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***Original Research Article***

# Accuracy of Combined Neutrophil to Lymphocyte Ratio and C-Reactive Protein for Diagnosis of Spontaneous Bacterial Peritonitis Among Cirrhotic Patients

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**Abstract:** *Spontaneous bacterial peritonitis (SBP) is a serious complication of liver cirrhosis associated with high morbidity and mortality. While ascitic fluid analysis remains the diagnostic gold standard, it is invasive and not always feasible. There is a need for simple, non-invasive, and cost-effective alternatives to diagnose SBP early, especially in resource-limited settings.* ***Objective:*** *To determine the diagnostic accuracy of combined neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) levels in diagnosing SBP among cirrhotic patients, using ascitic fluid PMN count as the gold standard.* ***Methods:*** *This descriptive cross-sectional study was conducted over six months from April 2024 to September 2024, at the Department of Medicine, Ibn-e-Siena Hospital, Multan. A total of 131 cirrhotic patients with ascites were included through non-probability consecutive sampling. All patients underwent diagnostic paracentesis. SBP was confirmed if PMN count in ascitic fluid was ≥250/mm³. NLR and CRP were assessed using venous blood samples. A cut-off of NLR ≥2.9 and CRP >11.3 mg/dL was used to define SBP positivity. Diagnostic indices were calculated using 2×2 contingency tables.* ***Results:*** *Out of 131 patients, 91 (69.5%) were confirmed to have SBP by ascitic fluid analysis. The combination of NLR and CRP showed a sensitivity of 94.5%, specificity of 85.0%, positive predictive value of 93.5%, negative predictive value of 87.2%, and overall diagnostic accuracy of 91.6%. Stratified analysis revealed consistent diagnostic performance across gender and duration of liver disease.* ***Conclusion:*** *Combined NLR and CRP are accurate, readily available, and non-invasive diagnostic markers for SBP in cirrhotic patients. Their application may complement or, in selected cases, substitute ascitic fluid analysis, improving early detection and outcomes in resource-limited settings such as Pakistan.*

**Keywords:** Spontaneous bacterial peritonitis, cirrhosis, neutrophil-to-lymphocyte ratio, C-reactive protein, non-invasive diagnostics, ascites

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## Introduction

Chronic liver disease (CLD), particularly cirrhosis, represents a major healthcare burden in Pakistan, contributing significantly to morbidity, hospital admissions, and mortality. Cirrhosis is commonly caused by hepatitis B and C, alcohol use, and non-alcoholic steatohepatitis in the region, and is frequently complicated by the accumulation of ascitic fluid in the peritoneal cavity (1). Among the most severe and life-threatening complications of decompensated cirrhosis is spontaneous bacterial peritonitis (SBP), an infection of previously sterile ascitic fluid in the absence of any identifiable intra-abdominal source. SBP is responsible for rapid clinical deterioration and is associated with high short-term mortality if not diagnosed and treated promptly (2).

In the context of Pakistan, where cirrhosis prevalence is high due to chronic viral hepatitis, the incidence of SBP is rising, particularly among patients presenting in tertiary care centers with advanced liver disease (3). Timely diagnosis of SBP is imperative to initiate empirical antibiotic therapy and prevent complications such as renal failure, hepatic encephalopathy, and sepsis. The gold standard for SBP diagnosis is the detection of polymorphonuclear neutrophil (PMN) counts ≥250 cells/mm³ in ascitic fluid obtained via diagnostic paracentesis (4). However, this procedure is invasive, painful, technically demanding in some patients (e.g., with coagulopathy), and carries risks such as bowel perforation, hemorrhage, persistent ascitic leakage, and peritonitis (5). Moreover, in some clinical settings across Pakistan, timely access to experienced staff or laboratory support for immediate ascitic analysis may be limited.

Therefore, there is an unmet need for simple, rapid, low-cost, and non-invasive tests that can aid clinicians in the early diagnosis of SBP, especially in high-risk cirrhotic patients. Two such promising biomarkers are the neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP). These biomarkers are readily available from routine blood investigations, widely accessible even in secondary and district-level hospitals across Pakistan, and provide indirect yet reliable indicators of systemic inflammation (6).

NLR is derived from a complete blood count (CBC) and reflects the balance between the body's innate (neutrophils) and adaptive (lymphocytes) immune responses. An elevated NLR indicates an inflammatory shift toward neutrophil predominance, which is common in bacterial infections such as SBP (7). CRP, on the other hand, is an acute-phase protein synthesized in the liver in response to interleukin-6 and tumor necrosis factor-alpha during systemic infections. Elevated CRP levels correlate with bacterial inflammation and have been shown to be significantly higher in SBP compared to non-SBP ascites (8).

Several recent international studies have demonstrated the diagnostic utility of NLR and CRP in identifying SBP among cirrhotic patients. In an Egyptian cohort, Elhendawy et al. found that a combined NLR >2.9 and CRP >15 mg/L predicted SBP with 95% sensitivity and 88% specificity (9). A study by Mousa et al. on 180 cirrhotic patients with ascites showed that combined NLR and CRP values had a diagnostic accuracy of 96.3% (10). These findings suggest that combining both markers improves diagnostic precision compared to using them independently.

Despite growing international evidence, there is a significant gap in local data from Pakistan evaluating the accuracy of these combined biomarkers. The diagnostic landscape in Pakistani public hospitals is often challenged by delays in obtaining paracentesis results and variable technical expertise. Hence, the integration of NLR and CRP as a combined, non-invasive surrogate diagnostic approach could have substantial implications in resource-constrained settings like ours.

Incorporating these markers could reduce reliance on invasive procedures, minimize diagnostic delays, and expedite treatment decisions—particularly critical in Pakistan where cirrhotic patients often present late with severe decompensation (11).

Moreover, stratifying biomarker performance across clinical variables such as age, gender, and duration of liver disease may offer personalized diagnostic thresholds and improve triage protocols in emergency and internal medicine departments. A 2023 meta-analysis underscored that the diagnostic accuracy of inflammatory biomarkers like NLR is influenced by these demographic and disease-related factors (12). Thus, assessing the stratified utility of these markers can help optimize their use in Pakistan's diverse clinical settings.

In Pakistan, the lack of standardized guidelines on SBP diagnosis in primary and secondary care settings often leads to delays in treatment, empirical antibiotic misuse, and increased hospital stays. Developing evidence-based protocols for SBP diagnosis using non-invasive tools such as NLR and CRP could revolutionize initial management in both rural and urban centers.

The rationale for this study stems from the urgent need to validate the use of combined NLR and CRP in diagnosing SBP among cirrhotic patients in a Pakistani population. If proven accurate, these markers—already widely used and economical—can serve as effective alternatives or adjuncts to ascitic PMN count in settings where paracentesis is delayed or contraindicated. This could lead to earlier diagnosis, faster treatment initiation, reduced procedural risks, and ultimately, better clinical outcomes. The findings of this study have the potential to guide future diagnostic pathways, reduce healthcare costs, and improve care quality for patients with decompensated cirrhosis in Pakistan.

**Methodology**

This descriptive cross-sectional study was conducted at the Department of Medicine, Ibn-e-Siena Hospital, Multan, over a duration of six months from April 2024 to September 2024, following the approval of the synopsis by the institutional ethics review committee. The study aimed to evaluate the diagnostic accuracy of combined neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) levels for the diagnosis of spontaneous bacterial peritonitis (SBP) in patients with liver cirrhosis and ascites. SBP is a potentially life-threatening complication of decompensated cirrhosis, and timely diagnosis is essential to reduce morbidity and mortality. Given the invasive nature and associated complications of diagnostic paracentesis, the study sought to assess whether the combination of NLR and CRP—both routine, non-invasive, and cost-effective blood markers—could serve as a reliable diagnostic alternative.

A total of 131 patients were enrolled in the study using non-probability consecutive sampling. The sample size was calculated using a single population proportion formula based on a sensitivity of 95.1%, specificity of 96.3%, a 70% prevalence of SBP among cirrhotic patients, a 95% confidence level, and an absolute precision of 6%. Inclusion criteria consisted of patients aged 18 to 65 years, of either gender, who were known cases of liver cirrhosis with clinical or ultrasound-confirmed ascites and presenting to the outpatient department. Patients with malignant ascites, ongoing skin or chest infections, secondary bacterial peritonitis due to surgical causes, recent antibiotic use, or those already on SBP prophylaxis were excluded based on history, clinical examination, and medical records.

Upon enrollment, informed consent was obtained from all participants. Demographic information such as age and gender, along with clinical data including duration of chronic liver disease (CLD), were recorded in a predesigned proforma. All patients underwent an aseptic ascitic tap, and the fluid samples were sent for polymorphonuclear neutrophil (PMN) count and culture sensitivity. A PMN count of $\geq 250/mm^3$ in the absence of an alternative source of intra-abdominal infection was used to confirm SBP, which served as the gold standard for diagnostic comparison.

Simultaneously, five milliliters of venous blood was drawn aseptically from each patient. Two milliliters were placed in an EDTA vacutainer for complete blood count (CBC) analysis, including neutrophil and lymphocyte counts to calculate the NLR. The remaining three milliliters were collected in a plain vacutainer, allowed to clot for approximately 30 minutes, then centrifuged at 1200 rpm to separate the serum. The serum was analyzed for CRP concentration. All hematological and biochemical analyses were performed in a single laboratory using standardized procedures to ensure consistency and minimize inter-laboratory variability.

For the purpose of this study, patients were labelled SBP-positive on NLR if the ratio was ≥2.9, and SBP-positive on CRP if the level was >11.3 mg/dL, as defined in the operational definitions. Combined SBP positivity was noted when both NLR and CRP met the aforementioned criteria. Data were entered and analyzed using SPSS version 23. Continuous variables such as age, CLD duration, NLR, and CRP levels were assessed for normality using the Shapiro-Wilk test and expressed as mean ± standard deviation or median with interquartile range, as appropriate. Categorical variables like gender and SBP status were summarized using frequencies and percentages.

A 2x2 contingency table was constructed using SBP confirmed by ascitic PMN count as the gold standard and compared against SBP diagnosed by the combined NLR and CRP criteria. From this table, diagnostic parameters including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated. The diagnostic performance was further stratified by age, gender, and duration of chronic liver disease, and post-stratification diagnostic indices were recalculated to identify any significant variability across subgroups. All statistical tests were two-tailed, and a p-value $\leq 0.05$ was considered statistically significant.

**Results**

This descriptive cross-sectional study included 131 patients diagnosed with liver cirrhosis and ascites, recruited from the Department of Medicine, Ibn-e-Siena Hospital, Multan, over a 6-month period. The mean age of patients was 49.6 ± 10.7 years, with a male predominance. The average duration of chronic liver disease (CLD) was 24.2 ± 12.5 months. The majority of patients presented with a history of decompensated cirrhosis and clinical suspicion of spontaneous bacterial peritonitis (SBP).

Table 1 shows that SBP was confirmed in 69.5% of cirrhotic patients via ascitic PMN count, which is consistent with the prevalence estimated in the sample size calculation.

Table 2 demonstrates elevated mean NLR and CRP levels in this cirrhotic population, with the majority meeting the defined cutoffs for SBP based on combined biomarker criteria.

These findings confirm high sensitivity and specificity of the combined NLR and CRP method for diagnosing SBP in cirrhotic patients, in line with international studies.

Table 4 shows comparable diagnostic accuracy across genders, slightly higher among females.

Table 5 indicates better diagnostic performance of the combined biomarkers in patients with longer-standing liver disease (>24 months), possibly due to a more pronounced inflammatory response.

SBP prevalence in this Pakistani cohort was 69.5%, aligning with international prevalence figures for decompensated cirrhosis.Combined use of NLR (≥2.9) and CRP (>11.3 mg/dl) showed 94.5% sensitivity, 85.0% specificity, and 91.6% diagnostic accuracy.Stratified analyses confirmed consistent diagnostic performance across gender and duration of liver disease subgroups.

**Table 1: Demographic and Clinical Characteristics of Study Participants (n = 131)**

| Variable | Frequency (%) / Mean ± SD |
|---|---|
| Age (years) | 49.6 ± 10.7 |
| Gender | |
| Male | 86 (65.6%) |
| Female | 45 (34.4%) |
| Duration of CLD (months) | 24.2 ± 12.5 |
| SBP confirmed on ascitic tap | 91 (69.5%) |
| SBP negative on ascitic tap | 40 (30.5%) |

**Table 2: Laboratory Parameters – NLR and CRP Levels Among Participants (n = 131)**

| Parameter | Mean ± SD | Range |
|---|---|---|
| Neutrophil-to-Lymphocyte Ratio (NLR) | 4.9 ± 2.8 | 1.2 – 14.6 |
| C-reactive Protein (CRP, mg/dl) | 19.4 ± 8.7 | 3.1 – 48.5 |
| Combined NLR ≥ 2.9 and CRP >11.3 | 84 (64.1%) | – |

**Table 3: Diagnostic Accuracy of Combined NLR and CRP Using Ascitic Fluid PMN Count as Gold Standard (n = 131)**

| SBP by Ascitic Tap (Gold Standard) | SBP by Combined NLR & CRP Positive | SBP by Combined NLR & CRP Negative | Total |
|---|---|---|---|
| Positive (≥250 PMNs/mm³) | 86 | 5 | 91 |
| Negative (<250 PMNs/mm³) | 6 | 34 | 40 |
| Total | 92 | 39 | 131 |
| | • Sensitivity: 86 / (86 + 5) = 94.5%<br>• Specificity: 34 / (34 + 6) = 85.0%<br>• Positive Predictive Value (PPV): 86 / (86 + 6) = 93.5%<br>• Negative Predictive Value (NPV): 34 / (34 + 5) = 87.2%<br>• Overall Accuracy: (86 + 34) / 131 = 91.6% | | |

**Table 4: Stratified Diagnostic Accuracy by Gender**

| Gender | Sensitivity (%) | Specificity (%) | Accuracy (%) |
|---|---|---|---|
| Male | 93.7% | 84.2% | 91.0% |
| Female | 95.8% | 86.7% | 92.5% |

**Table 5: Stratified Diagnostic Accuracy by Duration of Chronic Liver Disease**

| Duration of CLD (months) | Sensitivity (%) | Specificity (%) | Accuracy (%) |
|---|---|---|---|
| ≤ 24 months (n = 67) | 92.1% | 82.4% | 89.6% |
| > 24 months (n = 64) | 96.8% | 87.5% | 93.7% |

**Discussion**

This study evaluated the diagnostic accuracy of combined neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) in detecting spontaneous bacterial peritonitis (SBP) among patients with liver cirrhosis and ascites, using ascitic PMN count as the gold standard. The results showed a sensitivity of 94.5%, specificity of 85.0%, positive predictive value (PPV) of 93.5%, negative predictive value (NPV) of 87.2%, and overall diagnostic accuracy of 91.6%, indicating that the combination of these two blood-based markers is highly effective in diagnosing SBP in the Pakistani population.

Our findings are consistent with previous studies conducted internationally. Elhendawy et al., in an Egyptian cohort, reported that a combined NLR >2.9 and CRP >15 mg/L could diagnose SBP with 95% sensitivity and 88% specificity (13). These values closely mirror our own results, reinforcing the validity of using these cut-off points in clinical practice. Similarly, Mousa et al. studied 180 cirrhotic patients with ascites and reported that combined NLR and CRP yielded 95.1% sensitivity and 96.3% specificity, with an overall diagnostic accuracy exceeding 95% (14). Although our specificity was slightly lower (85.0%), this may reflect population-based variations or differences in underlying comorbidities.

Another comparable study by Kumar et al. in India also highlighted the value of NLR and CRP in SBP detection. They observed that an NLR >3.0 had 90% sensitivity and CRP >10 mg/dL had 92% specificity. The combination improved overall predictive accuracy in differentiating infectious from non-infectious ascites (15). These findings are aligned with our stratified analysis, where both short-term (≤24 months) and long-term (>24 months) cirrhosis patients showed high sensitivity and accuracy, suggesting that these markers perform consistently regardless of disease chronicity.

Our study also demonstrated that the diagnostic performance of the combined biomarkers was consistent across both genders, with slightly higher accuracy among female patients (92.5%) compared to males (91.0%). This is comparable to the results reported by Abdel-Razik et al., who found no significant gender-related variability in the performance of inflammatory markers in SBP diagnosis (16). This suggests that gender may not significantly impact the inflammatory response markers used in this context.

The superiority of using combined NLR and CRP over individual markers is supported by immunopathological rationale. Neutrophilia reflects acute inflammatory response, while lymphopenia may indicate immune suppression in cirrhotics, making the NLR a composite marker of immune dysregulation (17). Simultaneously, CRP is a well-established acute-

phase protein synthesized by hepatocytes, and its elevation in SBP signifies hepatic response to infection. The synergistic diagnostic capability of these markers is particularly important in resource-limited settings such as Pakistan, where delays in paracentesis or laboratory processing can hinder timely diagnosis and management.

Moreover, these findings gain relevance in light of current limitations in SBP diagnosis in our clinical environment. Ascitic tap, although considered the gold standard, is invasive and often delayed due to coagulopathy or lack of trained personnel. Therefore, a reliable blood-based diagnostic approach such as the combined NLR-CRP method may serve as a valuable initial screening tool. This could enable earlier initiation of empirical antibiotic therapy and potentially reduce SBP-related morbidity and mortality, especially in tertiary care hospitals with high patient turnover.

Our results also align with a meta-analysis by Huang et al., which confirmed that NLR and CRP have high diagnostic value in identifying SBP. The pooled sensitivity and specificity for combined markers were 92% and 89%, respectively, further validating our findings within a broader clinical context (18).

Despite its strengths, our study has limitations. Firstly, it was conducted at a single center, which may limit the generalizability of the findings. Secondly, the study did not assess the prognostic value of these biomarkers post-treatment or their correlation with clinical outcomes such as hospital stay or mortality. Future multicenter prospective studies with follow-up data are recommended to evaluate the longitudinal predictive value of these markers in SBP.

## Conclusion

In conclusion, this study confirms that combined NLR and CRP are accurate, accessible, and cost-effective markers for diagnosing SBP in cirrhotic patients with ascites in Pakistan. Their use may complement or even substitute invasive diagnostics in select cases, particularly in peripheral or overloaded healthcare settings. Integrating these markers into diagnostic algorithms could enhance early SBP detection, reduce reliance on invasive procedures, and improve patient outcomes.

## Declarations

**Data Availability statement**

All data generated or analysed during the study are included in the manuscript.

**Ethics approval and consent to participate**

Approved by the department concerned. (IRBEC-IBS-2399-24)

**Consent for publication**

Approved

**Funding**

Not applicable

## Conflict of interest

The authors declared the absence of a conflict of interest.

## Author Contribution

**AA** (PGR)
*Manuscript drafting, Study Design,*
**FS** (HO)
*Review of Literature, Data entry, Data analysis, and drafting article.*
**UF** (HO)
*Conception of Study, Development of Research Methodology Design,*
**ZN** (PGR)
*Study Design, manuscript review, critical input.*
*All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.*

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