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Serum Homocysteine and Lipid Profile In Type 2 Diabetes Mellitus Patients

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Abstract:

Aims and Objectives: *To evaluate the association of Homocysteine (Hcy) and Lipid profile with Type 2 Diabetes Mellitus (DM) and to assess affect of age, sex and smoking status on Hcy level.*

Materials And Methods: *The study was carried out in the department of Physiology in collaboration with Medicine and Biochemistry department, Regional Institute of Medical Sciences (RIMS), Imphal. A total of 122 diabetic volunteers fulfilling the criteria of diagnosis according to American Diabetic Association (ADA) and World Health Organization (WHO) were included in the study. Patients with congenital heart disease, signs of congestive heart failure and pericardial disease, chronic obstructive pulmonary disease, evidence of severe renal impairment, history of acute infections, thyroid dysfunction, prolong supplementation of B-complex vitamin especially Vitamin B6,B12 and folic acid, pregnancy and any seriously ill patients were excluded. Serum Hcyl were measured by ELISA and lipid profile by enzymatic colorimetric method. Student t-test and chi square test has been used for statistical analysis.*

Results: *The Hcy level increased in relation with impaired sugar level though not statistically significant (P= 0.124).Statistically significant correlation between Hcy with age was observed (P= 0.009). Higher levels of Hcy was observed in male (P=0.037).There was no significant difference in triglyceride level (P=0.224) with regard to glycaemic status though the severity of lipid alteration increase with high fasting blood sugar. Total cholesterol (P=0.003) and Low Density Lipoprotein (P=0.011) show significant correlation with Hcy level.*

Conclusion: *Elevated blood levels of Hcy have been linked with a wide range of health disorders including cardiovascular disease, stroke, macular degeneration, hearing loss, brain atrophy etc. The raised of Total Hcy in Type 2 diabetes may further increase the risk. These risk factors might be taken into consideration in addition to known risk factor during evaluation of Type 2 diabetic patients.*

Keywords: *Homocysteine, Lipid profile, Type 2 Diabetes.*

I. Introduction

Homocysteine (Hcy) is sulphur containing non-essential amino acid formed from demethylation of methionine. Instead, it is biosynthesized from methionine via a multistep process.[1] Approximately 70% of plasma Hcy is bound to albumin and the remaining 30% exist as free sulphides. The term total plasma Homocysteine (tHcy) refers to the sum of all Hcy species in plasma/serum including both the free and protein bound form.[2]The normal plasma levels of Hcy value ranges from 5-15µmol/L. Hyperhomocysteinemia refers to elevated Hcy in plasma generally greater than 15µmol/L.

Diabetes Mellitus (DM) represents a spectrum of metabolic disorders which has become a major health challenge worldwide. The prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity level as countries become more industrialized, and the aging of the population.[3]

Hyperhomocysteinemia is an important independent risk factor for atherosclerotic disease in both diabetic and non diabetic subjects. Hyperhomocysteinemia in diabetic patients may contribute to the development of chronic vascular complications. Inspite of many research works on Hcy in DM patients, the association between these two is not totally clear.[4]

DM affects several lipid metabolism mechanism. Obesity and Insulin resistance result in hypertriglyceridemia due to over production of Very Low Density Lipoprotein (VLDL).The characteristic pattern of dyslipidemia associated with type 2 DM includes high Triglyceride level, low High Density Lipoprotein (HDL) cholesterol and elevated Low Density Lipoprotein (LDL) cholesterol consisting of small dense LDL particles. The excess risk for Coronary Heart Disease (CHD) seen among diabetes is attributed to

diabetic dyslipidemia particularly increase in small dense LDL .[5]The present study was undertaken to evaluate the association of Hcy and lipid profile with Type 2 diabetes as elevated Hcy level has been linked with wide range of health disorders such as cardiovascular disease, stroke etc. and to assess affect of age, sex and smoking status on Hcy level.

II. Materials And Methods

The study was carried out in the department of Physiology in collaboration with the department of Medicine and Biochemistry, Regional Institute of Medical Sciences (RIMS), Imphal for a period from November 2012 to October 2014 after getting approval from Institutional Ethical Committee. The study was a cross-sectional study. A total of 122 diabetic volunteers fulfilling the criteria of diagnosis according to American Diabetic Association (ADA) and World Health Organization (WHO) criteria were selected from medicine ward irrespective of sex and socio-economic status to form the study group.

The exclusion criteria : Seriously ill patients whose sensorium and higher functions are altered, patients with congenital heart diseases, congestive heart failure and pericardial disease, chronic obstructive pulmonary disease, evidence of severe renal and or hepatic impairment, history of acute infections, thyroid dysfunction, prolong supplementation of B-complex vitamins specially Vitamin B6,Vitamin B12 and folic acid, pregnancy.

All the selected patients had given a voluntary consent. A detailed history such as age, sex, address, religion, occupation, marital status, personal history including dietary habit, alcohol consumption, history of cigarette smoking , past medical history, family history of diabetes, hypertension and levels of physical activity were recorded. Blood pressure was recorded using mercury sphygmomanometer in lying down position. Baseline investigation data, Electrocardiogram, Chest X-ray etc. available with the patient was taken for reference.Blood samples were collected in the morning after 8 hours of fasting in plain vials. The blood samples were centrifuged for 10 minutes at 3000rpm immediately. The serum were taken out and kept in the freezer compartment of refrigenerator for measuring Hcy and lipid profile. The serum Hcy levels were estimated by ELISA method using Axis-Homocysteine Enzyme Immunoassay (EIA) kit from Axis-Shield Diagnostic, UK. Serum lipid profile estimation were done by Enzymatic Colorimetric Test with Lipid clearing factor (LCF) by using Kits Human Gesellschaff fur Biochemical and Diagnostica mbH. The data were analyzed using Chi Square test, Pearson Correlation. P value < 0.05 was considered significant.

III. Results

Table 1: Demographic data of the study population

Parameters		Number	Percentage
Gender	Male	80	65.5
	Female	40	34.5
Age groups (yrs)	0-45	6	4.9
	46-55	42	34.4
	56-65	44	36
	66-83	30	24.5
Smoking habits	Smoker	41	33.6
	Non-smoker	81	66.3
Diet	Non-veg	108	88.5
	Veg	14	11.47
Employment	Yes	30	24.5
	No	92	75.4
Literacy	Literate	52	42.6
	Illiterate	70	57.3
Family history of Diabetes	Yes	70	57.3
	No	52	42.6

Table1 shows that 65.5% were males and 34.4% were females. Highest percentage (36%) of subjects included in the sample belong to the age group of 56-65 years and the lowest percentage (4.9%) belong to the age group 0-45 years. Among the participants, 33.6% were smokers and the remaining 66.3% were non-smokers. Majority (75.4%) of the subjects are unemployed and only 24.5% are employed. 57.3% patients have a family history of diabetes. 42.6% were literate and 57.3% were illiterate among the study population.

Table 2: Association between Homocysteine (Hcy) and fasting blood sugar (FBS)

Fasting blood sugar	Homocysteine level		P-value
	≤15µmol/dl	>15µmol/dl	
<100	8	0	0.124
100-125	28	16	
≥126	48	22	
Total	84	38	

Levels of Hcy increases with an impaired sugar level though statistically not significant.

Table 3: Association between Lipid profile and Fasting blood sugar

Lipid profile	mg/dl	FBS (mg/dl)			p- value
		<100	100-125	≥126	
Total cholesterol	<200	6	20	36	0.303
	≥200	2	24	34	
Triglyceride	<150	6	20	30	0.224
	≥150	2	24	40	
HDL	≤40	6	26	44	0.685
	>40	2	18	26	
LDL	<100	4	20	30	0.910
	≥100	4	24	40	

This table show no significant differences in triglyceride with regard to glycaemic status though the severity of lipid alteration increases in patients with high FBS.

Table 4: Homocysteine level in male and female groups

Homocysteine	Female	Male	P-value
≤15µmol/dl	34(40.5%)	50(59.5%)	0.037
>15µmol/dl	8(21.1%)	30(78.9%)	

Hyperhomocysteinaemia is observed in both sexes; males are affected more and found to be statistically significant (P=0.037).

Table 5: Homocysteine level in smoker and non-smoker

Subject	Homocysteine level		P- value
	≤15µmol/dl	>15µmol/dl	
Non- smoker	59 (72.8%)	22 (27.1%)	0.181
Smoker	25 (61%)	16 (39%)	

Table 8 shows that level of homocysteine was increased in smokers (39%) than non-smokers (27.1%) of study population but statistically not significant.

Table 6: Correlation between Hcy and Cardiovascular risk factors

Variable	r- value	P value
Age	0.235	0.009
BMI	0.021	0.815
Total cholesterol	-0.263	0.003
Systolic Blood pressure	0.160	0.077
Diastolic Blood pressure	0.070	0.446
HDL	-0.164	0.071
LDL	-0.231	0.011

The age, total cholesterol and LDL were found to have significant correlation with Hcy level as shown in table 6.

IV. Discussion

The present study consist of 122 diabetic patients having 80 number of males and 42 females. It was reported that type 2 DM usually develop after the age of 40[6,7] and the highest percentage of subjects in our study belongs to the age group of 56-65 years. The prevalence of diabetes was higher among unemployed individuals as well as individual with a family history of diabetes. This indicates that unemployment and family history are associated with Type 2 DM. Many studies reported that family history is a risk factor of diabetes.[8,9]

The result of the study showed increased Hcy level with increased impaired sugar level though not statistically significant. The elevated levels of Hcy are linked to type 2 diabetes. Hyperhomocysteinemia was also reported in Type 2 DM in other studies [10,11,12] and may contribute to the development of vascular complications.[4] Studies have shown that too much Hcy in the blood is related to a higher risk of coronary heart disease, stroke and peripheral vascular disease. A large multi-center European trial observed that among men and women younger than age 60, the overall risk of coronary and other vascular disease was 2.2 times higher in those with plasma total Hcy (tHcy)levels in the top fifth of the normal range compared with those in the bottom four fifth of the normal range.[13] Disturbances in intracellular Hcy metabolism lead in most cases to elevated tHcy concentrations. Genetically determined functional deficiencies of enzyme in Hcy metabolism like deficiency of Cystathionine β-synthetase (CBS) depletion of important co-factors for those enzymes including folate, vitamin B12 and vitamin B6 also have an extremely large impact on tHcy concentration.[14]

The association between lipid profile and fasting blood sugar in Type 2 DM were found to be not significant, however, severity of dyslipidemia increases in patients with increased FBS, this was observed in case of triglyceride and LDL, whereas cholesterol and HDL show negative relation with elevated sugar level

similar to the observation made by Ali et al.[15] Hypertriglyceridemia is the commonest lipid abnormality occurred in Type 2 diabetic patients (73.3%) .This finding was in agreement with Taylor R et al [16] who reported an increased in serum triglyceride concentration in Type 2 DM.

The present study show a significant correlation of Hcy with age similar to the findings of Framingham Offspring Cohort and The Hordaland Hcy study.[17,18] Refsum H et al reported that increasing age is one of the factor associated with increased tHcy levels. Changes in renal function impaired renal metabolism of Hcy or vitamin status or both may be responsible in part for the age-related changes in Hcy concentrations. Other factor such as fat free lean body mass, muscle mass and life style factors like smoking must have affected the age related changes in Hcy concentration in male.[19,20] This may partly explain the tendency to premature atherosclerosis in patients with hyperhomocysteinemia.

Significant sex difference in Hcy level was present with the values higher in males as in other studies .[21,22] Higher Hcy concentration in males may be explained by sex hormone status, body size, muscle mass and vitamin status.[22]

Increased in Hcy level was also observed among smokers similar to other studies .[23,24] This could be a direct effect of smoking, it is more likely reflecting the different nutritional status of smokers.

V. Conclusion

Hcy is known as an independent predictive biomarker for cardiovascular disease. Elevated blood levels have been linked with a wide range of health disorders including heart disease, stroke, macular degeneration, hearing loss etc. Raised tHcy in Type 2 diabetes further increased the risk of developing cardiovascular disease. All these risk factors might be taken in to consideration in addition to known risk factors during the evaluation of Type 2 diabetic patients.

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