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Original Article

Association of Homocysteine Levels with Cardiometabolic Risk Factors Reported at a Tertiary Care Unit of Karachi – Pakistan

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Abstract

Objective: To determine the association between homocysteine serum levels and metabolic risk factors in adults of Karachi – Pakistan.

Study type, settings & duration: This prospective study was carried out in peripheral out-patient department, primary care unit, affiliated with Baqai Institute of Diabetology and Endocrinology, Baqai Medical University, Karachi from November 2007 to June 2008.

Methodology: Non-diabetic subjects were selected after taking informed consent. Subjects were advised to visit with at least 8 to 12 hours of fasting for oral glucose test. The anthropometry parameters were measured and blood tests for glucose levels, lipid profile, serum insulin, and homocysteine levels were done.

Results: Of the 75 recruited subjects, 52% (n=39) were males and 48% (n=36) were females. Age (mean years) of the subjects was 44.26±10.98 and mean BMI kg/m^2 was found 27.33±4.17. Fasting homocysteine, serum insulin levels, and HOMA found 15.6±6.52, 16.96±8.26, and 5.02±3.06, respectively. A significant association of elevated homocysteine level was found with BMI value p <0.04, male gender p <0.026, and smoking p <0.006. Insignificant correlation was seen between elevated homocysteine levels and age, fasting plasma glucose, hypertension, serum lipid parameters and waist circumference.

Conclusion: Serum homocysteine level was significantly correlated with BMI, male gender, and smoking. Furthermore, an elevated homocysteine serum level was found in our study but not significantly associated with metabolic risk factors among population of Pakistan.

Key words: Diabetes, homocysteine levels, HOMA, OGTT.

Introduction

Metabolic disorder is a common disorder that has an adverse public health impact, the prevalence has raised to an epidemic portion as well.[1] This disorder cluster indulge resistance of insulin, obesity (central), lipid disorder, hypertension, dysfunction of endothelial cells which collectively developed adverse events cardiovascular disorder (CVD), fatty liver of non-alcoholic disease (NAFLD), and diabetes.[2]

Total homocysteine (tHcy) is an amino acid contain sulfur that is produced from methionine (Met) to cysteine (Cys) metabolism.[3] Homocysteine (Hcy) is categorized as moderate level 16-30, intermediate 31-100, and severe hyperhomocysteinemia ≥100(mmol/L), respectively.[4] Higher levels of circulating Hcy are directed as a risk indicator for coronary, peripheral, and cerebral atherosclerosis.[3] Individuals with elevated levels of this amino acid have decreased folate value, B6 and B12 (vitamins), a mutation in gene, kidney diseases, and methotrexate.[4]

Association of hypertension promoted by both hyper-homocysteinemia and elevated Hcy,but suppressed T2DM only with elevated Hcy that is well understood.[5] However, oxidative stress is

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Authors Contribution

MS, IAS, AB & AA conceptualized the project. AA & RAK did the data collection. IAS & AA performed the literature search. AA & AF did the statistical analysis. Drafting, revision & writing of manuscript were done by MS, IAS, AA, AF, AB & RAK.

increased in T2DM and matrix, these alterations are a prominent feature of diabetes, both of which probably make diabetic subjects more susceptible to the adverse effect of hyperhomocysteinemia.[6]

Significance between tHcy level and MetS is determined by using only baseline measurements of both. The potential causality is unclear due to variances results reports. For instance, tHcy is known to be an associated MetS risk factor.[7]

Because elevated homocysteine in the blood has been proved to be associated with severe health problems, studies are needed to explain its relation with lipid profile, plasma glucose, obesity and hypertension in the population. Therefore, the goal of our study was to find the association between serum homocysteine levels and lipid profile, plasma glucose, obesity and hypertension in the adult population of Karachi – Pakistan.

Methodology

This prospective study designed and carried out in peripheral OPD (out-patient department), Primary Care Unit, affiliated with Baqai Institute of Diabetology and Endocrinology (BIDE), Karachi from November 2007 to June 2008. Non diabetic subjects having age 18 years or above were selected after informed consent. Subjects were advised to visit with at least 8 to 12 hours of fasting for oral glucose test. Pre and post levels of blood was obtained following 75g glucose, was given to each study participant. Diabetes and pre-diabetes were categorized as per World Health Organization (WHO) criteria.[8] Subjects having a diabetes status, uncontrolled raised blood pressure, coronary artery illness, brain disease, kidney, and hepatic disease, and pregnant females were excluded. Data was obtained on a pre-designed questionnaire. The anthropometry parameters were measured and blood tests for glucose levels, lipid profile, serum insulin, and homocysteine levels were done. According to the results, subjects were divided into three groups; normal tolerance of glucose, impaired tolerance glucose and diabetes. Isolated impaired glucose fasting was distinct as fasting glucose between 110 and 125 (mg/dL) with 2-hour post glucose ≤140 (mg/dL) and/or <110 (mg/dL) and 2-h PGL between 141 to 199 (mg/dL). Diabetes was classified as FPG ≥126 (mg/dL) or 2-h PGL ≥ 200 (mg/dL) or both.[8] The data was further divided into two categories; normal (<15 µM/L) and higher (≥15µM/L) homocysteine levels. Normal range for total cholesterol was <200 mg/dL, triglycerides was <150 mg/dL, HDL was >40 mg/dL for males and >50 mg/dL for females and LDL was <130 mg/dL.[9]

Height was measured in centimeters (cm) then converted into meters (m) from participants to stand in an erect position using stadiometer. Weight in kilograms (kg) was measured using digital weighing machine on a flat surface. Obesity was recorded by BMI (body mass index) measurement as >25 kg/m^2.[10] Central obesity based on circumference of waist (WC) was taken ≥ 90 cm (men) and ≥ 80 cm (women), similar to other studies done in South Asians.[10] Raised BP was calculated as systolic/ diastolic blood pressure ≥140/90(mmHg).[11]

Glucose peroxidase oxidase method for plasma glucose was used. Cholesterol phenol oxidase 4-aminoperoxidase antipyrinemethod for cholesterol, glycerol oxidase phosphate -p-aminophenazone technique for triglycerides, high lipoprotein density cholesterol and low lipoprotein density cholesterol by enzymatic homogeneous colorimetric process were used.[12] Fasting plasma homocysteine total concentration was processed by a fluorometric detection system with high-performance liquid chromatography.[13]

Statistical examination was completed by using Social Sciences of Statistical Package (SPSS version 20). For continuous parameters, mean ± SD was calculated. Categorical variables were described in terms of number of observations and percentages; chi-square was applied to see the association. $p \leq 0.05$ was taken significant statistically.

The Ethical approval was obtained from Institutional Review Committee of Baqai Institute of Diabetology and Endocrinology, Baqai Medical University, Karachi.

Results

Of the 75 recruited participants, 52% (n=39) were males and 48% (n=36) were females. Table-1 shows the description of baseline parameters. Age (mean years) of participants was 44.26±10.98 and BMI was found 27.33± 4.17. Fasting homocysteine, serum insulin levels, and HOMA found 15.6±6.52, 16.96±8.26, and 5.02±3.06, respectively. Females were more hypertensive, having high BMI, waist circumference, fasting cholesterol (serum), HDL, LDL, and fasting insulin of serum levels while males were older, having greater fasting plasma glucose, TG levels, HOMA and elevated fasting serum homocysteine.

Association of serum homocysteine levels with different variables and their statistical significance is shown with *p*-values. Significant association of elevated homocysteine was found with BMI p <0.04, male gender p <0.026, and smoking p <0.006. Insignificant correlation was seen between elevated homocysteine levels and age, glucose plasma fasting, hypertension, cholesterol (serum), LDL, HDL, TG, and WC (Table-2).

Table 1: Baseline parameters of the study participants.

Variables	*Overall*	*Male*	*Female*
Age (yrs)	44.26±10.98	45.84±12.35	42.54±9.15
Systolic Blood Pressure (mmHg)	128±21.3	122.82±14.13	133.61±26.09
Diastolic Blood Pressure (mmHg)	81.06±10.44	80±8.58	82.22±12.15
Weight (kg)	70.36±11.23	73.05±12.26	67.44±9.3
Height (cm)	160.76±9.12	167.35±6.35	153.61±5.57
Body mass index (kg/m^2)	27.33±4.17	26.12±3.65	28.63±4.35
Waist circumference (cm)	96.04±11.81	95.41±10.19	96.73±13.47
Cholesterol (mg/dl)	190.2±48.21	188.35±47.76	192.19±49.3
Triglyceride (mg/dl)	159.54±93.73	182.15±116.84	135.05±50.65
HDL (mg/dl)	35.53±5.48	34.38±5.42	36.77±5.34
LDL (mg/dl)	123.38±28.54	121.20±24.86	125.75±32.25
Insulin (µIU/ml)	16.96±8.26	16.58±7.44	17.37±9.15
HOMA	5.02±3.06	5.09±3.33	4.94±2.77
Fasting homocysteine (µM/L)	15.6±6.52	17.30±7.59	12.41±4.59

Table 2: The association of serum homocysteine levels with different variables and their statistical significance as shown with *p*-values.

Variables	*Normal Homocysteine n (%)*	*High Homocysteine n (%)*	*p-value*
Age			
< 50	28(57.14)	21(42.85)	0.363
> 50	11(45.83)	13(54.16)	
BMI			
< 25	14(73.68)	5(26.31)	0.04
> 25 (obesity)	26(46.42)	30(53.57)	
Gender			
Male	16(41.02)	23(58.97)	0.026
Female	24(66.67)	12(33.33)	
Smoking			
No	35(62.5)	21(37.5)	0.006
Yes	5(26.31)	14(73.68)	
Fasting Plasma Glucose			
Normal	12(48)	13(52)	
Impaired	11(45.83)	13(54.16)	0.31
Diabetic	17(65.38)	9(34.61)	
Hypertension			
Normal	7(50)	7(50)	0.782
Hypertensive	33(54.09)	28(45.9)	
Cholesterol			
Normal	7(38.88)	11(61.11)	0.159
High	33(57.89)	24(42.10)	
LDL			
< 100	6(40)	9(60)	0.247
> 100	34(56.67)	26(43.33)	
HDL			
> 40 50	0(0)	2 (100)	0.125
< 40 50	40(54.79)	33(45.20)	
TG			
< 150	23(47.91)	25(52.08)	0.21
≥ 150	17(62.96)	10(37.03)	
Waist circumference			
Normal	7(53.84)	6(46.15)	0.967
Central obesity	33(53.22)	29(46.77)	

Discussion

In our study, mean homocysteine levels were found higher than the normal range. Similar findings of elevated mean homocysteine levels were also found in a study from Pakistan.[6] The increased serum level of homocysteine is also a risk factor of non-communicable diseases.[6] Further exploration needs to be done of this observation, as homocysteine is a potentially risk factor (modifiable) in cardiac people and the general population with a little economic burden.

The reason for elevated homocysteine levels in our study can be dietary factors. A previous study reported complex homocysteine serum levels in vegetarians related to omnivores. Because vegetables are not enough source for B12 vitamins

which is necessary essentially in remethylation of homocysteine to methionine.[14]

Homocysteine levels are found to be associated with obesity, smoking, and male gender in the current study. Statistical significance is observed when BMI is used as a criterion to define obesity. In other studies, BMI and cigarette smoking are found as risk factors for increased levels of plasma Hcy.[15,16]

The high serum concentration of homocysteine in men than women in present study was consistent with the result of another research.[17] It is suggested that sex hormones play an important role in homocysteine metabolism.[17] Gender differences in homocysteine may be due to sex hormones effect during and postmenopause in females and greater mass of muscles in male.[18]

Although advancing with age is correlated to increased homocysteine levels in the general population because of age-related metabolic syndrome.[19] Such kind of association was not found in this study may be because the mean age of the population is 44 years and by that time renal status is usually not compromised. This needs to be explored further in a larger scale study.

Limitations of this study are small sample size and future studies need to be carried out in a larger population. Also, nutritional status is not considered in our study. Certain vitamins play an important role in homocysteine metabolism like vitamins B12; folic acid and vitamin B6. These were not considered in our study.

Serum homocysteine level was significantly correlated with BMI, male gender, and smoking. Furthermore, an elevated homocysteine serum level was found in our study but not significantly associated with metabolic risk factors among population of Pakistan.

Conflict of interest: None declared.

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