TO STUDY THE VARIOUS ETIOLOGIES OF PLEURAL EFFUSION

Faheem Din Awan*, Zafar Ahmed*, Syed Ali Arsalan*

* Department of Pulmonology, Liaquat National Hospital & Medical College, Karach - Pakistan

Adress for correspondence:
Dr. Faheem Din Awan,
Department of Pulmonology, Liaquat National Hospital & Medical College, Karach - Pakistan
E-mail:
faheem.awan86@gmail.com

ABSTRACT

BACKGROUND: Pleural effusion is the abnormal collection of fluid in the pleural space. The etiological spectrum of pleural effusion depends on the geographical location and local incidence of different diseases that cause pleural effusions.[1,2] In developed countries the most common causes of pleural effusion are cardiac failure, malignancy and pneumonia whereas in developing countries, tuberculosis and para pneumonic effusion are more prevalent.[3-5]

OBJECTIVE: To study the various etiologies of pleural effusions in a tertiary care hospital of Pakistan.

METHODOLOGY: This was a prospective study of 4 months duration, carried out in the Department of Pulmonology, Liaquat National Hospital Karachi from the period September 2013 to December 2013. This study included all patients >15 years age who were admitted in chest unit or visited chest medicine Outdoor Department (OPD). Clinical records of the patients were reviewed for risk factors, more than 90% patients underwent thoracocentesis in which pleural fluid was aspirated and sent for biochemical, cytological and microbiological studies and additional clinical and radiological examinations were performed.

RESULTS: During the study period, total 70 cases of pleural effusions were identified;. There were 45 males (64.28%) and 25 females (35.71%) having a mean age of 54 years. Pleural effusion was exudative in 45 (64.28%) and transudative in 21 cases (30%) (total 70: also give characteristics of remaining 4 patients: borderline, empyema or hemorrhagic etc). Radiological results showed right sided pleural effusion in 33 (47.14%), left sided in 12 (17.14%), and bilateral pleural effusions in 21 cases (30%). The most frequent cause of pleural effusion was tuberculosis in 29 cases (42%), malignancy in 13 (18%), Congestive heart failure (CCF) in 10 (14%), pneumonia in 06 (08%), Chronic liver disease (CLD) in 04 (06%), Chronic Kidney Disease (CKD) with liver abscess, sepsis & pneumonia in 04 cases (06%) similar problem, trauma in 01 case (1.42%); while 04 cases remained undiagnosed (06%) and expired during the study period.

CONCLUSION: Our study confirms Tuberculosis being the most common cause of exudative pleural effusions while CCF remains the most common cause of a transudative pleural effusion in patients coming to Liaquat National Hospital Karachi.

KEY WORDS: Congestive Cardiac Failure (CCF); Etiology; Exudative; Pleural Effusion; Tuberculosis

This Article may be cited as: Awan FD, Ahmed Z, Arsalan SA. To study the various etiologies of pleural effusion. Pak J Chest Med 2015; 21(1): 20 - 5.

INTRODUCTION

Pleural effusion is defined as accumulation of fluid between the visceral and parietal layers of the pleura when there is an imbalance between formation and absorption in various disease states.[1,2]

To differentiate whether the pleural effusion is exudative or transudative, pleural fluid protein <25g/L is termed as transudative and pleural fluid protein >30g/L is called an exudates Data now suggest exudate as pleural fluid protein greater than 2.9 g/dL (29 g/L) and less than this value is called a transudate. In the patient with abnormal serum protein or in borderline cases (protein 25-35g/L) apply Light's criteria.[6]

Studies done worldwide showed tuberculosis, malignancy, bacterial infections, uremia, and sarcoiodosis as the most common cause of exudative pleural effusion while CCF, cirrhosis of liver, pulmonary embolism, nephrotic syndrome, peritoneal dialysis, superior vena cava obstruction, myxedema and urinothorax remain the common causes of transudative pleural effusions.[7] Pleural effusion is common problem confronting pulmonary and general physicians in Pakistan; this prompted us to conduct this study to evaluate various etiologies of pleural effusions in our hospital.

METHODS

This was a prospective study carried out in the Department of Pulmonology, Liaquat National Hospital Karachi from the period September 2013 to December 2013. This study included all patients >15 years age who were admitted in chest unit or visited chest medicine OPD. A total of 70 patients on clinical examination were identified to have pleural effusions which was later on confirmed by radiological examination according to British Thoracic Society (BTS) guidelines.[8]

Clinical records of the patients were reviewed for risk factors, more than 90% patients underwent thoracocentesis in which pleural fluid was drained and sent for biochemical, cytological and microbiological studies. At the same time blood samples were also taken for simultaneous pleural fluid and blood determination of total protein, albumin and Lactate dehydrogenase (LDH) levels.

The sediment from fluid was cultured for Mycobacterium Tuberculosis (MTB) species and pleural biopsy was sent for microbiology and histopathology and sputum samples were obtained from the patients (all patients or selected ones suspected of having TB/malignancy, specify) and sent for Acid fast Bacilli (AFB) smear and cytology. Additional examinations performed included bronchoscopy and, breast examination, Ultra Sound (U/S) abdomen, Echocardiography/Echocardiogram (Echo), Electrocardiogram (ECG), Ultrasound Kidney Ureter Bladder (U/KUB) and prostrate, bone scan, Fine Needle Aspiration Cytology (FNAC) of lung mass, bone scan.

Table 1: Etiology of pleural effusions in patients attending pulmonary unit

Etiology or type of pleural effusion	No	%	Age (Years) Mean
Tuberculosis	29	42	39 years
Malignancy	13	18	62 years
Congestive Cardiac Failure	14	14	63 years
Pneumonia	06	08	40.5 years
Chronic Liver Disease	04	06	62.5 years

Table 2: Site of pleural effusion in various etiologies

Etiology or type of pleural effusion	Right Sided Effusion		Left Sided Effusion		Bilateral Effusion		Total
	No	%	No	%	No	%	No
Tuberculosis	18	63	08	27	03	10.34	29
Malignancy	07	53.84	05	38.46	01	7.69	13
Congestive Cardiac Failure	02	20	01	10	07	70	10
Pneumonia	04	66.66	02	33.33	-	-	06
Chronic Liver Disease	-	-	-	-	04	06	04

RESULTS

Out of 70 patients admitted with the diagnosis of pleural effusion, there were 45 males (64.28%) and 25 females (35.71%), having a mean age of 54 years (range 18-84 years). Thirty two (45.71%), patients were cigarette smokers (average 40 pack years. Erythrocyte Sedimentation rate (ESR) was more than 70 in 25 cases (35.71%) and more than 100 in 10 cases (14.28%). Comorbid conditions including hypertension was present in 25 patients (35.71%), diabetes mellitus (DM) was found in 14 patients (20%), chronic liver disease was found in 04 patients (06%), chronic kidney disease (CKD) with liver abscess, sepsis & pneumonia in 04 cases (06%), trauma in 01 case (1.42%); while 04 cases remained undiagnosed (06%) and expired during the study period.

Pleural effusion was exudative in 45 (64.28%) and transudative in 21 cases (30%). Radiological results showed right sided pleural effusion in 33 (47.14%), left sided in 12 (17.14%), and bilateral pleural effusions in 21 cases (30%). The most frequent causes of pleural effusion was tuberculosis in 29 cases (42%).

Among patients with pleural tuberculosis, average age was 39 years (range 18-65 years), males were 17 (58.62%), female 12 (41.37%), and history of TB contact was positive in 07 cases (24.13%). In this group, right sided pleural effusion was found in 18 cases (63%), left sided 08 cases (27% cases), and bilateral pleural effusions in 03 cases (10.34%), exudative effusion in 29 cases (100%), mono-lymphocytic in 25 cases (86.7%). Mycobacterium Tuberculosis Polymerase Chain Reaction (MTB PCR), in 03 cases out of 13(23.07%), Acid Fast Bacilli Culture and Sensitivity (AFB CS), in 04 cases out of 14 (28.57%), Pleural Fluid (P/F), AFB smear positivity in 03 cases out of 29 (10.34%), pleural biopsy positive in 04 cases out of 13 (23.079%), ESR was raised in 12 cases and >100 in 06 cases (50%). Sputum AFB smear was positive in 04 cases out of 10 (40%).

Pleural metastatic malignancy was positive in 13 cases (18%), The characteristics of this group included: average age is was 62 years, males 08 (61.5%), females 05 (38.46%), cigarette smokers 10 (76.9%), ESR raised (> 50 in 07) and > 100 in 02 cases (28.57%). Malignant cytology was positive in 05 out of 11 (45.45%).

Pleural effusion was right sided in 07 cases (53.84%), left sided in 05 cases (38.46%) and bilateral in 01 case (7.69%),. Exudative effusion was found in 10 cases (76.89%), transudative in 03 cases (23.076%), mono-lymphocytic predominant in 11 cases (84.61%) and pPleural biopsy was positive in 02 cases out of 05 (40%).

Effusions associated with CCF were found in 10 cases (14%), among 06 (60%) males and 04 (40%) females. Average age of this group was 63 years, 02 (20%) were cigarette smokers, and ESR was > 50 but less than 100 in all 03 cases. Pleural effusion was bilateral in 07 cases (70%), right sided in 02 cases (20%), left sided in 01 cases (10%), and was tansudative in all cases (100%).

Parapneumonic pleural effusions were found in 06 cases (08%),. In this group, mean age was 40.5 years, among 05 (83.3%) males and 01(16.7%) female.

Table 3: Etiology of Exudative versus Transudative effusions

Etiology	No	%
Exudative		
Tuberculosis	29	42
Malignancy	13	18
Pneumonia	06	08
Transudative		
Congestive Cardiac Failure	10	18
Chronic Liver Disease	04	06

Table 4: Etiology of pleural effusions in patients attending pulmonary unit

Age Group (years)	Tuberculosis (n=29)	Malignancy (n=13)	Congestive Cardiac Failure (n=10)
18-65	25	06	05
>65	03	04	05

Table 5: Sensitivity of each of the criteria used for the definitive diagnosis of tuberculous pleurisy

Criterion	No of Positive / Total Cases	Percentage
Pleural Fluid		
Stain	03/29	10.34
Culture	04/14	28.57
Biopsy Tissue		
Stain	-	-
Culture	04/13	23.079
Pleural Biopsy		
Caseating Granulomas	04/13	23.079
Non- Caseating Granulomas	-	-
Sputum		
Stain	04/10	40
Culture	-	-

Exudative polymorphic (neutrophils) predominant effusion was present in 05 cases (83.33%), right sided 05 (66.66%), and left sided pleural effusion in 01 case (16.7%).

Effusions associated with CLD (hepatic hydrothoraces) were found in 04 cases (06%), having mean age of 62.5 years, among 02 (50%) males and 02 (50%) females. All 04 cases (100%) had bilateral transudative pleural effusions.

Effusions associated with CKD with liver abscess, sepsis & pneumonia were found in 04 cases (06%) & trauma associated effusion was present in 01 case (1.42%).

DISCUSSION

The mean age of the patients in this study (45 years) was lower than those described in other studies.[2,5,11-13] Furthermore there was predominance of male patients in our study. Tuberculosis was the most common cause of effusions in our study which is comparable with reports from Saudi Arabia, India, Malaysia, Lebanon, Iraq, Ghana and Spain[3-13] but different from those reported in other developed countries and the Islamic Republic of Iran.[1,2,14] This could be explained by the fact that tuberculosis is still endemic in Pakistan. Poor socioeconomic conditions and stress were other contributing factors to the high incidence of tuberculosis among most of the cases. The mean age of patients with tuberculous effusions (39 years) was lower than that of patients with other types of effusions, in agreement with previous reports.[5-13]

Tuberculous pleurisy is either a primary disease or a reactivation of previous parenchymal lung tuberculosis. In developed countries, these effusions have been increasingly associated with reactivation of tuberculosis,[3-5] whereas in developing countries tuberculous effusions are classically associated with primary tuberculous infection.[15]

Although this study was not designed to classify tuberculous pleurisy as primary or reactivated tuberculosis, the mean patient age together with the low association with pulmonary lesions in our study suggests that tuberculous pleurisy is still a primary disease, which is similar to that reported by Ibrahim et al.[15] Pleural fluid mycobacterial culture had a higher sensitivity than direct smear for AFB, in agreement with many reports worldwide.[3,5,9,13,16,17] This could be explained by the fact that direct examination requires bacilli concentration of 10 000 /mL, whereas the culture only requires the presence of 10–100 organisms /mL.[16] Closed pleural biopsy using Abram's needle was positive for caseating granulomas in 23.79% of our patients, which falls below the range of 51% to 83% described in many studies.[5,15-18] There was right-sided dominance of tuberculous effusions in our series which is comparable with many reports.[2-15]

Malignancy was the second most common cause of pleural effusions in our series accounting for approximately 18% of all cases, which falls within the range of 14.7% to 48% described in the literature;[21] it had a tendency to afflict both middle and older age groups in agreement with many reports worldwide.[11-14] Most of our patients tended to have effusions on the right side in agreement with the observations by other studies. A majority of these patients were over 60 years of age, which is comparable with many reports from both developed and developing countries.[1-14] In agreement with previous reports, the most common place of

origin of the tumour was the lung.[2,5,11-14,22] Direct tumour involvement of the pleura is most effectively diagnosed by pleural fluid cytology and/or pleural biopsy.[23-26] In our study, serial cytological examination of pleural fluid for malignant cells was positive in 45.45% of patients, which is similar to previously reported results. When pleural fluid cytology is non-diagnostic for a suspected malignant effusion, pleural biopsy is recommended. Although the specificity of closed needle biopsy (Abrams needles) for malignant effusion is high, reported sensitivities range widely between 7% and 72%.[27] In our series, closed pleural biopsy confirmed the diagnosis in 02/05 (40%) patients, which falls within the above mentioned range.

A total of 14% of our patients had cardiac failure, which is comparable with reports from Saudi Arabia[5] but different from other reports from the Czech Republic, Spain, the United States of America and the Islamic Republic of Iran[1,2,11,14]

Parapneumonic effusion was the 4th common cause of pleural effusion in our study 06/70 cases (8%) with predominance of exudative pleural effusion.

Cultures of empyema (empyemas not mentioned anywhere in results) fluid in this series yielded bacterial isolates in 32% of cases, which fits in the range of 11% to 82% previously reported.[27-31] The spectra of the most common organisms isolated from empyema fluid have varied depending on the patient populations studied by other investigators. In contrast to recent reports[29-31] Gram-positive organisms (not mentioned anywhere in results) were the most frequent isolates in our study accounting for 62.5% of all isolates. These results are consistent with previously reported figures.[32]

LIMITATIONS

Some limitations can be noted in our study. First, the study was hospital-based rather than population-based. Secondly, the number of cases was small. Only pulmonology indoor and OPD patients were there, many pts with CKD & CLD with effusions may be going to other departments

CONCLUSION

Pleural effusion is a common clinical problem confronting physicians in Pakistan. The most frequent cause of pleural exudates was tuberculosis, followed by malignancy and pneumonia, whereas the most common cause of transudative pleural effusion was cardiac failure. Pleural fluid examination and culture of pleural were the most useful diagnostic tests for tuberculosis effusions, whereas cytological examination of pleural fluid was the most useful test for malignant effusions.

REFERENCES

1. Light RW. Clinical practice. Pleural effusion. New England Journal of Medicine 2002; 346:1971–1977.
2. Marel MA, Light RW. The incidence of pleural effusion in a well-defined region. Epidemiologic study in central Bohemia. Chest Journal 1993; 104(5):1486–1489.
3. Ferrer J. Pleural tuberculosis. European Respiratory Journal1997; 10(4): 942-947.
4. Antoniskis D, Amin K, Barnes PF. Pleuritis as a manifestation of reactivation tuberculosis. American Journal of Medicine 1990; 89:447–450.
5. Moudgil H, Sridhar G, Leitch A. Reactivation disease: the commonest form of tuberculous pleural effusion in Edinburgh, 1980–1991. Respiratory Medicine 1994; 88:301–304.
6. Maskell NA, Butland RJ. Pleural Diseases Group, Standards of Care Committee, British Thoracic Society. BTS guidelines for the investigation of a unilateral pleural effusion in adults. Thorax 2003; 58.
7. Hirsch A, Ruffie P, Nebut M, Bignon J, Chretien J. Pleural effusion: laboratory tests in 300 cases. Thorax 1979; 34(1):106-112.
8. Davies HE, Davies RJ, Davies CW. Management of pleural infection in adults: British Thoracic Society pleural disease guideline.Thorax 2010; 65(Suppl 2), ii41-ii53.
9. Al-Alusi F. Pleural effusion in Iraq: a prospective study of 100 cases. Thorax 1986; 41:492–493.
10. Prabhudesai PP, Mahashur AA, Mehta N, Ajay R. Exudative pleural effusions in patients over forty years of age – an analysis of seventy six patients. Journal of Postgraduate Medicine 1993; 39(4):190–193.
11. Valdes L, Alvarez D, Valle JM, Pose A, San Jose E. The etiology of pleural effusions in an area with high incidence of tuberculosis. Chest Journal 1996; 109(1):158–162.
12. Kalaajieh WK. Etiology of exudative pleural effusions in adults in North Lebanon. Canadian Respiratory Journal 2001; 8:93–97.
13. Laim CK, Wong CM. Causes of pleural exudates in a region with a high incidence of tuberculosis. Respirology 2000; 5:33–38.

14. Golshan M, Faghihi M, Ghanbarian K, Ghanei M. Common Causes of Pleural Effusion in Referral Hospital in Isfahan, Iran 1997–1998 Asian Cardiovascular and Thoracic Annals 2002; 10(1):43–46.

15. Ibrahima WH Ghadban W, Khinji A, Yasin R, Soub H, Al-Khal AL, Bener A. Does pleural tuberculosis disease pattern differ among developed and developing countries. Respiratory Medicine 2005; 99(8):1038–1045.

16. How SH, Chin SP, Zal AR, Liam CK. Pleural effusions: role of commonly available investigations. Singapore Medical Journal 2006; 47(7):609–613.

17. Valdes L, Alvarez D, San Jose E, Penela P, Valle JM, Garcia-Pazos JM et al. Tuberculous pleurisy: a study of 254 patients. Archives of Internal Medicine 1998; 158(18):2017–2021.

18. Chan CHS, Arnold M, Chan CY, Mak TWL, Hoheisel GB. Clinical and pathological features of tuberculous pleural effusion and its long term consequences. Respiration 1991, 58:171–175.

19. Levine H, Metzger W, Lacera D, Kay L. Diagnosis of tuberculous pleurisy by culture of pleural biopsy specimen. Archives of Internal Medicine 1970; 126(2):269–271.

20. Seibert AF, Haynes J, Middleton R, Bass JB. Tuberculous pleural effusion. Twenty-year experience. Chest Journal 1991; 99(4):883–886.

21. Sahn SA. Malignant pleural effusions. In: Pulmonary diseases and disorders, 2nd ed. New York, McGraw–Hill 1988; 2159–2170.

22. Villena V, López EA, Echave-Sustaeta J, Alvarez MC, Martín EP. Prospective study of 1,000 consecutive patients with pleural effusion. Etiology of the effusion and characteristics of the patients. Archivos de Bronconeumologia 2002; 38(1):21–26.

23. Yang CT, Lee, M. H., Lan, R. S., & Chen, J. K. Telomerase activity in pleural effusions: diagnostic significance. Journal of Clinical Oncology 1998; 16(2):567–573.

24. Salyer WR, Eggleston JC, Erozon YS. Efficacy of pleural needle biopsy and pleural fluid cytopathology in the diagnosis of malignant neoplasm involving the pleura. Chest Journal 1975; 67:536–539.

25. Heffner JE. Diagnosis and management of malignant pleural effusions. Respirology 2008; 13:5–20.

26. Diacon AH, Van de Wal BW, Wyser C, Smedema JP, Bezuidenhout J, Bolliger CT, Walzl G. Diagnostic tools in tuberculous pleurisy: a direct comparative study. European Respiratory Journal 2003; 22(4):589–591.

27. Huang HC, Chang HY, Chen CW, Lee CH, Hsiue TR. Predicting Factors for outcome of tube thoracostomy in complicated parapneumonic effusion or empyema. Chest Journal 1999; 115(3):751–756.

28. Satpathy SK, Behera CK, Nanda P. Outcome of parapneumonic empyema. Indian Journal of Pediatrics 2005; 72:197–199.

29. Mohanty S, Kapil A, Das BK. Bacteriology of parapneumonic pleural effusions in an Indian hospital. Tropical Doctor 2007; 37:228–229.

30. Tareen S, Aman R, Hussain S, Masoom A, Zaman M, Massod, MK. Bacteriology of acute thoracic empyema in a tertiary care hospital. International Journal of Pathology 2007; 5(2):72–76.

31. Lin YC, Tu, CY, Chen W, Tsai YL, Chen HJ, Hsu WH, Shih CM. An urgent problem of aerobic Gram-negative pathogen infection in complicated parapneumonic effusions or empyemas. Internal Medicine 2007; 46(15):1137–1178.

32. Storm HK, Krasnik M, Bang K, Frimodt-Møller N. Treatment of pleural empyema secondary to pneumonia: thoracocentesis regimen versus tube drainage. Thorax 1992; 47(10):821–824.