

CLINICAL PROFILE OF STROKE IN RELATION TO GLYCEMIC STATUS OF THE PATIENTS

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**ABSTRACT****Introduction:** Stroke is the sudden death of brain cells that occurs due to lack of oxygen, caused by blockage of blood flow or rupture of an artery to the brain leading to permanent disability or death. Diabetes mellitus (DM) has been established as a major risk factor for stroke. However, this study was conducted to incorporate glycemetic status and its correlation with severity of stroke.**Materials and Methods:** A cross-sectional observational study was conducted in the Department of Internal Medicine, Neurosurgery, Emergency and Endocrinology of Bir Hospital. Ethical clearance was granted by Institutional Review board of National academy of medical sciences. A total of 50 patients with stroke presented within 72 hours of symptoms of stroke was included in the study. Data was collected and stored in MS-EXCEL sheet and analyzed using SPSS.**Results:** Among 50 patients with stroke enrolled for the purpose of this study, 54% had ischemic and 46% hemorrhagic stroke. Patient pool was predominantly 51-60 years of age. Majority of the patients were euglycemic, of these 56.67% suffered hemorrhagic stroke, while known diabetics predominantly suffered ischemic stroke. Euglycemic patients had CT lesion measuring 5-10mm compared to larger lesions of >10mm in known diabetics. Euglycemic patients had better outcome in contrast to newly diagnosed and known diabetics.**Conclusion:** The study found that patients with higher glucose levels had increased severity of stroke. Increased morbidity was documented among known diabetics and newly diagnosed cases of DM in comparison to euglycemics and patients with stress hyperglycemia.**Keywords:** diabetes mellitus; euglycemia; stroke**INTRODUCTION**

World Health Organization defines stroke as “the rapidly developing clinical symptoms and/or signs of focal [at times global] disturbance of cerebral functions, with symptoms lasting for more than 24 hours or leading to death with no apparent cause other than that of vascular origin”.¹ Symptoms of stroke are sudden loss of speech, weakness, or paralysis of one side of the body and these suspected may be confirmed by brain imaging.²

According to the world health organization data published in 2017, stroke deaths in Nepal reached 15,450 or 9.46% of total deaths.³ Ischemic strokes are due to reduction or complete blockage of blood flow. This reduction can be due to decreased systemic perfusion, severe stenosis, or occlusion of a blood vessel. The main causes of ischemia are thrombosis, embolization, and lacunar infarction from small vessel disease. Ischemic strokes represent about 80% of all strokes.⁴

Intracerebral hemorrhage accounts for ~10% of all strokes, and about 35–45% of patients die within the first month. Hypertension, coagulopathy, sympathomimetic drugs, and cerebral amyloid angiopathy cause the majority of these hemorrhages.⁵

OBJECTIVES

The general objective of the study was to study the clinical profile of stroke in relation to the glycemetic status of patient. The specific objectives were to study the type of stroke, to find the size of stroke, to determine the percentage of stroke patients with euglycemia, stress hyperglycemia, newly detected diabetes and known diabetes, to identify and establish the severity and correlation between stroke and glycemetic status of patient

METHODOLOGY

A cross-sectional observational study, conducted at Department of Internal Medicine, Neurosurgery,

Emergency and Endocrinology of Bir Hospital, from January 2019 to June 2019. Ethical clearance was taken from Institutional Review board of National Academy of Medical Sciences. (Reference no. 600)

Study enrolled all the cases admitted within 72 hours after stroke with exclusion of patients with pre-existing neurological deficit following previous stroke or any other condition.

Sample size was calculated using the formula

$$n = z^2 p (1-p) / d^2$$

Where, n=required sample size

z=statistical value for a level of confidence (for 95% level of confidence, z=1.96)

p=estimated proportion of diabetes in people with stroke in the population

d=precision or maximum tolerable error

The prevalence of stroke in patients with Type II Diabetes Mellitus is 10 and can be high as years after the onset of diabetes.⁶Hence considering z=1.96, p=0.1(proportion of stroke in Type II Diabetes Mellitus)⁶ and d=0.1 (precision of 10%), total sample size was around 34. However, I took 50 cases for convenience.

Data was collected using a structured Pro forma covering the relevant details. Informed written consent was obtained from patients. Data was collected and stored in MS-EXCEL sheet and analyzed using SPSS 22.0.

RESULTS

In this study, a total of 50 patients with stroke admitted in Bir hospital, Kathmandu in time period of 6 months were included and all had undergone history, physical examination and investigations.

Table 1: Risk factors profile

Risk Factors	Frequency	Percent
Smoking	35	70
Alcohol	22	44
Dyslipidemia	7	14
Valvular Heart Disease	1	2
Coronary Artery Disease	3	6
Type II Diabetes Mellitus	15	30
Hypertension	35	70

Study showed that smoking and hypertension were the most prevalent risk factor present among the study population. Type II Diabetes Mellitus was the third most common risk factor.

Table 2: Classification of patients according to their glycemic status

Glycemic status	Frequency	Percentage
Euglycemic	30	60
Stress hyperglycemia	5	10
Newly diagnosed Type II Diabetes Mellitus	3	6
Known diabetic	12	24
Total	50	100

In the study of 50 cases of stroke admitted in Bir Hospital, Kathmandu, 60% cases of stroke patients were euglycemic and 24% cases were known diabetics. Similarly, 10% of the patients had stress hyperglycemia and remaining 2% were newly diagnosed cases of diabetes.

Table 3: Types of stroke in study group

Type of stroke	Frequency	Percent
Hemorrhagic	23	46.0
Ischemic	27	54.0

Among 50 cases of stroke studied, 54% were ischemic stroke and the remaining were hemorrhagic stroke. Frequency of ischemic stroke is slightly higher compared to hemorrhagic stroke.

Table 4: Types of stroke in different glycemic status

Glycemic status	Hemorrhagic	Hemorrhagic %	Ischemic	Ischemic %	Total
Euglycemic	17	56.67	13	43.33	30
Stress hyperglycemia	3	60	2	40	5
Newly diagnosed Type II Diabetes Mellitus	1	33.33	2	66.67	3
Known diabetic	2	16.67	10	83.33	12
Total	23		27		50

In this study, total of 30 euglycemics were documented, of whom 57% had hemorrhagic stroke. Table shows that 60% of the hemorrhagic stroke cases had stress hyperglycemia. Newly diagnosed Diabetes Mellitus cases and known diabetics both predominantly suffered from ischemic stroke. Fisher exact value was calculated to be 6.22 and p-value at 0.08 which is statistically insignificant.

Table 5: Size of lesion (by computed tomography scan) at different glyceemic states

Glyceemic status	Small (0-5mm)	%	Medium (5-10mm)	%	Large (>10mm)	%	Total
Euglycemic	11	37	15	50	4	13	30
Stress hyperglycemia	1	20	1	20	3	60	5
Newly diagnosed type II Diabetes Mellitus	1	33.33	1	33.33	1	33.33	3
Known diabetic	1	8	3	25	8	67	12
Total	14	100	20	100	16	100	

Comparing the size of lesion in computed tomography with glyceemic status of the patients, the study shows that euglycemics have commonly lesion the size of 5-10mm. Large lesions i.e. >10mm was significantly higher in known diabetics at 67%. Fisher exact value was 13.24 and p-value was 0.01 which is statistically significant.

Table 6: Clinical outcome of patients based on their glyceemic status

Outcome	Eu-glycemic	Eu-glycemic outcome %	Stress hyperglycemia	Stress hyperglycemia outcome %	Newly diagnosed type II Diabetes Mellitus	Newly diagnosed type II Diabetes Mellitus outcome %	Known diabetic	Known diabetic outcome %	Total
Expired	0	0	0	0	1	33	1	8	2
Improved	30	100	5	100	2	67	11	92	48
Total	30	100	5	100	3	100	12	100	50

Study of the 50 cases of stroke enrolled for this study showed that all the patients with euglycemia and stress hyperglycemia improved. Whereas, 33% of stroke patients with newly diagnosed type II Diabetes Mellitus expired. 8% of the known diabetics expired while all others improved. Fisher exact value was 6.63 and p-value was 0.05.

Table 7: Distribution of type of stroke with Glycated Hemoglobin

Type of stroke	Glycated Hemoglobin				Total
	<7	<7(%)	>=7	>=7(%)	
Hemorrhagic	20	55.56	3	21.43	23
Ischemic	16	44.44	11	78.57	27
Total	36	100	14	100	50

In the study of 50 stroke cases, 36 patients had glycated hemoglobin <7 while remaining 14 had glycated hemoglobin >=7. Patients with glycated hemoglobin A1C >=7 were predominantly found to had suffered ischemic stroke at 78.57%. On the other hand, majority of patients with glycated hemoglobin <7 (55.56) suffered hemorrhagic stroke. Chi-square value was calculated to be 4.72 and p-value at 0.03 which is statistically significant.

DISCUSSION

Stroke ranks third in the causation of morbidity and mortality after ischemic heart disease and all kinds of cancers combined.⁶ Diabetes is the well-established risk factor for stroke. Improving stroke outcomes in individuals with diabetes requires prompt and persistent implementation of evidence-based medical therapies.⁷

This study showed that smoking and hypertension were the most prevalent risk factor present among the study population. Type II Diabetes Mellitus was the 3rd most common risk factor. Studies done at Nepal medical college Teaching Hospital by Pathak V, et al,⁸ Tribhuvan

University Teaching Hospital Nepal (TUTH) by Oli K.K. and Agrawal J.P,⁹ as well as the study at Nepal Medical college Teaching hospital by Devkota K.C. et al,¹⁰ show similar results. Bhatt VR et al concluded that among other risk factors, diabetes was an important risk factor for ischemic stroke but it was uncertain whether tight control of blood sugar in patients with diabetes reduces the risk of stroke.¹¹

In this study of 50 cases of stroke admitted in Bir Hospital, Kathmandu, 60% of stroke patients were euglycemic and 24% were known diabetics. Similarly, 10% of the patients

had stress hyperglycemia and remaining 2% were newly diagnosed diabetics. In the study of Singh KG et al. 40% of stroke patients were euglycemic, and remaining hyperglycemic including newly detected diabetes, and known diabetics.⁷ In a study done by Patil VM et al. among 80 patients, 62.5% of patients were euglycemics, 21.25% known diabetic, 8.75% freshly detected diabetic and 7.5% had stress hyperglycemia.¹²

This study found 54% patients had ischemic stroke and the remaining were hemorrhagic stroke. In a retrospective study done by Shrestha A et al. at Neurology ward of Bir hospital for Analysis of stroke and its risk factors, 210 patients with stroke were studied. Hemorrhagic strokes were 89 (42.95%) and Ischemic were 121 (57.62%). Frequency of ischemic stroke is slightly higher compared to hemorrhagic stroke.⁶ Patil VM et al. showed freshly detected diabetics had higher prevalence of ischemic infarct (85.7%) and known diabetics and euglycemics had comparable prevalence of ischemic infarct, 70.6% and 66% respectively.¹²

In this study, there were a total of 17 hemorrhagic and 13 ischemic stroke cases were found in euglycemics. Only 1 case (33.33%) of hemorrhagic and 2 cases (66.67%) of ischemic stroke were found in newly diagnosed cases of type II Diabetes Mellitus. Known diabetics predominantly suffered ischemic stroke i.e. 10 cases (83.33%). Stress hyperglycemia was also present in 60% and 40% cases of hemorrhagic and ischemic stroke respectively. In contrast, Singh KG et al 75% of cases of strokes in the euglycemic group presented as ischemia (15 out of 20) and 25% in the same group occurred as hemorrhage (5 out of 15). Patients with stress hyperglycemia and new diabetics all suffered hemorrhagic stroke. 85.71% of stroke in the known diabetic group were hemorrhagic strokes (12 out of 14). This shows that hemorrhagic strokes occurred in the hyperglycemic patients, maximum being in the stress hyperglycemia and new diabetics.⁷ In a study done by Bhatt VR et al. at TUTH from April 2008 to August 2008, to study the risk factors of stroke 61 patients were admitted with stroke, out of which 48 had ischemic stroke and 13 had hemorrhagic stroke. 21 patients had diabetes (34% prevalence).¹¹ In a study done by Goplani KR et al Known diabetics had higher prevalence of ischemic infarct (85.7%) and newly detected diabetics had comparable prevalence of ischemic infarct with that of euglycemic patients (66.7% and 71% resp.). The known diabetic patient had higher prevalence of larger infarct than euglycemic patients did.¹³

Comparing the size of lesion in computed tomography with glycemic status of the patients, this study showed that euglycemics have commonly medium sized (5-10mm) stroke lesion. Known diabetic and stress hyperglycemics have commonly large sized computed tomography lesion

(10mm), accounting 66.67% and 60% respectively. Singh KG et al shows large-sized strokes (> 10mm) occurred only in known diabetics (85.71%), new diabetics (100%), and stress hyperglycemia (100%). Small-sized strokes (0 to 5 mm) occurred only in euglycemic patients (50%), medium-sized strokes (> 5 to 10 mm) occurred in euglycemics (50%) and known diabetics (14.28%).⁷ In a study done by Kyadav k et al. in 2004, hyperglycemics of both the groups had larger sized stroke.¹⁴

In this study, all the patients with euglycemia and stress hyperglycemia improved. Whereas, 33% of stroke patients with newly diagnosed type II Diabetes Mellitus expired and 8% of known diabetic expired while all the others improved. In a study done by Goplani KR et al both known diabetic and newly diabetic patients with stroke are associated with higher mortality rate than euglycemic (57.1%, 66.7% and 34.8% respectively). Both known diabetic and newly diabetic patients with stroke are associated with higher percentage of poor outcome during 15 days follow-up (66.7%, 100%, and 50%). This concludes diabetes is an important risk factor for stroke especially thrombotic and associated with high morbidity and mortality.¹³ In a study done by Singh S et al. 50 patients with stroke were enrolled in this retrospective study done in year 2000 the mortality was significantly higher (67%) in stress hyperglycemics, 40% in newly detected diabetics, as compare to 16% in known diabetics and 10% in euglycaemics. As compared to euglycaemics, the mortality was significantly higher in newly diagnosed diabetics ($p < 0.001$), and stress hyperglycemic ($p < 0.001$) which was statistically significant.¹⁵ Kyadav k et al Neurological assessment showed statistically significant improvement in all neurological functions in euglycemic subgroup compared to hyperglycemic subgroup. Mortality was also found to be significantly higher in hyperglycemic subgroup in both groups as compared to euglycemic subgroup.¹⁴

The study conducted showed that, patients with glycated hemoglobin <7 had 55.56% cases of hemorrhagic and 44.44% cases of ischemic stroke. On the other hand, patients with glycated hemoglobin ≥ 7 had dominantly more cases of ischemic stroke accounting to 78.57%. P-value was calculated to be 0.03 which was statistically significant in this study. In a study done by Weir CJ et al., analysis was done on 750 non-diabetic patients, to determine whether raised plasma glucose concentration independently influences outcome after acute stroke or is a stress response reflecting increased stroke severity. 645 patients (86%) had ischemic stroke and 105 patients (14%) hemorrhagic stroke. The effect of glucose concentration on survival was greatest in the first month. Study concluded that plasma glucose concentration above 8 mmol/l after acute stroke predicts a poor prognosis after correcting for age, stroke severity,

and stroke subtype. Raised plasma glucose concentration was therefore unlikely to be solely a stress response and should arguably be treated actively.¹⁶

LIMITATION OF STUDY

Smaller sample size in comparison to other similar studies which may have influenced the result generation. Data was collected from only one hospital for a defined period of time. A multicenter study could have produced a clearer and convincing result with higher acceptance. We could not follow up the stroke patients beyond 1 week after admission and hence could not fully document the actual functional status and recovery from stroke on long term.

CONCLUSION

The study found that patients with higher glucose levels had increased severity of stroke. An increased morbidity was documented among known diabetics and newly diagnosed cases of Diabetes mellitus in comparison to euglycemics and patients with stress hyperglycemia. This concludes diabetes is an important risk factor for stroke and is associated with increased severity of stroke.

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