (34%) were female with male:female ratio of 1.9:1. The occurrence of tubercular pleural effusion was maximum in the 21–30 year age group. Malignant pleural effusion was more common above 60 years of age. Most cases of CCF were observed above 50 years age group.

Out of 172 tubercular pleural effusion patients, 39 (22.7%) had a definite history of contact with patients suffering from sputum positive tuberculosis and 54 (31.39%) had a prior history of smoking but among 35 malignant pleural effusion cases 24 (68.47%) had prior habit of smoking.

Tubercular pleural effusion (n −172) cases were presented commonly with fever (72.7%), dry cough (71.5%), and chest pain (68.1%) but malignant pleural effusion (n −35) cases were presented commonly with breathlessness (71.4%), chest pain (62.8%), cough (51.4%), and weight loss (51.4%).

Pleural effusion was more common on the right side (59.6%) in our study. 2% Cases were bilateral. Both tubercular and malignant pleural effusion cases were more commonly observed in the right side (60.5% and 54.3% among own group) but in CCF cases (n −5) bilateral effusion were seen in 60% and right sided in 40% cases.

All 250 cases were undergone pleurocentesis. Straw colored fluid was present in 177 (70.8%) cases. Among tubercular cases 151 (87.8% of same group) had straw-colored pleural fluid, 12 (7% of same group) had hemorrhagic pleural fluid but in malignant cases 22 (62.9% of same group) cases had

Table 1: Distribution of cases according to aetiology

Group	Etiology	Number of cases	% of total (n−250)
Exudative No. 243 (97.2%)	Tuberculosis	172	68.8
	Malignant	35	14
	Para pneumonic	6	2.4
	Empyema	15	6
	Rheumatic arthritis	1	0.4
	Pancreatitis	1	0.4
	Undiagnosed	13	5.2
Transudative No. 7 (2.8%)	CCF	5	2
	Cirrhosis of liver	1	0.4
	Chronic renal failure	1	0.4

CCF: Congestive cardiac failure

hemorrhagic pleural fluid, and 13 (37.1% of same group) had straw-colored pleural fluid. 80% of CCF cases had clear fluid and rest had yellowish colored fluid.

Most of the tubercular pleural effusion cases (133,77.3% of same group) had lymphocyte count more than 80% but among malignant pleural effusion cases most (26,74.3%) had lymphocyte count between 50% and 80%.

ADA were measured in 244 cases. Among 172 tubercular pleural effusion cases, 133 (77.3% of same group) had pleural fluid ADA level above 70 U/L. In malignant pleural effusion group, most (30 cases 93.7% of same group) had ADA level below 40 U/L.

Malignant cytology of pleural fluid was examined in 90 cases, and presence of malignant cell was found in 17 (48.57% of same group) cases.

Pleural biopsy with Abram's needle had been done in 41 cases, and it was possible to make a definitive diagnosis in 27 cases. Diagnosis of tuberculosis was made in 18 cases and malignancy in nine cases. Other 13 cases had histopathological features of chronic non-specific inflammation. Out of 41 cases, 13 (31.71%) developed complication during or after closed pleural biopsy. Most common complication was pneumothorax (7 cases, 17.06%), others were vasovagal attack, local sepsis and fever (2 cases each, 4.8%).

Image (CT) guided FNAC from lung mass was done in 16 cases, and diagnosis of lung malignancy was established in all cases.

FOB with biopsy was done in five cases, and malignant etiology was established in four cases. Presence of AFB in bronchoalveolar lavage fluid was found in one case.

Peripheral lymph node FNAC/biopsy was performed in 48 cases, presented with lymphadenopathy. Diagnosis of tubercular adenopathy was done in 22 (45.9%) cases, and metastatic deposit was found in 10 (20.8%) cases, but 16 (33.3%) cases showed features of reactive hyperplasia only.

Table 2 showing type of malignancy among cases of malignant origin diagnosed by either cytology or histopathology. Non-small cell carcinoma is the most common type.

AFB staining of pleural fluid elicited positive result in four cases. AFB culture (BACTEC) of pleural fluid was positive in six cases. Gram stain of pleural fluid (Pus) showed Gram-positive cocci and bacilli in five cases. It was possible to identify the organism by pyogenic culture in four cases. Two (0.8% among all cases) cases of tubercular pleural effusion were HIV seropositive.

Table 2: Cytological/histological type of malignant effusion

Type	Number of cases (%)
Non-small cell	11 (31.4)
Squamous cell	7 (20)
Adenocarcinoma	6 (17.1)
Non-Hodgkins lymphoma	1 (2.9)
Breast carcinoma	1 (2.9)
Unclassified	9 (25.7)
Total	35 (100)

DISCUSSION

The most common cause pleural effusion in this study was tuberculosis (68.8%), followed by malignancy (14%), empyema (6%), and transudative effusion (2.8%). Pleural effusion was commonly seen in male (66%). The occurrence of tubercular pleural effusion was maximum in the age group 21–30 years, but malignant pleural effusion was more common above 60 years of age. Right-sided effusions were more common. Estimation of pleural fluid ADA plays a significant role in the diagnosis of tubercular pleural effusion. Pleural fluid cytology and closed pleural biopsy can diagnose most of the cases of pleural effusion due to malignancy.

World Wide CCF is the most common cause of pleural effusion[2] but in India tuberculosis is the most common cause of pleural effusion.[3] In our study, we found tuberculosis as the most common etiology behind pleural effusion. Our study result is concordant with results observed by Jindal,[4] Valdés.[5] In our study, lower incidence of transudative effusion can be explained by the fact that we conducted our study at pulmonary medicine department of a teaching hospital where most of the cases of CCF, cirrhosis, nephrotic syndrome may attended in the respective department after triage from general OPD or emergency department. Some transudative cases of mild effusion may be missed due to failure to have chest X-ray before diuretic therapy. Majority of cases of pleural effusion were males as compared to females in our study (66% vs. 34%) with male:female ratio 1.9:1. It is similar among tuberculosis group also. Cases of pleural effusion have been studied earlier and there male outnumbered the female.[6] Similar observation also made by Sharma *et al.*[7] The ratio varies from study to study and probably depend on the nature of the selection of patients. In the present study, the patients with pleural effusion were found in all age groups through the patients aged between 21 and 30 represent the largest group (25.6%). One previous study found majority of their cases between 21 and 40 year of age,[8] another study found majority of their cases (29.6%) below 20 years of age.[6] In tubercular pleural effusion predominant symptoms were fever, cough, and chest pain and in malignant effusion dyspnea, chest pain, cough, and weight loss as per our study. In one earlier study by Berger

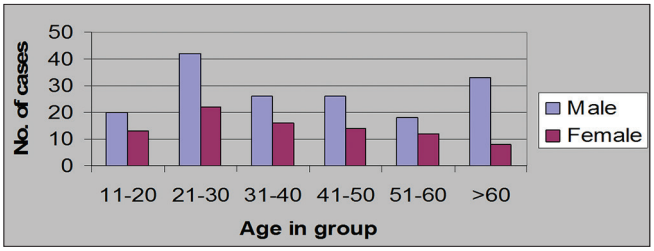

Figure 1: Multiple bar diagram showing the age distribution of cases of pleural effusion

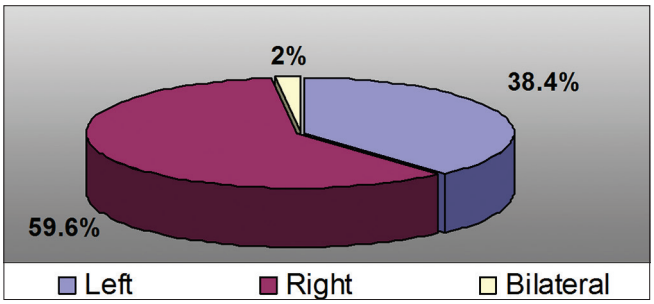

Figure 2: Pie diagram showing side of involvement in cases of pleural effusion

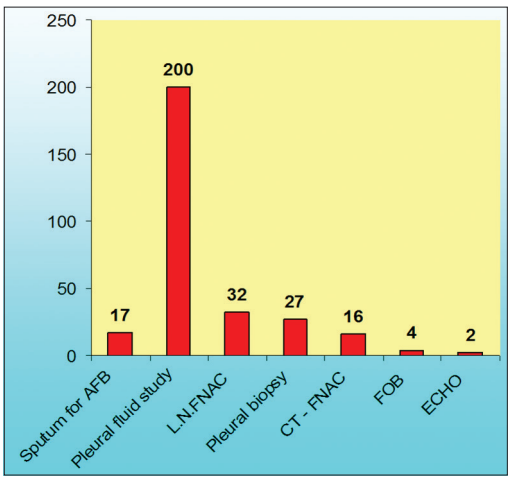

Figure 3: Bar diagram showing different investigations contributing to reach etiological diagnosis of pleural effusion

and Mejia, most patients with tubercular pleural effusions had cough, usually nonproductive, and many had chest pain, usually pleuritic in nature.[9] In another series, Chernow and Sahn reported that the most common symptom in malignant pleural effusions is dyspnea, which occurs in more than 50% and weight loss occurred in 32%.[10] Temperature elevation is significantly more common in patients with benign disease than in patients with malignant disease.[11] In our study, pleural effusions were predominantly observed in the right side. There are studies with a similar result.[12] Color of effusion is of immense diagnostic importance. Tubercular effusion was predominantly straw colored whereas malignant effusion was hemorrhagic. Turbid pleural fluid is suggestive of PPE. Transudative pleural effusions are generally clear.[2] Most of the cases in this study had predominantly lymphocytic pleural effusion. 83.2% cases had lymphocyte count of 50% or more. According to light in tubercular pleural effusion, the pleural fluid lymphocyte count is usually more than 50%.[2] Predominantly polymorphs are commonly found in PPE, empyema, pleural effusion due to pancreatic disease, and rheumatoid arthritis.[13] In the present study, 9 cases (3.6%) were found to have predominantly polymorphs in the pleural fluid, out of which 6 were in due to parapneumonic and one each due to tubercular, rheumatoid arthritis, and pancreatitis. Various authors have reported that the ADA level was significantly higher in cases of tubercular pleural effusion.[14,15] In our study, 77.3% of tubercular pleural effusion had pleural fluid ADA level above 70 U/L. We found presence of malignant cell in pleural fluid in 48.57% of cases of pleural effusion due to malignancy which is consistent with findings of Light.[2] In the present study during the histolopathogical examination of closed pleural biopsy sample in tubercular pleural effusion, tubercular granuloma was detected in 18 (43.9%) cases; in malignant pleural effusion, evidence of malignancy was found in 9 (21.9%) patients. Low yield in pleural biopsy may be due to nonrepresentative sample due to blind nature of the procedure. Pneumothorax and hemothorax are known complications of closed pleural biopsy, various studies show about 4–11% incidence rate of pneumothorax with pleural biopsy.[16,17] In the present study, 7 (17.06%) patients developed pneumothorax following pleural biopsy. They were managed successfully. There was no incident of hemothorax.

Our study was done in a low resource setup; hence, there was nonavailability of ultramodern instruments such as thoracoscopy and endobronchial ultrasonography to reach the final diagnosis in more number of cases. It was also limited by relatively small sample size and shorter study duration.

CONCLUSION

To conclude the etiological diagnosis of pleural effusion remains unchanged even after few decades in our country. Even after thorough investigations with the help of closed pleural biopsy, FOB, CT scan and CT guided FNAC, and others, 5.2% of cases could not be diagnosed. It has been also observed in another study where 15% cases remain undiagnosed.[3] Thoracoscopic pleural biopsy may narrow down this gap.

REFERENCES

1. Wong, CL, Holroyd-Leduc J, Straus SE. Does this patient have a pleural effusion? JAMA 2009;301:309-17.
2. Light RW. Clinical manifestations and useful tests. In: Pleural Diseases. 6th ed. Baltimore: Williams & Wilkins; 2013. p. 86-127.
3. Light RW. Clinical practice. Pleural effusion. N Engl J Med

2002;346:1971-7.
4. Jindal SK. Textbook of Pulmonary and Critical Care Medicine. 1st ed., Vol. 2. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.; 2011.
5. Valdés L, Alvarez D, Valle JM, Pose A, San José E. The etiology of pleural effusions in an area with high incidence of tuberculosis. Chest 1996;109:158-62.
6. Tandon RK, Mishra SR. Pleural biopsy: Analysis of 81 cases. Ind J Tubercul 1975;22:18.
7. Sharma SK, Suresh V, Mohan A, Kaur P, Saha P, Kumar A, *et al.* A prospective study of sensitivity and specificity of adenosine deaminase estimation in the diagnosis of tuberculosis pleural effusion. Indian J Chest Dis Allied Sci 2001;43:149-55.
8. Reddy DJ, Indira C. Needle biopsy of the parietal pleura in the aetiological diagnosis of pleural effusion. J Indian Med Assoc 1963;40:6-11.
9. Berger HW, Mejia E. Tuberculous pleurisy. Chest 1973;63:88-92.
10. Chernow B, Sahn SA. Carcinomatous involvement of pleura. Am J Med 1977;63:695-702.
11. Marel M, Stastny B, Melínová L, Svandová E, Light RW. Diagnosis of pleural effusions. Experience with clinical studies, 1986 to 1990. Chest 1995;107:1598-603.
12. al-Qorain A, Larbi EB, al-Muhanna F, Satti MB, Baloush A, Falha K, *et al.* Pattern of pleural effusion in eastern province of Saudi Arabia: A prospective study. East Afr Med J 1994;71:246-9.
13. Light RW, Ball CW, Erozan YS. Cells in pleura fluid: Their value in differential diagnosis. Arch Intern Med 1973;132:854-60.
14. Ungerer JP, Oosthulzen HM, Retief JH, Bissbort SH. Significance of ADA activity and its isoenzymes in tuberculous effusions. Chest 1994;106:33-7.
15. Shibagaki T, Hasegawa Y, Saito H, Yamori S, Shimokata K. Adenosine deaminase isozymes in tuberculous pleural effusion. J Lab Clin Med 1996;127:348-52.
16. Marco FP, Esther SJ, Lucia F, Antonio G, Jose A, González-Barcala F, *et al.* Role of blind closed pleural biopsy in the management o pleural exhudates. Can Respir J 2013;20:362-6.
17. Gouda AM, Dalati TA, Al-Shareef NS. A comparison between cope and abrams needle in the diagnosis of pleural effusion. Ann Thorac Med 2006;1:12-15.

How to cite this article: Maikap MK, Dhua A, Maitra MK. Etiology and clinical profile of pleural effusion. Int J Med Sci Public Health 2018;7(4):316-321.

Source of Support: Nil,**Conflict of Interest:** None declared.