



RESEARCH ARTICLE

COMPARATIVE UTILITY OF PLEURAL BIOPSY, CYTOLOGY AND BIOCHEMICAL ANALYSIS IN THE DIAGNOSIS OF PLEURAL EFFUSION

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ARTICLE INFO

Article History:

Received 23rd September, 2016
Received in revised form
17th October, 2016
Accepted 14th November, 2016
Published online 30th December, 2016

Key words:

Pleural effusion,
Tuberculosis,
Malignant Effusion.

ABSTRACT

Background: Pleural effusion refers to the excessive or abnormal accumulation of fluid in the pleural space. Pleural effusion often present as a common diagnostic dilemma to the physicians in clinical practice (1) as the differential diagnosis is wide and may indicate the presence of pleural, pulmonary, or extra pulmonary disease, as the no cause can be found in many cases in spite of care full evaluation

Methods: This study was carried out on 65 patients with pleural effusion admitted to the pulmonary medicine ward between August 2008 to August 2011. Etiological diagnosis of pleural effusion was confirmed according to appropriate clinical and /or laboratory findings or criteria.

Results: Sixty five patients with pleural effusion of different etiology were studied. The commonest type of effusion being tuberculosis 34(52.3%) followed by malignancy 17(26.15%), transudation effusion 7(10.7%) parapneumonic effusion 5(7.6%) and 2(3.07%) cases of empyema.

Conclusion: The findings of the present study in confirmation with previous studies indicate that tuberculosis and malignancy are the most probable cases of exudative pleural effusion. Additionally, those results confirm that, despite the development of new diagnostic procedures, pleural fluid analysis and pleural biopsy remain the best diagnostic methods for evaluation of pleural effusion, as well as for determining the etiology in patients with pleural effusion.

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Citation: Ashok Kumar, M. and Fayaz Ahmed Syed. 2016. "Comparative utility of pleural biopsy, cytology and biochemical analysis in the diagnosis of pleural effusion", *International Journal of Current Research*, 8, (12), 43637-43647.

INTRODUCTION

Pleural effusion refers to the excessive or abnormal accumulation of fluid in the pleural space. Pleural effusion often present as a common diagnostic dilemma to the physicians in clinical practice (Storey *et al.*, 1976) as the differential diagnosis is wide and may indicate the presence of pleural, pulmonary, or extra pulmonary disease, as the no cause can be found in many cases in spite of care full evaluation (Lesley *et al.*, 1995) It is important to establish an accurate etiological diagnosis, so that patient may be treated in the most appropriate and rationale manner. A better knowledge of spectrum of clinical history and clinical signs of pleural effusion along with radiological, biochemical, and etiological evaluation of pleural fluid helps in narrowing the diagnostic dilemma faced by physicians and helps better. The present study is contemplated the comparative utility of pleural biopsy, cytological and biochemical analysis in the diagnosis of pleural effusion, as patients admitted in the pulmonary medicine ward.

MATERIALS AND METHODS

The present study was conducted at our institute. This study was carried out on 65 patients with pleural effusion admitted to the pulmonary medicine ward between August 2008 to August 2011. Etiological diagnosis of pleural effusion was confirmed according to appropriate clinical and /or laboratory findings or criteria. Following selection criteria are observed.

Inclusion criteria

Thoracentesis and closed pleural biopsy with copes needle was performed in all patients with pleural effusion
Exudative effusion as per light's criteria
Patients age more than 18 years
patients who has given informed consent
Chest x-ray showing evidence of pleural effusion

Exclusive criteria

Un co-operative patient.
Patients with HIV seropositive.
Patient's with haemorrhagic diathesis.

Patient who have undergone repeated thoracentesis.
 Insufficient fluid to separate the parietal and visceral pleural surfaces and allow placement of the needle.
 Uncontrolled coughing.
 Local cutaneous lesions.Eg.:Pyoderma or Herpeszoster.

All patients were given a detailed history, clinical examination, routine blood investigations, sputum examination, chest x-ray, USG chest and pleural fluid analysis.Under local anaesthesia, a diagnostic thoracentesis was performed. Pleural fluid (10ml) were sent for biochemical, cytological study for tumour cells and bacteriologic studies. Pleural fluid analysis was performed protein concentration, glucose, LDH, ADA levels, cell count, and differential count, as well as cytological study for malignant cells. Bacteriological examination as well as examination for AFB were also performed. The serum LDH and proteins were estimated.Diagnosis of exudative pleural effusion was confirmed according to pleural fluid protien and LDH levels (light's criteria) and the size of the effusion was determined on the basis of chest radiographs

Light's criteria for exudative effusion

- Pleural fluid protein divided by serum protein greater than 0.5.
- Pleural fluid LDH divided by serum LDH greater than 0.6.
- Pleural fluid LDH more than two thirds the upper limit of normal serum LDH.

Closed Pleural biopsy with Cope's needle was performed in all patients, biopsies can be performed inferiorly, medially, and laterally but not superiorly because of the risk of serving an intercostal vessels. Four samples of pleural tissue were obtained for malignant pathology and one sample obtained for pleural tuberculosis for histological study (in 90% alcohol solution), after ward a chest radiograph was routinely obtained. Other diagnostic methods performed such as pleural fluid culture and 2 samples for examination of AFB. Standard tuberculin test was also performed for all patients. In patients with enlarged lymph nodes FNAC of lymph nodes was performed for diagnosis of tuberculosis and malignancy. Diagnosis of tubercular pleural effusion was confirmed by high ADA levels and predominant lymphocyte cytology and pleural biopsy samples by direct examination and identification of AFB from sputum samples.Presence of granulomas with caseous necrosis in biopsy specimen was confirmation of TB if clinical and radiological findings of TB were also available.Diagnosis of malignant pleural effusion was confirmed by identification of tumour cells from pleural fluid or pleural tissue samples. We consider a clinical history compatible with tuberculosis pleuritis in the case of a young patient with an acute illness, who has a cough, usually non-productive, low-grade fever, pleuritic chest pain, weight loss, and a chest roentgenogram with a pleural effusion. We also consider the tuberculin positivity and the response to treatment.

Concurrently we consider a clinical history compatible with neoplastic pleuritis in the case of a patient who had a known neoplastic disease and in which we have no other explanations for their pleural fluid. The sensitivity of diagnostic tests was calculated as the proportion of diseased individuals with positive test results i.e. diseased with positive test divided by all diseased.

RESULTS

A total of 65 cases of pleural effusion were included in the study and the following observations were made. Out of the 65 cases of pleural effusion most of the effusion were exudates 58 (89.2%).

Table 1. Final diagnosis of pleural effusion

S.No.	Final diagnosis	No. of cases	Percentage
1	Tuberculosis	34	52.3
2	Malignant	17	26.15
3	Transudative	7	10.7
4	Parapneumonic	5	7.6
5	Empyema	2	3.07

Among 65 cases of pleural effusion final diagnosis of tuberculosis was made in 34(52.3%) cases. 17(26.15%) cases were malignant effusion, 7(10.7%) were transudative effusion, 5(7.6%) cases were paraneumonic effusion, 2(3.07%) cases were empyema. Out of 65 cases of pleural effusion tuberculosis was the commonest cause, followed by malignant pleural effusion and transudative effusion.

Sex distribution

Among the 65 cases of pleural effusion there were 46 males and 19 females. The male: female ratios in the various group are as follows.

Table 2. Sex distribution of pleural effusion

S.No	Type of Effusion	No. of Cases	
		Male	Female
1.	Tuberculous	21	13
2.	Malignant	13	4
3.	Transudative	06	01
4.	Parapneumonic	04	01
5.	Empyema	02	-
	Total	46 (70.7%)	19 (29.2%)

Thus out of 65 cases 70.7% were males and 29.2% were females.

Table 3. Age distribution of pleural effusion

The age distribution among the cases are as follows

	Male		Female	
	No.	%	No.	%
01	03	04	6.15	
05	05	10	15.3	
10	4	14	21.5	
08	4	12	18.4	
10	01	11	16.9	
8	01	09	13.8	
4	01	5	7.6	
46	19	65	100%	

Among 65 cases of pleural effusion, patients age ranged from 11 to 80 years with mean age of 44.89 ± 16.3 years. 21.5% of patients were in the age group of 31-40 years, 18.4% of patients were in the age group off 41-50 years, 16.9% of patients were in the age group 51-60 years, 15.3% of patients were in the age group 21-30 years, 7.6% of patients were in the age group of 71-80 years, 6.15% of patients were in the age

group of 11-20 years. Among 65 cases of pleural effusion the more common in age group of 30 – 60 years.

Table 4. Site of effusion Distribution of site of effusion in pleural effusion

Sl.No.	Type of Pleural Effusion	Left	Right	Bilateral
1.	Tuberculosis	15	18	1
2.	Malignant	9	7	1
3.	Parapneumonic	1	4	-
4.	Transudative	-	3	4
5.	Empyema	-	2	-
	Total	25	34	6
	Percentage	38.4	52.3	9.2

Out of the 65cases of pleural effusion 34 (52.3%) were right side 25(38.4%) cases were left side 6(9.2%) patients had Bilateral effusions.

Amount of Pleural effusion

Out of the 65 cases 44 cases (67.69%) had moderate pleural effusion 12(18.46%) cases had a minimal effusion and 9(13.8%) cases had a massive pleural effusion.

Table 5. Presenting complaints

S.No	Symptoms	No. of cases	Percentage
1.	Cough	51	78.4
2.	Breathlessness	50	76.9
3.	Fever	46	70.1
4.	Weight Loss	43	66.15
5.	Loss of Appetite	37	56.9
6.	Chest pain	29	44.6
7.	Haemoptysis	10	15.3
8.	Puffiness of face	7	10.7
9.	Distension of abdomen	6	9.2
10.	Swelling of feet	6	9.2
11.	Decreased urine output	3	4.6

The most common presenting complaints were cough 51(78.4%) and breathlessness 50(76.9%) followed by fever 46(70.1%), wt loss 43(66.15%) loss of appetite 37(56.9%) and chest pain 29(44.6%) cases.

Table 6. Distribution of respiratory signs in pleural effusion

S.No.	Symptoms	No. of cases	Percentage
1.	Flat note	52	80
2.	Decreased/absent breath sounds	52	80
3.	Decreased VF, VR	52	80
4.	Decreased Respiratory Movements	48	73.8
5.	Mediastinal shift	38	58.4
6.	Crepitations	20	30.7
7.	Pleural rub	02	3

Respiratory findings on admission

The distributions of the various respiratory findings were as follows.52 (80%) cases had a stony dull note on percussion and 52 patients (80%) had decreased breath sounds, vocal fremities and vocal resonance. 48 cases (73.8%) showed decreased respiratory movements and 38 cases (58.4%) showed a mediastinal shift.

Montoux test: The Mantoux test was positive in 18 (52.9%) of the 34 cases with tuberculous pleural effusion.

FNAC of lymphnodes: Among 34 cases of tuberculars pleural effusion 2(5.88%) cases shows caseous granuloma in lymph

node tissue material. Among 17 cases of malignant pleural effusion 3(17.64%) cases shows malignant cells in lymph node tissue material.

Sputum for AFB: Sputum for AFB was positive in 3(8.8%) of 34 cases with tuberculous pleural effusion.

Radiology: All patients underwent chest x-ray PA view, lateral chest x-ray in few selected cases and ultrasound of thorax for approximate estimation of pleural fluid amount.

i) Chest X – ray

- Evidence of pleural effusion was seen in the chest X-ray in all the cases.
- Cavitary lesions were seen in the lung parenchyma in 3 cases.
- Lower lobe consolidation was seen in 5 cases.
- Cardiomegaly was present in 2 cases.
- Pulmonary filtrates – 4 cases.
- Fibrosis was present in 3 cases.
- Mass in the lung was present in 2 cases.

Table 7. Distribution of site of Effusion in CXR

S.No.	Type of Pleural Effusion	Left	Right	Bilateral
1.	Tuberculosis	15	18	1
2.	Malignant	9	7	1
3.	Parapneumonic	1	4	-
4.	Transudative	-	3	4
5.	Empyema	-	2	-
	Total	25	34	6
	Percentage	38.4	52.3	9.2

ii) Out of the 65cases of pleural effusion 34 (52.3%) were right side 25(38.4%) cases were left side 6(9.2%) patients had Bilateral effusions.

Table 8. USG estimation of pleural fluid volume

S. No.	Type of Pleural Effusion	Minimal 250-600ml	Moderate 600-1500ml	Severe >1500ml
1.	Tuberculosis	1	30	3
2.	Malignant	-	11	6
3.	Transudative	5	2	-
4.	Parapneumonic	5	-	-
5.	Empyema	1	1	-

iii) Amount of pleural effusion (including USG thorax):

Out of the 65 cases, 44 cases (67.69%) had a moderate pleural effusion, 12(18.46%) cases had a minimal effusion and 9(13.8%) had a massive pleural effusion. The cell count ranged from 96 to 5800 cells/mm³. The average cells count in Tubercular, Malignant, Transudative, Parapneumonic pleural effusion and Empyema was 1051, 840, 152, 4480 and 5800 cells/mm³ respectively. Lymphocytes were predominantly seen in patients with tuberculous effusion. Among 34 cases TB effusion 34 cases of 29(85.2%) cases showed predominant lymphocytes, 5(14.7%) cases shows polymorphs. Among 17 cases of malignant effusion 4(23.5%) shows lymphocytes, 12(70.5%) shows positive for malignant cells, 1(5.8%) shows polymorphs. All 7 cases of transudative effusion shows lymphocytes and all 5 cases of parapneumonic effusion and 2 cases of empyema shows polymorphs. (Table 12)

Table 9. Patients with characteristics and presenting features of tuberculous and malignant pleural effusions

Characteristics	Tuberculous pleurisy (n=34)	%	Malignant pleurisy (n=17)	%
Male	21	61.7	13	76.4
Bloody pleural fluid	2	5.8	8	47.05
Bilateral effusion	1	2.9	1	5.8
Left side effusion	15	44.1	9	52.9
Large effusion	3	8.8	6	35.2
Clinical presenting features				
Dyspnea	26	76.4	14	82.3
Cough	26	76.4	12	70.5
Pleuritic pain	17	50	5	29.4
Fever	19	55.8	7	41.1
Radiographic findings				
Pulmonary infiltrates	4	11.7	0	0
Cavitation	3	8.8	0	0
Pulmonary mass and atelectasis	0	0	2	11.7
Fibrosis	3	4.61	0	0

Table 10. Pleural fluid cytology

S.No.	Type of effusion	No. of cases	Cell count	Cell type predominant	Malignant cells
1	Tubercular	34	1051 ± 507	Lymphocytes	-
2	Malignant	17	840 ± 265	Lymphocytes	Positive in 12 cases
3	Transudative	7	152 ± 57	Lymphocytes	-
4	Parapneumonic	5	4480 ± 1622	Polymorphocytes	-
5	Empyema	2	5800 ± 282	Polymorphocytes	-

Table 11. Pleural fluid differential count in exudative and transudative pleural effusion

S.No.	Type of effusion	No. of cases	Differential count				
			Polymorphs	Lymphocytes	Eosinophils	Mesothelial cells	Malignant cells
1	Tubercular	34	5	29	-	-	-
2	Malignant	17	1	4	-	-	12
3	Transudative	7	-	7	-	-	-
4	Parapneumonic	5	-	-	-	-	-
5	Empyema	2	2	-	-	-	-

Pleural fluid cytology in tuberculous pleural effusion**Table 12. Tuberculous effusion lymphocyte count in 34 cases**

No. of samples	Lymphocyte count (%)	
	< 50	> 50
34	5	29

Among 34 cases of tuberculous pleural effusion 29(85.2%) shows lymphocytes count greater than 50%.

ii) Pleural fluid cytology in malignant effusion:**Table 13. Yield from cytology for malignant cells in malignant pleural effusion**

Cytology	Positive	Negative
17	12	5
100%	70.5%	29.4%

Pleural fluid cytology performed in all the patients with exudative. Among the 17 cases of malignant pleural effusion 12 (70.5%) cases of malignant pleural effusion had a positive cytology for malignant cells. The yield increased with the number of samples examines, but the number too small to draw a definite conclusion

13) Biochemical studies**i) Appearance:**

The pleural fluid was straw colored in 47 patients, colorless in 4 patients, turbid in 2 patients, hemorrhagic in 10 patients.

ii) The following biochemical parameters were analyzed in the present study

- Pleural fluid Glucose.
- Pleural fluid total Protein.
- Pleural fluid Lactate dehydrogenase.
- Pleural fluid Adenosine Deaminase.
- Serum glucose, protein, LDH.
- Ratio of protein, LDH.

They were divided into subjects with pleural effusion due to tubercular, malignant, transudative, parapneumonic and empyema groups.

Tubercular pleural effusion

The mean pleural fluid glucose levels in tubercular pleural effusion were in the range of 61±9.2 mg/dl and these concentrations were lower compared to Transudative pleural effusion and this difference was statistically highly significant (P<0.001). Further the mean pleural fluid glucose was higher in tuberculosis as compared to malignant pleural effusions and this difference was found to be statistically highly significant (P<0.001). The mean pleural fluid total protein levels in tubercular pleural effusion were in the range of 4.1±0.8 gm/dl which was higher as compared to Transudative pleural effusions and this difference was statistically significant (P=0.05). Among cases of tuberculosis pleural effusion, all cases which showed greatly elevates ADA levels in pleural effusion ranging from 40-150 U/Lit. With a mean value of 73.28 ± 21.38. in all cases responding to anti TB drugs ADA

Table 14. The estimated mean \pm SD of pleural fluid glucose, protein, LDH and serum protein, LDH and PF/S ratio of protein, LDH

S.No.	Type of Effusion	No. of cases	Pleural Fluid			Serum		Pl/s ratio	
			GLU(mg%)	PROT(gm%)	LDH(U/L)	PROT(gm%)	LDH(U/L)	PROT	LDH
1	Tubercular	34	61 \pm 9.2	4.1 \pm 0.8	236 \pm 37.52	6.5 \pm 0.7	340 \pm 50	>0.5	>0.3
2	Malignant	17	52 \pm 4	4.7 \pm 0.1	292 \pm 56.9	6.2 \pm 0.6	370 \pm 66	>0.5	>0.3
3	Transudative	7	84 \pm 11	2 \pm 0.7	95 \pm 24.5	6.0 \pm 0.5	360 \pm 28	<0.5	<0.3
4	Parapneumonic	5	48 \pm 15	4.7 \pm 0.3	530 \pm 89	6.9 \pm 0.8	351 \pm 53	>0.5	>0.3
5	Empyema	2	27 \pm 3.5	4.7 \pm 0.2	1225 \pm 247	7.3 \pm 0.2	367 \pm 45	>0.5	>0.3

Table 15. Pleural fluid ADA range with mean \pm SD in 65 cases of pleural effusion

S.No.	Disease	Range	Mean \pm SD	P - Value
1	Tubercular (n = 34)	50-150 U/L	73.28 \pm 21.38	< 0.0001
2	Malignant (n = 17)	20 - 40 U/L	32.66 \pm 6.03	< 0.0001
3	Transudative (n = 7)	13 - 25 U/L	19.28 \pm 4.2	< 0.001
4	Parapneumonic (n = 5)	25 - 30 U/L	27 \pm 2	< 0.001
5	Empyema (n = 2)	15 - 18 U/L	16.5 \pm 2.12	P=0.06 NS

levels were significantly raised compared to transudative and other exudative pleural effusion and this difference was statistically highly significant. $P < 0.0001$. By taking 95th percentile of control group (non-tuberculous pleural effusion). 40U/L as the cut off value, the activity of ADA test exhibited sensitivity and specificity of 100% and 100% respectively for the diagnosis of tuberculous pleural effusion. The pleural fluid LDH activity in tubercular effusion were in the range of 236.2 \pm 37.5 IU/L which was higher as compared to transudative pleural effusion and this difference was statistically highly significant ($P < 0.001$). We have observed increased concentration of pleural fluid total protein, along with the increased ADA and LDH activity whereas pleural fluid concentrations of glucose is decreased in tubercular pleural effusion.

Malignant pleural effusion

The mean pleural fluid glucose levels in malignant pleural effusion were in the range of 52 \pm 4 mg/dl which was lower as compared to Transudative pleural effusions and this difference was statistically highly significant ($P < 0.001$). Further the mean pleural fluid glucose was lower in malignant pleural effusion as compared to tubercular pleural effusion and this difference was found to be statistically highly significant ($P < 0.001$). The mean pleural fluid total protein levels in the range of 4.7 \pm 0.1 gm/dl which was higher as compared to Transudative pleural effusions and this difference was statistically significant ($P < 0.001$). Further the mean pleural fluid total protein was higher in malignant pleural effusion as compared to tubercular pleural effusion and this difference was found to be statistically highly significant ($P = 0.05$). The mean pleural fluid ADA levels in malignant pleural effusion were in the range of 32.66 \pm 6.03 IU/L which was lower as compared to tubercular pleural effusions and this difference was statistically highly significant ($P < 0.0001$). The pleural fluid LDH mean activity in malignancy were in the range of 292 \pm 56.9 IU/L which was higher as compared to Transudative pleural effusions and this difference was statistically highly significant ($P < 0.001$). Further the mean pleural fluid LDH activity was higher in malignant pleural effusion as compared to tubercular pleural effusion and this was found to be statistically highly significant ($P < 0.001$). By taking 95th percentile of the control group (non-malignant pleural group), 200.00 U/L as the cut-off value the

activity of LDH test exhibited 100% sensitivity and 100% specificity for the diagnosis of malignant pleural effusion.

Transudative pleural effusion

The mean pleural fluid glucose levels in Transudative pleural effusion were in the range 84 \pm 11 mg/dl which was higher as compared to exudative pleural effusions and this difference was statistically highly significant ($P < 0.001$). By taking pleural fluid glucose of >60.0 mg/dl as the cut-off value, the pleural fluid glucose test exhibited sensitivity and specificity of 100% and 93% respectively for the diagnosis of Transudative pleural effusion. The mean pleural fluid total protein levels in Transudative pleural effusion were in the range of 2 \pm 0.7 gm/dl which can be classified as Transudative form as compared to exudative form and this is of highly statistically significant ($P < 0.001$). By taking pleural fluid total protein of <3.0 gm/dl as the cut-off value, pleural fluid total protein test showed the sensitivity and specificity 90% and 95% respectively for the diagnosis of Transudative pleural effusion. The mean pleural fluid Adenosine deaminase activity in pleural effusion due to Transudative pleural effusion were in the range of 19.28 \pm 4.23 IU/L which was lower as compared to exudative pleural effusions and this difference was statistically highly significant ($P < 0.001$). The mean pleural fluid LDH activity in Transudative pleural effusion with pleural effusion were in the range of 95 \pm 24.5 IU/L which was lower as compared to 80 exudative pleural effusions and this difference was statistically highly significant ($P < 0.001$). The ratio of serum pleural fluid LDH was <0.6. We have observed that pleural fluid concentrations of glucose is more, whereas pleural fluid concentrations of total protein, activity of ADA and LDH are decreased in Transudative pleural effusion.

Parapneumonic pleural effusion

The mean pleural fluid glucose level in parapneumonic pleural effusion was in the range of 48 \pm 15 mg/dl and was found to be significant as compared to Transudative pleural effusions. The mean pleural fluid total protein in parapneumonic pleural effusion was in the range of 4.7 \pm 0.3 gm/dl. The mean pleural fluid total proteins were higher than the Transudative pleural effusions. The mean pleural fluid ADA activity in parapneumonic pleural effusion was in the range of 27 \pm 2 IU/L.

The mean levels of pleural fluid ADA were lower than the tubercular pleural effusion and this difference is statistically significant ($P < 0.001$). The mean level of pleural fluid LDH activity in parapneumonic pleural effusion was in the range of 530 ± 89 IU/L. The mean level of pleural fluid LDH in parapneumonic pleural effusion was lower than the malignant pleural effusion. We have observed increased concentration of pleural fluid total protein, and LDH activity whereas pleural fluid glucose and ADA activity are decreased in parapneumonic pleural effusion.

Empyema

The mean pleural fluid glucose level in empyema effusion was in the range of 27 ± 3.5 mg/dl and was found to be significantly less as compared to transudative pleural effusions. The mean pleural fluid total protein in empyema effusion was in the range of 4.7 ± 0.2 gm/dl. The mean pleural fluid total proteins were higher than the Transudative pleural effusions. The mean pleural fluid ADA activity in empyema effusion was in the range of 16.5 ± 2.12 IU/L. The mean levels of pleural fluid ADA were lower than the tubercular pleural effusion and this difference is statistically not significant ($P = 0.006$ NS). The mean level of pleural fluid LDH activity in empyema effusion was in the range of 1225 ± 125 IU/L. The mean level of pleural fluid LDH in empyema effusion was lower than the malignant pleural effusion. We have observed increased concentration of pleural fluid total protein, and LDH activity whereas pleural fluid glucose and ADA activity are decreased in empyema effusion

Table 16. Pleural biopsy results in 65 patients

Pleural biopsy	No. of cases	Percent
Pleural biopsy showed caseous granuloma	19	29.2
Pleural biopsy showed malignancy	7	10.7
Chronic specific inflammation	28	43
Inadequate	11	16.9

Table 17. Pleural fluid ADA levels in 65 cases

S. No.	Etiology	Total	0-20	21-40	41-60	61-80	> 80	Mean \pm SD	P-Value
1	Tuberculous	34	0	1	10	15	8	73.28 \pm 21.38	< 0.0001
2	Malignant	17	1	16	0	0	0	32.66 \pm 6.03	< 0.0001
3	Transudates	7	5	2	0	0	0	19.28 \pm 4.23	< 0.001
4	Parapneumonic	5	0	5	0	0	0	27 \pm 2	< 0.001
5	Empyema	2	2	0	0	0	0	16.5 \pm 2.12	P= 0.06 NS

Table 18. Pleural fluid ADA levels in Biopsy positive cases

S.No.	Etiology	Total	0-20	21-40	41-60	61-80	> 80	Mean \pm SD	P-Value
1	Tuberculous	19	0	1	5	8	5	80.15 \pm 28.97	< 0.001
2	Malignant	7	3	4	0	0	0	27.71 \pm 9.53	< 0.001

Pleural biopsy

Pleural biopsy using the cope's needle was undertaken in 65 patients with pleural effusion. Adequate tissue specimen was obtained in 54 (83%) patients. Biopsy gave a definitive diagnosis in 26 patients (19 patients with tubercular effusion, and 7 patients with a malignant effusion) with a yield of 40%. Rest of the 28 (43%) patients had chronic non specific inflammation. 13 of them were treated as suspected tubercular effusion. 3 had malignant effusion (cytology positive), 12 had no diagnosis established, 11(16.9) patients adequate tissue was

not obtained. Complications occur in 7(10.7%) patients, 5(7.6%) patients had pneumothorax, that resolved spontaneously. In 2 (3%) patients subcutaneous emphysema arose, resolving completely without treatment.

Pleural biopsy verses pleural fluid analysis

Tubercular pleural effusion:

All 34 (52.3%) cases of tubercular pleural effusion were exudates. Among 34 patients of tubercular pleural effusion, 19 (29.2%) were shows caseating granuloma in biopsy tissue. The pleural fluid of tubercular pleural effusion is usually predominantly lymphocytic. Among 34 cases of tubercular pleural effusion, 29 (85.2%) cases had more than 50% lymphocytes. 5(14.7%) cases shows polymorphs. Among case of tubercular pleural effusion, there were 34 cases which showed greatly elevated ADA levels in pleural fluid ranging from 40 to 150 U/Lit. With mean ADA concentration value of (73.28 \pm 21.38). These values were significantly raised compared to other cases of pleural effusion ($P < 0.0001$). In malignant effusion showed pleural fluid ADA levels from 20U to 40U/Lit. With mean of 32.66 \pm 6.03. ($P < 0.0001$). All 5 cases of parapneumonic effusion had pleural fluid ADA between 25-30U/Lit. With a mean value of 27 \pm 2 U/L. ($P < 0.001$). All 7 cases of trasudative pleural effusion showed values of pleural fluid ADA ranging from 12-25 U/Lit with a mean value of 19.28 \pm 4.23. Among 2 cases of empyema pleural effusion showed values of pleural fluid ADA from ranging 15-80 U/Lit with a mean value of 16.5 \pm 2.1. (Table-17) Among 19 case of biopsy confirmed tubecular cases, significant raised ADA levels were obtained in pleural biopsy confirmed cases, with mean ADA value of 80.15 \pm 28.97 ($P < 0.001$). Among 7 cases of pleural biopsy confirmed malignant pleural effusion with a mean ADA value of 27.71 \pm 9.53 ($P < 0.001$). (Table-18) All the patients with tubercular pleural effusion had ADA level diagnostic cut off value above 40U/L.

All non-tuberculous pleural effusion cases had ADA values <40 U/L. The values of pleural fluid ADA levels in tuberculosis were significantly raised when compared with malignant pleural effusion $P < 0.0001$, parapneumonic pleural effusion $P < 0.001$, trasudative effusion ($P < 0.001$), empyema ($P = 0.006$ ns). Accordingly the sensitivity of the test for diagnosis of Tuberculous Pleural Effusion is 100%, specificity 100%. None of the patients with tubercular effusion had ADA less than 40 U/L. In addition we failed encounter a correlation between the ADA activity and the total lymphocyte count. Pleural fluid

culture did not grow mycobacterium in any case, and pleural fluid for AFB not demonstrated in any case.

Table 19. Sensitivities of pleural biopsy and pleural fluid analysis in tubercular pleural effusion in 34 patients

Diagnostic method	n	%
Pleural biopsy	19	55.8
Lymphocyte count > 50%	29	85.2
ADA level diagnostic cut off above 40 U/L	34	100

In our patients, the sensitivity (100%) of ADA activity for diagnosis of tubercular effusion was higher comparative other methods. As compared to pleural biopsy ADA estimation is a simple, cheap, non invasive, biochemical test for diagnosis of tubercular pleural effusion.

Malignant pleural effusion

Table 20. Sensitivities of pleural biopsy and cytology in malignant pleural effusion in 17 patients

Diagnostic method	n	%
Pleural biopsy showed malignancy	7	41.17
Pleural fluid cytology positive for malignant cells	12	70.5

Among 17 cases of malignant pleural effusion 7(41.17%) were diagnosed by pleural biopsy showed neoplastic infiltration. 12 (70.5%) of the 17 patients had pleural fluid cytology was positive for malignant cells.

Table 21. Samples and yield of cytology in 17 cases of malignant pleural effusion

Sample(number)	Positive (%)
First (10)	7 (41.7%)
Second (5)	3 (17.6%)
Third (2)	2 (11.7%)
Total	12 (70.5%)

The diagnosis was established on the first specimen in 7 (41.7%) cases on the second in 3 (17.6%), on the third in 2 (11.7%) cases. Pleural fluid cytology alone was diagnostic of malignancy in 9 cases (52.9%), while pleural biopsy alone was diagnostic of malignancy in 4 (23.5%) cases.

Table 22. Types of neoplasms in 17 patients with malignant pleural effusion

Type of malignancy	No. of cases (%)	Total
Primary Carcinoma of lung		
Adenocarcinoma	6(35.2%)	
Squamous cell carcinoma	1(5.8%)	
Poorly differentiated carcinoma	2(11.7%)	9
Breast carcinoma	1(5.8%)	1
Lymphoma	2(11.7%)	2
Malignant pleural effusion with unknown primary	5(29.4%)	5
TOTAL		17

Out of 17 cases of malignant pleural effusion the origin of primary cancers were determined which included carcinoma lung 9(52.9%), breast carcinoma 1(5.8%), lymphoma 2(11.7%), malignant pleural effusion unknown primary 5(29.4%). Among 9(52.9%) cases of carcinoma of lung 6(35.2%) were adenocarcinoma, 1(5.8%) is squamous cell carcinoma, 2(11.7%) were poorly differentiated carcinoma. In our patients the sensitivity (70.5%) of pleural effusion fluid

cytology for malignant cells for the diagnosis of malignant pleural effusion was higher compared to pleural biopsy.

DISCUSSION

Pleural effusion is one of the most common problem with which patients come to the pulmonary physician. The present study examined the effectiveness of pleural fluid analysis and pleural biopsy in diagnosis of pleural effusion and differentiation of tuberculosis and malignancy in 65 hospitalized patients with pleural effusion. In the diagnostic work up of pleural effusion, biochemical, cytological and microbiological analysis, and pleural biopsy can provide the diagnosis in all cases of exudative effusion, transudative effusion and empyema. Tuberculosis and malignant pleural effusion are first two most important causes of pleural effusion with which a patient presents to a tertiary care hospital. 65 patients with pleural effusion were studied of which 34(52.30%) were cases of tuberculous effusion and 31(47.6%) were cases of non tuberculous effusion. The present study is particularly relevant in our country, has it has a high prevalence of tuberculous.

Etiology of Pleural Effusion

The causes of exudative pleural effusion vary according to geographic region as well as the study population ; crowding, poverty, malnutrition are associated with increased rise of TB; age, smoking habits; exposure to environmental factors or occupational risk factors may increase the risk of malignancies. According to time table of tuberculosis (Wallgrein time table) tuberculous pleural effusion was manifest usually within 3-6 months after primary infection. In our study out of the 65 cases of pleural effusion, 34 (52.30%) cases were of tuberculous effusion. This was reflective of the high prevalence of tuberculosis in the area being studied. The remaining 31 cases, 17(26.15%) were malignant effusion 7 (10.7%) were transudative effusion 5 (7.6%) were para pneumonic effusion and 2 (3.07%) cases empyema. In comparison, the etiology of pleural effusion in some of the previous studies are Prabhu Desai *et al.* (1993)-tubercular effusion comprises 64% of infective cause and 8% were of empyema. In patients of age more than 40 yrs, malignant effusion was more common, Al quarainet *al.*(1994)-common diagnose was tubercular (37%) followed by neoplasm (8%), parapneumonic (14%) and congestive cardiac failure (14%), Mamumet *al.*(2005) – also showed tubercular and malignancy were the major causes of pleural effusion, Valdes *et al.*(3) showed tubercular and transudative were commonest causes.

Sex Distribution

In our study there were a greater number of male patients than female patients in this study with 70.7% males and 29.2% females. In comparison, the sex distribution in some of the previous studies are: Subhakar *et al.* (1991).-77.5% males and 22.5% females; Leesly J. Burges *et al.* (1995) - 58% males and 42% females, Al Quorian *et al.* (1994) of 101 cases 45 were males and 31 females.

Age Distribution

The present study comprised of patients aged from 18 years to 80 years (mean age : 44.89 ± 16.3 years). The mean age in case of tuberculous effusion was 37.44 ± 10.7 years, with the

maximum number of patients between 20 – 60. The mean ages in cases of malignant, parapneumonic and Transudative effusion were 65.23 ± 7.57 years, 26.2 ± 1.92 years and 44.42 ± 17.28 years respectively. In comparison, the age distributions in some of the previous studies are: Lesley J. Burgess *et al.* (1997) – the ages of the patients ranged from 6 months 98 years with a mean age of 49 ± 20.72 years; Subhakar *et al.* (1991) – 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.

Presenting complaints

In our study the following were the presenting complaints among the patients, on admission. The commonest symptoms were cough (78.4%) and breathlessness (76.9%), followed by fever 70.1%, weight loss 66.15%, chest pain 44.6%, loss of appetite 56.9% and hemoptysis 15.3%. A small percentage (33.7%) had various other symptoms like distension of abdomen, puffiness of face, swelling of feet, decreased urine output. Most of the patients with parapneumonic 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 *et al.* (1991) main complaints were fever (41/44), chest pain (41.44) and weight loss (34.44).

Clinical Findings

In our study out of the 65 patients with pleural effusion 34 patients had a right sided effusion and 25 patients had a left sided effusion and 6 patients had bilateral effusion. 2 cases of empyema were on right side. In comparison to other studies: AL Quarain *et al.* (1994)- pleural effusion was more common in right side (55%) than on the left (32%). In Follander *et al.* (1988) both right and left side effusion were of equal distribution. 52(80%) patients had a flat note on percussion of the chest, due to the fluid in the pleural cavity. Flat note is the most important sign of pleural effusion. The breath sounds were diminished or absent in 52(80%) of the patients and the vocal fremitus and vocal resonance were also decreased in 52(80%) of the patients. Decreased respiratory movements were noted 48(73.8%) of the cases and mediastinal shift in 38(58.4%) of the cases. Crepitations were present 20(30.7%) of the cases and 2(3%) had a pleural rub. Other associated findings were seen like ascitis (6%) hepatomegaly (6%) and elevated jugular venous pressure (6%).

Mantoux test

In our study the Mantoux test was positive 18 (52.9%) of the 34 patients with tuberculous effusion. The patients with tuberculous effusion, in whom the Mantoux test was negative, were poorly nourished and emaciated which was probably the reason for the decreased sensitivity, thus producing a false negative response to the Mantoux test.

Sputum for AFB

In this study, out of the 34 cases of tuberculous effusion, in 3(8.8%) cases acid fast bacilli could be demonstrated in the sputum by Ziehl Nielson's staining. The detection of AFB in the sputum in the tuberculous depends upon the associated lung parenchymal lesion. In comparison to other study: Subhakar

et al. (1991).-7 of the 62 patients with tuberculous pleural effusion showed sputum positivity for AFB (i.e.,11%).

Radiology

In our study chest X-ray showed the presence of fluid in all the patients and was diagnostic of pleural effusion. 19 of the patients also had associated pulmonary lesions. In USG estimation of pleural fluid volume – majority of tubercular (30 cases) had moderate effusion. 6 cases of malignant effusion had massive effusion but, parapneumonic and empyema had minimal effusion. In Follander *et al.* study (1991) of radiological had shown parenchymal lesions in 23% of cases. Bowen *et al.* (1931) in his study in quantitative study of pleural effusion, divided pleural effusion into mild (250-600) and massive (>1500) pleural effusion. Majority of malignant effusion had massive effusion and parapneumonic had minimal effusion.

Pleural Fluid Analysis

1. Pleural fluid Cytology: In our study the cell count in the pleural fluid ranged from 96 to 5800 cells/mm³. The average cell counts in tubercular, malignant, transudative, synpneumonic and empyema was 1051, 840, 152, 480 and 5800 respectively. Lymphocytes were predominantly seen in tuberculous effusion. In our study 29(85.2%) tubercular effusion had more 50% lymphocytes were present in pleural fluid. Lymphocytes were also seen in 4(23.5%) cases of malignant effusion and 5(71.4%) cases of transudative effusion. Transudates also showed a significant number of mesothelial cells. Malignant cells could be demonstrated in 12(70.5%) cases of malignant effusion. In comparison to other studies; (9) Epstein *et al.* (1987) shows that majority of tuberculars effusion had more than 50% lymphocytes. Light *et al.* (1973) showed more than 50% of the WBC in an exudative pleural effusion are small lymphocytes. 96 of 211 exudative pleural effusion had more than 50% lymphocytes. Of these 96 effusion 90 (94%) were due to tuberculosis or malignant disease. Aggarwal *et al.* showed that tuberculars effusions rarely contains more than 5% meothelial cells which is similar to our study. Follander *et al.* (1994) demonstrated predominance of lymphocytes and scarcity of mesothelial cells in tubercular effusion: Nance (1991) KV-Cytology for malignancy was diagnostic in 71%; Light (1973) large number of neutrophils indicated the presence of bacterial pneumonia. Lymphocytes predominant in tubercular pleural effusion. Cytology for malignant cells was positive in 33-87%; Kumar *et al.* (2001) 70.8% has positive cytological findings in pleural fluid. Indicate that cytological evolution of pleural fluid is more effusions in the diagnosis of malignant pleural effusion. Light *et al.* (1980) demonstrated predominantly polymorphs in bacterial pneumonia.

2. Proteins: In our study the amount of proteins in the pleural fluid ranged from 1.2 gm/dl to 6.2 gm/dl. The mean protein level in tuberculous effusion was 4.1 ± 0.8 gm/dl, in malignant effusion was 4.7 ± 0.1 and in parapneumonic effusion was 4.7 ± 0.3 gm/dl, in empyema it was 4.7 ± 0.2 and in case of transudative it was 2 ± 0.7 gm/dl. The pleural fluid and serum protein ratio was >0.5 gm/dl% in tubercular, malignant, parapneumonic and empyema but <0.5 gm% in transudative pleural effusion. In comparison to other studies: Follader *et al.* (1991), Lakhotia *et al.* (1980) Light *et al.* (1996) ratio was >0.5 in exudates and <0.5 in transudates: in Anthony Seaton *et*

al. (2008) and Richard W. Light *et al.* (2004) pleural protein was more than 3 gm%.

3. Glucose: The glucose level in the pleural fluid ranged from 48 to 148 mg%. Low glucose levels were associated with tuberculous effusions, parapneumonic, empyema and malignant effusion and high glucose levels were seen in transudate. In our study, the mean values of pleural fluid glucose were: tuberculous effusion -61 ± 9.2 mg%, malignant effusion -52 ± 4 mg%, parapneumonic effusion -48 ± 15 mg%, empyema -27 ± 3.5 gm% and in case of transudate -84 ± 11 mg%. In comparison to other studies: Antony Seaton *et al.* (2008) showed glucose level <60 mg% in parapneumonic, empyema, tubercular and malignancy and >60 mg% in transudates; Light *et al.* (1983) pleural fluid glucose level below 40 mg% in parapneumonic and empyema; Carr *et al.* (1968) 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.

4. Lactate dehydrogenase: In our study the average LDH value in tubercular effusion -236.2 ± 37.5 , malignant -292 ± 56.9 , transudative -95 ± 24.5 , parapneumonic -530 ± 80 and empyema -1225 ± 125 . The mean LDH in exudative effusion was higher as compared to transudative effusions which was highly significant. By taking ratio of pleural and serum LDH >0.6 cut off, the activity of LDH exhibited 100% sensitivity and 100% specificity. In comparison to other studies; Lakhotia *et al.* (Suri *et al.*, 1991) pleural fluid LDH >200 U/L and pleural fluid to serum ratio >0.6 helps to classify the effusion as transudance. The same view was held by Santiago Romero *et al.* (1993) and Marina Costa *et al.* (1995) Richard W. Light *et al.* (2004) also classified transudates and exudates with same criteria.

5. Adenosine Deaminase levels: In our study 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 73.2 ± 21.38 IU/L, in malignant effusion the mean ADA level was 32.66 ± 6.03 IU/L and in transudates, the mean ADA level was 19.28 ± 4.2 IU/L. In the present study, the pleural fluid ADA values were significantly higher in tuberculous effusions ($p < 0.0001$) compared to other causes of pleural effusion. Using 40 IU/L as the cut off value, pleural fluid ADA estimation has a sensitivity and specificity of 100% in differentiating tuberculous from non-tuberculous effusion. ADA estimation in pleural fluid has long been taken as a marker for tuberculous pleurisy; The distinction between malignant and tuberculous effusions can usually be made on the basis of ADA activity. In general malignant effusions have lower ADA levels than those found in TB. The ADA is an enzyme involved in the purine catabolism. It catalyzes the deamination of adenosine to inosine and of deoxyadenosine to deoxyinosine. Adenosine deaminase is involved in the proliferation and differentiation of lymphocytes, specifically the T-lymphocytes. The T-cells release ADA during the process of activation in the presence of live intracellular pathogens. Thus ADA has been looked upon as a marker of cell mediated immune response and specifically T-cell activation. There are several known isoforms of ADA, which arise from different gene loci (Guptha *et al.*, 1990) out of which ADA-1 is found in all cells including lymphocytes and monocytes, while ADA-2 is found exclusively in monocytes. ADA-2 isoform is the one raised in tuberculous pleurisy, accounting for almost 88% of total ADA activity. Rise in ADA-1 activity is more commonly associated

with pyogenic bacterial infection of the pleural cavity, contributing to a median 70% of total ADA activity (Marina Costa *et al.*, 1995) However there is no clear advantage of using the ADA-2 over the total ADA activity in clinical practice (Tom Petterson *et al.*, 1984). The total ADA activity assay is in fact preferred for its rapid turnover and low cost. In comparison to other studies: Tom Patterson *et al.* (1984) stated that the high ADA activity in tubercular effusion is because ADA is being locally synthesized by T-lymphocytes within the pleural cavity and this is a reflection of a local cellular immune response. This view was also shared by Lesley J. Burgess *et al.*, M.F. Bagahana *et al.* (1988) Chopra *et al.* Ribera *et al.* (1990), Valdes *et al.* (1993), and Muranishi *et al.* (1992). Stated that above 40 u/L indicate pleural tuberculosis with sensitivity 81 to 100% and specificity 83 to 100%. Other workers Valdes *et al.* (1993); Roth *et al.* (1990) Burgess *et al.* (1991). have observed that this cut off indicates a still higher sensitivity of 90-100% and specificity of 89-100%.

Porcel *et al.* (2009) studied in areas with TB prevalence, pleural fluid ADA levels greater than 40 U/L argue, strongly for TB. The specificity of this enzyme increases if only lymphocyte exudates are considered. Indian workers Gilhotra *et al.* (1989) Maldhure *et al.* (1994), Ghelani *et al.* (1999), Raj *et al.* (1985), have observed that above 40 IU/L cut off indicates a sensitivity of 100% and specificity of 0.9, 0.34, 0.59 respectively. In our study we obtained a yield of 19(55.8%) for pleural biopsy in diagnosis of tuberculous pleural effusion and 7(41.17%) for malignant pleural effusion. In our study diagnostic yield of pleural biopsy in all cases of exudative pleural effusion was 26(40%). One of the reasons of this low diagnostic yield in our study was that in all the cases pleural biopsy was done only once, because of un-co-operation of the patients. In comparison to other studies; Poe *et al.* (1984) Suri *et al.* (1991) diagnostic yield of pleural biopsy in all cases of pleural effusion is about 60-80%. Suri *et al.* (1991) Kirsch *et al.* (1997), Jimenez *et al.* (2002) show that repeat pleural biopsy increased the diagnostic yield of pleural biopsy upto 89 to 100%. In our study for diagnosis of tuberculous pleural effusion, closed pleural biopsy yielded the diagnosis in 19(55.8%) cases of tubercular pleural effusion. In comparison to other studies Kettle *et al.* (1967) stated that diagnostic yield of closed pleural biopsy in tubercular pleural effusion ranges from 60 to 95%. In one of the largest reviews of over 2500 pleural biopsies Tomolson *et al.* (1987) reported a diagnostic yield of 75% for pleural tuberculosis. In an Indian study Christopher *et al.* (2004) reported that the diagnostic yield of pleural biopsy was 75% for pleural tuberculosis. In an Indian study on role of serial pleural biopsies in the diagnosis of pleural effusion, Suri *et al.* (1991) showed that in case of tubercular pleural effusion three serial pleural biopsies increases the yield from 60 to 93%.

In our study closed pleural biopsy yield the 7(41.17%) for diagnosis of malignant pleural effusion. Compared to various studies Prakash *et al.* (1985), Sahn *et al.* (1988) in malignant pleural effusion the diagnostic yield of close pleural biopsy is about 43% and 46% respectively. Other studies Salyer *et al.* (1975), Sisson and Weiss *et al.* (1962). Hampson and Karlishe *et al.* (1961) the diagnostic yield of pleural biopsy is about 56%, 59% and 55% respectively. In an Indian study Christopher *et al.* (Richard W. Light, 2004) reported the diagnostic yield of pleural biopsy was 71% for malignant pleural effusion. The present study we compare the diagnostic efficacy of pleural biopsy and pleural fluid ADA activity in the diagnosis of

tuberculous pleural effusion and other types of pleural effusion. In our study we obtained a yield of 55% for pleural biopsy in the diagnosis of tuberculous pleural effusion. In our study pleural fluid ADA in case of tuberculous pleural effusion is $73.2\% \pm 21.8\%$ which is significantly higher ($p < 0.0001$) as compared to other types of pleural effusions. All 34 cases of tuberculosis pleural effusion had pleural fluid ADA value above 40 U/L; at this cut off value pleural fluid ADA estimation has a sensitivity and specificity of 100%. Compared to various studies. Ribera *et al.* (1990) Valdes *et al.* (1993), and Muranishi *et al.* (1992). Stated that above 40 U/L indicate pleural tuberculosis with sensitivity 81 to 100% and specificity 83 to 100%. Other workers Valdes *et al.* (1993) Roth *et al.* (1990), Burgess *et al.* (1991). Have observed that this cut off indicates a still higher sensitivity of 90-100% and specificity of 89-100%. Indian workers Gilhotra *et al.* (1989); Raj *et al.* (1990), Maldhure *et al.* (1994), Ghelani Dn *et al.* (1999) have observed that above 40 IU/L cut off indicates a sensitivity of 100% and specificity of 0.34-0.9.

The pleural fluid ADA values reported by various authors are Piras *et al.* (1978) 83.24 \pm 25.5 U/Lit, Blake and Berman (20) (1982) 46 \pm 13 U/Lit. O'cana *et al.* (1983) 92.43 \pm 29.43 U/Lit, Patterson *et al.* (1984) 32.0 \pm 3.3 U/Lit. The pleural fluid ADA values reported by Indian authors are Sinha *et al.* (1985) 76.8 \pm 23.8 U/Lit. Raj *et al.* (1985), 99.56 \pm 9.78 U/Lit, Chopra *et al.* (1968), 114.2 \pm 7.22 U/Lit and Gilthotra *et al.* (1989), 82.9 \pm 30.32 U/Lit respectively. In addition we failed to encounter a correlation between ADA activity and the total lymphocyte count. Pleural fluid culture did not grow mycobacterium in any case; and pleural fluid cob web not demonstrated AFB in any case. Thus, ADA estimation being simple, low cost, rapid and non invasive biochemical test, should become an integral part of the diagnostic work up of exudative pleural effusion in suspected cases of tuberculosis and differentiate tubercular pleural effusion from other etiologies of pleural effusion compared to pleural biopsy. In our study the sensitivity (100%) ADA activity for diagnosis of tuberculous effusion was higher compared to pleural biopsy. In the present study we compare the diagnostic efficacy of pleural biopsy and pleural fluid cytology in the diagnosis of malignant pleural effusion. In our study we obtained a diagnostic yield of 7 (41.7%) cases for pleural biopsy and 12 (70.5%) cases for pleural fluid cytology positive for malignant cells. In comparative various studies Suri *et al.* (1991) Light *et al.* (1995) pleural fluid cytology diagnostic yield in malignant pleural effusion range from 40 to 87%. Nance *et al.* (1991) reported a diagnostic yield of 45% for closed pleural biopsy and 71% for pleural fluid cytology in case of malignant pleural effusion. Shans *et al.* (1988) reported yield of 46% for closed pleural biopsy and 66% for pleural fluid cytology for diagnosis of malignant pleural effusion.

Prakash *et al.* (1985) reported a diagnostic yield of 43% for closed pleural biopsy and 57.6% for pleural fluid cytology for diagnosis of malignant pleural effusion. Salyer *et al.* (1975) reported a diagnostic yield of 56% for closed pleural biopsy and 72% for pleural fluid cytology for diagnosis of malignant pleural effusion, stated that repeated submission of pleural fluid samples for cytological examinations increases the diagnostic yield. In our study diagnostic yield of pleural fluid cytology and pleural biopsy was 70.5% and 41.17% respectively in the case of malignant pleural effusion. In our study shows that cytologic analysis has a higher sensitivity (70.5%) compared to needle biopsy for diagnosis of malignant pleural effusion.

All tubercular pleural effusion patients were put on treatment with antitubercular drugs along with steroids for rapid absorption of fluid and prevent subsequent pleural thickening. Malignant pleural cases were referred to higher centre for further evaluation and management. Parapneumonic effusion responded to appropriate antibiotics given for 2 weeks. Empyema patients required intercostals drainage and antibiotics were given for 3 weeks. All patients received other supportive measures. Chest x-ray were done when and where necessary.

Summary and Conclusion

- Pleural effusion is one of the most common problem, with which patients come to the pulmonary physician and in our country, the commonest cause is tuberculosis, as is evidenced from the present study.
- Sixty five patients with pleural effusion of different etiology were studied. The commonest type of effusion being tuberculosis 34(52.3%) followed by malignancy 17(26.15%), transudation effusion 7(10.7%) parapneumonic effusion 5(7.6%) and 2(3.07%) cases of empyema.
- In summary, the findings of the present study in confirmation with previous studies indicate that tuberculosis and malignancy are the most probable causes of exudative pleural effusion. Additionally, those results confirm that, despite the development of new diagnostic procedures, pleural fluid analysis and pleural biopsy remain the best diagnostic methods for evaluation of pleural effusion, as well as for determining the etiology in patients with pleural effusion.

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