

Stroke in Persons with Diabetes Mellitus in Jos, Nigeria

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ABSTRACT

Background: Mortality and morbidity from stroke in patients with diabetes are on the increase. Epidemiological surveys are most crucial in planning and allocating resources as they provide critical information for good policy formulation in a resource poor country. The purpose of this study was to determine the frequency of stroke in patients with diabetes mellitus attending the Medical out Patient unit of Jos University Teaching Hospital.

Methods: A total of one hundred and twenty Nigerians with diabetes mellitus were consecutively selected and age-sex matched with sixty non-diabetic controls in a ratio of two to one respectively.

Results: The mean age of the diabetics was 53.0 ± 12.4 years while that of the controls was 54.5 ± 13.9 . The mean duration of DM was 8.4 ± 6.9 years. Sixty five percent of the diabetics had their disease for up to five years. Eight (6.7%) of diabetic patients had ischaemic stroke while 3(5%) of the controls had stroke.

Conclusion: The frequency and risk factors for stroke in persons with diabetes mellitus in Jos, Nigeria are similar to those obtained in other parts of the world. A differing result of hyperlipidaemia as a major determinant for stroke in persons with diabetes mellitus is worth studying in future in a large prospective study.

KEYWORDS: Diabetes mellitus; Hypertension; Nigeria; Stroke.

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INTRODUCTION

Stroke is the third commonest cause of death (after coronary artery disease and cancer) in developed countries¹. It is the third commonest neurological disease, after infections and epilepsy in black Africans from community based studies². Several hospital based reports have indicated that stroke is a major cause of mortality and morbidity in black Africans^{2,3}.

It was believed that stroke was no more common in diabetics than in the general population⁴. Large autopsy studies, however, have shown an increase in encephalomalacia (cerebral infarcts) in diabetics. Stroke is two to six times more common in diabetics

than in non-diabetics and it is responsible for about 25 per cent of diabetic deaths⁵. This increase in stroke rate is probably attributable to an increase in cerebral atherosclerosis⁶. The important factors include hypertension, which is common in diabetics and also contribute to atherosclerosis, promotes both intracranial small vessel disease and heart disease, which can lead to lacunar and embolic infarction respectively⁶.

Stroke is an important health issue world wide and expressing and interpreting risk factors provide vital epidemiological information⁷. Understanding the risk factors of a disease is an important aspect for clinicians in prevention strategy. The attending physicians also play a role in providing information on risk factors reduction. The purpose of this study was to determine the frequency of stroke in patients with diabetes mellitus attending the Medical Out Patient unit of the University Teaching Hospital and assess the contribution of the various risk variables or determinants in the occurrence of stroke in these patients. The study also compares the linear regression statistics of metric and non-metric component of risk determinant of stroke in patients with diabetes mellitus.

MATERIALS AND METHODS

Setting and study design

This is a cross sectional study to determine the frequency of stroke in patients with diabetes mellitus (DM) seen in Jos University Teaching Hospital (JUTH), a referral centre for Plateau state and North Central Nigeria. The study period was from December 2002 to July 2003.

Subjects

Consecutive patients with diabetes mellitus attending the Endocrine Clinic of JUTH, other clinics of the Medical Out Patient Departments and/or admitted to the medical wards were screened and examined for stroke. Diabetes mellitus was diagnosed according to American Diabetes Association, ADA/WHO consultation criteria⁸. A similar population of non-diabetic patients attending the General out Patients Department (GOPD) for minor ailments served as

controls.

The study was approved by the Research and Ethical Committee of JUTH. Informed consent was obtained from the subjects and controls before enlistment for the study. Excluded from the study were pregnant women, patients with DM of specific aetiology, patients with diabetic emergencies, positive HIV or VDRL serology and positive family history of diabetes mellitus among controls.

Study procedure

Demographic data, clinical history, laboratory tests and physical findings of each subject were documented using a proforma. Nervous system examination included full assessment of cranial nerves, deep tendon reflexes, motor and sensory functions. Tuning fork of 128 Hz was used to assess vibration sense and 10-g filament tensiometer to assess light touch perception.

Definitions

Stroke was defined as sudden or rapid onset of focal or global brain dysfunction of vascular origin, lasting for more than 24 hours in the absence of causes such as meningitis and space occupying lesions (tumors, abscesses etc, traumatic cerebral haemorrhage and subdural collections, including haematoma). Stroke was considered to be thromboembolic when a focal neurological event occurred without prolonged unconsciousness, nuchal rigidity, fever, prominent leucocytosis or bloody spinal fluid. The diagnosis of haemorrhagic stroke was made when the neurological event was accompanied by headache, loss of consciousness and bloody spinal fluid⁹.

Statistical analysis

Data obtained was analyzed using the EPI info-2000 statistical soft ware¹⁰. Results were expressed as means (SD) or with ranges for continuous variables and proportions for categorical variables. Fisher's exact results were used where expected frequencies were less than five. The Mantel-Haensnel was used to estimate the chi-square for significance of association between groups or proportions. Logistic regression analysis was used to assess independent contribution of the risk variables. A p-value less than 0.05 were considered significant.

RESULTS

Clinical characteristics of study subjects

Table I shows the clinical characteristics of the study subjects. The mean age of the diabetics was 53.0

± 12.4 years while that of the controls was 54.5 ± 13.9, (p=0.056). Their ages ranged from 22 to 87 years. The mean duration of DM was 8.4 ± 6.9 years. Sixty five percent of the diabetics had their disease for up to five years.

Frequency of stroke in study subjects

Table II shows the frequency of stroke in study subjects. Eight (6.7%) of diabetic patients had stroke while 3(5%) of the controls had stroke. None of the subjects had haemorrhagic stroke based on CT-scan and clinical factors.

Comparison of characteristics of diabetics with stroke and without stroke

Table III compares the various characteristics of diabetes mellitus patients with stroke and those without stroke. This was done to explain the differences in the two groups using independent sample test to look at the effect of age, duration of DM, hypertension, BMI, total cholesterol, fasting plasma glucose, and retinopathy. There was no influence of gender, fasting plasma glucose, obesity, triglyceride, and diastolic blood pressure on the occurrence of stroke. Age, duration of DM, systolic blood pressure and total cholesterol were all significant for the presence of stroke in DM patients. The mean BMI of diabetics with stroke was 24.86± 4.93(P=0.001). Seven of the eight diabetics with stroke had retinopathy; with at least retinal exudates, compared to 52 (46.4%) of diabetics without stroke. This was significant with P=0.001

Multiple logistic regression analysis

The test variables that were significant for stroke; such as age, duration of DM, systolic blood pressure, Total-Cholesterol and diabetic retinopathy were subjected to multiple regression analysis. Total-Cholesterol was independently significant for stroke in diabetic persons. (Odds Ratio=2.95, r=1.08, P=0.009). This is shown on Table IV.

Table I. Characteristics of Study Subjects

Characteristics	Diabetics	Controls
Number (M/F)	58/62	29/31
Age, years (mean, SD)	53.0 ± 12.4	54.5 ± 13.9
Duration of DM (years)	8.4 ± 6.9	---
Mode of treatment (%)		---
OHA	82.5	
Insulin	12.5	
Diet alone	5	

OHA =Oral Hypoglycaemic Agents.

Table II. Frequency of stroke among diabetics and controls

Status	Without Stroke	With Stroke	Total
Control	57(95%)	3(5.0)	60(100)
Diabetics	112(93.3%)	8(6.7)	120 (100)
Total	169 (93.89)	11(6.11)	180(100)

($\chi^2=0.19$) Odds Ratio: 1.36; 95% CI (0.35-5.31)

Fisher exact P= 0.056 (not significant).

() = values in parentheses are percentages.

Table III. Comparison of Characteristics of Diabetics with Stroke and Without Stroke

Risk Determinants	Stroke present(n=8)	Stroke absent (n=112)	P-Value
Age (yr.)			
mean \pm SD	61.6 \pm 9.6	52.4 \pm 12.4	0.03(S)
Sex M:F	3:5	53:59	0.08(NS)
Duration of DM (yr) mean \pm SD	13.1 \pm 6.3	8.0 \pm 6.8	0.02(S)
Fasting plasma glucose mean \pm SD	8.4 \pm 2.5	8.3 \pm 3.6	0.87(NS)
SBP mean \pm SD	154.5 \pm 19.4	137.4 \pm 4.1	0.02(S)
DBP mean \pm SD	95.0 \pm 5.8	88.7 \pm 15.2	0.24(NS)
BMI Mean \pm SD	24.8 \pm 4.9	25.3 \pm 5.0	0.80(NS)
Total cholesterol Mean \pm SD	6.1 \pm 1.9	4.3 \pm 1.8	0.02(S)
HDL Mean \pm SD	1.7 \pm 0.9	2.2 \pm 1.1	0.16(NS)
Triglyceride Mean \pm SD	2.1 \pm 1.8	2.2 \pm 1.5	0.90(NS)
Retinopathy (present)	7(87.4%)	52(46.4%)	0.001(S)

Table IV. Multiple Regression Analysis

Variable	*OR	95%CI	Coefficient	SE	Z	P value
Age	1.44	0.94-1.14	0.042	0.048	0.865	0.38
Duration	1.06	0.93-1.20	0.068	0.062	0.985	0.32
ϕ TC	2.96	1.30-6.67	1.08	0.416	2.600	0.009
Retinopathy	5.80	0.426-79.15	1.75	1.332	1.319	0.186
ψ SBP	1.018	0.98-1.05	0.017	0.017	1.037	0.299
Constant	---	---	-15.99	5.16	-3.09	0.002

ϕ =Total cholesterol, ψ =Systolic Blood Pressure, π =Odds Ratio, SE= Standard Error, Z=Z-score.

DISCUSSION

The prevalence of stroke in our study in Jos University Teaching Hospital is 6.7%. Diabetes is a clear risk factor for stroke, though data supporting DM as risk for stroke is sparse and available data are mainly in the southern part of Nigeria¹¹. This low prevalence of stroke among diabetes mellitus patients is in agreement with Famuyiwa and colleagues¹², Zargar and coworkers¹³; the reason being that stroke in the diabetics is usually

fatal and patients do not live long and hence the low prevalence. However, the report of Bell and colleagues⁶ and Barret-Conner and colleagues¹⁴ is in contrast with this finding. They reported a higher prevalence in a population survey^{6, 14}. Little information is available on cerebrovascular disease in diabetic patients and few studies have reported low prevalence of stroke among patients with DM in Nigeria¹¹.

The result of our study only shows that the occurrence of stroke in diabetics compared with non diabetics is lower than the two to six times reported in the western world^{7, 15} although stroke related mortality and morbidity are on the increase among diabetics¹⁵. In addition, the well known macrovascular diseases such as atherosclerosis cause a great deal of mortality in the diabetic population. Diabetes associated dyslipidaemias strongly promote atherogenesis; therefore non-enzymatic glycation of lipoproteins may be important as a cause of cerebrovascular disease in diabetics¹⁶. Many more factors may contribute to the development of stroke in patients with DM. Many researchers uphold the view that when the major determinants of diabetic stroke (duration of diabetes and effectiveness of glycaemic control) are adequately controlled for, other such factors as age, sex, family history of diabetes, hyperlipidaemia do not contribute much to the development of stroke⁷. Many such factors may just be epidemiologic associations¹⁶.

The result of this study showed that hypertension was clearly associated with stroke, sixty-six (55%) of diabetics were previously diagnosed as hypertensive and were on treatment. The mean supine systolic blood pressure for diabetics with stroke was 154.5 \pm 19.4, (P=0.002), mean age was 61.63 \pm 9.65 which was clearly significant when compared to diabetics without stroke. This is consistent with an observational analysis of UKPDS that showed that clinical complications (i.e. micro and macrovascular) were significantly associated with systolic blood pressure, and each 10 mmHg of mean systolic blood pressure reductions was associated with 12% reduction risk for any complication related to DM and 13% for macrovascular complications¹⁸. Based on these findings, there is need to re-emphasize assiduous treatment of hypertension to the target required if diabetic stroke complications are to be minimized.

It has been documented that hypercholesterolemia and hyperlipidaemia are not well established risk factors for first or recurrent stroke in contrast to what is seen with cardiac disease. Observational cohort studies have shown positive association for cholesterol level and risk

of ischaemic stroke¹⁷. Our results did not show any association between serum triglycerides and stroke but there was significant association with Total-Cholesterol and stroke. A multiple regression analysis of age, duration of DM, systolic blood pressure, Total-Cholesterol and diabetic retinopathy showed that Total-Cholesterol was independently significant for ischaemic stroke in persons with diabetes mellitus. This is in agreement with the National Cholesterol Education Program (NCEP) recommendations on management of lipids in persons with stroke; reduction in saturated fats and cholesterol intake, weight reduction and increase in physical exercise. They also approved the use of statins such as pravastatins and simvastatins in persons with stroke and Coronary Heart Disease¹⁸. Evidence in the literature suggests that obesity is not an independent risk factor for stroke in DM patients¹⁸. However, increased risk of stroke in DM patients may be indirectly mediated by obesity through an increase in atherosclerosis, which is a known risk factor for stroke¹⁹.

Our study was not without limitations as we were unable to carry out CT-scan on most of our subjects. Subjects were referred to distant town to have CT-scan done.

In conclusion, this study has determined the frequency of stroke among diabetes patients in Jos, a developing area of Nigeria where rational treatment of DM is still developing. The study was able to identify that, age, duration of DM, Systolic hypertension, total cholesterol and retinopathy were all significant risk factors for stroke in diabetics. Diabetic retinopathy was highly associated with stroke in DM patients which had been widely reported. This calls for regular eye examination in diabetics as this may prevent the risk of stroke in those that are positive for retinal exudates.

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