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Original Research Article

To Determine Peripheral Blood Neutrophil to Lymphocyte Ratio as a Pridictive Markar of Mortality and Morbidity in Patient with Hemorrhagic Stroke

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Abstract:

Background and Objectives: Peripheral blood neutrophil-to-lymphocyte ratio (NLR) has recently emerged as a prognostic biomarker in many disease states. The aim of this study was to evaluate the diagnostic utility of NLR to predict poor functional outcomes in patients with hemorrhagic stroke and to compare it with the intracranial hemorrhage (ICH) score.

Materials and methods: Patients who presented to the emergency department with clinical features suggestive of stroke were evaluated with computed tomography (CT) brain to identify ICH. The ICH scores and NLR were estimated at the time of admission. Modified Rankin Scale (mRS) score equal to or greater than 3 at 90 days was used to define poor functional outcomes (major disability or death). Receiver operating characteristic (ROC) curve was plotted with NLR and the ICH score to analyze and compare their discriminative ability to predict poor functional outcomes.

Conclusion: In patients with hemorrhagic stroke, NLR at admission is a good predictor of functional outcomes at 90 days. When compared to the ICH score, NLR is more sensitive but less specific in predicting poor functional outcomes.

Keywords: Functional outcomes, Hemorrhagic stroke, Intracranial hemorrhage, Modified Rankin scale, Neutrophil-to-lymphocyte ratio..

Introduction

Hemorrhagic strokes are caused by rupture of a blood vessel resulting in bleeding into the cerebral parenchyma with or without extension into the ventricles. They account for 10–20% of all strokes.[1] Intracranial hemorrhage (ICH) has high mortality and morbidity in spite of recent advances in medical intensive care and neurosurgical interventions. Approx 6 million deaths and more than 10% over all deaths every year world wide about 40% of all stroke deaths are due to hemorrhagic stroke the inflammatory mediators release after ICH including p selectin, cytokines , chemokines, protease. These fore all brain cells and peripheral immune cells (such as neutrophils and lymphocytes are major factors for post stroke inflammation, Release of chemical mediators related to more tissue damage and poor neurological outcome, At the same time stroke could trigger a special immunosuppressive stage, Such as the neutrophils activation leads to decrease in lymphocytes count, Several meta analysis that indicate increase NLR is a negative prognostic indicator in acute stroke and spontaneous ICH, The study by sun et ai has failed to determine between NLR association and functional outcomes or mortality in ICH. So our aim to conduct a compreshensive evaluation of relationship between baseline NLR and hemorrhagic stroke.

Objectives

To identify the role of NLR as a indicator for prognosis in patients with hemorrhagic stroke and to compare it with the ICH score to predict mortality and morbidity outcome.

Material and method

This Prospective, Observational Study will be conducted on 100 patients admitted in icu at Indira Gandhi Institute of Medical Sciences, Patna. After

obtaining Institutional research and ethical committee approval.

Inclusion criteria

- Within 24hrs of onset of stroke symptoms
- Age greater then 18yrs
- Evidence of hemorrhagic stroke in Ct brain

Exclusion Criteria

*current on anti coagulant medication
*prior stroke
*Trauma

Sample size 100 data regarding baseline demographic and ICH score. At presentation taken all vitals parameters like pulse, BP,Spo2, respiration, GCS, collected and documented the values of absolute neutrophil count ANC and absolute lymphocyte count ALC were obtained from the complete blood count results at admission and NLR is calculated for each patient at presentations .the study end point is mortality morbidity predict at 90days. It was assessed by mobile phone conversation and using modified Renkin scale (mRS) patient having mRS greater than or equal to 3 were taken underf poor outcome.

Statistical analysis

Categorical and quantitative variables wiil be expressed as frequency % and mean+_ standard deviation (SD), respectively. Descriptive statistics such as mean +_ SD, median with interquartile range (IQR), minimum, and maximum will be used to describe quantitative parameters. Receiver operating characristic (ROC) graphs were plotted, and the area under the curve (AUC) would be calculated to assess diagnostic accuracy of NLR and the ICH score in detecting poor outcomes and to assess the optimal cutoff scores. Sensitivity , specificity , positive predictive value (PPV), negative predictive value (NPV), and accuracy would be calculated . for all statistical interpretations. Statistical analysis will be performed using the statistical software package SPSS, version 20.0.

Results

A total of 100 patients were included in this study, The mean age of the study group was 66.5 years (SD = 12.6). The baseline demographic characteristics and the ICH score.

Of the total 100 patients, (67.7%) had mRS score greater than or equal to 3 at 90 days. These patients were categorized as the poor functional outcome group. Fifty-one patients (32.27%) had mRS score less than 3 at 90 days and were categorized as the good outcome group.

Functional status at 90 days	
Poor functional outcomes, mRS ≥3, *N* (%)	107 (67.7%)
Good functional outcomes, mRS <3, *N* (%)	51 (32.27%)
Fatal outcomes, mRS = 6, *N* (%)	27 (17.1%)
mRS, modified Rankin scale	

The mean ANC, ALC, and NLR on admission are presented .The mean NLR of the study population was 5.34 (SD = 4.74). The mean NLR of the poor outcome group was 6.57 (SD = 5.24) and that of the good outcome group was 2.75 (SD = 1.56). The difference was statistically significant with a *p*-value of 0.001. The mean ANC of the poor outcome group (mean ANC: 9327, SD = 2531.9) was higher when compared to the good outcome group (mean ANC: 6880, SD = 1986.6) and the difference was statistically different with a *p*-value of 0.001. Similarly, mean ALC of the poor outcome group (mean ALC: 2084, SD = 1084.4) was significantly lower compared to the good outcome group (mean ALC: 2868, SD = 877.6) and this difference was also statistically significant with a *p*-value of 0.001

Laboratory variables on admission				
	Mean ± SD	***Median (IQR)***	***Minimum***	***Maximum***
ANC (cells/μL)	8537.3 ± 2627.2	8499.5 (6825.5–10262.75)	1400.0	16425.0
ALC (cells/μL)	2337.9 ± 1083.8	2344 (1506.75–3163.5)	289.0	5250.0
NLR	5.3 ± 4.7	3.73 (2.22–6.79)	0.7	31.7
ANC, absolute neutrophil count; ALC, absolute lymphocyte count; NLR, neutrophil-to-lymphocyte ratio				

The mean age of the good outcome group was 63 years (SD = 11.3) and that of poor outcome group was 68.17 years (SD = 12.9). This difference was also found to be statistically significant with a *p*-value of 0.017

The mean ICH score at admission was 2.40 (SD of 1.32). The poor functional outcome group had a higher mean ICH score of 2.83(SD = 1.25) compared to the good outcome group that had a mean ICH score of 1.49 (SD = 0.94). This difference was statistically significant with a *p*-value of 0.001

The ROC analysis with respect to NLR and mRS at 90 days. NLR was found to be a good predictor of functional outcomes with AUC of 0.814 (*p*-value less than 0.05). The best predictive cutoff value for NLR was 3.4 at which it had a sensitivity of 84% and a specificity of 66.3% to predict poor functional outcomes at 90 days.

The comparison between NLR and the ICH score in predicting poor functional outcomes at 90 days, At their cutoff values, NLR compared to the ICH score was found to be more sensitive (84.0 vs 66.7%) but less specific (66.3 vs 78.3%). There was no significant difference in accuracy between NLR and the ICH score (74.7 and 72.8%).

Discussion

This study explores the clinical significance of NLR in patients with hemorrhagic stroke with respect to functional outcomes. NLR is a simple parameter that can be calculated easily at the bedside from the results of routine blood investigations readily available to the clinicians. This index incorporates the changes in ANC as well as ALC, making it a potential cell-based biomarker to assess the inflammatory response occurring in the body. Previous studies have shown that NLR shows good correlation with other traditional biomarkers of inflammation such as C-reactive protein and IL-6 (interleukin-6) or with oxidative stress markers.[13–15]

We have observed in this study that derangements in NLR occur early in the course of hemorrhagic stroke and this supports the hypothesis that inflammation plays an important role in the pathophysiology of ICH-associated brain injury. In our study, it is found that high ANC, low ALC, and high NLR on admission are associated with major disability at 90 days. These findings are consistent with the results of studies by Lattanzi et al. and by Geide-Jeppe et al.[7,8] Hence, it can be inferred that the initial inflammatory response, especially when intense, has a detrimental effect on the course and outcome of the disease.

Apart from NLR, it is also observed in this study that statistically significant difference exists between good and poor outcome group with respect to age and ICH score also. The mean age of the group with poor outcomes is found to be higher when compared to the mean age of the good outcome group (68 vs 63 years). This finding is in congruence with the findings of Tekinarslan et al. where age more than 65 years was found to be an important poor prognostic factor in patients with hemorrhagic stroke.

The diagnostic ability of NLR in predicting poor functional outcomes at 90 days is good and is comparable with clinical prognostic models like the ICH score. In this study, the ROC analysis has demonstrated that both NLR and the ICH score have nearly equal to AUC. At their cutoff values, NLR was found to be more sensitive but less specific than ICH score but their overall accuracy was nearly the same. This difference in sensitivity and specificity can be explained by the fact that the ICH score is a composite score that integrates multiple clinical and radiological data, which strongly influences the disease outcomes while NLR reflects only the intensity of the inflammatory response occurring in response to ICH. Both NLR and the ICH score have a good discriminating ability to predict poor functional outcomes in hemorrhagic stroke patients but should be used in the correct clinical context in accordance with their differences in sensitivity and specificity. We are of the opinion that, in view of its better sensitivity, NLR can prove to be valuable as a screening tool in the early risk stratification of patients with hemorrhagic stroke.

Conclusion

In patients with hemorrhagic stroke, NLR at admission is a good predictor of functional outcomes at 90 days. When compared to the ICH score, NLR is more sensitive but less specific in predicting poor functional outcomes.

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