



**International Journal of Biology, Pharmacy
and Allied Sciences (IJBPAS)**
'A Bridge Between Laboratory and Reader'

www.ijbpas.com

STUDY OF SERUM TOTAL HOMOCYSTEINE LEVEL IN TYPE 2 DIABETES PATIENTS AND THEIR ASSOCIATION WITH DIABETIC COMPLICATIONS

MAHSHID MOHAMMADIAN^{2,3*}, MOHADESEH NEMATI^{2,3}, NARMIN MOKARIZADEH³, ELMIRA ROSHANI ASL^{2,3}, SIAMAK RASHIDI¹, FARHAD FATHI YONESI¹

1: Aria medical Laboratory, Sanandaj, Iran

2: Student Research Committee, Urmia University of Medical Science, Urmia, IR Iran

3: Department of Biochemistry, School of Medicine, Urmia University of Medical Science, Urmia, Iran

***Corresponding Author: Mahshid Mohammadian**

ABSTRACT

The aim of this study was to determine and surveys of total homocysteine (tHcys) in patients with type 2 diabetes mellitus disease. Patients group (n=120) compared to 120 healthy individuals as control group were enrolled into this study. Lipid profile, HbA1C as glycemic control, fasting blood sugar (FBS) and total plasma homocysteine and socioeconomic condition analyzed. The results of this study showed a higher level of tHcy in patients with type 2 diabetes compared to controls. Elevated level of Homocysteine was associated with chronic diabetes complication. (higher level of FBS, LDL-c, TG, TC) in the patients. Further study is necessary for detection of precise role of tHcy on the development of type 2 diabetes mellitus.

Keywords: Diabetes Mellitus type 2, Homocysteine

INTRODUCTION

Homocysteine is a α -amino acid with a sulfur agent, that could be made in metabolism of methionin. This amino acid, is a risk factor for cardiovascular diseases and diabetes. [1-6] previous studies demonstrated mild elevations in plasma homocysteine as

independent factor could be related with increased risk for cardiovascular disease. Increased level of homocysteine in the blood promote inflammation and blood vessels endothelial cell dysfunction, insulin resistance which could result in

atherogenesis and ischemic injury and type 2 diabetes [7-15]. Several investigations indicated that elevated homocysteine levels could predict the risk of coronary complications in diabetic patients [10-19]. In patients with diabetes mellitus type 2, however, plasma homocysteine levels have been reported to be increased [8, 11, 15]. Also studies reported that tHcy was an independent risk factor of ischemic stroke [15-22]. Circulating homocysteine levels in patients with diabetes is a prominent factor that worsens the diabetic complications. In addition, environmental factors such as lifestyle, smoking and drug, alcohol and coffee intake, could be associated with higher homocysteine concentrations including positive associations with diabetes. The aim of our study was to survey the circulating homocysteine levels in patients with diabetes and study of relationships between homocysteine and type 2 diabetes [4, 20-25].

METHODS AND MATERIALS

The case-control based study was on a population in western of Iran were performed. Subjects selected among type 2 diabetic patients (76 female, 44 male) with average age of 54.2 ± 8.1 years, that already diagnosed as diabetes for more than four years referred to Aria Medical Laboratory, Sanandaj, Iran. Our control population were 120 randomly selected healthy subjects

under 70 years of age (34 males and 86 females) Age range from 35–60 years (mean 43.2 ± 3.1). Venous blood samples from patients and healthy subjects were drawn and then collected. 12-hour overnight fasting was necessary for getting blood samples. Samples were analyzed for measuring Fasting blood sugar (FBS), triglyceride (TG), HbA1c, total cholesterol (TC), total Homocystein (tHcy). Diagnosis parameters in patient group based on Trained diabetes physician certified and biochemical analysis was done. Plasmatic Hcy concentration was determined by Immulite System (Siemens, Germany). This is a chemiluminescence Immunoassay. For HbA1c was measured by Particle enhanced immune assay (PEIA) method (Bionic, Iran). The plasma level of triglycerides, total cholesterol and fasting blood sugar (FBS) was determined using spectrophotometry and commercially available kits (Pars Azmoun, Iran). Low density lipoprotein-cholesterol (LDL-c) was calculated by using the Friedewald formula. All statistical analysis was performed using SPSS software (Version 21, USA). Comparisons between groups were performed by using the chi-square and the unpaired t-test and $P < 0.05$ was considered significant. Pearson's correlation coefficient was used to explain the relationship of the tHcy and the studied variables: glucose, total

cholesterol, TG, LDL-c, and HbA1c. and P<0.05 was considered significant status.

RESULTS

In our study total Hcy, serum fasting glucose, total cholesterol, triglycerides, LDL-c, and glyceimic control analyte (HbA1c) measured in patients with diabetes type 2 and in the control group. Our result indicated Higher values of Hcy in the total of diabetic patients compared to control group (p < 0.05)which were statistically significant in fact there was positive correlations between Total serum homocysteine and other biochemical

parameters (TG, HbA1C,FBS, TC,LDL-c). Demographic and biochemical characteristics of the studied subjects in two groups presented in **Table 1**.

Statistical multiple regression analysis revealed that all study parameters were significantly correlated with Hcy levels in diabetic patients group. Correlation of serum total homocysteine levels with HbA1C, serum triglycerides (TG) LDL-c, Fasting Blood Sugar (FBS), Triglyceride (TG), Total cholesterol (TC), in patients group shown in **Table 2**.

Table 1: Demographic and biochemical characteristics of the studied subjects in two groups

Parameters	patients	Controls	P Value
Number of participants	120	120	—
Age (year)	54.2±8.1	43.2±3.1	P<0.05
TC (mg/dl)	252.6 ± 121.3	184.8 ± 31	P<0.05
LDL-c	141.3 ±9.7	73.6±8.5	P<0.05
FBS (mg/dl)	175.4±90.1	87.9±7.7	P<0.05
TG (mg/dl)	209.6 ± 121.3	136.1 ± 43.1	P<0.05
tHcy	11.35 ± 4.59	8.4 ± 5.2	P<0.05
HbA1c (%)	8.37±1.3	4.20±0.96	P<0.05

Data are expressed as mean ± standard deviation., TC: total cholesterol; LDL-C: low-density lipoprotein cholesterol; tHcy: Total homocysteine; TG: Triglyceride, FBS fasting blood sugar, HbA1c:glycosilated Hemoglobin (as glyceimic control)

Table 2: Correlation of serum total homocysteine levels with HbA1C, serum triglycerides (TG) LDL-c, Fasting Blood Sugar FBS, Triglyceride TG, Total cholesterol TC, in patients group.

	HbA1c	FBS	LDL	TG	T.C
Pearson correlation	0.346	0.289	0.411	0.391	0.275
Significancy	Sig	Sig	Sig	Sig	Sig
Pv	>0.05	>0.05	>0.05	>0.05	>0.05

DISCUSSION

Diabetes is a hyperglycemic chronic diseases that are the major source of morbidity and mortality world width. Prevalence of diabetes continues to increase. In all communities the importance of protecting the body from hyperglycemia can

be Inevitable, also the Deleterious effects of hyperglycemia are separated into vascular disease Included coronary artery disease. There are an important issue to understand the association of diabetes and coronary artery disease. Elevated level of plasma homocysteine may be a risk factor for

atherosclerosis in the General community. In human plasma, homocysteine exists in multiple forms. About 70–80% homocysteine is bound to albumin by a disulphide bond, residual homocysteine in form of homocystine Or in combination with cysteine exist, There are only a small percentage of homocysteine exist as a free form.(<1%). measurement of the multiple forms of plasma homocysteine, which is expressed as total homocysteine (tHcy) [19, 20-25]. Indeed Homocysteine play an important role in vascular endothelium injuries .and could be induces essential effect in diabetic conflicts.our study performed for investigation of relationships between diabetes conflicts and total serum homocystein. Based on results we found higher serum homocysteine concentration in patient group. Also there was significant difference in the mean plasma homocysteine concentration between subjects with and without diabetes. We can say increase in plasma homocysteine concentration was an predictor of increased risk of diabetic complications. In fact there was correlations between homocysteine and demographic and biochemical parameters (TG, HbA1C, FBS, TC, LDL-c). Indeed statistical multiple regression analysis revealed that, all study parameters were significantly correlated with tHcy levels in diabetic patients group. Result shown the existence

of conflicts. In patients could be related to elevated level of Serum homocysteine. Homocysteine may be a Appropriate biomarker for increased risk of diabetes conflicts that dependent on higher levels of it .Finally results indicated a role for homocysteine in diabetic conflicts as Potential risk factor.

REFERENCES

- [1] F Brian Boudi, MD, FACP; Chief Editor: Yasmine Subhi Ali, MD, MSCI, FACC, FACP Noncoronary Atherosclerosis Overview of Atherosclerosis
- [2] M. Dalton and J. S. Williams, “How best to approach point-of-care testing,” *CAP Today*, vol. 11, no. 12, pp. 46–50, 1997.
- [3] H. Wang, M. Yoshizumi, K. Lai *et al.*, “Inhibition of growth and p21 (ras) methylation in vascular endothelial cells by homocysteine but not cysteine,” *Journal of Biological Chemistry*, vol. 272, no. 40, pp. 25380–25385, 1997.
- [4] J. Selhub, P. F. Jacques, A. G. Bostom *et al.*, “Association between plasma homocysteine concentrations and extracranial carotid-artery stenosis,” *The New England Journal of Medicine*, vol. 332, no. 5, pp. 286–291, 1995.

- [5] B. M. Coull, M. R. Malinow, N. Beamer, G. Sexton, F. Nordt, and P. De Garmo, "Elevated plasma homocyst(e)ine concentration as a possible independent risk factor for stroke," *Stroke*, vol. 21, no. 4, pp. 572–576, 1990.
- [6] Hofmann MA, Kohl B, Zumbach MS, Borcea V, Bierhaus A, Henkels M, et al. Hyperhomocysteinemia and endothelial dysfunction in IDDM. *Diabetes Care* 1998; 21: 841e8.
- [7] Meigs JB, Jacques PF, Selhub J, Singer DE, Nathan DM, Rifai N, et al. Framingham Offspring Study. Fasting plasma homocysteine levels in the insulin resistance syndrome: the Framingham offspring study. *Diabetes Care* 2001; 24: 1403e10.
- [8] Aso Y, Yoshida N, Okumura K, Wakabayashi S, Matsutomo R, Takebayashi K, et al. Coagulation and inflammation in overt diabetic nephropathy: association with hyperhomocysteinemia. *Clin. Chim. Acta.* 2004; 348: 139e45.
- [9] Stehouwer CD, Gall MA, Hougaard P, Jakobs C, Parving HH. Plasma homocysteine concentration predicts mortality in non-insulin-dependent diabetic patients with and without albuminuria. *Kidney Int.* 1999; 55: 308e14.
- [10] Kark JD, Selhub J, Bostom A, Adler B, Rosenberg IH. Plasma homocysteine and all-cause mortality in diabetes. *Lancet*, 1999; 353: 1936e7
- [11] Hoogeveen EK, Kostense PJ, Jakobs C, Dekker JM, Nijpels G, Heine RJ, et al. Hyperhomocysteinemia increases risk of death, especially in type 2 diabetes: 5-year follow-up of the Hoorn Study. *Circulation* 2000; 101: 1506e11.
- [12] Iso H, Moriyama Y, Sato S, Kitamura A, Tanigawa T, Shimamoto T, et al. Serum total homocysteine concentrations and risk of stroke and its subtypes in Japanese. *Circulation.* 2004; 109:2766–72
- [13] Kawamoto R, Kajiwara T, Oka Y, Takagi Y. An association between plasma homocysteine concentrations and ischemic stroke in elderly Japanese. *J Atheroscler Thromb.* 2001; 9: 121–5.
- [14] Smulders YM, Rakic M, Slaats EH, Treskes M, Sijbrands EJ, Odekerken DA, et al. Fasting and post-methionine homocysteine levels in NIDDM. Determinants

- and correlations with retinopathy, albuminuria, and cardiovascular disease. *Diabetes Care* 1999; 22: 125e32
- [15] Davies L, Wilmshurst EG, McElduff A, Gunton J, Clifton-Bligh P, Fulcher GR. The relationship between homocysteine, creatinine clearance, and albuminuria in patients with type 2 diabetes. *Diabetes Care* 2001; 24:1805e9.
- [16] Clarke R., *et al*, Homocysteine Lowering Trialist's Collaboration (1998) Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomized trials. *Br Med J.* 316:894–898.
- [17] Still R.A, McDowell I.F.M. (1998) Clinical implications of plasma homocysteine measurement in cardiovascular disease. *J Clin Pathol.*, 51:183–188.
- [18] Emoto M, Kanda H, Shoji T, Kawagishi T, Komatsu M, Mori K, *et al*. Impact of insulin resistance and nephropathy on homocysteine in type 2 diabetes. *Diabetes Care* 2001; 24: 533e8.
- [19] Welch GN, Loscalzo J. Homocysteine and athero thrombosis. *N Engl J Med* 1998; 338:1042. e50.
- [20] Stehouwer CD, Gall MA, Hougaard P, Jakobs C, Parving HH. Plasma homocysteine concentration predicts mortality in non-insulin-dependent diabetic patients with and without albuminuria. *Kidney Int* 1999; 55: 308e14.
- [21] Kark JD, Selhub J, Bostom A, Adler B, Rosenberg IH. Plasma homocysteine and all-cause mortality in diabetes. *Lancet* 1999; 353: 1936e7.
- [22] Hoogeveen EK, Kostense PJ, Jakobs C, Dekker JM, Nijpels G, Heine RJ, *et al*. Hyperhomocysteinemia increases risk of death, especially in type 2 diabetes: 5-year follow-up of the Hoorn Study. *Circulation* 2000; 101: 1506e11.
- [23] O. Aydemir, P. T̄urkc̄, ̄uōglu, M. Ḡuler *et al.*, "Plasma and vitreous homocysteine concentrations in patients with proliferative diabetic retinopathy," *Retina*, vol. 28, no. 5, pp. 741–743, 2008.
- [24] M. Goldstein, I. Leibovitch, I. Yeffimov, S. Gavendo, B.-A. Sela, and A. Loewenstein, Hyperhomocysteinemia in patients with diabetes mellitus with and without diabetic retinopathy," *Eye*, vol. 18, no. 5, pp. 460–465, 2004.

- [25] H. C. Cho, The relationship among homocysteine, bilirubin, and diabetic retinopathy,” *Diabetes & Metabolism*, Vol. 35, no. 6, 595–601, 2011.