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Risk Profile in Reference to Glycated Hemoglobin and Lipid Profile in Stroke Patient with Type-2 Diabetes Mellitus

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Abstract: ***Introduction: Diabetic mellitus (DM) is characterized by chronic hyperglycemia with disturbances of carbohydrate, lipid and protein metabolism. we evaluated the level of HbA_{1C} and lipid profile in type2 diabetes mellitus patient and found out the correlation between HbA_{1C} and lipid profile parameters in stroke patients with type-2 DM. Methods: A cross sectional study was done among 50 patients of stroke with DM type-2 at a centre in North Karnataka. A detailed history and clinical examination with relevant investigations were done. The serum sample was used for the measurement of lipid profile and HbA_{1C} level. Results: In this study of 50 patients, 30 (60%) were male and 20 (40%) were female. The mean age of the cases studied was 61.6±11.06 years. The mean HbA_{1C} 8.46±1.26, the mean lipid value TC = 194.15±36.77, TG=157.94±49.73, HDL = 34.06±9.47, LDL=126.36±35.54 and VLDL=31.76±10.06. The present study showed a statistically significant positive correlation between serum HbA_{1C} level and serum lipid levels ($p<0.05$). Conclusions: The dual biomarker HbA_{1C}, glycemic control as well as lipid profile can be used for screening of high risk patients for early diagnosis of dyslipidemia. Thereby the cerebrovascular and peripheral complications can be prevented by timely intervention of the disease.***

Keywords: Dyslipidemia; Diabetes Mellitus; HbA_{1C}; Lipid profile

1. Introduction

Cerebrovascular diseases include some of the most common and devastating disorders: ischemic stroke and hemorrhagic stroke. Stroke is the second leading cause of death worldwide, causing 6.2 million deaths in 2011 [1]. The incidence of cerebrovascular diseases increases with age, and the number of strokes is projected to increase as the elderly population grows, with a doubling in stroke deaths in the United States by 2030[2]. A stroke, or cerebrovascular accident, is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause. Thus, the definition of stroke is clinical, and laboratory studies including brain imaging are used to support the diagnosis. Cerebral ischemia is caused by a reduction in blood flow that lasts longer than several seconds. Neurologic symptoms manifests within seconds. Stroke has occurred if the neurologic signs and symptoms last for >24 h or brain infarction is demonstrated. Focal ischemia or infarction, is usually caused by thrombosis of the cerebral vessels themselves or by emboli from a proximal arterial source or the heart. Intracranial hemorrhage is caused by bleeding directly into or around the brain; it produces neurologic symptoms by producing amass effect on neural structures, from the toxic effects of blood itself, or by increasing intracranial pressure[3]. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. An increasing incidence worldwide, DM will be likely a leading cause of morbidity and mortality in the future. The worldwide prevalence of DM has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to 382 million in 2013[4]. Based on current trends, the International Diabetes Federation projects that 592 million individuals will have diabetes by the year 2035[5].In the most recent estimate for the United States (2012), the Centers for Disease Control and Prevention (CDC) estimated that 9.3% of the population had diabetes (~28% of the individuals with diabetes were undiagnosed; globally, it is estimated that 50% of individuals may be undiagnosed). The CDC estimated that the incidence and prevalence of diabetes doubled from 1990–2008, but appears to have plateaued from 2008–2012[6]. DM increases with age. Worldwide, most individuals with diabetes are between the ages of 40 and 59 years[7]. The ADA recommends screening all individuals >45 years every 3 years and screening individuals at an earlier age if they are overweight (BMI >25 kg/m2 or ethnically relevant definition for overweight) and have one additional risk factor for diabetes[8].

2. Material and Methods

This is a cross sectional study conducted at Khaja Banda Nawaz Teaching and General Hospital, in North Karnataka. A total number of 50 cases were selected for the present study. A pre-structural proforma will be used to collect baseline data detailed clinical history with clinical examination and relevant investigation including, complete blood count, random blood sugar, serum creatinine, blood urea, serum electrolytes, urine routine, fasting blood glucose, post prandial blood sugar, HbA_{1C}, lipid profile, CT brain plain was done on participating individuals after the permission of ethics committee of the institute.

Inclusion Criteria

Patient with age more than 18 years , type 2 Diabetes mellitus, hypertension, smoking history, history of previous stroke

Exclusion Criteria

Patient with age less than 18 year, type 1 Diabetes mellitus, stroke mimickers - unusual manifestations of nonvascular conditions that may resemble acute stroke syndrome, seizure / postictal, subdural hematoma, abscess, intracranial tumors, hypertensive encephalopathy, multiple sclerosis, psychiatric problems, factitious disorders.

3. Results

Table 1: Distribution of Age and Gender

Age (years)	*Gender*		*Total*
	Female	*Male*	
41 - 50	5 (55.55%)	4 (44.44%)	9 (18.00%)
51 - 60	5 (27.77%)	13 (72.22%)	18 (36.00%)
61 - 70	4 (30.76%)	9 (69.23%)	13 (26.00%)
71+	6 (60.00%)	4 (40.00%)	10 (20.00%)
Total	20 (40.00%)	30 (60.00%)	50 (100%)

Mean ± SD of age (years) were 61.82 ± 11.06

Total number of patients in the present study were 50. Out of 50 patients, 30 were males and 20 were females. The mean age in the present study is 61.82±11.06 years.

Table 2: Distribution of HbA_{1C} with Gender

HbA_{1C}	*Sex*		*Total*
	Female	*Male*	
≤7.0	1 (20.00%)	4 (80.00%)	5 (10.00%)
7.1 - 8.0	9 (64.28%)	5 (35.71%)	14 (28.00%)
8.1 - 9.0	6 (33.33%)	12 (66.66%)	18 (36.00%)
>9.0	4 (30.76%)	9 (69.23%)	13 (26.00%)
Total	**20 (40.00%)**	**30 (60.00%)**	**50 (100%)**

Mean ± SD of HbA_{1C} is 8.460 ± 1.26

Out of 50 patients, 5 patients (10%) had HbA_{1C} levels ≤7, among which one was female and 4 were male. The HbA_{1C} levels among 9 female (64.28%) and 5 male (35.71%) observed was between 7.1-8.0. 18 (36%) patients had HbA_{1C} levels between 8.1-9.0, while 13 patients i.e., 26% had HbA_{1C} levels >9.

Table 4: HbA_{1C} Vs HTN & No H/o of HTN

HbA_{1C}	*HTN*	*No. H/o HTN*	*Total*
≤ 7.0	4 (80%)	1(20%)	5 (100%)
7.1 - 8.0	11 (78.57%)	3 (21.42%)	14 (100%)
8.1 - 9.0	12 (66.66%)	6 (33.33%)	18 (100%)
>9.0	10 (76.92%)	3 (23.07%)	13 (100%)
Total	37 (74%)	13 (26%)	50 (100%)

Out of 50 patients, 37 (74%) had hypertension and 13 (26%) patients had no history of hypertension. Out of 37 (75%) patients with hypertension, 4 patients had HbA_{1C} levels ≤7.0, 11 had HbA_{1C} levels 7.1-8.0, 12 had HbA_{1C} levels 8.1-9.0, while 12 patients had HbA_{1C} levels >9.0. Out of 13 patients (26%) with no history of hypertension, 1 patients had HbA_{1C} levels ≤7, 3 had 7.0-8.0, 6 had HbA_{1C} levels between 8.1-9.0 and 3 had HbA_{1C} levels >9.0.

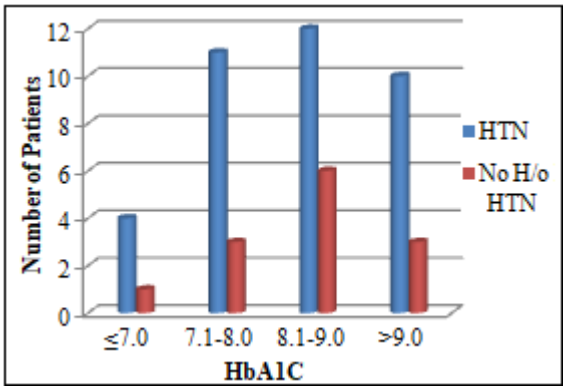

Figure 7: HbA_{1C} levels in relation to Hypertension

Table 5: Relationship between HbA_{1C} with incidence of stroke

Stroke		*HbA_{1C}*				*Total*
		≤7.0	*7.1 - 8.0*	*8.1 - 9.0*	*>9.0*	
Isc. stroke	**No.**	5	9	15	8	**37**
	%	13.51%	24.32%	40.54%	21.62%	100
TIA	No	0	3	1	1	05
	%	0%	60%	20%	20%	100
Hem. Stroke	No	0	2	2	4	8
	%	0%	25%	25%	50%	100
Total Percentage	No	5	14	18	13	50
	%	10%	28%	36%	26%	100

Out of 5 TIA patients, 3 had HbA_{1C} levels >7.1-8.0, 1 had HbA_{1C} levels 8.1-9.0 and 1 had HbA_{1C} levels >9.0. Among 37 patients of ischemic stroke, 5 had HbA_{1C} levels ≤7.0, 9 had 7.1-8.0, 15 patients had HbA_{1C} levels 8.1-9.0 and 8 patients had HbA_{1C} levels >9.0. Out of 8 hemorrhagic stroke patients, 2 patients had HbA_{1C} levels >7.1, 2 patients had HbA_{1C} levels >8.1, while 4 patients had HbA_{1C} levels >9.0.

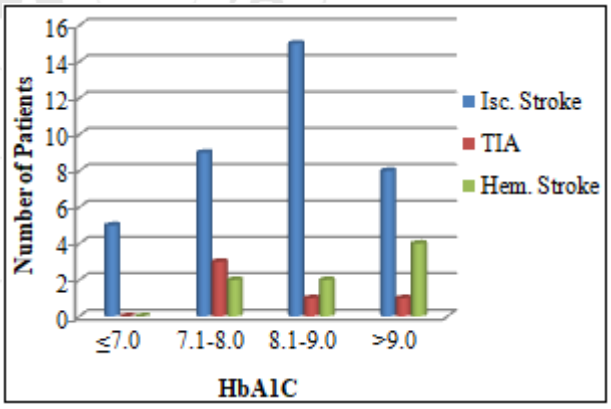

Figure 8: Relationship between HbA_{1C} with incidence of stroke

Table 6: Relationship between lipid levels (LDL &HDL) with incidence of stroke

Strokes	*Lipids*		
	TIA	*Isc. Stroke*	*Hem. Stroke*
TC	185.8 ± 40.95	201.66 ± 49.66	207 ± 23.31
TG	168.87 ± 29.31	155.32 ± 53.91	168.87 ± 29.31
HDL	30.25 ± 6.75	35.21 ± 10.31	30.25 ± 6.75
LDL	119.8 ± 40.03	124.81 ± 37.50	137.62 ± 22.51
VLDL	34.4 ± 10.87	31.05 ± 10.66	33.37 ± 6.75

P<0.05 were statistically significant

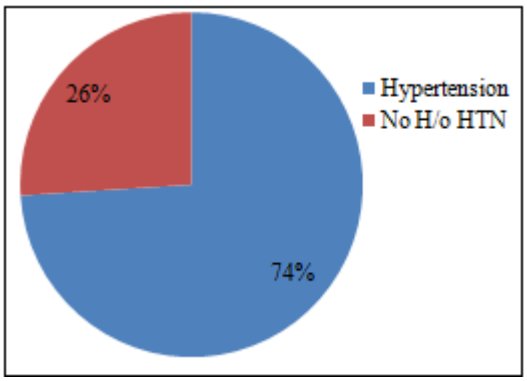

Figure 9: Distribution of Hypertension and No H/o HTN

Out of 50 patients studied, no history of hypertension was found in 13 patients (26%) and 37 patients (74%) had history of hypertension.

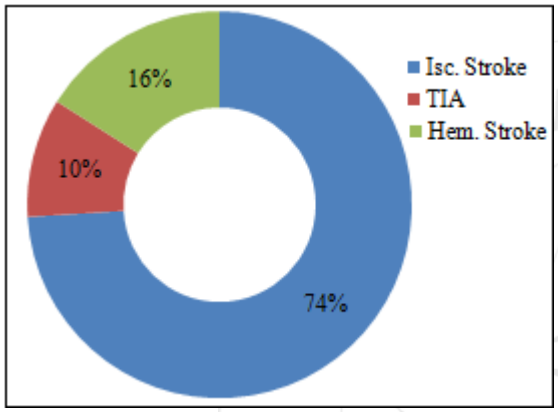

Figure 10: Patients based on type of strokes

Out of 50 patients studied, 5 patients had TIA, 8 had hemorrhagic stroke and 37 had ischemic stroke.

Table 7: Association of HbA_{1C} level with lipid parmeter

Lipid Levels Vs HbA_{1C}	*Mean ± SD*	*P-value*	*Significant/ insignificant*
TC	194.15 ± 36.77 (8.46±1.261)	P<0.05*	significant
TG	157.94 ± 49.73 (8.46±1.261)	P<0.05*	significant
HDL	34.06 ± 9.47 (8.46±1.261)	P<0.05*	significant
LDL	126.36 ± 35.54 (8.46±1.261)	P<0.05*	significant
VLDL	31.76 ± 10.062 (8.46±1.261)	P<0.05*	significant

***P<0.05 were statistically significant and p>0.05 is insignificant.**

Table 9: CT Findings

CT Findings	*No*	*%*
Acute Bleed In Right Thalamus & Right Deep Periventricular White Matter	1	2
Acute Bleed In Right Thalamus & Right Gangliocapsular Region	1	2
Acute Infarct In Left Gangliocapsular Region, Insular Cortex &Parietal	1	2
Hematoma In Left Fronto Parietal Region	1	2
Hemorrhage Inleft Side Internal Capsule	1	2
Infarct In B/L Frontal & Subcortical Region	1	2
Infarct In B/L Fronto Parietal Lobe	1	2
Infarct In Left Basal Ganglia	1	2
Infarct In Left Cerebellar Hemisphere	1	2
Infarct In Left Corona Radiata	3	6
Infarct In Left Fronto Tempo Parietal Cortex	1	2
Infarct In Left Gangliocapsular Region	2	4
Infarct In Left Internal Capsule	3	6
Infarct In Left Parafalcine Gyrus & Rt Precentral Gyrus	1	2
Infarct In Left Temporal & Parietal Cortex	2	4
Infarct In Right Temporal & Parietal Cortex	1	2
Infarct In Right Basal Ganglia	1	2
Infarct In Right Fronto Parietal Region	2	4
Infarct In Right Parieto Temporal Region	1	2
Infarct In Right Pca Territory	1	2
Infarct In Right Post Frontal / Parietal & Subcortical Region	1	2
Infarct In Rt. Corona Radiata & B/L Infarct In Basal Ganglia	1	2
Infarction In B/L Fronto Parietal Lobe	1	2
Infarction In Left Tempo Parietal Lobe	1	2
Intra Parenchymal Hemorrhage Right Cerebral Peduncle & Pons	1	2
Intracerebral Hemorrhage In Right Gangliocapsular Region	2	4
Lacunar Infarct In B/L Fronto Parietal Subcortical Whitematter	1	2
Lacunar Infarct In Genu Of Right Internal Capsule	1	2
Lacunar Infarct In Left Basal Gangia	2	4
Lacunar Infarct In Left Lentiform Nucleas & Corona Radiata	1	2
Lacunar Infarct In Right Fronto Parietal Subcortical Region	1	2
Lacunar Infarct In Right Internal Capsule	1	2
Lacunar Infarct In Right Thalamus	1	2
Lacunar Infarct Inleft Thalamus & Left Basal Ganglia	1	2
Lacunar Infarct Inleft Thalamus &Pons	1	2
Left Intra Parenchymal Hemorrhage	1	2
Normal	5	10
Total	50	100

Statistical Analysis:
The mean levels of various fractions were correlated with basal reference values for normal individuals. Relevant statistical methods like Normal distribution test were used to see the significance of difference in mean values between groups and to know the correlation between inter and intragroup variations.

4. Discussion

Ischemic stroke is an important cause of morbidity and mortality worldwide and currently the leading cause of adult disability in developed countries[9], [10]. Several studies have shown a higher prevalence of ischemic stroke in subjects with diabetes mellitus[11], [12], [13]. Among patients with diabetes several risk factors play a role together to promote the development of ischemic stroke. In the analysis of these risk factors can be identified diabetes-specific factors such as hyperglycemia and vascular risk factors such as hypertension and dyslipidemia [14].

In addition to these also genetic, demographic, and lifestyle factors contribute in varying degrees to the overall risk of people with diabetes. As a whole, all these factors, contribute to the characteristic atherogenic profile of the

patients with diabetes mellitus, in which there is a complex interplay of several variables with inflammatory metabolic disorders and their effect on the cardiovascular system that may accelerate the atherosclerotic process both in intracranial that extracranial vessels[15].

This could result in pathophysiological changes of cerebral vessels in people with diabetes and increase the risk of stroke [16].
The SVD play an important role in the context of diabetic microangiopathy, in fact the subtype of stroke that is mainly found in the subjects with diabetes mellitus is the lacunar type[17]. Thus, diabetes is associated with a more insidious ischemic damage to the brain, mainly manifesting as lacunar infarcts and thus increase the risk of dementia and lead to a steeper decline in cognitive function. On the other and the hyperglycemia play an important pathogenetic role in the acute phase of ischemic stroke as direct effector of neuronal damage and it is well known as a negative prognostic factor [18].

Therefore, the interaction between diabetes and stroke is a bidirectional interaction and this underlines the close relationship between these two common diseases which often arise together [19].

Finally the higher risk of stroke, especially lacunar type, that is observed in people with diabetes underline the importance of preventing the higher cerebrovascular risk which characterizes this class of patients with a multifactorial treatment of risk factors for stroke, in particular lifestyle factors, hypertension, and dyslipidemia with the aim to prevent a substantial number of these disabling strokes among patients with diabetes [20].

5. Conclusion

HbA_{1C} may be a better indicator of glycemic status than RBS in stroke. Achieving HbA_{1C} target to less than 7% in diabetic patient is very important to prevent stroke. The patient with hemorrhagic stroke had significantly higher blood pressure level. It is also confirmed that hypertension remained the most dominant risk factor for stroke. Diabetic patient with stroke tend to have higher level of lipid fraction – (TC, TG, LDL) and lower level of HDL. This suggest that there appears to be some relation between the genesis of various vascular complication and presence of lipid abnormality. The dual biomarker HbA_{1C}, glycemic control as well as lipid profile can be used for screening of high risk patients for early diagnosis of dyslipidemia, thereby the cerebrovascular and peripheral complications can be prevented by timely intervention of the disease. This is a small study. A large controlled trial will help in coming on a conclusion.

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