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1. Respir Res. 2005 Dec 28;6:153

NEUROLOGY

Role of Neutrophil/Lymphocyte Ratio as a Severity Indicator in Patients with Acute Ischemic Stroke and Comparison with National Institutes of Health Stroke Scale

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ABSTRACT

Introduction: Stroke is one of the leading causes of disability in the world. There is no simple laboratory marker available for assessing the severity of stroke. We studied neutrophil/lymphocyte (N/L) ratio as an indicator of stroke severity and compared it with National Institutes of Health Stroke Scale (NIHSS), used as the gold standard marker for assessing severity of stroke. **Material and methods:** A cross-sectional study was conducted taking 100 subjects fulfilling inclusion and exclusion criteria of the study. N/L ratio was calculated using standard techniques. **Observations:** Patients with moderate stroke had higher N/L ratio than those with mild stroke (p = 0.004). **Conclusion:** N/L ratio can be used as a simple, calculative laboratory marker for assessing the severity of stroke.

Keywords: Stroke, N/L ratio, severity, ischemic stroke

The World Health Organization (WHO) defines stroke as a clinical syndrome consisting of rapidly developing signs of focal or global (in case of coma) disturbance of cerebral functions lasting more than 24 hours or leading to death with no apparent cause other than a vascular origin.

Stroke is more disabling than fatal. Approximately 20 million people each year suffer from stroke and out of these, 5 million will not survive after stroke. Projections show that by 2030, stroke prevalence will increase by more than 20% than in 2012. There is no simple laboratory maker to predict stroke severity.

AIMS AND OBJECTIVE

To study the changes in neutrophil/lymphocyte (N/L) ratio in patients of acute ischemic stroke and to compare the efficacy of N/L ratio as a marker of severity in comparison with National Institutes of Health Stroke Scale (NIHSS).

OBSERVATIONS AND RESULTS

A total of 100 subjects were included in our study, out of which 70% were females and 30% were males. Nearly 51% were >60 years of age and 49% were <60 years of age (Table 1). Severity of stroke according to NIHSS score was mild (0-7) in 24% patients, moderate (8-14) in 41% patients and severe (>14) in 35% patients (Table 2). A significant difference in N/L ratio was found in studied stroke patients. Patients with moderate stroke had higher N/L ratio than those with mild stroke (p = 0.004). P value for mild vs. moderate was 0.463, for mild vs. severe was 0.001 (significant) and moderate vs. severe was 0.025 (significant) (Table 3 and Fig. 1).

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Table 1. Age and Sex Distribution of Study Subjects

Age group (years)	Male		Female		Total	
	N	%	N	%	N	%
21-40	2	6.7	6	8.6	8	8
41-60	2	6.7	39	55.7	41	41
>60	26	86.6	25	35.7	51	51
Total	**30**	**30**	**70**	**70**	**100**	**100**

Table 2. Severity of Stroke According to NIHSS Score

Severity	NIHSS	N	Percentage (%)
Mild	0-7	24	24
Moderate	8-14	41	41
Severe	>14	35	35
Total		**100**	**100**

Table 3. N/L Ratio in Relation to Severity of Stroke

Severity	N	Mean	SD	P value
Mild	24	6.5	3.8	
Moderate	41	7.2	5.1	0.004 (S)
Severe	35	10.5	5.6	
Multiple comparison	**Mild vs. moderate**	**Mild vs. severe**	**Moderate vs. severe**	
P value	0.463	0.001 (S)	0.025 (S)	

SD = Standard deviation; S = Significant
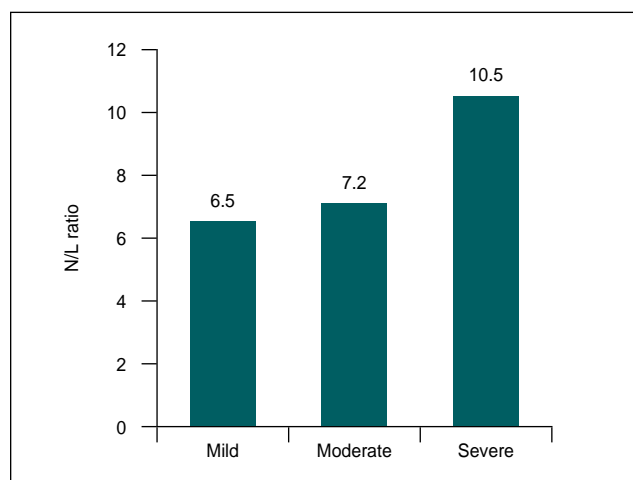
Figure 1. N/L ratio in relation to severity of stroke.

DISCUSSION

The NIHSS (Table 4) which measures neurological function in stroke patients, has been well validated and is commonly used in both the clinical and research settings. However, this score involves use of 15 different individual clinical parameters for patient's clinical status assessment, which is cumbersome and time consuming especially in emergent situations. Secondly, being subjective, it is entirely a clinical parameter based score, and it's validity and objectivity is further limited.

In stroke patients, a rise in total peripheral leukocyte count in the first 72 hours after stroke onset is associated with larger final infarct volumes on computed tomography (CT) and magnetic resonance imaging (MRI) and increase stroke severity. Experimental models of stroke have shown that within minutes of the onset of focal ischemia, there is activation of microglia followed by increased trafficking of leukocytes into the ischemic territory. Neutrophils are the earliest leukocyte subtype to show substantial upregulation in gene expression and to infiltrate areas of brain ischemia. Early neutrophil activation has been implicated in the potentiation of post-ischemic brain injury, and animal stroke models have suggested that depleting circulating neutrophils either before or at the onset of stroke reduces the size of infarction. Hence, N/L ratio could be an alternative and easy, approachable and calculative option in comparison to several other cumbersome scoring systems used to quantify the degree of severity of stroke like Glasgow Coma Scale, Canadian Neurological Scale, Scandinavian Stroke Scale and NIHSS.

In our study, a significant association was found between severity of stroke according to NIHSS criteria and N/L ratio (p = 0.004). Xue et al conducted a study which aimed to assess N/L ratio as a prognostic marker in acute ischemic stroke. A total of 280 patients with acute ischemic stroke were included in the study. Patients were divided into 3 groups according to the N/L ratio value (<2, 2-3 and >3). Demographic, clinical and laboratory data were accumulated for all patients. After adjustment for potential confounders, N/L ratio was associated with an increased risk of stroke severity on admission (odds ratio [OR] 1.364, 95% confidence interval [CI] 1.101-1.690, p = 0.005) and primary unfavorable outcome (OR 1.455, 95% CI 1.083-1.956, p = 0.013). After a median of 1.13 years (interquartile range 0.91-1.42) of follow-up, N/L ratio was associated with recurrent ischemic stroke after adjustment (hazard ratio 1.499, 95% CI 1.161-1.935, p = 0.002). The findings were in corroboration with our study. Yu et al also conducted a study to investigate whether N/L ratio is associated with early clinical outcomes in patients with acute ischemic stroke. Data were collected from a tertiary hospital's stroke registry including admitted patients with a first-ever acute ischemic stroke within 72 hours of onset. White blood cell counts and peripheral differential counts were measured on admission. Early clinical outcomes were in-hospital mortality and disability at discharge assessed by the modified Rankin Scale (mRS). Among 1,131 stroke patients, 454 patients were included and classified into tertile groups based on N/L ratio on admission. Patients in higher tertiles of N/L ratio were likely to have severe neurologic deficit

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Table 4. National Institutes of Health Stroke Scale

Response	Score	Response	Score
Level of consciousness	Alert = 0 Drowsy = 1 Stuporous = 2 Coma = 3	**Motor arm (Left and Right)**	No drift = 0 Drift before 10 sec = 1 Falls before 10 sec = 2 No effort against gravity = 3 No movement = 4
Level of consciousness questions **How old are you?** **What month is this?**	Answers both correctly = 0 Answers one correctly = 1 Answers both incorrect = 2	**Motor leg (Left and Right)**	No drift = 0 Drift before 5-10 sec = 1 Falls before 5-10 sec = 2 No effort against gravity = 3 No movement = 4
Level of consciousness commands **Squeeze my hand (using nonparetic hand)** **Close your eyes**	Performs both correctly = 0 Performs one correctly = 1 Performs neither = 2	**Limb ataxia**	Absent = 0 Present in one limb = 1 Present in two limbs = 2
Pupillary response	Both reactive = 0 One reactive = 1 Neither reactive = 2	**Sensory**	Normal = 0 Mild = 1 Severe loss = 2
Gaze	Normal = 0 Partial gaze palsy = 1 Total gaze palsy = 2	**Language**	Normal = 0 Mild aphasia = 1 Severe aphasia = 2 Mute/Global aphasia = 3
Visual field	No visual loss = 0 Partial hemianopsia = 1 Complete hemianopsia = 2 Bilateral hemianopsia = 3	**Facial palsy**	Normal = 0 Minor = 1 Partial = 2 Complete = 3
Dysarthria	Normal = 0 Mild = 1 Severe = 2	**Extinction and inattention**	Normal = 0 Mild = 1 Severe = 2

Maximum score - 42.

Source: Goldszmidt AJ, Caplan LR. Thrombolytic therapy for acute ischemic stroke (Chap. 3). In: Stroke Essentials. 2 nd Edition, Jones and Bartlett Publishers; Sudbury, Massachusetts; 2010. p. 33.

at discharge. Higher N/L ratio tertiles were associated with an unfavorable shift of mRS score (p < 0.0001). This association remained significant after adjustment for clinical and laboratory variables including age, sex, hypertension, hypercholesterolemia, atrial fibrillation, stroke severity and glucose level (p = 0.032 for trend). Celikbilek et al conducted a study which aimed to analyze the predictive ability of N/L ratio in acute ischemic cerebrovascular disease. In all, 190 patients including 70 patients with first-ever atherothrombotic acute ischemic stroke (AAIS), 50 patients with transient ischemic attack and 70 healthy subjects were enrolled in this study. N/L ratio was found to increase significantly in AAIS patients than the controls (p < 0.001). In addition, N/L ratio values were found to increase significantly in dead patients (p = 0.029). A cut-off value of 4.1 for N/L ratio was detected in predicting mortality with a sensitivity of 66.7% and a specificity of 74.1% (κ = 0.299, p = 0.006). These findings also support the role of N/L ratio as a simple, inexpensive and readily available marker of prognosis in acute ischemic stroke, as we found in our study.

CONCLUSION

Our study indicates that N/L ratio can be used as a simple laboratory marker for assessing the severity of stroke and prognosis in patients with acute ischemic stroke.

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