

Frequency of Newly Diagnosed Diabetes in Hemorrhagic Stroke Patients Presenting to a Tertiary Care Hospital in Peshawar



Salim Badshah¹, Muhammad Bilal¹, Adeela Masood¹, Yaseen Khan¹

Abstract

Background: The present study aimed to determine the frequency of newly diagnosed diabetes in Hemorrhagic stroke patients presenting to a tertiary care hospital in Peshawar.

Methods: This cross-sectional study was conducted at the Department of Medicine, Lady Reading Hospital, Peshawar, for six months from December 2019 to June 2020. The ethical approval was obtained from Lady Reading Hospital ethical review committee. The sample size of 210 was calculated using the WHO sample size calculator. All hemorrhagic stroke patients between 31 to 80 years of age, having a hyperdense (white area) on CT brain for the first time, were included in the study. While those having an ischemic stroke and other causes of sudden-onset neurologic symptoms mimicking strokes were excluded from the study. Patient history was obtained following detailed clinical examination and necessary tests such as CT brain, HbA1c. The data were recorded using a structured questionnaire and analyzed using SPSS version 22.0. A Chi-square test was applied to assess the effect of various risk factors on the frequency of newly diagnosed diabetes mellitus.

Results: Out of the total, there were 66.70% males and 33.30% females, with a mean age of 55.90 ± 9.28 years. 53.3% were hypertensive, and only 27.60% had active smoking status. We found 63 (30.0%) new cases of diabetes mellitus. The most common risk factors among the enrolled newly diagnosed diabetic subjects were family history of diabetes, hypertension, and BMI ($P < 0.05$).

Conclusion: It is concluded that newly diagnosed diabetes mellitus is fairly common in hemorrhagic stroke patients.

Keywords: Diabetes Mellitus, hemorrhagic stroke, risk factors

¹MTI Lady Reading Hospital, Peshawar.

Correspondence:
Muhammad Bilal
dr_bilal79@hotmail.com

Introduction

Stroke is the second leading global cause of death after heart disease accounting for 11.8% of the total deaths worldwide (1). Over the years, the incidence of stroke, morbidity, and mortality has significantly increased (2). Around 13% of all stroke cases are hemorrhagic type (3). A Global Burden of Disease (GBD) study of the year 2010 reported 5.3 million hemorrhagic stroke cases and over 3 million associated deaths, out of which about 80% cases and 63% deaths occurred in low and middle-income countries (4).

There are several modifiable and non-modifiable risk factors associated with hemorrhagic stroke incidence. Increasing age, smoking status, alcohol intake, lack of physical activity, hypertension, dyslipidemia, diabetes mellitus, cardiovascular diseases, obesity, genetic risk factors, etc., are to name a few (5-7). Diabetes remains one of the consistent predictors of recurrent stroke and coronary heart disease. The diabetic patients are at 2.1 to 5.6 times greater risk of recurrent stroke than

their non-diabetic counterparts (8). Moreover, up to 42% of all stroke patients have undiagnosed diabetes (9).

Most human studies suggest that the worst clinical outcomes have been observed among diabetic or non-diabetic acute stroke patients with admission hyperglycemia. Evidently, elevated glucose concentrations are representative of underlying glucose intolerance or diabetes (10). Despite known, hyperglycemia is often neglected under such circumstances as it is considered to be exclusively related to the physiological stress due to acute stroke (10). However, the underdiagnosis of diabetes and the correlation of diabetes with stroke emphasizes the need to screen all hyperglycemic stroke patients for diabetes. It would assist in the disease management and control of associated risk factors (11,12).

Locally, a study from KPK, Pakistan, presented the frequency of diabetes to be 7.9% among cardiovascular disease (CVD) patients (13). As of 2018, a meta-analysis of 39 studies predicted the

prevalence of diabetes to be 28%; the rate was higher in ischemic 33%, compared with hemorrhagic stroke 26%. Most of the included studies concluded that diabetes mellitus and acute hyperglycemia lead to worse neurological and functional events and prolonged hospital stay in both hemorrhagic and ischemic stroke patients (14).

There is a lack of local data regarding the underdiagnosis of diabetes among hemorrhagic stroke patients. Hence the present study aimed to determine the frequency of newly diagnosed diabetes mellitus among hemorrhagic stroke patients.

Methodology

A total of 210 hemorrhagic stroke patients presenting at the Medicine Department of Lady Reading Hospital, Peshawar-Pakistan, between December 2019 to June 2020 were recruited for this cross-sectional study. The sample size was calculated using the World Health Organization (WHO) sample size calculator keeping margin of error 6.5%, confidence level of 95%, and the prevalence of newly diagnosed diabetes mellitus in hemorrhagic stroke patients of 36% (15).

Both male and female patients between 31 to 80 years of age, having a hyperdense (white area) on CT brain for the first time (new onset), were included in the study. While those having an ischemic stroke and other causes of sudden-onset neurologic symptoms mimicking strokes like epilepsy, dural sinus thrombosis, migraine, subdural hematoma, space-occupying lesions, etc. were excluded from the study. Moreover, all known diabetic patients and those having a non-lacunar stroke were also kept under exclusion criteria.

The study protocol was approved by the ethical review committee of Lady Reading Hospital, (Reference no; 22/LRH Dated: 04/12/2018), and prior to inclusion, written informed consent was obtained. While the consents were obtained from the next of kin among disoriented or unconscious cases (assessed via Glasgow coma scale). Patient data, including demographic details, clinical examination such as computerized tomography (CT) brain findings, Glycated hemoglobin (HbA1c) levels, were determined and recorded using a pre-structure questionnaire.

The data was analyzed using SPSS version 22.0; all categorical variables like gender, newly diagnosed diabetes mellitus, positive family history of diabetes, smoking status, and hypertension were presented as frequency and percentages. While mean and standard deviation was calculated for continuous variables like age, weight, height, BMI, and HbA1c. A Chi-square test was applied to assess the effect of various risk factors on the frequency of newly diagnosed diabetes mellitus, where a p-value ≤ 0.05 was considered statistically significant.

Results

Out of the total 210 patients with hemorrhagic stroke majority were males (66.70%). Upon investigation, it was found that 30% of hemorrhagic stroke patients were newly diagnosed with diabetes mellitus.

Table 1: Baseline characteristics of the patients with hemorrhagic stroke.

Variables		n=210
Age; mean \pm SD (years)		55.90 \pm 9.28
	31-40 years	8(3.80)
	41-50 years	56(26.6)
	51-60 years	81(38.57)
	61-70 years	50(23.80)
	71-80 years	15(7.14)
Gender		
	Male	140(66.70)
	Female	70(33.30)
Family history of DM		
	Yes	65(31.0)
	No	145(69.0)
Smoking Status		
	Smoker	58(27.60)
	Non-smoker	152(72.40)
Hypertension		
	Yes	112(53.3)
	No	98(46.7)
BMI; mean \pm SD (kg/m²)		24.98 \pm 3.39
	Normal	116(55.23)
	Overweight	69(32.85)
	Obese	25(11.90)
HbA1c; mean \pm SD (%)		5.80 \pm 1.17
Newly diagnosed DM		
	Yes	63(30.0)
	No	147(70.0)

Values are given as mean \pm SD or n(%)

BMI-Body Mass Index; HbA1c-Glycated Hemoglobin; DM-Diabetic Mellitus

The most common risk factor associated with the frequency of the newly diagnosed DM among the hemorrhagic stroke patients were hypertension (30%), family history of DM (20%), and obesity (29.0%). These proportions were significantly high among newly diagnosed DM patients as compared to non-diabetic patients (p<0.05).

Table 2: Distribution of risk factors of newly diagnosed diabetes mellitus in hemorrhagic stroke patients.

Variables		Newly diagnosed DM		p-value
		Yes (n=63)	No (n=147)	
Age groups	31-40 years	2(3.17)	6(4.08)	0.333
	41-50 years	13(20.63)	43(29.25)	
	51-60 years	23(36.50)	58(39.45)	
	61-70 years	16(25.39)	34(23.12)	
	71-80 years	9(14.28)	6(4.08)	
Gender	Male	47(22.4)	93(44.3)	0.074
	Female	16(7.6)	54(25.7)	
Family history of DM		42(20.0)	23(11.0)	<
Hypertension		63(30.0)	49(23.3)	<
Smoking status		19(9.0)	38(18.6)	0.315
BMI	Normal	1(1.58)	115(78.23)	<
	Overweight	37(58.7)	32(21.76)	
	Obese	25(39.6)	-	
Classification				0.001*

Values are given as mean \pm SD or n(%)

BMI-Body Mass Index; HbA1c-Glycated Hemoglobin; DM-Diabetic Mellitus

*p<0.05 is considered statistically significant

Discussion

Our data confirm that newly diagnosed diabetes mellitus is quite common among hemorrhagic stroke patients. We found 30% newly diagnosed diabetic cases among the enrolled hemorrhagic stroke cases. Five different studies, including patients with hemorrhagic stroke, indicated that the frequency of diabetes ranges between 8.2 and 50.2% (16-20). Likewise, a meta-analysis showed that diabetes is 20 to 33% more prevalent among stroke patients than the normal population (21-24), which is comparatively high among ischemic stroke cases than those with hemorrhagic stroke (25). There is a paucity of local data on the frequency of diabetes among hemorrhagic stroke patients, while a study from Karachi-Pakistan assessed its frequency among ischemic stroke cases, i.e., 20%, lower than that observed in hemorrhagic stroke patients of the present study (26).

Irrespective of diabetic status, stress hyperglycemia has been associated with the worst functional outcomes and leads to early mortality among patients with acute hemorrhagic stroke after adjusting for stroke severity and subtypes (16, 18, 19, 27, 28). Snarska et al., in their study including stroke patients, determined a frequent association between admission hyperglycemia and increased in-hospital mortality (27). Another similar study reports that with every 1.0 mmol/L increase in plasma glucose concentration, the likelihood of 30-day mortality in hemorrhagic stroke patients increases by 33% after adjusting for diabetic status. But due to underdiagnosis and reporting, the risk remains underestimated among unrecognized diabetes cases (27).

It is to note that the frequency of hypertension (30%), family history of DM (20%), and obesity (29.0%) was significantly high among newly diagnosed DM patients as compared to non-diabetic patients ($p < 0.05$), hence, these were the common risk factors associated with the frequency of newly diagnosed DM among patients with hemorrhagic stroke. Although family history is a non-modifiable risk factor, but it signifies the importance of early screening of diabetes among stroke patients with a positive family history of diabetes. While the other two modifiable risk factors, hypertension, and obesity, could be controlled through lifestyle and dietary modifications. An extensive review including studies highlighting the association between diabetes and stroke outcomes suggests that age, gender, BMI, antihyperglycemic medication, and diabetes complications are the co-founding factors associated with frequency of diabetes among stroke patients and its associated outcomes (29).

It is essential to control the risk of diabetes and hyperglycemia among stroke patients; early and accurate screening of diabetes is required to minimize the progressive burden on the global healthcare system concerning the two concomitant conditions. Given the weak infrastructure of healthcare facilities in Pakistan, disease burden, and sub-optimal management, this high frequency of newly diagnosed diabetic patients among hemorrhagic

stroke patients attending the specific study center is alarming. It denotes the un-awareness of the disease and its complexities and highlights the extent of under-diagnosis in the region.

The study had certain limitations that need consideration; the foremost was the limited sample size. Secondly, the data was specific to a single center of Peshawar, and hence the outcomes lack generalizability concerning the local population. Furthermore, the present study did not include stroke outcomes, i.e., the frequency of newly diagnosed DM among these patients might alter the stroke outcomes. Larger prospective studies are required to further investigate the relation between diabetes and stroke outcome measures.

Conclusion

It is concluded from the study results that newly diagnosed diabetes is prevalent among hemorrhagic stroke patients, 30% patients of hemorrhagic stroke had un-diagnosed diabetes.

We recommend that hemorrhagic stroke patients with hypertension, family history of DM, and obesity must be screened for diabetes to reduce associated morbidity and mortality.

References

1. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Executive summary: heart disease and stroke statistics-2016 update: a report from the American Heart Association. *Circulation*. 2016;133(4):447-54.
2. Feigin VL, Krishnamurthi RV, Parmar P, Norrving B, Mensah GA, Bennett DA, et al. Update on the global burden of ischemic and hemorrhagic stroke in 1990-2013: the GBD 2013 study. *Neuroepidemiology*. 2015;45(3):161-76.
3. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *circulation*. 2015;131(4):e29-322.
4. Krishnamurthi RV, Moran AE, Forouzanfar MH, Bennett DA, Mensah GA, Lawes CM, et al. The global burden of hemorrhagic stroke: a summary of findings from the GBD 2010 study. *Global heart*. 2014;9(1):101-6.
5. Younis H, Younis S, Ahmad S. Awareness regarding complications of type II diabetes mellitus among diabetics in Karachi, Pakistan. *Int. j. endorsing health sci. res.* 2019;7(1):47-54.
6. Hopewell JC, Clarke R. Emerging Risk Factors for Stroke: What Have We Learned from Mendelian Randomization Studies? *Stroke*. 2016;47(6):1673-1678.
7. Von Sarnowski B, Putaala J, Grittner U, Gaertner B, Schminke U, Curtze S, et al. Lifestyle risk factors for ischemic stroke and transient ischemic attack in young adults in the stroke in young fabry patients study. *Stroke*. 2013;44(1):119-125.
8. Air EL, Kissela BM. Diabetes, the metabolic syndrome, and ischaemic stroke: epidemiology and possible mechanisms. *Diabetes Care* 2007; 30(12):3131-3.
9. Christopher SG, Janice EOC, Hilary L. Diabetes hyperglycemia and recovery from stroke. *Geriatr Gerontol Int*. 2001; 1(1-2):87-94.
10. Karapanayiotides T, Piechowski-Jozwiak B, Van Melle G, Bogousslavsky J, Devuyst G. Stroke patterns, etiology and prognosis in patients with diabetes mellitus. *Neurology* 2004; 62(9):1558-62.
11. Scott MG, Diane B, Luther C, Richard SC, Margo AD James H, et al. Evaluation, and treatment of high blood cholesterol in adults (adult treatment Panel III). The National Cholesterol Education Program Expert Panel on Detection; 2002.

12. Imran M, Begum S, Kandhro AH, Ahmed N, Qasim R. The management of glycemic control in associated disorders. *Int. j. endorsing health sci. res.* 2017;5(2):37-42.
13. Khan S, Iqbal S, Ullah R, Shah ST, Khan MN, Saidullah S. Prevalence of cardiovascular risk factors in the rural areas of khyber pakhtunkhwa. *Pak Heart J.* 2015;48(3):147-152
14. Lau LH, Lew J, Borschmann K, Thijs V, Ekinci EI. Prevalence of diabetes and its effects on stroke outcomes: A meta-analysis and literature review. *J Diabetes Investig.* 2019;10(3):780-792.
15. Zhang X, Jing J, Zheng H, Jia Q, Zhao X, Liu L, et al. Prognosis of Intracerebral Hemorrhage with Newly Diagnosed Diabetes Mellitus According to Hemoglobin A1c Criteria. *J Stroke Cerebrovasc Dis.* 2018;27(5):1127-1133.
16. Godoy DA, Piñero GR, Svampa S, Papa F, Di Napoli M. Hyperglycemia and short-term outcome in patients with spontaneous intracerebral hemorrhage. *Neurocrit Care.* 2008;9(2):217-29.
17. Munoz-Rivas N, Méndez-Bailón M, Hernández-Barrera V, de Miguel-Yanes JM, Jimenez-Garcia R, Esteban-Hernández J, et al. Type 2 diabetes and hemorrhagic stroke: a population-based study in Spain from 2003 to 2012. *J Stroke Cerebrovasc Dis.* 2016;25(6):1431-43.
18. Tapia-Perez JH, Gehring S, Zilke R, Schneider T. Effect of increased glucose levels on short-term outcome in hypertensive spontaneous intracerebral hemorrhage. *Clin Neurol Neurosurg.* 2014;118:37-43.
19. Stead LG, Jain A, Bellolio MF, Odufuye A, Gilmore RM, Rabinstein A, et al. Emergency department hyperglycemia as a predictor of early mortality and worse functional outcome after intracerebral hemorrhage. *Neurocrit Care* 2010; 13(1): 67–74.
20. Wang Q, Wang D, Liu M, Fang Y, You C, Dong W, et al. Is diabetes a predictor of worse outcome for spontaneous intracerebral hemorrhage? *Clin Neurol Neurosurg* 2015; 134: 67–71.
21. Baker ST, Chiang CY, Zajac JD, Bach LA, Jerums G, MacIsaac RJ. Outcomes for general medical inpatients with diabetes mellitus and new hyperglycaemia. *Med J Aust* 2008; 188(6): 340–343.
22. Nanayakkara N, Nguyen H, Churilov L, Kong A, Pang N, Hart GK, et al. Inpatient HbA1c testing: a prospective observational study. *BMJ Open Diabetes Res Care* 2015; 3: e000113–e000113.
23. Silverman RA, Thakker U, Ellman T, Wong I, Smith K, Ito K, et al. Hemoglobin A1c as a screen for previously undiagnosed prediabetes and diabetes in an acute-care setting. *Diabetes Care.* 2011;34(9):1908-12.
24. Wexler DJ, Nathan DM, Grant RW, Regan S, Van Leuvan AL, Cagliero E. Prevalence of elevated hemoglobin A1c among patients admitted to the hospital without a diagnosis of diabetes. *J Clin Endocrinol Metab.* 2008;93(11):4238-44.
25. Tsai CF, Anderson N, Thomas B, Sudlow CL. Comparing risk factor profiles between intracerebral hemorrhage and ischemic stroke in chinese and white populations: systematic review and meta-analysis. *PLoS ONE* 2016; 11: e0151743.
26. Zahra F, Kidwai SS, Siddiqi SA, Khan RM. Frequency of newly diagnosed diabetes mellitus in acute ischaemic stroke patients. *J Coll Physicians Surg Pak.* 2012 Apr 1;22(4):226-9.
27. Snarska KK, Bachórzewska-Gajewska H, Kapica-Topczewska K, Drozdowski W, Chorąży M, Kułakowska A, Małyszko J. Hyperglycemia and diabetes have different impacts on outcome of ischemic and hemorrhagic stroke. *Arch Med Sci* 2017;13(1):100–108.
28. Saxena A, Anderson CS, Wang X, Sato S, Arima H, Chan E, et al. Prognostic significance of hyperglycemia in acute intracerebral hemorrhage: the INTERACT2 Study. *Stroke* 2016; 47(3):682-8.
29. Lau LH, Lew J, Borschmann K, Thijs V, Ekinci EI. Prevalence of diabetes and its effects on stroke outcomes: A meta-analysis and literature review. *Journal of diabetes investigation.* 2019;10(3):780-792.