

## A Study of Aetiopathological Profile of Pleural Fluid

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### Abstract

### Original Research Article

The aspiration of pleural fluid is a bedside procedure. The routine, microscopic and cytological examinations of pleural fluid have been an important diagnostic value to find out the cause of pleural effusion. The routine examination can help in differentiation of transudative and exudative fluid, microscopic examination, culture sensitivity and PCR testing can help to identify microbiological organism and cytological examination helps in the diagnosis and typing of malignancy in pleural fluid. The present study includes 300 cases of pleural effusion. The aspiration of pleural fluid was done with aseptic precautions and fluid was submitted for routine and microscopy, cytological examination and ADA estimation. The transudative type of fluid detected in 71(23.7%) cases and exudative fluid detected in 229(76.3%) cases. The inflammatory fluid in 178(77.7%) cases and malignancy in 40(17.5%) cases were detected and 11(4.8%) cases were suspicious of malignancy. Adenocarcinoma in male and carcinoma is commonest cause on cytological study in 45 cases (19.6%). In case of malignant pleural fluid different cytomorphological features along with clinical and radiological image study help to identify type of malignancy in lungs and pleura as well as extra thoracic causes of pleural effusion. The type of malignant lesion can be confirmed by histopathology after surgery or by various available biopsy techniques like bronchoscopic and direct CT guided lung biopsy. ADA level in body fluids is 93.5% specific and 95.9% sensitive for diagnosis of tuberculous pleural fluid and positive predictive value was 95.9% and negative predictive value was 92.1%. ADA level more than 40 IU/ML is diagnostic of tuberculous etiology of pleural fluid.

**Keywords:** Pleural effusion Pleural fluid Cytology ADA.

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## INTRODUCTION

Localized, breath holding and sharp chest pain is a manifestation of pleuritis and it is followed by pleural effusion. Pleural effusion is due to numerous causes [1] Pleural effusion paracentesis by needle aspiration, introduction of drainage catheter or intercostal drainage device is a bedside procedure. The aspirated pleural fluid has been sent for different investigations due to its diagnostic value. The study has been conducted to assess different laboratory tests of pleural fluid and its value in etiology of the pleural and lung disease. The pleural fluid examination includes gross examination, routine and microscopic examination with different stains, ADA estimation cytological examination and immune-histological study. The routine examination is helpful in differentiate transudative fluid from exudative fluid while microscopic examination is important for detection of infective etiology while ADA estimation and cytological examination is useful for diagnosis of tuberculous and malignancy respectively. The study is organized to evaluate the examination of pleural fluid

and its etiological, pathological and clinical correlations.

## MATERIAL AND METHODS

Pleural effusion is diagnosed by correlating clinical, X-ray chest (PA), ultrasonogram of thorax, CT thorax and laboratory methods were used to differentiate malignant, tuberculous and others causes. In the present study the total 300 cases of pleural fluids were studied from indoor patients of tertiary care hospital Jamnagar, Gujarat. The routine, microscopic and sensitivity cytological examination was done in Department of Pathology in tertiary care hospital. All patients underwent abdominal paracentesis under aseptic conditions using 18 gauge needles. The total 30 ml of pleural fluid were obtained for laboratory tests and cytological examination. The fluid specimen was examined within 2 hours of its withdrawal but on delay processing, the specimens were refrigerated. The routine examination of pleural fluid includes quantity of fluid, its appearance correlated with its color clear yellow-transudate, milky white or hemorrhagic and

exudative fluid. Its turbidity was observed as in transudate is clear fluid and in the exudates the presence of turbidity due is to presence protein. The protein was measured by biuret method. The transudate has <3.0g% of total protein. In exudative fluid has >3.0g% of total protein. The glucose was measured by glucose-oxidase-peroxidase method. In the pleural fluid the cell count was done in automated cell counter. Cytological examination: The smears were prepared from the sediment on to glass slide by a thin cotton swab applicator stick and immediately fixed in 95% ethyl alcohol, when the pleural fluid sample was rich in RBC's saline rehydration technique was used. In the present study, the slides were stained by Haematoxyline and Eosin (H & E), Periodic Acid Schiff (PAS), Mucicarmine, and Papanicolaou(PAP) stain and were studied. In transudate, the smear showed less cellularity,

few inflammatory cells and absence of malignant cells. In 1749xudates, smear of malignancy and inflammation showed high cellularity with malignant cells and inflammatory cells respectively. In tuberculosis, mainly chronic inflammatory cells like lymphocytes and groups of epithelioid cells were seen. In malignancy high cellularity and presence of malignant cells having large pleomorphic nuclei and increase nuclear / cytoplasmic ratio were seen, cells in groups or clusters were seen. The various cytomorphological criteria were used for diagnosis and type of neoplasm and for determining the primary site of tumor. Technique of ADA estimation: The spectrophotometric method or the sensitive colorimetric method of Galanti and Guisti were used. The present study ADA values were collected from patients' data and calculation done as under.

**Table-1: The statistical analysis method for sensitivity and specificity of ADA estimation in pleural fluid**

Test Results	Disease Present	Disease Absent
Test Positive	a	b
Test Negative	c	d

a = True Positive b = False Positive c = False Negative d = True Negative

$$\text{Sensitivity} = \frac{a}{a + c} \times 100 \quad \text{Specificity} = \frac{b}{b + d} \times 100$$

$$\text{Predictive value of positive test} = \frac{a}{a + b} \times 100$$

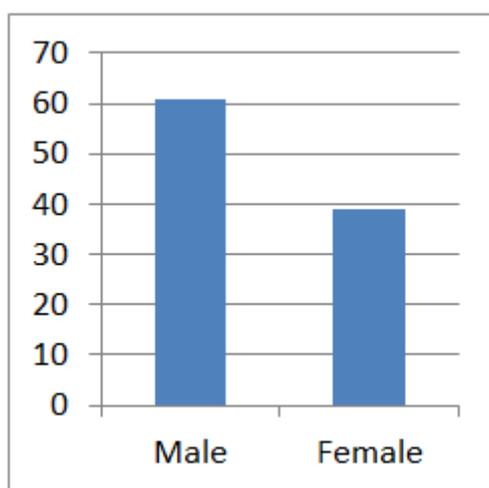
$$\text{Predictive value of negative test} = \frac{d}{c + d} \times 100$$

Sensitivity: Defined as ability of a test to detect disease when it is present true positive.

Specificity: Defined as ability of a test to exclude disease when it is not present

Cut –off: It is a point between disease and normality. Data analysis was done using Microsoft excel ver.2007 and SPSS ver. 12.

## RESULTS



**Chart-1: The gender incidence of pleural fluid (n = 300)**

Chart 1 show that out of total 300 cases (100%) of pleural fluid, male 219(61%) were

predominantly affected as compared to female71 (39%).

**Table-1: The age incidences of the pleural fluid cases**

Sr. No.	Age of patient (Yrs)	Pleural fluid cases (%)
1.	00-10	13(4.3%)
2.	11-20	25(8.3%)
3.	21-30	19(6.3%)
4.	31-40	35(11.6%)
5.	41-50	70(23.3%)
6.	51-60	111(37%)
7.	61 onwards	27(9%)
TOTAL		300(100%)

Table 1 show that maximum cases of pleural effusion were recorded in 5<sup>th</sup> and 6<sup>th</sup> decade of life.

**Table-2: The side distribution of the pleural fluid distribution**

Side of pleural effusion	Cases	Percentage
Right side	124	41.3%
Left side	74	24.7%
Bilateral	102	34%
Total	300	100%

Table 2 shows most common site of pleural effusion is right side(41.3%)as compared to left side(24.7%) and bilateral(34%). As right bronchus is straight, more in line with main bronchus as compared to left bronchus and also right bronchus is more wide

than left, so most of the infection affect right lung. In present study 135(45%) cases out of 300 cases of pleural effusion were due to infectious etiology so right side pleural effusion was common.

**Table-3: The naked eye examination of pleural fluid**

Sr. No.	Gross examination	Pleural fluid cases (%)
1.	Serous	133 (44.3%)
2.	Turbid	92 (30.7%)
3.	Purulent	14 (4.7%)
4.	Hemorrhagic	61 (20.3%)
Total		300(100%)

Table 3 shows that out of total 300 cases of pleural fluid 133(44.3%) were serous, 92(30.7%) were turbid, 14(4.7%) were pleurulent and 61(20.3%) were hemorrhagic. Serous fluids were found to be

transudative in most of the cases but some were turnout exudative. While turbid fluids were suggestive of exudates and hemorrhagic fluid almost shows positive for malignant fluid.

**Table-4: The routine examination of pleural fluid**

Sr. No.	Routine examination(transudate/exudate)	No. of cases
1.	Transudate (Protein<3.0g/dl)	71(23.7%)
2.	Exudate (Protein>3.0g/dl)	229(76.3%)
Total		300(100%)

Table 4 shows that out of total 300 cases of pleural fluid, 71(23.7%) were transudative and 229(76.3%) were exudative type.

**Table-5: The cytological finding in pleural fluid**

Sr. No.	Cytological examination of exudative fluid	No. of pleural fluid cases (%)
1.	Inflammatory	178(77.7%)
2.	Malignant	40(17.5%)
3.	Suspicious	11(4.8%)
Total		229(100%)

Table 5 shows in case of pleural fluid 178(77.7%) cases were inflammatory, 40(17.5%) were malignant and 11(4.8%) were suspicious of malignancy.

**Table-6: The distribution of histological patterns of exudative pleural fluids**

Morphological patterns	No. of cases (%)
Adenocarcinoma cell	45(20.5%)
Squamous cell carcinoma	2(1%)
Lymphocyte rich effusion	99(45.2%)
Polymorph rich effusion	45(20.5%)
Reactive mesothelial cells	34(15.5%)
Total	219(100%)

Table 6 shows that out of total 229 cases of exudative pleural fluid, 45 cases of adenocarcinoma, 2 cases of squamous cell carcinoma and 4 were of

mesothelioma, 99 cases were lymphocyte rich effusion, 45 cases of polymorph rich effusion, and in 34 cases reactive mesothelial cells were observed.

**Table-7: The gender specific incidence of malignancy in pleural fluid**

Sr. No.	Type of malignancy	Male	Female
1.	Adenocarcinoma lung	20	12
2.	Breast carcinoma	0	10
3.	Squamous cell carcinoma lung	2	0
4.	Malignant mesothelioma	4	0
5.	Metastasis in pleura (unknown 1 <sup>0</sup> )	3	0
5.	Total	51	

Table 7 shows that 32 cases were from with adenocarcinoma of lung amongst the total number of 51 specimens studied.

**Table-8: The distribution of total pleural fluids advised ADA estimation**

Group code	Category of patients	Pleural fluid
a	Tuberculous etiology	94
b	Non tuberculous etiology	45
Total		139

Table 8 shows that 94 cases were of tuberculous pleural fluid and 45 cases of non-tuberculous pleural fluid.

**Table-9: The distribution of observation according to ADA level in pleural fluids**

Range $\mu/L$	Tuberculous pleural Fluid	Non tuberculous pleural Fluid
00-10	-	02
11-20	-	17
21-30	-	20
31-40	03	03
41-50	20	03
51-60	25	-
61-70	24	-
71-80	12	-
>81	10	-
Total	94	45

Table 9 shows that most of patient of tuberculous fluid 81 out of 94 cases (%) were in range of 41-80U/L of ADA, while for patients of non-

tuberculous pleural fluids, the range was between 11-30U/L of ADA, 37/45(%) of patient fall in this category.

**Table-10: No. of true positive and true negative cases according to cut off level (>40u/l) of ADA in pleural fluids**

ADA level	Tuberculous effusion	Non tuberculous effusion	Total
Positive cases(>40U/L)	91	03	25
Negative cases(≤40U/L)	03	41	16
Total	94	45	41

(Chi value- 143.02, df-1, p<0.05).

Table 10 shows that 91 cases of tuberculous effusion were showing pleural fluid ADA level above 40U/L, considered as true positive cases and 3 patients were showing ADA level below 40U/L, considered as a false negative cases. In non-tuberculous effusion cases were showing ascites fluid ADA level below 40U/L, that are true negative 41 cases and 03 cases were showing ADA level above 40U/L considered as false

positive cases. From these finding the sensitivity and specificity of test counted as follows. On checking association between ADA level with TB effusion and non TB effusion, it was found that there was a association between them and it was found statistically significant (Chi value- 143.02, df-1, p<0.05). The results had great significance in diagnosis of tuberculous pleural effusion.

**Table-11: The sensitivity and specificity percentage of ADA value above 40U/ML is diagnosis of tuberculous pleural fluid**

Sensitivity	95.9%
Specificity	93.5%
Positive predictive value	95.9%
Negative predictive value	92.1%

On considering the 40U/L of fluid ADA level as cut off value sensitivity was 95.9%, specificity was

93.5%, positive predictive value was 95.9% and negative predictive value was 92.1%.

## DISCUSSION

**Table-12: The age distribution of pleural effusion cases**

Sr. No.	Author	No. of patient	Maximum cases age range Years
1.	Irani <i>et al.</i> [2]	109	25-90
2.	Valdes <i>et al.</i> [3]	253	41-70
3.	Ram and Singh [4]	40	20-60
4.	Present study	300	40-60

In the present study 300 cases were studied and maximum cases recorded in 4<sup>th</sup> to 6<sup>th</sup> decade. According to above observations by various authors, it is apparent that pleural effusion is very common in age

group between 30-60 years and the results of present study are quite comparable with others. The tuberculous and malignant pleural effusions were common 4<sup>th</sup> to 6<sup>th</sup> decade.

**Table-13: The gender incidence of pleural fluids**

Author	Year	Male	(%)	Female	(%)	Total no. of Cases
Valdes <i>et al.</i> [3]	1991	156	61.6%	117	38.4%	253
Ram and Singh [4]	1995	35	87.5%	05	12.5%	40
Present study	2012	183	61%	117	39%	300

In the present study 183 cases, (61%) were male patients and 117 (39%) were female patients, which shows a higher incidence of pleural fluid

occurring in males and this corresponds with study of Valdes *et al.* and Ram and Singh.

**Table-14: The transudative and exudative pleural cases noted by routine examination mainly based on protein estimation of fluid**

Author	Year	Transudate Less than 3 gm% of	Exudate,more Than 3 gm%	Total no. of cases
Storey <i>et al.</i> [5]	1976	35	70	105
Hirsch <i>et al.</i> [6]	1979	92	208	300
Chandrashekhar <i>et al.</i> [7]	1969	08	72	80
Present study	2012	71	229	300

Table 14 shows that differentiation of transudative and exudative by routine examination of fluid mainly based on protein estimation of fluid. In the present study, total 300 cases of pleural effusion include 71 cases of transudative effusion and 229 cases of

exudative effusion were comparable to Hirsch *et al.* study. The exudative pleural effusion is more common cause noted due to infection and malignancy involves pleura frequently.

**Table-15: The comparative of studies between malignant and non-malignant diseases by cytological examination of pleural fluid**

Author	Year	Total no. of cases	Malignancy	Others
Storey <i>et al.</i> [5]	1976	146	20	126
Hirsch <i>et al.</i> [6]	1979	300	117	183
Cordozo <i>et al.</i> [7]	1966	1248	373	875
Bakalos <i>et al.</i> [8]	1974	62	42	20
Sears <i>et al.</i> [9]	1987	1846	812	1034
Irani <i>et al.</i> [10]	1987	109	64	45
Present study	2012	300	51	249

Table 15 shows correlation of malignancy with others by cytology examination. In present study of 300 specimens of pleural fluid, 51 were diagnosed as malignant and amongst 249 cases, were diagnosed as

tuberculous inflammatory, other inflammatory conditions and transudative is comparable with other studies. The tuberculosis was detected as the cause of pleural effusion in more cases.

**Table-16: The sensitivity and specificity at different cut off value of body fluid ADA of various authors and present study**

Sr. No	Authors	Year	Cut-off value of ADA(U/L)	Sensitivity	Specificity
1	Rajendra psrasad [10]	1992	30	100%	100%
2	Bharat kumar [11]	2010	40	92.8%	90%
3	Y. Aoki [12]	1994	45	100%	75%
4	Bina Solanki [13]	1995	40	85%	100%
5	E. perez Rodriquez [14]	1999	40	88.8%	92%
6	Present study	2012	40	95.9%	93.5%

Table 16 shows that the sensitivity and specificity of the test at cut off value > 40U/L was 95.9% and 93.5% respectively, this data is comparable with other studies. The estimation of ADA is diagnostic to considered tuberculous etiology in pleural effusion if level of ADA is more than 40 U/L.

## CONCLUSION

The routine and cytological examination of pleural fluid has an important diagnostic value to find out the cause of pleural effusion. The routine examination can help in differentiation of transudative and exudative fluids and cytological examination helps in the diagnosis and typing of malignancy respectively. In case of malignant effusion different cytomorphological features along with clinical and radiological findings helps to diagnose the type of

malignancy. The type of malignant lesion can be confirmed by histopathology after surgery or by various available biopsy techniques like laparoscopic and endoscopic. The knowledge of cytology of pleural fluid is at greater help to the patients having inoperable malignancies where palliative treatment is needed and by avoiding unnecessary agony of surgery to the patients. The ADA level in pleural fluids is 93.5% specific and 95.9% sensitive for diagnosis of tuberculous pleural effusion. Thus, a collective approach in body fluid analysis by physical, chemical, cytological method and special technique like cytospin preparation and special test like ADA level helps in making more accurate diagnosis than any single investigation.

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