Comparison Between Stroke Patients and Normal Subjects on Hypertension and Blood Biochemical Parameters

***Farha Matin Juliana*[1], *Md. Muniruzzaman Bhuiyan*[2], *Hasan Zahidur Rahman*[2] *and Yearul Kabir*[1]**

[1]Department of Biochemistry, University of Dhaka, Dhaka-1000, [2]Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka-1000

Abstract

A study was conducted to investigate the profile of serum lipids, vitamin C and minerals (Fe, Zn, Cu, Ca) in stroke patients and compared with control subjects. Out of 72 patients 72.3% were male and 27.7% were female. The age of the patients ranged from 25 to 75 years and the mean age was 54.3 years. CT scan of the brain showed that 81.9% had cerebral infarction and only 18.1% had intracerebral hemorrhage. Hypertension was found in 63.9% patients. This study demonstrated a strong association between hypertension and stroke. No significant difference was found between the mean serum total cholesterol of stroke patients (168.9 mg/dl) and control (169.5 mg/dl). On the other hand, the mean serum HDL-cholesterol level of the ischaemic patients (28.6 mg/dl) was significantly lower compared to the control subjects (34.4 mg/dl) but not with hemorrhagic patients (32.3mg/dl). The mean serum LDL-cholesterol levels among two types of stroke patients and control subjects did not differ significantly. The mean value of triglyceride levels in cerebral infarction (209.0 mg/dl) was significantly higher than that of the intracerebral hemorrhage (188.7 mg/dl) and control (157.2 mg/dl). The results suggested that lower level of HDL-cholesterol and higher level of triglyceride are some of the risk factors for the incidence of stroke. The stoke patients, especially intracerebral hemorrhage had significantly ($P<0.05$) lower vitamin C levels (1.2mg/dl) compared to the control (2.4mg/dl) and a close correlation was also postulated between vitamin C and the risk for the incidence of stroke. The mean serum iron, zinc, copper and calcium levels in cerebral infarction patients were significantly lower than that of control subjects suggesting that inadequate intake of these minerals may also be responsible for the incidence of cerebral infarction although physiological significance of these findings need further investigation.

Key Words: Stroke, Risk Factor, Lipid Profile, Vitamin C, Minerals.

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Author for correspondence.

Introduction

A stroke or cerebrovascular accident is a rapidly developing episode of focal and at times global loss of cerebral function, with symptoms more than 24 hours, and with adequate investigation, with no apparent cause other than that of vascular origin. In developed countries it is the third most common cause of death after heart disease and cancer and is responsible for much of physical and mental disability in elderly. In Bangladesh there is no epidemiological data or cerebrovascular disease. The risk factors related to this dreadful disease are yet to be determined.

The search for risk factors for stroke was begun later than studies of risk factors for coronary heart disease. Cross-sectional and prospective epidemiological studies have identified various risk factors for stroke and the most important of these, is hypertension[1,2,3]. It is said to be the single most important risk factor possibly accounting for 70% of stroke. Overall, the age adjusted relative risk of stroke among definite hypertensive persons, compared to normotensive persons is 3.1 in men and 2.9 in women, and even borderline levels carry 50% increased stroke risk[4]. A substantial portion of stroke incidence is directly attributable to hypertension, and a portion of stroke in the population would be eliminated if hypertension was effectively treated. In the study about 64% patient were hypertensive.

Although the relationship between serum lipids to coronary heart disease is well established, its relation to stroke is less clear. Prospective studies of Japanese patients in Japan and of Japanese American men in the Honolulu indicate an inverse association of the serum cholesterol level with the occurrence of intracerebral hemorrhage and no significant relation of serum cholesterol to the risk of cerebral infarction was observed[3]. Some other studies shows no significant association with any type of stroke or cerebral infarction[5,6]. Xu *et al.*[7] suggested that the disturbance of blood lipid metabolism is a risk factor for cerebral infarction. Studies with Bangladeshi population also show hypercholesterolaemia as a risk factor for stroke[8,9]. However it is difficult to assess whether stroke is due specifically to hyperlipidaemia or combination of conditions that include hyperlipidaemia[10].

The importance of nutrition in protecting the living organism against the potentially lethal effects of reactive oxygen species and toxic environmental chemicals has recently been realized. The emerging newer concepts focus on the involvement of trace elements like iron, zinc, selenium, copper and manganese in antioxidant defense mechanism. Inadequate intake of these nutrients has been associated with ischemic heart disease, stroke and cancer where pathogenic role of free radicals is suggested by Lall *et al.*[11] Leinonen *et al.*[12] have suggested that the antioxidant activity of plasma ascorbic acid an important factor providing protection from neurological damage caused by stroke associated oxidative stress.

Despite recent advance in technique and equipment, the reported relationship between trace elements and ischemic cerebral vascular disease remain inconclusive. The demonstration and quantification of such a relationship would be of clinical importance in view of trace elements that often participate in the pathophysiological processes of maintenance of the normal structures and functions of CNS.

Considering the above facts, a study was conducted in stroke patients to find out the relationship and possible influence of serum lipids e.g. total cholesterol, HDL-cholesterol, LDL-cholestrol, and triglycerides to stroke and to asses the potential role of zinc, iron, copper, calcium and vitamin C as associated factors in stroke patients (intracerebral hemorrhage versus infarctions) with control subjects.

Materials and Methods

Study design and population

This study was carried out from September 2000 to February 2001. A total number of 72 (male = 52, Female = 20) clinically diagnosed stroke patient and 27 control subjects were selected from Neurology department of Bangabandhu Sheikh Mujib Medical University and Bangladesh Medical College respectively. The biochemical analysis was done in the Department of Biochemistry, University of Dhaka. Stroke was diagnosed following the WHO Criteria. Patients and controls were between 25 and 75 years old. The patients were selected before any medication was given.

Analytical methods

Under all aseptic condition 5 ml venous blood sample was collected from each of the subjects. Blood sample was kept undisturbed for at least 60 min and was centrifuged at 3000 rpm for 10 min. Serum thus extracted was stored at–20°c for biochmical analysis of serum parameters. Serum cholesterol, HDL-cholestrol, LDL-cholesterol, triglyceride were measured enzymatically according to the method of Allaine *et al*[13], Gordon and Gordon[14], Wielant and Seidel[15], and Jacobs *et al.*[16] respectively. Serum ascorbic acid was estimated with the modified method of Lowry *et al*[17]. Analysis of iron, zinc, copper and calcium were done by an atomic absorption spectophotometer (AAS, Perkin Elmer, M-3110, USA).

Data analysis

Results were expressed as mean ± SD. Data were analysed using SPSS version 4.1.

Results

A total number of 99 men and women aged between 25 to 75 years who concord with the WHO's definition of stroke (patients) and controls took part in the study. Among 99 participants 72 were stroke patients and 27 were control subjects.

Table 1 shows the sex distribution of the stroke patients by age. There were more male patients than female (ration 2.6:1) but it varies with age. Before 60 years age male to female ratio is 1.93: 1, i.e. male is 48.15% higher and above 60 years male to female ratio is 4.17: 1, i.e. males are 76% more likely to have stroke than females.

Table 1. Sex distribution by age of stroke patients

Age (Years)	**Male No. (%)**	**Female No. (%)**
upto 49	9 (12.50)	10 (13.88)
50-59	18 (25.00)	4 (5.55)
≥ 60	25 (34.72)	6 (8.33)
Total	**52(72.22)**	**20(27.78)**

Total (n=72)

On the other hand, CT scan of the stroke patients showed that of all patients 59 (81.9%) had cerebral infarction (CI) and 13 (18.0%) had intracerebral hemorrhage (ICH). Thus of CI was found 4.5 times higher than ICH (Fig-1). Among the patients, about 64% were found hypertensive (Fig-2). All controls were taken hypertensive as a risk factor for stroke.

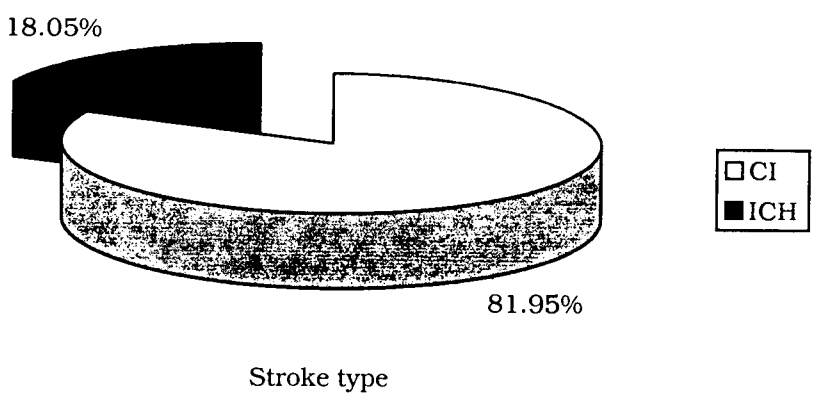

Figure 1. Percentage distribution of stroke by CT scan findings of patients. CI=Cerebral Infarction. ICH=Intracerebral Hemorrhage.

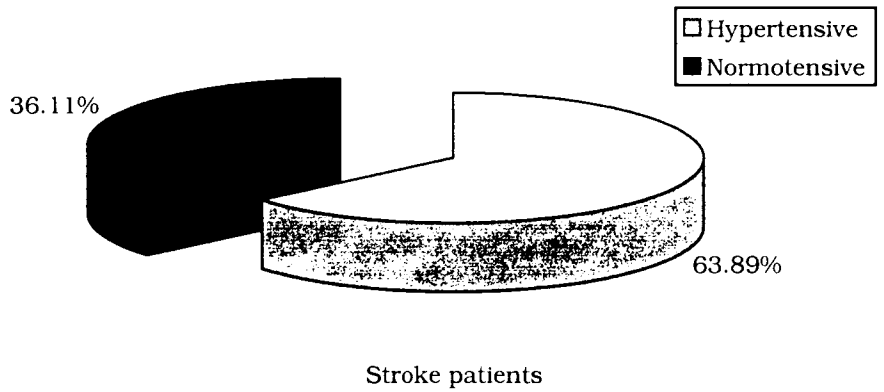

Figure 2. Percentage distribution of stroke patients by hypertension.

The mean value of cholesterol level of cerebral infarction stroke patients (173.5 mg/dl) did not differ significantly from the control (169.5 mg /dl) but significantly different (P<0.01) from intra cerebral hemorrhage patients (148.4 mg /dl). The mean value of serum HDL-cholesterol level was significantly lower (P<0.001) in cerebral infarction stroke patients (28.6 mg/dl) but not in intra cerebral hemorrhage patients (32.3 mg /dl) as compare to control (34.5 mg /dl). The mean HDL-cholesterol level was also significantly different (P<0.01) between the two types of stroke (Table-2). On the other hand, the mean LDL-cholesterol value did not significantly differ among the groups (Table-2). The mean value of serum triglyceride level was significantly (P<0.01) higher in cerebral infarction stroke patients (209.0 mg /dl) compared to control (157.2 mg /dl). No significant difference was found between two types of stroke (Table-2). The mean serum vitamin C value is significantly lower (P<0.05) in intra cerebral hemorrhage patients (1.2 mg /dl) compared to control (2.40 mg /dl) and also with cerebral infarction (1.4 mg /dl) stroke patients.

Table 2. Serum cholesterol, HDL-cholesterol, LDL-cholesterol, triglyceride and vitamin C levels in stroke patients (CI and ICH) and control subjects

Variables (mg/dl)	Stroke patient (n=72)		Control subject (n = 27)	P-Value
	CI (n=59)	ICH (n=13)		
Cholesterol	173.5±39.6*	148.4±37.3	169.5±41.3	*P<0.01
HDL-cholesterol	28.6±8.0*	32.3±10.6	34.4 ± 5.9	* P<0.001
LDL-cholesterol	114.6±38.3	116.8±43.9	116.9 ± 34.7	NS
Triglyceride	209.0 ±106.7*	188.7 ± 70.5	157.2± 71.5	* P<0.01
Vitamin C	1.4 ± 0.94	1.2 ± 0.75*	2.4 ± 2.0	* P<0.05

CI = Cerebral Infarction, ICH = Intracerebral Hemorrhage.
Results are expressed as mean ± SD.

The mean ±SD values of serum iron, zinc, copper and calcium are given in Table-3.

Table 3. Serum iron, zinc, copper and calcium levels in stroke patients (CI and ICH) and control subjects

Variables	Stroke patient (n=72)		Control subject (n = 27)	P-Value
	CI (n=59)	ICH (n=13)		
Iron (μg/dl)	112.0±44.2**	108.3±53.3*	174.9±78.4	* P<0.001
Zinc (μg/dl)	97.0±35.9*	105.9±90.9	123.4 ± 40.5	* P<0.01
Copper (μg/dl)	123.6 ±24.6*	130.8 ± 17.2	132.6± 26.5	* P<0.01
Calcium (mg/dl)	11.6 ± 2.6*	11.0 ± 2.2*	13.9 ± 3.5	* P<0.01

CI = Cerebral Infarction, ICH = Intracerebral Hemorrhage.
Results are expressed as mean ± SD.

Among the stroke patients the mean value of serum iron was more significantly lower (P<0.001) in intracerebral hemorrhage patients (108.3 μg/dl) than in cerebral infarction patients (112.0 μg /dl) as compared to control (174.9 μg/dl). About 5% of the cerebral infarction stroke patients were found deficient in iron. Mean value of serum zinc levels was significantly lower (P<0.01) in cerebral infarction patients (97.0 μg/dl) compared to control (123.4μg/dl) and intra cerebral hemorrhage patients (105.8 μg/dl). About 14% of cerebral infarction patients and 1.38% of intra cerebral hemorrhage stroke patients were found deficient in zinc. Serum copper level in cerebral infarction stroke patients (123.6 μg/dl) was significantly lower (P<0.01) from intra cerebral hemorrhage stroke patients (130.7 μg/dl) and control (132.6 μg/dl). Also about 1.69% of the stroke patients had serum copper levels below the normal value. Serum calcium level was also significantly low (p<0.01) in both types of stroke patients (11.6 mg /dl and 11.0 mg/dl) compared to control subjects (13.8 mg /dl). Only 1.38% cerebral infarction stoke patients had serum calcium levels below the normal value, whereas 15.3% both intra cerebral hemorrhage stroke patients and control subjects were found deficient in calcium.

Discussion

The male to female ratio of the stroke patients in this study was 2.6:1. Male cases was 61.53% higher than that of female which varied with respect to age (Table-1). Before 60 years, male to female ratio was 1.93: 1, but after 60 years 76% higher. These findings are in good agreement with those of the other studies[18,19,20]. In our study maximum number of patients (about 74%) were between 50 to 75 years age and the percentage had declined sharply below the ages. In the present study it was found that the frequency of stroke increases with increase of age, especially in case of male patients. This findings corroborates the results of other reports[19,21] that most of the cases were between 50 to 70 years. CT scan finding of the stroke patients showed that 81.95% patients had cerebral infarction and only 18.05% had intracerebral hemorrhage (Fig-1). This finding is similar to the findings of Brown[22], where they found 85% cerebral infarction and 10% intracerebral

hemorrhage. The present finding are in good agreement with other studied carried out in Bangladesh.

It has been found that there is an association between the risk of stroke and the level of blood pressure. Champman[23] reported that the incidence of stroke among hypertensive patients was higher than that of normotensive subjects. In the present study 63.9% stroke patients had hypertension (Fig-2). The strong association between hypertension and stroke is definitely a major contributor of stroke in Bangladesh as the finding at this study showed higher number of stroke patients with hypertension.

In this study, we found no significant difference between the mean total cholesterol of stroke patients (173.5 mg/dl and 148.4 mg/dl) and control subjects (169.5 mg/dl). But when the mean value of serum total cholesterol level was compared between two types of stroke patients, ischemic stroke patients (173.4 mg/dl) had significantly higher ($P<0.01$) serum cholesterol level than hemorrhage stroke patients (148.4 mg/dl). Iso *et al.*[24] in their study also detected higher cholesterol level in ischemic stroke and lower value in hemorrhage stroke patients. In this study the mean serum HDL-cholesterol level of the Cl type of stroke patients (28.6 mg/dl) was significantly lower in comparison to control (34.4 mg/dl) the ICH patients also had lower level of HDL-cholesterol but the difference was not significant with control subjects. The cerebral infarction patients had relatively more lower value than that of intracerebral hemorrhage. Quizibash *et al.*[25] in their study of TIA and minor stroke detected significantly lower value of HDL-cholesterol than their age and sex-matched controls and concluded that lower HDL-cholesterol as one of the risk factors for ischaemic stroke. On the other hand the mean LDL-cholesterol levels among ischemic, hemorrhagic patients (114.6 mg/dl, 116.8 mg/dl) and control subjects (116.9 mg/dl) did not differ significantly. But some study reported higher LDL-cholesterol levels in stroke patients compared to matched controls[25,26]. Controversis exist regarding the role of lipoprotein, lipids in case of different type of stroke[27,28].

The mean value of triglyceride levels in cerebral infraction (209.0 mg/dl) was significantly higher ($P<0.01$) than that of intracerebnal haemorrhage (188.7 mg/dl) and control (157.2 mg/dl) which is in good agreement with the study carried out in 204 stroke patients by Xu *et al.*[7]. They reported that the levels of triglyceide in patients with cerebral infarction were significantly higher than those in the cerebral haremorrhagic patients and controls but there is no significant difference in blood lipid levels between the patients with cerebral hemorrhage and controls. The results of the present study suggest that the disturbance of triglycerides metabolism is a risk factor for cerebral infarction in our population as also indicated by Xu *et al.*[7]

The most important dietary antioxidant is vitamin C and some studies have links low intake of this vitamin with increased rates of stroke[29,30]. In the present study the stroke patients had much lower mean vitamin C levels (1.4 mg/dl and 1.2 mg/dl) compared to control (2.4 mg/dl) and the mean value of vitamin C in intracerebral hemorrhage is significantly lower ($P<0.05$) as compared to control. The present result indicate that the lower level of serum vitamin C may be a risk factor for stroke.

It has been reported that inadequate intake of copper with other trace elements is associated with stroke[31,11]. In the present study, however no such correlation could be established.

The present study generated a valuable baseline information to form a biochemical and nutritional basis in assessing the risk factor for stroke. Based on the results presented in this study, it is concluded that difference in the level of serum lipids, vitamin C, minerals (Fe, Zn, Cu, Ca) and hypertension between stroke patients and controls are somehow related to the incidence of different types of stroke in the studied population. Further community based prospective study with large sample size is required to establish the actual risk factors for stroke to take preventive and curative measures in our population.

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