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Research Article

A CLINICAL, BIOCHEMICAL & CYTOLOGICAL PROFILE IN PATIENTS OF PLEURAL EFFUSION ATTENDING A TERTIARY CARE CENTRE IN KUMAON REGION OF UTTARAKHAND

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ABSTRACT

Aim: To evaluate the reliability & diagnostic efficacy of pleural glucose, total protein, Lactate dehydrogenase(LDH), Adenosine Deaminase(ADA) and cholesterol in diagnosis of pleural effusion (PE) & to study clinical, biochemical & cytological markers which helps in establishing the exact diagnosis of different causes of pleural effusion. **Materials and Methods:** A Prospective observational-study done at Department of General Medicine of Govt. Medical College Haldwani over 2 years (2016 -2018) period. 122 patients above the age of 16 years with pleural effusion were included in our study. Thoracocentesis was done and an adequate amount of pleural fluid was aspirated to carry out the requisite tests. **Results:** The mean age of the studied patients was 44.72±17.3 years. 65.6% were males. Fever and cough were the commonest clinical findings. Sputum test for AFB was found positive only in 9.0% cases. Cytology of pleural fluid for malignant cells was found to be positive in 10.7% of the studied patients and 9.8% mortality rate due to pleural effusion was found. **Conclusion:** The most useful tool in establishing the exact diagnosis of PE was pleural fluid cytology and pleural fluid cell count.

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INTRODUCTION

Pleural effusion (PE) is excessive or abnormal collection of fluid in the pleural space. Pleural effusion is of 2 types depending on the underlying pathophysiology i.e., 'transudates' and 'exudates'. Transudates happen when the mechanical component influencing the emergence or reabsorption of pleural fluid are altered. Exudate outputs from inflammation or irritation or other disease process implicating the pleura, resulting in increased permeability.¹ Tuberculosis is the commonest cause of exudative PE in different areas of the world.^{2,3} According to different studies the occurrence of synpneumonic effusions with pneumonia span from 20% to 57%,⁴ and the occurrence of pleural effusion in decompensated congestive heart failure (CHF) is the highest with 87% occurrence.⁵

In India, the occurrence of pleural effusion in descending order is Tubercular pleural effusion (TPE) followed by malignant effusion⁶ and a very few due to synpneumonic effusion.⁸ Previous studies have shown that the precision of cytological findings of pleural fluid in diagnosing malignant pleural effusion varies from centre to centre and has been described to

be between 40% and 87%.⁷ Under physiological conditions, pleural fluid (PF) is an ultrafiltrate of plasma with an estimated quantity of 0.15 mL/kg in each hemithorax.⁸ The pleural fluid is normally composed of approximately 1.5 g of protein per dL and contains a less number of macrophages, mesothelial cells, and lymphocytes. Through echocardiography, even a minimal film of PF, approximately 3-mm, can be observed in 30% of healthy individuals.⁹

The diagnosis of tuberculous pleural effusion (TPE) depends on the confirmation of tubercle bacilli in pleural fluid, a pleural biopsy sputum, or the confirmation of granulomas in the pleura.¹⁰ Since pleural tissue sampling is more difficult than simple thoracocentesis, pleural fluid markers of TPE have been extensively evaluated as an attractive alternative.¹¹

Polymerase chain reaction (PCR) is a new quick strategy to diagnose mycobacterial DNA in pleural fluid depending on the area of the genome that is amplified and the technique used for DNA extraction.¹² High levels of ADA have also been described in non-infectious conditions related with pleural fluid lymphocytosis including malignancies (e.g., adenocarcinomas, leukemias, and lymphomas) & collagen vascular diseases (e.g.,

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rheumatoid pleuritis and systemic lupus erythematosus), which makes the finding less useful in countries with a low incidence of tuberculosis.^{13,14}

MATERIALS AND METHODS

Our study was a prospective Observational Study done in the department of general medicine of GMC Haldwani and associated STM Hospital Haldwani from October 2016 to October 2018 on the 122 patients with pleural effusion. The study was approved by ethical Committee. All patients above the age of 16 years with pleural effusion were included. A written consent was taken from all 122 patients, detailed history and physical examinations were done that was recorded on predesigned proforma. Patient's demographic profile, personal history, physical examination, radiographic findings were recorded. Evaluation of biochemical & cytological profile of pleural effusion was done by thoracentesis. Chest x ray (PA) view was taken in every patient and lateral view was taken, if necessary.¹⁵ Complete blood counts and ESR were done. Plasma total and differential protein and LDH were used to calculate the ratio using light's criteria for Pleural fluid. Macroscopic appearance of pleural aspirates was also recorded. Pleural fluid was examined by May-grunwald staining, H & E staining, staining for AFB, and PAS staining used for evaluation of pleural fluid. Differential white cell counts of pleural fluid were recorded & calculated as percentage (%). Calculation of pleural fluid total protein concentration (g/l), LDH (U/L), total cholesterol (mmol/l) and sugar (mmol/l) were performed by COB S501 auto analyser. The data was analyzed using Statistical Package for Social Sciences, version 23 (SPSS Inc., Chicago, Illinois, USA).

OBSERVATION AND RESULTS

The majority of the patients were of the age group 21-40 years (39.3%) followed by 41-60 years (34.4%) while the least were of the age above 80 years (1.6%). Males (65.6%) were dominant than female (34.4%). Most of patients have studied till high school (35.2%) followed by Intermediate (27.9%) and illiterate patients (21.3%) and the least were Graduate or above (15.6%). On the basis of their geographical region and the majority of patients were from hilly and cold region (64.7%) followed by the plain region (35.3%) (Table 1).

Table 1 Distribution of demographic profile of patients

Variable	No. of patients (n=122)	Percentage (%)
Age	≤20	6.6
	21-40	39.3
	41-60	34.4
	61-80	18.0
	>80	1.6
Gender	Males	65.6
	Females	34.4
	Illiterate	21.3
Literacy	High School	35.2
	Intermediate	27.9
	Graduation and above	15.6
Region	Hilly	64.7
	Plain	35.3

On the basis of clinical findings, fever (73.8%) was most common followed by cough (47.5%) and Chest discomfort/heaviness (23.8%) while the least patients were suffering from dyspnea (9.8%). (Table 2)

Table 2 Clinical findings of patients

Chief complaints	Frequency(n=122)	Percentage (%)
Fever	90	73.8
Cough	58	47.5
Breathlessness	11	9.0
Chest discomfort/heaviness	29	23.8
Weight loss	16	13.1

Side involved in pleural effusion, 58.2% were diagnosed with unilateral sides (Right and Left) followed by bilateral sides (41.8%). (Fig.1)

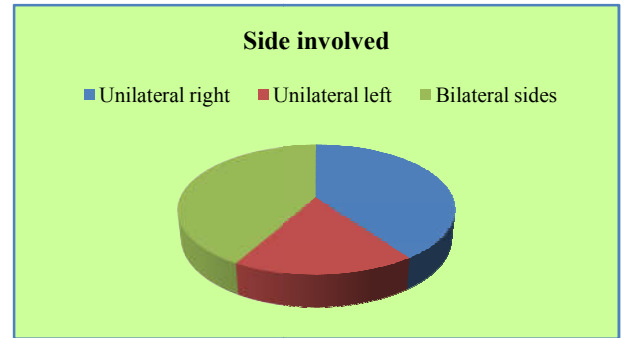


Fig 1 Side involved in pleural effusion

Morphology of pleural fluid findings showed Straw colored fluid (41.8%) followed by Clear Fluid (24.6%) and Turbid fluid (15.6%) while the least having Dark yellow fluid (6.6%) and Yellow color (3.3%)(Fig. 2).

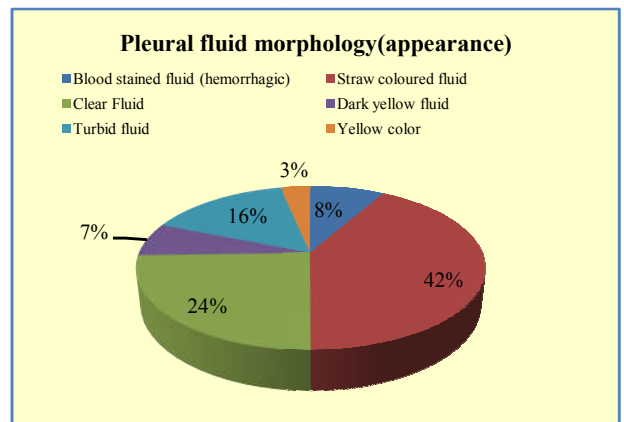


Fig 2 Morphology of pleural fluids

Biochemical, Hematological, and peripheral blood hematological findings were also recorded (Table 3).

Table 3 Blood investigations of patients

Findings	Mean ± SD	
Biochemical Variables	Pleural Fluid ADA(U/L)	21.48±2.56
	Pleural Fluid Glucose(mg/dl)	58.41±30.39
	Pleural Fluid Protein(g/dl)	2.21±1.23
	LDH	265.59±161.48
Pleural fluids	Pleural fluid Cholesterol(mmol/L)	2.14±1.26
	Total Cell count(TLC)	2121.30 ± 2295.90
	Neutrophils (%Total WBC)	19.0± 10.40
	Lymphocytes (%Total WBC)	80.91±10.39
Hematological variables	Plenty of RBC	--
	Plenty of RBC + mesothelial cells	--
	Haemoglobin (g/dl)	12.46 ± 9.00
	Total Cell count(TLC) mm ³	10954 ± 4151
	Serum Albumin(g/dl)	2.9 ± 0.7

The quantification of effusion with different etiology in the studied patients where massive size was present in 18 patients, moderate was in 55 cases while mild size was in 49 cases with 83 cases of tubercular followed by malignant and Synpneumonic with 12 cases each and the association was found to be statistically significant ($p < 0.05$) (Table 4).

Table 4 Size of effusion with different etiology

Size	Tubercular	Malignant	Synpneumonic	Empyema	Pancreatic	P value
Massive	9	6	0	3	0	<0.001
Moderate	45	3	2	3	2	
Mild	29	3	10	3	4	
Total	83	12	12	9	6	

Pleural fluid biochemical findings with different etiology were also recorded (Table 5).

Table 5 Pleural fluid biochemical findings with different etiology

Type of effusion	No. of cases	Pleural fluid				
		Glucose (mg %)	Protein (gm %)	LDH (U/L)	ADA (IU/L)	CHOL (mg %)
Tubercular effusion	83	61±9.4	4.8±1.5	238±34	79.5±9.8	71.56±10.2
Malignant effusion	12	51±4.2	4.6±0.8	340±47.8	41.5±8.4	78.45±11.5
Synpneumonic effusion	12	46.8±16	4.5±0.5	520±84	42.3±18.6	74.8±5.8
Empyema	9	29.8±5.6	4.4±0.6	1128±284	32.56±5.9	73.56±5.4
Pancreatic effusion	6	34.9±8.4	4.3±0.4	421±95	35.6±9.8	74.8±6.1

Correlation between symptoms and etiologies was found to be highly significant ($p < 0.05$). Pleural fluid cytology for malignant cells was found positive in 10.7% patients (Figure 3)

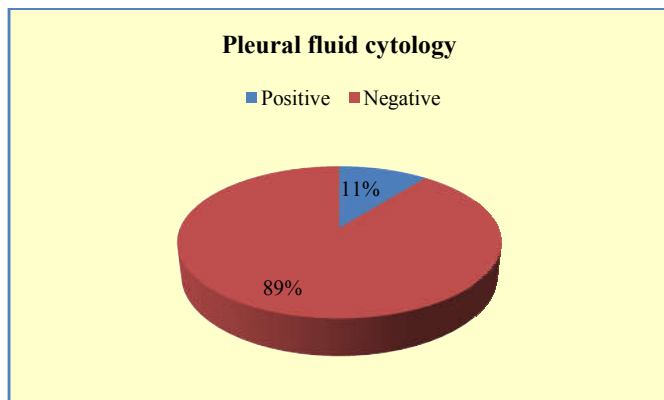


Figure 3 Pleural fluid cytology for malignant cells

A total of 9.8% mortality was reported and the most common cause of mortality was respiratory failure in 8 patients followed by shock & septicemia with 4 patients in each.

LDH was 83.3% sensitive and 77.3% specific whereas cholesterol was 83.3% sensitive and 70.0% specific. For glucose, protein and ADA sensitivity was 41.7%, 50.0% and 25.0% respectively, similarly, specificity was 29.1%, 40.0% and 20.9% respectively. (Table 7)

Table 7 Sensitivity and specificity of Test Result Variables

Test Result Variable(s)	Cutoff	Sensitivity (%)	Specificity (%)
Glucose (mg %)	52.50	41.7	29.1
Protein (gm %)	4.750	50.0	40.0
LDH(U/L)	325.50	83.3	77.3
ADA(IU/L)	47.00	25.0	20.9
CHOL (mg %)	77.50	83.3	70.0

DISCUSSION

The difficulty in ascertaining the exact cause of PE was shown by the fact that in many series “unknown aetiology” still constituted nearly 15%.

Demographic

The mean age was found to be 44.72±17.3 years and majority of the patients were of the age group 21-40 years (39.3%) followed by 41-60 years (34.4%) while the least were in the age group above 80 years (1.6%). Similar findings regarding the mean age were also observed by Soe Z *et al*¹⁶, Vasireddy A *et al* and Lokesh MR¹⁷ who reported the mean age to be 42.60±16.34, 41.85±15.39 and 41.85±15.39 years respectively in their studies. This implied that the majority of patients suffering from pleural effusion were in the 4th and 5th decade of their life.

Pleural effusion were males (65.6%) dominant than females (34.4%) in the study that is in accordance with the study performed in the past by Kelam MA¹⁸, Suvernakar SV *et al*, Lokesh MR and Vasireddy A reported the predominance of males over females in their respective studies. This implied that males were more afflicted with pleural effusion as compared to females.

Clinical Findings

The majority of patients were suffering from fever (73.8%) followed by a cough (47.5%) and Chest discomfort/heaviness (23.8%) while the least patients were suffering from dyspnea (9.8%) that was similar to Vasireddy A *et al* & Follador EC *et al*¹⁹ studies. Another study by Rao MRR *et al* depicted the commonest symptoms as a cough (78.32%) and breathlessness (74.76%) followed by fever 71.20%, weight loss 67.64%, chest pain 44.50%, loss of appetite 62.30%, and haemoptysis 17.80%.

Pleural Effusion side involved

The majority of patients were diagnosed with unilateral involvement. (right sided pleural effusion (40.2%) and left sided pleural effusion (18.0%)) 58.2% followed by bilateral pleural effusion (41.8%). Similar findings were reported by Rao *et al*, Al-Quarain²⁰, Follador *et al* and Vasireddy A *et al* in their respective studies.

Morphology of pleural fluids

Majority of the patients showed straw colored fluid (41.8%) followed by clear fluid (24.6%) and turbid fluid (15.6%) while the least number had a dark yellow fluid (6.6%) and yellow color (3.3%). Soe Z *et al* reported that out of 108 patients with tubercular pleural effusion, seven patients revealed blood stained pleural fluid (6.48%). The rest had straw colored aspirates. Vasireddy A *et al* & Lokesh MR *et al* also reported the majority of effusions were of straw colored.

Correlation of the etiology of pleural effusion with the amount of fluid

The massive size was commonly associated with the malignant etiology (50.0%) while moderate size of the pleural effusion was commonly associated with the tubercular (54.2%) and the mild was also common in tubercular (34.9%) followed by

synpneumonic (83.3%) etiology and the association was found to be statistically significant ($p < 0.05$). Rao *et al* found that massive effusion with haemorrhagic pleural fluid is commonly associated with malignant effusion similar to that observed, by Maher *et al* (55%).²¹

Biochemical findings with different etiology of pleural effusion

In our study the mean glucose level was significantly higher in tubercular effusion than any other pleural effusion etiology; mean protein level was almost similar in all the etiologies of the pleural effusion, LDH level was also very much higher in empyema than in malignant or tubercular etiology of pleural effusion, ADA was the highest in Tubercular effusion and was almost similar in other effusions and there was no statistical difference in the cholesterol levels of the effusions. Our study was in accordance with Rao *et al* who stated that pleural fluid ADA was significantly elevated in tubercular pleural effusion. Exudative effusion had decreased glucose, but increased protein, LDH, and cholesterol compared to transudative effusion. In study by Richard W. Light²² pleural protein was more than 3gm%.

Pleural fluid cytology

Pleural fluid cytology for malignant cells was done and the majority of the patients were diagnosed as a negative result (89.3%) followed by the positive result (10.7%). Our findings were comparable to the study performed by Vasireddy A *et al* who observed 62.0% of malignant effusions were negative while 38.0% were found to be positive.

Mortality

In the present study, 90.2% patient of pleural effusion had survived and mortality was reported in only 9.8%. The primary causes of mortality was respiratory failure (6.6%) followed by shock and septicemia with 3.3% each while the least common causes were MODS and Malignancy with 1.6% each. No such comparative studies in the past had been performed depicting the mortality and the primary causes of the mortality in cases of pleural effusion.

On the basis of correlation between malignancy and their correlated factors in our study, we found that LDH and Cholesterol plays a significant role in PE patients for their positive malignancy, it was shown that LDH and Cholesterol has plays a significant role in PE patients for their malignancy. LDH was 83.3% sensitive & 77.3% specific at level of 325.50 U/L whereas Cholesterol was 83.3% sensitive & 70.0% specific at level of 77.50 mg% in our pleural effusion population.

CONCLUSION

Our study demonstrated that the most practical test in demonstrating the exact diagnosis of pleural effusion was pleural fluid cytology and pleural fluid cell count.

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