Study of Homocysteine Level in Patients with Diabetes Mellitus Type 2

THESIS

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Internal Medicine

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Abstract:

Homocysteine (Hcy) is an independent risk factor for cardiovascular disease, which is the leading cause of morbidity and mortality among Type 2 Diabetes Mellitus (T2DM) patients. 60 T2DM patients and 20 apparently healthy volunteers were included as controls in this study. Hcy was significantly higher in patients versus controls ($p<0.\cdot01$), Hcy was also higher in patients with vascular complications compared to those without complications, ($p<0.\cdot01$). There was a highly significant positive correlation between Hcy and the duration of Diabetes, blood pressure, the dose of metformin, glycated hemoglobin, total cholesterol, low-density lipoprotein cholesterol, Triglycerides and a negative highly significant correlation with high-density lipoprotein cholesterol. In diabetic patients with vascular complications, there was a highly significant correlation between fasting total homocysteine and both ischemic heart disease and urinary albumin to creatinine ratio, ($p<0.\cdot01$).

Key Words:

- Homocysteine.
- Type 2 Diabetes.
- Vascular complications.

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List of Abbreviations

ABCA1	ATP-Binding Cassette, sub-family A, member 1.
ACCORD	Action to Control Cardiovascular Risk in Diabetes.
ACEI	Angiotensin Converting Enzyme Inhibitor.
ACR	Albumin Creatinine Ratio.
AD	Alzheimer's Disease.
ADA	American Diabetes Association.
ADMA	Asymmetric Di-Methyl Arginine.
ADT	Anethole Dithiole-Thione.
ADVANCE	Action in Diabetes and Vascular Disease.
AGEs	Advanced Glycation End Products.
ANOVA	Analysis of Variance.
ARB	Angiotensin Receptor Blocker.
BHMT	Betaine-Homocysteine *S*-Methyl-Transferase.
BMI	Body Mass Index.
CAD	Coronary Artery Disease.
CBS	Cystathionine-B-Synthase.
CGL	Cystathionine γ-Lyase.
CKD	Chronic Kidney Disease.
CVD	Cardio Vascular Disease.
DCCT	Diabetes Control and Complications Trial.
DD	Disc Diameter.
DM	Diabetes Mellitus.
DMG	Di-Methyl-Glycine.
DMO	Diabetic Macular Edema.
DN	Diabetic Nephropathy.
DNA	Deoxyribo-Nucleic Acid.
DPP	Diabetes Prevention Program.
DR	Diabetic Retinopathy.
EDIC	Observational Epidemiology of Diabetes Interventions and Complications.
EDTA	Ethylene Diamine Tetra-acetic Acid.
ESRD	End Stage Renal Disease.
FFA	Free Fatty Acids.
FPG	Fasting Plasma Glucose.
GABA	γ-Amino-Butyric Acid.
GFR	Glomerular Filtration Rate.
Hcy	Homocysteine.
HDL	High-Density Lipoprotein.
HHcy	Hyper-Homocysteinemia.

IFG	Impaired Fasting Glucose.
IGT	Impaired Glucose Tolerance.
IHD	Ischemic Heart Disease.
LDL	Low-Density Lipoprotein.
MS	Multiple Sclerosis.
MTHFR	Methylene –Tetra- Hydro- Folate- Reductase.
MTs	Methyl-Transferases.
NGSP	National Glycohemoglobin Standardization Program.
NPDR	Non-Proliferative Diabetic Retinopathy.
OGGT	Oral Glucose Tolerance Test.
PD	Parkinson's Disease.
PDR	Proliferative Diabetic Retinopathy.
RAGE	Receptor for Advanced Glycation End Products.
RRMS	Relapsing Remitting Multiple Sclerosis.
SAH	*S*-Adenosyl Homocysteine.
SAM	S-Adenosyl Methionine.
SHMT	Serine Hydroxy Methyl Transferase.
T1DM	Type 1 Diabetes Mellitus.
T2DM	Type 2 Diabetes Mellitus.
THF	Tetra-Hydro-Folate.
UKPDS	United Kingdom Prospective Diabetes Study.
VADT	Veterans Affairs Diabetes Trial.
VEGF	Vascular Endothelial Growth Factor.
VLDL	Very Low Density Lipoprotein.

INTRODUCTION

Background:

Diabetes mellitus is a major epidemic of this century, which has increased in incidence by 50% over the past 10 years **(Forbes and Cooper, 2013)** and Type 2 Diabetes mellitus (T2DM) accounts for ~90–95% of diabetic patients **(American Diabetes Association, 2015**).

The magnitude of the global health burden of diabetes is well documented and complications of diabetes are the cause of the vast majority of this burden, it also account for substantial costs **(Tin et al 2014)**.

Macrovascular complications are the largest contributor to the direct and indirect costs of diabetes. Cardiovascular complications are the leading cause of morbidity and mortality among patients with type 2 diabetes mellitus and cardiovascular disease risk is 2- to 8-fold higher in the diabetic population than it is in non-diabetic individuals of a similar age, sex and ethnicity **(Papa et al, 2013)**.

As obesity, hypertension and dyslipidemia, which are known to be frequently associated with type 2 diabetes, are insufficient in explaining the increase in risk of cardiovascular disease; researchers are focusing on investigating other risk factors **(Kangabam et al, 2013).**

Homocysteine

Homocysteine (Hcy), a sulphur containing amino acid produced during the metabolism of methionine **(Kangabam et al 2013),** is an independent cardiovascular risk factor. An association between elevated levels of Hcy and the vascular complications of diabetes has been reported. However; studies on circulating Hcy levels in Type 2 Diabetes (T2DM) have given conflicting results **(Huang et al, 2013)**.

The risk of cardiovascular disease and for mortality attributed to Hyperhomocysteinemia (HHcy) is stronger in patients with type 2 diabetes than in subjects without diabetes **(Jung et al, 2013).** HHcy is also associated with atherosclerosis, and this association is stronger in individuals with diabetes than in nondiabetic subjects **(Mohammed et al, 2013)**.