The Prognostic Value of Serum Uric Acid in the Acute Phase of Ischemic Stroke in Black Africans

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Background: The association between hyperuricemia and stroke outcome still remains controversial worldwide. This study aims to determine the prevalence of hyperuricemia and its association with the outcome of patients with acute ischemic stroke in a tertiary care hospital. *Methods:* This was a hospital-based prospective cohort study that included patients with ischemic stroke with baseline uric acid levels and 3-month post-stroke follow-up data. Associations between hyperuricemia and stroke outcomes were analyzed using multiple logistic regression, Kaplan–Meier, and Cox proportional hazards regression analysis. *Results:* A total of 480 patients were reviewed with a mean age of 62.8 ± 13.3 years. The prevalence of hyperuricemia was 52.3% with mean uricemia of 71.1 ± 25.3 mg/dL. There was a significant association between hyperuricemia and mortality with unadjusted odds ratio (OR) = 4.120 [95% (confidence interval [CI]: 2.466-7.153); $P = .001$)], but on multivariate analysis, hyperuricemia was not an independent predictor of stroke mortality [OR = 1.270 (CI: .547-2.946); $P = .578$)]. An independent association between increasing uric acid levels and mortality was noted on Cox proportional hazards regression; adjusted hazard ratio (95% CI) of 3.395 (2.114-5.452), P value greater than .001. Stroke mortality significantly increased across higher uric acid quintiles in patients with acute stroke ($P < .001$). Hyperuricemia was an independent predictor of poor functional outcome within 3 months after stroke with adjusted OR (95% CI) of 2.820 (1.359-5.851); $P = .005$. *Conclusions:* Half of black African patients with ischemic stroke present with hyperuricemia, and hyperuricemia is a predictor of mortality and adverse functional outcomes. Further studies are therefore warranted to determine whether reducing hyperuricemia after stroke would be beneficial within our setting. **Key Words:** Hyperuricemia—acute ischemic stroke—mortality—functional outcome.

Introduction

Stroke is a common and devastating disorder and is currently the second leading cause of death worldwide.[1] The mortality rate of stroke in the acute phase is as high as 20% and it remains higher for several years after the acute event in patients with stroke than in the general population.[2] In Africa, 6-month post-stroke mortality rates range from 44% to 47%.[3,4] Stroke is also an important cause of morbidity and long-term disability: up to 40% of survivors are not expected to recover their independence with self-care and 25% become unable to walk independently.[5] Despite previous epidemiological evidence, the role of serum uric acid (SUA) as an independent marker of cardiovascular risk has been controversial for over 50 years. The Framingham Heart Study concluded that the association

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of SUA levels with cardiovascular disease merely reflects the link between SUA levels and other risk factors, including hypertension, kidney disease, elevated lipoprotein levels, and use of diuretics.[6,7] SUA is a powerful antioxidant contributing to approximately two thirds of free radical scavenging in plasma.[8,9] Oxidative stress in the acute phase of ischemic stroke increases brain injury.[8,10] Oxidative stress reflects an imbalance between potentially harmful oxidants and protective antioxidants and predisposes to local tissue damage, partly through excess free radical activity.[10] SUA could act as a free radical scavenger, reducing oxidative stress in patients with acute ischemic stroke (AIS) and protects cells in the ischemic penumbra.[11] In this perspective, an interventional study showed that administration of uric acid in healthy volunteers with low baseline serum concentrations increased the antioxidant capacity.[11] Although some authors have demonstrated that elevated SUA predicts good outcome during the acute phase of stroke,[12,13] others have demonstrated that hyperuricemia is associated with poor outcomes.[14-17] This shows that despite previous and current studies, there are still controversies as to whether there is a relation between SUA levels and functional outcome after AIS. It is also not clear whether this relation is either causal or circumstantial. Moreover, the association between SUA with mortality and functional outcomes in black patients with stroke in Africa, where there is no routine measurement of SUA levels in patients with acute stroke, has received scant attention in world literature. Therefore, we determined the prevalence of hyperuricemia and assessed its association with the outcome in patients with AIS.

Methods and Patients

Study Design

We carried out a hospital-based prospective cohort study in a tertiary care hospital in Douala, Cameroon. We included consenting patients admitted for AIS in the neurology unit of the department of internal medicine and the intensive care unit (ICU) of the Douala General Hospital (DGH) from January 2010 to January 2016. This study was approved by the Institutional Ethics Committee of Research on Human Health of the University of Douala and the study hospital— Douala General Hospital. Patients who were admitted for confirmed AIS within 7 days of onset of symptoms were included in our study. Patients with hemorrhagic stroke (including subarachnoid hemorrhage, spontaneous intracerebral and intraventricular hemorrhage) and cerebral venous thrombosis were excluded.

Data Collection

Demographic data, including age, gender, and relevant medical history such as hypertension, diabetes mellitus (DM), smoking history, alcohol abuse, use of diuretics, history of diseases such as chronic kidney disease, gout and other cardiovascular events such as atrial fibrillation, congestive heart failure, coronary artery disease, and ischemic heart disease were recorded. Baseline vital and anthropometric parameters such as blood pressure, pulse, respiratory rate, oxygen saturation weight, height, and an abdominal circumference values were recorded using standard operating procedures. The following definitions and standard operating techniques were used to identify risk factors for stroke in each subject: hypertension was defined as patient with medical history of hypertension, treated or not, and patient with persistent high blood pressure higher than 140/90 mmHg after stroke. DM was defined as patient with medical history of diabetes, treated or not, random serum glucose greater than or equal to 2 g/L, or venous fasting glucose test greater than or equal to 1.26 g/L. Dyslipidemia was defined as patient with medical history of dyslipidemia or total cholesterol greater than 2 g/L or low-density lipoprotein greater than 1 g/L, or high-density lipoprotein less than .40 g/L in men or less than .50 g/L in women, and triglycerides greater than 1.50 g/L. Metabolic syndrome is defined as per the National Cholesterol Education Program Adult Treatment Panel III guidelines.[18] Alcohol abuse is defined as daily alcohol intake of more than 40 g/L. Obesity was defined as patient with a body mass index (BMI) greater than 30, and when it is impossible to have the body mass index, we use the abdominal circumference: greater than 102 cm in men and greater than 88 cm in women. Smoking was defined as patient with history of smoking (current smokers and ex-smokers) quantified in pack-years. Patients with severe conditions such as a Glasgow Coma Scale of less than 8 of 15 or septic shock were directly admitted in ICU, whereas other cases were hospitalized in the neurology unit.

Blood sample was collected from all patients during the first 24 hours of admission to check SUA levels, fasting blood sugar, complete metabolic panel (urea, creatinine, uric acid, electrolytes) and lipid profile using the Cobas 311 autoanalyzers. A full blood count with platelet counts, prothrombin time, cephaline-kaolin time, C-reactive protein, erythrocyte sedimentation rate, and HIV serology were done. Other tests were prescribed if required by the patient's conditions: chest X-ray, urine culture, hemoculture, and thick blood film to check for *Plasmodium falciparum*. Neurological assessment was done by a neurologist or an intensive care specialist. Interpretation of computed tomography scans was done by both radiologist and neurologist, and its findings were recorded. Electrocardiography, transthoracic, and supra-aortic Doppler ultrasound was systematically done, except for those with severe conditions. On admission, stroke severity was evaluated using the Glasgow Coma Scale (GCS) and the National Institute of Health Stroke Scale (NIHSS), whereas the modified Rankin score (mRS) was