Original Article

Association Between Hyperglycemia and Short-Term Outcome in Patients with Ischemic Stroke

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Objective: We aimed to explore the differenceof short-term prognosis in controlled, uncontrolled and non-diabetic patients suffering from ischemic stroke.

Methods: This was a prospective observational study conducted at Neurology department of Services Hospital, Lahore over a period of 6 months from January 2014 to June 2014. A total of 113 patients with first-time ischemic stroke (confirmed on CT scan) were admitted in our department. In all patients fasting blood glucose (FBG) level was monitored on 1st admission day and history of Diabetes Mellitis (DM) was acquired. FBG >126mg/dl was taken as cut-off level. In all patients with positive history of DM, HbA1C level was evaluated. So it divided our patients into four groups: A) Uncontrolled Diabetics (HbA1C ≥6.5%, positive history of DM); B) Controlled Diabetics (HbA1C 5.7-6.5%, positive history of DM); C) Impaired glucose group (Deranged FBG, No history of DM); D) Normoglycemics (FBG <126mg/dl, No history of DM). The outcome in all patients was measures in terms of early neurological deterioration (increase in the NIH Stroke Scale (NIHSS) of ≥2 points during the first 14 days after admission) and poor short-term outcome (30-day modified Ranking Scale [mRS] score 2-6) was evaluated.

Results: Of 113 patients, 17 patients were in group A (uncontrolled diabetics), 7 patients were in group B (controlled diabetics), 4 patients were in group C (Impaires glucose group) and 85 patients (75.2%) were in group D (Normoglycemics). All the groups were comparable regarding demographic details. The risk of early neurological deterioration was higher in group A (9/17 patients) (ORs=1.839; 95% CI, 0.707-4.782),) than group B (3/7 patients) (ORs=1.48; 95% CI, 0.35-6.31),), group C (1/4 patients) (ORs=0.868; 95% CI, 0.091-8.238), and group D (19/85 patients). Similarly the risk of poor short-term outcome was also significantly higher in the group A (13/17 patients)(ORs=2.75; 95% CI, 0.83-8.238; p=0.047) than group B (5/7 patients) (ORs=2.12; 95% CI, 0.389-11.54; p=0.207), group C (2/4 patients) (ORs=0.847; 95% CI, 0.114-6.301; p=0.440), and group D (46/85 patients).

Conclusion: In our study population, patients having hyperglycemia with history of DM were associated with poor short-term prognosis than those with normal glycemic readings after ischemic stroke.

Key words: stroke; ischemic; outcome; diabetes mellitis; diabetics.

Introduction

Stroke is a leading cause of death in adult population following cardiac diseases and is responsible for about 9% of total deaths each year. Also it contributes as a major cause in long-term morbidity among survivors, as about 40% of the sufferers don't get independent in their future life.[1] According to estimation by World Health Organization (WHO), about 15 million peoplesuffer from stroke per year worldwide.[2]

Diabetes is an established risk factor for the developmentof stroke. In a study by Doi Y and colleagues, The Hisayama study, the risk of stroke in general Japanese population was found twice higher in diabetics than non-diabetics.[3] Also outcome after stroke was worse in diabetics than non-diabetics. Previous studies have demonstrated residual neurological deficits and functional outcome to be worse in diabetics as compared with nondiabetics. Therefore, hospital and long-term mortality were worse indiabetic patients than nondiabetics, although afew other studies did not confirm these effects[4] A few studies have compared the difference in outcome between controlled, uncontrolled and non-diabetics. Therefore, we planned this study to explore the difference of short-term prognosis in controlled, uncontrolled and non-diabetic patients suffering from ischemic stroke.

Methods

After approval from hospital ethical review board, this study was planned. It was a Descriptive

observational study conducted at department of neurology, Services Institute of Medical Sciences (SIMS), Services hospital, Lahore over a period of one year, from January, 2014 to December, 2014.All the patients with first time ischemic stroke (confirmed by CT scan) presenting in emergency department were included in the study. Those having subarachnoid hemorrhage and venous etiology of stroke on CT scan brain and previous history of stroke were excluded from the study. Also those patients who died within 30 days after stroke were excluded. Written informed consent for inclusion in the study was acquired from all the patients. In all patients fasting blood glucose (FBG) level was monitored on 1st admission day and history of Diabetes Mellitis (DM) was acquired. FBG >126mg/dl was taken as cut-off level. In all patients with positive history of DM, HbA1C level was evaluated. So it divided our patients into four groups: A) Uncontrolled Diabetics (HbA1C ≥6.5%, positive history of DM); B) Controlled Diabetics (HbA1C 5.7-6.5%, positive history of DM); C) Impaired glucose group (Deranged FBG, No history of DM); D) Normoglycemics (FBG <126mg/dl, No history of DM). All the patients were assessed at 1st admission day as per the NIH Stroke Scale (NIHSS). They were managed as per policy of the department and after discharge they were followed up at 14th and 30th post-stroke day. At 14th day they were assessed again by NIHSS. At 30th day they were assessed by modified Ranking Scale (mRS). The outcome in all the patients was measured in terms of early neurological deterioration (if there was increase in the NIHSS of ≥2 points during the first 14 days after admission) and short-term outcome (30day mRS score). Short-term outcome was labelled as poor if it was between 2-6.

The collected data was entered and analyzed accordingly using SPSS version 21 through its statistical program. The variables were analyzed using simple descriptive statistics, calculating mean and standard deviation for numerical values like age. Frequencies and percentages were calculated for qualitative variables like gender and scores in all groups (using NIHSS and mRS scale). The Odd's Ratio (OR) and 95% confidence interval (95% CI) for outcomes were determined in all stroke patients in each group.

Results

A total of 113 patients were included in the study. Of these 113 patients, 17 patients were in group A, 7 patients were in group B, 4 patients were in group C and 85 patients (75.2%) were in group D. All the groups were comparable regarding demographic details **(Table 1).**

Of all the included patients, 24 patients (21.2%) had previous history of DM and 70.8% of them were having uncontrolled DM while remaining 29.2% had controlled DM. Four patients in the study had first time deranged FBG and 2 of them later on were labelled as diabetics after full evaluation.

The percentage of patients developing early neurologic disability was higher in group A than others (group A: 52.9%; group B:42.8% ; group C: 25%; group D: 22.3%). OR was calculated for each group which is summarized in Table 2. Similarly poor short-term outcome was noted and it was highest among group A patients than others (group A: 76.4%; group B: 71.4%; group C: 50%; group D: 54.1%). or for each group is summarized in **Table**

Table-1: Demographic details of the patients in four groups.

		Group A (n=17)	Group B (n=7)	Group C (n=4)	Group D (n=85)
Age (mean in years)		55.75±10.34	59.5±9.97	56.70±16.21	57.03±14.5
Gender	Male	10	4	3	49
	Female	7	3	1	36
Socio-econmic status	Poor	12	5	5	69
	Middle	4	1	2	11
	High	1	1		5
Hypertension		13	5	2	40
Ischemic Heart Disease		4	2	0	18
Current cigarette smokers		10	4	2	9

Table-1: Demographic details of the patients in four groups.

	Early Neurological Deterioration		
	Yes	% age of Pts.	Odd's Ratio
Group A	9/17	52.9%	ORs=1.839; 95% CI, 0.707-4.782
Group B	3/7	42.8%	ORs=1.48; 95% CI, 0.35-6.31
Group C	1/4	25%	ORs=0.868; 95% CI, 0.091-8.238
Group D	19/85	22.1%	ORs=0.332; 95% CI, 0.134-0.817

Table-1: Demographic details of the patients in four groups.

	Short-Term Poor Outcome		
	Yes	% age of Pts.	Odd's Ratio
Group A	13/17	52.9%	ORs=2.75; 95% CI, 0.83-8.238; p=0.047
Group B	5/7	42.8%	ORs=2.12; 95% CI, 0.389-11.54; p=0.207
Group C	2/4	25%	ORs=0.847; 95% CI, 0.114-6.301; p=0.440
Group D	46/85	22.1%	ORs=0.412; 95% CI, 0.158-1.079; p=0.348

Discussion

It has been mentioned in many clinical trials that admission hyperglycemia is an indicator of extensive brain damage which ultimately leads to rise in stress hormones leading to hyperglycemia.[5] However, animal studies have shown that administration of insulin is associated with better outcome after stroke. It suggest that hyperglycemia post-stroke is not just a response to stress, rather it is of pathophysiological significance.[6]

Admission hyperglycemia is a well-known and established predictor of poor outcome after ischemic stroke. In a study it was found that diabetic patients have a 2 fold higher relative risk of mortality after ischemic stroke within 30 days.[7] Although there is minimal data available in the literature regarding the optimal cut-off level of random blood sugar during treatment, however American stroke association recommended glucose level of <300mg/dl to be targeted.[8] Zsuga and colleagues conducted a trial in patients with ischemic stroke and they found that even a mild rise in glucose levels in these patients is an independent predictor of 30-days mortality.[9]

In our study 24 of 113 patietns (21.2%) were known patients of DM. In a large study conducted in Chinese population, Fang Y and colleagues had found DM in 23% of the general population presenting with ischemic stroke.[10] In another study by Cruz- and colleagues, DM was found in 24.2% of all the patients with ischemic stroke.[11]

For early neurologic deterioration we used NIHS scale which is a commonly used scale at all centers. We found the worst outcome in known diabetics while outcome was relatively better in those having controlled diabetes. In a large The Fukuoka Stroke Registry, it was found that pre-stroke glycemic control is important and a significant independent factor for better outcome in stroke patietns.[12] In antoher study, it was found that early neurological deterioration was more in diabetics than non-diabetic patients.[13] These findings are in accordance to our results. There are several reasons for poor functional outcome in daibetics than non-diabetics. In an animal study conducted on mice, it was found that there was release of higher inflammatory response after stroke and also higher neuroprotective heat-shock chaperone gene attenuation.[14] Also DM induces the release of metalloproteases which ultimately leads t increased permeability of blood brain barrier and greater inflammatory response, thus resulting in poor outcome after stroke.[15] These factors support our results of poor outcome in diabetics than non-diabetics.

Also short-term outcome was poor in diabetics than non-diabetics. In our study, 4 patients had deranged FBD who were not previously known diabetics and out of these 4, 2 patients later on turned out to be diabetics. Tanaka et al found that pre-diabetics and patients with underlying hyperglycemia also suffer from longer hyperglycemic states and thus have poor outcome.[13] Other than glycemic control, some other factors are also there playing their role in the outcome of stroke patients. Toyoda and co-workers found that in patients with poor glycemic control, blood pressure was significantly higher than those having better controls. Therefore, blood pressure level in stroke patients is associated with the outcome.[16] Also Zhou J and colleagues found that when hyperglycemia was associated with raised levels of markers of inflammation, the ultimate outcome was poor in patients with stroke.[17]

Our study had several limitations. Firstly it was a short-term outcome study and no long-term outcome was analyzed. It had limited sample size as it was a single center study. Therefore we suggesta multicenter study with longer duration to unreveal long-term outcomes in diabetic patients presenting with stroke.

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