ASSOCIATION BETWEEN HBA1C AND FUNCTIONAL OUTCOME OF NEW ONSET ISCHEMIC STROKE IN DIABETIC PATIENTS

SINA H[1], ANWAR ULLAH AKM[2], DEY SK[3], HOSSAIN MA[4], ARIFUZZAMAN M[5], AHMED SU[6], HOSSAIN MS[7], SIDDIQUE AR[8], HOSSAIN MZ[9], HASAN MR[10], AZAD KAK[11]

Abstract

Background: *Abnormal glucose metabolism is an independent risk factor for poor outcome following acute ischemic stroke.*

Objective: *To evaluate the association between high HbA1c level and poor functional outcome in new onset ischemic stroke patient with diabetes mellitus.*

Method: *This Cross sectional study was carried out in the Department of Neurology, BSMMU, Dhaka, from February 2013 to September 2014 on 50 patients with first attack of ischemic stroke with DM. modified Rankin Scale (mRS) and HbA1c were measured on 14th day of the stroke. During this period other important relevant investigations were also recorded.*

Result: *Majority of the patients (40.0%) were in age group 51-60 years. The mean age was 58.9 ± 9.6 years with a range from 30 to 75 years. Males were 52.0% and females were 48.0%. Male to female ratio was 1.08:1. It was observed that more than one third (36.0%) patients were current smoker, 9(18.0%) were former smoker and 23(46.0%) were non smoker. Majority of the 29(58.0%) patients had hypertension. Mean systolic BP was found 129 ±16 mmHg with a range from 90 to 160 mmHg. The mean diastolic BP was found 81±11 mmHg with a range from 60 to 100 mmHg. HbA1c has significant positive correlation with modified ranking scale on 14th day of stroke [r= 0.504 (p<0.001)].*

Conclusion: *As per study result it can be concluded that increase level of HbA1c is associated with higher level of mRS.*

Keywords: *HbA1c, Iischemic stroke, diabetes mellitus*

J Dhaka Med Coll. 2018; 27(1) : 5-8

Introduction:

Acute stroke is characterized by rapid appearance (usually over minutes) of a nonconvulsive focal deficit of brain function, most commonly a hemiplegia with or without signs of focal higher cerebral dysfunction (such as aphasia, hemisemory loss and visual field defect) or brain stem deficit. Care needs to be taken to exclude other differential diagnosis if symptoms progress over hours or days.[1]

In 1990 alone, World Health Organization estimated that there were over 2.1 million people who died of stroke. In Asia, burden of stroke is likely to increase substantially in the near future because of the aging population. Stroke is the third leading cause of death worldwide and the leading cause of acquired disability in adults in most regions.[2] Countries of low and middle income have the largest burden of stroke, but few reliable data are available to identify risk factors for stroke in most of these regions.

The existing studies have shown that the main cause of ischemic stroke is the lesion of vascular wall. Diabetes mellitus is one of the major risk factors of atherosclerosis, which can accelerate the process of vascular lesion.[3]

1. Dr. Hashmi Sina, Assistant Professor of Neurology, Dhaka Medical College Hospital, Dhaka.
2. Dr. A K M Anwar Ullah, Professor of Neurology , BSMMU, Dhaka.
3. Dr. Subash Kanti Dey, Associate Professor of Neurology , BSMMU, Dhaka.
4. Dr. Md. Amir Hossain, Assistant Professor of Neurology, NINS, Dhaka.
5. Dr. Sharif Uddin Ahmed, Assistant Professor of Neurology, OSD, DGHS.
6. Dr. Md. Shahadat Hossain, Assistant Professor of Medicine, OSD, DGHS.
7. Dr. Md. Arifuzzaman, Assistant Professor of Neurology, Dhaka Medical College Hospital, Dhaka.
8. Dr. Abu Raihan Siddique, Assistant Professor of Gastroenterology, OSD, DGHS.
9. Dr. Mohammad Zakir Hossain, Junior Consultant Medicine, UHS, Keraniganj, Dhaka
10. Dr. Md. Rashedul Hasan, Junior Consultant, Medicine, Tangail Medical College, Tangail
11. Prof. Khan Abul Kalam Azad, Professor, Department of Medicine, Dhaka Medical College, Dhaka

Correspondence: Dr. Hashmi Sina, Assistant Professor, Neurology, Dhaka Medical College Hospital, Email – hashmi.sina49@gmail.com Mobile - 01789675269

Received: *25 March 2017* ***Revision:*** *26 August 2017* ***Accepted:*** *30 September 2017*
DOI: http://dx.doi.org/10.3329/jdmc.v27i1.38886

About 90% of Hb is HbA (adult type). Approximately 8% of HbA is made up of minor component that are chemically slightly different. These minor components include HbA1c, HbA1b, HbA1a1 & HbA1a2. HbA1c is a minor component of Hb to which glucose is bound. Glycosylated hemoglobin is a variety of non enzymetic glycation reaction product generated by the Hb in the role of continuous glucose exposure and their formation is irreversible, its synthesis rate is proportional to the blood glucose concentration. Its main form is HbA1c, which represents, the average blood glucose level in previous 2-3 months. The new guidelines issued by American diabetic association (ADA) in 2010 takes HbA1c e" 6.5% as one of the diagnostic criteria for DM, takes e" 5.7% as one of the screening criteria of DM[4] and <7 as target for diabetic patients by American Diabetic Association and <6.5 by NICE guideline.

Krishnamurti & Steffes[5] have shown that if HbAlc increases in the blood it will continually accumulate in the vessel wall that lead to increase production of thromboxane A2 and protein kinase which causes to excessive collagen fibers cross-link by reducing the release of nitric oxide. These ultimately cause hardening of the blood vessel wall and decline of artery compliance. On the other hand higher content of HbA1c allows shifting of oxyhaemoglobin dissociation curve to the left, resulting in oxygen dissociation barrier, nerve tissue ischemia and hypoxia, myelin loss, nerve degeneration, dysfunction and necrosis.

Method:

This Cross sectional study was carried out in the Department of Neurology, BSMMU, Dhaka, from February 2013 to September 2014. This study was conducted on 50 patients with first attack of ischemic stroke with DM. On 14th day of stroke, patient's mRS was done along with HbA1c. During this period other important relevant investigations were recorded. Pearson Correlation Test was also used to show the relation between HbA1c and mRS. Statistical software SPSS 12.0 was used for analysis. A p value of <0.05 was taken as level of significance.

Results:

In this study, it was observed that majority of the patients (40.0%) were in age group 51-60 years. The mean age was found 58.9 ± 9.6 years with a range from 30 to 75 years. 26(52.0%) patients were male and 24(48.0%) were female. Male to female ratio was 1.08:1. It was observed that more than one third (36.0%) of the patients were current smoker, 9(18.0%) were former smoker and 23(46.0%) were non smoker. It was observed that majority of the 29(58.0%) patients had hypertension. It was observed that mean systolic BP was found 129 ± 16 mmHg with a range from 90 to 160 mmHg. The mean diastolic BP was found 81±11 mmHg with a range from 60 to 100 mmHg. Significant positive correlation was found between HbA1c and modified ranking scale on 14th day of stroke [r= 0.504 (p<0.001)].

A total of 31 patients had slight disability on 14th day of stroke, among them 7 patients had d"6.5 HbA1c and 24 patients had > 6.5 HbA1c. Total 19 patients had moderate to severe disability, among them only 1 patient had d"6.5 HbA1c and 18 patients had >6.5 HbA1c. However, chi-square statistics does not provide any significant conclusion about association between.

HbA1c level significantly positively correlated with mRS. The estimated odds ratio suggests that there is 2.3 times greater likelihood of facing severe disability for 1 unit increase in HbA1c level.

Table I

Demographic and clinical profile of the study subjects (n=50)

	Frequency	Percentage
Age (years)		
<40	4	8.0
41-50	5	10.0
51-60	20	40.0
61-70	19	38.0
>70	2	4.0
Mean ±SD	58.9 ± 9.6	
Range (min-max)	(30-75)	
Gender		
Male	26	52.0
Female	24	48.0
Smoking habit		
Current	18	36.0
Former	9	18.0
Non smoker	23	46.0
Hypertension	29	58.0
Systolic BP (mmHg)	[Mean ±SD]	129 ± 16
Diastolic BP (mmHg)	[Mean ±SD]	81 ± 11

Table II

Cross tabulation between HbA1c categories and mRS categories

mRS categories	HbA1c		Total	P-value
	<6.5	>6.5		
Slight disability	7 (87.5)	24 (57.1)	31 (62.0)	0.134^{ns}
Moderate to severe disability	1 (12.5)	18 (42.9)	19 (38.0)	
Total	8 (100.0)	42 (100.0)	50 (100.0)	

Table III

Multivariate logistical regression analysis of modified ranking Scale for Stroke Severity (mRS) and the outcome variables

Independent variables	Wald	S.E.	Sig. (p value)	OR	95% CI for OR	
					Lower	Upper
Age	5.421	0.046	0.020*	1.112	1.017	1.216
Sex	3.650	1.390	0.056	0.070	0.005	1.071
Smoking	2.479	0.870	0.115	0.254	0.046	1.399
Hypertension	1.702	0.756	0.192	0.373	0.085	1.641
HBA1c	6.025	0.345	0.014*	2.332	1.186	4.584

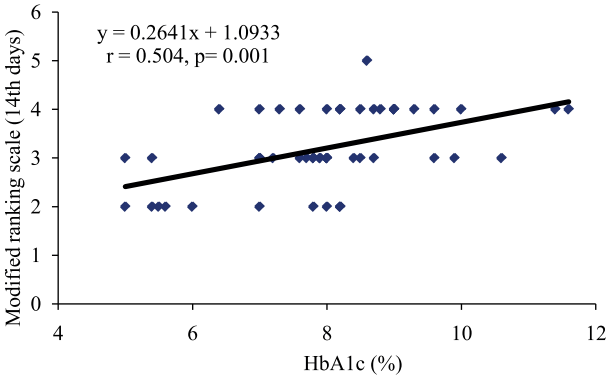

Fig.-1: *The scatter diagram shows significant positive correlation between HbA1c with modified ranking scale on 14th day of stroke [r= 0.504 (p<0.001)].*

Discussion:

In this series it was observed that majority (78.0%) patients were in 6th and 7th decade and the mean age was 58.96±9.58 years with range from 30 to 75 years. Shuangxi et al.[4] and Basu et al.[6] showed the mean age was 60.5±8.65 years varied from 45 to 81 years and the average age was 60.0 ±13 years varied from 25 to 88 years respectively. Similarly, Doi et al.[7] obtained the mean age 58.0±10.0 years, which is consistent with the current study. On the other hand, Rathore et al.[8] has observed higher mean age, which was 64.78±9.404 years varied from 45–85 years and the maximum frequency was seen between ages 55 –74 years. Similarly, Kamouchi et al.[9] and Sare et al.[10] showed the mean age of the study subjects was 69±12 years and 68.9±12.1 years respectively. The higher mean age may be due to increased life expectancy, geographical variations, racial and ethnic differences may have significant impacts.

In this study it was observed that 52.0% patients were male and 48.0% female and male to female ratio was 1.08:1, which is closely resembled with Shuangxi et al.[4], Kamouchi et al.[9], Rathore et al.[8], Sare et al.[10] and Basu et al.[6] series, where all the above investigators found male predominance in their study.

In this present studies it was observed that more than one third (36.0%) of the patients were current smoker, 18.0% were former smoker and 46.0% were non smoker. Shuangxi et al.[4], Kamouchi et al.[9] and Rathore et al.[8] showed 38.9%, 46.0% and 57.0% study subjects were current smoker respectively. In another study, Doi et al.[7] observed 50.1% patients were current smoker in their study, which were comparable with the current study.

In this current study it was observed that 58.0% patients had hypertension. Similarly, Shuangxi et al.[4] and Doi et al.[7] found 55.6% and 43.3% of their study patients were hypertensive, respectively. Kamouchi et al.[9] found 70.9% of patients hypertensive, Sare et al.[10] found history of hypertension in 73.2% and Basu et al.[6] obtained that the majority of the patients were hypertensive (74.0%). Above results were higher than the current study.

In this present study, it was observed that the mean systolic BP was 129.25±15.98 mmHg which varied from 90 to 160 mmHg. The mean diastolic BP was 81±10.77 mmHg which varied from 60 to 100 mmHg. Doi et al.[7] showed that the mean systolic blood pressure was 134.0±20.0 mmHg and mean diastolic blood pressure was 81.0±11 mmHg, which was consistent with the current study. Kamouchi et al.[9] showed the mean systolic blood pressure was 161.0±30.0 mmHg and mean diastolic blood pressure was 88.0±18.0 mmHg, which were higher than the current study. Similarly higher systolic and diastolic blood pressure was also revealed by Rathore et al.[8] and Sare et al.[10].

In this series it was observed that a significant positive relationship [r= 0.504 (p<0.001)] between HbA1c and modified ranking scale on 14th day of stroke. Shuangxi et al.[4] showed that the serum HbAlc and mRS score in patients with ischemic stroke was positively correlated (P<0.001). In 2010, from the Fukuoka Stroke Registry (FSR) a multicentre stroke registry in Japan, 3627 patient with first ever ischemic stroke within 24 hours after onset were included in the analysis. ORs for neurological deterioration and a poor functional outcome were higher in patients with poorer PSGC status.[9] Hussain et al.[11] examined the relationship between HbA1c and discharge modified rankin scale (mRS) in patients with acute ischemic stroke receiving IV rt-pa. All patients who received IV rt-PA had HbA1c and discharge mRS record. Clinical outcomes quantified by discharge mRS in patients with ischemic strokes treated with rt-PA is indeed dependent on HbA1c levels.

Conclusion:

Patients having new onset ischemic stroke with Diabetic Mellitus were predominant in 6th decade and above and more common in male subjects. Finally it can be concluded that increase level of HbA1c is associated with higher mRS, so more stroke severity.

References:

1. Allan HR and Martina AS. Adams and Victors Principle's of Neurology, 9th edn, Mc Graw Hill Medical, USA. 2009
2. Langhorne P. 'Stroke disease' In: Walker B, Colledge N, Ralton S, Penman I. 22nd ed. 2014. Davidson's Principles and Practice of Medicine, Elsevier, London.
3. Pearson ER and McCrimmon RJ. 'Diabetes mellitus' In: Walker B, Colledge N, Ralton S, Penman I 22nd ed. 2014. Davidson's Principles and Practice of Medicine, Elsevier, London.
4. Shuangxi G, Song T, Bo S, Avinash C, Anna M, Hui F, Si C, Yuming X. Study of the relationship of glycated hemoglobin levels and neurological impairment and three months prognosis in patients with acute ischemic stroke. Life Sci J. 2012;9(2):119-21.
5. Krishnamurti U, Steffes MW. Glycohemoglobin: a primary predictor of the development or reversal of complications of diabetes mellitus. Clinical chemistry. 2001 Jul 1;47(7):1157-65.
6. Basu S, Sanyal D, Roy K, Bhattacharya KB. Is post-stroke hyperglycemia a marker of stroke severity and prognosis: A pilot study. Neurology Asia. 2007 Jun;12:13-9.
7. Doi Y, Ninomiya T, Hata J, Fukuhara M, Yonemoto K, Iwase M, Iida M, Kiyohara Y. Impact of Glucose Tolerance Status on Development of Ischemic Stroke and Coronary Heart Disease in a General Japanese Population. Stroke. 2010 Feb 1;41(2):203-9.
8. Rathore JA, Kango ZA, Mehraj A. Predictors of mortality after acute stroke a prospective hospital based study. J Ayub Med Coll Abbottabad. 2011 Jun 1;23(2):144-6.
9. Kamouchi M, Matsuki T, Hata J, Kuwashiro T, Ago T, Sambongi Y, Fukushima Y, Sugimori H, Kitazono T, FSR Investigators. Prestroke glycemic control is associated with the functional outcome in acute ischemic stroke. Stroke. 2011 Oct 1;42(10):2788-94.
10. Sare GM, Ali M, Shuaib A, Bath PM. Relationship between hyperacute blood pressure and outcome after ischemic stroke. Stroke. 2009 Jun 1;40(6):2098-103.
11. Hussain M, Dababneh H, Mehta S, Dass P, Ahmad J, Moussavi M, Panezai S, Kirmani J. Effect of HbA1c Level on Discharge Modified Rankin Scale Who Received rt-PA in Acute Ischemic Stroke (P01. 224). Neurology. 2013 Feb 12;80(7 Supplement):P01-224.