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PREVALENCE OF HYPERHOMOCYSTEINEMIA IN TYPE ٢ DIABETIC PATIENTS AND ITS RELATION TO THE DIFFERENT THERAPEUTIC MODALITIES FOR DIABETES

Thesis
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LIST OF ABBREVIATION

ACEI	Angiotensin converting enzyme inhibitor.
ADMA	Asymmetric dimethyl arginine.
AT	Alpha tocopherol.
BHMT	Betaine homocysteine methyltransferase.
BMI	Body mass index.
BMD	Bone Mineral Density
BNP	B-type natriuretic peptide.
CAD	Coronary artery disease.
CAN	Cardiac autonomic neuropathy.
CBS	Cystathionine-β synthase.
CGL	Cystathionine-δ lyase.
CHD	Coronary heart disease.
CRF	Chronic renal failure.
CRP	C-reactive protein.
CVD	Cardiovascular disease.
DM	Diabetes mellitus.
E gr.١	Early growth response gene–١
eNOS	Endothelial nitric oxide synthase.
ESRD	End-stage renal disease.
FFAs	Free fatty acids.
FMD	Flow mediated dilatation.
FPG	Fasting plasma glucose.
FPIA	Fluorescence polarization immunoassay.
GDM	Gestational diabetes mellitus.
GFR	Glomerular filtration rate.
Hcy	Homocysteine.
HDL	High- density lipoprotein.
HMG CoA	Hydroxy methyl glutryl Co A.
HOPE	Heart Outcome Prevention Evaluation.
ICAM	Intercellular adhesion molecule.
IFG	Impaired fasting glucose.
IGF-١	Insulin growth factor-١.
IGT	Impaired glucose tolerance.
IHD	Ischemic heart disease.
IL-٦	Interieukin-٦.
IMT	Intima-media thickness.
IRS	Insulin resistance syndrome.
LDL	Low-density lipoprotein.
Lp (a)	Lipoprotein (a).
MAT	Methionine adenosyltransferase.
MeTHF	Methyltetrahydrofolate.
MI	Myocardial infarction.

MICRO-HOPE Microalbuminuria, Cardiovascular and Renal Outcomes in HOPE.
MNC Mononuclear cells
MS Methionine synthase.
NAC N-acetylcysteine.
NO Nitric oxide.
NOS Nitric oxide synthase.
NPDR Non-proliferative diabetic retinopathy.
OC Oral contraceptives.
PAI-١ Plasminogen activator inhibitor type ١.
PDR Proliferative diabetic retinopathy.
PPAR Peroxisome proliferators-activated receptors.
SAH S-adenosylhomocysteine.
SAM S-adenosylmethionine.
TF Tissue factor.
tHcy Total homocysteine.
TGF-β Transforming growth factor β.
TNF–α Tumor necrosis factor α.
TZDs Thiazolidinediones.
UKPDS United Kingdom Prospective Diabetes Study.
VCAM Vascular cell adhesion molecule.
VLDL Very low density lipoprotein.
vWF von Willebrand factor.

INTRODUCTION

Diabetes mellitus has been defined as a coronary heart disease risk equivalent. Therefore, there has been a major focus on preventing cardiovascular disease and controlling cardiovascular disease risk factors in the diabetic patient, and more aggressive treatment goals have been proposed for diabetic patients ***(American Diabetes Association, ٢٠٠٦).***

Traditional risk factor such as hypertension, dyslipidemia and poor metabolic control has been well identified in type ٢ diabetic patients. However, they do not fully explain the acceleration in macro-vascular disease in those patients **(*Hoogeveen et al., ٢٠٠٠a).*** Thus, non traditional risk factors came into focus.

Hyperhomocysteinemia is an independent risk factor for cardiovascular disease **(*Guilliams, ٢٠٠٤).*** It has been identified also as a modest predictor and stroke risk in healthy population **(*The Homocysteine Studies Collaboration, ٢٠٠٢),*** and even correlated with the angiographic extent of coronary artery disease **(*Bozkurt, ٢٠٠٤).***

Diabetes mellitus is associated with impaired homocysteine metabolism which might contribute to endothelial- myocyte dysfunction in the heart of diabetic patients **(*Tyagi et al., ٢٠٠٥b).*** In addition, metformin; a key treatment option in type ٢ diabetes, decreases vitamin B١٢

levels and subsequently increases homocysteine levels **(*Wulffele et al., ٢٠٠٣*).** On the contrary, sulfonylureas were associated with lower serum levels of homocysteine when compared to diet and physical activity alone ***(Hellgren et al., ٢٠٠٥*).**

AIM OF THE WORK

To study the prevalence of hyperhomocysteinemia among type ٢ diabetic patients receiving different anti-diabetic therapies.

NON TRADITIONAL RISK FACTORS & MACROVASCULAR COMPLICATIONS IN TYPE ٢ DIABETES MELLITUS

Diabetes mellitus is defined as a group of metabolic diseases characterized by hyperglycemia due to defects in insulin secretion, insulin action or both ***(American Diabetes Association, ٢٠٠٧).***

Several distinct types of diabetes mellitus (DM) exist and are caused by a complex interaction of genetics, environmental factors, and life-style choices. Depending on the etiology of the DM, factors contributing to hyperglycemia may include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiological changes in multiple organ systems that impose burden on the individual with diabetes and on the health care system. In the United States, DM is the leading cause of end-stage renal disease (ESRD), non traumatic lower extremity amputations, and adult blindness. With an increasing incidence worldwide, DM will be a leading cause of morbidity and mortality for the foreseeable future ***(Gillam & Landsberg, ٢٠٠٣).***

*Etiologic Classification of Diabetes Mellitus: *By (American Diabetes Association, ٢٠٠٧).*

I. Type ١ diabetes (β-cell destruction, usually leading to absolute insulin deficiency):

A. Immune-mediated.