

Predictive Value of Neutrophil to Lymphocyte Ratio Combined with C-Reactive Protein for Diagnosis of Spontaneous Bacterial Peritonitis among Cirrhotic Patients

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ABSTRACT

Background: A serious problem for cirrhotic individuals is spontaneous bacterial peritonitis (SBP). Clinical significance of SBP's C-reactive protein (CRP) as well as neutrophil-to-lymphocyte ratio (NLR) have been discovered using varying threshold levels. **Objective:** The aim of the current work was to assess the validity of diagnostic paracentesis with the use of combined blood NLR and CRP as a non-invasive predictor for early diagnosis of SBP.

Patients and Methods: This case control study included a total of 60 cirrhotic decompensated patients, admitted at Department of Tropical Medicine, Zagazig University Hospitals. Patients were categorized into two groups (30 each) according to neutrophil count in Ascitic fluid; **Group I** with SBP and **Group II** free from SBP. Both NLR and CRP were assessed among all subjects.

Results: NLR was statistically significant higher in SBP group. A cut-off value of blood NLR >2.9 on ROC curve had a specificity of 88% as well as sensitivity of 95% for SBP diagnosis in cirrhotic patients. CRP level differed significantly among cirrhotic patients diagnosed with SBP. A cut-off >15 mg/L had a sensitivity and specificity of 85% and 90 % respectively in diagnosing SBP in cirrhotic patients. Combination NLR and CRP had a cut-off >22.6 mg/L, had a sensitivity and specificity of 86%, 91 % respectively in SBP diagnosis among cirrhotic patients.

Conclusions: Combined NLR and CRP with cut of >2.9 , and >15 mg/dl respectively could be used as a novel, non-invasive predictor for SBP diagnosis.

Keywords: Spontaneous Bacterial Peritonitis, NLR, CRP.

INTRODUCTION

In severe cases of liver disease, ascites may develop. It's the leading reason why people with cirrhosis end up in the hospital. Ascites infections caused by bacteria can increase mortality in cirrhotic individuals by a factor of four or more. The chances of acquiring a bacterial infection among people with cirrhosis is four to five times higher than among the general population. Cirrhotic patients usually deteriorate because of infections ⁽¹⁾. In patients with decompensated liver cirrhosis, hepatorenal syndrome or systemic sepsis can precipitate the development of life-threatening spontaneous bacterial peritonitis (SBP), which has a high recurrent incidence of over 70% throughout one year of follow up. While in the hospital, 10%-30% of those people have it. About 50% of patients admitted have SBP, and another 50% will develop it while they are hospitalized ⁽²⁾. Ascites with more than 250 polymorphonuclear neutrophils (PMN)/mm³ and no other obvious cause of intra-abdominal infection are diagnostic of SBP ⁽³⁾.

Risks of Diagnostic paracentesis involves, peritonitis, hemoperitoneum, persistent leak abdominal wall hematoma as well as visceral perforation, which is the most common complication ⁽⁴⁾.

When inflammation occurs in a living organism, C reactive protein (CRP) levels rise in the blood. In response to a bacterial infection, macrophages secrete cytokines such interleukin-1, interleukin-6, and tumor necrosis factor, which stimulate the liver to produce serum CRP ⁽⁵⁾.

The neutrophil-to-lymphocyte ratio (NLR) in the blood is a simple and inexpensive way to gauge how well your immune system is functioning and how much

systemic inflammation you may be experiencing ⁽⁶⁾. As an indicator of the interplay between these two arms of the immune system, the neutrophil-to-lymphocyte ratio (NLR) was proposed as a diagnostic marker for bacterial peritonitis that develops on its own. The presence of neutrophils indicates the presence of active inflammation, while lymphocytes are indicative of the immunological regulation mechanism. Patients with peritonitis caused by bacteria on their own have had their outcomes predicted using the NLR ⁽⁷⁾. It has been shown that platelet indices, C-reactive protein, and total white blood cell counts can foretell infection in ascites fluid. Clinically useful diagnostic criteria for SBP were postulated by Janum and coworkers using NLR alone and in combination with CRP ⁽⁸⁾.

This study objective was to assess the validity of diagnostic paracentesis with the use of combined blood NLR and CRP as a non-invasive predictor for early diagnosing of SBP.

SUBJECTS AND METHODS

This case control study included a total of 60 cirrhotic decompensated patients, admitted at Department of Tropical Medicine, Zagazig University Hospitals.

Patients were categorized into two groups according to Neutrophil count in Ascitic fluid; **Group I** included 30 patients with SBP (neutrophil more than 250 /ml), and **Group II** included 30 patients free from SBP (neutrophil less than 250 cells / ml).

Inclusion criteria:All patients diagnosed with cirrhosis and ascites by clinical, laboratory and radiological criteria who were free of other infections (chest, skin, urinary ...etc.)

Exclusion criteria:

Non cirrhotic ascites “exudative ascites”, Immunocompromised or sepsis cases, Patients who had been receiving antibiotics for SBP prophylaxis for at least one month before hospitalization, cases with hematological disorders on anticoagulant medications.

All patients were subjected to:

1. Complete history taking, and thorough clinical examination.
2. **Lab investigations:**
 - Complete blood count (CBC).
 - Neutrophil-lymphocyte ratio, determined by dividing the number of neutrophils by the total number of lymphocytes, is manually computed as follows: NLR levels outside of this range, especially in adults, are considered abnormal.
 - Liver function tests: (alanine transaminase, aspartate transaminase, total protein, total and direct bilirubin as well as albumin).
 - Kidney function tests (serum creatinine and urea).
 - Urine and stool analysis.
 - ESR, random plasma sugar, alpha fetoprotein.
 - Coagulation profile (INR, prothrombin time and concentration).
 - C - reactive protein
3. Pelviabdominal ultrasonography
4. Ascitic fluid analysis “Diagnostic Paracentesis”:
 - a. 40 ml of ascitic fluid were withdrawn using aseptic techniques, then transferred to the testing tubes and bottles (including blood culture bottles). The fluid was tested for total protein, glucose, lactate dehydrogenase, and albumin. Serum ascitic albumin gradient (SAAG) was calculated. A high SAAG (>1.1g/dL) indicated that ascites was due to portal hypertension (transudate), Ascites

without portal hypertension and a SAAG level below 1.1 g/dL was likely an exudate.

Cytological analysis: Culture of organisms was done, and ascitic fluid microscopy offers vital information on the amount and kind of red and white cells within the fluid that can assist restrict the differential diagnosis.

Ethical approval:

This experiment was ethically approved by the Zagazig University's Research Ethics Committee. After being fully informed, all participants provided written consent. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Statistical Analysis

Statistics were analyzed using SPSS 20 (Statistical Package for the Social Services). It was found that using visual aids like tables and graphs helped best express the results. The quantitative information was displayed as the mean, median, standard deviation, and confidence intervals. Stats like frequency and % were used to help illustrate the data's quality. When dealing with quantitative independent variables, the student's t test (T) is employed to evaluate the data. Chi-Square for Linear Trend (X2) and Pearson Chi-Square were used to evaluate the linear independence of qualitative data. For statistical significance, a P value of 0.05 or less was established.

RESULTS

Table 1 shows that the average age for SBP group was 60.96±8.36 years, and for non-SBS group was 60.93±10.94 years. 63.3% of SBP group were males and 36.7% were females. In this study, hepatitis C virus (HCV) was the leading cause of cirrhosis (66.7%) in the SBP group and 80% in the non-SBP group, whereas hepatitis B virus was the second leading cause of cirrhosis (33.3%) in the SBP group and 20% in the non-SBP group.

Table (1): Comparing patients with SBP and patients without SBP regarding basic characteristics.

Basic characteristics	SBP group (N=30)		Without SBP group (N=30)		Test	p-value (Sig.)
	No.	%	No.	%		
Sex						
Male	19	63.3%	17	56.7%	0.278 ^a	0.598
Female	11	36.7%	13	43.3%		(NS)
Age (years)						
Mean± SD	60.96±8.36		60.93±10.94		0.013 ^b	0.989
Median (Range)	60 (45 – 80)		62 (38 – 80)			(NS)
HBV						
Negative	20	66.7%	24	80%	1.364 ^a	0.243
Positive	10	33.3%	6	20%		(NS)
HCV						
Negative	10	33.3%	6	20%	1.364 ^a	0.243
Positive	20	66.7%	24	80%		(NS)

a: Chi-Square Test; b: Independent samples Student's t-test

Table 2 shows the Child Paugh score in all patients of the study: in SBP group 60% were child C, and 40% were Child B, while in non SBP group 66.7% were Child B

Table (2): Comparing cases with SBP and cases without SBP regarding Child Pugh score and classification.

Child Pugh score and classification	SBP group (N=30)		Without SBP group (N=30)		Test	p-value (Sig.)
	No.	%	No.	%		
Child Pugh class						
Child B	12	40%	20	66.7%	4.286 ^a	0.038
Child C	18	60%	10	33.3%		(S)
Child Pugh score						
Mean± SD	10.30±2.08		9.13±1.45		-2.296 ^c	0.022
Median (Range)	10 (7 – 15)		9 (7 – 12)			(S)

a: Chi-Square Test; c: Mann Whitney U test

Table 3 shows that there was positive correlation between some serum biomarkers level and SBP, they were found to be increased in SBP group: ESR, CRP, NLR were markedly increased among SBP group. Both combination of NLR and CRP were markedly increased together in SBP. Either Summation or multiplication of both ratios were found to be obviously elevated among SBP group.

Table (3): Comparing cases with SBP and cases without SBP regarding biomarkers of infection.

Biomarkers of infection	SBP group (N=30)	Without SBP group (N=30)	Test	p-value (Sig.)
ESR (mm/hr)			2.048 ^b	0.046
Median (Range)	40 (10–85)	25 (0–90)		(S)
CRP (mg/L)			-6.660 ^c	<0.001
Median (Range)	71.50 (36–206)	10 (1.20–20)		(HS)
NLR			-6.659 ^c	<0.001
Median (Range)	7.50 (1.60–12.80)	2.40 (1–2.90)		(HS)
NLR+CRP			-6.653 ^c	<0.001
Median (Range)	81.15 (42.60–220.40)	12.65 (2.70–22.60)		(HS)
NLR*CRP			6.653 ^c	<0.001
Median (Range)	697.50 (237.60–2966.40)	24.15 (1.80–52)		(HS)

Median and Range: non-parametric test

a: Chi-Square Test; b: Independent samples Student's t-test; c: Mann Whitney U test

A statistically significant split can be seen between the two groups in this table. In terms of the ascitic sample analysis parameters where: Patients with SBP had a dramatically elevated total leucocytic count, especially of neutrophils, proteins, and lactate dehydrogenase.

Table (4): Comparison between patients with SBP and patients without SBP regarding ascitic fluid biochemical analysis.

Ascitic fluid biochemical analysis.	SBP group (N=30)	Without SBP group (N=30)	Test	p-value (Sig.)
TLC (/cc)				
Median (Range)	1450 (500–5000)	175 (30–370)	-6.655 ^c	<0.001 (HS)
PNL (/cc)				
Median (Range)	900 (260–2500)	92.50 (20–200)	-6.656 ^c	<0.001 (HS)
Glucose (mg/dl)				
Median (Range)	100 (2–315)	112 (79–236)	-1.479 ^c	0.139 (NS)
Protein (mg/dl)				
Median (Range)	1069 (40–3143)	620 (138–1741)	-3.253 ^c	0.001 (S)
LDH (mg/dl)				
Median (Range)	108.50 (39–416)	50 (2–150)	-5.730 ^c	<0.001 (HS)

Median and Range: non-parametric test; c: Mann Whitney U test, PNL: polymorphnuclear leucocytes. LDH: lactate dehydrogenase.

We assessed NLR and compared patients with and without SBP for ascitic cirrhosis; the difference was statistically significant (p 0.001). The sensitivity of detecting SBP in cirrhotic patients was 95% when using a blood NLR cut-off value of >2.9, while the specificity was 88%.

Table (5): Diagnostic utility of the neutrophil-to-lymphocyte ratio (NLR) for patients with cirrhosis who have had spontaneous bacterial peritonitis (SBP); ROC curve analysis.

Neutrophil to Lymphocyte Ratio (NLR)	
Cut-off value	>2.9
Specificity (95% CI)	88% (80.0– 88)
Sensitivity (95% CI)	95% (80.0 – 95)
NPV (95% CI)	90%
PPV (95% CI)	92%
AUROC (95% CI)	0.85 (0.80 – 0.85)
Accuracy (95% CI)	92%
p-value (Sig.)	<0.001 (HS)

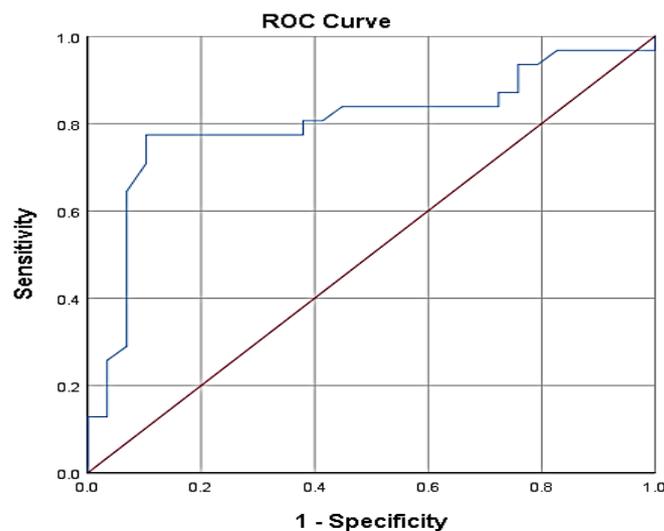


Figure (1): ROC curve of Diagnostic utility of the neutrophil-to-lymphocyte ratio (NLR) for patients with cirrhosis who have had spontaneous bacterial peritonitis (SBP).

The CRP levels of cirrhotic individuals with SBP were found to be significantly higher than those of patients without cirrhosis (p 0.001). The sensitivity and

specificity of a cut-off >15 mg/L for identifying SBP in cirrhotic patients were 92% and 85%, respectively.

Table (6): C-reactive protein (CRP) in cirrhotic individuals as a diagnostic tool for spontaneous bacterial peritonitis (SBP); ROC curve analysis.

C-reactive protein (CRP)	
Cut-off value	>15 mg/L
Specificity (95% CI)	85% (78.0– 85)
Sensitivity (95% CI)	92% (78.0 – 92)
NPV (95% CI)	88%
PPV (95% CI)	90%
AUROC (95% CI)	0.80 (0.75 – 0.80)
Accuracy	90%
p-value (Sig.)	<0.001 (HS)

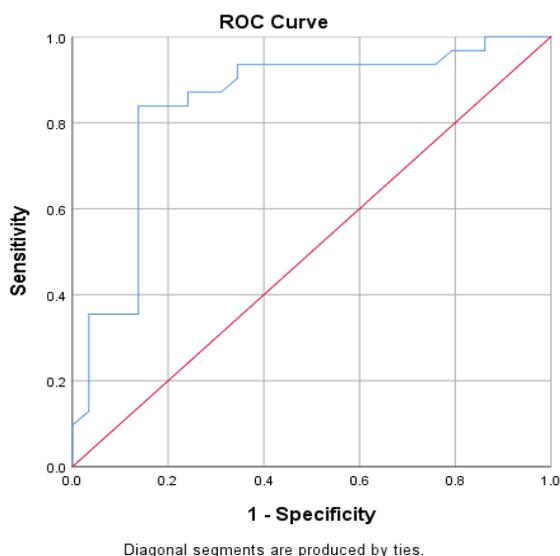


Figure (2): Diagnostic accuracy of C-reactive protein (CRP) for spontaneous bacterial peritonitis (SBP) in cirrhotic patients as shown by a receiver operating characteristic (ROC) curve.

The predictive power of NLR (at the cut of >2.9) in conjunction with CRP (at the cut of >15 mg/dl) for SBP was evaluated.

Table (7): Diagnosing spontaneous bacterial peritonitis (SBP) in cirrhotic patients using a ratio of neutrophils to lymphocytes (NLR) combined with C-reactive protein (CRP): ROC curve analysis.

NLR+CRP	
Cut-off value	>22.6
Specificity (95% CI)	92% (85.4 – 90)
Sensitivity (95% CI)	96% (87.4 – 96)
NPV (95% CI)	90%
PPV (95% CI)	92%
AUROC (95% CI)	0.89 (0.78 – 1.85)
Accuracy (95% CI)	95% (88.4 – 100)
p-value (Sig.)	<0.001 (HS)

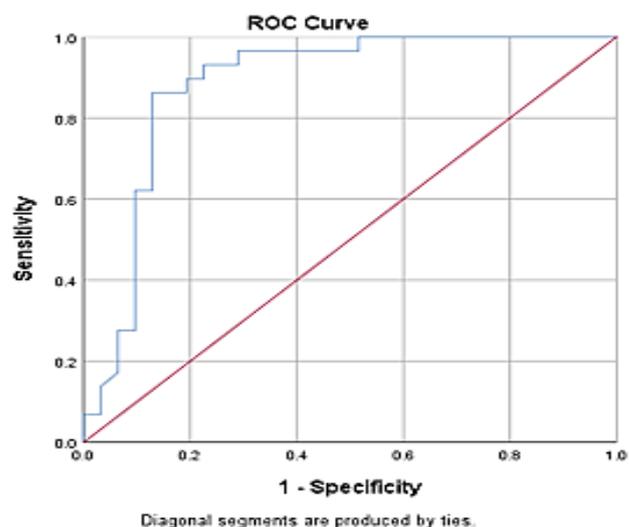


Figure (3): Neutrophil-to-lymphocyte ratio and C-reactive protein in the diagnosis of spontaneous bacterial peritonitis in patients with cirrhosis.

DISCUSSION

Ascites and cirrhosis are a lethal combination, and septic shock is a common consequence of cirrhosis. Early diagnosis and antimicrobial therapy have reduced the prevalence of SBP to about 20%. It is recommended that clinical vigilance, rapid diagnosis, and fast therapy be applied when caring for these individuals ⁽⁹⁾.

After considering the patient's MELD score and renal dysfunction, a 2.7-fold increase in the risk of in-hospital death is associated with delayed paracentesis in patients with SBP. Patients with cirrhosis and ascites may benefit from a diagnostic paracentesis performed within 12 hours of hospital admission, according to the results of a retrospective research conducted in the United States ⁽¹⁰⁾.

Some less invasive biomarkers, including the combination of NLR and CRP, have been established for the prediction of SBP. The neutrophil-to-lymphocyte ratio (NLR) in the blood is a useful indicator of overall immunological and inflammatory health. Prediction of ascitic fluid infection is reported using platelet indices and total white blood cell counts ⁽¹¹⁾.

When an inflammatory lesion forms in a living organism, C-reactive protein [CRP] levels increase in the blood. In response to a bacterial infection, macrophages release cytokines, which trigger the production of C-reactive protein (CRP) in the liver. Interleukin-1, interleukin-6, and tumor necrosis factor are examples of cytokines ⁽¹²⁾.

In this study, non-statistically significant differences were found between the two study groups in terms of age, sex, the underlying etiology of the cirrhosis (HBV or HCV), or the duration of the disease.

The results were nearly agreed with the study of **Baweja et al.** ⁽¹³⁾ who found no significant difference in age between infected and uninfected people. These

findings disprove the hypothesis that socioeconomic status is a major confounding factor.

In our study of 60 cirrhotic patients, 32 were classified as Child B, and 28 as Child C; we also stated that the proportion of SBP patients with severe cirrhosis increased dramatically, with around 60% being "Child C."

This was consistent with the results of **Paul et al.** ⁽¹⁴⁾ who demonstrated that 10-30% of cirrhotic patients also had SBP. Seventy percent of cirrhotic individuals with SBP fall into the Child Class C category. The incidence of SBP varies among these individuals, rising in those with more severe liver failure; this condition is also linked to a dismal prognosis in the long run.

NLR is a straightforward, noninvasive metric that may be measured on many patients to indicate their inflammatory condition. It demonstrates the connection between two distinct immune pathways and has been proposed as a measure of systemic inflammation. Subclinical inflammation is indicated by neutrophil-lymphocyte ratio (NLR), while the lymphocyte count shows the immune regulatory mechanism. A serious infection may be in its early stages if the peripheral blood shows an increase in neutrophils and a reduction in lymphocytes. Several studies have shown that NLR is useful in the clinic as a diagnostic indicator of bacterial infection ⁽¹³⁾.

In this study A cut-off value of blood NLR >2.9 on ROC curve had a specificity of 88% as well as sensitivity of 95% for SBP diagnosis in cirrhotic patients. CRP level differed significantly among cirrhotic patients diagnosed with SBP. A cut-off >15 mg/L had a sensitivity and specificity of 85% and 90 % respectively in diagnosing SBP in cirrhotic patients. Combination NLR and CRP had a cut-off >22.6 mg/L, has a sensitivity and specificity of 86%, 91 % respectively in SBP diagnosis among cirrhotic patients.

NLR's usefulness as a marker for spontaneous bacterial peritonitis has been the subject of numerous recent research, often in conjunction with CRP, a study by **Mousa and his colleagues** ⁽¹⁵⁾ which had analyzed NLR's contribution to SBP diagnosis alongside CRP. 180 cirrhotic patients with and without SBP were compared for NLR. Patients with SBP had a mean NLR of 4.5 (3.2-8.7) and patients without SBP had a mean NLR of 2.1 (1.6-2.6), both with a p value of 0.001 and a cut off value of >2.89. Patients with SBP also had a mean CRP of 48 (12-90) and patients without SBP had a mean CRP of 3.74 (2.3-5.2), both with a p value of <0.001. This study show agreement with the results found in the current study.

Another study done by **Baweja and his colleagues** ⁽¹³⁾ found that blood NLR >3.38 was shown to be a cut-off value for identifying SBP in patients with ascites, with a sensitivity of 94% and a specificity of 80% among those with the condition. Similarly, high-sensitivity C-reactive protein (hsCRP) was elevated compared to normal in both cases and controls, although

patients with and without SBP/CNNA did not differ significantly from one another statistically (p value=0.194).

Several investigations found an association between SBP and CRP elevations, prompting researchers to conclude that CRP levels may be used to predict SBP on their own ^(16,17).

The enzyme lactate dehydrogenase (LDH) can be found in a variety of tissues throughout the body. It's an enzyme that uses NAD⁺ as a hydrogen acceptor to catalyze the conversion of L-lactate to pyruvate ⁽¹⁸⁾. Therefore, either diffusion from the blood or release by dissolving AF neutrophils can account for the elevated LDH level found in infected ascitic fluid.

Ascitic fluid LDH was estimated in 150 patients over the course of a recent study conducted in the medical wards of a tertiary care hospital in North India. Ascitic fluid LDH was observed to be considerably elevated in SBP patients (p=0.001) ⁽¹⁹⁾.

The findings of the current study agreed with the previous study, A highly significant increase in ascitic LDH was found among patients with SBP with p-value <0.001.

Talaat et al. ⁽²⁰⁾ found that Both the neutrophil count and the lactate dehydrogenase level in the ascitic fluid of patients with spontaneous bacterial peritonitis were significantly greater than those of individuals with cirrhosis of the liver but no peritonitis symptoms (group II) (P-value 0.000 and 0.003, respectively), Patients in Group I had considerably lower levels of total proteins, albumin, and glucose (Pvalue 0.000, 0.028 and 0.021, respectively).

In similar, **Ahmed and colleagues** ⁽²¹⁾ observed that the ratio of ascitic fluid LDH to serum LDH was significantly different (p0.001) and that the ascitic fluid LDH level was significantly different (p0.001).

CONCLUSION

Combined NLR and CRP with cut of >2.9, and >15 mg/dl respectively could be used as a novel, non-invasive predictor for SBP diagnosis.

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Competing interests: Nil.

REFERENCES

1. **Fernandez J, Gustot T (2012):** Management of bacterial infections in cirrhosis. *J Hepatol.*, 56: 1-12.
2. **Jalan R, Fernandez J, Wiest R et al. (2014):** Bacterial infections in cirrhosis: a position statement based on the EASL Special Conference 2013. *J Hepatol.*, 60:1310-1324.
3. **Barreales M, Fernandez I (2011):** Spontaneous bacterial peritonitis. *Rev Esp Enferm.*, 103(5):255-63.
4. **Grabau C, Crago S, Hoff L et al. (2004):** Performance standards for therapeutic abdominal paracentesis. *Hepatology*, 40(2):484-8.
5. **Sproston N, Ashworth J (2018):** Role of C-Reactive Protein at Sites of Inflammation and Infection. *Frontiers*

- in *Immunology*, 9: 754. doi: 10.3389/fimmu.2018.00754.
6. **Xue T, Zhang L, Xie X *et al.* (2014):** Prognostic significance of the neutrophil-to-lymphocyte ratio in primary liver cancer: a meta-analysis. *PLoS One*, 9(5): e96072. doi: 10.1371/journal.pone.0096072
 7. **Avanzas P, Quiles J, Lopez De Sa E *et al.* (2004):** Neutrophil count and infarct size in patients with acute myocardial infarction. *Int J Cardiol.*, 97 (1):155-6.
 8. **Janum S, Søvsø M, Gradel K *et al.* (2011):** C-reactive protein level as a predictor of mortality in liver disease patients with bacteremia. *Scand J Gastroenterol.*, 46(12):1478-83.
 9. **Oladimeji A, Temi A, Adekunle A *et al.* (2013):** Prevalence of spontaneous bacterial peritonitis in liver cirrhosis with ascites. *The Pan African Medical Journal*, 15: 128. doi: 10.11604/pamj.2013.15.128.2702
 10. **Kim J, Tsukamoto M, Mathur A *et al.* (2014):** Delayed paracentesis is associated with increased in-hospital mortality in patients with spontaneous bacterial peritonitis. *Am J Gastroenterol.*, 109: 1436–1442.
 11. **Awad S, Ahmed E, Mohamed E (2020):** Role of Combined Blood Neutrophil- Lymphocyte Ratio and C-reactive Protein in Diagnosis of Spontaneous Bacterial Peritonitis. *Benha Journal of Applied Sciences*, 5: 43-49.
 12. **Papp M, Vitalis Z, Altorjay I *et al.* (2012):** Acute phase proteins in the diagnosis and prediction of cirrhosis associated bacterial infections. *Liver Int.*, 32(4):603-11.
 13. **Baweja A, Jhamb R, Kumar R *et al.* (2021):** Clinical utility of neutrophil lymphocyte ratio (nlr) as a marker of spontaneous bacterial peritonitis (sbp) in patients with cirrhosis-an exploratory study. *International Journal of Science and Research Archive*, 3(2):031-42.
 14. **Paul K, Kaur J, Kazal H (2015):** To Study the Incidence, Predictive Factors and Clinical Outcome of Spontaneous Bacterial Peritonitis in Patients of Cirrhosis with Ascites. *J Clin Diagn Res.*, 9(7): 9-12.
 15. **Mousa N, Besheer T, Abdel-Razik A *et al.* (2018):** Can combined blood neutrophil to lymphocyte ratio and C-reactive protein be used for diagnosis of spontaneous bacterial peritonitis? *Br J Biomed Sci.*, 75(2): 71–75.
 16. **Preto-Zamperlini M, Farhat S, Perondi M *et al.* (2014):** Elevated C-reactive protein and spontaneous bacterial peritonitis in children with chronic liver disease and ascites. *J Pediatr Gastroenterol Nutr.*, 58(1):96-8.
 17. **Kadam N, Acharya S, Shukla S *et al.* (2016).** Ascitic Fluid High Sensitive C-Reactive Protein (hs-CRP). A Prognostic Marker in Cirrhosis with Spontaneous Bacterial Peritonitis. *Journal of Clinical and Diagnostic Research*, 10: 20-24.
 18. **Ekpe E, Omotoso A (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.
 19. **Sandhya S, Loomba R, Loomba V *et al.* (2021):** Ascitic Fluid Lactate Dehydrogenase (LDH) - A Marker for Spontaneous Bacterial Peritonitis. *Journal, Indian Academy of Clinical Medicine*, 22(1-2):26-29.
 20. **Talaat A, Kamal E, Osman R *et al.* (2012):** Role of ascitic fluid C3 in spontaneous bacterial peritonitis, *Egyptian Journal of Medical Human Genetics*, 13: 81-85.
 21. **Ahmed S, Ahmed M, Khan S (2021):** Study of ascitic fluid lactate dehydrogenase (LDH): A marker for diagnosis of spontaneous bacterial peritonitis at a tertiary hospital. *MedPulse International Journal of Medicine*, 20(3): 194-197.