A BIOCHEMICAL APPROACH TO LACTATE DEHYDROGENASE IN ASCITIC/PLEURAL FLUID IN A TERTIARY CARE HOSPITAL

Vivek Sinha[1], Poonam Kachhawa[2]

[1]Associate Professor, Department of Biochemistry, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India.
[2]Assistant Professor, Department of Biochemistry, Saraswathi Institute of Medical Sciences, Hapur, Uttar Pradesh, India.

ABSTRACT

BACKGROUND

Lactate dehydrogenase (LDH) is an enzyme which is found in almost all living cells. LDH is a tetramer composed of two different subunits, M and H. It catalyses the interconversion of lactate and pyruvate, as it interconverts NAD^+ and NADH.

The aim of this study was to evaluate the diagnostic significance of estimating lactate dehydrogenase in ascitic and pleural fluid.

MATERIALS AND METHODS

The current study was conducted in the department of biochemistry at Saraswathi Institute of Medical Sciences, Hapur. This descriptive study was performed on 60 subjects suffering from ascites/pleural effusion, who satisfy the inclusion and exclusion criteria. Since the duration of the study was less, patients were selected by convenience technique.

RESULTS

Estimating the fluid lactate dehydrogenase levels in patients presenting with ascites helps in differentiating between malignant and non-malignant effusions. 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 effusions. It is highly sensitive (100%) and highly specific (100%).

CONCLUSION

Biochemical analysis of LDH in ascitic fluid helps in differentiating malignant and non-malignant aetiology (Negative Predictive Value= 100%, Confidence Interval= 75.3-100%).

KEY WORDS

Lactate Dehydrogenase, Ascites, Pericardial Effusion.

BACKGROUND

Lactate Dehydrogenase (LDH) is a tetrameric molecule used to detect cell damage or cell death.[1-5] It is composed of four polypeptide chains. It is composed of five different polypeptide chains encoded by separate genes (M and H). LDH_1 is composed of four H subunits, and LDH_5 of four M subunits. The biochemical analysis of extravascular body fluids is considered an important clinical tool in the patient management plan.

Aim

To study the diagnostic significance of estimating lactate dehydrogenase in ascitic and pleural fluid.

MATERIALS AND METHODS

Study Setting

This descriptive study was performed on a minimum of 60 subjects suffering from Ascites/ Pleural Effusion, who satisfy the inclusion and exclusion criteria. The aetiology of the

subjects to be studied in our study has already been established as per the diagnostic criteria of the disease concerned. This study was conducted in the department of department of biochemistry at Saraswathi institute of medical sciences in the period of March 2016 to Jun 2018.

Study Period

March 2016 to Jun 2018.

Study Design

Descriptive study.

Study Subjects

This study will be performed on a minimum of 60 subjects suffering from Ascites/ Pleural Effusion, who satisfy the inclusion and exclusion criteria. The aetiology of the subjects to be studied in our study has already been established as per the diagnostic criteria of the disease concerned.

Sample Size

This study will be performed on a minimum of 60 subjects suffering from Ascites/ Pleural Effusion, who satisfy the inclusion and exclusion criteria. The aetiology of the subjects to be studied in our study has already been established as per the diagnostic criteria of the disease concerned. Sample size was also calculated by convenience. Pre-tested semi-structured Questionnaire to assess: Socio-demographic characteristics of the study participants. Inclusion and exclusion criteria were also taken in to consideration. General physical and CVS examination in study subjects.

Inclusion Criteria
- All cases of Ascites/ Pleural Effusion of larger duration.
- Rapid filling of both the serous sacs after tapping.

Exclusion Criteria
Patients suffering from one of the following conditions:
- Acute Myocardial Infarction.
- Haemolysis.
- Trauma.
- Pulmonary Embolism.
- Post-operative cases.

After taking informed consent and ethical clearances, all subjects in the study will be studied with reference to-
- A complete physical and medical examination.
- Basic Anthropometry.
- Blood Urea, Serum Creatinine, Serum Albumin, SGOT, SGPT, FBS.
- Ascitic fluid for Lactate Dehydrogenase.
- Pleural fluid for Lactate Dehydrogenase.
- Serum Lactate Dehydrogenase.
- Ascitic/Pleural fluid - Protein, albumin, sugar, cells, malignant cells (When indicated)
- USG Whole Abdomen.
- X-Ray Chest.

All biochemical investigations were done by semi-automated biochemistry analyzer. All assays were performed according to the respective manufacturer's instructions.

Statistical Analysis
Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Statistical tests were applied as follows-
1. Quantitative variables were compared using Independent T test.
2. Qualitative variables were correlated using Chi-Square test.
3. The data was entered in MS Excel spreadsheet and analysis was done using SPSS.

Version 20.Data was entered in Microsoft excel and Descriptive statistical analysis was done. Results on categorical measurements are presented as Percentages. Significance is assessed at 5 % level of significance. p value <0.001 statistically significant. Fisher's exact test/ Chi square test was used to find out the significance of study parameters on a categorical scale between two groups.

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%).

	Ascitic Fluid Malignant	Ascitic Fluid Non-Malignant	p-Value
1. Age			
Sample Size	12	18	
Mean ± S.D.	47.5± 11.09	55.78 ± 10.82	
Median	45	53.5	0.052
Min-Max	34-70	42-75	
Inter Quartile Range	39-55.500	45-65	
2. Ascitic Albumin			
Sample Size	12	18	
Mean ± S.D.	2.38 ± 0.25	1.82 ± 0.67	
Median	2.35	2.05	0.003
Min-Max	2-2.8	0.8-2.7	
Inter Quartile Range	2.200-2.600	1.900-2.300	
3. Ascitic LDH			
Sample Size	12	18	
Mean± S.D.	523.58 ± 127.62	142.56 ± 42.6	
Median	473	145.5	<0.001
Min-Max	384-724	18-195	
Inter Quartile Range	409.50-636	126-173	
4. Serum Albumin			
Sample Size	12	18	
Mean±S.D.	3.23±0.27	3.94±0.62	
Median	3.25	3.85	0.003
Min-Max	2.8-3.7	3.5	
Inter Quartile Range	3-3.450	3.500-4.300	

Table 1. Comparison of Parameters Between Ascitic Fluid Malignant and Ascitic Fluid Non-Malignant

		Ascitic Fluid Malignant	Ascitic Fluid Non-Malignant	Total	P Value
Age	1)≤50	66.67 %	50.0 %	17	
	2)≥50	33.33 %	50.0 %	13	
Total		12 (100%)	18 (100%)	30 (100%)	

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

Parameters	Ascitic Fluid Malignant (Mean ± S.D)	Ascitic Fluid Non-Malignant (Mean ± S.D)	P -value
Age	47.5 ± 11.09	55.78 ± 10.82	0.052
Ascitic Albumi	2.38 ± 0.25	1.82 ± 0.67	0.003
Ascitic LDH	523.58 ± 127.62	142.56 ± 42.6	<0.001
Serum Albumi	3.23 ± 0.27	3.94 ± 0.62	0.003
SAAG	0.85 ± 0.23	2.14 ± 0.49	0.004
SGOT	68.33 ± 24.5	28.72 ± 6.22	<0.001
SGPT	65.20 ± 22.4	23.11 ± 7.43	<0.001

Table 3. Comparison of Parameters in Malignant Ascites and Non-Malignant Ascites

DISCUSSION
Table 1 shows 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. Initially, it was found that there was uniformly high levels of LDH in

malignant effusions and low levels of LDH in non-malignant effusions.[6-9] It was observed that the mean ascitic fluid LDH level was much lower in patients with liver diseases than in those with malignant ascites (167±9 vs 913±228 SU).[10] We inferred a similar result from our study i.e. fluid LDH level in patients with malignant ascites was higher (523.8) as compared to fluid LDH level in non-malignant ascites (142.5) with a p value <0.001. 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.

LDH values were higher in patients with an SAAG greater than 1.1 g/dL or less than in those with a SAAG greater than 1.1 g/dL.[11,12] 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.[13] 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.[14-16] 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.[17,18]

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 <0.001. The mean value of transaminases was raised in patients with malignant ascites which is similar to earlier studies.[19-22] In India, Pleural effusion occurs in a number of pathological conditions.[23] It is important to classify pleural effusion as transudative or exudative as 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. If the effusion is exudative a more extensive diagnostic work-up is required to distinguish between the many possible causes of exudative effusion.[24-29] In India, tubercular effusion is common. The various criteria that have been employed include pleural fluid specific gravity, protein levels and lactic dehydrogenase (LDH) levels.[30-34] In patients with malignant cells in the pleural effusion, it was seen that LDH activity is higher than in the corresponding serum.[35] It was assumed 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 tumours contiguous with the effusion.[36-37] 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 average 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.

CONCLUSION
- Patients 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%).

Due 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 study.

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