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Pathology

ETIOLOGICAL SPECTRUM OF EXUDATIVE PLEURAL EFFUSION AT TERTIARY CARE CENTRE

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ABSTRACT **Background:** A pleural effusion is abnormal collection of fluid in pleural cavity that can result from excess fluid formation or decreased absorption. This prospective study was done to find out the etiology of exudative pleural effusion at Jhalawar region and correlate the clinical diagnosis with cytological biochemical and microbiological parameters and its incidence with respect to age and sex. **Methodology** The prospective study was carried out at pathology department in Jhalawar medical college and SRG and SHKBM hospital Rajasthan in year 2020 to 2021. Detailed history of patients, physical examination, cytological biochemical and microbiological correlation was done. **Results:** The prospective study of 180 patients with exudative pleural effusion majority of patients lie within the age group of 31 to 40 followed by 41 to 50 years and more than two third were men. The three most common cause of exudative effusion in this study were tuberculosis, malignancy, synpneumonic effusions. The most common symptom encountered by our TB patients were fever (100%) followed by cough (70.56%) and chest pain (46.67%). Pleural fluid cytology was performed in all the patients with exudative effusions. Among malignant effusion only 85.7% of the effusion showed malignant cells on cytological examination. A pleural fluid ADA above 70IU/L is diagnostic of tuberculosis it has to be considered if the pleural fluid ADA lies between 40 IU/L and 70 IU/L. An ADA level less than 40IU/L probably rules out pleural tuberculosis. **Conclusion** The most common cause of exudative pleural effusion still remains tuberculosis in India. Majority of patient affected are male. Pleural fluid analysis with biochemical and microbiological investigation together with detailed clinical history of patient play an important role to diagnose underlying etiology.

KEYWORDS : Adenosine deaminase, synpneumonic, Tuberculosis.

INTRODUCTION

A pleural effusion is abnormal collection of fluid in pleural cavity that can result from excess fluid formation or decreased absorption. (Dr. Rishi Kumar Sharma) It is one of the major leading causes of pulmonary morbidity and mortality.

Pleural effusion can be classified as exudative and transudative on the basis of Modified Light's criteria. According to these criteria, all exudates have at least one of the following while transudates have none.

Ratio of pleural fluid protein to serum protein >0.5.

Ratio of pleural fluid lactate dehydrogenase (LDH) to serum LDH >0.6.

Pleural fluid LDH > 2/3 of the upper limit of serum LDH.[1]. (G Selvamani)

Symptoms (Adithya Cattamanchi html)

Some people with pleural effusion do not present with any symptoms. They may have symptoms of many underlying disease, such as a cough or fever.

Depending on the cause, a person with pleural effusion may also have:

- Chest pain
- Cough
- Fever
- Shortness of breath
- Hemoptysis

Physiology and pathophysiology (Berthold Jany)

Both the visceral and the parietal pleura play an important role in maintaining the fluid homeostasis in the pleural space. The mean rate of both the production and the absorption of pleural fluid is normally 0.2 mL/kg/hr, which shows that the entire volume of the pleural fluid normally turns over within one hour [(2)]. The parietal side of the pleura that accounts for most of the production of pleural fluid, and as well as its resorption. Pleural effusion due to left-heart failure is one of the exception to this rule, in which the fluid comes from the visceral pleura. The volume of the pleural fluid is determined by the balance of the hydrostatic and oncotic pressure differences that is present between the systemic and pulmonary circulation and the pleural space [(2).] Pleural fluid is resorbed via lymphatic vessels in the parietal pleura. The flow in these vessels can be increased by a factor of 20 if more than the normal amount of pleural fluid is produced; thus, the pleural lymphatic resorbing system has a large reserve capacity. In health, the production and resorption of pleural fluid are usually at equilibrium. A pleural effusion represents a unbalance of this equilibrium, probably because of both increased production and decreased resorption. Low oncotic pressure (e.g., in hypoalbuminemia), elevated pulmonary capillary pressure, increased permeability, lymphatic obstruction, and diminished negative intrapleural pressure are all pathophysiological components that lead to the clinically relevant and discriminating features of a pleural effusion—transudate vs. exudate.

Most common cause of Pleural effusion is (Maulik P. Saliya)

- bacterial pneumoni
- tuberculosi
- dengue
- heart failure
- nephrotic syndrome
- diaphragmatic abscess
- rheumatic and rheumatoid diseases
- uremia
- pancreatitis
- Hemothorax
- Trauma
- Surgery
- Cirrhosis
- Ascites

Analysis of pleural fluid can have an important contribution for investigation of patients with pleural effusion. [4] Cytological examination not only helps for diagnosing cancer but also for staging and prognosis of underlying diseases. [5] Levels of adenosine deaminase (ADA) are particularly very useful in areas where the prevalence of tuberculosis is high. [6] Closed pleural biopsy gives the highest diagnostic yield in cases of pleural tuberculosis and malignancy, the two most important causes of exudative pleural effusion. (Biswajit Biswas)

Aims and Objectives

1. To know the etiology of exudative pleural effusion at tertiary care centre.
2. To correlate clinical diagnosis with cytological biochemical and microbiological parameters.
3. To compare the incidence of exudative pleural effusion with respect to age and sex.

Materials and Methods

1. Study design

The prospective, observational study was carried out in the Department of Pathology in Jhalawar Medical college, SRG hospital and SHKBM hospital over a period of 1 year.

2.Source of data The study comprised of pleural fluid sample received in cytopathology and central lab.

3.Inclusion criteria

1.All pleural fluid sample that was exudative in nature were included in the study with reference to all age and sex.
2. Patient who had given consent.

4.Exclusion criteria

1.All pleural fluid sample that are transudative in nature were excluded
2.Those patients who did not give consent.

5. Methodology

a. After obtaining approval and clearance from the ethical committee, only those patients meeting the inclusion and exclusion criteria were enrolled for the study.

b. Informed consent was obtained from each participant.

c. After enrolment the following parameters was considered and measured in all patient's: name age, gender, occupation, address, General physical examination systemic examination.

6.Study design

This study was prospective study from March 2020 to march 2021.This study was carried out in department of pathology, Jhalawar medical college, Jhalawar.

7.Sample size: Case available during the period of one year were taken for study.

OBSERVATIONS AND RESULTS

TABLE-1: DISTRIBUTION OF PATIENTS ACCORDING TO AGE GROUP

AGE GROUP	FREQUENCY	PERCENT
<21	13	7.2
21-30	32	17.8
31-40	37	20.6
41-50	36	20
51-60	28	15.6
61-70	25	13.9
71-80	8	4.4
81-90	1	0.6
TOTAL	180	100

In the above table, majority of 37(20.6%) patients were in the age group between 31-40 years and the remaining 36(20%) were in the age group 41-50 years.

TABLE-2: DISTRIBUTION OF PATIENTS ACCORDING TO GENDER

GENDER	FREQUENCY	PERCENT
FEMALE	40	22.2
MALE	140	77.8
TOTAL	180	100

In this study, majority of 140(77.8%) patients were male followed by 40(22.2%) of female.

TABLE-3: DISTRIBUTION OF PATIENTS ACCORDING TO ETIOLOGY

ETIOLOGY	FREQUENCY	PERCENT
DEFINITE TB	44	24.4
PROBABLE TB	89	49.4
MALIGNANCY	14	7.8
SYNPNEUMONIC EFFUSION	19	10.6
EMPYEMA	8	4.4
OTHERS	2	1.1
UNKNOWN	4	2.2
TOTAL	180	100

In the above table, majority of 89(49.4%) patients had probable TB and the remaining had other etiology.

TABLE-4: COMPARISON OF PATIENTS PLEURAL LDH/SERUM LDH RATIO AND ETIOLOGY

PLEURAL LDH/SERUM LDH RATIO	ETIOLOGY							TOTAL
	DEFINITE TB	PROBABLE TB	MALIGNANT EFFUSION	SYNPNEUMONIC EFFUSION	EMPYEMA	OTHERS	UNKNOWN	
0.6-1.0	6 (13.6%)	11 (12.4%)	0	0	0	0	0	17 (9.4%)
1.0-2.0	14 (31.8%)	48 (53.9%)	10 (71.4%)	9 (47.4%)	0	0	2 (50%)	83 (46.1%)
>2.0	24 (54.5%)	30 (33.7%)	4 (28.6%)	10 (52.6%)	8 (100%)		2 (50%)	80 (44.4%)
TOTAL	44	89	14	19	8	2	4	180
CHI-SQUARE VALUE=27.13; P-VALUE=0.007; SIGNIFICANT								

In the above table, it observed that there was a significant association between pleural LDH/serum LDH ratio and etiology with p-value<0.005.

TABLE-5: COMPARISON OF PATIENTS ADA (IU/L) AND ETIOLOGY

ADA (IU/L)	DEFINITE TB	PROBABLE TB	MALIGNANT EFFUSION	SYNPNEUMONIC EFFUSI	EMPYEMA	OTHERS	UNKNOWN	TOTAL
<30	0	0	0	0	8(100%)	2(100%)	.	10 (5.6%)
30-40	2(4.5%)	21 (23.6)	12 (85.7%)	14 (73.7%)	0	0	4(100%)	45 (35%)
40-70	6(13.6%)	34 (38.2)	0		0	0	0	32 (25%)
>70	34(77.3%)	34 (38.2%)	2 (14.3%)	0	0	0	0	70 (38.9%)
UD	2(4.5%)	0	0	0	0	0	0	2 (1.1%)
TOTAL	44	89	4	19	8	2	4	180
CHI-SQUARE VALUE=252.5; P-VALUE=0.001; SIGNIFICANT								

In the above table, it observed that there was a significant association between ADA (IU/L) and etiology with p-value<0.005.

Discussion

Age and sex

In the prospective study of 180 patients with exudative pleural effusion majority of patients lie within the age group of 31 to 40 followed by 41 to 50 years and more than two third were men. The three most common cause of exudative effusion in this study were tuberculosis , malignancy , synpneumonic effusions and empyema. The patient with tuberculosis were younger than those patient who had malignancy Their mean age was 36 years, consistent with Luis Valdes et al (34years)[7] and S.K.Sharma et al (33 years) [8]. Earlier studies that was done in United States by Epstein et al 55 and Aho K et al. [9] showed a mean age of 54 and 28 years respectively.

Malignant effusions in this study were seen in older age 50 to 70 years group (mean 64yrs). This is older than that reported by Sharma et al (mean age 47 years), but similar to that of reports from the West (65 years) [7]. It is how ever well known that Indian patients with malignancy

are 15 years younger as compared to the West as seen by Pathak et al[10]. Incidence

The commonest exudative effusion in this study was tuberculosis (probable and definite 73.8%) followed by malignant effusion (7.8%) and synpneumonic effusion (10.6%) and empyema. (4.4%) . In India effusion caused by tuberculosis is the commonest cause of all exudative effusions. This is similar to the observation in another study from India by Maldhure et al[3] where they showed that the tubercular effusions constitute 66% of the effusions, malignancy 15%, and parapneumonic effusion 4.8%.

This observation is different from that of the West where the incidence of parapneumonic effusion and malignant effusion are much higher compared than that of tubercular effusion. This is consistent with the fact that India has a very high prevalence of tuberculosis in the general population even after implementing various strategies to get a control over this disease.

ADA

As per the literature pleural fluid adenosine deaminase (ADA) has got a good discriminative value in differentiating tuberculous effusions from malignant effusion. Although a pleural fluid ADA above 70IU/L is diagnostic of tuberculosis[13] it has to be considered if the pleural fluid ADA lies between 40 IU/L and 70 IU/L. An ADA level less than 40IU/L probably rules out pleural tuberculosis. But different authors have used different cut off levels for pleural fluid ADA that is ranging between 33 IU/L to 50 IU/L.[14,15,16,17,18] In our study out of 24.4% patients with definite tuberculosis pleural fluid 34 (38.2%) of them had a level more than 40IU/L but [13] .6% showed a level of less than 40IU/L. Though studies done in the West demonstrate pleural fluid ADA more than 70 IU/L (Valdes et al[19] and Burgess et al[20]). But also significant percent of patients with different diagnosis had a pleural fluid ADA less than 30IU/L. The mean ADA were high in the 2 Indian studies done by Rajendra Prasad et al[21], and Gilhotra et al[22] with the mean ADA level ranging between 76.8±23.8 IU/L - 95.8±57.5 IU/L.

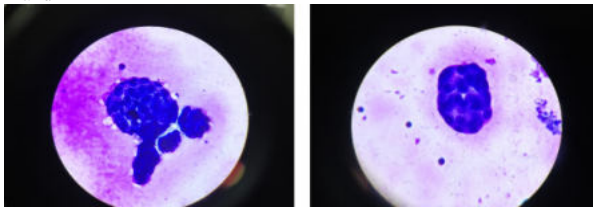
ADA level (> 30IU/L) does not establish TB but helps rule out malignancy as none of our malignant effusions had a level greater than 30.

Cytology

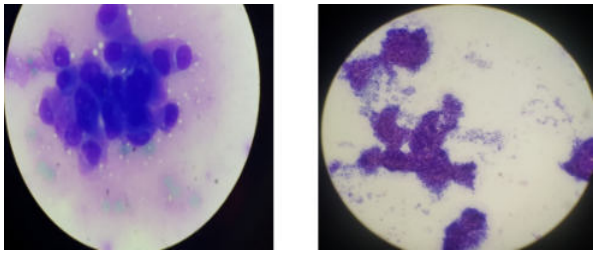
Pleural fluid cytology was performed in all the patients with exudative effusions. Among malignant effusion only 85.7% of the effusion showed malignant cells on cytological examination. In other studies the percentage demonstrating malignant cells ranged from 40% to 87%[79] in the literature cytology has a more sensitive test to diagnose malignancy when compared to biopsy. The yield increases with the number of samples examined and reaches a maximum (100%) with 3 samples.

Among the 2 patients who were classified as “unknown”, 2 of them were lost to follow up.

A and B



C and D



Photomicrograph A and B showing Reactive mesothelial cells and C and D showing Malignant pleural effusion.

CONCLUSION

Tubercular effusion remains the most common etiology of all exudative effusions in our study It commonly involves the young and is associated with fever and cough as the most common presenting symptoms.

Malignant effusions were usually seen in older age group with fever cough and breathlessness as common symptoms.

Massive effusion with hemorrhagic pleural fluid is commonly seen in malignant effusion.

Pleural fluid eosinophilia is not associated with either malignancy or pulmonary tuberculosis

Pleural fluid, with low glucose (<60 mg/dl) was seen predominantly in parapneumonic effusions and empyemas. They were not associated with TB or malignancy.

A pleural fluid ADA more than 40 IU/L increases the chances of a tubercular effusion while a value below 30 IU/L rules out tuberculosis.

Pleural fluid analysis with biochemical and microbiological investigation together with detailed clinical history of patient play an important role to diagnose underlying etiology.

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