



Clinico-radiological and etiological profile of pleural effusion patients diagnosed at Tertiary Care hospital of Rajasthan

Singh AK^{1*}, Jain VK², Mishra M³, Maan L⁴

¹ Junior resident, Department of Respiratory Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

² Professor and HOD, Department of Respiratory Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

³ Professor, Department of Respiratory Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India.

⁴ Associate Professor, Department of Respiratory Medicine, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

Abstract

Objective: clinic-radiological and etiological diagnosis of pleural effusion by collecting relevant clinical as well as laboratory data using the recent modalities available in tertiary care hospital.

Materials and Methods: This is a prospective study which was conducted in patients who presented with pleural effusion in department of Respiratory medicine of Mahatma Gandhi medical college Hospital, Jaipur which is a tertiary care center. All the patients who are clinic radiologically suspected were broadly evaluated clinically by the Presenting complaints, detailed history, general followed by systemic examination and routine investigations like Complete Blood Count (CBC), pleural fluid cyto-pathological, biochemistry, microbiological and CBNAAT (Cartridge Based Nucleic Acid Amplification Test) examination were done.

Results: Majority of patients were in the age group of 31-40 years (n=70) 35% followed by 20-30 years (n=47) 23.5%. The most common symptom was breathlessness (51.5%), followed by fever (39%), chest pain (38.5%), cough (35%) and weight loss (30%). 116 (58%) cases were of exudative effusion and 84 (42%) cases of transudative effusion. CCF (42/84) 50% is commonest cause of transudative pleural effusion followed by CKD (23/84) 27.3% and cirrhosis (15/84) 17.8%. Tuberculosis 46.5% was the common cause of exudative pleural effusion followed by malignancy (27.5%), empyema (11.2%) and Synpneumonic (6.03%). High level of ADA (above 40) were seen in 72.2% (39/54). CBNAAT detected MTB in 21.5% cases among exudative effusion, while cytochemistry and pleural biopsy favour tuberculosis 37.1% and 1.7% respectively in exudative effusion.

Conclusion: While evaluating a case of pleural effusion, a combined approach, involving clinical evaluation, radiographic and sonographic evaluation, pleural fluid analysis, pleural fluid cytology, and in cases where possible thoracoscopic pleural biopsy, must be utilized to fruitful and accurate diagnosis. CBNAAT could also be useful rapid diagnostic tool for suspected tuberculous pleural effusion/empyema.

Keywords: biopsy, CBNAAT, pleural effusion

Introduction

Pleural effusion is an indicator of a pathologic process that may be of primary pulmonary origin or of an origin related to another organ system or occasionally the first evidence of some other systemic disease. It may occur in the setting of acute or chronic disease and is not a diagnosis in itself. The occurrence of pleural effusion [PE] is a common finding, with higher incidence of effusions secondary to non-infective pathology in the western studies and infective pathology in India^[1].

India has the highest prevalence of tuberculosis in the world with 2/3rd of all TB patients being in India^[2]. Tuberculosis is the mainly cause of effusion in India as compared to the other countries where malignancy and parapneumonic effusions are more common. Pleural tuberculosis is second in frequency after TB lymphadenitis. Diagnosing the aetiology of pleural effusions clinically with certainty is a challenging task for physicians.

Congestive heart failure is the biggest condition that produces transudative pleural effusion followed by hepatic

hydrothorax. Nephrotic syndrome, hypoproteinemia are some other common causes^[3]. Common causes of exudative effusion include tuberculosis, parapneumonic effusion, viral infections, and malignancy^[4]. Other causes include hypothyroidism pulmonary embolism with infarction, connective tissue disorders, pancreatitis, esophageal rupture (Boerhaave's syndrome), collagen vascular disorders, chylothorax, and hemothorax.

With various diagnostic aids like pleural fluid analysis, pleural fluid cytology, pleural biopsy, ultrasonography, bronchoscopy, thoracoscopy, serological tests like ANA, ADA, Rheumatoid factor, CT thorax help the physician to arrive at the diagnosis at an earlier course of the disease^[5]

Determining the aetiological and clinical profile of PE helps in adoption of regionally optimized diagnosis & therapeutic approach. Here we have made an attempt to arrive at the clinic-radiological and etiological diagnosis of pleural effusion by collecting relevant clinical as well as laboratory data using the recent modalities available in tertiary care hospital.

Material and Methods

This Prospective study was conducted in the Department of Respiratory Medicine, Mahatma Gandhi Medical College & Hospital, Sitapura, Jaipur

- Institute Ethics Committee approval will be obtained before starting the study.
- Informed and written consent will be obtained from all the patients and / or attendants before enrolment to the study.

Methods

This is a prospective study which was conducted in patients who presented with pleural effusion in department of Respiratory medicine of Mahatma Gandhi medical college Hospital, Jaipur which is a tertiary care center. All the patients who are clinic radiologically suspected was broadly evaluated clinically by the Presenting com-plaints, detailed history, general and systemic examination. Routine investigations like Complete Blood Count (CBC), pleural fluid cyto-pathological, biochemistry, microbiological and CBNAAT (Cartridge Based Nucleic Acid Amplification Test) examination. Sputum examination was done for AFB staining by Ziel Nelson technique in all cases, Gram staining and Culture & sensitivity in specific cases. Chest X-ray PA view was done in all cases and chest sonography, CT chest was done if required. Other specific investigation like pleural biopsy (by Abrahms needle) and fiberoptic bronchoscopy

was done if required as per nature of Specific Diseases.

Eligibility Criteria

Inclusion criteria

- All cases in which Patient/ relative of patient giving informed consent.
- All cases of pleural effusion admitted in mgmc(age>15yrs) with clinically or radiologically documented pleural effusion were included in present study.

Exclusion criteria

- Patients who are moribund, not fit, refusal for consent
- Patients who have bleeding disorder.
- Patients with Trauma chest will be excluded

Statistically analysis

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of percentages, means and standard deviations. The data were checked for normality before statistical analysis using Shapiro–Wilk test. Chi-square test and Fisher exact test were used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at $P \leq 0.05$. ROC curve was also

Table 1: Demographic details of the study subjects

Age	N	%
20-30 years	47	23.5
31-40 years	70	35
41-50 years	36	18
51-60 years	29	14.5
>61	18	9
Mean±SD	32.4±2.31	
Gender		
Male	131	65.5
female	69	34.5
Residence		
Rural	145	72.5
Urban	55	27.5
Total	200	100

Table 2: Distribution of various symptoms in study subjects

Symptoms	N	%
Breathlessness	103	51.5
Chest pain	77	38.5
Cough	70	35
Weight loss	60	30
Night sweats	38	19
Fever	78	39
Icterus	19	9.5

Table 3: Etiologic spectrum of the study subjects

Etiology		N	%
Transudative (N=84)	Cardiac causes-CCF	42	50
	CKD	23	27.3
	Cirrhosis	15	17.8
	Etiology unknown	4	4.76
Exudative (N=116)	Tuberculosis	54	46.5
	Malignancy	32	27.5
	Empyema (bacterial)	13	11.2
	Synpneumonic	7	6.03
	Pancreatitis	3	2.58
Etiology unknown	7	6.03	

Table 4: Association of ADA levels with etiological spectrum

Etiology	<40 IU	40-70IU	>70 IU	Total
Tuberculosis	15	32	7	54
CCF	28	10	4	42
Malignancy	23	4	5	32
CKD	17	4	2	23
Cirrhosis	11	3	1	15
Empyema (Bacterial)	0	3	10	13
Synpneumonic	5	1	1	7
Pancreatitis	3	0	0	3
Etiology unknown	6	2	3	12
Total	108	59	33	200
P value	0.001 (S)			

Table 5: Radiological profile of the study subjects

Radiographic profile	Mild	Moderate	Massive	Total
Tuberculosis	17	31	6	54
CCF	16	24	2	42
Malignancy	1	11	20	32
CKD	8	15	0	23
Empyema	4	11	0	13
Synpneumonic	2	5	0	15
Cirrhosis	0	8	7	7
Pancreatitis	2	1	0	3
Etiology	1	8	6	12
Total	51	107	42	200

Table 6: Diagnostic yield of various investigation

Microbiological method	N	%
CBNAAT detect MTB	25	21.5
Cyto biochemistry favour MTB	43	37.1
Pleural biopsy in favour MTB	2	1.7
AFB stain detect MTB	7	6.03

Discussion

The present study was done in patients of pleural effusion reporting to tertiary care teaching hospital. The total number of cases studied were 200 with male predominance that is 131 with male is to female ratio 2:1. Most of the studies reported almost similar gender pattern with male predominate and profile of these are, Pandit *et al* (1.79:1) [6], Valdes L [7] *et al*-62.5% males and 37.5% females with a ratio of 1.6:1; while little more higher ratio of male by Al Quorian *et al*. [8] of 201 cases 145 cases were males (72%) and 56 females (27.9%) with a ratio of 2.58:1. Although the general understanding is that the incidence of pleural effusion is equal between both sexes, unless specific etiological profile, the ratio varies from study to study and probably depends on nature of the selection of patients [9]

Our study, the patients are in the age groups between 15 to more than 61 years with mean age of the patients was 32 years. The similar mean age in case of effusion was also reported as 34, 33 and 31 years by Valdes L *et al*, Sharma SK [10] *et al* and Subhakar K [11] *et al* respectively. In our study, near three fourth (72.5%) patients were from rural area and near one fourth (27.5%) from urban area. This rural predominance could be due to our hospital caters rural population.

The most common symptom in our study is breathlessness (51.5%), followed by fever (39%), chest pain (38.5%), cough (35%), and weight loss (30%). These similar finding are compatible with the studies done by Porcel and Vives (2003) [12]. Light RW and Ball WC [13] also observed noticed 51% breathlessness in their study. Breathlessness is predominant

symptom which compels the patient to report health facility. Majority of Pleural fluid were Unilateral 76% of that maximum right sided 58% followed by left sided 42%. bilateral pleural effusion was in near one fourth (25%) in our study. study done in western UP, India, out of 135 patients of pleural effusion, 89 right-sided, 37 left-sided, and 9 were bilateral effusions [14].

In our study, more than half of the cases (53.5%) were of moderate radiological grade followed by near one fourth mild (25.5%) and massive (21%) which was similar to Reddy L *et al* [15].

In our study, High level of ADA (above 40) was seen in 72% (39/54) in tuberculosis patients and empyema was 100%. Pleural fluid ADA >40U/l was taken as diagnostic cut off for tuberculous effusion and it yielded 97.1% sensitivity, 83.14% specificity, 82% positive predictive value, 94.6% negative. Although a pleural fluid ADA 70IU/L is diagnostic of tuberculosis. In another study by Bandrés Gimeno (1994) [16] *et al.*, the cut-off value of ADA >23 U/L had sensitivity, specificity, positive, and negative predictive values were 96%, 100%, 1.0%, and 0.94%, respectively, for differentiating tuberculous pleuritis or neoplasia with lymphocytic exudate. Sharma SK *et al* also recorded cut off value 35 IU/L with 83% sensitivity and 66% specificity in Indian Population. Gupta A *et al* in 2018 showed, about 70% had raised ADA levels, predominantly in exudative effusion (94%) and almost 99% of these patients had tuberculosis. It appears that pleural fluid ADA level above 70 U/L is highly suggestive of tuberculous pleuritis whereas pleural fluid ADA level below 40 U/L virtually rules out the diagnosis of

tuberculosis [17]. This finding correlate well with our finding where 27 patients had ADA level > 70 U/, ADA value is sensitive and specific test for the diagnosis of tuberculous pleurisy. our study also support that results of ADA levels should be interpreted in parallel with clinical findings and other pleural fluid parameters such as lymphocyte to polymorphs ratio, glucose levels, and cytopathology to differentiate between tuberculous effusion and parapneumonic effusion

CBNAAT detected tuberculosis in 25(21.55%) patients out of 116 patients of exudative pleural effusion. Out of 54 tubercular pleural effusion and 13 patients of empyema CBNAAT detected MTB in 17 and 8 patients respectively. Study by Gupta *et al.* showed 25% of total patients having exudative pleural effusion detected MTB by CBNAAT of pleural effusion, while study by Chakarboty A *et al.* [18] showed 32% (24/75) of cases of tubercular pleural effusion detected MTB by CBNAAT, out of which 2 were rifampicin resistant. In our study and other studies have shown CBNAAT has the potential to significantly authenticate tubercular etiology in pleural fluid specimens with rapid test results and it has an added advantage to assess the rifampicin drug sensitivity.

There were about 58% cases of exudative effusion and 42% cases of transudative effusion in our study. Study done by Shashikant A and Gupta A (2017) [19] observed similar pattern, 66% cases of exudative and 34% transudative. In our study, tuberculosis (54/116) 46.5% was the most common etiology of exudative pleural effusion. It was followed by malignancy (32/116) 27.5%, empyema (13/116) 11.2% and Synpneumonic (7/116) 6.03% in terms of etiology. Desai PP (1993) [20] *et al* reported tubercular effusion comprises 22.4% and 64% were of malignancy, this study has predominance of elder age group, this may be the reason for malignancy out number tuberculosis In our study congestive cardiac failure (42/84) 50% commonest etiology of transudative effusion followed CKD 27% and Cirrhosis 18%.

In study by Al Quarain [21] *et al* common etiology was tubercular (37%) followed by malignancy (18%), parapneumonic (14%) and congestive cardiac failure (14%); Valdes L *et al* showed tubercular (25%), malignancy (22.9%) and transudative (17.9%) were commonest causes of pleural effusion. Similar results were observed in a study done by Al Alusi FA (2003) *et al.* [22] in Iraq and by Afful B (1986) *et al.* [23] showing tuberculosis the leading cause of exudative pleural effusion and CCF among commonest ethology for transudative pleural effusion. Yam LT *et al.* [24] have shown that predominant lymphocytes in pleural fluid are suggestive of either tuberculosis or malignancy in the majority of cases. Pandit *et al.* was reported, 75% and 41% of diagnosed tuberculosis and malignancy patients respectively had predominant lymphocytes in their pleural fluid.

In our study pleural biopsy was needed in undiagnosed exudative pleural effusion only 7 in number, out of which 4 were nonspecific inflammation followed by tuberculosis 2 and malignant in 1 patient. Good number of studies is available in which they used pleural biopsy / medical thoracoscopy as a primary tool for the diagnosis of pleural effusion. Study by Hucker *et al.* [25] found 21 cases (20.6%), Hansen *et al.* [26] found 45 cases (31%), and Blanc *et al.* [27] observed 57 cases (38.2%) of chronic nonspecific inflammation. In study by Patil C *et al.* [28] out of 18 cases, five patients the histopathology report had chronic inflammation; and in one patient it was normal pleura [29].

While we needed biopsy only 7 out of 116 patients, we were able to make diagnosis with simple biochemical, molecular test and cytopathological examination. Our study suggest that thoracoscopy /pleural biopsy is not required in all the cases of exudative pleural effusion, it used should be limited to only undiagnosed pleural effusion.

Limitation

An obvious limitation of the study was that the number of patients is small and duration is less time period, which could limit the general applicability of our findings to the larger community setup and a possible selection bias, as patients with advanced malignancy may have been referred directly for palliative care, without further investigations. In the present study, diagnosed cases of pleural effusion that might be on conservative management before enrolment were included. So, effect of previous treatment, which may affect our diagnostic workup and differential diagnosis, were not taken into account

Conclusion

The present study concludes that despite the revised national tuberculosis control program in India, the tubercular effusions are still at large. The cause is usually the noncompliance with antitubercular therapy. The malignant pleural effusion cases are far less than tuberculosis, but their incidence is rising as compared to previous studies. While evaluating a case of pleural effusion, a combined approach, involving clinical evaluation, radiographic and sonographic evaluation, pleural fluid analysis, pleural fluid cytology, and in cases where possible thoracoscopic pleural biopsy, must be utilized to fruitful and accurate diagnosis.

CBNAAT is also useful rapid diagnostic tool for suspected tuberculous pleural effusion/empyema considering the advantage of rapid test result and information about drug resistance pattern, especially in high burden country such as India.

References

1. Duke J, Good J, *et al.* Frontline assessment of common pulmonary presentations. Snowdrift Pulmonary Foundation, Inc, 2001.
2. Park K. Text book of preventive and social medicine. Epidemiology of Tuberculosis. 18th edition 2005, Bansarilal publications Park. Text book of preventive and social medicine. Epidemiology of Tuberculosis. 18th edition, Bansarilal publications, 2005.
3. Chetty KG. Transudative pleural effusions. Clin Chest Med. 1985; 6:49-54.
4. Collins TR, Sahn SA. Thoracentesis. Clinical value, complications, technical problems, and patient experience. Chest. 1987; 91:817-22.
5. Lokeswara Reddy A, Sundar Raj G, Md Badusha, Ramanjula Reddy C, Yugandhar P, Nilofer SK, *et al.* Analytical Study of Clinical And Etiological Profile of Patients Presenting with Pleural Effusions to a Tertiary Hospital. Journal of Evolution of Medical and Dental Sciences 2015; 4(88):15305-15312.
6. Pandit S, Chaudhuri AD, Datta SB, Dey A, Bhanja P. Role of pleural biopsy in etiological diagnosis of pleural effusion. Lung India. 2010; 27(4):202-204. doi:10.4103/0970-2113.71941

7. Vlades L, Alvarez D, *et al.* The etiology of pleural effusion in an area with high prevalence of tuberculosis. *Chest.* 1996; 109:158-162.
8. Al-Quarain, F GI-Muhanna, FB Larbi. Pattern of pleural effusion in Eastern province of Saudi Arabia a prospective study in *East African Medical Journal.* 1994; 71(4):246-249.
9. Available at:
<https://emedicine.medscape.com/article/299959-overview>
10. Sharma SK, Suresh V, Mohan A, *et al.* A prospective study of sensitivity and specificity of adenosine deaminase in the diagnosis of tubercular pleural effusion. *Indian J Chest Dis Allied Sci.* 2001; 43:149-155.
11. Subhakar K, *et al.* Adenosine Deaminase Activity in Pleural Effusions. *Lung India.* 1991; 10:p57-60.
12. Porcel JM, Vives M. Etiology and Pleural fluid characteristics of large and massive pleural effusions. *Chest.* 2003; 124:978-983
13. Light RW, Ball WC. Glucose and amylase in pleural effusion. *JAMA.* 1973; 225:257-60.
14. Agrawal A, Tandon R, Singh L, Chawla A. Clinico-pathological profile and course of malignant pleural effusion in a tertiary care teaching hospital in western U.P. with special reference to lung cancer. *Lung India.* 2015; 32:326-30.
15. Reddy AL, Raj GS, Reddy BCR, Yugandhar P, Nilofer SK, Sri SS. Analytical Study of Clinical And Etiological Profile of Patients Presenting with Pleural Effusions to a Tertiary Hospital. *Journal of Evolution of Medical and Dental Sciences.* 2015; 4(88):15305-12.
16. BandrésGimeno R, Abal Arca J, Blanco Pérez J, Gómez-González MC, Cueto Baelo M, Piñeiro Amigo L, *et al.* Adenosine deaminase activity in the pleural effusion. A study of 64 cases. *Arch Bronconeumol.* 1994; 30:8-11.
17. Light RW. 4th ed. Lippincott Williams and Wilkings. *Approach to the patient. In pleural diseases,* 2001, pp. 42-86.
18. Chakraborty K, Bossaer JB, Patel R, Krishnan. Successful treatment of nilotinib-induced pleural effusion with prednisone. *Journal of Oncology Pharmacy Practice,* 2013.
19. Shashikant A, Gupta A. A study of clinicoetiological profile of patients with pleural effusion. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS).* 2017; 16(1):23-27.
20. Prabhudesai PP, Mahashur AA, Mehta N, Ajay R. Exudative pleural effusions in patients over forty years of age – an analysis of seventy-six patients. *J Post grad Med,* 1993, 39:190.
21. Al-Quarain, F GI-Muhanna, FB Larbi. Pattern of pleural effusion in Eastern province of Saudi Arabia a prospective study in *East African Medical Journal.* 1994; 71(4):246-249
22. Al Alusi FA. Pleural effusion in Iraq: A prospective study of 100 cases. *Thorax.* 1986; 41:492-493.
23. Afful B, Murphy S, Antunes G, Dudzevicius V. The characteristics and causes of pleural effusions in Kumasi Ghana, a prospective study. *Tropical Doctor.* 2008; 38:219-20
24. Yam LT. Diagnostic significance of lymphocytes in pleural effusion. *Ann Intern Med.* 1967; 66:972-82.
25. Hucker J, Bhatnagar NK, Al-Jilaihawi AN, Forrester-Wood CP. Thoracoscopy in the diagnosis and management of recurrent pleural effusions. *Ann Thorac Surg.* 1991; 52:1145-7.
26. Hansen M, Faurschou P, Clementsen P. Medical thoracoscopy, results and complications in 146 patients: A retrospective study. *Respir Med.* 1998; 92:228-32.
27. Blanc FX, Atassi K, Bignon J, Housset B. Diagnostic value of medical thoracoscopy in pleural disease: A 6-year retrospective study. *Chest.* 2002; 121:1677-83.
28. Patil C, Dixit R, Gupta N, Indushekar V. Thoracoscopic evaluation of 129 cases having undiagnosed exudative pleural effusions. *Lung India.* 2016; 33(5):502-506.
29. Hira HS, Ranjan R. Role of percutaneous closed needle pleural biopsy among patients of undiagnosed exudative pleural effusion. *Lung India.* 2011; 28(2):101-104.