Original Research Article

Lactate dehydrogenase levels in pleural fluid of effusive pleural diseases

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Abstract

Background: The present study was aimed to evaluate and access the sensitive marker for the differentiation of fluid, protein content and LDH. **Material and methods:** The present study was observational cross sectional study carried out in patients attending chest clinic of Nair hospital, Mumbai. For comparison, healthy individuals without any past history of chest disease admitted in the Nair hospital were selected as controls. Serum and fluid were processed for estimation of glucose, protein electrophoresis, total LDH and its isoenzyme. **Results:** Total 63 patients were included in the study of which 45 were males and 18 were females. The majority of population belonged to age group of 21-40 years. Tuberculosis followed by Nephrotic syndrome and bacterial empyema were the common causes of pleural effusion. The pleural fluids were classified into transudative and exudative based on the protein content and LDH content in plasma as well as pleural fluid. In present study, high levels of total LDH are observed in tuberculosis and empyema both in serum as well as in pleural fluid. In malignant effusion, serum LDH is lowered and pleural fluid LDH is high. In pseudopancreatic cyst and cirrhosis of liver, serum LDH is normal and pleural fluid LDH is low. **Conclusion:** Determination of protein content alone does not serve as a sensitive marker but LDH also should be taken into consideration as one of the sensitive marker for the differentiation of pleural fluid into transudate or exudate.
Key Word: Serum, Pleural fluid, LDH, Total Protein, Pleural effusion.

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INTRODUCTION

Pleural effusion is an accumulation of fluid in the pleural space as a result of excessive transudation or exudation from the pleural surfaces[1]. Transudate is a fluid substance that passed through a membrane or has been extruded from tissue. A transudate has high fluidity and low content of proteins, cells or solid matters derived from cells. In contrast to a transudate, exudate is a fluid with high protein content and cellular debris that has escaped from blood vessels and has been deposited in tissues or on tissue surfaces[2]. The differentiation of pleural effusion into exudates and transudate is of considerable diagnostic importance[3]. Lactate dehydrogenase is a fermentative oxidoreductase enzyme[4]. It has been extensively studied to differentiate between various causes of pleural effusion and various observations have been putforth[5]. Sources of enzyme under normal conditions are combination of intracellular synthesis and normal cell replacement. A rise of specific enzyme therefore indicates necrobiosis or functional damage in a particular tissue. LDH levels are increased in the presence of inflammation. Acute inflammation results in an increased permeability of the vascular supply of the pleura thereby leading to exudation of pleural proteins including LDH along with leucocytes into pleural fluids or LDH may be derived from pleural fluid leucocytes.

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Leucocytes are the rich sources of LDH which may explain its higher value in septic effusion and empyema. It has been shown to alter in body fluids in absence of acute tissue necrosis[6].Effusion containing malignant cells demonstrated to have greater LDH activity compared to its serum levels[7]. The increase in production of enzyme by tumour cells is other possible mechanism[8]. If pleural fluid to serum LDH ratio is more than 0.6 or if total LDH of pleural fluid is more than 200 IU or if the pleural fluid of serum protein ratio is more than 0.5, then the pleural fluid is an exudate[5]. The diagnostic and prognostic value of LDH has been investigated by various authors[9,10,11,12]. Many patients of myelogenous leukemia, lymphosarcoma and disseminated carcinoma have increased serum LDH levels[11].It is reported that in malignant effusion, pleural fluid LDH is more that serum LDH[7,13,14,15]. LDH values are high in empyema[16,17,18,19]. Gastrin[16] found lower LDH levels in malignant patients while Brook[18] reported high LDH values in 77% of patients with pleural effusion. Wroblewski[11] reported lower LDH levels in effusion of benign condition as compared to that with malignant conditions. The aim of present study was to evaluate the LDH status in patients with pleural effusion due to various causes.

METHODOLOGY

The present study was a cross sectional type of observational study. The patients selected for the present study were among those who attended Chest OPD and being admitted in the wards of BYL Nair Charitable Hospital, Mumbai. The individuals who attended Chest Clinic with evidence of accumulation of fluid in lungs on radiological examination, of both gender and all age groups, irrespective of co morbidities were included in the study. At the same time, healthy individuals without any past history of chest disease admitted in the hospital for minor surgery, who had undergone complete medical and laboratory examinations including chest normal X ray, were selected as controls. Patients as well as control's blood was processed for the estimation of Total LDH, iso enzymes of LDH and protein electrophoresis. Patients and controls who fulfilled the criteria for enrollment of the study were allowed to have dinner in the evening prior to collection of specimen. Next day morning, after 12-14 hours of overnight fasting, blood was collected in fluoride bulb. Estimation of total protein was done by Biuret reaction. LDH was measured by colorimetric method as described by King. The LDH isoenzymes were determined by Polyacrylamide gel electophoretic method.

RESULTS

Table 1: Distribution Of Age And Sex

Age	Males	Females	Total	Percentage
11-20 yrs	2	2	4	6.35
21-30 yrs	18	10	28	44.44
31-40 yrs	14	3	17	26.98
41-50 yrs	8	1	9	14.29
51-60 yrs	3	2	5	7.94
Total	45	18	63	

Table no. 1 shows the distribution of patients in different age group and sex. In the present study, pleural effusion was seen predominantly more common in middle age group i.e, 21-40 years (71.4%).

Table 2: Distribution of cases in different diseased groups

S. No	Diseases	No of patients	Percentage
1	Tuberculosis	29	46.03
2	Nephrotic syndrome	7	11.11
3	Bacterial empyema	7	11.11
4	Malignant effusion	5	7.94
5	Subpneumonic effusion	5	7.94
6	Pseudopancreatci cyst	5	7.94
7	Cirrhosis of liver	5	7.94
	Total	63	

As seen in Table no. 2, most of the patients of pleural effusion in the present study were diagnosed with tuberculosis. Table no. 3 below shows the classification of pleural fluid in transudate/exudates groups. Pleural fluid protein level of 3g/100ml is frequently used to separate transudates from exudates; however this dividing line has consistently led to the misclassification of many effusions. If the fluid protein content is more than 3gm% , then pleural effusion is said to be exudative.

Table 3: Difference of pleural effusion between exudates and transudates

S. No	Diseases	Number	From total protein content of Pleural fluid	From pleural fluid to serum protein ration	From total LDH of pleural fluid	From pleural fluid LDH to serum LDH ration
1	Tuberculosis	29				
	Exudate	22	18	19	22	24
	Transudate	7	11	10	7	5
2	Nephrotic syndrome	7				
	Exudate	0	0	0	2	1
	Transudate	7	7	7	5	6
3	Bacterial empyema	7				
	Exudate	6	6	5	7	7
	Transudate	1	1	2	0	0
4	Malignant effusion	5				
	Exudate	3	3	3	4	5
	Transudate	2	2	2	1	0
5	Subpneumonic effusion	5				
	Exudate	4	4	3	5	4
	Transudate	1	1	2	0	1
6	Pseudopancreatic cyst	5				
	Exudate	1	0	2	0	1
	Transudate	4	5	3	5	4
7	Cirrhosis of liver	5				
	Exudate	1	0	1	1	2
	Transudate	4	5	4	4	3

In the present study, all the effusion associated with nephrotic syndrome, cirrhosis of liver and pseudopancreatic cyst are transudative. In empyema and tuberculosis, majority of the cases are exudative.

Table 4: Total LDH of serum in different groups

S. no	Diseases	No of patients	<200 IU	200-300 IU	300-600 IU	>600 IU
1	Tuberculosis	29	2	26	1	0
2	Nephrotic syndrome	7	4	3	0	0
3	Bacterial empyema	7	0	2	5	0
4	Malignant effusion	5	4	0	1	0
5	Subpneumonic effusion	5	2	3	0	0
6	Pseudopancreatic cyst	5	1	4	0	0
7	Cirrhosis of liver	5	0	5	0	0

Table 5: Pleural fluid Total LDH (IU) in different groups

S. no	Diseases	No of patients	<200 IU	200-300 IU	300-600 IU	>600 IU
1	Tuberculosis	29	20	3	0	0
2	Nephrotic syndrome	7	7	0	0	0
3	Bacterial empyema	7	0	0	0	7
4	Malignant effusion	5	1	0	4	0
5	Subpneumonic effusion	5	0	0	5	0
6	Pseudopancreatci cyst	5	4	1	0	0
7	Cirrhosis of liver	5	4	1	0	0

Table no. 4 and 5 show total LDH in serum and pleural fluid. Serum and pleural fluid value of total LDH in tuberculous effusion in present study is variable though majority had LDH more than 200IU.

DISCUSSION

Table no.2 represents diseases associated with pleural effusion. Tuberculosis (46%) was the most common cause of effusion. In a study by Finney, the 274 patients of pleural effusion were diagnosed, the most common cause (30%) was carcinoma[20]. Hirsch[21] found cancer followed by tuberculosis and bacterial infection to the common cause of pleural effusion. Lueallen[22], in his study on 436 patients, observed that Tuberculosis was the most common cause (66.6%) of pleural effusion. It can be

seen that the prevalence of tuberculosis and malignancy was common among the patients of pleural effusion. Tuberculosis was more common in our setting due to higher prevalence of tuberculosis in community.

In the present study, all the effusion associated with nephrotic syndrome, cirrhosis of liver and pseudopancreatic cyst are transudative (Table no 3). In empyema and tuberculosis, majority of the cases are exudative, which is similar to the study carried out by Carr[23], who found that all 29 tuberculosis pleural fluids he studied contained more than 3gm% protein. Berger[24]found 77% of his cases having protein concentration more than 5gm%, while Epstein[25] found all his cases as exudates. Light[5] observed that 8% of transudates and 11% of exudates in his study being misclassified on the basis of total protein content of pleural fluid. He proposed that any pleural effusion to be termed as exudates should have at least:

1. Pleural protein to serum protein ratio more than 0.5
2. Total LDH of pleural fluid more than 200IU or
3. Pleural fluid LDH to serum LDH ratio more than 0.6.

Applying these criteria to differentiate between tuberculous exudates and transudates, pleural fluid to serum LDH ration is most useful indicator. In present study, out of 29 cases pleural fluid to serum LDH ratio is more than0.6 in 24 cases and total LDH is more than 200IU in 22 patients. In nephrotic syndrome, total protein and pleural fluid to serum protein ratio is the most sensitive indicator to differentiate between exudates and transudate. By using this criteria all the 7 cases of nephrotic syndrome shows transudate in nature while LDH does not serve as a sensitive marker. Total LDH in bacterial empyema is more than 200IU in all 7 cases and also pleural fluid to serum LDH ratio is more than 0.6 in all 7 cases. So both these indicators are useful to differentiate the fluid in exudates or transudate. In malignant effusion and synpneumonic effusion, total LDH of pleural fluid and pleural fluid to serum LDH ratio is more useful to distinguish between exudate and transudate. Total protein and total LDH of pleural fluid is more useful indicator to differentiate pleural fluid in pseudopancreatic cyst. In cirrhosis of liver, total protein is less than 3gm% in all 5 cases studied. Pleural fluid to serum protein ratio is less than 0.5 and total LDH is less than 200IU in four cases respectively. So these three criteria are useful to differentiate pleural fluid is transudate in nature in cirrhosis of liver. Total protein and pleural fluid protein to serum protein ratio are more useful indicator to differentiate pleural fluid in nephrotic syndrome and cirrhosis of liver. Total LDH can serve as useful indicator to differentiate between exudates or transudate nature of pleural fluid in empyema, malignancy, synpneumonic effusion, pseudopancreatic cyst and in cirrhosis of liver. However pleural fluid LDH to serum LDH ratio is more useful for differentiation of fluid as exudates or transudate in tuberculosis, empyema, malignancy and synpneumonic effusion. Table no. 4 and 5 show total LDH in serum and pleural fluid. Serum and pleural fluid value of total LDH in tuberculous effusion in present study is variable though majority had LDH more than 200IU, which confirm study by Brook[18], Berger[24]. They also reported high LDH value in 77% tuberculous pleural effusion. Pleural fluid total LDH in all transudates secondary to nephrotic syndrome, four cases of cirrhosis of liver and pseudopancreatic cyst were less than 200IU in the present study (Table no. 5). In all cases of empyema, pleural fluid LDH was greater than 600IU (Table no. 5), which confirms previous studies that empyema fluid contains high LDH[16,17,19]. Light[5]proposes that LDH level more than 1000IU in parapneumonic effusion suggests that the effusion is infected. It is reported that in malignant effusion, pleural fluid LDH is more than serum LDH[7,13,14,15]. These findings are comparable with the present study. Low LDH secondary to cirrhosis could be result of two factors. Relative absence of cellular elements limits LDH from this source. In addition, low albumin concentration in such fluid might result in decreased LDH activation or preservation[9]. Similar mechanism may operate for low LDH in other transudates. Elevated lactate in body fluids during pathological processes is due to anaerobic conditions in the tissues[26]. This in turn may depend on increased production of lactate; partly by the tissue cells and partly by the bacterial cells.

CONCLUSION

Total LDH in Nephrotic syndrome, Pseudopancreatic cyst and Cirrhosis of liver is lowered in pleural fluid. In empyema it is raised both in serum and pleural fluid. In malignant effusion, pleural fluid LDH was considerably raised. For differentiation of pleural fluid in exudates and transudate, pleural fluid LDH to serum LDH ratio was more useful marker in tuberculosis, empyema, malignancy and synpneumonic effusion. Thus, determination of protein content alone does not serve as a sensitive marker but LDH also should be taken into consideration as one of the sensitive marker for the differentiation of pleural fluid into transudate or exudate.

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