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Study of Clinicoetiological Analysis of Pleural Effusion-Its Radiological, Biochemical, Cytological and Bacteriological Correlation.

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ABSTRACT

Background: Pleural effusion (PE) have varied pathological processes and etiological diseases prevalence. We aim to study clinicoetiological analysis of PE in its radiological, biochemical, cytological and bacteriological correlation in different diseases prevalence in our setup.

Methods: A total of 100 patients with PE were studied over a period of one year in a Regional Hospital in collaboration with a tertiary care hospital catering rural and urban population. Thoracocentesis was performed with standard technique and pleural fluid thus obtained was appropriately evaluated and analysed statistically.

Results: Patients of PE with age-range from 19 to 78 years were found mostly in younger age group of 20 -40 years (59%), more in males (66%) vs females (34%). Modified Light's criteria was satisfied in 81(81%) patients of PE to classify them as exudative and remaining 19(19%) as transudative. Tuberculosis (56%) was found the most common cause and dyspnoea (76%) the most common symptom of PE.

Conclusion: Tuberculosis was found the most common cause of PE, therefore, all the patients with PE are recommended to be evaluated meticulously for tuberculosis for early case detection and treatment, hence prevention of the disease incidence and prevalence.

Keywords: Adenosine deaminase, Exudative, Parapneumonic, Pleural effusion, Transudative, Tuberculosis.

I. INTRODUCTION

Pleural effusion (PE) refers to excessive and abnormal accumulation of fluid in the pleural space. It is accompanied by wide variety of diseases of lungs, pleura and other systemic pathologies. Chest physicians report around 4% of all the cases in out patients clinics alone.[1] India exhibits high incidence of tuberculosis (TB) which forms the most common cause of PE.[2] Accurate etiological diagnosis is very important for effective management of PE. It often poses a diagnostic dilemma, as no cause may be found in about 19% of cases.[3] With clinical, biochemical and cytological evaluation, an etiological diagnosis can be established in approximately 75% of patients.[4]

Pleural space lies between parietal pleura, outer layer of loose connective tissue and visceral pleura, inner layer of thick connective tissue containing blood vessels, lymphatics and mesothelial cells.[5] Fluid that enters the pleural space originates in the pleural capillaries, interstitial spaces of the lungs, intrathoracic blood vessels and lymphatics or peritoneal cavity. Movement of fluid between pleural surface and capillaries is governed by Starling's law of transcapillary exchange.[1] Pleural fluid enters the pleural space from interstitial space of the lungs either by high pressure or high permeability of capillaries.Pulmonary edema can lead to accumulation of the pleural fluid in this manner.[6] Pleural fluid formation takes place because of increased formation or decreased absorption or both.[7]

It is necessary to separate pleural fluid into transudative and exudative, as extensive diagnostic workup is required to delineate the cause for exudative PE. For many years, protein levels > 3gm% in pleural fluid were used to separate exudates from transudates which alone leads to misclassification of 10% of PE. In 1972, Richard W. Light added lactic acid dehydrogenase (LDH) levels in both serum and pleural fluid which correctly classifies 99% of PE into exudates and transudates.[8] Pleural fluid protein to serum protein ratio >0.5, to LDH ratio > 0.6 and pleural fluid LDH > two third of upper limit of normal for serum LDH meet the criteria for exudative PE. In

recent years, tests have been proposed for PE to differentiate transudates from exudates; cholesterol greater than 60 mg% is used for the differentiation. [9,10] Romero et al[11], in a study found Light's criteria superior to serum effusion albumin gradient, the effusion cholesterol or pleural fluid and serum bilirubin gradient. Light's criteria with a sensitivity of 98% and a specificity of 77% for exudates, showed best accuracy (95.2%). Modified Light's criteria classify 98% exudates and 77% transudates correctly. Infectious, neoplastic, gastrointestinal and connective tissue disorders (CTD) are the main etiological causes for exudative PE, whereas heart failure, cirrhosis of liver, nephrotic syndrome and constrictive pericarditis are the main etiological causes for transudative PE. Initial evaluation of PE includes meticulous history and complete physical examination. Dyspnea, cough, pleuritic chest pain, dullness on percussion, absent tactile fremitus, decreased breath sounds and absence of vocal transmission are the main clinical features of PE. Erect chest X-ray is more evident of PE in > 250 - 600 ml, lateral decubitus is sensitive in lesser volume and supine film is least sensitive.[12,13] Ultrasound (USG) of thorax detects PE amount as small 3-5 ml than X-ray detecting the fluid > 50ml. USG thorax can be used for minimal fluid assessment, thoracocentesis guidance,diagnosis and management. [14] Computed tomography (CT) of chest can help distinguish transudates and exudates and also PE and empyema.[15]Thoracocentesis should be performed in all patients in > 1 cm height of fluid on lateral decubitus, USG or CT, of unknown origin.[16] Pleural fluid analysis includes appreciation of appearance of fluid.[17]Transudates have white blood cell (WBC) counts below 1000 $mm^3$and most exudates have counts above 1000mm^3. WBC counts > 10,000 mm^3, most commonly occurs in parapneumonic, pancreatitis,TBand Dressler's syndrome.[18,19] In differential cell counts neutrophils predominate in acute inflammatory response with characteristic degeneration in pleural infection whereas lymphocytes predominate in PE in malignant diseases, TB and post coronary bypass graft.[18,20] In biochemical measurement proteins differentiate exudates from transudates but may not fulfill the Light's criteria in parapneumonic and malignant effusion where LDH has a better discriminatory value.[21,22]LDH, a reliable indicator of inflammation is used to separate transudate from exudate.[23] Low glucose (<60mg%) levels suggest parapneumonic, malignant, TB effusion and Rheumatoid disease.[24]Empyema is the presence of pus in the pleural cavity, where pleural fluid glucose < 40mg%, PH<7.0, positive gram staining and culture and LDH> three times of upper limit for serum LDH indicate bad prognostic sign.[25]TB is the commonest cause of PE and should be considered in differential diagnosis of all patients with exudative PE.[2,26,27] Characteristically, TB effusion have proteins > 5gm% and adenosine deaminase (ADA) levels >70 IU/L with sensitivity of 99% and specificity of 98% at 37 IU/L cut off value, and lymphocyte to neutrophil ratio (L:N) >0.75.

ADA are chiefly present in T-lymphocytes and the activity of ADA is found high where cellular activity is stimulated. ADA_2 chiefly found in monocytes contributes approximately 20% of total ADA activity.[28] Malignant pleural effusion is exudative and revealed malignant cells in PE where the patients fall into stage IV diseases.[29,30]Pleural biopsy is indicated in malignant PE if cytology is negative and thoracoscopy is not available.[31] PE develops with increased incidence in rheumatoid arthritis, systemic lupus erythematosus and other CTDs.[32,33]The incidenceof PE in Acquired Immune Deficiency Syndrome (AIDS) is 14.6% with different causes including opportunistic organisms and fungal infections leading to PE.[34,35] PE in AIDS is commonly associated with pulmonary TB. Viruses and atypical organisms may lead to development of moderate to large PE. Other diagnostics tests including flowcytometry, tumor markers, immunohistochemical and carcinoembryonic antigen (CEA) can be done in PE for specific diagnosis. Cartridge based nucleic acid amplification test (CBNAAT) or Gene-X-pert based polymerase chain reaction (PCR) assay can be done in PE for resistant TB.

II. MATERIALS AND METHODS

This cross-sectional, descriptive analytical study was conducted on patients of department of General
Medicine at Regional Hospital Solan in collaboration with Indira Gandhi Medical College and Hospital Shimla, Himachal Pradesh in a hilly northern part of India.

Study Design: Cross-sectional, descriptive analytical study.

Study Duration: July 2018 to June 2019.

Study Location and Subjects selection: Outdoor and admitted patients registered at Regional Hospital Solan catering rural and urban areas.

Sample size: 100 patients.

Sample size calculation: The study population was drawn using population size of Solan of 5,80,000 persons. Percentage frequency of tubercular pleural effusion was estimated, 62% ± 10% according to Parikh et al.[36] We assumed the confidence limits of

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10% and confidence level of 95%. The sample size actually estimated for this study was 91+10% using open epidemiological calculator version 3.01. We planned to include 100 patients.

Inclusion criteria

1. Patients, aged 18 years and above of both sexes with pleural effusion diagnosed clinically and radiographically and
2. Patients undergoing thoracocentesis, yielding minimal amount of fluid enough to carry out all tests for analysis were included in the study.

Exclusion criteria

1. Patients, aged <18 years, non consenting and seriously ill and
2. Patients with non-aspirable pleural fluid quantity estimated clinically or radiographically, were excluded from the study.

Procedure methodology

After taking approval from Institutional ethics committee, the patients were thoroughly evaluated for symptomology and laboratory investigations, and assessed for pleural effusion size clinically and radiographically (chest radiograph postero-anterior view or ultrasonography or CT of chest) and leveled broadly as mild (<one third), moderate (one third to two third) and massive (more than two third) on the basis of opacification of hemithorax. After taking informed consent, a diagnostic (therapeutic where indicated) thoracocentesis was then performed on all patients under aseptic conditions.Patients were positioned as recommended by R.W. Light[1] where the patient sits by the side of the bed with arms and head resting on one or more pillows on a bed side table with a foot stool placed below for foot rest and with the side containing the fluid towards the foot of the bed. Thoracocentesis was performed in the midaxillary line one interspace below the dull tactile fremitus or confirming the exact location radiographically in case of minimal fluid , necessitating ultrasound guided aspiration of fluid as well . The ideal interspace was selected 7th, 8th or 9thin midaxillary line or midway between posterior axillary and midline.3-way stopcock and 22 gauge needle were used for aspiration of pleural fluid and Abram´s needle for pleural biopsy, where indicated.Pleural fluid aspirated was sent appropriately for biochemical, cytological and bacteriological analysis.

Statistical analysis

Data of all patients were collected, entered into Microsoft excel spreadsheet and transferred to Epi info 7.1 software for statistical analysis. Continuous variables were expressed as means and standard deviations while categorical variables as proportions, percentage and 95% confidence interval (CI). Chi – square test (χ^2)for comparison of categorial variables and Student's ´t´ test for comparison of means were used. For association, p value < 0.05 was considered as statistically significant.

III. RESULTS

A total of 100 patients with PE attending outdoor and admitted in General Medicine department were studied over a period of one year for pleural fluid analysis. The patients ages ranged from 19 to 78 years with maximum 59 (59%) patients in middle age group between 20-40 years as compared to 46(46%) patients above 40 years. There were a total of 66 (66%) males and 34 (34%) females with male to female ratio of 1.9:1 (Table1). Maximum patients haled from rural (83%) than urban (17%) area.

Table 1: Age and sex distribution of patients.

Age (years)	No. of patients No (%)	Males No (%)	Females No(%)
18-20	5 (5%)	3 (3%)	2 (2%)
21-30	25 (25%)	18 (18%)	7 (7%)
31-40	24 (24%)	15 (15%)	9 (9%)
41-50	14 (14%)	9 (9%)	5 (5%)
51-60	17 (17%)	11 (11%)	6 (6%)
61-70	13 (13%)	9 (9%)	4 (4%)
71-80	2 (2%)	1 (1%)	1 (1%)
Total	100 (100%)	66(66%)	34(34%)

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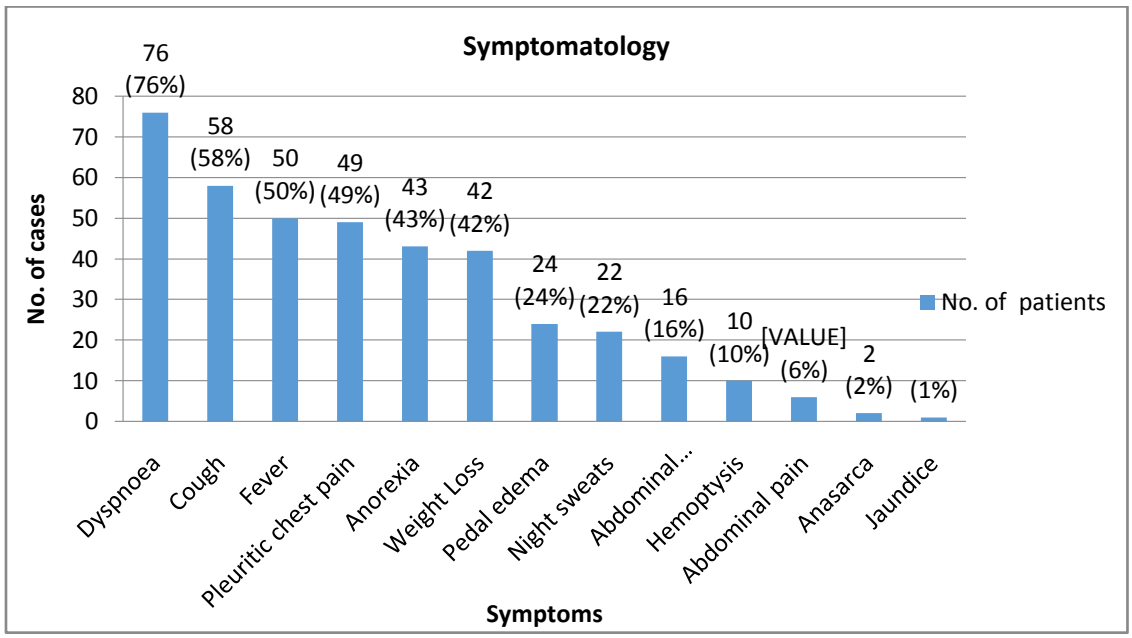

Figure 1: Frequency of symptoms in pleural effusion

Dyspnea (76%) was the most common symptom followed by cough (58%), fever (50%) and pleuritic chest pain (49%) in decreasing order (Figure 1). Diminished breath sound (82%) and reduced vocal resonance (70%) were the most sensitive examination maneuvers followed by reduced tactile fremitus (68%),asymmetric chest expansion (62%) and crackles (58%) on auscultation in decreasing order of sensitivity (Table 2).

Table 2: Sensitivity of physical examination maneuvers in pleural effusion.

Examination maneuvers	Pleural effusion		Sensitivity	Positive likelihood ratio (95% CI)
	Suggestive	Non-suggestive		
Asymmetric chest expansion	62	38	62	0.62
Dullness on percussion	54	46	54	0.54
Crackles	58	42	58	0.58
Diminished breath sounds	82	18	82	0.82
Pleural rub	2	98	2	0.02
Reduced tactile fremitus	68	32	68	0.68
Reduced vocal resonance	70	30	70	0.70

PE in the present study revealed varied etiology.Most of the effusions were tubercular (56%) followed by parapneumonic (16%) and CCF (12%), hepatic hydrothorax(7%), empyema(4%), malignancy(3%) and CTD(2%) in decreasing frequency of occurrence of PE(Table 3). In all, there were a total of 81(81%) patients of exudative and 19 (19%) patients of transudative PE. 51(51%) patients had moderate, 32 (32%) patients mild and 17 (17%) patients had massive PE.

Table 3: Etiology of pleural effusion

Diagnosis	No. of cases	Percentage (%)
Tubercular	56	56%
Parapneumonic	16	16%
Congestive cardiac failure	12	12%

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Hepatic hydrothorax	7	7%
Empyema	4	4%
Malignancy	3	3%
Connective tissue disorders	2	2%
Total	100	100%

Most of exudative tubercular and parapneumonic PE had moderate amount (38% and 9%) followed by mild amount (10% and 6%) and massive amount (8% and 1%) respectively.Of all cases 47% patients of TB had clear or straw colored PE,7% patients had turbid and only 2% patients had hemorrhagic PE. All the patients of empyema had turbid (3%) and hemorrhagic (1%) PE.All the patients of malignancy and CTD had clear or straw colored PE (Figure 2).

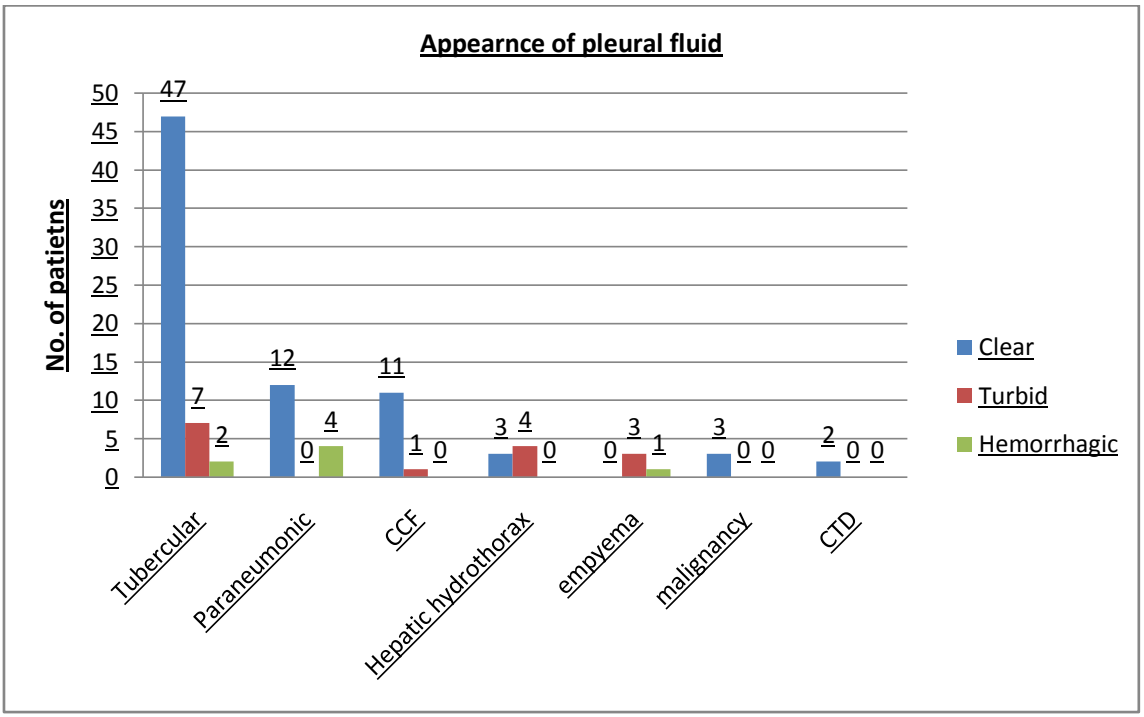

Figure 2: Appearance of pleural fluid. CCF, Congestive cardiac failure; CTD, Connective tissue disorders.

Maximum patients of tubercular and parapneumonic PE had proteins >3gm%; 53(94.6%) and 15(93.8%) respectively.All the patients 4(100%) with empyema had pleural fluid proteins> 3gm%.Most of the patients of PE in CCF and hepatic hydrothorax had pleural fluid proteins < 3gm%; 10 (83.3%) and 5(71.4%) respectively (Figure 3).

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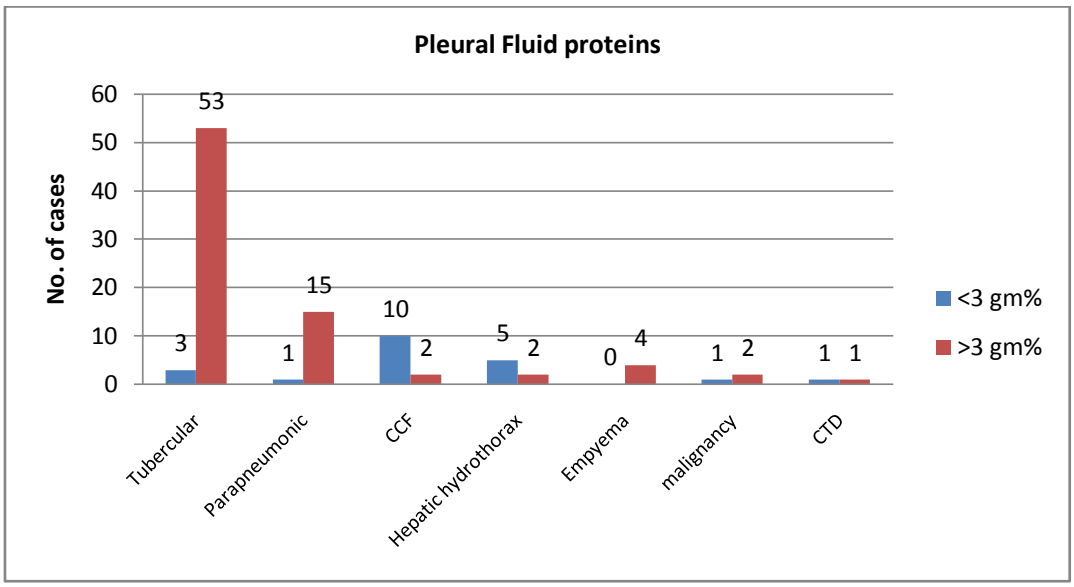

Figure3: Pleural fluid proteins. CCF, Congestive cardiac failure; CTD, Connective tissue disorders.

Pleural fluid LDH in TB and parapneumonic PE > 200 IU/L had frequency of 48% and 14% and < 200 IU/Lhad frequency of 8% and 2% respectively.Most of cases of PE in CCF and hepatic hydrothorax had LDH < 200 IU/L in 11 (11%) and 4 (4%) patients respectively.All the 4 (4%) patients with empyema had pleural fluid LDH > 200 IU/L (Figure 4).

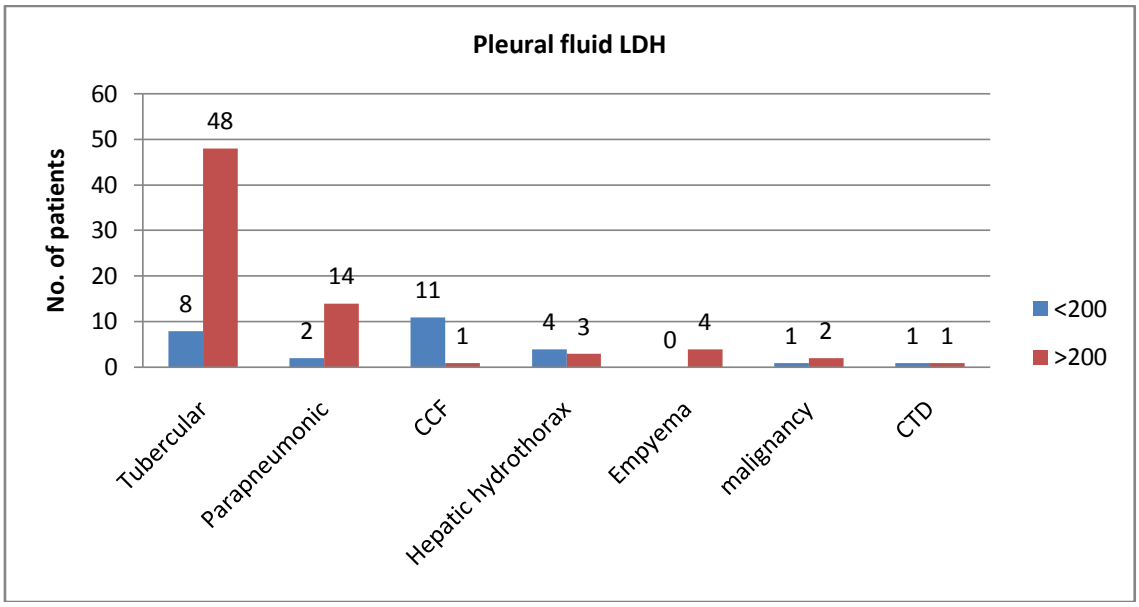

Figure 4: Pleural fluid lactate dehydrogenase(LDH). CCF, Congestive cardiac failure; CTD, Connective tissue disorders.

Most of the patients with TB 44(44%), parapneumonic and CCF 9(9%) each, and hepatic hydrothorax 6(6%) had pleural fluid glucose levels between 60-120mg%. 12(12%) patients in TB and 7(7%) patients in parapneumonic PE had glucose levels< 60mg%.All the 4 (4%) patients in empyema had blood glucose level <60mg% (Figure 5).

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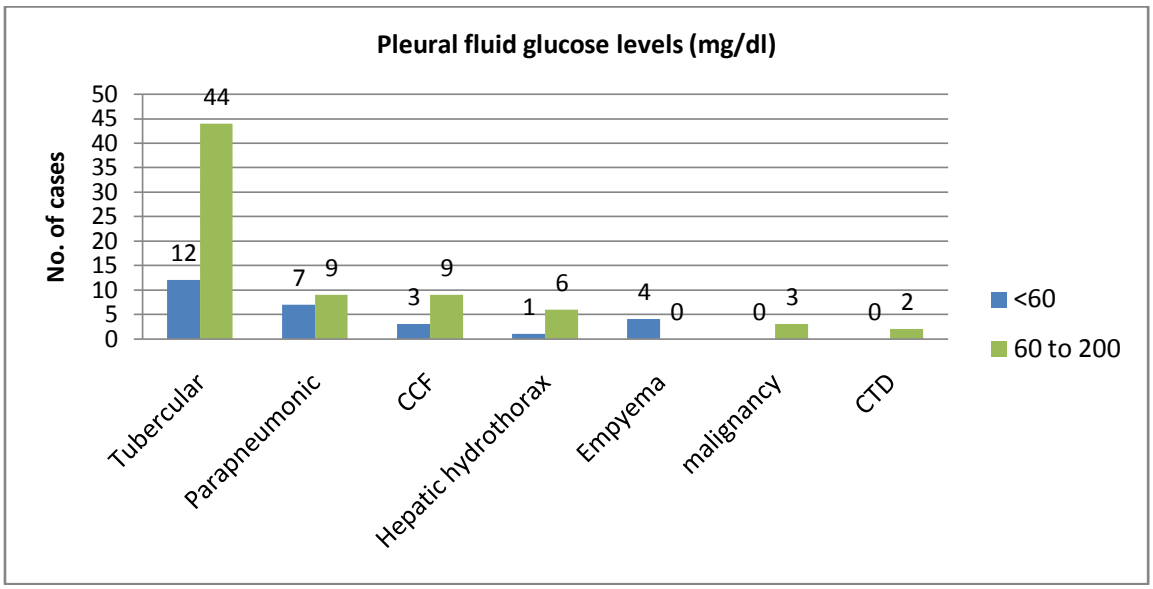

Figure 5: Pleural fluid glucose. CCF, Congestive cardiac failure; CTD, Connective tissue disorders.

44 (44%) patients in TB had pleural fluid ADA levels between 60-200 IU/L and 4 (4%) patients had > 200 IU/L. 7(7%) patients in each parapneumonic and CCF had ADA levels >200 IU/L. All the patients of empyema and CTD effusion had ADA levels < 60 IU/L (Figure 6).

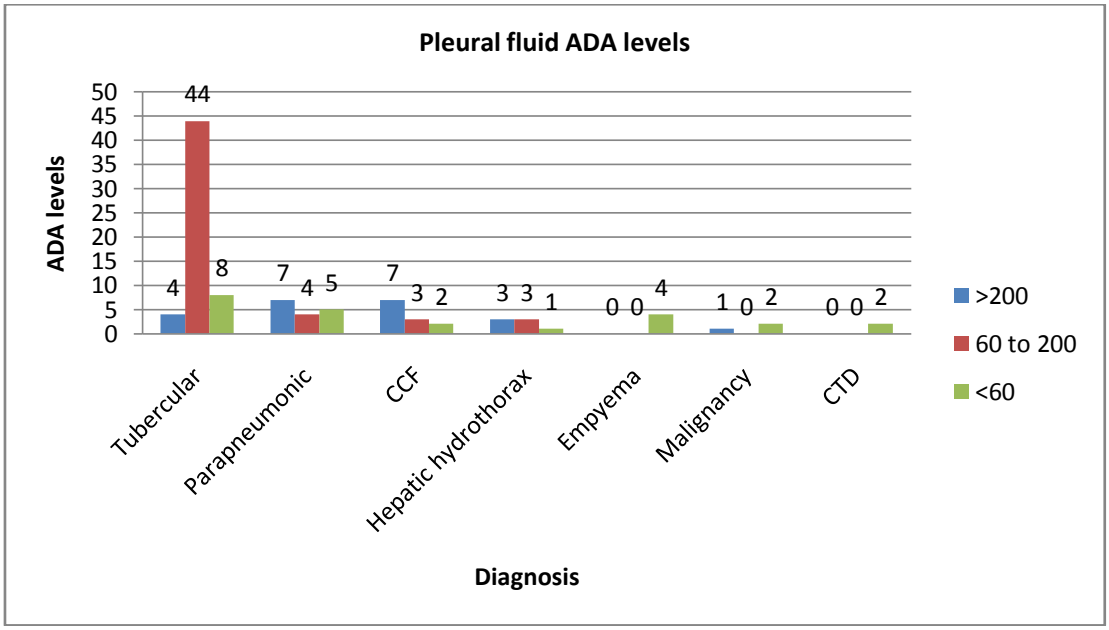

Figure 6: Pleural fluid Adenosine deaminase(ADA). CCF, Congestive cardiac failure; CTD, Connective tissue disorders.

40 (40%) patients in tubercular PE had WBC counts > 1000 mm^3, 14 (14%) patients, between 250-1000 mm^3 and 2 (2%) patients had < 250 mm^3.All the patients of CCF and parapneumonic PE had WBC counts between 250 mm^3- 1000 mm^3 and > 1000 mm^3. All the 4 (4%) patients with empyema had WBC counts>1000 mm^3.Tubercular PE revealed lymphocytic predominance whereas parapneumonic PE and empyema revealed neutrophilic predominance(Table 4).

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Table 4: White blood cell(WBC) counts in pleural effusion.

	Pleural fluid WBC_($x10^3$/dl)		
Diagnosis	**0-250**	**250-1000**	**>1000**
Tubercular	2(2%)	14(14%)	40(40%)
Parapneumonic	0(0%)	6(6%)	10(10%)
Congestive cardiac failure	0(0%)	9(9%)	3(3%)
Hepatic hydrothorax	1(1%)	2(2%)	4(4%)
Empyema	0(0%)	0(0%)	4(4%)
Malignancy	0(0%)	1(1%)	2(2%)
Connective tissue disorders	0(0%)	0(0%)	2(2%)
Total	3(3%)	32(32%)	65(65%)

81 (81%) cases of PE satisfied the modified Light's criteria and were grouped as exudative PE whereas remaining 19 (19%) were classified as transudative PE. Means and Standard deviation of the pleural fluid parameters were calculated for comparison by P value and 't' score. All the parameters except pleural fluid glucose have been found to have statistically significance difference between transudates and exudates (Table 5).

Table 5:consolidated parameters –statistical analysis.

Parameter	Transudate		Exudate		T score	P value
	Mean	Stdev	Mean	Stdev		
Pleural proteins	1.16	0.29	4.79	0.78	20.09	<0.001*
Pf/sr.protein ratio	0.61	0.07	0.38	0.06	14.94	<0.002*
Serum protein	1.93	0.58	13.09	3.04	15.87	<0.003*
Pleural fluid LDH	52.89	24.33	384.46	200.04	7.18	<0.004*
Pf/sr. LDH ratio	0.66	0.05	0.49	0.06	14.04	<0.005*
Serum LDH	34.89	15.84	188.77	104.72	6.38	<0.006*
Pf glucose	120.53	53.58	107.93	52.82	0.98	0.33
Pf ADA	241.74	113.08	103.94	108.97	4.97	<0.008*
WBC count	915.79	544.12	1432.35	714.17	2.96	<0.009*

*Significant; Pf/sr., Pleural fluid to serum; LDH, Lactate dehydrogenase; ADA, Adenosine deaminase; St dev, standard deviation.

Out of total 56 patients of tubercular PE, CBNAAT was positive in 43 (77%) patients and negative in 13 (23%) patients. The patients of pleural effusion in the study revealed clinic-etiological, radiological, biochemical, cytological and bacteriological correlations. None of the patients had pleural biopsy and bronchoscopy done.

IV. DISCUSSION

The present study was conducted over a period of one year recruiting 100 patients of PE in a Regional Hospital, Solan in collaboration with Indira Gandhi Medical College Shimla a tertiary care hospital in the state of Himachal Pradesh, catering both urban and rural area patients in a hill station in north India. TB has high prevalence in India, the most common cause of PE reported was tubercular followed by malignancy.[36,37] Therefore, we aimed to analyse the PE to find the aetiological cause of it to know the disease prevalence in our setup. In this study, the patients revealed the age-range from 19 to 78 years, and PE frequency of 59%, mostly in the age group between 20-40 years, more in males (66%) than females (34%) with male to female ratio of 1.9:1. These observations were similar to the studies from India, by Parikh et al[36] who studied 100 patients and reported PE in mostly in younger age group of 31-40 years (36%) and 40-50 years (28%) with a total (60%) of all patients,more common in males (68%) vs females (32%), and Gupta et al[37] who in a study of 1000 patients with age range (18-70 years) of PE from

north India reported most of cases (54%) in age group of 18-40 years, more in males (75%) vs female (25%). In the present study dyspnoea (76%) was the most common symptom followed by cough (58%), fever (50%) and pleuritic chest pain (49%). Parikh et al[36] reported chest pain (72%) the most common symptom followed by fever (62%), cough (61%), and dyspnoea (58%). In the present study, the physical examination maneuver with most sensitivity and positive likelihood ratio was diminished breath sounds (82%) followed by reduced vocal resonance (70%), reduced tactile fremitus (68%) and asymmetric chest expansion (62%) in predicting the case of PE. The findings of this study were similar to the findings of the study by Kalantri et al[38] who reported diminished breath sounds (88%) the most sensitive predictor of PE followed by reduced vocal resonance (76%) and asymmetric chest expansion (74%).In the present study, 78% of PE were clear or straw coloured, 15% turbid and 7% were haemorrhagic. 47% patients in tubercular PE had clear or straw coloured and 2% had haemorrhagic pleural fluid (Figure 2). In a similar study done by Khamar et al[39], 74% of the cases had clear or straw coloured pleural fluid followed by haemorrhagic (16%) and turbid (10%). Most of the cases in our study were of moderate sized PE (51%) and 17% were massive, consistent with the findings of other studies.[36-38]

In the present study, 81(81%) cases of PE satisfied the modified Light's criteria and were classified as exudative and the remaining 19(19%) as transudative as compared to a study of a 1000 patients by Gupta et al [37] where 89.8% cases of PE were exudative and 10.2% cases were transudative. Most of the effusions in our study, were of tubercular (56%) followed by parapneumonic (16%) and CCF (12%) whereas malignant PE was reported only in 3% cases (Table3). These findings closely matched the findings of the studies from India, by Parikh et al[36] who reported 62% cases of tubercular, 10% cases of parapneumonic and 5% cases of CCF, and by Gupta et al[37] who reported 69.5% cases of tubercular and 16% cases of malignant PE. However, the study of 3,000 thoracocentesis done by Porcel et al[40] in Spain, reported malignancy (27%) the most common etiology in causing PE followed by CCF (21%), parapneumonic (19%) and tubercular (9%)which revealed the diseases prevalence there. The biochemical parameters, proteins, LDH, glucose and ADA differentiated the exudative and transudative pleural fluid and correlated with etiological causes of PE as also reported by several other studies.[36-40] Similarly, exudative PE, in tubercular and parapneumonic PE revealed WBC counts with lymphocytic and neutrophilic predominance respectively. Consolidated parameters (Table 5) revealed strong statistical significance in PE analysis. Our study revealed clinico-etiological, biochemical, cytological, bacteriological, and radiological correlations of PE, defining the diseases prevalence.

V. CONCLUSION

Most of the PE was exudative and TB was the commonest cause of PE, found mainly in the patients from rural than urban area. TB is the most prevalent disease in India, therefore, all the patients with PE should be meticulously investigated for TB for early case detection and treatment, hence prevention of incidence and prevalence of TB.

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Conflict of Interest: None declared.
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

[1]. Light RW. Pleural diseases. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2013.
[2]. Chinchkar NJ, Talwar D, Jain SK. A stepwise approach to the etiologic diagnosis of pleural effusion in respiratory intensive care unit and short-term evaluation of treatment. Lung India 2015;32(2):107.
[3]. Diaz-Guzman E, Budev MM. Accuracy of the physical examination in evaluating pleural effusion. Cleve Clin J Med 2008 ;75(4):297–303.
[4]. Collins TR, Sahn SA. Thoracocentesis. Clinical value, complications, technical problems, and patient experience. Chest 1987;91(6):817–22.
[5]. Finley DJ, Rusch VW. Anatomy of the pleura. Thorac Surg Clin. 2011;21(2):157–63.
[6]. Light RW. Pleural Effusion. N Engl J Med 2002;346(25):1971–7.
[7]. D'Agostino HP, Edens MA. Physiology, Pleural Fluid. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2019 [cited 2019 Jun 23]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK513353/
[8]. Light RW. The Light criteria: the beginning and why they are useful 40 years later. Clin Chest Med 2013 ;34(1):21–6.
[9]. Maskell NA, Butland RJA, 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: 8-17.
[10]. Roth BJ, O'Meara TF, Cragun WH. The serum-effusion albumin gradient in the evaluation of pleural effusions. Chest 1990;98(3):546–9.
[11]. Romero S, Candela A, Martín C, Hernández L, Trigo C, Gil J. Evaluation of different criteria for the separation of pleural transudates from exudates. Chest 1993;104(2):399–404.
[12]. Konik E, Schirger J. Chest X-ray of a patient with history of pleural effusion. BMJ Case Rep. 2017 Jun 18;2017.
[13]. Emamian SA, Kaasbol MA, Olsen JF, Pedersen JF. Accuracy of the diagnosis of pleural effusion on supine chest X-ray. Eur Radiol 1997;7(1):57–60.
[14]. Soni NJ, Franco R, Velez MI, Schnobrich D, Dancel R, Restrepo MI, et al. Ultrasound in the Diagnosis & Management of Pleural Effusions. J Hosp Med 2015;10(12):811–6.
[15]. Çullu N, Kalemci S, Karakaş Ö, Eser İ, Yalçın F, Boyacı FN, et al. Efficacy of CT in diagnosis of transudates and exudates in patients with pleural effusion. Diagn IntervRadiol 2014;20(2):116–20.
[16]. Porcel JM, Light RW. Diagnostic Approach to Pleural Effusion in Adults. Am Fam Physician. 2006;73(7):1211–20.
[17]. Villena V, López-Encuentra A, García-Luján R, Echave-Sustaeta J, Martínez CJ. Clinical implications of appearance of pleural fluid at thoracentesis. Chest 2004;125(1):156–9.
[18]. Conner BD, Lee YCG, Branca P, Rogers JT, Rodriguez RM, Light RW. Variations in pleural fluid WBC count and differential counts with different sample containers and different methods. Chest 2003;123(4):1181–7.
[19]. Liam CK, Lim KH, Wong CM. Differences in pleural fluid characteristics, white cell count and biochemistry of tuberculous and malignant pleural effusions. Med J Malaysia 2000;55(1):21–8.
[20]. Light RW. Cells in Pleural Fluid: Their Value in Differential Diagnosis. Arch Intern Med 1973; 132(6):854-60.
[21]. Tarn AC, Lapworth R. Biochemical analysis of pleural fluid: what should we measure? Ann Clin Biochem 2001 ;38:311–22.
[22]. Rungta R, Jha RK. Comparative analysis of pleural fluid biochemical parameters with cholesterol to differentiate transudates from exudates.J Assoc Chest Physicians 2013;1: 54-7.
[23]. Saint-Rémy P, Buret J, Radermecker M. Significance of lactate dehydrogenases in pleural effusions. Rev Pneumol Clin 1986;42(2):74–81.
[24]. Vorster MJ, Allwood BW, Diacon AH, Koegelenberg CFN. Tuberculous pleural effusions: advances and controversies. J Thorac Dis 2015 ;7(6):981–91.
[25]. Shebl E, Paul M. Parapneumonic Pleural Effusions And Empyema Thoracis. In: StatPearls[Internet].Treasure Island (FL): StatPearls Publishing; 2019[cited 2019 june 23]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK534297/
[26]. Ferrer Sancho J. Pleural tuberculosis: incidence, pathogenesis, diagnosis, and treatment. Curr Opin Pulm Med 1996;2(4):327–34.
[27]. Bansal P, Bansal,Kansal HM,Goyal S, Bansal, P. Tuberculous Pleural Effusion: A study on 250 patients. J Med Sci Res 2010;1:46–9.
[28]. Verma SK, Dubey AL, Singh PA, Tewerson SL, Sharma D. Adenosine Deaminase (ADA) Level in Tubercular Pleural Effusion. Lung India Off Organ Indian Chest Soc 2008;25(3):109–10.
[29]. Porcel JM. Malignant pleural effusions because of lung cancer. Curr Opin Pulm Med.2016;22(:356–61.
[30]. Desai NR, Lee HJ. Diagnosis and management of malignant pleural effusions: state of the art in 2017. J Thorac Dis. 2017 ;9(10):1111–22.
[31]. Bhattacharya S, Bairagya TD, Das A, Mandal A, Das SK. Closed Pleural Biopsy is Still Useful in the Evaluation of Malignant Pleural Effusion. J Lab Physicians 2012;4(1):35–8.
[32]. Walker WC, Wright V. Rheumatoid pleuritis. Ann Rheum Dis. 1967 ;26(6):467–74.
[33]. Choi BY, Yoon MJ, Shin K, Lee YJ, Song YW. Characteristics of pleural effusions in systemic lupus erythematosus: differential diagnosis of lupus pleuritis. Lupus 2015;24(3):321–6.
[34]. Bhattacharya AK. Pleural effusion in AIDS. Lung India 2005;22(3):101-4.
[35]. Miller RF, Howling SJ, Reid AJ, Shaw PJ. Pleural effusions in patients with AIDS. Sex Transm Infect 2000;76(2):122–5.

[36]. Parikh P, Odhwani J, Ganagajalia C. Study of 100 cases of pleural effusion with reference to diagnostic approach. Int J Adv Med 2016;3(2):328-31.
[37]. Gupta R, Gupta A, Ilyas M. Spectrum of pleural effusion etiology revisited in 18–70 years of age group: A tertiary care center-based study of 1000 patients.CHRISMED J Health Res 2018; 5(2): 110-3.
[38]. Kalantri S, Joshi R, Lokhande T, Singh A, Morgan M, Colford JM, et al. Accuracy and reliability of physical signs in the diagnosis of pleural effusion. Respir Med. 2007;101(3):431–8.
[39]. Khamar ND, Gohil PR, Thacker RN, Gediya US. A clinical study of pleural effusion and its radiological, biochemical, bacteriological and cytological correlation. J Integr Health Sci. 2017 ;5(1):8.
[40]. Porcel JM, Esquerda A, Vives M, Bielsa S. Etiology of pleural effusions: analysis of more than 3, 000 consecutive thoracenteses. Arch Bronconeumol. 2014 ;50(5):161–5.