EVALUATION OF THE RELATIONSHIP BETWEEN CREATININE CLEARANCE AND PRESENCE OF LOWER LIMB ARTERIAL DISEASE IN DIABETIC ISCHEMIC HEART DISEASE PATIENTS

Thesis

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Evaluation of The Relationship Between Creatinine Clearance And Presence of Lower Limb Arterial Disease in Diabetic Ischemic Heart Disease Patients

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ABSTRACT

The present study was done to investigate the association between creatinine clearance and presence of lower limb arterial disease in diabetic ischemic heart disease patients

The study was conducted on 50 cases was selected from patients who were admitted to cardiology department of Ain shams university hospital.

The cases include patients with coronary artery disease, diabetes mellitus and those with chronic kidney disease (CKD) (stage 2 kidney damage) their creatinine clearance 60-89 ml/min/1.73m2. (Normal value: 90-160 ml/min/1.73m2).

Patients were subjected to full medical history, through physical examination**,** fasting blood sugar, Lipid profile (total cholesterol and triglycerides), serum creatinine, and creatinine clearance.

Blood pressure measurements for calculation of the ankle brachial index (ABI) obtained using Doppler probe on bilateral brachial, posterior tibial, and dorsalis pedis arteries by ABI Doppler smartdop 30 ex. PAD was defined by ABI < 0.9.

Correlation of both PAD and traditional risk factors resulted in significant relation with sex, dyslipidemia, smoking and hypretension but the relation was not significant with age.

In the present study it was found that PAD was more prevalent among patients with increased levels of serum creatnine (p=0.021).and also with decreased levels of creatnine clearance (p=0.034) and the difference was statistically significant

Finally, ABI is a bed-side tool can be useful for PAD screen in patients with ischemic heart disease, diabetes mellitus and chronic kidney disease.

LIST OF ABBREVIATIONS

ABI	**:**	Ankle / Brachial Index
ACC	**:**	American Colleague of Cardiology
ACE	**:**	Angiotensin-converting enzyme
ACS	**:**	Acute Coronary Syndrome
AHA	**:**	American Heart Association
AMI	**:**	Acute myocardial infarction
CABAG	**:**	Coronary Artery Bypass And Grafting
CAD	**:**	Coronary artery disease
CCU	**:**	Cardiac care unite
CKD	**:**	Chronic Kidney Disease
CRP	**:**	C-reactive protein
CTA	**:**	Computed Tomography Angiography
CVD	**:**	Cardio vascular disease
DM	**:**	Diabetes mellitus
ECG	**:**	Electrocardiogram
EPIC	**:**	European Prospective Investigation into Cancer
ESRD	**:**	End-Stage Renal Disease
FFA	**:**	Free fatty acids
GFR	**:**	glomerular filtration rate
HDL	**:**	high density lipoprotein
HOPE	**:**	Heart Outcomes Prevention Evaluation
IDDM	**:**	Insulin dependent diabetes mellitus
IHD	**:**	Ischemic heart disease
IL	**:**	Interlukin

IR	**:**	Insulin resistance
LDL	**:**	Low density lipoprotein
LVH	**:**	Left ventricular hypertrophy
LVH	**:**	Left Ventricular Hypertrophy
MONICA	**:**	Multinational Monitoring of Trends and Determinants in Cardiovascular Diseas
MRA	**:**	Magnetic Resonance Angiography
NCEP	**:**	National Cholesterol Education Program
NCEP	**:**	National Cholesterol Education Panel
NIDDM	**:**	Non insulin dependent diabetes mellitus
Non STEMI	**:**	Non ST elevation myocardial infarction
NOS	**:**	Nitric oxide synthase
PAD	**:**	Peripheral Arterial Disease
PAI-1	**:**	Tissue plasminogen activator inhibitor type 1
PCI	**:**	Percutenous Coronary Intervention
PREVEND-IT	**:**	Prevention of Renal and Vascular Endstage Disease Intervention Trial
PVRs	**:**	Pulse-Volume recordings
STEMI	**:**	ST elevation myocardial infarction
tHcy	**:**	Total homocysteine
tPA	**:**	Tissue plasminogen activator
VLDL	**:**	Very low density lipoprotein
VSMC	**:**	Vascular Smooth Muscle Cell

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INTRODUCTION

Peripheral artery disease (PAD) describes the pathologic states that lead to stenosis and aneurysm in noncoronary arterial circulation.

Atherosclerosis is the most common cause of lower extremity (PAD). Traditional risk factor include age, smoking, hyperlipidemia, hypertension, and diabetes mellitus. Other risk factor include elevated markers of inflammation such as C- reactive protein, fibrinogen, and interlukin (IL-6), hypercoagulable state, possibly genetic predisposition and chronic kidney disease**.(Eric j. topol et al 2009)**

Nephropathy is associated with increased risk of cardiovascular morbidity and mortality **(johensen et al. 1999, Hillege et al 2002)** as well as high–risk populations including diabetic patients **(Valmadrid et al 2000)** and those with known hypertension and left ventricular hypertrophy **(Wachtel K. et al 2003)**

Nephropathy has been shown to be associated with higher carotid intima–medial thickness in diabetic subjects **(Mykanen L. et al 1997)** and this may explain the relationship between nephropathy and generalized early atherosclerotic disease and

atherosclerotic peripheral arterial disease **(**PAD**)** of the lower extremities.

Most epidemiologic studies have shown an increased risk of **(**PAD) in patients with chronic kidney disease **(Wattankit K. et al 2007, O'Hare IS et al 2004).**

Cardiac diseases accounts for the majority of deaths in patients with (PAD), in whom the relative risk of death from cardiac causes is increased more than six fold.

Approximately one-third to one-half of all patients of (PAD) will have concomitant coronary artery disease and thus (PAD) is considered a coronary artery disease risk equivalent. **(Eric j. topol et al 2009)**

AIM OF THE WORK

The study is aiming at evaluating the relationship between creatinine clearance and presence of lower limb arterial disease in diabetic ischemic heart disease patients.

REVIEW

DIABAETIC NEPHROPATHY

Diabetic nephropathy is the leading cause of end-stage renal disease (ESRD) in the United States, accounting for nearly 40% of incident ESRD (**USA National Institutes of Health annual report, 2002**). Diabetes mellitus (DM) is also an independent and strong risk factor for ESRD ascribed to causes other than diabetes **(Brancati FL et al 1997**), such as hypertension, pyelonephritis, and other forms of glomerulopathies that can lead to chronic renal disease. Diabetic nephropathy is a major microvascular complication of both type 1 and type 2 diabetes.

Between 35% and 57% of type 1 diabetics (**Andersen AR et al 1983, Hasslacher C et al 1989, Rossing P et al 1995**,) and 25% and 46% of type 2 patients with long-lasting diabetes (**Hasslacher C et al 1989**, **Melton L Jr, et al. 1988**), develop clinically detectable nephropathy, indicated by proteinuria and/or renal insufficiency. In fact, the prevalence of proteinuria is the same in both types of diabetes, after adjustment for differences in diabetes duration(**Hasslacher C et al 1989**, **Stephenson JM et al 1995**).

Crossectional studies indicate that 20% of type 2 DM have microalbuminuria, many at the time diabetes is diagnosed. The prevalence increases to nearly 50% in those with advanced retinopathy (**Delcourt C et al 1996**). Approximately 2–3% of patients with type 2 diabetes progress to overt proteinuria yearly (**Adler AI et al 2003**).

PATHOGENESIS:

Recent large-scale intervention trials have provided compelling evidence for the role of hyperglycemia in the development and progression of nephropathy in type 1 and type 2 diabetes ((**UKPDS) Group. Lancet 1998**). However the fact that only a proportion of individuals with diabetes develop nephropathy suggests that factors other than the hyperglycemic environment are involved in the pathogenesis of nephropathy. Genetic, ethnic, and familial factors may also play significant roles in the development of nephropathy.

Recent investigations have identified a number of candidate gene polymorphism that may contribute to diabetic nephropathy. The angiotensin-converting enzyme (ACE) gene variant with a deletion (D) of a 287 base pair sequence is one such polymorphism.