Journal of Health and Nutrition Research
Vol. 4, No. 2, 2025, pg. 815-821, https://doi.org/10.56303/jhnresearch.v4i2.497
Journal homepage: https://journalmpci.com/index.php/jhnr/index

e-ISSN: **2829-9760**

Evaluation of C-Reactive Protein, Neutrophil-To-Lymphocyte Ratio, and Absolute Neutrophil Count as Simple Diagnostic Markers for Spontaneous Bacterial Peritonitis

Ayu Sekarani Damana Putri[1]*, Supriono[2], Vera Diana Tonowidjojo[1], Junjun Fitriani[1], Gede Nanda Utama[1], Andi Alfia Muthmainah[1], Andi Nur Asrinawati[1]

[1] Faculty of Medicine, Tadulako University, Palu, Indonesia
[2] Faculty of Medicine, Brawijaya University, Malang, Indonesia

Corresponding Author Email: ayusekaranidp@gmail.com

ORIGINAL ARTICLES

Submitted: 7 June 2025

Accepted: 4 July 2025

Keywords:
Spontaneous Bacterial Peritonitis; Neutrophil-To-Lymphocyte-Ratio; Diagnostic Tools; Liver Cirrhosis

ABSTRACT

Spontaneous bacterial peritonitis (SBP) is a serious complication of liver cirrhosis with high morbidity and mortality. Early diagnosis is crucial; however, ascitic fluid analysis is invasive and often yields a low culture positivity rate. This study aimed to evaluate the diagnostic performance of C-reactive protein (CRP), absolute neutrophil count (ANC), and neutrophil-to-lymphocyte ratio (NLR) as non-invasive markers for the early detection of SBP. A prospective observational study was conducted on 90 liver cirrhosis patients with ascites undergoing diagnostic paracentesis at Saiful Anwar Hospital, Indonesia. CRP, ANC, and NLR levels were compared between the SBP and non-SBP groups. Receiver operating characteristic (ROC) curves were used to assess diagnostic accuracy, and logistic regression identified independent predictors. NLR and ANC levels were significantly higher in SBP patients ($p = 0.004$ and $p = 0.033$, respectively), while the difference in CRP levels was not statistically significant ($p = 0.372$). NLR showed the best performance (sensitivity 81.8%, specificity 68.2%) at a cut-off of 6.8 and was independently associated with SBP (OR = 11.09, $p = 0.019$). ANC had similar sensitivity but lower specificity, while CRP demonstrated the weakest predictive value. In conclusion, NLR and ANC are emerging as promising, simple, and cost-effective non-invasive biomarkers for the early screening of SBP in cirrhotic patients, particularly in settings where paracentesis is not readily available. NLR, in particular, holds significant diagnostic value. Conversely, CRP may be less reliable in this patient population. Larger multicenter studies are needed to validate these findings

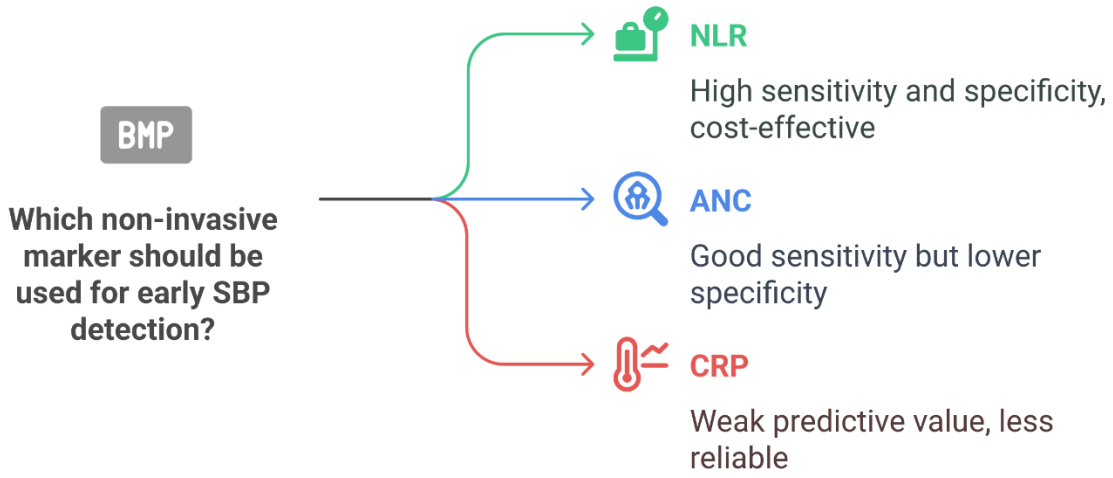
Key Messages:

- The neutrophil-to-lymphocyte ratio (NLR) demonstrates superior diagnostic accuracy over absolute neutrophil count (ANC) and C-reactive protein (CRP), emerging as a promising, simple, and cost-effective non-invasive biomarker for the early screening of spontaneous bacterial peritonitis in patients with liver cirrhosis.

Access this article online

Quick Response Code

GRAPHICAL ABSTRACT



INTRODUCTION

Cirrhotic individuals have impaired defensive mechanisms against microorganisms, resulting in diminished bacterial clearance(1). Bacterial infections are a significant complication of cirrhosis, accounting for 25%-46% of hospitalizations due to acute decompensation events in patients with cirrhosis(2). Spontaneous bacterial peritonitis (SBP) is a severe bacterial infection occurring in the ascitic fluid of liver cirrhotic patients without a discernible source of infection. The prevalence of SBP in cirrhotic patients varies, ranging from 3.5% in outpatients to 36% in hospitalized patients(1,3). Early screening is essential because delayed diagnosis can lead to high mortality rates, with reported mortality rates as high as 40% (4).

The current gold standard for SBP diagnosis is diagnostic paracentesis followed by ascitic fluid analysis. SBP is confirmed by a polymorphonuclear leukocyte (PMN) count of ≥250 cells/mm^3, regardless of positive culture results. However, this approach has limitations: culture-positive rates remain low (30-50%), particularly in patients who have received previous antibiotics, and the process is invasive, time-consuming, and operator-dependent(5,6). Furthermore, logistical challenges in resource-constrained settings may delay paracentesis and microbiological examination, increasing the risk of treatment delays (7). To overcome these challenges, researchers have increasingly concentrated on creating simple, quick, and low-cost marker methods for SBP screening and diagnosis.

Systemic inflammatory indicators such as C-reactive protein (CRP), absolute neutrophil count (ANC), and neutrophil-to-lymphocyte ratio (NLR) have emerged as promising early detection tools for SBP. CRP is an acute-phase reactant produced by the liver in response to infection and inflammation, whereas ANC is a direct marker of circulating neutrophils—key effectors in bacterial defense(8–11). The NLR, calculated from a standard blood count, reflects the balance between the neutrophil-driven inflammatory response and the lymphocyte-mediated immune regulation(12). NLR, in particular, has been established as a robust prognostic and diagnostic marker in various other acute bacterial infections, including sepsis and pneumonia, suggesting its potential applicability in SBP (13–15). While a few preliminary studies have explored NLR for diagnosing SBP (13), their results have been inconsistent, and a definitive optimal cut-off value has not been established, highlighting a critical research gap.

This study aims to assess the diagnostic performance of CRP, ANC, and NLR in detecting SBP and to develop non-invasive ways to improve clinical practice, particularly in locations where quick paracentesis or ascitic fluid analysis is not readily available.

METHODS

This prospective observational study aimed to evaluate the diagnostic value of ANC, NLR, and CRP as early markers for spontaneous bacterial peritonitis (SBP) in patients with liver cirrhosis and ascites.

https://doi.org/10.56303/jhnresearch.v4i2.497

The study was conducted at Hospitals in Palu and Malang, Indonesia during 2022-2025, enrolling adult patients (≥18 years) with clinically, radiologically, or histologically confirmed liver cirrhosis who presented with ascites and underwent diagnostic paracentesis. Patients were excluded if they had secondary peritonitis, ongoing systemic infections outside the peritoneum, active malignancy, hematological disorders affecting leukocyte profiles, or if they had received antibiotic treatment prior to paracentesis.

Upon enrollment, demographic data, clinical characteristics, and laboratory parameters were collected. Blood samples were analyzed for complete blood count (CBC) with differential to determine ANC and calculate NLR, as well as for serum CRP levels. Diagnostic paracentesis was performed within six hours of hospital admission or clinical indication, with ascitic fluid analyzed for cell count and differential, culture and sensitivity, and biochemical parameters. SBP was diagnosed based on an ascitic fluid polymorphonuclear neutrophil (PMN) count of ≥250 cells/mm^3, with or without positive ascitic fluid culture.(16) Descriptive statistics were utilized to summarize the patient features. ANC, NLR, and CRP were compared between SBP and non-SBP groups using Mann-Whitney U-test. Diagnostic accuracy was determined using receiver operating characteristic (ROC) curve analysis, which calculated the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for each biomarker. Furthermore, multivariate logistic regression was used to find independent predictors of SBP. A p-value of <0.05 indicated statistical significance.

RESULTS

Characteristic of Subjects

Table 1 show the baseline clinical and laboratory characteristics of the study subjects, stratified into Spontaneous Bacterial Peritonitis (SBP) (n=47) and Non-SBP (n=47) groups. Demographically, the SBP was slightly older and predominantly male (81.80%) compared to the Non-SBP group (63.60%). While Hepatitis B was the leading etiology of liver disease in both cohorts, alcoholic liver disease was observed exclusively in patients with SBP. Clinically, the SBP group presented with markers indicative of more severe systemic inflammation and organ dysfunction. This is evidenced by a substantially higher mean white blood cell (WBC) count (15,672 vs. 10,054.71 /µL) and lower hemoglobin (8.68 vs. 10.76 g/dL). Furthermore, patients with SBP demonstrated signs of more advanced liver decompensation, including lower mean serum albumin (2.41 vs. 2.62 g/dL) and elevated AST (178.96 vs. 102.57 U/L). A critical distinction was observed in renal function, with mean urea (103.46 vs. 61.69 mg/dL) and creatinine (2.17 vs. 1.20 mg/dL) levels being markedly higher in the SBP group, suggesting a high prevalence of concurrent acute kidney injury.

Table 1 Baseline Characteristic of Subjects

Characteristic	SBP Group (n=47)	Non-SBP Group (n=47)
Age, years (mean ± SD)	56.28 ± 9.52	53.1 ± 7.40
Male, n (%)	81.80%	63.60%
Female, n (%)	18.20%	36.40%
Etiology of Liver Disease		
- Hepatitis B, n (%)	33 (73.3%)	38 (80.8%)
- Hepatitis C, n (%)	6 (13.3%)	6 (13.3%)
- Alcoholic Liver Disease, n (%)	3 (6.4%)	0 (0%)
- Others, n (%)	5 (11.1%)	3 (6.3%)
Hemoglobin, g/dL (mean ± SD)	8.68 ± 2.14	10.76 ± 3.59
WBC, /µL (mean ± SD)	15672 ± 8364.50	10054.71 ± 6951.54
Platelet, /µL (mean ± SD)	218184.44 ± 109274.36	197143.17 ± 158408.53
AST, U/L (mean ± SD)	178.96 ± 118.68	102.57 ± 49.39
ALT, U/L (mean ± SD)	74.78 ± 54.18	76.15 ± 20.49
Albumin, g/dL (mean ± SD)	2.41 ± 0.50	2.62 ± 1.74
Urea, mg/dL (mean ± SD)	103.46 ± 74.62	61.69 ± 23.91
Creatinine, mg/dL (mean ± SD)	2.17 ± 1.38	1.20 ± 0.41

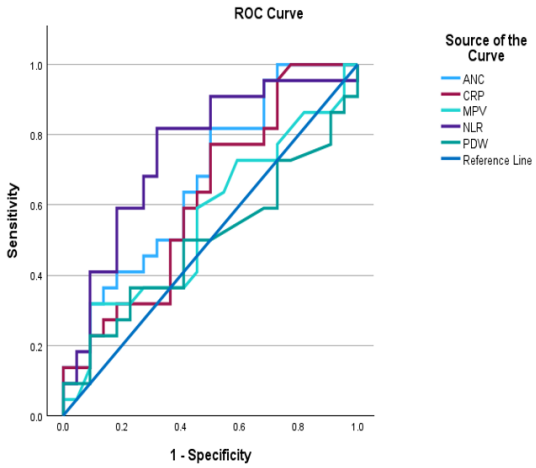
https://doi.org/10.56303/jhnresearch.v4i2.497

The comparison of inflammatory markers between groups demonstrated that patients with ascitic SBP had higher NLR, ANC, and CRP levels compared to non-SBP patients. The mean NLR was significantly higher in the SBP group (28.05±0.52) compared to the non-SBP (16.95 ± 07.42, p = 0.004) group. Similarly, the mean ANC was significantly elevated in SBP patients (14.65 ± 9.75 × 10^3/µL) compared to non-SBP patients (9.32 ± 5.74 × 10^3/µL, p = 0.033). Although CRP levels were higher in the SBP group (24.23 mg/L) than in the non-SBP group (20.77 mg/L), the difference was not statistically significant (p = 0.372) (Table 2).

Table 2. Comparison of Inflammatory Markers Between SBP and Non-SBP Groups

Marker	SBP Group (n=47)	Non-SBP Group (n=47)	p-value
NLR (mean ± SD)	28.05 ± 05.23	16.95 ± 07.42	0.004*
ANC (×10^3/µL, mean ± SD)	14.65 ± 9.75	9.32 ± 5.74	0.033*
CRP (mg/L, mean)	24.23	20.77	0.372
PMN Count in Ascitic Fluid (cells/mm^3, mean ± SD)	23326.20 ± 144292.98	368.49 ± 975.46	0.0023*

Among the markers assessed, NLR demonstrated the highest sensitivity (81.8%) and a specificity of 68.2% at a cut-off value of 6.8. CRP exhibited a sensitivity of 77.3% and a lower specificity of 50% with a cut-off value of 4.57. ANC showed a sensitivity of 81.8% but similarly limited specificity at 50% using a cut-off of 8.4 × 10^3/µL (Figure 1).



Variable	Sensitivity	Specificity	Cut-Off
NLR	81.8%	68.2%	6.8
CRP	77.3%	50%	4.57
ANC	81.8%	50%	8.4

Figure 1. Sensitivity, specificity and Cut-Off points of NLR, CRP, ANC

Table 3. Correlation between Inflammatory Markers and SBP Status

Marker	p-value	OR	95% CI	R^2
NLR	0.019	11.09	1.45–82.75	0.412
CRP	0.351	2.3	0.39–14.09	
ANC	0.845	0.824	0.12–5.68	

Statistical analysis revealed that NLR was significantly associated with the presence of SBP (p = 0.019), with an odds ratio (OR) of 11.09 (95% CI: 1.45–82.75) and an R^2 value of 0.412, indicating a strong predictive relationship. In contrast, CRP and ANC did not show statistically significant associations with SBP status (p = 0.351 and p = 0.845, respectively) (Table 3). Comparatively, NLR demonstrated superior diagnostic performance over CRP and ANC, underscoring its potential as a reliable and readily available screening tool for early SBP detection in cirrhotic patients.

DISCUSSION

SBP is one of the leading causes of mortality among people with end-stage liver disease(5). The clinical presentation of SBP ranges greatly, from asymptomatic individuals to those with fever, abdominal

https://doi.org/10.56303/jhnresearch.v4i2.497

discomfort, acute renal damage, abnormal liver function tests, and hepatic encephalopathy(17). While ascitic fluid analysis is critical for detecting SBP, conducting a paracentesis presents various hurdles. As an invasive procedure, paracentesis carries inherent risks, such as haemorrhage and intestinal perforation, often necessitating safety measures like ultrasound guidance to minimize complications(18). Thrombocytopenia and coagulopathy, which are frequent in cirrhosis, enhance the procedural risk, restricting its usage, especially in resource-limited settings(18,19). As a result, diagnostic paracentesis is routinely underused, potentially leading to misdiagnosis, delayed therapy, or ineffective antibiotic administration. This emphasizes the need for a quick, non-invasive, and simply applied biomarker to help predict SBP in cirrhotic patients with ascites.

This study demonstrated that NLR and ANC were significantly elevated in patients with ascites-SBP compared to those with ascites without SBP. NLR showed the strongest association with SBP status, with a sensitivity of 81.8% and specificity of 68.2% at a cut-off value of 6.8. ANC also displayed significant diagnostic potential, although its specificity was lower. While CRP levels were higher in SBP patients, the difference was not statistically significant. Our analysis found no significant correlation between these serum inflammatory markers and ascitic fluid PMN counts.

The findings regarding NLR are consistent with previous studies that have highlighted NLR as a reliable marker for infections, including SBP, in cirrhotic patients(20). NLR is a simple parameter to easily assess the inflammatory status of a subject. Infection can cause the medulla to produce more neutrophils and reduce lymphocyte counts by apoptosis if the source of infection is not completely eliminated(21). Similarly, ANC was significantly higher among SBP patients in this study, corroborating findings that demonstrated ANC as a strong diagnostic marker with high sensitivity and specificity(11). For instance, Sheta et al. (2022) showed that an ANC >2.804 could discriminate SBP from non-SBP with a sensitivity of 84% and a specificity of 78% (22). Our NLR cut-off aligns with findings from Mousa et al., who reported that an NLR value >2.89 distinguished SBP from non-SBP cases with 80.3% sensitivity and 88.9% specificity, supporting its role as an accessible diagnostic tool(20). Neutrophils play a key defensive role through phagocytosis, degranulation, and reactive oxygen species (ROS) production, following chemokine-directed migration to infection sites(12). Cirrhosis is associated with increased bacterial translocation, especially across the intestinal barrier, even without active infection. Despite this heightened inflammatory activity, cirrhosis impairs overall immune competence due to reduced expression of toll-like receptors and cytopenia, making patients more vulnerable to infections(23,24). Lymphopenia, commonly due to hypersplenism from portal hypertension, also contributes to immune imbalance. This shift in white blood cell composition—particularly an elevated neutrophil-to-lymphocyte ratio—reflects both immune activation and suppression, as seen in various disease states(25).

Conversely, the results regarding CRP were less definitive. While some have suggested that CRP may be a useful adjunct in diagnosing infections in cirrhosis, others reported that its diagnostic accuracy decreases in advanced liver disease, possibly explaining the nonsignificant results observed in this cohort(26–29). As reported by Pieri et al., baseline CRP in cirrhotic patients is already elevated, and in the setting of infection, the increase in CRP may be blunted in those with more severe liver dysfunction (30,31).

This study had several limitations. A primary limitation was the relatively small sample size, which may have introduced selection bias and reduced the statistical power for subgroup analyses. The single-center design may limit the generalizability of the results. Potential confounding factors, such as the severity of liver disease (e.g., MELD scores), concomitant infections, and the timing of paracentesis relative to symptom onset, were not fully controlled for. Additionally, missing data and unmeasured variables may have influenced the diagnostic accuracy estimates.

.

CONCLUSION

The significant association between elevated NLR and SBP supports its use as a simple, rapid, and inexpensive screening tool for the early identification of SBP in cirrhotic patients presenting with ascites. Future multicenter studies with larger sample sizes are needed to validate the diagnostic value of NLR, ANC, and CRP in diverse patient populations. Prospective studies that incorporate comprehensive liver disease severity assessments and standardized timing of paracentesis could help refine existing prediction

https://doi.org/10.56303/jhnresearch.v4i2.497

models.

FUNDING

This research received no external funding.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Huang CH, Lee CH, Chang C. Spontaneous Bacterial Peritonitis in Decompensated Liver Cirrhosis—A Literature Review. Livers. 2022;2(3):214–32.
2. Piano S, Morando F, Angeli P. Spontaneous Bacterial Peritonitis in Patients with Cirrhosis and Ascites. 2011;559–75.
3. Bello KE, Irekeola AA, Al-Mhanna SB, Oseni OML, Omebije AP, Shueb RH, dkk. Prevalence of Spontaneous Bacterial Peritonitis (SBP) in Hepatitis B (HBV), and Hepatitis C (HCV) Liver Cirrhosis: A Systematic Review and Meta-Analysis. Healthc Switz. 2023;11(2):1–17.
4. Kim JH, Choe WH, Kwon SY, Yoo B chul. Prognosis of Spontaneous Bacterial Peritonitis in Hepatocellular Carcinoma Patients. J Korean Med Sci. 28 November 2018;33(52):e335.
5. Numan L, Elkafrawy A, Kaddourah O, Brotherton T, Saeed L, Zafar Y, dkk. Spontaneous Bacterial Peritonitis: We Are Still Behind. Cureus. 2020;12(4):0–5.
6. Yin X, Qin E, Song R, Bao X, Dong J, Hou W, dkk. Diagnostic model for spontaneous bacterial peritonitis in cirrhotic patients with ascites: a multicenter cohort study. Eur J Gastroenterol Hepatol. 2024;36(11):1319–28.
7. Alaniz C, Regal RE. Spontaneous Bacterial Peritonitis. Pharm Ther. April 2009;34(4):204–10.
8. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. Front Immunol. 2018;9(APR):1–11.
9. Ngwa DN, Agrawal A. Structure-function relationships of C-reactive protein in bacterial infection. Front Immunol. 2019;10(FEB).
10. Levinson T, Wasserman A. C-Reactive Protein Velocity (CRPv) as a New Biomarker for the Early Detection of Acute Infection/Inflammation. Int J Mol Sci. 2022;23(15).
11. Sheta T, El-mesery A, Salama K, El-Wakeel N, El-Emam O, Habib A. Diagnostic utility of absolute neutrophil count as a new marker of spontaneous bacterial peritonitis; multicenter study. Med J Viral Hepat. 2022;6.3(3):12–8.
12. Burn GL, Foti A, Marsman G, Patel DF, Zychlinsky A. The Neutrophil. Immunity. 2021;54(7):1377–91.
13. Abudeif A, Elbadry MI, Ahmed NM. Validation of the diagnostic accuracy of neutrophil to lymphocyte ratio (NLR) and mean platelet volume (MPV) in cirrhotic patients with spontaneous bacterial peritonitis. Egypt Liver J. 13 Februari 2023;13(1):9.
14. Drăgoescu AN, Pădureanu V, Stănculescu AD, Chiuțu LC, Tomescu P, Geormăneanu C, dkk. Neutrophil to Lymphocyte Ratio (NLR)—A Useful Tool for the Prognosis of Sepsis in the ICU. Biomedicines. 30 Desember 2021;10(1):75.
15. Efrina D, Priyanto H, Andayani N, Arliny Y, Yanti B. Neutrophil To Lymphocyte Ratio as A Marker of COVID-19 Disease Severity in Banda Aceh. J Respirologi Indones. 27 November 2021;41(4):272–8.
16. PPHI. Penatalaksanaam Hipertensi Portal. 2021;1–95.
17. Marciano S, Díaz JM, Dirchwolf M, Gadano A. Spontaneous bacterial peritonitis in patients with cirrhosis: incidence, outcomes, and treatment strategies. Hepatic Med Evid Res. 2019;Volume 11:13–22.
18. Sideris A, Patel P, Charles HW, Park J, Feldman D, Deipolyi AR. Imaging and clinical predictors of spontaneous bacterial peritonitis diagnosed by ultrasound-guided paracentesis. Bayl Univ Med Cent Proc. 2017;30(3):262–4.

https://doi.org/10.56303/jhnresearch.v4i2.497

19. Raco J, Bufalini J, Dreer J, Shah V, King L, Wang L, dkk. Safety of abdominal paracentesis in hospitalised patients receiving uninterrupted therapeutic or prophylactic anticoagulants. Intern Med J. 2024;55:77–83.
20. Mousa N, Besheer T, Abdel-Razik A, Hamed M, Deiab AG, Sheta T, dkk. Can combined blood neutrophil to lymphocyte ratio and C-reactive protein be used for diagnosis of spontaneous bacterial peritonitis? Br J Biomed Sci. 2018;75(2):71–5.
21. Moreau N, Wittebole X, Fleury Y, Forget P, Laterre PF, Castanares-Zapatero D. Neutrophil-to-Lymphocyte Ratio Predicts Death in Acute-on-Chronic Liver Failure Patients Admitted to the Intensive Care Unit: A Retrospective Cohort Study. Shock. 2018;49(4):385–92.
22. Sheta T, El-mesery A, Salama K, El-Wakeel N, El-Emam O, Habib A. Diagnostic utility of absolute neutrophil count as a new marker of spontaneous bacterial peritonitis; multicenter study. Med J Viral Hepat. 2022;6.3(3):12–8.
23. Engelmann C, Clària J, Szabo G, Bosch J, Bernardi M. Pathophysiology of decompensated cirrhosis: Portal hypertension, circulatory dysfunction, inflammation, metabolism and mitochondrial dysfunction. J Hepatol. 2021;75(Suppl 1):S49–66.
24. Van der Merwe S, Chokshi S, Bernsmeier C, Albillos A. The multifactorial mechanisms of bacterial infection in decompensated cirrhosis. J Hepatol. 2021;75:S82–100.
25. Seyedi SA, Nabipoorashrafi SA, Hernandez J, Nguyen A, Lucke-Wold B, Nourigheimasi S, dkk. Neutrophil to Lymphocyte Ratio and Spontaneous Bacterial Peritonitis among Cirrhotic Patients: A Systematic Review and Meta-analysis. Can J Gastroenterol Hepatol. 2022;2022.
26. Verma R, Satapathy SK, Bilal M. Procalcitonin and C-reactive protein in the diagnosis of spontaneous bacterial peritonitis. Transl Gastroenterol Hepatol. 2022;7(October).
27. Abdel-wahab AA. Serum and Ascitic Fluid High Sensitive C Reactive Protein As Prognostic Marker In Patients With Spontaneous Bacterial Peritonitis. Zagazig Univ Med J. 2019;0(0):0–0.
28. Barutcu S. Lymphocyte to Monocyte Ratio and C-Reactive Protein Combination as the Best Simple Predictor of Treatment Response in Cirrhotic Patients With Culture Negative Neutrocytic Ascites. SiSli Etfal Hastan Tip Bul Med Bull Sisli Hosp. 2021;56(1):77–83.
29. Kalvandi G, Haghighat M, Honar N, Shahramian I, Delaramnasab M, Bazi A. A comparative study on ascetic fluid biochemical markers in cirrhotic children with and without spontaneous bacterial peritonitis: A cross-sectional observation. J Compr Pediatr. 2019;10(3).
30. Pieri G, Agarwal B, Burroughs AK. C-reactive protein and bacterial infection in cirrhosis. Ann Gastroenterol. 2014;27(2):113–20.
31. Evaluation of C Reactive Protein Levels in Spontaneous Bacterial Peritonitis in Patients with Decompensated Chronic Liver Disease. 2020;8(2):40–5.

https://doi.org/10.56303/jhnresearch.v4i2.497