ISSN - 2250-1991 | IF : 5.761 | IC Value : 79.96

Original Research Paper Medicine

Pleural fluid and serum amylase ratio for differentiation between malignant and tuberculous pleural effusion.

Rajesh Chetiwal (M.D.) Professor, Deptt. of Medicine, ESI PGIMSR, New Delhi.

R.K. Bhimwal (M.D.) Professor, Dr. SN Medical College and attached hospitals, Jodhpur.

ABSTRACT

Background: Pleural effusion provide the opportunity to diagnose the disease causing the effusion with analysis of fluid obtained by thoracentesis, which is "diagnostic" in approximately 75% of patients and useful in management in an additional 15-20% 2.

Objective: The present study is planned to estimate pleural fluid and serum amylase levels and their ratio in cases of exudative pleural effusions and its role in differentiating malignant from tuberculous pleural effusion.

Study design: A prospective observational study was conducted on 63 patients of exudative pleural effusion, admitted in various medical wards with the diagnosis of 33 as tubercular and 30 as malignant effusion, in a tertiary care teaching hospital in western Rajasthan, India.

Methodology: After detailed history and through clinical examination cases of pleural effusion from February 2009 to January 2011 were taken in the study to establish etiological diagnosis. Pleural fluid was collected after thoracocentesis and sent for cytological and biochemical testing including amylase. Serum amylase was also measured to estimate the ratio of pleural fluid and serum amylase.

Results: In this prospective observational study 63 patients were enrolled, 33 patients are of tubercular and 30 were of malignant effusion. The pleural fluid/serum amylase ration ranging from 0.93 to 3.11 with the mean of 1.48±0.43 in malignant pleural effusion, whereas this ratio was ranging from 0.41 to 1.07 with the mean of 0.70±0.19 in tuberculous pleural effusion ($p<0.001$). The pleural fluid/serum amylase ratio was more than one in (96.66%) patients of malignant pleural effusion. The pleural fluid/serum amylase ratio was less than one in (96.96%), patients of tuberculous pleural effusion.

Conclusion: The pleural fluid amylase was more than 200 SU/dl and pleural fluid/serum amylase ratio was more than one in malignant pleural effusion. Whereas these values were lower, (pleural fluid amylase less than 200 and pleural fluid/serum amylase ration less than one), in tuberculous pleural effusion.

KEYWORDS pleural effusion, malignant, tubercular, amylase.

Introduction:
The spectrum of diagnosis causing exudative pleural effusion is extensive and presents more of a diagnostic dilemma. However, tuberculosis should be considered as diagnostic possibility in any patient with an exudative pleural effusion in the developing countries and malignant pleural effusions (MPE) are the more common in patients over the age of 60 years. Etiological diagnosis (presumptive or definitive) can be established in approximately 75% of patients [2].

Definitive diagnosis of tuberculous and malignant pleural effusion rests on pleural biopsy for histopathological, immuno histochemical studies and pleural fluid for AFB stain and culture, ADA and PCR.[3] The above test are not easily available everywhere as both the conditions tuberculosis and malignant pleural effusion have exudative nature. Pleural fluid may be haemorrhagic or may contain mesothelial cells therefore pose difficulty in diagnosis. In such cases estimation of pleural fluid amylase may be helpful in diagnosis.[4,5]

Serum and pleural fluid amylase and pleural/serum amylase ratio in malignant pleural effusions are found to be significantly raised as compared to tuberculous and non tuberculous pleural effusions. Therefore, the present study is planned to estimate pleural fluid and serum amylase levels and their ratio in cases of exudative pleural effusion. Cut–off value for pleural fluid amylase is more than 100 SU/dl and for pleural fluid/serum amylase ratio of >1 helps in differentiating malignant from tuberculous pleural effusion.[6]

Aims and objectives:
Estimation of pleural fluid and serum amylase levels and the Study of pleural fluid/serum amylase ratio in differentiating malignant pleural effusion from tubercular pleural effusion.

Material and Methods:
This was a prospective observational study done in a tertiary care teaching hospital from February 2009 to Jan 2011. After taking ethical committee approval, patient's history, examination and personal data were entered on predesigned proforma.

Sixty three patients admitted to the medicine wards with exudative pleural effusion were included. Thirty three of tubercular and thirty of malignant etiology. Patients of liver cirrhosis, hepato cellular disease with concurrent illness, pancreatitis and esophageal perforation were excluded from this study.

Samples were collected in ethylene diamine tetra acetic acid (EDTA) , citrated and plane tubes for complete blood count (CBC), Total leukocyte count (TLC), Platelet count, ESR, Peripheral smear, Blood urea, Serum creatinine, electrolytes, Liver function tests (LFT) ,blood sugar following routine and special investigations were carried out in a patient of pleural effusion to establish etiology. Chest X–Ray, Sputum for AFB, sputum for malignant cells, USG abdomen/Thorax, C.T. Thorax and Pleural Biopsy.

Pleural fluid was sent for Cytology including cell count and type with malignant cells, also sent for Protein, sugar, ADA and amylase. Pleural fluid/Serum amylase ratio was calculated. Quantitative data tabulated in Microsoft excel sheet and presented in proportion.

Results :
Majority 24 out of 30 (80%) of the patients of malignant pleural effusion were above the age of 50 years, whereas 25 out of 33 (75.75%) patients of tuberculous pleural effusion were under the age of 40 years. incidence of malignant as well as tuberculous pleural effusion was twice in males than in females.

70% patients were diagnosed by pleural fluid cytology and 50%

were diagnosed by bronchial aspirate. 26.67%, 20% and 10% patients were diagnosed by bronchial biopsy, lymphonde FNAC/ biopsy and malignant cells in sputum, respectively.

Eight cases were found to be positive with pleural fluid cytology as well as bronchial aspirate. Two cases we found to be positive for malignant cells in sputum, pleural fluid cytology and bronchial biopsy. One case was found to be positive for malignancy with all five methods.

Patients were diagnosed by pleural fluid for AFB culture in 30.30% and 27.27% were diagnosed by bronchial aspirate for AFB. 18.18% and 15.15% patients diagnosed by lymphonde FNAC/ biopsy and sputum for AFB, respectively, whereas pleural biopsy for HP and pleural fluid for AFB smear was positive in 9.09%, found to be positive in 3 patients.

Four cases were found to be positive with pleural fluid for AFB culture as well as bronchial aspirate for AFB. Two cases were found to be positive with pleural fluid for AFB culture as well as pleural fluid for AFB smear. One case was found to be positive with sputum for AFB as well as bronchial aspirate for AFB.

The serum amylase is higher in malignant pleural effusion than in tuberculous pleural effusion. Majority 21 out of 30 (70%) of patients exhibited pleural fluid amylase more than 200 SU/dl. Adenocarcinoma and metastatic carcinoma showed highest pleural fluid amylase. The mean pleural fluid amylase in malignant pleural effusion was significantly higher than the mean pleural fluid amylase in tuberculous pleural effusion.

The pleural fluid amylase and serum amylase ratio was almost always more than one in malignant pleural effusion, whereas it is less than one in tuberculous pleural effusion.

The pleural fluid amylase value of more than 200 SU/dl was found in majority (21 out of 30 (70%) of patients of malignant pleural effusion. All patients of tuberculous pleural effusion had pleural fluid amylase value less than 200 SU/dl. Maximum value of pleural fluid amylase was observed in adenocarcinoma and metastatic carcinoma patients.

Discussion:

Majority (80%) of the malignant pleural effusion patients were above the age of 50 years, whereas 75.75% patients of tuberculous pleural effusion were under the age of 40 years. Incidence of malignant as well as tuberculous pleural effusion was about two times more in males than in females. This is in conformity with the study by Chernow et al (1977).[11]

Incidence of malignant pleural effusion (54.05%) is higher than tuberculous pleural effusion (49.94%) in smokers. 75.60% male patients were smokers, whereas only 27.20% female patients were smokers. 64.51% of male smokers had malignant pleural effusion, whereas only 37.83% of male smokers had tuberculous pleural effusion. 8.10% of female smokers had malignant and tuberculous pleural effusion, each. It is supported by the fact that the risk of malignant pleural effusion increases in smokers.

In the present study, majority of patients of malignant pleural effusion were diagnosed by pleural fluid cytology (70%) and bronchial aspirate (50%). Similar results were also observed by Grunze et al (1964)[5] Dekher et al (1978)[13], Prakash (1985)[14], Sahn et al (1988)[8] and Bueno et al (1990)[9] ranges from 40-87%.

The present study showed, adenocarcinoma (43.33%) was the most common type of cancer, followed by metastatic carcinoma (20%), squamous cell carcinoma (10%) and undifferentiated cell carcinoma (10%) in patients of malignant pleural effusion. In a study by Chernow et al (1977) patients of carcinomatous involvement of the pleura and observed that pleural effusions occur with all the cell types of lung carcinoma, but appear to be most frequent with adenocarcinoma[11]. Johnston et al (1985) reviewed cytopathologic diagnosis of 584 specimens from 472 consecutive patients and found adenocarcinoma as the most common cell type in patients of malignant pleural effusion[12]. Small cell carcinoma (3.33%) was the least common type of cancer, found only in one case in the present study, whereas Heerstedt et al (1992)[17] found the incidence of pleural effusions in patients with small cell lung carcinoma is about 10%.

Our study showed, majority of patients of tuberculous pleural effusion were diagnosed by pleural fluid for AFB culture (30.30%) and bronchial aspirate for AFB (27.27%). 18.18% and 15.15% patients diagnosed by lymph node FNAC / biopsy and sputum for AFB, respectively. Berger et al (1973)[7] observed that pleural fluid cultures were positive for AFB in fewer than 25% cases. Sahn et al (1988)[8] reported this yield in the range of 25-70% and pleural fluid smear was positive for AFB in < 10% cases.

Twenty seven percent of patients of tuberculous pleural effusion also had parenchymatous lesion in chest-x-ray. P.A. view and 55.55% of these patients were also positive for AFB in sputum in our study. Berger et al (1973)[7] reported coexisting parenchymal disease can be detected radiographically in about one third of patients. The effusion is almost ipsilateral to the infiltrate and is a marker of active parenchymal disease.

In our study, amylase activity, in pleural fluid samples of malignant pleural effusion ranged from 108 to 457.1 SU/dl with a mean of 250.04±98.[10] SU/dl, whereas it was in the range of 72.70 to 186.6 SU/dl with a mean of 117.82±27.54 SU/dl in tuberculous pleural effusion. Foresti et al (1994)[15] observed in his study that pleural fluid amylase concentrations were significantly higher in malignant pleural effusion than in tuberculous pleural effusion (106.3±101 SU/dl, ranging from 4 to 485 SU/dl, vs 62+45.8 SU/dl, ranging from 14 to 195 SU/dl, $p < 0.02$). Prasop Leelyana et al (1998)[16] observed pleural fluid amylase more than 220 SU/dl in 91.67% patients of malignant pleural effusion. The mean level of pleural fluid amylase in malignant pleural effusion was statistical significant higher than tuberculous pleural effusion ($p<0.001$). K.B. Gupta et al (2001)[6] observed with his study that pleural fluid amylase concentrations were significantly higher in malignant pleural effusion than in tuberculous pleural effusion (163.33±82.09 SU/dl, vs 62.73±20.11 SU/dl, $p < 0.001$).

So, it is fairly evident in our study that the pleural fluid amylase is significantly higher in malignant pleural effusion than the pleural fluid amylase in tuberculous pleural effusion ($p < 0.001$). Similar results were observed by Foresti et al(1994)[15], Prasop Leelyana et al (1994)[16]and K.B. Gupta (2001)[6].

Our study showed, the mean serum amylase 177.70±79.61 SU/dl in malignant pleural effusion was also higher than the mean serum amylase 173.09±34.71 SU/dl in tuberculous pleural effusion. The relation between both these groups was found to be statistically insignificant ($P>0.05$). It was observed that the amylase activity in pleural fluid samples was higher than in serum samples of both groups. In our study results were similar to those reported by Foresti et al (1994)[15] that serum amylase concentrations did not show statistically significant differences among the two groups studied (malignant pleural effusion 122.7±74.8 SU/dl and tuberculous pleural effusion 122.6±57.6 SU/dl).

In our study, adenocarcinoma (3 cases) and metastatic carcinoma (2 cases) exhibited the highest pleural fluid amylase and in conformity with above studies. Higher pleural fluid amylase activity in these patients could be explained by the fact that these were the most common cell type and owing to its peripheral location and propensity for contiguous spread to the pleural surfaces, adenocarcinomas are mostly responsible for majority of malignant pleural effusion. Furthermore, pleural metastasis increases the permeability of pleural surfaces, leading to shedding or exfoliation of affected cells that could result in leakage of amylase in pleural fluid.

The pleural fluid amylase was compared in patients of malignant and tuberculous pleural effusion. It was evident that the pleural

fluid amylase was less than 200 SU/dl in all patients of tuberculous pleural effusion, whereas the pleural fluid amylase was more than 200 SU/dl in majority 21/30 (70%) of patients of malignant pleural effusion.

The pleural fluid/serum amylase ration ranging from 0.93 to 3.11 with the mean of 1.48±0.43 in malignant pleural effusion, whereas this ration was ranging from 0.41 to 1.07 with the mean of 0.70±0.19 in tuberculous pleural effusion (p<0.001). The pleural fluid/serum amylase ratio was more than one in (96.66%) patients of malignant pleural effusion. The pleural fluid/serum amylase ratio was less than one in (96.96%), patients of tuberculous pleural effusion.

Conclusion:

In conclusion the pleural fluid amylase was more than 200 SU/dl and pleural fluid/serum amylase ratio was more than one in malignant pleural effusion. Whereas these values were lower, (pleural fluid amylase less than 200 and pleural fluid/serum amylase ration less than one), in tuberculous pleural effusion. So this can be helpful in early diagnosis and patient management.

Table 1: Age and sex wise distribution of patients.

S. No.	Age group (in years)	Malignant pleural effusion		Tuberculous pleural effusion	
		Female	Male	Female	Male
1.	18–30	–	–	5	7
2.	31–40	1	2	4	9
3.	41–50	2	1	2	2
4.	51–60	2	6	1	1
5.	61–70	4	7	–	1
6.	>71	1	4	–	1
	Total	**10**	**20**	**12**	**21**

Table 2: Laboratory means by which diagnosis of malignant pleural effusion confirmed.

S.No.	Method of Confirmation	No. of Patients	%
1.	Pleural fluid	21	70.00
2.	Bornchial aspirate	15	50.00
3.	Bronchial biopsy	8	26.67
4.	Lymph node FNAC/Biopsy	6	20.00
5.	Sputum for malignant cells	3	10.00

Table 3: Laboratory means by which diagnosis of tuberculous pleural effusion confirmed.

S.No.	Method of Confirmation	No. of Patients	%
1.	Sputum for AFB	5	15.15
2.	Pleural fluid for AFB Culture	10	30.30
3.	Pleural fluid for AFB smear	3	9.09
4.	Bronchial aspirate for AFB	9	27.27
5.	Pleural biopsy for HP	3	9.09
6.	Lymph node FNAC/Biopsy	6	18.18

Table 4: Amylase value in pleural fluid of malignant pleural effusion.

S. No.	Histological Types of Cancer	Amylase value in pleural fluid (SU/dl)			
		100 to 200	201 to 300	301 to 400	401 to 500
1.	Adenocarcinoma	4	7	–	3
2.	Squamous cell carcinoma	1	3	–	–
3.	Metastatic carcinoma	2	3	–	2
4.	Undifferentiated cell carcinoma	1	–	2	–
5.	Small cell carcinoma	1	1	–	–

Table 5 : Mean amylase value in pleural fluid and serum.

Disease		Malignant Pleural Effusion	Tuberculous pleural effusion
Amylase (Pleural fluid)	Mean±SD	250.04±98.42	117.82±27.54**
Amylase (Serum)	Mean±SD	177.70±79.61	173.09±34.71
Pleural fluid : Serum amylase ratio	Mean±SD	1.47±0.43	0.70±0.19**
	Range	0.933–3.11	0.41–1.07

**P<0.001

References:

1. Albertine K.H.,Weiner Kromish J.P. Basta: Protein exit and entry in pleural space. J of Applied Physiology 1971,70: 123-124.
2. Collin TR, Sahn SA. Thoracocentesis: Complication, patients experience and diagnostic value. Chest 1987, 91: 817-22.
3. Light RW. Malignant Pleural Effusion. In: Retford DC, editor. Pleural disease.3rd Ed. Philadelphia. Williams and Wilkins 1995, 94-116.
4. Harper's Biochemistry-Roberts K. Murray, Daryl K. Granner, Peter A, Mayes, Victor W Rodwell, 23rd Edi, 1993; 772.
5. Kitazawa M., Makagawa M, Baba O, Sumiyashi K, Saito Y, Bamba T et al. A case of amylase producing lung cancer. Kokyo To Junkan 1993, 41(4) : 393.
6. K.B. Gupta et al: Estimation of serum and pleural fluid amylase and isoenzyme in cases of malignant pleural effusion. Ind. J. Tub. 2001; 48 : 87.
7. Berger H.W., Mejia E: Tuberculous pleurisy. Chest 1973; 63: 88-92.
8. Sahn SA, Good Jt : Jr Pleural fluid pH in malignant pleural effusions, Diagnostic, prognostic and therapeutic implications. Ann Intern Med 1988; 108 : 345-349.
9. Bueno CE Clemente G, Castro BC, Martin LM, Ramos SR, Panizo AG, Glez-Rio JW. Cytologic and bacteriologic analysis of fluid and pleural biopsy specimens with cope's needle. Arch Intern Med 1990; 150 : 1190-1994.
10. Levy H, Wayne LG, Anderson Barnes PF, Light RW. Anti mycobacterial antibody levels in pleural fluids reflect passive diffusion from serum. Chest 1989; 92: 1855.
11. Chernow B, Sahn SA. Carcinomatous involvement of the pleura: Analysis of 96 patients. Am J Med 1977; 63: 695-702.
12. Johnston WW. The malignant pleural effusion: a review of cytopathologic diagnosis of 584 specimens from 472 consecutive patient. Cancer; 56: 905-909.
13. Grunze H: The comparative diagnostic accuracy, efficiency and specificity of cytologic techniques used in the diagnosis of malignant neoplasm in serous effusion of the pleural land pericardinal caviies. Acta cytol 1964; 8: 150-164.
14. Prakash URS, Reiman HW: Comparison of needle biopsy with cytologic analysis for the evaluation of pleural effusion: analysis of 414 cases. Mayo Clin Proc 1985: 60: 158-164.
15. Fresti V, Villa A, Zubani R : Amylase concentrations in pleural effusion. Chest 1994; 105 : 1625.
16. Prasop Leelyana: Pleural fluid amylase level in malignant and tuberculosis pleural effusion: Division of pulmonary disease, Department of Medicine, Rajavith, Hospital, Bangkok, Thailand.
17. Herrstedt J, Clementren P, Hansen OP. Increased myelosuppression during cytostatic treatment and pleural effusion in patients with small cell lung cancer. Eur J cancer 1992; 28A: 1070 – 1073.