PJN
ISSN 1680-5194

PAKISTAN JOURNAL OF NUTRITION

ANSInet
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan
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Pakistan Journal of Nutrition 8 (11): 1753-1755, 2009
ISSN 1680-5194

Hyperhomocysteinemia, a Risk Factor for Myocardial Infarction in Patients with Type-2 Diabetes in Southern Sindh, Pakistan

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Abstract: Hyperhomocysteinemia is a major risk factor for Myocardial Infarction (MI) in patients with type 2 diabetes, in general population of Pakistan. However, the role of increase plasma homocysteine level in the development of Coronary Heart Disease (CHD) in patients with type 2 diabetes is still unknown. Therefore this study was designed to determine the relation ship between plasma homocysteine level and the incidence of MI in patients with type 2 diabetes. The study group consists of 107 patients (71 male and 36 female) who are admitted in different hospital of Hyderabad and Mirpurkhas with myocardial infarction. Plasma total homocysteine level, lipid profile and HbA1c were measured. All patients were identified as diabetic by using WHO criteria. Group A indicates patients (Diabetes Mellitus [DM]) with Myocardial Infarction ([MI] n = 107) Group B include controls (non-Diabetes Mellitus [non-DM] having MI). The plasma homocysteine level was significantly high in patients then in control (21.3±1.8 Vs 13.9±1.2 μmol/L, p = 0.0008). It seems clear relationship between hyperhomocystenia and an increase risk of MI in patients with type 2 diabetes.

Key words: Hyperhomocysteine, type 2 diabetes, myocardial infarction

INTRODUCTION

Myocardial infarction is a major consequence of coronary artery disease. A part from traditional risk factors of myocardial infarction, recently many reports have suggested that hyperhomocysteinemia plays an important role in myocardial infarction or lower homocysteine levels are associated with lower rates of coronary heart disease and stroke (Okada *et al*., 1999; Aamir *et al*., 2004).

Homocysteine is a nonessential, sulfur containing amino acid and is an intermediate form of metabolic demethylation of methionine. It is present in plasma in four forms:

Free thiol (1%), disulfide (5-10%), mixed disulfide (5-10%) and protein bound thiol groups (80-90%). The combined pool of all four forms of homocysteine is referrers as "total plasma homocysteine". The total homocysteine level in plasma has been reported to be in the range of 5-15 mmol/L in healthy individuals (Aamir *et al*., 2004; Iqbal *et al*., 2005).

Altered homocysteine metabolism plays a potential role in the pathogenesis of atherosclerosis, thromboembolism and vascular endothelial damage. Individuals untreated for hyperhomosteinemia may develop the major cardiovascular complications.

In patients with type 2 diabetes, several parameters including glucose intolerance, increased body weight, hypertension, hyperglyceridemia and decreased HDL cholesterol level are recognized cardiovascular risk factors (Iqbal *et al*., 2005; Zafar *et al*., 2004; Ismail *et al*., 2004; Iqbal *et al*., 2004).

Type 2 diabetes is known to be associated with several other cardiovascular risk factors, including dyslipidemia and hypertension, but these do not fully explain the excess mortality rates in type 2 diabetes (Aamir *et al*., 2004). Cardiovascular disease is the major cause of death in diabetic and nondiabetic subjects. The overall cardiovascular mortality rates are 2-4 times higher in type 2 diabetic patients than in nondiabetic subjects. Therefore, increased risk must be due, at least in part, to diabetes itself, poor metabolic control, or other factors. (Deepa *et al*., 2001; Prasad, 1999).

MATERIALS AND METHODS

This study was designed as cross sectional case control comparative study spanning over a period of 2.5 years and carried out at Institute of Biochemistry, University of Sindh, Jamshoro.

The study groups consisted of 160 (91 male and 69 female) hospitalized 40-65 year old patients of myocardial infarction, 110 patients of them were diabetic and 50 age and gender-matched control which were non-diabetic. Subjects in pernicious anaemia, severe hepatic impairment, renal impairment, psoriasis, hypothyroidism, systemic lupus erythematosus, anorexia nervosa, organ transplantation, malignanciec of breast, overy, pancreas and acute lymphoblastic leukaemia excluded from the study. Patients were admitted in different hospitals of southern sindh and adjoining area including Hyderabad and Mirpurkhas.

A verbal consent was obtained from each patient. Recording of demographic details, brief clinical history and physical examination of the subject and the presence or absence of diabetes mellitus, hypertension, and smoking status.

A 10 ml fasting venous blood specimen was collected and divided into two parts, 5 ml in a plain BD vacutainer (without anticoagulant for Serum) for estimation of blood glucose level and lipid profile, 5 ml in BD vacutainer containing K2 EDTA for the analysis of total plasma homocysteine level.

Estimation of total plasma homocysteine, blood glucose, total lipids, total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol: Determination of plasma total homocysteine by standardized High-Pressure Liquid Chromatography (HPLC) method for homocysteine measurement using Dithiothreitol (DTT) as reductant. Fasting serum glucose, serum lipid profile was estimated by commercial colorimetric kits methods on semi-automated chemistry analyzer.

RESULTS

Of the 160 patients of myocardial infarction were studied. 110 were in the group with type 2 Diabetes Mellitus (DM), and 50 were non-Diabetes Mellitus (Non-DM). The results of total plasma homocysteine in the group with DM are 23.14±2.4 µmol/L and highest frequency was observed in 56-60 years of age. Non-diabetic patients of MI were analyzed as a control among them 30 was male and 20 were female In the group with non-DM the mean homocysteine concentration is 13.1±1.8 µmol/L and highest frequency was observed in age group between 61-65. Table 1 shows the comparison of results of DM-MI and non-diabetic patients with MI.

DISCUSSION

The present study was carried out to assess the level of homocysteine in patient of type 2 diabetes and its role in the development of myocardial infarction and its correlation with non-diabetes subjects having myocardial infarction. Other was assessed parameters including (Lipid profile, Total blood glucose level, Total Homocysteine level in both groups).

In this study we observed the comparison of frequency and percentage of patients and controls of different age groups. Were observed along with high frequency of incidence of MI in patients in the age between 56-60 years that is 34.50%, out of 110 patients 38 were found in this age group. We observed the significance difference in the incidence of MI in controls. In control groups the incidence of MI in the age of more then 60 years.

An other study of Iqbal MP (Iqbal *et al*., 2005) reported that the mean age 52.83±9.12 year in patients having MI and 51.23±7.95 non-MI diabetes patients.

Iqbal *et al*. (2005) studied the effect of age on concentrations of folate, PLP, B12 and homocysteine. The author divided the case and control subjects into two age groups (52 years) because 52 years was the mean age group when cases and controls were combined. With the exception of B12 concentration in the

Table 1: Demographic and clinical characteristics of patients

	Control (n = 50)		Patients (n = 110)	
	Values (mean+/-SD)	Frequency (%)	Values (mean+/-SD)	Frequency (%)
Age (Years)				
Gender	56.4+/-6.16		53.76+/-7.6	
Male		30 (60.0)		71 (64.5)
Female		20 (40.3)		39 (45.5)
Smoking status				
Smokers		26 (52.0)		61 (55.4)
Nonsmokers		24 (48.0)		49 (44.6)
Diet				
Vegetarian		03 (6.0)		06 (5.5)
Non-vegetarian		47 (94.0)		104 (94.5)
Parental history of MI				
Yes		24 (48.0)		45 (40.0)
No		26 (52.0)		65 (65.0)
Hypertension				
Yes		26 (52.0)		78 (70.0)
No		24 (48.0)		32 (30.0)
Homocysteine	13.1±1.8 µmol/L		23.14±2.4 µmol/L	
Glucose (Fasting) (60-115 mg/dl)	76.4+/-16.82		206+/-23.23	
Total lipid	815.2+/-75.2		689.5+/-34.4	
Total Cholesterol (200-240 mg/dl)	228.7+/-25.3		201.5+/-19.8	
Triglyceride	210.0+/-56.0		224.3+/-69	
HDL-Cholesterol	34.1+/-09.1		28.4+/-8.7	
LDL-Cholesterol	118.1+/-23.5		132.6+/-35.5	

control group, which was significantly lower in the older subjects, p Z 0.02, there was no significant difference in mean values of folate, PLP, B12 and homocysteine between elder and younger groups .

In comparison of smoking status in patients and controls, it was observed that 55.4% patients were smokers and 44.6% were non-smokers. In control group 52.0% were smokers and 48.0% were non-smokers. Iqbal *et al.* (2005) reported that 43.3% patients and 18.3% control were smokers. In this effect of smoking on mean serum/plasma concentrations of folate, PLP, B12 and homocysteine, authors analyzed the values of these variables among smokers and nonsmokers in healthy subjects and AMI patients.

This study shows that the total lipid, LDL-cholesterol, VLDL-cholesterol level is significantly high in patients then control but total cholesterol level and HDL-cholesterol level is significantly lower then control. Triacyglycerol level shows no significant difference.

Marouf *et al.* (2006) showed the same results as in our case. Aamir *et al.* (2004) and Iqbal *et al.* (2005) also reported the same results of lipid profile as in our study. It is reported that the increased level of total cholesterol, LDL-cholesterol and triglyceridesand low level of HDL-cholesterol in serum cause cardiac disease. In Pakistan the food contains high levels of triglycerides and cholesterol (Malinow *et al.*, 1996). Plasma lipid concentration and lipoprotein patterns are labile and affected by eating, smoking, alcohol intake, stress and changes in posture. It is essential that the samples will be collected under standard conditions (Lonn *et al.*, 2006).

Total plasma homocysteine level reveal the results in group with DM is 23.14±2.4 µmol/L and in Non-DM is 13.1±1.8 µmol/L. Significantly increased level of homocysteine in patients with type 2 diabetes was observed in this study.

Iqbal *et al.* (2005) reported homocysteine 19.33± µmol/L in male patients which is significantly high then the normal limits which is reported as 5-15 µmol/L. Many other studies also conform these results, which as in our case.

Conclusion: Moderately high levels of plasma homocysteine are associated with subsequent risk of MI independent of other coronary risk factors. Because high levels can often be easily treated with vitamin supplements, homocysteine may be an independent, modifiable risk factor.

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