

Study of ascitic fluid lactate dehydrogenase (LDH): A marker for diagnosis of spontaneous bacterial peritonitis at a tertiary hospital

Syed Faiz Ahmed^{1*}, Md Muneer Ahmed², Saba Khan³

¹Assistant Professor, ²Senior Resident, ³Post Graduate, Department of General Medicine / Internal Medicine, Deccan College of Medical Sciences (DCMS), Kanchanbagh, Hyderabad, Telangana State -500058, INDIA.

Email: dr786faiz@yahoo.com

Abstract

Background: Spontaneous Bacterial Peritonitis (SBP) is defined as polymorph nuclear (PMN) count $\geq 250/\mu\text{L}$ ascitic fluid regardless of ascetic fluid (AF) culture results. Value of biochemical parameters including ascitic fluid pH, lactate dehydrogenase (LDH), glucose and total proteins compared to their blood levels in diagnosing culture-negative patients for diagnosis of Spontaneous Bacterial Peritonitis (SBP) are studied. Present study was aimed to ascitic fluid lactate dehydrogenase(LDH) as a marker for spontaneous bacterial peritonitis. **Material and Methods:** Present study was hospital-based cross-sectional study, conducted in patients >18 years, admitted with ascites, underwent abdominal paracentesis, consented for participation in study. The differences in AFLDH (ascitic fluid LDH) and AFLDH/SeL DH (serum LDH) ratio between SBP and non-SBP group were compared. **Results:** In present study, 210 patients of ascites were studied. Majority were of 41-60 year age group (43.33 %), male (74.76 %), diagnosed as alcoholic liver disease (57.62%), cryptogenic (16.19 %), malignancy (11.90 %) with co-morbidities such as Hypertension (29.05 %), Diabetes mellitus (26.19 %), Hepatitis C virus (10.00 %) and Hypothyroidism (7.14 %). Spontaneous bacterial peritonitis was noted in 26 patients (12.38 %). We noted statistically significant difference in levels of Ascitic Fluid LDH (SBP - 239.81 ± 159.26 and Non-SBP - 65.47 ± 28.75) and Ascitic Fluid LDH/ Serum LDH ratio SBP - 0.65 ± 0.21 and Non-SBP - 0.18 ± 0.12 in SBP and non-SBP group ($p < 0.001$). **Conclusion:** Ascitic Fluid LDH >125 as well as Ascitic Fluid LDH/ Serum LDH > 0.05 is useful, sensitive and specific, as well as widely available diagnostic tool. for diagnosis of SBP.

Keywords: SBP, Ascitic Fluid LDH, Serum LDH > 0.05 , ascites

*Address for Correspondence:

Dr Syed Faiz Ahmed, Assistant Professor, Department of General Medicine / Internal Medicine, Deccan College Of Medical Sciences (Dcms), Kanchanbagh, Hyderabad, Telangana State -500058, INDIA.

Email: dr786faiz@yahoo.com

Received Date: 28/06/2021 Revised Date: 16/07/2021 Accepted Date: 23/08/2021

This work is licensed under a [Creative Commons Attribution-NonCommercial 4.0 International License](https://creativecommons.org/licenses/by-nc/4.0/) 

Access this article online

Quick Response Code:	Website: www.medpulse.in
	DOI: https://doi.org/10.26611/102120329

INTRODUCTION

Spontaneous Bacterial Peritonitis (SBP) is defined as polymorph nuclear (PMN) count $\geq 250/\mu\text{L}$ ascitic fluid regardless of ascetic fluid (AF) culture results.¹ SBP is the

most common source of infection in liver cirrhosis, accounting for approximately 25% of bacterial infections.² Mortality due to SBP ranges between 30% and 90% within the first year of diagnosis.³ The risk for spontaneous bacterial peritonitis is 15% within the first 3 years after the onset of ascites.⁴ Spontaneous bacterial peritonitis is the result of overgrowth of a specific organism in the intestine, translocation of that microbe from the intestine to mesenteric lymph nodes, and resulting spontaneous bacteremia and subsequent colonization of susceptible ascitic fluid. Spontaneous bacterial peritonitis is probably related to several impaired defense mechanisms, such as depressed reticuloendothelial system phagocytic activity, leukocyte dysfunction, reduced serum complement, and low bactericidal activity of ascitic fluid.^{5,6} Value of biochemical parameters including ascitic fluid pH, lactate

dehydrogenase (LDH), glucose and total proteins compared to their blood levels in diagnosing culture-negative patients for diagnosis of Spontaneous Bacterial Peritonitis (SBP) are studied.⁷ Present study was aimed to ascitic fluid lactate dehydrogenase(LDH) as a marker for spontaneous bacterial peritonitis.

MATERIAL AND METHODS

Present study was hospital-based cross-sectional study, conducted in Department of General Medicine / Internal Medicine, Deccan College of Medical Sciences (DCMS), Kanchanbagh, Hyderabad, India. Study duration was of 2 years (July 2018 to June 2020). Study was approved by institutional ethical committee. Study was discussed with patients and included in study after taking an informed consent in writing.

Inclusion criteria: Patients >18 years, admitted with ascites, underwent abdominal paracentesis, consented for participation in study

Exclusion criteria: Pregnant women and recent postpartum (within 6 months of delivery). Patients not willing to participate

RESULTS

In present study, 210 patients of ascites were studied. Majority were of 41-60 year age group (43.33 %), male (74.76 %), diagnosed as alcoholic liver disease (57.62 %), cryptogenic (16.19 %), malignancy (11.90 %) with co-morbidities such as Hypertension (29.05 %), Diabetes mellitus (26.19 %), Hepatitis C virus (10.00 %) and Hypothyroidism (7.14 %). Spontaneous bacterial peritonitis was noted in 26 patients (12.38 %).

History, any previous medical records, examination findings were noted in proforma. Relevant hematological (CBC, PT/INR, LFTs, RFTs), urine examination, radiological (USG- abdomen with pelvis, if required CT/MRI) and ascites fluid investigations (ascitic fluid pH, lactate dehydrogenase (LDH), glucose and total proteins) were done in all patients. The ascitic fluid and corresponding blood samples were sent for LDH estimation. LDH values of ascitic fluid and blood were correlated with the clinical, pathological and radiological findings. Spontaneous Bacterial Peritonitis (SBP) was diagnosed with polymorph nuclear (PMN) count $\geq 250/\mu\text{L}$ ascitic fluid regardless of ascetic fluid (AF) culture results. The differences in AFLDH (ascitic fluid LDH) and AFLDH/SeLDH (serum LDH) ratio between SBP and non-SBP group were compared.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated using appropriate formulas.

Table 1: General characteristics

Characteristics	Frequency (N = 210)	Percentage
Age (years)		
19-40	44	20.95%
41-60	91	43.33%
>60	75	35.71%
Gender		
Male	157	74.76%
Female	53	25.24%
Diagnosis		0.00%
Alcoholic liver disease	121	57.62%
Cryptogenic	34	16.19%
Malignancy	25	11.90%
Tuberculosis	19	9.05%
Cardiogenic	11	5.24%
Co-morbidities		
Hypertension	61	29.05%
Diabetes mellitus	55	26.19%
Hepatitis C virus	21	10.00%
Hypothyroidism	15	7.14%
Hepatitis B virus	12	5.71%
HIV	9	4.29%
Hepatitis E virus	3	1.43%
Spontaneous bacterial peritonitis		
Present	26	12.38%
Absent	184	87.62%

We noted statistically significant difference in levels of Ascitic Fluid LDH (SBP - 239.81 ± 159.26 and Non-SBP - 65.47 ± 28.75) and Ascitic Fluid LDH/ Serum LDH ratio SBP - 0.65 ± 0.21 and Non-SBP - 0.18 ± 0.12) in SBP and non-SBP group ($p < 0.001$).

Table 2: LDH levels

Parameter	SBP (N = 26)	Non-SBP (N = 184)	P value
Ascitic Fluid LDH	239.81 ± 159.26	65.47 ± 28.75	<0.001
Ascitic Fluid LDH/ Serum LDH	0.65 ± 0.21	0.18 ± 0.12	<0.001

DISCUSSION

Ascites is the Consequence of portal hypertension which is characteristic clinical feature of cirrhosis. The development of ascites is a marker of prognosis in liver cirrhosis, as it indicates a reduction in 1- and 5-year survival rates by 15% and 23.5%, respectively.² Spontaneous bacterial peritonitis is diagnosed when (a) the ascitic fluid culture grows pathogenic bacteria (almost always pure growth of a single type of organism), (b) the ascitic fluid neutrophils count ≥ 250 cells /mm³ and (c) there is no evidence of surgically treatable intra-abdominal sources of infection.⁸ Although SBP occurs most commonly in conjunction with cirrhosis of the liver and ascites, it is sometimes reported in patients with ascites from other causes such as nephrotic syndrome, systemic lupus erythematosus, or malignancies.⁹ Spontaneous Bacterial Peritonitis (SBP) occurs when a bacterial infection spreads to the AF through the gut wall or lymphatics but less commonly via hematogenous spread in absence of a recognized intra-abdominal source of bacterial infection or malignancy.⁶ The mesenteric lymph nodes are the most common site of translocation, and the bacterial species that most commonly translocate include *Escherichia coli*, *Klebsiella pneumoniae*, the streptococcal species, and other microorganisms, of the family Enterobacteriaceae.^{10,11} Patients with decompensated cirrhosis often have a compromised host defense system due to impaired phagocytic activity of neutrophils and macrophages and deficient complement activation.¹⁰ Lactate Dehydrogenase is widely distributed in many body tissues. It is a hydrogen transfer enzyme that catalyzes the oxidation of L-lactate to pyruvate with the mediation of NAD⁺ as a hydrogen acceptor.¹² Consequently, the high LDH level in infected ascitic fluid can be explained by either diffusion from the blood or by the release from disintegrating AF neutrophils.¹³ El Motasem *et al.*,¹⁴ noted that patients with clinical suspicion of SBP showed a highly significant ascites inflammatory response than patients without SBP, confirmed by more AF LDH (IU/L) (mean \pm SD 185.06 ± 58.39 IU/L vs mean \pm SD 84.37 ± 33.65 IU/L respectively, $p < 0.001$). Similar findings were noted in present study. In study by, El-Shabrawi MH *et al.*,¹⁵ mean lactate dehydrogenase (LDH) level was significantly higher in ascitic fluid in the infected versus sterile cases ($p < 0.002$). A ratio of ascitic/serum LDH \geq

0.5 gave a sensitivity of 80%, specificity of 88%, positive predictive value (PPV) of 66.7%, negative predictive value (NPV) of 93.7% and accuracy of 63.3%. Similar findings were noted in present study. In a comparative study with 170 patients S Sandhya *et al.*,¹⁶ noted that ascitic fluid LDH (AFLDH) was significantly raised in SBP as compared to non SBP patients ($p < 0.0001$). For SBP, AFLDH ≥ 127.5 IU/L had sensitivity of 76.5%, specificity of 75.2%, PPV of 28.3% and NPV of 96.2%. For SBP, AFLDH/ SeLDH ratio with a cut-off value of ≥ 0.50 had specificity of 81.2%, sensitivity of 47.1%, PPV of 25.7% and NPV of 93%. For AFLDH in SBP, the area under the curve was 0.820 with 95% CI 0.737 - 0.904 (p value < 0.001). Amany Talaat *et al.*,¹⁷ noted that ascitic fluid neutrophil count and LDH level was significantly higher in patients of spontaneous bacterial peritonitis (group I) compared to those in cirrhotic ascites without evidence of peritonitis (group II) (P-value 0.000 and 0.003, respectively), while total proteins, albumin and glucose levels were significantly lower in the patient of group I (P-value 0.000, 0.028 and 0.021, respectively) Although PMN count is an accurate diagnostic test, this is concerned with individuals born errors that can affect the results. Furthermore, there is a possibility for lysis and missing PMN in AF while handling the specimens leading to pseudo negative results. High degree of suspicion, routine diagnostic paracentesis, standardization of diagnostic criteria of ascitic fluid infection and use of non-nephrotoxic antibiotics is essential for early diagnosis and management. Early diagnosed and treated SBP episodes resolved satisfactorily and improved short-term prognosis.

CONCLUSION

Among the various biochemical parameters for early diagnosis of SBP, Ascitic Fluid LDH >125 as well as Ascitic Fluid LDH/ Serum LDH > 0.05 is useful, sensitive and specific, as well as widely available diagnostic tool. Further studies are recommended for confirmation of present study findings.

REFERENCES

1. Navasa M, Rodés J. Bacterial infections in cirrhosis. *Liver Int* 2004;24:277-80.
2. Vilstrup H. Cirrhosis and bacterial infections. *Rom J Gastroenterol* 2003;12:297-302.

3. Fernandez J, Navasa M, Gomez J, Colmenero J, Vila J, Arroyo V, et al. Bacterial Infections in cirrhosis: Epidemiological changes with invasive procedures and norfloxacin prophylaxis. *Hepatology* 2002;35:140-8.
4. Turnage RH, Li DLB, McDonald JC. Abdominal wall umbilicus, peritoneum, mesenteries, omentum. In: Sabiston Textbook of Surgery – The biological basis of modern surgical practice. 17th edn. Philadelphia: Elsevier Saunders; 2004: 1182-6.
5. Caruntu, F. and Benea, L. (2006) Spontaneous Bacterial Peritonitis: Pathogenesis, Diagnosis, Treatment. *Journal of Gastrointestinal and Liver Diseases*, 15, 51-56.
6. Yildirim, B., Sari, R. and Sezgin, N. (2002) Complement and Immunoglobulin Levels in Serum and Ascitic Fluid of Patients with Spontaneous Bacterial Peritonitis, Malignant Ascites, and Tuberculous peritonitis. *Southern Medical Journal*, 29, 1158-1162.
7. El-Shabrawi MH, El-Sisi O, Okasha S, et al. Diagnosis of spontaneous bacterial peritonitis in infants and children with chronic liver disease: A cohort study. *Ital J Pediatr*. 2011;37:26.
8. Runyon BA (2004): Early events in spontaneous bacterial peritonitis. *Gut* 63:782-4.
9. Bac D V, de Marie S, van Blankenstein M (1996): Spontaneous bacterial peritonitis complicating malignancy-related ascites. *Dig Dis Sci* 41:131-132.
10. Wiest R, Krag A, Gerbes A. Spontaneous bacterial peritonitis: Recent guidelines and beyond. *Gut* 2012;61:297-310.
11. Wells CL. Relationship between intestinal microecology and the translocation of intestinal bacteria. *Antonie Van Leeuwenhoek* 1990;58:87-93.
12. Ekpe, E. E. L., and Omotoso, A. J. (2015). The Relevance of Ascitic Lactate Dehydrogenase (LDH) and Serum Ascites Albumin Gradient (SAAG) in the Differential Diagnosis of Ascites among Patients in a Nigerian Hospital. *Journal of Advances in Medicine and Medical Research*, 8(3), 211-219.
13. Runyon BA. Management of adult patients with ascites caused by cirrhosis. *Hepatology* 2004;27:264–72.
14. El Motasem, E. , Heikal, A. , El Haddad, H. , Hamdy, A. , Samie, R. and El Din, H. (2015) Value of Different Diagnostic Markers in Spontaneous Bacterial Peritonitis in HCV Egyptian Cirrhotic Patients. *Open Journal of Gastroenterology*, 5, 119-128.
15. El-Shabrawi MH, El-Sisi O, Okasha S, et al. Diagnosis of spontaneous bacterial peritonitis in infants and children with chronic liver disease: A cohort study. *Ital J Pediatr*. 2011;37:26.
16. S Sandhya, Rinchu Loomba, V Loomba, N Malhotra, Ascitic Fluid Lactate Dehydrogenase (LDH) – A Marker for Spontaneous Bacterial Peritonitis *Journal, Indian Academy of Clinical Medicine IACM* 2021; 22(1-2): 26-29
17. Amany Talaat, Kamal Eman Nagib, Osman Rasha, Youssef Shahin, Role of ascitic fluid C3 in spontaneous bacterial peritonitis, *Egyptian Journal of Medical Human Genetics* Volume 13, Issue 1, February 2012, Pages 81-85.



Source of Support: None Declared
Conflict of Interest: None Declared