

Relation of Homocysteine With Malondialdehyde and Dyslipidemia in Type 2 Diabetic Patients with Coronary Artery Diseases

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Abstract

Diabetes mellitus(DM) is one of the most common chronic disorder widely prevalent throughout the world. DM is characterized by elevation of blood glucose (hyperglycemia). Hyperglycemia, with time, led to several serious macro and microvascular complications.

The purpose of study was to investigate the relation of Homocysteine(Hcy) with oxidative stress (malondialdehyde"MDA") and dyslipidemia in type 2 diabetic patients with coronary artery diseases in comparison to patients of coronary artery diseases(CAD) without DM.

Methods: The present study included 60 patients of coronary artery disease. Patients divided into two groups: group1 = 30 coronary artery disease patients without diabetic and group2 = 30 coronary artery disease patients with type2 diabetes. Homocysteine was estimated by competitive ELISA test using commercially available kit. MDA was estimated by colorimetric method. Lipid profiles were determined by using commercial available kits.

Results: Plasma levels of Hcy and MDA in group1 and group2 were significantly higher ($p < 0.05$) than controls. In group1 Hcy shows significant ($P < 0.05$) positive correlation with MDA and Total Cholesterol (TC). Hcy shows no significant ($p > 0.05$) positive correlation with very low density lipoprotein (VLDL), low density lipoprotein (LDL), and Triglyceride(TG). Hcy shows negative significant ($p < 0.05$) correlation with high density lipoprotein(HDL). While in group2 Hcy shows significant ($P < 0.05$) positive correlation with MDA, TC, VLDL, LDL and TG. Hcy shows negative significant ($p < 0.05$) correlation with HDL. Hcy, MDA, TC, TG, LDL and VLDL were higher without significant in CAD diabetic patients than non-diabetic CAD patients. HDL was lower in diabetic coronary artery disease patients than non-diabetic coronary artery disease patients but without significant importance.

Conclusion: In this study Hcy and MDA levels obtained were found to be positively correlated with dyslipidemia in patients in both groups. Hcy may be one of the cause for development and progress of macro- and microvascular disease. Hcy, MDA and dyslipidemia were higher in CAD with DM than CAD without DM this shows that hyperglycemia may be is another factor to increase atherosclerotic process.

Keywords : *Diabetes mellitus, Homocysteine, Malondialdehyde, Dyslipidemia.*

Introduction

Diabetes mellitus (DM) is epidemical disease widely prevalent throughout the world. DM is a significant cause of mortality and morbidity worldwide because of its serious complications such as micro- and macroangiopathic complications^[1,2]. Globally studies shows about 300 million people will suffering from diabetes in 2025^[1]. One of diabetic complication is

coronary artery disease or cardiovascular diseases(CAD or CVD). CAD is the commonest cause of heart disease and the most important cause of death in the different countries of worldwide. Beside the known classical risk factors of CAD like hypertension, cigarette smoking, diabetes mellitus, low HDL, obesity and reduce physical inactivity, a few new parameters at last few years have been identified and studied as risk

factors for development and progress of the CAD such as prothrombotic factor, pro-inflammatory factor and homocysteine^[3]. Homocysteine is sulfur containing amino acid formed as intermediate product in normal biosynthesis of methionine. In human body there are two major pathways to metabolize homocysteine, both of these pathways required vitamin B6, B12 and folic acid^[4]. One of the ways by which homocysteine increases the damage to the cardiovascular system is the formation of reactive oxygen species (ROS) by auto-oxidation of homocysteine. The ROS produces by auto-oxidation of homocysteine including hydrogen peroxide and superoxide which enhances oxidative stress by production free radicals which causes lipid peroxidation to formation aldehydes. The most commonly measured compound produced by action of free radical is malondialdehyde (MDA)^[5]. The results of many clinical and epidemiological studies have been showed a positive correlation between pathogenesis of CAD and increasing homocysteine levels. Few studies have been carried out to established correlation between homocysteine and oxidative stress in diabetic patients with and without CAD^[6-10]. Therefore the study has been current to establish the correlation of hyperhomocysteinemia with oxidative stress as one of the risk factors for coronary artery disease in diabetic patients.

Materials and Method

The present study is conducted on 85 male subjects, 60 subjects were of coronary artery disease patients who visited Consultative Clinic of Baquba Teaching hospital in June-July 2017. The 60 CAD patients divided into two groups: group1 = 30 coronary artery disease patients without diabetic and group2 = 30 diabetic patients with coronary artery disease. The patients were compared with 25 healthy subjects were chosen as control group in

study, whom age and BMI matched with patients.

All samples were collected in the morning after overnight (8-12 hours) of fasting. 6 ml of vein blood was drawn by venipuncture using a 10 ml disposable syringes from each subjects. 3ml of blood transferred into an EDTA containing vacutainer tube for determination of plasma MDA and homocysteine, and 3 ml of blood was transferred into a plain tube for evaluation of lipid profile. Estimation of plasma homocysteine was done by competitive Elisa test using commercially available kit. Estimation of serum TC, HDL-C and TG were done by using commercially available kits. Serum LDL-C and VLDL-C were calculated by using Friedewald's formula. Estimation of plasma MDA malondialdehyde was done by colorimetric method.

Statistical analysis were done for tabulated results of all undertaken parameters by the Pearson correlation and t-test from which p value were obtained.

Results

Table1 below represents the Mean±SD values for different parameters in group1 as compared with control group. The patients of group1 and healthy controls were matched in age and body mass index(BMI), but fasting blood glucose was, higher non-significantly in patients of group1 than control group. Plasma level of Hcy and MDA were significantly higher ($p < 0.05$) in group1 than controls. Levels of TC, TG, LDL-C and VLDL-C were higher in group1 than in controls, whereas level of HDL-C was lower in the group1 in comparison to controls. The difference is statistically significant only for TC, VLDL-C and HDL-C. Hcy showed significant positive correlation with TC, and significant negative correlation with HDL-C as shown in table2.

Table1 : Shows the comparison of M±SD for parameters of group1 with control group

Parameter	Mean ± SD of control (n=25)	Mean ± SD of group1(n=30)	P-value
Age (years)	48.34±12.23	51.65±13.56	0.34
BMI(Kg/m ²)	24.6 ± 5.32	26.65 ± 4.98	0.42
FBS(mg/dl)	95.67±12.33	107.78±54.91	0.101
Hcy μmol/L	13.4467 ± .9488	25.6917 ± 1.789	0.001
MDA μmol/L	0.517 ± 0.0449	1.183 ±0.1108	0.001
TC (mg/dl)	172.30 ± 6.60	189.62 ± 8.42	0.02

Cont... Table1 : Shows the comparison of M±SD for parameters of group1 with control group

TG (mg/dl)	122.27± 7.40	150.05 ± 8.35	0.053
LDL-C (mg/dl)	107.30 ± 6.19	120.67 ± 7.17	0.197
VLDL-C (mg/dl)	23.5 ± 1.42	30.95 ± 2.36	0.036
HDL-C (mg/dl)	42.03 ± 1.36	37.35 ± 1.33	0.03

Table 2: shows the correlations between parameters of group1

	TG	TC	LDL	VLDL	HDL	MDA
Hcy	0.190	0.333*	0.121	0.211	-0.288*	0.617*
MDA	0.157	0.403*	0.203	0.225	-0.182	1

Table3 below also represents the Mean±SD values obtained for different parameters in group2 in comparison with control group. As in group1 patients of group2 and healthy controls were matched in age and body mass index(BMI), but fasting blood glucose was normally, significantly higher in diabetic patients of group2 than control group. Hcy and MDA levels were significantly higher ($p < 0.05$) in group2 than controls. The TC, TG, LDL-C and VLDL-C levels also, were higher in group2 than in controls, whereas level of HDL-C was lower in the group2 in comparison to controls. The difference is significant statistically only for TC, TG, VLDL-C and HDL-C. Hcy showed significant positive correlation with TC, LDL-C, VLDL-C and TG and negative significant correlation with HDL-C as shown in table4.

Table 3: Shows the comparison of M±SD for parameters of group2 with control group

Parameter	Mean ± SD of control (n=25)	Mean ± SD of group1(n=30)	P-value
Age(years)	48.34±12.23	53.44±14	0.23
BMI(Kg/m ²)	24.6 ± 5.32	25.11±7.21	0.44
FBG(mg/dl)	95.67±12.33	196.34±98.66	0.000
Hcy μmol/L	13.4467 ± .9488	27.971 ± 1.789	0.001
MDA μmol/L	0.517 ± 0.0449	1.253 ±0.181	0.000
TG (mg/dl)	122.27± 7.40	175.15 ± 12. 53	0.025
TC (mg/dl)	172.30 ± 6.60	208. 96 ± 30.22	0.019
LDL-C (mg/dl)	107.30 ± 6.19	132.77 ± 9.37	0.097
VLDL-C (mg/dl)	23.5 ± 1.42	35.90 ± 3. 26	0.028
HDL-C (mg/dl)	42.03 ± 1.36	33.35 ± 1.33	0.021

Table4: shows the correlations between parameters of group2.

parameter	TG	TC	LDL	VLDL	HDL	MDA
Hcy	0.390*	0.441*	0.321*	0.411*	-0.328*	0.617*
MDA	0.357*	0.413*	0.204	0.275*	-0.182	1

Generally, all levels of studied parameters showed increasing in group2 (diabetic patients with CAD) in comparison to group1(CAD without diabetic patients) but the differences do not showed statistical significant(p>0.05) as shown in table5.

Table5: shows the comparison between group1 and group2

Parameters	Mean ± SD of group1(n=30)	Mean ± SD of group2(n=30)	P-value
FBG(mg/dl)	107.78±54.91	196.34±98.66	0.15
Hcy µmol/L	25.6917 ± 1.789	27.971 ± 1.789	0.27
MDA µmol/L	1.183 ±0.1108	1.253 ±0.181	0.21
TC (mg/dl)	189.62 ± 8.42	208.96 ± 30.22	0.13
TG (mg/dl)	150.05 ± 8.35	175.15 ± 12.53	0.09
LDL-C (mg/dl)	120.67 ± 7.17	132.77 ± 9.37	0.16
VLDL-C (mg/dl)	30.95 ± 2.36	35.90 ± 3.26	0.19
HDL-C (mg/dl)	37.35 ± 1.33	33.35 ± 1.33	0.34

Discussion

The statistical positive significant correlation between Hcy and MDA levels that obtained in study is agreed with some previous studies^[6-11] that shows positive correlation between Hcy and MDA levels (p<0.05). The exact mechanism of toxicity by Hcy is still unknown well, but it's believed that homocysteine or compounds liberated from its metabolize enhancing atherosclerosis by several mechanisms for example the hydrogen peroxide generated by auto oxidation of homocysteine which affect toxically on endothelial cells^[11-13]. Generated hydrogen peroxide promotes oxidation of low density lipoproteins(LDL) and lipids peroxidation. The oxidized LDL causes alteration of metabolism for nitric oxide (NO) the oxidative damages also causes alteration of functions on vascular endothelial cells and platelets^[5]. Auto-oxidation of homocysteine beside generation of hydrogen peroxide, it is also generates superoxide anion and hydroxyl radical, and all these compounds are factors contributing for vascular injury that is associated with hyperhomocysteinemia^[11-14]. Also the auto-oxidation of Homocysteine to produce the free radicals which are the

initiators of lipid peroxidation in cells. Lipid peroxidation induced by homocysteine is more occurrence in hyperlipidemic state which can increases the production of MDA through enhance oxidative stress^[11-14]. As shown in table3 diabetes mellitus increases risk factors levels of CAD. Although, the possible role of hyper Hcy in diabetes is not clear. Hyperglycemia may another risk factor with HHcy increases the oxidative stress and contributes to acceleration the atherosclerotic process in diabetes mellitus^[15]. So, HHcy may accelerate vascular damage related to diabetes. Some studies re-searching the relationship between plasma Hcy and diabetes have shown that type 2 diabetic patients have a higher prevalence of HHcy than control subjects^[16,17].

Conclusion

Hcy and MDA levels obtained in this study were found to be positively correlated with each other and with lipid parameters in CAD patients without diabetic and diabetic patients with CAD but the increase were higher in diabetic patients with CAD than CAD patients whom without diabetic. This indicates that Hcy enhances

the oxidative stress by lipid peroxidation, HHcy may accelerate vascular damage related to diabetes this may be one of the cause for development of coronary artery disease in diabetes rapidly, and, Hyperglycemia may another risk factor with HHcy increases the oxidative stress and contributes to acceleration the atherosclerotic process in diabetes mellitus.

Ethical Clearance- This study was conducted with the consent of the volunteers and without mentioning the names with the complete privacy of volunteers

Source of Funding - Self

Conflict of Interest – There were no

Conflicts of Interest: in this study.

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