ORIGINAL RESEARCH PAPER

Neurosurgery

A PROSPECTIVE STUDY TO EVALUATE THE ROLE OF MONOCYTE TO LYMPHOCYTE RATIO AS A PREDICTOR OF ACUTE TRAUMATIC INTRAPARENCHYMAL HEMORRHAGE EXPANSION AFTER CEREBRAL CONTUSION

KEY WORDS: Monocyte to lymphocyte ratio, acute tICH, primary cerebral contusion.

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ABSTRACT

Background: The present study was conducted to evaluate the role of monocyte to lymphocyte ratio as a predictor of acute traumatic intraparenchymal hemorrhage expansion after cerebral contusion. **Materials and methods:** A total of 300 patients diagnosed with primary cerebral contusion were included in the study. Demographic parameters, mode and severity of the injury, signs and symptoms pupillary reactions and Glasgow Coma Scale scores were recorded. MLR was obtained from routine blood tests and baseline and follow-up (within 24 hrs) hematoma volumes was calculated from the CT images using semi-automated computer-assisted volumetric analysis. Fisher's exact test, Pearson's chi square test, independent t test and logistic regression were used for statistical analysis. **Results:** Both baseline and follow-up tICH volumes significantly higher in patients with acute tICH expansion (p=0.016 and p=0.004 respectively). The MLR was significantly higher in the patients with acute tICH expansion (p=0.001). **Conclusion:** MLR at hospital admission can be used as a significant factor to predict acute traumatic tICH expansion after cerebral contusion.

INTRODUCTION

Traumatic brain injury (TBI) continues to play a substantial role in neurological morbidity and death all over the world. [1,2] Hematomas and contusions are the most frequent lesions connected to traumatic brain injury (TBI), occurring in 13% to 35% of patients. [3,4] Traumatic intraparenchymal haemorrhages (tIPH) are a particular kind of TBI that can leave victims permanently disabled in their cognitive, physical, and mental abilities. Acute tICH expansion is found in 38% to 63% of the patients suffering from TBI that has significant association with the outcomes. [5] Hence, targeting acute tICH expansion at the initial phases of the treatment of cerebral contusion is crucial. Despite substantial research and advancements in critical care, no previous study addressing the numerous clinical factors on rates of volumetric haemorrhage expansion has been carried out. [6]

After a brain contusion, neuro-inflammation is one of the main characteristics of tICH. [7] There is evidence of release of various cytokine and chemokines immediately after TBI. This neuro-inflammation affects the course of the tICH disease and contributes to it. Under normal physiological settings, the infiltration of inflammatory cells are mostly controlled through the blood brain barrier (BBB). However, following cerebral contusions, the monocytic, neutrophils and lymphocytic infiltration from the periphery is observed which makes the situation more critical. [8,9]

Monocyte level is an important factor in subsequent brain damage following tICH. The neutrophilic infiltration in the brain, has been shown to be facilitated by increased level of monocytes after cerebral trauma. [10-11] Lower lymphocyte counts have been linked to spontaneous intraparenchymal hematoma expansion and clinical worsening, even though their significance in the acute intraparenchymal bleeding following the TBI is not clearly understood. [12-14]

The monocyte to lymphocyte ratio (MLR) serves as a straightforward indicator of immunological status and inflammatory level and shows the equilibrium between innate immunity and adaptive immunity. MLR has lately been proposed in order to evaluate the prognosis in neurological diseases, cardiovascular diseases and cancer. It is an affordable and easily accessible biomarker that helps to take faster decision regarding the management of the patients. [15-21] The present study was conducted to evaluate the role of lymphocyte to monocyte ratio as a predictor of acute traumatic intraparenchymal hemorrhage expansion after cerebral contusion.

MATERIALS AND METHODS

Sampling

This prospective study was carried out on the patients who were admitted in the trauma centre with diagnosis of primary cerebral contusion from July 2021 to April 2022 at Department of Neurosurgery, SMS Hospital, Jaipur. The ethical approval was obtained from the institutional ethical committee. The principles of the Declaration of Helsinki was followed to establish the ethical standards. After obtaining informed and written consent, the patients were included in the study. Patients with history of any previous intra cranial procedures, brain tumor, history of brain trauma or spontaneous ICH, with baseline CT performed over 6 hours or the follow-up CT over 24 hours after cerebral contusion, with surgical evacuation of the hematoma before the follow-up CT, with no initial blood test within 24 hours after cerebral contusion, with bleeding diathesis or taking anticoagulant drugs were excluded. The G*Power 3.1.9.2 software was used for calculation of sample size. Considering 5% alpha error, 10% beta error and 90% power for the study, the sample size was calculated as 294. We had taken a total of 300 samples after matching the inclusion and exclusion criteria.

Methodology

A detailed history about the demographic parameters, mode and severity of the injury, signs and symptoms were recorded and a thorough clinical examination was done. Pupillary reactions and Glasgow Coma Scale scores were noted.

Routine blood tests along with leukocyte count, monocyte count and lymphocyte count were done. The monocyte-lymphocyte ratio (MLR) was calculated as the ratio between the absolute monocyte and lymphocyte counts. Patients was identified as having a coagulation disorder if the activated

partial thromboplastin time (APTT) is more or equal to 36 seconds, the international normalized ratio (INR) is more than 1.2, or the platelet count (PT) is less than 120 × 10^9 platelets/L at admission.

Axial non contrast CT images (5 mm slice thickness) were analysed to know the location, side and midline shift of the contusion. Baseline and follow-up (within 24 hrs) volumes of the hematoma were calculated from the CT images using semi-automated computer-assisted volumetric analysis. The total volume was taken into consideration in case there were many small areas of intraparenchymal hematomas (ICHs) were observed in the region of contusion. Acute tICH expansion was defined as a relative expansion of ≥33% or absolute hematoma expansion of more than 5 ml from the initial CT.

Statistical analysis of data

The data subjected to statistical analysis were tabulated first in the Microsoft excel and analysed with SPSS V.24 software. The variables were expressed with mean (SD) in case they are continuous and frequency (%) in case they are categorical. Fisher's exact test, Pearson's chi square test, independent t test and logistic regression were used. The p value ≤0.05 is considered as statistically significant.

RESULTS

Out of the 300 patients, 166 patients had acute tICH expansion. Table 1 shows the comparison of various parameters between patients with and without acute tICH expansion. The demographic parameters (sex and age) were comparable between the groups. In both the groups, as per Glasgow coma scale score, majority of the patients had mild head injury followed by severe and moderate type. The mean arterial pressure was significantly higher in the patients with acute tICH expansion (p=0.037). Although more number of patients with acute tICH expansion had history of hypertension, diabetes and coagulopathy, no statistically significant association were found.

Among the distributions of hemorrhages in different locations, subarachnoid and subdural hemorrhages were found to be significantly higher in patients with acute tICH expansion (p=0.003 and p<0.001 respectively). Both the groups showed greater number of contusion in frontal and temporal regions in comparison to the other regions. Both baseline and follow-up tICH volumes significantly higher in patients with acute tICH expansion (p=0.016 and p=0.004 respectively). Leukocyte count and monocyte count were significantly higher and lymphocyte count was significantly lower in patients with acute tICH expansion (p=0.008, p=0.035 and p=0.022 respectively). The MLR was significantly higher in the patients with acute tICH expansion (p=0.001).

The MLR was established as a significant risk factor for tICH expansion after various other independent risk factors were adjusted (OR, 6.14; 95% CI, 3.79-9.35) in the logistic regression analysis. The chance of occurring acute tICH expansion significantly is raised when MLR was greater than 0.91 (Table 2).

DISCUSSION

Results obtained from the current study shows that, there is a significant association between MLR and the acute tICH expansion in the cerebral contusion. The application of MLR in various diseases of CNS is in the assessment of the prognosis of spontaneous intracerebral hemorrhage and acute ischemic stroke [22-24]. Additionally, the MLR is independently linked to brain atrophy in multiple sclerosis and neurological impairments. Song et al (2020) reported that, Lower MLR was independently related to higher risk of hemorrhagic transformation in patients with acute ischemic stroke [20]. Hemond et al (2019) showed higher MLR was associated with whole brain atrophy [21].

A crucial component of acute cerebral contusion connected to tICH enlargement, which is neuroinflammation, can affect the course of the condition and may serve as a target for treatment [25-27]. The neuroinflammation starts following the initiation of the brain contusion. The initial hematoma is caused by tissue being sheared and micro vessels being broken as a result of the impact injury. Additionally, the peripheral leukocytes trigger a number of inflammatory pathways, such as the NF-B signal, which is essential for inducing the cellular death of vascular endothelium. As a result, subsequent tICH expansion and fragmentation of the micro vessels are seen around the hematoma. Additionally, elevated levels of matrix metalloproteinases (MMPs) following the ICH leads to increase in the vascular permeability as the integrity of the vessels are lost [27,28]. Additionally, MMPs encourage the breakdown of the BBB and aids in neutrophil and monocyte infiltration [29].

In consequence, extravasation of leukocytic infiltration into the brain parenchyma along with the expansion of the ICH intensify the responses, worsen the tICH expansion and edoema, and ultimately impair the recovery from cerebral trauma [29,30]. Sheng et al (2020) reported that the MLR upon hospital admission is an independent risk factor for the acute tICH expansion and the long-term unfavorable outcome [14].

Uncertainty exists regarding lymphocytes' contribution to the acute tICH expansion. In line with earlier research, the current study demonstrates reduced lymphocyte counts in patients suffering from tICH expansion, which are most likely caused by lowered T lymphocyte counts [31,32]. In patients with traumatic brain injury, the decrease in T lymphocyte count is linked to a striking decline in neurologic outcomes and a rise in lung infection [33]. Wang et al (2020) showed that, low MHR was associated with 1.81-fold increase of Hemorrhagic transformation and 3.82-fold increase of symptomatic Hemorrhagic transformation [34].

The potential participation of T lymphocytes in the acute tICH expansion may be complicated due to the existence of several subtypes and bidirectional immunomodulatory functions. However, further clinical research is still required to examine the part played by T lymphocytes in the immediate tICH expansion and long-term prognosis following brain trauma.

CONCLUSION

The results of the current study establishes MLR at hospital admission as a distinct risk factor for patients suffering from acute tICH expansion. The chance of occurring acute tICH expansion significantly is raised when MLR was greater than 0.91. The tICH treatment continues to be supportive within a framework of the overall critical care management because in the current clinical setting, no therapy targeting the tICH-induced primary damage has produced definite advantages. Our research could therefore be used to locate new potential targets for neuroinflammation and create fresh treatment plans.

Table 1: Comparison of various parameters between patients with and without Acute tICH expansion

Parameters	Acute tICH expansion		P value
	Yes (n=166)	No (n=134)	
Demographics and clinical variables			
Male sex, no. (%)	126 (75.85%)	100 (74.62%)	0.798
Mean age (SD) (years)	52.16 (19.16)	49.78 (18.97)	0.053
Severity of injury mechanism			0.783
Mild, no. (%)	48 (29.16%)	37 (27.56%)	

Moderate, no. (%)	6 (3.61%)	7 (5.56%)	
Severe, no. (%), no. (%)	112 (67.23%)	90 (66.88%)	
Level on Glasgow Coma Scale score			0.090
Mild (13–15 points), no. (%)	82 (49.28%)	83 (61.92%)	
Moderate (9–12 points), no. (%)	37 (22.37%)	21 (15.61%)	
Severe (3–8 points), no. (%)	47 (28.42%)	30 (22.47%)	
Mean arterial pressure, mean (SD) (mmHg)	105.65 (45.57)	103.53 (44.34)	0.037
Hypertension, no. (%)	19 (11.71%)	13 (9.38%)	0.626
Diabetes, no. (%)	9 (5.17%)	5 (3.84%)	0.490
Coagulopathy, no. (%)	20 (12.27%)	12 (8.65%)	0.388
Imaging variables			
Intraventricular hemorrhage, no. (%)	11 (6.65%)	8 (5.81%)	0.815
Subarachnoid hemorrhage, no. (%)	136 (81.69%)	90 (66.89%)	0.003
Subdural hemorrhage, no. (%)	127 (76.74%)	68 (50.68%)	<0.001
Extradural hemorrhage, no. (%)	34 (20.47%)	27 (20.14%)	0.943
Location of contusion			0.421
Frontal, no. (%)	76 (45.97%)	55 (41.13%)	
Temporal, no. (%)	76 (45.97%)	59 (43.86%)	
Parietal, no. (%)	6 (3.58%)	9 (6.83%)	
Occipital, no. (%)	3 (1.79%)	4 (2.73%)	
Basal ganglia, brainstem, or cerebellum, no. (%)	4 (2.68%)	7 (5.46%)	
Baseline tICH volume, mean (SD) (mL)	6.00 (9.21)	3.03 (6.71)	0.016
Follow-up tICH volume, mean (SD) (mL)	15.64 (20.78)	3.31 (10.15)	0.004
Inflammatory index parameters			
Leukocyte count, mean (SD) (× 109 cells/L)	17.30 (5.77)	15.20 (5.82)	0.008
Monocyte count, mean (SD) (× 109 cells/L)	0.93 (0.52)	0.88 (0.51)	0.035
Lymphocyte count, mean (SD) (× 109 cells/L)	1.04 (0.47)	1.75 (1.01)	0.022
MLR, mean (SD)	1.14 (1.11)	0.63 (0.39)	0.001

Table 2: Associations of MLR with acute tICH expansion.

Models	Unadjusted		Adjusted*	
	OR (95% CI)	P value	OR (95% CI)	P value
MLR	9.31 (7.22, 13.64)	<0.001	6.14 (3.79, 9.35)	<0.001
MLR<0.91	27.29 (15.76, 53.82)	<0.001	22.58 (11.09, 51.24)	<0.001
MLR≥0.91	4.06 (2.62, 7.55)	<0.001	3.86 (1.95, 6.84)	<0.001

*Adjustment by sex, age, coagulopathy, subdural hemorrhage, baseline traumatic intracerebral hematoma volume, and location of contusion.

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