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Screening of Lactate dehydrogenasein ascitic/pleural fluid in Saraswathi institute of Medical Sciences, Hapur

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Introduction*: Aims To investigate lactate dehydrogenase (LDH) measurements in fluids.These are more sensitive and specific markers for differentiating between exudates and transudates, as confirmed clinically, than the measurement of fluid total protein concentrations alone.*
Materials and Method: *The study was conducted in the department of medicine and department of biochemistry at Saraswathi institute of medical sciences. Pleural fluid, and ascitic fluid from patients were analysed retrospectively for LDH, cholesterol, and total protein. Clinical classification of transudate or exudate was reached independently by reviewing clinical details and laboratory data.*
Observation and Result: *Estimating the Fluid Lactate Dehydrogenase levels in patients presenting with ascites helps in differentiating between malignant and non malignant effusion. It is highly sensitive (100%) and highly specific (100%). Estimating the Fluid Lactate Dehydrogenase level in patients presenting with pleural effusion helps in differentiating between transudative and exudative effusion. It is highly sensitive (100%) and highly specific (100%).*
Conclusion: *Biochemical analysis of LDH in ascitic fluid helps in differentiating malignant and non-malignant etiology (Negative Predictive Value = 100%, confidence interval= 75.3-100%). Biochemical analysis of F.LDH (Ascitic Fluid)/ S. LDH helps in differentiating malignant and non-malignant etiology (Negative Predictive Value = 100%, confidence interval = 75.3-100%).*
Keywords: *pleural effusion, peritoneal effusion, pericardial effusion*

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I. Introduction

Lactate dehydrogenase (LD or LDH) is an enzyme involved in energy production that is found in almost all of the body's cells, with the highest levels found in the cells of the heart, liver, muscles, kidneys, lungs, and in blood cells; bacteria also produce LD. This test measures the level of LD in the blood or sometimes other body fluids.The lactate dehydrogenase (LDH) molecule is a tetramer composed of four polypeptide chains. Three characteristics of an exudate, ie, an ascitic fluid lactic dehydrogenase (LDH) level of > 400 Sigma units (SU), an ascitic fluid-serum LDH ratio of > 0.6, and an ascitic fluid-serum protein ratio of > 0.5, were studied in a prospective fashion to determine their usefulness in the differential diagnosis of ascites. The ascitic fluid LDH level did not exceed 400 SU in any patient with uncomplicated chronic liver disease, whereas in patients with malignant, tuberculous, or pancreatic ascites it exceeded 500 SU in 12/19 patients. The finding of two of the three characteristics indicated a nonhepatic cause for the ascites whereas the absence of all three strongly suggested uncomplicated liver disease as the sole cause. The ascitic fluid WBC count was also useful in that values exceeded 500/cu mm in bacterial and tuberculous peritonitis whereas it was low (297 ± 49/cu mm) in chronic liver disease.There are five component iso-enzymes as a result of the five different combinations that are produced by two polypeptide chains encoded by separate genes (M and H). The extracellular appearance of LDH is used to detect cell damage or cell death (1-3). LDH-1 is composed of four H subunits, and LDH5 of four M subunits. Since patient management depends on right and timely diagnosis, biochemical analysis of extravascular body fluids is considered a valuable tool in the patient management process. The biochemical evaluation of serous fluids includes the determination of gross appearance, differentiation of transudative from exudative effusions and additional specific biochemical testing to assess the effusion etiology.In conclusion LDH a cytoplasmatic enzyme present in essentially all organ systems is thought

to be released only after cell death. Various cell types are characterized by LDH isoenzyme profiles. Therefore LDH isoenzyme activity patterns can be used to localize cellular injury.

II. Materials and Method

Present study was carried out in the department of Medicalbiochemistry at Sarswathi Institute of Medical Science, AnwarpurHapur U.P, on the clinically diagnosed cases of Diabetes mellitus. The study period was from August 2016 to July 2018 . Study Design Open labelled, Cross sectional, observational study Subjects

- **Subjects**

This study will be performed on a minimum of 80 subjects suffering from Ascites/ Pleural Effusion, who satisfy the inclusion and exclusion criteria. The etiology of the subjects to be studied in our study has already been established as per the diagnostic criteria of the disease concerned.The data collected from each patient included Age, Sex, Duration of Disease, Body Mass Index (BMI), Fasting & Post Prandial Glucose Level, HbA1c, TSH, Total Cholesterol, Triglycerides, HDL, LDL and VLDL.

Study Design

Study Design Open labelled, Cross sectional, observational study

- **Blood Collection**

5 ml of blood was drawn from all the above subjects from the anterior cubital vein using sterile disposable syringe.

Statistical Analysis

The statistical analyses were performed using SPSS version 20. The descriptive results were expressed as mean ± standard deviation and percentage. An independent t-test was used to compare mean values of each parameter among the groups. To observe possible relationships between parameters, Pearson's correlation coefficient (r) was used. All variables with p- value less than 0.05 were considered as statistical significance.

- **Study Methodology**

After taking consent and ethical clearances, all subjects in the study will be studied with reference to:

- A complete physical and medical examination.
- Basic Anthropometry
- H b, TLC, DLC,ESR
- Blood Urea, Creatinine,SerumCreatinine, LFT, FBS
- Ascitic fluid for Lactate Dehydrogenase
- Pleural fluid for Lactate Dehydrogenase
- Serum Lactate Dehydrogenase, Albumin
- Ascitic/ Pleuralfluid - Protein, albumin, sugar, cells, malignant cells.

III. Observations and Results

Estimating the Fluid Lactate Dehydrogenase levels in patients presenting with ascites helps in differentiating between malignant and non malignant effusion. It is highly sensitive (100%) and highly specific (100%).Estimating the Fluid Lactate Dehydrogenase level in patients presenting with pleural effusion helps in differentiating between transudative and exudative effusion. It is highly sensitive (100%) and highly specific (100%).

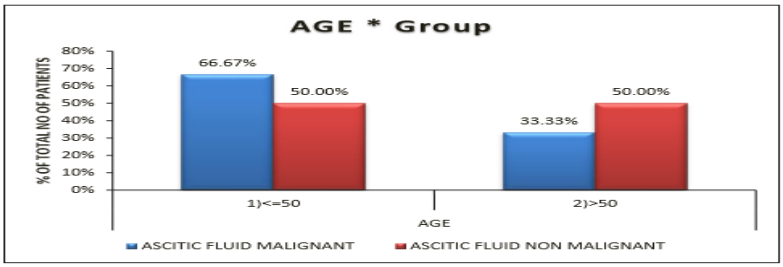
Table 1:- Total no. of 12 patients with Ascites having malignancy were enrolled. The mean age of patient was 47.5 years. The youngest being 34 years old and oldest aged 70 years. 18 patients had ascites due to non-malignant causes. The youngest being 42 years and oldest 75 years.

	Ascitic Fluid Malignant	Ascitic Fluid Non-malignant	P - value
AGE			0.051
Sample size	14	16	
Mean ± S.D	37.5± 11.09	65.78 ± 10.82	
Median	46	56.5	
Min-Max	34-70	42-75	
Inter quartile range	39-55.500	45-65	
ASCITIC ALBUMIN Sample size	14		0.002
Mean± S.D	2.38± 0.25		

Median	2.35		
Min-Max	2-2.8	0.8-2.7	
Inter quartile range	2.200-2.600	18	
Ascitic LDH		1.82 ± 0.67	.0001
Sample size	12	2.05	
Mean± S.D	523.58±127.62	142.56±42.6	
Median	470	142.5	
Min-Max	389-726	18-195	
Inter quartile range	409.500-636	126-173	
S-ALBUMIN			0.0003
Sample size	12	18	
Mean±SD	3.23±0.27	3.94±0.62	
Median	3.25	3.85	
Min-Max	2.8-3.7	3.5	
Inter quartile range	3-3.450	3.500-4.300	

Table 2 :- More young patients (<50 years) were seen having malignant Ascites i.e. 66.67% in comparison to just 33.3% of old patients (>50 years) with malignant Ascites.

		Ascitic fluid Malignant	Ascitic fluid Non-malignant	Total	P Value
AGE	1)≤50	66.67	50.0	17	0.465
	2)≥50	33.33	50.00	13	
Total		12(100.00)	18(100.00)	30(100.00)	



In malignant ascites

	Ascitic fluid malignant	Ascitic fluid Non-malignant
Age	37.3	55.78
Ascitic -Albumin	2.38	1.82
Ascitic LDH	524.58	142.56
S-Albumin	3.23	3.94
SAAG	0.85	2.14
SGOT	70.33	28.72
SGPT	65	23.11

RESULT

Our results showed that: a pleural fluid/serum LDH ratio above 0.7 indicates that the fluid is an exudate; however, in about 10% of inflammatory pleural effusions due to infection or cancer this ratio is comprised between 0.5 and 0.7; the enzyme profile of transudates only differs from that of normal serum by a slight increase in isoLDH 4 and 5; in exudates this profile is the reverse of the normal serum profile, with a decrease in isoLDH 1 and 2 and an increase in isoLDH 4 and 5; the enzyme profile provides little information on the origin of exudates, although a more than 30% rise in isoLDH 2 is in favour of a malignancy (mesothelioma excluded); polymorphonuclears contain more isoLDH 4 and 5 than mononuclears; activation of mononucleate cells is attended by a significant increase in intracellular isoLDH 4 and 5; the presence of red blood cells and/or haemolysis in an exudate cannot account for its high isoLDH 4 and isoLDH 5 content; the high content seems to be due, at least partly, to release of these enzymes by the polymorphonuclears and/or mononucleate cells involved in pleural inflammation. The cut off values for three parameters in ascitic fluid for differentiation between hepatic and non-hepatic ascites are as follows: LDH of 400SU, fluid/serum LDH ratio of 0.6, and fluid/serum total protein ratio of 0.5. Ascitic levels higher than the cut offs for any two out of three parameters indicate a non-hepatic cause of ascites, whereas values below the cut offs for all three parameters strongly suggest a hepatic cause of ascites. According to Gokturk et al, LDH values were higher in patients with an SAAG greater than 1.1g/dL or less than in those with a SAAG greater than 1.1 g/dL. [55]. We inferred a similar result from our study i.e. mean SAAG of 2.14 in patients with non-malignant ascites as compared to 0.85

in malignant ascites. However Sevinc et al. reported that in patients with malignant ascites, ascitic fluid LDH values had high sensitivity but low specificity for the diagnosis of the disease, and a low value of LDH did not necessarily exclude malignancy.[56] We inferred the same from our study i.e. Fluid LDH had a high sensitivity and specificity in differentiating malignant from non-malignant ascites. Of the 30 patients of ascites taken in our study 12 patients were found to have malignant ascites with a mean age of 47.5 years and the most common cause being liver cell carcinoma. 18 patients were found to have non-malignant ascites with mean age of 55.7 years and the most common cause being congestive cardiac failure. In our study we also found that the mean serum LDH values were higher in patients with malignant ascites (393) as compared to that of patients with non-malignant ascites (157) with a p value of <0.0001. The mean value of transaminases was raised in patients with malignant ascites which is similar to earlier studies. Pleural effusion occurs in a number of pathological conditions and even exhaustive .Diagnostic tests fail to reveal the etiology in as many as 15%–20% of cases. The classification of pleural effusion as transudative or exudative is the primary diagnostic step because, if the effusion is a transudate, no further diagnostic procedures are necessary and therapy is directed towards the underlying disease process. However, if the effusion is exudative a more extensive diagnostic work-up is required to distinguish between the many possible causes of exudative effusion. In India, tubercular effusion is common and may occur in a setting where the patient is predisposed to develop an effusion due to other causes. The various criteria that have been employed include pleural fluid specific gravity, protein levels and lactic dehydrogenase (LDH) levels. In a series of patients with malignant cells in the pleural effusion, Wroblewski&Wroblewski (1958) found an LDH activity higher than in the corresponding serum. They assume that the increase in LDH activity is caused not only by the neoplastic cells which are proliferating in the effusion but also by the malignant tumors contiguous with the effusion. We inferred a similar result from our study i.e. mean Fluid LDH levels were higher in exudative effusion (331) to that of transudative effusions (87) with a p value of <0.0001. In our study, we found that out of the 30 patients of pleural effusion taken for the study 17 patients were found to have exudative effusion and 13 patients were found to have transudative effusion. The mean age of patients with exudative effusion was 51 years whereas 52.7 years in patients with transudative effusion. The mean serum LDH was also found to be higher in patients with exudative effusions (393) to that with transudative effusions (157) with p value <0.0001. In our study we found that the most common cause of transudative effusion in the study group was congestive heart failure and that of exudative effusion was Tuberculosis. In conclusion, estimation of Fluid LDH levels may contribute to the differential diagnosis of effusion etiology. In patients with malignant/exudative effusion Fluid LDH levels have a high sensitivity and high specificity for disease groups. However, owing to the relatively small study population, further studies with longer sample size are indicated to confirm the utility of Fluid LDH in the diagnostic evaluation of ascites/ pleural effusion and to confirm the findings of our studies.

IV. Conclusions

Hence we conclude thatPatients with malignant diseases show increased LDH activity in serum and malignant effusion.Estimating the Fluid Lactate Dehydrogenase levels in patients presenting with ascites helps in differentiating between malignant and non malignant effusion. It is highly sensitive (100%) and highly specific (100%).Estimating the Fluid Lactate Dehydrogenase level in patients presenting with pleural effusion helps in differentiating between transudative and exudative effusion. It is highly sensitive (100%) and highly specific (100%).Biochemical analysis of LDH in ascitic fluid helps in differentiating malignant and non-malignant etiology (Negative Predictive Value = 100%, confidence interval = 75.3-100%).Biochemical analysis of F.LDH (Ascitic Fluid)/ S. LDH helps in differentiating malignant and non-malignant etiology (Negative Predictive Value = 100%, confidence interval = 75.3-100%).

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