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Homocysteine and Atherogenic lipid profile as Markers of Atherotherombatic Disease among Sudanese Patients with Diabetes Mellitus

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Abstract: Atherosclerosis is associated with increased inflammatory activity and risk of vascular disease. However, the factors that promote inflammation are not apparently clear. The aim of the present study was to detect homocysteine (Hcy) in urine as a marker for a therothombatic disease among Sudanese patients with Type2 diabetes mellitus with other markers as predictors of cardiovascular disease. A case control study , was conducted included a total of 100 individuals (60 patients and 40 apparently healthy) age was matched in both groups (ranged from 35 to 75 years) 65% male and 35% female, atherogenic lipid profile and HbA1c were measured by Biosystem 350 and Hcy was detected qualitativly by using Spaeth and Barber Modification method Silver – Nitroprusside test. Data analysis was done by using SPSS version 21 and the results revealed that 25 % of the patients had Hcy positive (+ve) while 35 % had Hcy negative (-ve). There was a significant increase of level of total cholesterol, LDLc, HbA1c and significant decreased level of HDLc between study groups. No statistical deffirance was found in levels across gender of patients. The results showed a positive correlation between total cholesterol, LDLc, HDLc and duration while a negative correlation was found with duration and HDLc. Positive correlation was found between BMI and HbA1c, total cholesterol, LDLc, HDLc. In conclusion, Homocysteine is related to CVD risk mildly elevated of homocysteine being an independent risk factor for atherothrombatic disease among Type2 Diabetes Mellitus.
Keywords: Homocystine, Cardiovascular disease, Atherogenic lipid, HbA1c, BMI

INTRODUCTION

Homocysteinuria was described in 1962 in mentaly retarded children [1].The defect in CBS was identified [2] and it was reported that such patients frequently had thromboembolic events [3 , 4]. Severe MTHFR deficiency [5, 6] and certain defects in intracellular co-balamin metabolism were later reported to be cause a similar clinical picture [7].

In 1969 McCully described the vascular pathology of homocysetinuria [8]. He noted that thromboembotic disease was a characteristic feature of homocysteinuria independent of the site of the metabolic defect, pointing to Hcy as the causal agent. This is the basis for Hcy theory of atherosclerosis, which implies that moderately elevation of tHcy may be a cardiovascular risk factor in the general population [9]. Homocysteine (Hcy) is one of more than 200 identified risk factor for cardiovascular disease (CVD) [10]. A correlation between tHcy level and total -cholesterol, LDL, HDL has been shown in some studies [11] two recent studies have demonstrated that tHcy is an independent predictor of atherosclerotic events [12] and of carotid intimat medical thikness [13].

Diabetes mellitus is on the tract to become one of the major global of the 21stcountry [14]. Diabetes mellitus is characterized by hyperglycemia due to absolutus or relative deficiency of insulin [15]. Type2 diabetes mellitus (T2DM) accounts for 90% of global diabetic population and 9% of annual global mortality with health and socioeconomic proplems [16]. Peripheral neuropathy is the most common complication of T2DM followed by cardiovascular, renal and ophthalmic complication and hyper lipideamia [17].

Any disease that affects the heart as well as all of the blood vessels in the body referred as cardiovascular disease. atherosclerosis is one of these elements ,and is caused by a buildup of plaque in a person's arteries, this build up can accumulate to the

point that a clot forms and clogs the artery completely, leading to either stroke or a heart attack [18]. If that happened and LDLc, Cho causes atherosclerosis, logic indicates that there should be a strong correlation between LDLc, cholesterol levels and atherosclerosis [19]. Then plaque buildup inside the coronary arteries called coronary artery disease or coronary heart disease (CHD), high blood cholesterol level is the one of the major risk factors of coronary heart disease [20].

LDLc carries about 70% of total cholesterol, recently, there has been great interest in measuring LDLc sub fraction, because small dense, LDLc particles have been shown to be more pro –atherogenic and may be better marker for cholesterol risk [21].

The HDLc has antioxidant, anti-inflammatory and antithrombotic properties which contribute to its atheroprotective effect [22] Low HDLc is known to be an independent and powerful predictor of atherosclerosis [23].

MATERIAL AND METHODS

Study population and study area

A case control study was conducted at Academy Charity Teaching Hospital, Sudan. Khartoum State During period of February to May 2017. A total of 100 were enrolled in the study 60 patients diagnosed with T2DM (as cases) and 40 apparently healthy subjects (as control), age was matched (35-75 year).

Inclusion Criteria

Diagnosed patients with Type2 DM as cases and apparently health individual

Exclusion Criteria

Patients who are taking supplements (folic acid, B6, and B12 Vitamins), or diagnosed with CVD, renal disorders or other disorder that may affect the Hcy or lipid levels was excluded.

Ethical consideration

The ethical approval was obtained from research .Committee of the faculty of medical laboratory sciences Al Neelain University and a verbal consent was obtained from all participants.

Sampling

5ml of venous blood was collected from each subject in to EDTA containers, heparin containers, and plain containers, then serum and plasma is obtained and analyzed. Urine sample was collected in a clean container; standard methods of collection were used.

Data collection techniques and tools

Demographic Data were collected by predesigned structural questionnaire.

Methods

Homocysteinuria was detected quantitatively by using Spaeth and Barber modification method Silver-Nitroprusside test. Atherognic lipid profile and HbA1 c were measured by Biosystems 350spain. BMI was calculated by using formula (weight/ (height) ^{2}.

Data processing and statistical analysis

Data was analyzed using SASS version 21. The results express as frequency, percentage and mean+ SD, independent T. test was used to compare study parameters in cases and control, Person's correlation was used to study correlations.

Quality control

Pathological and normal control sera were used to confirm accuracy and precision of results and to verify the performance of the tests.

RESULTS

Statistical analysis revealed that 25% of the patients had Hcy +ve while35 % had –ve Hay was significant increased among patients compered to control subjects (Table 1). There is a significant increase of level of Total Cholsterol, LDLc, HbA1c, among study group compared to control subjects, and significant decreased level of HDLc between study groups (Table2). The results showed a significant increase of HDLc and decreased of Total Cholesterol and LDLc among control subjects (Table3). No statistical difference was found in levels a cross gender of patients (Table 4). The results showed a positive correlation between, Total Cholesterol, LDLc, and duration. While negative correlation was found with duration and HDLc (Figures-2, 3, 4,) respectively. And positive correlation between Total Cholesterol, LDLc, HDLc and HbA1c (Figures 5, 6, 7) respectively**.** The results also showed a positive correlation between HbA1c, Total Cholesterol, LDLc, HDLc and BMI (Figures 8, 9, 10, 11) respectively.

Table-1: Comparison of Homocysteine level among the case and control group

Group	Homocysteine		Total
	Positive	Negative	
Case	25 (25.0%)	35 (35.0%)	60 (60.0%)
Control	0 (0.0%)	40 (40.0%)	40 (40.0%)
Total	25 (25.0%)	75 (75.0%)	100 (100.0%)
P-value	0.000		

Table-2: Comparison of HbA1c and thermogenic lipid profile among the study groups

Variable	Case (Means)	Control (Means)	*P-value*
HbA1c (%)	9.02±2.15	4.78±0.38	0.000
Cholesterol (mg/dl)	201.66±18.75	178.45±6.41	0.000
LDL c (mg/dl)	98.08±16.24	73.82±13.52	0.000
HDL c (mg/dl)	37.40±4.21	46.80±4.02	0.000

Table-3: Comparison of HbA1c and lipid profile among uncontrolled and controlled patients

Parameters	Uncontrolled (Means)	Control (Means)	*P-value*
T. Cholesterol (mg/dl)	202.66±19.69	180.78±8.34	0.000
LDL c (mg/dl)	98.32±17.22	77.17±14.92	0.000
HDL c (mg/dl)	36.96±3.86	45.89±4.73	0.000

Table-4: Comparison of HbA1c and lipid profile across the gender of patients

Parameters	Male (Means)	Female (Means)	*P-value*
HbA1c (%)	9.14±2.36	8.80±1.71	0.524
T. Cholesterol (mg/dl)	202.30±17.95	200.47±20.56	0.722
LDL c (mg/dl)	98.76±15.06	96.81±18.56	0.660
HDL c (mg/dl)	37.46±4.08	37.28±4.53	0.887

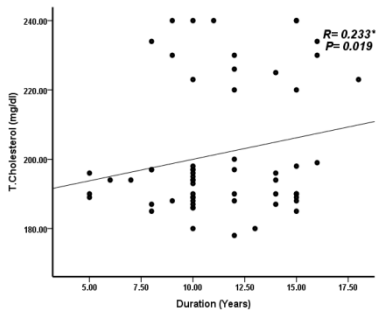

Fig-2: correlation between duration and T. Cholesterol

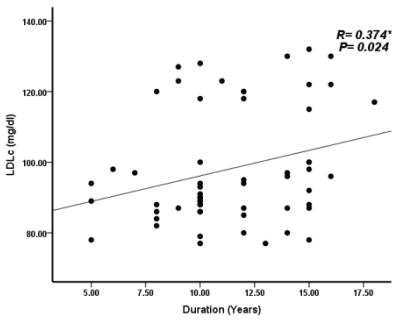

Fig-3: correlation between duration and LDLc

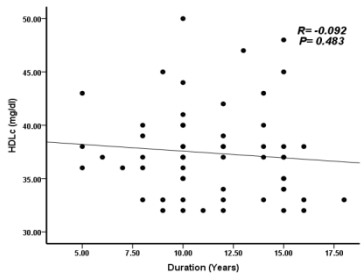

Fig-4: correlation between duration and HDLc

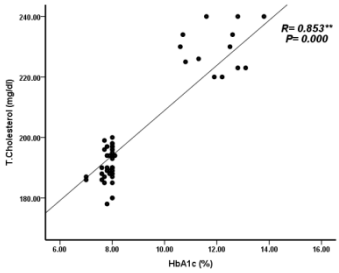

Fig-5: correlation between HbA1c% and Cholesterol

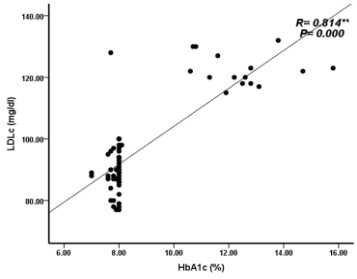

Fig-6: correlation between HbA1c% and LDLc

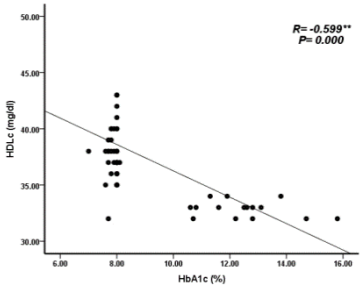

Fig-7: correlation between HbA1c and HDLc

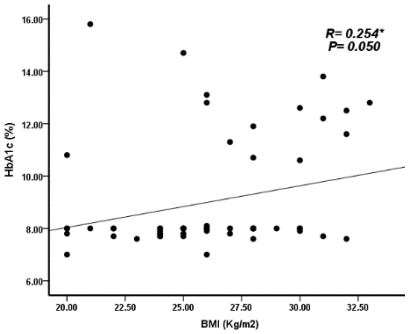

Fig-8: correlation between BMI and bA1c

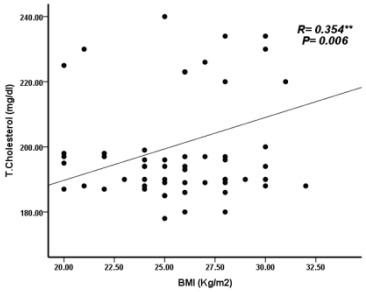

Fig-9: correlation between BMI and T. Cholesterol

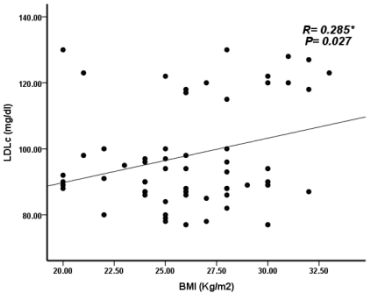

Fig-10: correlation between BMI and LDLc

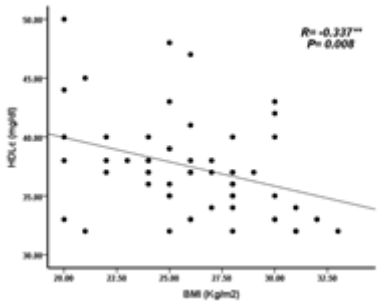

Fig-11: correlations between BMI and HD

DISCUSSION

The current study reveals that 25% of the patients had +ve Hcy while 35% had –ve Hcy was significantly increased among patients compered to control group. This result agreed with Ashok Sahu, *et al*. [24] who reported at 2015 in India that plasma Hcy level werer increased significantly in cardiovascular disease patients when compared to control and also Hcy is the best predictor of CHD risk amongst other conventional risk factor in CVD Patients. Other study by Joseph, *et al*. [25] reported that Hcy is related to CVD risk since the lowring of plasma Hcy levels did not reduced the risk mildly elevated of Hcy being an independent risk factor for CVD. With elevated Hcy levels have a risk of suffering from CVD events independent of others risk factors as age, and renal function it is the close relation between Hcy and CVD confirms the atherosclerotic roles. The present study results revealed that the HbA1c, Total Cholestrol, LDLc levels were significantly increased in Type 2 Diabetes Mellitus patients compered to control group while HDL level was significantly decreased in Type 2 Diabetes Mellitus patients compered to control group. This agreed with Glueck CJ, *et al*. [26] who reported that a correlation between tHcy level and total Cholestrol, HDLc, or LDLc has been shown. The study results showed a significant increase of HDLc level and decreased Total Cholestrol**,** LDLc levels among control group These agreed with GeraLd H, *et al.* [27] who repoted that low HDLc is known to be an independent and powerful predictor of atherosclerosis. The results showed no statistical difference was found in levels a cross gender of patients. The present study showed positive correlation between duration and Total Cholestrol, LDLc, while negative correlation was found with duration and HDLc. There was also a positive correlation found between HbA1c and Total Cholestrol, LDLc, HDLc. And the present study results revealed positive correlation between BMI and HbA1c, Total Cholestrol, LDLc, HDLc.

CONCLUSION

Homocysteine is related to CVD risk mildly elevated of homocysteine being an independent risk factor for atherothrombatic disease among Type2 Diabetes Mellitus.

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