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The Study of Relationship of Glycated Haemoglobin with Carotid Artery Intimal Thickness in Patients with Ischaemic Stroke.

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ABSTRACT

Background: Long term uncontrolled hyperglycemia, which is indicated by HbA1c levels, is strongly suspected of promoting atheogensis.An accurate marker for assessing the risk of stroke is the carotid artery intima-media thickening (IMT), assessed by Doppler ultrasound. Increased common carotid artery IMT is correlated with silent cerebral infarcts.This study aimed to show the association between marker of uncontrolled long term hyperglycemia (HbA1C) and marker of atherosclerosis (Carotid intima media thickness [CIMT]) in ischemic stroke patients. **Methods:** This study was conducted In Deptt. of Medicine, Rajindra hospital Patiala in collabroration with Deptt. Of Radiology and Deptt. of Biochemistry. **Results:** This study included a total number of 75 patients admitted in various ward of Medicine Deptt. Rajindra Hospital Patiala.CIMT was found to be significantly increased in the patients having diabetics mellitus than non diabetic patients. **Conclusion:**There is seen a positive correlation of HbA1C with CIMT in our study which included only the ischemic stroke patients.

Keywords: Glycated Hemoglobin, CIMT, Ischaemic Stroke.

INTRODUCTION

A Stroke is rapidly developing clinical symptom and/or signs of focal and at times global loss of brain function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than vascular origin.[1,2] Strokes are broadly classified as ischemic or hemorrhagic. Ischemic stroke is due to occlusion of cerebral blood vessel and causes cerebral infarction.[3] Atherosclerosis is the most common pathological feature of vascular obstruction resulting in thrombotic stroke.[4] People with diabetes have more than double the risk of ischemic stroke after correction for other risk factor, relative to individuals without diabetes. Even when adjusted for increased risk of cardiovascular disease in comparison to non diabetic people. Therefore, long term uncontrolled hyperglycemia, which is indicated by HbA1c levels, is strongly suspected of promoting atheogensis.

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Glycatedhemoglobin (HbA1c) is a form of hemoglobin that is measured primarily to indentify the average plasma glucose concentration over prolonged periods of time. It is formed In a non-enzymatic glycation pathway by hemoglobin's exposure to plasma glucose.HbA1c is a measure of the beta-N-1-deoxy frutosyl component of hemoglobin.4This serves as a marker for average blood glucose levels over the previous 3 months prior to the measurement as this is the half life of red blood cells.

Atherosclerosis within the carotid artery occurs frequently within the common carotid bifurcation and proximal internal carotid artery. Male gender, older age, smoking, hypertension, diabetes and hypercholesterolemia are risk factors for Carotid disease, as they are for stroke in general. Carotid atherosclerosis produces an estimated 10% of Ischemic stroke. Symptomatic carotid disease implies that the patient has experienced a stroke or TIA within the vascular distribution of the artery, and it is associated with a greater risk of subsequent stroke than asymptomatic stenosis, in which the patient is symptom free and the stenosis is detected through screening. Greater risk of arterial narrowing is generally associated with a greater risk of stroke.[5] Carotid atherosclerosis plaque with resultant stenosis

usually involves the internal carotid artery within 2cm of carotid bifurcation.

According to North American Symptomatic Carotid Endarterectomy Trial (NASCET), patients with a severe carotid stenosis (70-90%) have a risk of cerebral ischemic events of 28% in the following 2 years.[6] An accurate marker for assessing the risk of stroke as the carotid artery intima-media thickening (IMT) assessed by Doppler ultrasound.[7] Increased common carotid artery IMT is correlated with silent cerebral infarcts as a recent study on Japanese subjects showed.[8] The marker has predictive value for stroke occurrence and recurrence. For each standard deviation of 0.163 mm the relative risk increases with 1.57, while for every additional 0.1 mm in addition the risk of recurrent stroke increased by 18%.[9]

MATERIALS AND METHODS

This study was conducted In Deptt. of Medicine, Rajindra hospital Patiala in collabroration with Deptt. of Radiology and Deptt. of Biochemistry, Rajindra Hospital Patiala. This study included a total number of 75 patients admitted in various ward of Medicine Deptt. Rajindra Hospital Patiala.

Inclusion Criteria

1. Patients with ischemic stroke with symptoms persisting for more than 24 hours.
2. Patients with age more than 30 years.

Exclusion Criteria

1. Patients with isolated transient ischemic attack.
2. Stroke caused by vasculitic syndromes.
3. Patients with subarachnoid hemorrhage, intra cerebral haemorrhage.
4. Patents with coagulation disorders.

Method

Patients fulfilling the inclusion criteria after thorough screening were included in the study. All the patients and their relatives were informed about the study in their vernacular language. Written consent was taken. A details history of each patient was taken as per Performa attached. Complete clinical examination was done and all the routine investigation as in profoemawere sent.

All subjects also underwent Color Doppler of Carotid arteries and also had their HbA1c levels checked. Doppler Ultrasound was performed with Philips Envisor ultrasound machine with a 7.5 Mhz linear array transducer.

RESULTS

This study was conducted over 75 patients of stroke admitted in various wards of Deptt. of Medicine, Rajindra Hosptial Patiala. Careful history examination and laboratory parameters were recorded in present proforma. Then data was analysed statistically.

Table 1: Sex Distribution.

Sex	No. of cases	%age
Male	48	64.00
Female	27	36.00
Total	75	100

[Table 1] shows the distribution of cases according to gender. 48 out of the 75 patients ie 64% were males while 27 patients ie 36% were females.

Table 2: Age Distribution

Age Group (in years)	No. of cases	%age
31-40	1	1.33
41-50	10	13.33
51-60	16	21.34
61-70	24	32.00
>70	24	32.00
Total	75	100

[Table 2] shows the distribution of cases according to age. The age ranges from 35 years to 85 years. Most of the patients were above 60 years of age. The youngest patients was 35 years old and was a female, the oldest patient was an 85 years old male.

Table 3: Distribution of Diabetes Mellitus.

Type of patients	Number of Cases		Total
Patients with DM	17	17	34
Patients without DM	31	10	41
Total	48	27	75

[Table 3] shows distribution of diabetes mellitus in the study group. 34 patients out of 75 had a known history of type 2 diabetes mellitus out of which 17 were males and 17 were females. 3 patients who had no prior history of diabetes were found to be diabetic after admission.

Table 4: Glycemic Status of the patients.

DM	HbA1C		
	<5.7%	5.7%-6.4%	>6.5%
Yes	0	0	34
No	8	29	4
Total	8	29	38

[Table 4] shows the association of HbA1C with diabetes mellitus. All diabetics had their HbA1c value >6.5%, hence a significant relation was found.

Table 5: Relation of CIMT with Diabetes Mellitus.

	CIMT	
	<0.8mm	>0.8mm
Diabetic	0	34
Non-diabetic	25	16
Total	25	50
P Value		<0.05

[Table 5] shows correlation of CIMT with diabetes mellitus. All patients of diabetes had CIMT >0.8 mm and 16 non diabetic patients had CIMT >0.8mm.

Table 6: Relation of HBA1C with CIMT

CIMT	HBA1C		
	<5.7%	5.7%-6.4%	>6.5%
<0.8mm	8	17	0
>0.8mm	0	12	35
Total	8	29	38

Table 7: Correlation of HBA1C with CIMT

	HBA1C	CIMT
Mean + SD	7.35+1.73%	0.840+0.94mm
Range	5.10 -11.50	0.68 - .0107mm
Pearson's Correlation Coefficient ®		0.952
Significance		P<0.05(S)

[Table No 6 & 7] shows the correlation between Hba1c and CIMT. The mean Hba1c in the study population was 7.35 +1.73% and its and the mean CIMT was 0.840 +0.094 mm. This statistical analysis shows that there is significant Positive correlation of CIMT with HBA1C i.e. Higher HBA1C values is associated with increase in CIMT.

Table 8: Correlation of HBA1C with CIMT in MALES

	HBA1C	CIMT
Mean + SD	7.05 + 1.70%	0.825 + 0.094mm
Range	5.10 – 11.50%	0.680 – 0.107 mm
Pearson's Correlation Coefficient ®		0.956
Significance		P<0.05(S)

[Table 8] shows the association between HBA1C and CIMT in males. The mean HBA1C value for males was 7.05 + 1.70% and the mean value for CIMT was 8.25 + 0.94 mm. This statistical analysis shows that there is significant Positive correlation of CIMT with HBA1C higher HBA1C values are associated with increase in CIMT in males.

Table 9: Correlation of HBA1C with CIMT in FEMALES

	HBA1C	CIMT
Mean + SD	7.89+1.69%	0.867 + 0.09mm
Range	0.520 –0.108mm	0.69 – 0.105mm
Pearson's Correlation Coefficient ®		0.938
Significance		P<0.05(S)

[Table 9] shows the correlation of HBA1c with CIMT in females. The mean HBA1C was 7.89 + 1.69% and the mean CIMT was 7.89 + 1.69mm. This statistical analysis shows that there is significant Positive correlation of CIMT with HBA1C i.e higher HBA1C values are associated with increase CIMT in females.

DISCUSSION

Glycated hemoglobin (HbA1C) indicates long term uncontrolled hyperglycemia in the body, which in diabetic patients leads to various vascular complications as a part of generalized atherosclerosis culminating ultimately into ischemic stroke.

This study aimed to show the association between marker of uncontrolled long term hyperglycemia (HbA1C) and marker of atherosclerosis (Carotid intima media thickness [CIMT]) in ischemic stroke patients.

Table 10: Correlation of HBA1C with Diabetes Mellitus.

Studies	Mean HBA1C in diabetics	Mean HBA1C in non diabetics	P value
Singh AS et al[9]	9.29+1.74	6.65+0.89	<0.0001
Present study	9.02 + 1.12	5.96+0.39	<0.0001

[Table 10] shows the correlation between diabetic status of the patient and HBA1C levels. Higher values of HBA1C were found in diabetic patients as compared to non diabetics and this relation was statistically significant which was in concordance with Singh AS et al.[9]

Table 11: Association of CIMT with diabetic status of the patient.

Studies	Mean CIMT in diabetics (in mm)	Mean CIMT in non diabetics (in mm)
Jhamb R et al[7]	0.72 + 0.087	0.5813 + 0.085
Larsen J R[6]	0.86 + 0.164	0.605 +0.082
Osheiba Z F et al[10]	0.54 + 0.08	0.41 + 0.04
Perumal K Et al[11]	0.82 + 0.08	0.59 + 0.050
Gupta A et al[8]	0.775 + 0.21	0.583 + 0.22
Present study	0.920 + 0.0715	0.774 + 0.047

[Table 11] shows the correlation between CIMT and diabetic status of the patient. CIMT was found to be significantly increased in the patients having diabetic's mellitus than non-diabetic patients; this was in concordance with other studies as mentioned above. The mean CIMT of diabetic's patients was 0.72 + .0087 mm as compared to 0.581 + 0.085 mm in non-diabetics in the study conducted by Jhamb R et al.

Table 12: Correlation between HBA1C and CIMT

Studies	P Value
Singh As et al[9]	0.008
Ja"rvisalo J.M. et al	0.001
Jhamb R et al[7]	0.0036
Osheiba F.Z. et al[10]	0.012
Perumal K.K et al[11]	0.001
Saba L. et al[5]	0.0007
Zhu W. et al[12]	0.0009
Present study	0.001

[Table 12] shows the correlation between HbA1C and CIMT among various studies. There is found a positive correlation between HbA1C and CIMT on comparing the values of HbA1C and CIMT among different studies. There is seen a positive correlation of HbA1C with CIMT in our study which included

only the ischemic stroke patients. This positive correlation was also found in several other studies which were conducted by Singh As et al, Jhamb R et al and the above mentioned ones having different study populations. However in a study conducted by Doruk et al, it was seen that HbA1c levels are neither correlated with age nor with thecarotid IMT. This study only included healthy geriatric population.

In this study, a significant correlation was seen between CIMT and HbA1c. CIMT describe early atherosclerotic changes, thus HbA1c not only confirm diagnose of diabetes but also confirms upcoming fatal events like stroke as a complication of atherosclerosis developed in diabetics patients. Thus a good glycemic control as predicted by the HbA1c levels can help in slowing the progression of atherosclerosis and its complications.

CONCLUSION

Majority of the patients (64%) were male and 36% were females. Mean age of the patients included was 63.75 + 10.4 years with a range of 35 to 85 years. Among the patients, 30 had a history of Hypertension out of which 20 were males and 10 were females. Among the patients, 34 were diabetic and 41 without diabetics. Three patients who had no prior history of diabetics were later diagnosed as having diabetes after admission. Twenty-Three patients (30.66%) of the total were known smokers and 22 patients (29.33%) were alcoholic. The mean fasting blood glucose of all ischemic stroke patients was 124.12 + 45.34 mg/dl and postprandial value was 194.33 + 45.34 mf/dl.The mean HbA1C of the study population was 7.35 + 1.73%. The mean HbA1C levels among the diabetics were 9.023 + 1.12% and among the non-diabetics were 5.97 + 0.39%.The mean carotid artery intima media thickness among the study population was 0.84 + 0.094mm. The patients with high CIMT had a higher values of HbA1C than that of normal CIMT patients which was statistically significant ($p<0.05$).

Thus, we conclude that there is a strong correlation between HbA1c, which is a marker of glycemic control and carotid artery intima media thickness, which can be used as a marker for atherosclerosis in patients with ischemic stroke..Good control of glycemia levels can thus help in preventing and planning strategies against atherosclerotic complications like cerebrovascular and coronary artery disease, which are a major cause of morbidity and mortality in these patients.

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