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Relationship Between Serum Uric Acid Level And Ischemic Stroke In Patients With Type 2 Diabetes Mellitus In Nassiriyah City

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ABSTRACT :

Background: The role of serum uric acid as a risk factor for ischemic stroke in patients with type 2 Diabetes Mellitus is controversial and there is little information about it.

Aim of the study: This study was done to estimate serum uric acid levels in diabetic patients with ischemic stroke and to assess its risk factor potential.

Methods: It is a case control study carried out in the medical ward at Al Hussein Teaching Hospital at Al Nassiriyah city at southern of Iraq from June 2018 till December 2018, carried on 119 patient mean ages is 61.89 years. 56 of them was diabetic patients with ischemic stroke were enrolled as a case group and compared with 63 non diabetic patients presented with ischemic stroke also as a control group, Serum uric acid levels were measured in cases and controls (within 24 hours of stroke). The results were statistically analyzed and studied with other risk factors.

Results: Mean serum uric acid level in cases was 6.02 mg/dl where as it was 5.34mg/dl in controls. Hyperurecemia found in 25% of cases , with significant statistical association with increase in TG Cholesterol level p value is0.028 , and hyperurecemia was significant only in old age diabetic (p value less than 0.05) .

Conclusions: There was no significant statistical association between Serum uric acid level and stroke in type 2 DM, but it found to increase other risk factor for stroke especially in old age group , so it can be considered as a risk factor for ischemic stroke in type 2 DM.

Keywords: URIC ACID, ISCHEMIC STROKE, Diabetes Mellitus.

Introduction :

Stroke, or cerebrovascular accident, is defined as an abrupt onset of a neurologic deficit that is caused by a focal vascular cause, thus the definition of stroke is clinical and laboratory studies including brain imaging to support the diagnosis. It is considered the second cause of death worldwide, with 6.2 million dying from stroke in 2015(1). CVA represents a high socioeconomic burden due to increased mortality and morbidity. Early identification of individual at risk could be of help in designing primary prevention strategies. (2). There are two major types of stroke : ischemic and hemorrhagic types. Overall, approximately 85% of strokes are related to ischemic disease, of which 44% attributable to atherosclerosis, 21% to cardiogenic embolism, and 20% to small-vessel disease (3).

Stroke and DM Several population-based studies have shown that subjects With type 2 DM have a twofold to fourfold greater risk of all manifestations of atherosclerotic vascular disease, including Stroke, compared with nondiabetic subjects. The increased risk of stroke is only partly explained by the adverse effects of type 2 DM on classic risk factors (4,5,6 and 7). The risk of stroke associated with diabetes is higher in women than in men (8). Dyslipidemia, endothelial dysfunction, and platelet and coagulation abnormalities are among the risk factors that may promote the development of carotid atherosclerosis in diabetics, both large and small blood vessels seem to be affected (32). impaired glucose tolerance may be a risk factor for ischemic stroke in patients with a history of transient ischemic attack (TIA) or minor ischemic stroke (9). It may also be a risk factor for carotid atherosclerosis, as illustrated by studies in nondiabetics showing that elevated serum hemoglobin A1C is associated with an increased risk of carotid plaque development (10, 11). URIC ACID Uric acid is the ultimate catabolite of purine metabolism in human and higher primates (12). It exists in the extracellular compartment as sodium urate, and it is cleared from the plasma through the kidney (13). Uric acid levels are influenced by age and sex. Prior to puberty, the average serum uric acid is 3.6 mg/dl for males and female; following Puberty, value rises to adult levels with women typically 1 mg/dl less 4 than men. This lower level in women apparently reflects estrogen related enhancement of renal urate clearance (14). Several large studies have provided conflicting results regarding the clinical significance of elevated serum uric acid levels in cerebrovascular diseases. Many studies including the National Health and Nutrition Examination Survey (NHANES) study concluded that uric acid is an independent risk factor for development of cardiovascular and cerebrovascular diseases(15).

Patient and methods

●The consent was obtained from all patients or their relative who was responsible for them.

●The present study was carried out on 133 patients , admitted to medical wards of Al Hussein Teaching Hospital at Al Nassirryha city at southern of Iraq from June 2018 till December who satisfy the selection criteria , their age 45 years old and above , of acute ischemic stroke. All

patients were diagnosed with acute stroke according to American Heart Association/American Stroke Association Guideline definition of stroke which defined as "An episode of acute neurological dysfunction presumed to be caused by ischemia or hemorrhage, persisting ≥24 hours or until death, based on neuropathological, neuroimaging, and/or clinical evidence of permanent injury" (3). All stroke patients should have brain imaging with computed tomography or magnetic resonance imaging (MRI) to distinguish between ischemic and hemorrhagic events. We excluded 14 patients due to missing data on serum UA levels. So the final number of the patients was 119. Participants: Acute stroke patients were classified into two groups: diabetics and non diabetics. Diabetics were involving those with the following criteria: a self-reported physician diagnosis, use of hypoglycemic medications (for example, insulin or sulfonylurea), or having American Diabetic Association laboratory reading criteria of DM (16). Non diabetics were those who did not meet the above criteria.

On admission to the hospital detailed history was taken on medical records of the patient or their next of kin. Demographic data, including age, gender, residence, occupation and level of education. Relevant medical history such as hypertension (HTN), history of diseases like chronic kidney disease (CKD), gout and others. Cardiovascular events such as atrial fibrillation, congestive Heart failure (CHF), coronary artery disease (CAD), and Ischemic heart disease (IHD) was recorded. Detailed drug history like use of diuretics , history of contraceptive pills use for women. Smoking history ; Smoking defined as respondents who had smoked ≥100cigarettes during their lifetime and responded "every day" or "some days" to the question, "Do you now smoke cigarettes every day, some days, or not at all?")(17). Thorough possible physical examination was done also(18). 8 **Biochemical measurements** Within 24 hours of admission to the ward, all the patients were subjected to hematological tests after an 8-12 h overnight fasting, venous blood samples were obtained for measuring SUA, serum triglyceride (TG), low-density lipoprotein cholesterol (LDLC), High-density lipoprotein cholesterol (HDL-C) and HbA1c levels. SUA levels were measured by enzymatic methods (Abbott Diagnostic C400). The participants were divided into quintiles of the SUA levels with cut off values for two age groups ; Normal SUA if the level is equal or less than 7.2 mg ldl , High SUA level if more than 7.2 mg ldl. Blood sugar, urea, serum creatinine, serum electrolytes and ECG was done in every case to detect atrial fibrillation, IHD and left ventricular hypertrophy. Complete blood count and brain imaging study in form of computed tomography and /or magnetic resonance imaging (MRI) An abnormal lipid profile was considered when LDL-C > 100 mg/dl and HDL-C < 40 mg/dl) (19). According to American Diabetes Association, fasting plasma glucose (FPG) ≥ 126 mg/dl was considered abnormal. Glycated hemoglobin (Hb-A1c) was done for diabetic patients and those non diabetics who have abnormal fasting plasma glucose. Assuming Hb-A1c ≥ 6.5% diagnosed diabetes mellitus in non diabetics and considered as uncontrolled diabetes mellitus for acute stroke patients.

Results

Total number of the controls accounted for (63) while total number of the cases accounted for (56). Normal SUA accounted for (58) and (42) patients within the controls and the cases respectively;

while High SUA accounted for (5) and (14) patients within the controls and the case respectively in total sampled population. as shown in Figure 1.

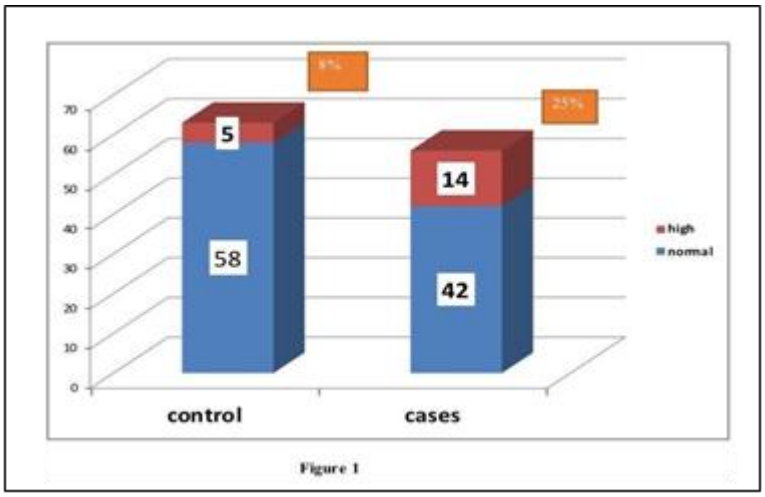

Figure 1

TABLE 1 A: Socio-demographic features of the studied population according to gender.

Table(1 A) Socio-demography of studied Population according to gender

Socio-demography			Gender		Total
			Male	Female	
Age	45-	No.	37	34	71
		%	52.1%	47.9%	59.6%
	≥65	No.	19	29	48
		%	39.6%	40.4%	40.4%
Occupation	Employed	No.	3	0	3
		%	100%	0.0%	2.5%
	Self Employed	No.	42	1	43
		%	97.7%	2.3%	36.1%
	Others	No.	11	62	73
		%	15.1%	84.9%	61.4%
Address	Rural	No.	12	22	34
		%	35.3%	64.7%	28.5%
	Urban	No.	44	41	85
		%	51.8%	48.2%	71.5%
Total		No.	56	63	119
		%	47.1%	52.9%	100.0%

TABLE 1 B: There was no significant statistical association between type of the studied population, (whether cases or control) and age, gender, occupation, residence, where the P value was higher than 0.05 .

Table(1 B): Socio-demography of studied population						
Socio-demography			Sample		Total	X^2,P value
			Control	Cases		
Age	45-	No.	35	36	30	0.939,0.27
		%	49.3%	50.7%	100%	
	≥65	No.	28	20	48	
		%	58.3%	41.7%	100 %	
Sex	M	No.	30	26	56	0.123,0956
		%	53.6%	46.4%	100%	
	F	No.	33	30	63	
		%	52.4%	47.6%	100%	
Occupation	Employed	No.	2	1	3	0.288, 0.565
		%	66.7%	33.3%	100%	
	Self Employed	No.	22	21	43	
		%	51.2%	48.8%	100%	
	Others	No.	39	34	73	
		%	53.4%	46.6%	100%	
			51.8%	48.2%	100%	
Address	Rural	No.	24	10	34	5.958 ,0.08
		%	70.6%	29.4%	100%	
	Urban	No.	39	46	85	
		%	45.9%	54.1%	100%	
Total		No.	63	56	119	
		%	52.9%	47.1%	100%	

TABLE 2: Shows means of parameters that studied for cases and controls.

Table 2 Comparison of Some Parameter's Means between Cases and Control

Variables	Sample type	Mean	Std. Deviation
Age	Control	62.39	11.841
	Cases	61.39	8.976
FBS	Control	104.01	19.624
	Cases	159.07	81.793
B Urea	Control	33.47	12.036
	Cases	33.39	10.627
S Creatinine	Control	0.77	0.1720
	Cases	0.726	0.1290
eGFR	Control	90	17.333
	Cases	94.35	13.221
SUA	Control	5.34	1.366
	Cases	6.02	2.687
TG	Control	126.76	45.795
	Cases	159.75	97.311
Cholesterol.	Control	172.52	49.648
	Cases	174.48	41.520
HDL	Control	43.04	9.777
	Cases	39.03	9.004
HbA1c	Cases	8.3214	1.81796

TABLE 3: There was no significant statistical difference in the distribution of the cases and control according to the smoking status.

Table(3)Behavioral characters of studied population

Socio-demography			Sample		Total	X^2,P value, O.R.
			Control	Cases		
Smoking	Yes	No.	22	20	42	0.008a,
		%	52.4%	47.6%	35.2%	0.152, .966
	No	No.	41	36	77	
		%	53.2%	46.8%	64.8%	
			53.4%	46.6%	97.5%	

Smokers accounted for 35.2% of the sampled population.

Controls and cases had the higher extents within the (Non- Smokers) (53.2%) and (Smokers) (47.6%) respectively.

TABLE 4 (A): There was no significant statistical difference in the distribution of the cases and control according to their age in comparison of their SUA, where P value was > 0.05.

Table 4 Distribution of the serum uric acid values according to the Age groups

Sample				SUA		Total	X^2
				Normal	High		P value
Control	Age	<65	No.	32	3	35	
			%	91.4%	8.6%	100.0%	
		>65	No.	26	2	28	.043[c],.607
			%	92.9%	7.1%	100.0%	
	Total		No.	No.	5	63	
			%	%	7.9%	100.0%	
Cases	ag e	<65	No.	29	7	36	
			%	80.6%	19.4%	100.0%	
		>65	No.	13	7	20	1.659[d], .167
			%	65.0%	35.0%	100.0%	
	Total		No.	No.	14	56	
			%	%	25.0%	100.0%	
Total	ag e	<65	No.	61	10	71	
			%	85.9%	14.1%	100.0%	
		>65	No.	39	9	48	0.465 .332
			%	81.3%	18.8%	100.0%	
	Total		No.	No.	19	119	
			%	%	16.0%	100.0%	

Discussion:

The total number of the patients was 119 patients included in a case control study , 56 of them were men and 63 of them were women . Both groups (cases and controls) were comparable for baseline characteristics representing the mean age, sex distribution, kidney function parameters . The mean age of cases (61.39±8.976) was comparable to controls (62.39±11.841). This means of age group as matched to many studies (20,21). In this study; 59.6 % of the patients was middle age group (45- 65) years old, while 40.4 % of them was old age (65 years or older) (22). Most of the old age patients with stroke was female; about 60.4 %.this can be explained by a fact that women live longer than men (35 - 38). Of the total studied patients; 53% of them was female while 47 % was male also comparable parameter. Both groups were comparable for the kidney function the cases i.e. blood urea(33.39±10.627mg/dl) and serum creatinine (0.726±0.129mg/dl) was also found to be comparable to controls, 33.47 ±12.036mg/dl and 0.77±0.172mg/dl, respectively. eGFR was also comparable i.e. for cases was 94.35±13.221, for control was 90±17.333. Regarding other demographic parameters like (residence and occupations), there was no significant differences between diabetic and non diabetic patients. In present study, old age diabetic appears to be at risk for hyperuricemia ; Out of 20, old age (65 years or older) diabetic patient 7 of them appear to be hyperuricemic (35%) , compared to only (7.1%) in control group of the same age. The difference was found to be statistically significant (p 0.05 as shown in table 4 (A).

Conclusion

The prevalence of hyperuricemia is quite high ; as about 1 in 4 diabetic Patients (25%) with ischemic stroke had hyperuricemia on admission ,and its accompanying increase in TG cholesterol levels can be considered it as a risk factor for acute ischemic stroke in type 2 DM especially in old age diabetics.

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