PATTERN OF STROKE IN TYPE 2 DIABETIC SUBJECTS VERSUS NON DIABETIC SUBJECTS

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Background: Diabetes mellitus is a well-recognized risk factor for ischaemic stroke. Stroke in diabetic patients is different from stroke in non-diabetics from several perspectives. There is no local study on this topic. This is the first study from Pakistan, in which pattern of stroke in diabetics have been described and compared with non-diabetics. The object of this study was to compare pattern of stroke in diabetic subjects with non-diabetics. **Methods**: This is a prospective comparative cross sectional study, carried out at Liaquat national hospital, Karachi, neurology department from October to March 2006. Fifty patients were enrolled in diabetic group and 50 in non-diabetic. Clinical features, risk factors and stroke patterns were identified. **Results**: Mean age was 59.5 (±11.82) in diabetics and 60.4 (±14.8) in non diabetics. There was slight preponderance of male patients in non diabetic group. Out of 50 diabetic patients, 44 (88.0%) had ischaemic stroke and 6 (12.0%) had intracerebral haemorrhage. In non-diabetics, 29 (58.0%) had ischaemic stroke while 21 (42.0%) had intracerebral haemorrhage. On further analysis of ischaemic stroke, cortical infarcts (CI) was found in 22, sub cortical infarcts (SCI) in 14, brainstem in 5 and cerebellar in 2 diabetic patients. CI was also the commonest subtype of ischaemic stroke in non-diabetics. **Conclusion**: Patterns of stroke in diabetics are different from non-diabetics. Ischaemic stroke is more prevalent than hemorrhagic stroke in diabetics. Sub cortical infarcts are more common in diabetics than non diabetics (p=0.04).

Keywords: Stroke, diabetes mellitus, stroke pattern.

INTRODUCTION

DM is a modifiable risk factor for a first ischaemic stroke.[1] In people with type 2 diabetes mellitus, there is a 2 to 5 fold increased risk for stroke compared with those without diabetes.[2] Modifiable risk factors for stroke include hypertension, diabetes mellitus, hyperlipidemia, cigarette smoking, cardiac disease, drug abuse, heavy alcohol consumption, and AIDS.[3] Presence of diabetes mellitus and ischaemic heart disease predict ischaemic stroke in a patient with hypertension.[4] Risk factors for stroke in diabetic patients include elevated blood pressure, smoking, age, male sex, atrial fibrillation and hyperglycemia.[5] In recently published observation of 5017 patients with different types of ischaemic stroke, the prevalence of diabetes was significantly higher in subjects with small vessel cerebrovascular accidents (35.5%) compared to patients with large vessel atherosclerosis (29.0%) or cardio-embolic (28.1%), while it was less common in subjects with other combined etiologies of stroke (9.4%).[6]

The significance of diabetes as a risk factor for hemorrhagic stroke could differ depending on ethnicity. In the Honolulu Heart Program, diabetes was not associated with an increased risk of hemorrhagic stroke in Japanese-American men, while in the Framingham study; there was a 4.5-fold excess risk of this type of stroke in white men with diabetes. [7] In a population based study from Finland, diabetes was a risk factor for cerebral infarction (RR-3.26) and unclassified stroke (RR-5.76), while there was no association between diabetes and sub arachnoidal and intracerebral hemorrhage.[8]

In one recently published study [9], diabetic individuals were older than non-diabetics. Intracerebral haemorrhage was less frequent in diabetic patients who have had a stroke. SCI were more frequent in diabetics, whereas complete middle cerebral artery (MCA) territory infarcts were less frequent. The association of diabetes mellitus with lacunar infarcts (LI) or SCI suggests small vessel disease (SVD) as the underlying pathophysiology.

In one study,[10] lacunar strokes was the most common subtype of stroke in our population, which was considered to be due to high burden of inadequately treated hypertension and diabetes. As diabetic angiopathy is presumed to differ from atherosclerotic angiopathy, strokes experienced by diabetic versus non-diabetic individuals may also differ. However, data on stroke type, topography, and outcome in diabetic persons conflict.[11] Diabetes is an independent risk factor of death from stroke. Tuomilehto *et al*[12] calculated that 16% of all stroke mortality in men and 33% in women could be directly attributed to diabetes. However, one local study could not show much difference in the outcome in the diabetics versus non diabetics.[13]

One large[14] prospective European multicentre study calculated that stroke in diabetic patients was different from stroke in non-diabetics from several perspectives. In diabetic patients, the frequency of intracerebral haemorrhage was lower,

the rate of lacunes was higher, recovery of handicap by Rankin scale score was worse and mortality was not increased.

Though there is extensive data on diabetic retinopathy, neuropathy and peripheral vascular disease, there is not enough data on pattern of stroke in type 2 diabetics.[15]

As there is a paucity of local data on this topic, this study is therefore planned to identify patterns of stroke in our population with diabetes mellitus.

MATERIAL AND METHODS

All patients older than 25 years presenting with features of stroke as hemiparesis, hemianaesthesia, language dysfunction, vertigo and altered level of consciousness were enrolled in the study. Informed verbal consent was taken. Patients were assessed for their glucose metabolism. All those who had history of diabetes in past, or had random blood glucose level more than 200 mg/dl or fasting blood glucose level more than 126 mg/dl before the onset of stroke (treated with either insulin, oral hypoglycemic agents or not treated) were included in diabetic group. HbA1c was checked in patients who were diabetics. Those who had no history of diabetes mellitus in past and had normal blood glucose level at time of admission were included in non diabetic group.

Patients with either stress hyperglycemia, i.e., no history of diabetes in past and normal HbA1c level but elevated blood glucose at the onset of stroke or diabetes diagnosed at the onset of stroke were excluded from the study. Patients with history of head injury, or usage of anticoagulant drugs or steroids prior to onset of stroke were also not included in the study.

Presence of other risk factors as age, sex, hypertension (systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg), smoking (habitual tobacco smoking), dyslipidemia (elevated plasma cholesterol and/or triglycerides or a low high density lipoprotein level that contribute to atherosclerosis), previous history of transient ischaemic attack (a neurological deficit lasting less than 24 hours, that is attributed to focal cerebral or retinal ischaemia), ischaemic heart disease (coronary artery diseases caused by compromised coronary vascular supply as angina, myocardial infarction or heart failure) or/and cerebrovascular accidents (CVA) was noted.

Routine laboratory tests including complete blood count, random blood glucose level, HbA1c, fasting lipid profile and electrocardiogram (ECG) were done. CT scan (computed tomography) or/and MRI (Magnetic Resonance Imaging) of brain was done to identify the type of stroke. Stroke was classified into ischaemic or hemorrhagic type according to CT scan or MRI brain. Ischaemic stroke was further typified into four categories.

1. Cortical Infarcts [CI] (infarcts in the territory of the middle cerebral artery [MCA]; anterior cerebral artery [ACA], or posterior cerebral artery [PCA]).
2. Subcortical infarcts [SCI]
3. Cerebellum
4. Brainstem

Further investigations as carotid ultrasound Doppler and/or echocardiography were done where needed. Findings were entered on proforma.

Data was analysed by SPSS version 10.0. Relevant descriptive statistics, frequency and percentage were computed for hypertension, dyslipidemia, smoking, ischaemic heart disease, CVA and TIA. Mean and standard deviation were computed for age. Chi-square test was used to check proportion between diabetics and non diabetics for qualitative variables with 0.05 level of significance.

RESULTS

Fifty patients were included in diabetic group and 50 in non-diabetic group. Mean age was 59.5 (±11.82) in diabetic group and 60.4(±14.8) in non-diabetic group. Demographic characteristics are presented in Table-1.

Table-1: Demographic characteristic

Demographic characteristics	Diabetics (n=50)	Non diabetics (n=50)	*p* value
Age	59.5 (±11.82)	60.4 (±14.80)	1.000
Males	28 (56%)	34 (68.0%)	0.493
Hypertension	46 (92.0%)	43.0 (86.0%)	0.5
Ischaemic heart disease	16 (32.0%)	14 (28.0%)	0.7
Dyslipidemia	6 (12.0%)	5 (10.0%)	0.8
CVA	9 (18.0%)	9 (18.0%)	0.89
TIA	1 (2.0%)	3 (6.0%)	0.5
Current or previous smokers	20 (40.0%)	16 (32.0%)	0.28

Low-density lipoprotein (LDL) was checked in 47 diabetic and 45 non-diabetic subjects. High-density lipoprotein (HDL) was checked in 46 diabetic and 45 non-diabetics. In non-diabetics, individuals who had hemorrhagic stroke were found to have high HDL as compared to those who had ischaemic stroke, i.e., 63.32±30.02 versus 44.62±10.90.

CT scan was done in 39 diabetic and 42 non-diabetic subjects. MRI was done in 13 diabetic and 8 non-diabetic patients.

Forty-four (88.0%) diabetics as compared to 29 (58.0%) non-diabetics were found to have ischaemic stroke. Frequency of hemorrhagic stroke was high, i.e., 21 (42.0%) in non-diabetics as compared to 6 (12.0%) in diabetics. Ischaemic strokes were significantly more common in diabetics

(p=0.001). Frequency of hemorrhagic stroke in diabetics was significantly low (p= 0.002) (Table-2).

CI was the commonest subtype of ischaemic stroke in both groups. However, SCI were more common in diabetics as compared to non-diabetics (p=0.04). Subtypes of ischaemic stroke in both groups are described in Table-2.

Table-2: Types and subtypes of stroke

Type of stroke	Diabetics	Non diabetics	*p* value
Ischaemic stroke	**44 (88%)**	**29 (58.0%)**	**0.001**
CI	22	19	0.5
SCI	14	6	0.04
Brain stem	5	2	0.93
Cerebellum	2	1	0.65
Un identified	1	1	0.99
Haemorrhagic stroke	**6 (12.0%)**	**21 (42.0%)**	**0.002**
Basal ganglia	4	12	0.16
Thalamic	1	6	0.26
Lobar	1	2	0.94
Brain stem	--	1	0.79

Etiologic factors of ischaemic stroke are explained in Figure-1. Large vessel disease was more common than small vessel disease in both groups. Similar results were described in one more study.[9] However, small vessel disease was more common in diabetics as compared to non diabetics.

Frequency of significant extra cranial carotid artery disease (i.e., stenosis >70%) was 8% in diabetics and 10% in non-diabetics.

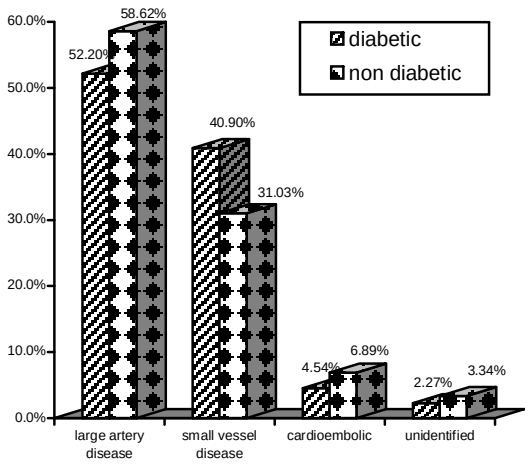

Figure-1: Etiology of ischaemic stroke in diabetics and non-diabetics

DISCUSSION

Our study did not show significance age difference between 2 groups. This contrasts with another study[9] in which diabetic individuals were on average 5.3 years older than non-diabetics. However, similar findings were observed in other studies as well.[14,16]

Frequency of other risk factors for stroke as hypertension, ischaemic heart disease, hyperlipidemia were also similar. While other studies[9,17] have found that diabetic patients are more likely to have hypertension, myocardial infarction, and high cholesterol than their non diabetic counterparts suggesting that diabetics have high cerebrovascular and cardiovascular risk. Ischaemic stroke was more prevalent in diabetics as compared to non-diabetics and haemorrhagic stroke was significantly less prevalent in diabetics. In one more study,[9] diabetic individuals had a lower relative prevalence of intracerebral haemorrhage (ICH: 6.4 versus 9.7%; p=0.011). Also, low frequency of intracerebral haemorrhage in diabetics is well known.[16] This may be explained by the fact that severity of fibrinoid necrosis of small cerebral arteriole walls, which is usually associated with ICH, is less pronounced in patients with diabetes and arterial hypertension compared to those with hypertension alone.[18] However, Stegmayr and Asplund[19] found a two time higher incidence of ICH in diabetic subjects compared to non diabetic subjects.

Previous history of TIA was less frequent in diabetics. One study[20] also showed low incidence of TIA in diabetics. A lower incidence of TIA, taken together with the high prevalence of major stroke, could be explained by a worse tolerance of the same insult to cerebral circulation in diabetic patients, leading to the development of full blown cerebral damage, whereas in non diabetic subjects, the cerebrovascular disturbance of the same extent would not lead to permanent morphologically recognized cerebral infarction.[21] The sub-types and topography of ischaemic stroke are presumed to differ between diabetic and non diabetic individuals according to the type of angiopathy induced by diabetes mellitus. Lacunar (small, less than 15 mm in diameter infarction, cyst like, frequently multiple) is the typical type of stroke in diabetic subjects.[22] Lacunar infarcts (LI) are typically found in the distribution of deep perforating arteries.[23]

Our study found significant differences in subtypes of ischaemic stroke in diabetics and non-diabetics. CI was the commonest subtype in both groups and SCI were more frequent in diabetics than non-diabetics. As far as the aetiology of ischaemic stroke is concerned, large artery disease was more common than small vessel disease in diabetic group. Similar result was described in one more study.[9] Higher frequency of large artery disease can be the result of an increased incidence of large vessel intracranial vascular disease in diabetics,[24] as significant extracranial carotid stenosis was found in

only 8% of diabetic patients in our study. Frequency of extracranial carotid artery stenosis is almost same in both groups showing that diabetes does not seem to put the patients at increased risk of extracranial carotid artery stenosis.

CONCLUSION

There is no significant age difference between diabetics and non-diabetics with stroke. Patterns of stroke are different in diabetics as compared to non-diabetics as SCI is more common in diabetics. Furthermore, diabetes mellitus has been found a risk factor for ischaemic stroke and not for hemorrhagic stroke (p=0.002).

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REFERENCES

1. Gordick PB, Sacco RL, Smith DB, Albert M, Mustone-Alexander L, Rader D, *et al.* Prevention of a first stroke: a review of guidelines and multidisciplinary consensus statement from the National Stroke Association. JAMA 1999;281:1112–20.
2. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes. Other risk factors and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. Diabetes Care 1993;16: 434–44.
3. Jafari FH, Ahmed SI, Qureshi HA. Presentation, progression and prognosis of stroke in Hypertensives, the Diabetic and the Normotensive Normoglycemic. J Rawalpindi Med Coll 2000;4:47–9.
4. Khealani BA, Syed NA, Maken S, Mapari UU, Hameed B, Ali S, *et al*. Presence of diabetes mellitus and ischemic heart disease predict ischemic stroke in a patient with hypertension. .J Coll Physicians Surg Pak 2005;15:22–5.
5. UKPDS Group. Association of systolic blood pressure with macrovascular and microvascular complications of type 2 Diabetes (UKPDS 36). BMJ 2000;321:412–9.
6. Grau AJ, Weimer C, Buggle F, Heinrich A, Goetler M, Neumaier S, *et al.* Risk factors, outcome,, and treatment in subtypes of ischemic stroke. The German stroke data bank. Stroke 2001;32:2559–66.
7. Rodriguez BL, D' Agostino R, Abbott RD, Kagan A, Burchfiel CM, Yano K, *et al.* Risk of hospitalized stroke in men enrolled in Honolulu Heart Program and the Framingham Study: A comparison of incidence and risk factor effects. Stroke 2002;33:230–6.
8. Njolstad I, Arnesen E, Lund-Larsen PG. Body height, cardiovascular risk factors, and risk of stroke in middle- aged men and women. A14- year follow-up of the Finnmark study. Circulation 1996;94:2877–82.
9. Karapanayiotides T, Piechowski-Jozwiak B, van Melle G, Bogousslavasky J, Devuyst G. Stroke patterns, etiology, and prognosis in patients with diabetes mellitus. Neurology 2004;62:1558–62.
10. Syed NA, Khealani BA, Ali S, Hasan A, Akhtar N, Brohi H, *et al*. Ischemic stroke subtypes in Pakistan: the Aga Khan University Data Bank. J Pak Med Assoc 2003;53:584–8.
11. Abbott RD, Donahue RP, MacMahan SW, Reed DM, Yano K. Diabetes and the risk of stroke: the Honolulu Heart Program. JAMA 1987;257:949–52.
12. Tuomilehto J, Rastenyte D, Jousilahti P, Sarti C, Vartiainen E. Diabetes mellitus as a risk factor for death from stroke. Prospective study of the middle-aged Finnish population. Stroke 1996;27:210–15.
13. Basir F, Ali S, Aziz H. Stroke recovery and outcome in diabetes. J Coll Physicians Surg Pak 2001;11:736–8.
14. Megherbi S-E, Milan C, Minier D, Couvreur G, Osseby G-V, Tilling K, *et al*. Association between diabetes and stroke subtypes on survival and functional outcome 3 months after stroke. Data from the European BIOMED Stroke Project. Stroke 2003;34:688–94.
15. Sarkar RN, Banarjee S, Basu A. Comparative evaluation of diabetic and non- diabetic stroke--effect of glycemia on outcome. J Indian Med Assoc 2004;102:551–3.
16. Jorgensen H, Nakayma H, Raaschou HO, Oslen TS. Stroke in patients with diabetes. The Copenhagen Stroke Study. Stroke 1994;25:1977–84.
17. Kiessla BM, Khoury J, Kleindorfer D, Woo D, Schneider A, Alwell K, *et al*. Epidemiology of ischemic stroke in patients with diabetes: the greater Cincinnati/Northern Kentucky Stroke Study. Diabetes Care 2005;28:355–9.
18. Aronson SM. Intracranial vascular lesion in patients with diabetes mellitus. J Neuropathol Exp Neurol 1973;32:183–96.
19. Stegmayr B, Asplund K. Diabetes as a risk factor for stroke. A population perspective. Diabetologia 1995;38:1061–8.
20. Fritz VU, Bilchik T, Levien LJ. Diabetes as a risk factor for transient ischemic attacks opposed to stroke. Eur J Vasc Surg 1987;1:259–62.
21. Mankovsky BN, Zeigler D. Stroke in patients with diabetes mellitus. Diabetes Metab Res Rev 2004;20:268–87.
22. Ghika A, Bogousslavsky J, Regli F. Infarcts in the territory of the deep perforators from the carotid system. Neurology 1989;39:507–12.
23. Mohr JP, Caplan LR, Melski JW, Goldstein RJ, Duncan GW, Kistler JP, *et al.* The Harvard Cooperative Stroke Registry: A prospective registry. Neurology 1978;28:754–62.
24. Baliga BS, Weinberger J. Diabetes and stroke: part one—risk factors and pathophysiology. Curr Cardiol Rep 2006;8:23–8.

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