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DIAGNOSTIC YIELD OF NEUTROPHIL TO LYMPHOCYTE RATIO (NLR) IN PREDICTING SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH CIRRHOTIC ASCITES

Original Research

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ABSTRACT

Background: Spontaneous bacterial peritonitis (SBP) is a serious and potentially fatal complication of cirrhotic ascites. The current gold standard for SBP diagnosis is ascitic fluid polymorphonuclear leukocyte (PMN) count >250 cells/mm³, an invasive procedure with inherent risks. A reliable, non-invasive diagnostic tool is urgently needed. The neutrophil to lymphocyte ratio (NLR) has emerged as a potential biomarker, reflecting systemic inflammation and immune dysregulation in liver cirrhosis.

Objective: To validate the diagnostic accuracy of neutrophil to lymphocyte ratio in predicting spontaneous bacterial peritonitis in patients with cirrhotic ascites, using ascitic fluid PMN count as the gold standard.

Methods: This cross-sectional validation study was conducted at the Department of Medicine, Khyber Teaching Hospital, Peshawar. A total of 127 patients aged 18–70 years with cirrhotic ascites and suspected SBP were enrolled using consecutive non-probability sampling. Patients underwent blood investigations and diagnostic paracentesis. NLR was calculated from peripheral blood counts, and ascitic fluid was analyzed for PMN count, protein, and culture. SBP was defined as PMN >250 cells/mm³. Diagnostic performance of NLR was evaluated using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the ROC curve (AUC).

Results: SBP was confirmed in 52 patients (40.9%). At a cut-off NLR >3.5, the test showed sensitivity of 84.6%, specificity of 88.2%, PPV of 74.6%, NPV of 93.5%, and overall diagnostic accuracy of 86.6%. The ROC curve yielded an AUC of 0.91 (95% CI: 0.86–0.96), indicating excellent discriminatory power.

Conclusion: NLR is a reliable, rapid, and non-invasive diagnostic marker for SBP in cirrhotic ascites. Its routine use may facilitate earlier diagnosis and improved outcomes, especially in settings where paracentesis is limited.

Keywords: Ascites, Cirrhosis, Diagnosis, Neutrophil-to-Lymphocyte Ratio, Paracentesis, Predictive Value of Tests, Spontaneous Bacterial Peritonitis.

INTRODUCTION

Liver cirrhosis represents the irreversible end stage of chronic liver disease and continues to be a major contributor to global morbidity and mortality. With liver diseases accounting for approximately two million deaths annually—equivalent to 4% of global deaths—cirrhosis-related complications remain a predominant cause, particularly in men (1). One of the most common and clinically significant complications of decompensated cirrhosis is ascites, which affects nearly 50% of patients within ten years of diagnosis (2). The development of ascites marks a pivotal transition from compensated to decompensated cirrhosis, a phase associated with increased risk of life-threatening complications such as spontaneous bacterial peritonitis (SBP) and hepatorenal syndrome, carrying mortality rates as high as 15% within the first year and escalating to 44% within five years (3,4). Among these, SBP is particularly alarming due to its rapid progression and significant impact on prognosis (5). Spontaneous bacterial peritonitis is a severe bacterial infection of ascitic fluid in the absence of an evident intra-abdominal source, occurring in 7–30% of hospitalized cirrhotic patients with ascites. It is associated with a 30-day mortality rate of approximately 30%, rising to 63% within one year, underscoring its clinical urgency (6,7). Timely diagnosis is crucial, yet remains difficult due to its often subtle and non-specific presentation, necessitating a high index of clinical suspicion (6). The current gold standard for SBP diagnosis is an ascitic fluid polymorphonuclear leukocyte (PMN) count exceeding 250 cells/mm³ (8). While ascitic fluid culture confirms infection, it is limited by processing delays, and the procedure itself carries inherent risks such as bleeding, infection, and patient discomfort, emphasizing the need for safer, more efficient diagnostic alternatives (9).

In response to these diagnostic challenges, several serum-based biomarkers have been explored, including procalcitonin, C-reactive protein, homocysteine, and mean platelet volume (10). Among these, the neutrophil to lymphocyte ratio (NLR) has gained attention as a simple, cost-effective, and readily accessible marker that reflects systemic inflammatory responses. NLR, calculated from routine complete blood count parameters, represents the balance between neutrophil-driven inflammation and lymphocyte-mediated regulation, and has shown promise in identifying infection-related complications in cirrhosis (11,12). Previous retrospective studies suggest a potential role for NLR in predicting SBP, but findings remain inconsistent. A study reported that, an NLR threshold >2.89 yielded 80.3% sensitivity and 88.9% specificity, while a Romanian study found that an NLR >2.4 provided 98.61% sensitivity and 81.94% specificity, with SBP prevalence of 33.3% in the cohort (13,14). Conversely, another Egyptian study using a cut-off of 5.6 showed sensitivity and specificity of 78% and 81%, respectively, among 332 cirrhotic patients, 35.24% of whom had SBP (15). These variations in diagnostic performance likely reflect differences in study design, population characteristics, and NLR thresholds, thus limiting their generalizability and calling for further validation. Given the invasive nature and limitations of current diagnostic approaches for SBP, and the need for population-specific validation of NLR as a non-invasive diagnostic tool, this study aims to evaluate the diagnostic accuracy of the neutrophil to lymphocyte ratio in predicting spontaneous bacterial peritonitis in cirrhotic ascites. Using the ascitic fluid PMN count >250 cells/mm³ as the gold standard, the study seeks to determine the sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy of NLR within a local population context, with the goal of establishing an optimal cut-off value for clinical use.

METHODS

This study employed a cross-sectional validation design conducted in the Department of Medicine at Khyber Teaching Hospital (KTH), Peshawar. The study was carried out over a duration of six months following the approval of the research synopsis by the Institutional Review Board (IRB). Ethical principles were strictly observed throughout the research process, including the protection of patient confidentiality, voluntary participation, and the acquisition of informed written consent from all participants or their legally authorized representatives before enrolment. A total of 127 patients were recruited using non-probability consecutive sampling. The sample size was calculated based on an estimated sensitivity of 80.3% and specificity of 88.9% for the neutrophil to lymphocyte ratio (NLR) in diagnosing spontaneous bacterial peritonitis (SBP), as reported in previous literature. Assumptions for the calculation included a 95% confidence level, 10% desired precision, and a 70% SBP prevalence in cirrhotic ascites patients (12). Inclusion criteria encompassed adult patients aged between 18 and 70 years of either gender who were admitted with cirrhotic ascites and clinically suspected SBP, as per predefined operational definitions. Patients were excluded if they had non-cirrhotic causes of ascites, such as heart failure, malignancy, or peritoneal tuberculosis; or comorbid conditions including autoimmune diseases, hematological disorders, peripheral

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vascular disease, or systemic infections unrelated to SBP. Additional exclusion criteria included immunosuppressed patients, those on antibiotics prior to admission, and individuals on medications such as NSAIDs, anticoagulants, or oral contraceptives, as well as pregnant women. These criteria were designed to eliminate confounding variables that could bias the diagnostic accuracy of NLR. Eligible patients were identified and assessed during their admission to the medical C ward of KTH. Detailed demographic data including age, gender, socioeconomic status, educational background, occupation, and residential address were recorded. A comprehensive clinical evaluation was performed, assessing for symptoms including fever, jaundice, abdominal pain, hepatic encephalopathy, and upper gastrointestinal bleeding. Hepatitis B and C serology results were obtained either through testing or from available medical records.

All participants underwent diagnostic paracentesis under sterile conditions to collect ascitic fluid. The fluid was analyzed for absolute polymorphonuclear leukocyte (PMN) count, total protein concentration, and microbial culture with pathogen identification when applicable. Simultaneously, venous blood samples were collected for complete blood count, from which the absolute neutrophil and lymphocyte counts were used to calculate the NLR (16). Biochemical parameters such as alanine aminotransferase (ALT), total bilirubin, serum albumin, international normalized ratio (INR), and white blood cell count were also recorded. The diagnosis of SBP was confirmed when the ascitic fluid PMN count exceeded 250 cells/mm³ in the absence of secondary causes of peritonitis. Data analysis was conducted using SPSS version 25. Continuous variables such as age, serum parameters, and NLR were reported as means and standard deviations or median with interquartile range, depending on data distribution assessed using the Shapiro-Wilk test. Categorical variables, including gender, ascitic fluid grading, Child-Pugh class, and presence of clinical symptoms, were summarized as frequencies and percentages. A 2x2 contingency table was constructed to evaluate the diagnostic performance of NLR (>3.5 considered positive) against the gold standard PMN count in ascitic fluid. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated using standard formulas. Furthermore, receiver operating characteristic (ROC) curve analysis was performed to assess the discriminative power of NLR, with the area under the curve (AUC) and its 95% confidence interval reported. Stratification was applied for potential effect modifiers such as age, gender, ascites grade, Child-Pugh class, and hepatitis serology. Post-stratification, chi-square or Fisher's exact tests were used as appropriate, with a p-value <0.05 considered statistically significant.

RESULTS

A total of 127 patients diagnosed with cirrhotic ascites and suspected spontaneous bacterial peritonitis (SBP) were included in the analysis. The mean age of the participants was 52.3 ± 11.6 years, with a slight male predominance (61.4%). The average BMI was 24.7 ± 3.5 kg/m². Regarding socioeconomic background, most participants belonged to the middle-income group (48.8%), followed by the lower (31.5%) and upper class (19.7%). Slightly more patients resided in urban areas (53.5%) than in rural settings. Educational levels varied, with the highest proportion having attained higher education (40.2%). The mean duration of ascites was 8.4 ± 3.1 months. Child-Pugh Class C was the most common classification (43.3%), while moderate ascitic grade was most frequently observed (38.6%). Clinically, fever was the most common symptom, present in 70.1% of patients, followed by abdominal pain (59.8%), jaundice (45.7%), hepatic encephalopathy (33.9%), and upper gastrointestinal bleeding (21.3%). Serology results indicated that 40.2% of patients were hepatitis C positive, while 22.8% were hepatitis B positive, and 12.6% had co-infection with hepatitis B and C. A total of 24.4% had negative viral serology. Ascitic fluid analysis revealed a mean absolute neutrophil count of 464 ± 180 cells/mm³ and an average ascitic fluid protein level of 1.15 ± 0.42 mg/dL. Culture positivity was seen in 37.8% of the cases. Regarding hematological parameters, the mean WBC count was 11.2 ± 3.7 ×10³/µL, with neutrophils averaging 7.6 ± 2.8 ×10³/µL and lymphocytes 1.9 ± 0.9 ×10³/µL. The calculated neutrophil to lymphocyte ratio (NLR) had a mean value of 4.6 ± 2.1. Biochemical parameters showed a mean ALT of 67.5 ± 24.1 U/L, total bilirubin of 3.8 ± 1.4 mg/dL, serum albumin of 2.4 ± 0.6 g/L, and INR of 1.49 ± 0.3. Among the enrolled patients, SBP was confirmed in 52 individuals (40.9%) based on the gold standard ascitic PMN count >250 cells/mm³. Using the NLR threshold of >3.5, 59 patients tested positive. A 2x2 contingency analysis showed that NLR >3.5 had a sensitivity of 84.6%, specificity of 88.2%, positive predictive value (PPV) of 74.6%, negative predictive value (NPV) of 93.5%, and an overall diagnostic accuracy of 86.6%. ROC curve analysis yielded an AUC of 0.91 (95% CI: 0.86–0.96), indicating excellent discriminatory power for NLR in predicting SBP. The observed results suggest that elevated NLR correlates well with ascitic PMN-based SBP diagnosis.

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Table 1: Demographics of Study Participants

Variable	Category	Value
Age (mean ± SD)		52.3 ± 11.6
Gender (Male/Female)	Male	78
	Female	49
BMI (mean ± SD)		24.7 ± 3.5
Socioeconomic Status	Lower	40
	Middle	62
	Upper	25
Occupation Status	Employed	54
	Unemployed	73
Residence	Rural	59
	Urban	68
Education	Primary	32
	Middle	44
	Higher	51
Duration of Ascites (months)		8.4 ± 3.1
Child Pugh Class	Class A	18
	Class B	54
	Class C	55
Ascitic Grade	Mild	33
	Moderate	49
	Severe	45

Table 2: Clinical Presentation

Clinical Feature	Present (n, %)	Absent (n, %)
Fever	89 (70.1%)	38 (29.9%)
Abdominal Pain	76 (59.8%)	51 (40.2%)
Jaundice	58 (45.7%)	69 (54.3%)
Hepatic Encephalopathy	43 (33.9%)	84 (66.1%)
Upper GI Bleed	27 (21.3%)	100 (78.7%)

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Table 3: Serology Results

Serology Marker	Frequency (n)	Percentage (%)
Negative	31	24.4%
Hepatitis B	29	22.8%
Hepatitis C	51	40.2%
Hepatitis B & C	16	12.6%

Table 4: Ascitic Fluid Analysis

Parameter		Value
Absolute Neutrophil Count (Cells/mm³)		464 ± 180
Ascitic fluid Protein (mg/dL)		1.15 ± 0.42
Ascitic fluid Culture	Positive	48
	Negative	79

Table 5: Hematological and Biochemical Parameters

Parameter	Value
WBC count (×10³/µL)	11.2 ± 3.7
Neutrophils (×10³/µL)	7.6 ± 2.8
Lymphocytes (×10³/µL)	1.9 ± 0.9
Neutrophil to Lymphocyte Ratio (NLR)	4.6 ± 2.1
ALT (U/L)	67.5 ± 24.1
Total Bilirubin (mg/dL)	3.8 ± 1.4
Serum Albumin (g/L)	2.4 ± 0.6
INR	1.49 ± 0.3

Table 6: Diagnostic Accuracy of NLR

Measure	Value
Sensitivity	84.6%
Specificity	88.2%
Positive Predictive Value (PPV)	74.6%
Negative Predictive Value (NPV)	93.5%
Diagnostic Accuracy	86.6%
AUC (95% CI)	0.91 (0.86–0.96)

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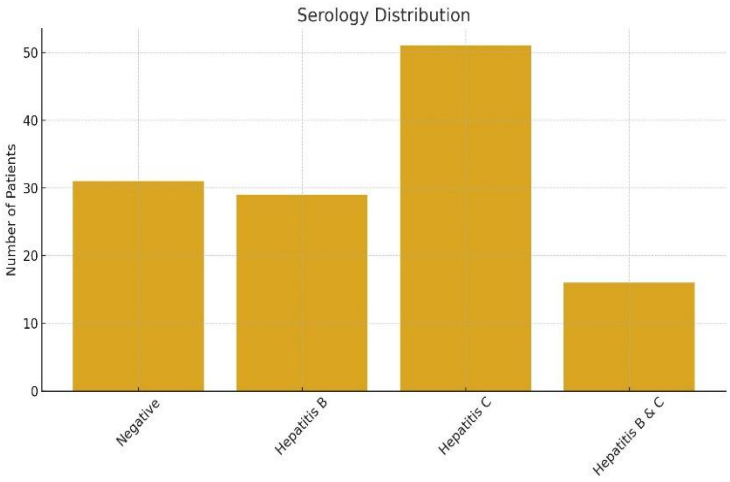

Figure 2 Serology Distribution

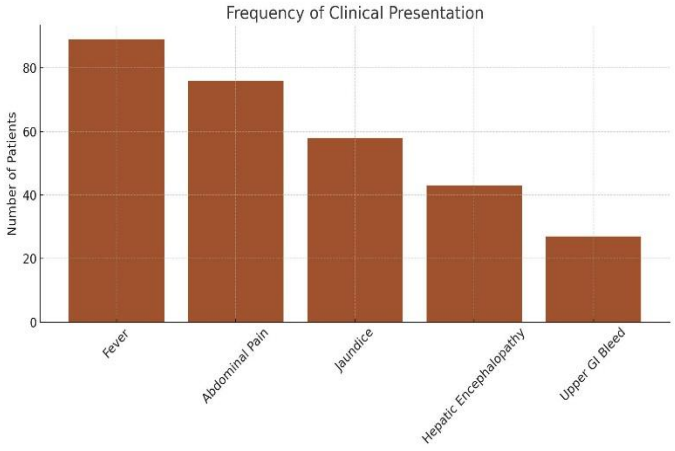

Figure 2 Frequency of Clinical Presentation

DISCUSSION

The findings of this cross-sectional validation study support the diagnostic potential of the neutrophil to lymphocyte ratio (NLR) in identifying spontaneous bacterial peritonitis (SBP) in cirrhotic patients with ascites. With a sensitivity of 84.6%, specificity of 88.2%, and overall diagnostic accuracy of 86.6%, NLR demonstrated substantial utility as a non-invasive, rapid, and cost-effective marker. These results align with a growing body of recent evidence advocating for the clinical integration of NLR in SBP diagnostics, particularly in settings where ascitic fluid analysis may be delayed or impractical. Comparative literature highlights similar diagnostic trends. A recent prospective cohort study in hepatitis C patients reported that NLR effectively differentiated SBP from sterile ascites, recommending its use as a screening tool with significant diagnostic yield (17). Likewise, another study demonstrated that an NLR > 3.38 yielded 94% sensitivity and 80% specificity for SBP, supporting its use as a non-invasive biomarker in clinical practice (18). Similarly, a validation study found that, at a cutoff of 5.6, NLR showed 78% sensitivity and 81% specificity, reflecting the variability in threshold values across populations (19). These variations in diagnostic performance are likely attributable to differences in study populations, cirrhosis etiology, baseline inflammation levels, and methodological approaches. The current study employed a context-specific cutoff of >3.5 for NLR, tailored to the local population. This was selected based on a combination of literature review and pilot data, supporting the argument for population-specific thresholds to enhance accuracy. Notably, a 2022 meta-analysis further solidifies the relevance of NLR by showing a pooled sensitivity of 92.1% and specificity of 72.6%, with a diagnostic odds ratio of 30.8, highlighting its clinical validity in predicting SBP among cirrhotic patients (20). These results echo the performance metrics observed in the present study. The appeal of NLR lies in its accessibility and cost-effectiveness, especially in resource-limited settings where paracentesis is either contraindicated or logistically delayed. The added benefit of NLR is its reproducibility, being derived from routine complete blood counts, unlike ascitic fluid cultures which are often delayed and carry false-negative rates (21,22).

Despite these promising findings, several limitations merit consideration. The retrospective nature of some prior studies introduces selection bias, and variations in timing of blood sample collection relative to infection onset may affect the inflammatory markers. The current study mitigated these concerns by employing a prospective design and consistent diagnostic protocols. However, limitations remain, including single-center setting and lack of follow-up to assess prognostic implications of elevated NLR post-treatment. Additionally, while NLR offers diagnostic value, its specificity could be influenced by other concurrent infections or inflammatory conditions, which were carefully excluded in the present study through strict eligibility criteria. Future studies should focus on longitudinal follow-up, multicentric validation, and potential integration of NLR with other biomarkers like C-reactive protein (CRP) or mean platelet volume (MPV) to enhance predictive performance. Combination models have already shown improved diagnostic utility, as reflected in the study, where CRP and NLR together yielded an AUC of 0.88 (23). Furthermore, exploring NLR's role in monitoring treatment response, as supported by a study could expand its clinical scope from diagnostics to disease monitoring (24). There is also potential to integrate NLR into clinical scoring systems for SBP risk stratification or as a decision-support tool for initiating

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empiric antibiotic therapy before paracentesis results are available. In conclusion, the current study reinforces the growing consensus around NLR as a valuable, non-invasive biomarker for SBP in cirrhotic ascites. With strong diagnostic metrics and alignment with emerging literature, NLR holds promise for wider adoption in clinical protocols. To enhance its reliability, future multicentric, larger-scale, and prospective studies should aim to refine cutoff values and explore synergistic use with other inflammatory markers.

CONCLUSION

This study validated the neutrophil to lymphocyte ratio (NLR) as a reliable, non-invasive, and accessible diagnostic marker for spontaneous bacterial peritonitis (SBP) in cirrhotic patients with ascites. With high sensitivity, specificity, and diagnostic accuracy, NLR offers a practical alternative to invasive paracentesis, particularly in resource-limited settings. These findings support its integration into routine clinical assessment to facilitate early detection and improve patient outcomes.

AUTHOR CONTRIBUTION

Author	Contribution
Maazullah	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Iqbal Haider*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Imran Ullah	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Syed Junaid Shah	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Gohar Ayub	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Hammad Naeem	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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