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Original Research Article

Correlation between neutrophil lymphocyte count ratio and outcomes of severe traumatic head injury

Tamajyoti Ghosh*, Subir Dey

Department of Neurosurgery, Armed Forces, Medical College, Pune, Maharashtra, India

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***Correspondence:**
Dr. Tamajyoti Ghosh,
E-mail: tamajyoti@gmail.com

ABSTRACT

Background: Raised peripheral neutrophil lymphocyte ratio is associated with poorer outcomes in conditions such as severe brain injury, ICH, cardiovascular conditions, cancer.
Methods: Retrospective analysis of 96 severe Traumatic Brain injury data treated at our institute over a period of 1 year. The patients were followed up for a period of at least 1 month. The primary outcome of the study was 1 month GOS and the various variables which may be associated with the poor GOS at 1 month follow up. Model based analysis was done for NLCR <24 hrs at 48 hrs and GCS at the time of presentation and discriminative ability of the models were studied by the Area under the curve.
Results: Univariate analysis were done of 96 patients of severe traumatic brain injury for various variables such as age, sex, mode of head injury, type of head injury, presenting GCS and NLCR at 24 hrs and 48 hrs to that of GOS at 1 month follow up. Initial GCS <7 (p=0.0138) with AUC=0.6689 and peak NLCR (<24 hr) of > 9.6 (AUC=0.931) with a p value of <0.001 with sensitivity of 100% and specificity of 79.27% and peak NLCR (48 hrs) of >12.4 (AUC= 0.973) with a p value of <0.001 with sensitivity of 100% and specificity of 89.02% were associated with unfavourable outcome.
Conclusions: High NLCR and initial poor GCS are independent unfavourable prognostic factors in 1 month GOS following severe traumatic head injury.

Keywords: Head Injury, Neutrophil Lymphocyte count ratio, Glasgow outcome score, Glasgow coma scale

INTRODUCTION

Traumatic brain injury (TBI) is a critical public health and socioeconomic problem throughout the world.[1-3] TBI is a major health and socioeconomic problem that affects all societies around the world. More than 10 million people worldwide suffer TBI serious enough to result in death or hospitalization each year NLCR is a marker of inflammatory response of the body.[4] It can thus be utilised as a clinical marker in judging the severity of outcome following traumatic brain injury. In India reported incidence of TBI is 55-120 per 100000 population.[5,6] A study from tertiary care institute has reported that the occurrence of TBI is approximately 42.5% in rural and 57.5% in urban area.[7] According to WHO data, by the year 2020, head trauma will be third largest killer in the developing world. In India studies by traffic police have shown that on an average one person dies every six min and 70% of these attributed to head and spinal trauma.[8] Road traffic accidents account for 45-60 per cent of traumatic brain injuries in different parts of India.[9] While primary brain injury is irreversible, secondary damage-consequent to neuronal dysfunction related to trauma induced oxidative stress, ischemia,

edema, and inflammatory response is amenable for treatment.[10] Tissue destruction, leading to release of intracellular components and production of reactive nitrogen and oxygen species, activates immune cells within the central nervous system.[11] The uncontrolled release of metalloproteinases, inflammatory cytokines, and proteases and the inappropriate activation of endothelial cells may further impair the integrity of the blood-brain barrier (BBB), leading to proteinaceous fluid extravasation into the interstitial space and significant leukocyte infiltration.[12-14] Anti-inflammatory cytokines such as interleukin 4 or 10 (IL-4, IL-10) stimulate alternative microglial phenotypes ("alternate activation" M2a state, or "acquired deactivated" M2c state) that act to suppress the destructive M1 immune response and promote repair processes after TBI.[15] Neutrophils are recruited to the area to phagocytize and clear cellular debris.[16] The first peak of increased BBB permeability is observed within the first few hours after injury and persists for 3-4 days; a second peak may occur after 5 days as a result of microglial activation.[17-19] Peak in peripheral WBC has been seen in cerebral ischemia in conditions such as cerebral vasospasm following SAH.[20] Neutrophil count to lymphocyte ratio has been found to be a sensitive and cost effective biomarker corresponds with the inflammatory status of the immune system in different conditions such as malignancy cardiovascular diseases stroke.[21-24] NLCR is also valuable in prediction of clinical outcomes in traumatic brain injury.[25] Patients with high NLCR is associated with poor outcome.[26,27] NLRC ratio also varies depending with the type of injury.[27-29] The purpose of this study is to determine whether there is a correlation between the raised NLCR and outcome of TBI as well as difference in NLRC in various type of TBI.

Aim and objectives

Aim and objectives of current study were to correlate between the NLRC ratio and the outcome of head injury. Secondary aim was to find out if there was any correlation of any other variables with outcomes of head injury

METHODS

This was a retrospective study involving 96 patients of severe traumatic brain injury admitted at AFMC during the period 31 January 2018 to 30 January 2020.

Inclusion criteria

Inclusion criteria for current study were; patients ≥18 years of age and patients with severe traumatic brain injury GCS less than or equal to 8.

Exclusion criteria

Exclusion criteria for current study were; patients <18 years of age, patients with mild or moderate traumatic head injury, patients with other co morbid conditions such as pregnancy, malignancy, cardiovascular disorder, CVA, patients with injuries involving other systems**.** Data were collected regarding the patients demographic profile, mode of injury, types of head injury (diffuse head injury, cerebral contusion, EDH, SDH, IVH, cerebral edema, traumatic SAH), GCS, any other injury, Day 1 to day 6 NLRC (ratio between absolute neutrophil count and lymphocyte count) and the Glasgow outcome score followed up at 04 week post discharge through a preformed questionnaire from the history sheets of the patients. The details were recorded in performa and data processed using Microsoft Excel 2010 and analysed by using SPSS version 2020.

Table 1: Glasgow coma scale.

Parameter	Score
Eye opening response	
Spontaneously	4
To Speech	3
To Pain	2
No response	1
Best verbral response	
Oriented to time place and person	5
Confused	4
Inappropriate words	3
Incomprehensible sounds	2
No response	1
Best motor response	
Obeys commands	6
Localises Pain	5
Withdraws from pain	4
Abnormal flexion, decorticate posture	3
Extension, decerebrate posture	2
No motor response	1

Note: Wright J. 2011 Glasgow Coma Scale. In: Kreutzer J.S., DeLuca J., Caplan B. (eds) Encyclopedia of Clinical Neuropsychology. Springer, New York, NY. https://doi.org/10.1007/978-0-387-79948-3_1840.

Table 2: Severity scale of brain injury.

Severity of brain injury	GCS
Mild	15-13
Moderate	12-9
Severe	8-1

Note: Pangilinan PH, et al Classification and Complications of Traumatic Brain Injury. Practice Essential Epidemiology and Pathophysiology. http:// emedicine. Medscape.com/article/ 326643-overview#a4. Updated March 02, 2020.

Unfavourable outcomes

Patients who expired while undergoing treatment at our institution and those patients who had Glasgow outcome score of 1 or 2 at 1 month follow up following discharge.

Table 3: Glasgow outcome score.

GOS	Functional status	Description
5	Good recovery	Return to original functional level and employment with no deficit
4	Moderate disability	Minor neurological deficit that does not interfere with daily function or work
3	Severe disability	Significant neurological deficit that interferes with daily activities or prevents return to employment
2	Persistent vegetative state	Coma or severe deficit rendering the patient total dependent
1	Death	Self- explanatory

Note: Wright J. 2011 Glasgow Coma Scale. In: Kreutzer J.S., DeLuca J., Caplan B. (eds) Encyclopedia of Clinical Neuropsychology. Springer, New York, NY. https://doi.org/10.1007/978-0-387-79948-3_1840.

RESULTS

A total of 96 patients were included in the study with 92 (95.83%) male and 4 (4.16%) female. Out of which 11 patients (11.45%) died. The median age of patients 34 years (18-72 years). Modes of Injury RTA 76% (M:F= 69:4), Fall from height 17.7% (M=17), Sports Injury 3.12% (M=3), Assault 3.12% (M=3). The median admission GCS was 8 (Range 5-8). On 6 month follow up total of 13 patients (13.54%) had unfavourable outcome. On univariate analysis Sex, age, mode of injury and type of head injury is found to have no co relation with outcomes whereas GCS at presentation (p=0.138) and NLCR at admission (p<0.01) had corelation with outcomes favourable of head injury. Predictor model involving ROC curve of NLCR and GCS at presentation shows a sensitivity of 100% and specificity of 79.27% at peak NLCR (<24 hr) of >9.6 (AUC=0.931) with a p value of <0.001 and sensitivity of 100% and specificity of 89.02% at peak NLCR (48 hrs) of >12.4 (AUC=0.973) with a p<0.001 The predictor performance of GCS was poor than NLCR with p value of 0.039 with sensitivity 53.85% and specificity of 75.61% at GCS <7 (AUC 0.669).

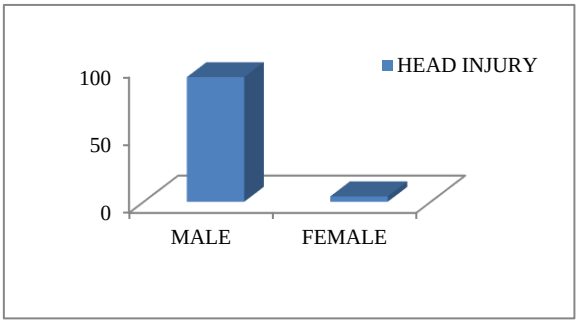

Figure 1: Sex distribution of head injuries.

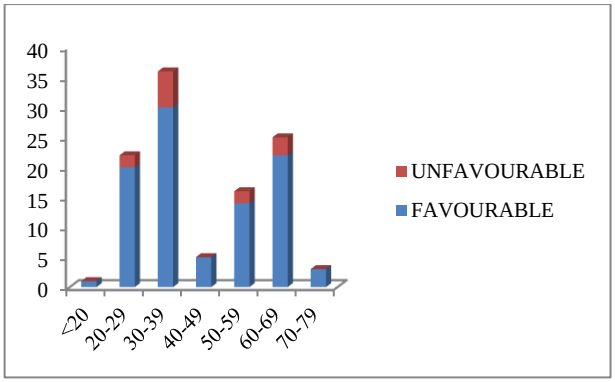

Figure 2: Age wise distribution of favourable outcome of head injuries.

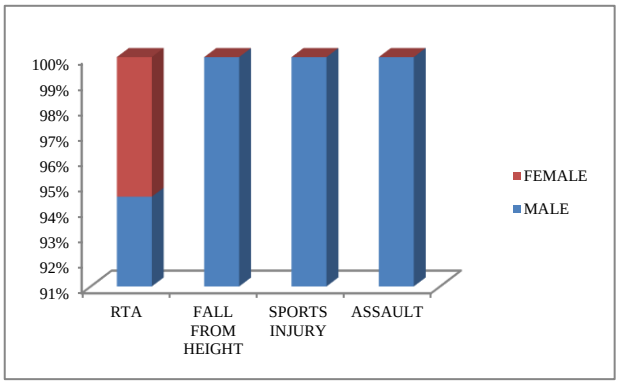

Figure 3: Sex wise distribution of different modes of head injury.

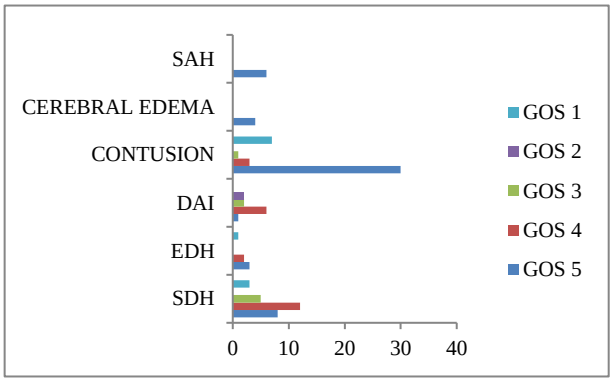

Figure 4: Distribution of different types of head injuries according to outcomes.

DISCUSSION

Our study showed that NLCR more importantly a rising trend in NLCR has prognostic value in predicting the outcomes of severe head injury at 1 month follow up. Patients with higher NLCR following severe head injury had poorer GOS. During the study initial presenting GCS of less than 7 was also found to have positive co relation with low GOS at the end of 01 month. Unlike other studies.[10-17] Age was not associated with outcomes of head injury. Traumatic brain injury has got 2 components

Initially injury occurs due to damage of neurons following direct trauma followed by bodies own inflammatory response to the injury causing blood brain barrier disruption, migration of inflammatory cells in CNS causing neurotoxicity, cell death and degeneration.[18-23]

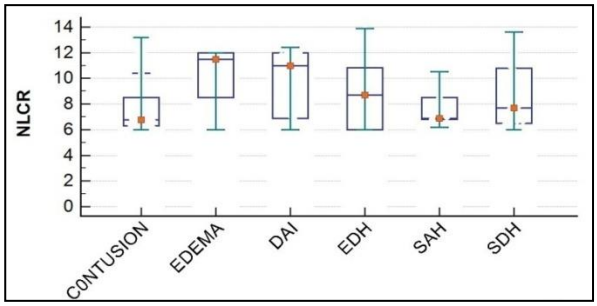

Figure 5: Mean NLCR according to the type of head injury.

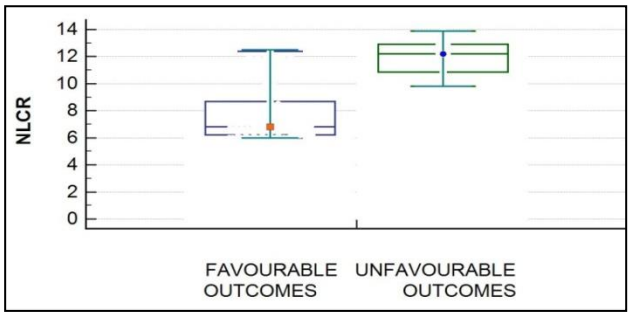

Figure 6: Distribution of NLCR values according to different outcomes in head injury patients.

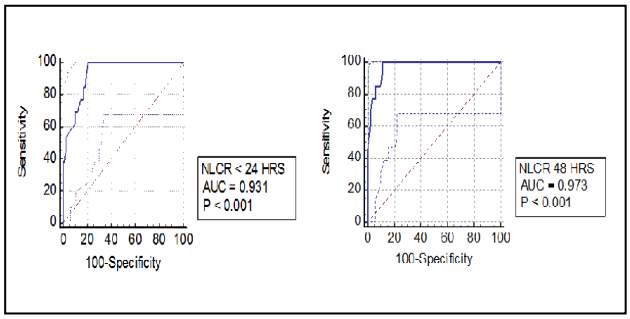

Figure 7: ROC curve of NLCR model shows AUC for NLCR at 48 hrs is more than AUC for NLCR <24 hours.

Neutrophils rapidly infiltrate brain through meningeal vessels and choroid plexus and facilitate neuronal injury by oxidative mechanism.[24,25] Lymphocyte also plays a critical role in mediating inflammatory response through cytokine mediated activation of T Lymphocyte which causes activation of microglial cells and repair of neuronal tissue.[26,27] Decrease in lymphocyte count is found to be associated with signs of brain damage 12 hours following injury.[28] Thus in our study the values of NLCR is an indirect measure of the secondary injury to the brain which effects the future outcome of the patient. NLCR has the advantage of being an objective clinical marker unlike GCS accurate assessment of which may be compromised in severe Head injury patients due to intubation, sedation, periorbital swelling, motor weakness. Minute changes in patients condition such as change in respiratory pattern and brain stem reflexes are not reflected in GCS.[29]

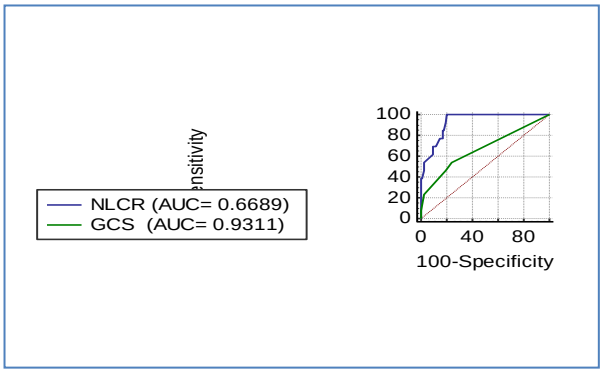

Figure 8: Predictor model of NLCR and GCS at the time of presentation shows AUC of NLCR is more as compared to GCS suggestive better predicting value in determining unfavourable outcomes of head injury.

Limitations

Limitation of our study is due to the retrospective analysis of patient data which have might have lead to selection bias. Secondly our centre being a tertiary centre catering a large area patients are brought after lapse of significant time post injury. Also the patients the reactionary changes of blood counts following emergency surgical procedure were not taken into account.

CONCLUSION

NLCR is a useful measure for predicting the outcomes of severe traumatic brain injury. High NLCR along with initial GCS is associated with unfavourable outcome in head Injury patients. NLCR being a rountinely used and cost effective blood test it can be used in prognostication in Head injury cases for potential therapeutic intervention in those patients with high NLCR. However precise collection time and following the rising trend of NLCR is more important for it to be used as an effective clinical marker for head injury prognosis.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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