ORIGINAL ARTICLE

Frequency of Newly Diagnosed Diabetes Mellitus in Acute Ischaemic Stroke Patients

Fatima Zahra[1], Saera Suhail Kidwai[2], Shaista A. Siddiqi[3] and Rashid Mohammad Khan[4]

ABSTRACT

Objective: To determine the frequency of newly diagnosed diabetes mellitus in acute ischaemic stroke patients.

Study Design: Observational study.

Place and Duration of Study: Jinnah Postgraduate Medical Centre, Karachi, from June 2007 - June 2008.

Methodology: This study included adult patients (age > 30 years, both genders) with the diagnosis of acute ischaemic stroke. Patients who were known to have diabetes mellitus prior to stroke, had a non-lacunar stroke or were admitted to intensive care units for any reason were excluded. Detailed history and examination, fasting blood sugar, fasting lipid profile, a non-enhanced CT scan brain and electrocardiogram were done on every patient. Data were entered on a preformed proforma. The results were analyzed on SPSS version 10. Chi-square test was applied. P-value <0.05 was considered to be statistically significant.

Results: A total of 250 patients were enrolled. The male: female ratio was 1: 0.9. Mean age was observed as 60.9±10.1 years. In total, 50 new cases of diabetes mellitus were identified (20%). Average fasting blood sugar in diabetic subjects was 148±10 mg/dl. The most common risk factors in the newly diagnosed diabetic subjects were hypertension 26 (52%), smoking 18 (36%) and hyperlipidemia 14 (28%). Atrial fibrillation and myocardial infarction were seen in 12 subjects (24%) and 9 subjects (18%) respectively.

Conclusion: Twenty percent patients with acute ischaemic stroke had un-diagnosed diabetes. Therefore, it is advisable to screen acute stroke patients for diabetes to reduce their long-term morbidity and mortality.

Key words: *Diabetes mellitus. Hypertension. Ischaemic stroke.*

INTRODUCTION

Stroke is considered the third largest cause of death in the world and the largest cause of disability in the United States. Diabetes mellitus remains an independent risk factor of stroke and coronary heart disease. Diabetes is also one of the most consistent predictors of recurrent stroke or stroke after transient ischaemic attack (TIA). The increased risk of recurrent stroke due to diabetes ranges from 2.1 to 5.6 times that of non-diabetic patients and is independent of glucose control during interstroke period.[1] Approximately one-third of all patients with diabetes have undiagnosed diabetes (i.e. not recognized by their clinician) and usually present as complications like stroke, myocardial infarction and diabetic foot.[2] The prevalence of previously recognized diabetes mellitus in acute stroke patients is estimated between 8 - 20%. About 6 - 42% of acute stroke patients have previously un-recognized diabetes mellitus.[3] In a study of supratentorial strokes, diabetes mellitus was diagnosed in 24.8% patients while transient hyperglycemia was seen in 36.3% of patients.[4]

Most human studies have shown that in acute stroke, admission hyperglycemia in patients with or without diabetes is associated with a worst clinical outcome than in patients without hyperglycemia. Evidence suggests that elevated glucose levels may reflect underlying glucose intolerance or diabetes.[5] Given these facts, hyperglycemia, however, is often ignored in these events as it is solely attributed to physiological stress of acute stroke event. Interestingly, the rate of screening for diabetes in hyperglycemic stroke patients without a prior diagnoses of diabetes was found at its best to be 20%.[6]

The under diagnosis of diabetes in the general population together with the strong association of diabetes with stroke suggest a rationale for screening all hyperglycemic stroke patients for diabetes. The diagnosis of diabetes in a stroke patient would change the initial management of that patient, specifically with respect to other risk factors like lipid and blood pressure management.[7]

Since, there is a paucity of local data regarding un-diagnosed diabetes in stroke patients, the current study was conducted to determine the frequency of newly diagnosed diabetes in acute ischaemic stroke patients.

[1] *Department of Medical, Jinnah Postgraduate Medical Centre.*
[2] *Department of Medicine / Neurology[3] / Pharmacology[4], Jinnah Medical College Hospital, Karachi.*

Correspondence: *Dr. Saera Suhail Kidwai, Department of Medicine, Jinnah Medical College Hospital, SR-6, Sec 7A, Industrial Area, Korangi, Karachi.*
E-mail: saerakhan@hotmail.com

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METHODOLOGY

Consecutive adult patients admitted to the medical units of Jinnah Postgraduate Medical Centre, Karachi, from June 2007 to June 2008 with established acute ischaemic stroke after radiological confirmation using non-constrast enhanced CT scan brain were included for the study. All the patients who gave their consent to participate in the study were questioned about their medical history and were examined in detail for their neurological deficits. Patients who were known diabetics, had non-lacunar stroke or were admitted to intensive care units were excluded.

All subjects had their random blood sugar checked at the time of admission followed by fasting blood sugar for the next consecutive days till discharge. Patients were checked for hyperlipidemia and an electrocardiogram was done to screen for any acute ischaemia or arrhythmia.

Data was entered on a preformed proforma. The results were analyzed on Statistical Package for Social Sciences (SPSS) version 10. Relevant descriptive statistics, frequency and percentage were computed for hypertension, dyslipidemia, smoking, myocardial infarction, and atrial fibrillation. Mean and standard deviation were computed for continuous variables e.g., age, glucose levels etc. Chi-square test was used to check proportion between diabetics and non-diabetics for qualitative variables. Statistical significance was considered at $p < 0.05$.

Stroke was defined according to WHO criteria as a rapidly developing symptoms/signs of focal and at time global loss of cerebral function without apparent cause other than that of vascular origin. Fasting glucose $\geq$ 126 mg/dl was the standard measure used to diagnose diabetes mellitus.[8] Hypertension was diagnosed if patients were on anti-hypertensive drugs or have systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg more than two readings during hospitalization. Hyperlipidemia was diagnosed if patients were on lipid lowering agents or with elevated serum cholesterol (> 200 mg/dl) and / or triglyceride (> 150 mg/dl) and/ or a low high density lipoprotein level (< 40 mg/dl) and/or a high low density lipoproteins (> 160).[7]

RESULTS

A total of 250 patients fulfilling the inclusion criteria were enrolled after informed consent. Out of them, 130 were males (52%) and 120 were female (48%) with a male: female ratio of 1: 0.9. Mean age was 60.9±10.1 years, ranging from 30-80 years. Mean age of males was 59.9±9.2 years and that of females was 61.1±10 years. They were further sub-divided in the following age groups; in group 1 (30 - 44 years), 14 were males and 12 were females. In group 2 (age 45 - 59 years) there were 40 males and 33 females; in group 3 (60 - 74 years) there were 55 males and 59 females; and in group 4 (age > 74 years) 17 males and 20 females were found. Dysphasia was seen in 145 subjects (58%). Monoparesis was seen in 63 non-diabetic (31.5%) as compared to 27 of the newly diagnosed diabetic subjects (54%) (p=0.003). Average systolic blood pressure in diabetic patients is 139±20 and in non-diabetics 133±18 mmHg. Average diastolic pressure in diabetics is 83±10 and 81±10 mmHg in non-diabetics.

Fifty new cases of diabetes mellitus were identified (20%). Average fasting blood sugar in diabetic subjects was 148±10 mg/dl with an average subject age of 62.1±11.2 years. Comparative age distributions between diabetic and non-diabetic patients are presented in Figure I.

The most common risk factor for stroke in the newly diagnosed diabetic subjects was hypertension (n=26, 52%) followed by smoking (n=18, 36%) and hyper-lipidemia (n=14, 28%). Atrial fibrillation was found in (n=12, 24%) and myocardial infarction in 9 cases (18%) of the newly diagnosed diabetic patients. These proportions were significantly high (all p -value < .05) as compared to non-diabetic patients as shown in Table I.

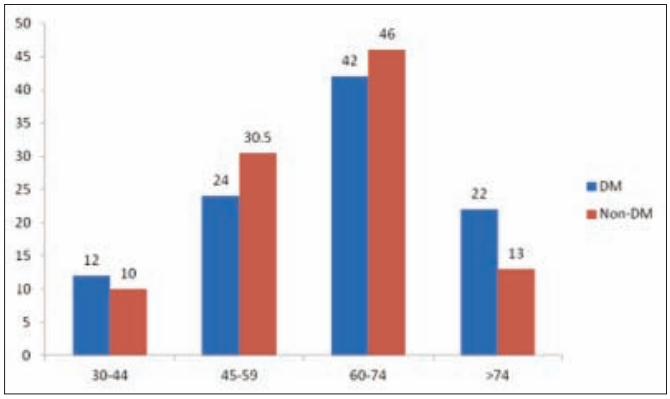

Figure 1: Age distribution in diabetics (DM, n=50) and non-diabetics (non-DM, n=200).

Table I: Distribution of risk factors of ischaemic stroke (n = 250).

History	Non-diabetic n=200	Newly diagnosed DM n=50	p- values*
Hypertension	71 (35.5%)	26 (52%)	0.032
Smoking	42 (21%)	18 (36%)	0.026
Hyperlipidemia	21 (10.5%)	14 (28%)	0.001
Atrial fibrillation	12 (6%)	12 (24%)	< 0.001
Myocardial infarction	08 (4%)	09 (18%)	< 0.001

** by chi-square test.*

DISCUSSION

Diabetes mellitus is a well-known risk factor for stroke, however, the magnitude of the risk varies widely between studies.[9] The number of adults in the developed world with diabetes is predicted to rise by 42% between 1995 and 2025.[10] According to an

international study, in 1995, Pakistan had a population of 132 million of which 5.54 million people were suffering from diabetes with a prevalence of 4.19%.[11]

This prevalence will increase to 4.66% by year 2000. The International Diabetes Federation estimates that this number will grow to 11.5 million by 2025 unless adequate measures are taken to control the disease.[12]

The increasing prevalence of diabetes mellitus makes it one of the most serious health problems in Pakistan. The risk is compounded more when the risk of diabetes mellitus causing stroke is added to this clinical picture.

Insulin resistance is the underlying defect in > 90% of patients with type 2 diabetes mellitus. Type 2 diabetes patients have both an increased susceptibility to atherosclerosis and an increased prevalence of atherogenic risk factors, notably hypertension, obesity, and abnormal blood lipids that contributes to stroke incidence.[2,13]

Hyperglycemic stroke patients without a previous diagnosis of diabetes are not routinely screened for diabetes.[4] Diabetes guidelines recommend aggressive screening for type 2 diabetes mellitus in Asian patients as they are considered to have a higher risk of developing diabetes and potentially worse prognosis.[1] Current guidelines also recommend screening patients for diabetes if they have 1 or more risk factors for diabetes for e.g. age > 45 years, hypertension, lipid abnormalities, vascular disease.[11]

Cerebral infarction accounts for 80% - 85% of cases of stroke.[14] Lacunar strokes is the most common sub-type of stroke in local population, which is considered to be due to high burden of inadequately treated hypertension and diabetes.[15]

Hyperglycemia is common in patients with acute stroke, occurring in upto 60% of patients and is believed to aggravate cerebral ischaemia.[4] It leads to intracellular acidosis, accumulation of extra cellular Glutamate, cerebral oedema, blood-brain barrier disruption, and tendency for haemorrhagic transformation.[16] It is observed that between 20 - 40% of patients admitted with ischaemic stroke are hyperglycemic, often without a pre-existing diagnosis of diabetes,[3] which can be due to stress hyperglycemia or undiagnosed diabetes exposed during an acute incident.

However, van Kooten *et al*. who also found a significant association between hyperglycemia on admission and stroke outcome, did not find a correlation between catecholamine and glucose levels, implying that increased stress was not responsible for the hyperglycemia.[17] In conclusion, although the association between admission hyperglycemia and worse outcome in acute stroke has been shown in most studies, it is still unclear whether it is related to diabetes (diagnosed or un-diagnosed previously) or to a stress reaction.[14]

We found a relatively equal proportion of male and female stroke patients (52% vs. 48%) with a male: female ratio of 1: 0.9, this is similar to the study by Farrukh *et al*.[18] however, other published studies have shown a greater prevalence in the male gender.[4,13,19-21] Mulnier *et al*. confirmed that diabetes dramatically increases the risk of stroke in younger subjects as well as women.[22]

In this study, a substantial peak in stroke risk is seen in the 60 - 74 years age groups in diabetic as well as non-diabetic patients. Amongst the un-modifiable risk factors for stroke, age is the single most important risk in the general population.[23]

Diabetes was diagnosed in 50 of 250 patients (20%) with ischaemic stroke included in this cross-sectional study over 1 year period. This is consistent with the study by Arboix in which the prevalence of diabetes was 21% in acute ischaemic stroke patients.[24] Sheikh *et al*. have shown the presence of diabetes in 35.2% of a Pakistani cohort of ischaemic stroke subjects, however, they did not mention the frequency of newly diagnosed diabetes in this study.[25]

Hypertension, smoking and hyperlipidemia were the frequently encountered co-morbids of stroke in this cohort. This finding is in assertion with the international data which show a proven relationship between stroke and these co-morbidities.[7,13,20] Surprisingly, significant p-values were obtained for atrial fibrillation and myocardial infarction for newly diagnosed diabetes. This is interesting as diabetic patients are seen to suffer from lacunar strokes secondary to atherosclerosis as compared to cardio-embolic strokes.[18]

Marjukka *et al*. observed that diabetes, both previously diagnosed and screen-detected, was associated with clearly increased risk of ischaemic stroke.[26]

This study has many limitations for example in every diabetic patient HbAIC should have been measured to further confirm the diagnosis of diabetes. Secondly, ophthalmic examination would have given an insight about the duration of diabetes underlying this event and would have further confirmed the presence of diabetes. Also, urine for microalbuminuria would also be helpful in identifying the duration of diabetes. Still the results are comparable with many local and international studies, since the study size is quite ample and the presence of risk factors in newly diagnosed as well as in non-diabetic patients is very significant with a p-value of < 0.005.

Given the weak infrastructure facilities and high load of patients in tertiary care hospitals, this figure of 1 new diabetic patient in every 5 stroke patient is very alarming. In addition, the un-awareness for the disease in low socio-economic strata adds further to the complexity of the situation. The morbidity of these patients if not treated and rehabilitated properly would add to the economic burden of our country. Not only the physicians should screen the stroke patients for diabetes and then follow accordingly but health awareness counselling

sessions should also be arranged for making patient understandable towards this disease.

CONCLUSION

Stroke patients represent an enriched population for undiagnosed diabetes. We have observed 1 patient of newly diagnosed diabetes mellitus in every 5 ischaemic stroke patients. It is, therefore, advisable for the clinicians to screen every ischaemic stroke patient for diabetes in order to reduce their long-term morbidity and mortality. Interestingly, we have also observed an increased frequency of other risk factors for ischaemic stroke in our diabetic subects. Therefore, modification of these risk factors (diabetes, hypertension, hyper-lipidemia, atrial fibrillation, myocardial ischaemia and smoking), if managed aggressively, can play a beneficial role in the secondary prevention of stroke.

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