Systemic Inflammatory Response Syndrome Predicts Severity of Stroke and Outcome

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Background: This study was undertaken to evaluate the frequency of systemic inflammatory response syndrome (SIRS) at admission and its correlation with clinical and radiological severity of stroke and outcome. *Methods:* Two hundred consecutive stroke patients within 48 hours of ictus were prospectively included, and their clinical details including Glasgow Coma Scale (GCS), National Institutes of Health Stroke Scale (NIHSS), and feature of raised intracranial tension were noted. Computed tomography/magnetic resonance imaging finding included stroke type, location, size, midline shift, herniation, and intraventricular hemorrhage score. SIRS was noted on days 1, 2, 7, and 15. Death and outcome at 3 months were based on modified Rankin Scale (mRS) score. *Results:* Seventy-five (37.5%) had infraction and 125(62.5%) intracranial hemorrhage (ICH). SIRS was present in 120 (60%) patients: all the features in 56 (28%), 3 in 48 (24%), and 2 in 16 (8%). The presence of SIRS decreased with time: on the second day in 57%, seventh day in 43%, and 15th day in 21% of patients. Admission SIRS correlated with the GCS score ($P < .001$), NIHSS score ($P < .001$), volume of ICH ($P < .001$), infarction size ($P < .001$), hypernatremia ($P = .001$), and respiratory paralysis ($P < .001$). Thirty-one (15.5%) patients died, and 30 (97%) of them had SIRS. At 3 months, 110 (55%) patients had poor outcome (mRS >2) and of them 90 (82%) had SIRS ($P < .001$). On multivariate regression analysis, the number of SIRS criteria ($P = .16$) was not significantly related to 3-month outcome and death but independently related to NIHSS score at admission (odds ratio [OR] = 1.39; 95% confidence interval [CI] = 1.22-1.56; $P < .001$), GCS score (OR = 1.32; 95% CI = 1.01-1.71; $P = .04$), and duration of hospitalization (OR = 1.07; 95% CI = 1.01-1.15; $P = .03$). *Conclusions:* SIRS at presentation is a useful marker for clinicoradiological severity of stroke but not an independent marker of death and disability. **Key Words:** Stroke—infarction—intracerebral hemorrhage—systemic inflammatory response syndrome—death—outcome.

Stroke is a cause of acute stress resulting in biochemical events such as liberation of oxidative stress markers, glutamate, and cytokines.[1-3] These biomarkers are known to produce leukocytosis or leucopenia, raised temperature, and tissue hypoxia resulting in manifestation of systemic inflammatory response syndrome (SIRS).[1-5] Presence of SIRS in intensive care unit patients has been reported to correlate with death and disability.[6,7] In stroke, SIRS may be a manifestation of systemic infection and its outcome may not be similar to noninfective cause. In the recent years, role of SIRS in stroke in terms of mortality, functional outcome, and complication during hospital stay, such as pneumonia,

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liver and kidney dysfunction, has been reported. Most of these studies, however, based on ischemic stroke and in these studies SIRS at admission were related to volume of stroke, clinical severity, and outcome.[8-10] In patients with subarachnoid hemorrhage, SIRS was related to death, vasospasm, and disability.[11] For volumetric analysis of stroke, a dedicated software is needed along with a neuroradiologist. Moreover, associated edema may also contribute to stroke severity rather than stroke volume only. There is a paucity of study evaluating the role of SIRS in defining the severity of outcome in intracerebral hemorrhage (ICH). There is no study comparing SIRS in patients with ICH and ischemic stroke. In this study, we therefore evaluate the role of SIRS in ICH and ischemic stroke in terms of clinical and radiological severity of stroke, biochemical changes, and outcome.

Patients and Methods

Consecutive patients with computed tomography/magnetic resonance imaging–proven ischemic and primary spontaneous hemorrhagic stroke during 2011 and 2012 admitted to neurology service within 48 hours of ictus were prospectively included. Patients with arteriovenous malformation, aneurysmal bleed, pregnancy, coagulopathy bleed, bleeding diathesis, immunosuppression, organ transplantation, malignancy, existing septicemia before ICH, lack of consent; patients on antiplatelet, oral anticoagulant, and corticosteroid drugs; patients undergoing surgical intervention and tissue plasminogen activator therapy, and children aged 15 years or below were excluded. The study was approved by the Institute's Ethics Committee (No: 2013-73-IP-70).

Their clinical details including their demographic and stroke risk factors were noted. Their age, gender, education, residence, dietary habit, life style, smoking, alcohol and tobacco chewing habit were also noted. Patients were considered hypertensive if their recorded blood pressure (BP) was high in 2 occasions (Eighth Joint National Committee criteria) or they were on antihypertensive drugs.[12] Patients were considered diabetic if they were on insulin or oral hypoglycemic drugs, and if their fasting blood sugar was greater than 126 mg/dL, postprandial blood sugar greater than 200 mg or HbA1c more than 6.5gm/dL.[13] Family history of stroke, hypertension, and diabetes in the first-degree relatives were noted.

Evaluation

The consciousness was assessed by Glasgow Coma Scale (GCS) score and severity of stroke by National Institutes of Health Stroke Scale (NIHSS) score. The presence of tachycardia (pulse >90/min) or bradyarrhythmia (pulse <60/min), irregular heart rate, ictal BP, hyperventilation, and extensor posturing was noted. And the presence of cranial nerve palsy, pupillary symmetry, and papilledema was also noted. Muscle power was graded on the basis of Medical Research Council (MRC) into severe (MRC grade, 0-2), moderate (2-3), and mild (grade 4). Muscle tone and tendon reflexes were categorized into increased, reduced, and decreased. Sensations and cerebellar signs were tested in the patients who could co-operate. Cardiovascular and chest examination findings and organomegaly were also noted. The presence of raised intracranial tension (ICT) was noted based on surrogate markers of raised ICT such as extensor posturing, hyperventilation, pupillary asymmetry, or contralateral pyramidal signs.

Investigations

Blood counts, hemoglobin, erythrocyte sedimentation rate at the first hour, C reactive protein, blood sugar, blood urea nitrogen, serum creatinine, albumin, transaminases, bilirubin, lactate dehydrogenase, sodium, and potassium were measured. Arterial blood gas analysis and electrocardiogram and chest radiography were done. Lipid profile was analyzed on the next day morning. CT scan was taken within 1 hour of admission to emergency using a third-generation CT scanner. In patients with a suspected ischemic stroke, MRI was preferred. If CT revealed ICH, MRI was not taken but in ischemic stroke patients, MRI was taken in most of the cases as MRI delineates infarct better. Echocardiography was done in patients with thrombotic or cardioembolic stroke. The location of infarct (anterior/posterior circulation and cortical versus subcortical) and its size (large—more than half of a lobe or multiple lobes; medium—less than half of a lobe; and small—single or multiple lacunar infarcts in CT/MRI scan of brain) were noted.[14] ICH was categorized based on the location (lobar, ganglionic, thalamic, brain stem, and cerebellar) and size (large, >60 mL; medium, 30-60 mL; and small, <30 mL).[15] Presence of midline shift and brain herniation was also noted both in ischemic stroke and in ICH. In patients with ICH, intraventricular and subarachnoid extension of blood was noted. Intraventricular volume of blood was measured by intraventricular hemorrhage (IVH) score calculated as $3(RV + LV) + III + IV + 3 \times H$, where RV, right ventricle score, LV, left ventricle score, III, third ventricle score, IV, fourth ventricle score, and H, hydrocephalous.[16] The volume of parenchymal blood was measured by $A \times B \times C/2$, where A is the greatest hemorrhage diameter by CT, B is the diameter 90° to A, and C is the approximate number of CT slices with hemorrhage multiplied by the slice thickness.[17]

Definition of SIRS

The presence of SIRS was considered if 2 or more of the following criteria are met: (1) temperature of less than 36°C or more than 38°C; (2) heart rate of more than 90 bpm; (3) respiratory rate of more than 20 breaths/minute;