Atherogenic Index of Plasma as a Predictor of Atherosclerosis in Hemodialysis Patients

Thesis

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By

Eman Magdy Abdellatif Hegazy

M.B., B. Ch, Faculty of Medicine, Ain Shams University

Under Supervision of

Prof. Dr. Osama Mahmoud Mohammad Kamal

Professor of Internal Medicine and Nephrology

Faculty of Medicine - Ain Shams University

Ass. Prof. Dr. Hussien Sayed Hussien

Assistant Professor of Internal Medicine and Nephrology

Faculty of Medicine - Ain Shams University

Faculty of Medicine
Ain Shams University
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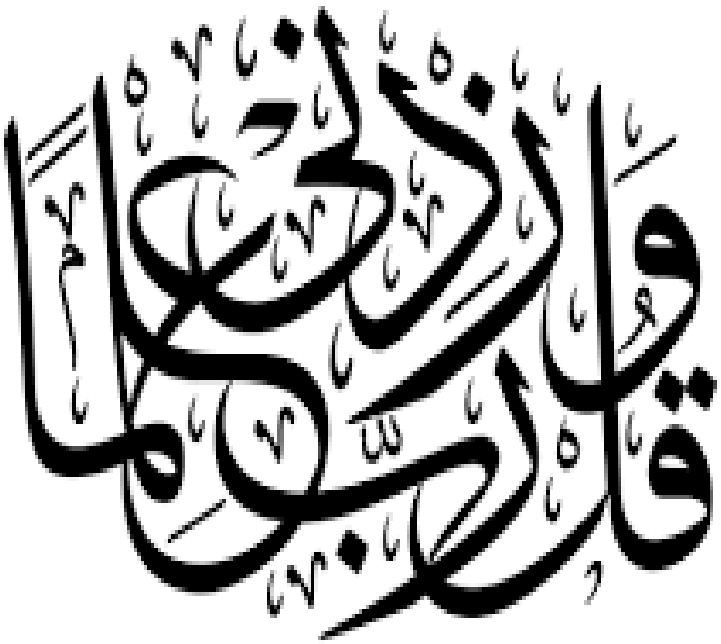
وقل رب زدني علما

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Eman Magdy

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List of Abbreviations

Abb.	Full term
ACEIs	Angiotensin converting enzyme inhibitors
ACR	Albumin creatinine ratio
ADMA	Asymmetric dimethyl arginine
AIP	Atherogenic index of plasma
AKI	Acute kidney injury
Apo B	Apolipoprotein B
ApoA-1	Apolipoprotein A-1
ARBs	Angiotensin 2 receptor blockers
ARF	Acute renal failure
ASCVD	Atherosclerotic cardiovascular disease
BMI	Body mass index
BUN	Blood urea nitrogen
CAC	Coronary artery calcium
CAD	Coronary artery disease
CETP	Cholesteryl ester transfer protein
CHD	Coronary heart disease
CI	Confidence interval
CIMT	Carotid intima media thickness
CKD	Chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CKD-MBD	Chronic kidney disease – mineral bone disorder
CRP	C-reactive protein
CV	Cardiovascular

Abb.	Full term
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DM	Diabetes mellitus
eGFR	Estimated glomerular filtration rate
ELISA	Enzyme-linked immunosorbent assay
ESRD	End-stage renal disease
FGF-23	Fibroblast growth factor 23
GFR	Glomerular filtration rate
HD	Hemodialysis
HDL-C	High density lipoprotein cholesterol
hs-CRP	Serum high sensitivity C-reactive protein
ICAM	Intercellular adhesion molecule
IDL	Intermediate density lipoprotein
IL	Interleukin
IMT	Intima media thickness
iPTH	Intact parathyroid hormone serum level
IRS1	Insulin receptor substrate1
KDIGO	Kidney Disease, Improving Global Outcomes
KDOQI	Kidney Disease Outcomes Quality Initiative
LCAT	Lecithin cholesterol acyltransferase
LDL-c	Low density lipoprotein cholesterol
LDL-p	Low density lipoprotein particle
Lp(a)	Lipoprotein (a)
LPL	Lipoprotein lipase
Lp-PLA2	Lipoprotein-associated phospholipase A_2

Abb.	Full term
LRP	Low density lipoprotein receptor-related protein
MBDs	Mineral and bone disorders
MCP	Monocyte chemotactic protein
MDRD	Modification of diet in renal disease
MI	Myocardial infarction
MIA	Malnutrition–inflammation–atherosclerosis complex
MRI	Magnetic resonance imaging
mtDNA	Mitochondrial DNA
NO	Nitric oxide
non-HDL-c	Non-high-density lipoprotein cholesterol
ox-LDL	Oxidized low density lipoprotein
PP	Pulse pressure
PWV	Pulse wave velocity
ROS	Reactive oxygen species
RR	Relative risk
RRT	Renal replacement therapy
SBP	Systolic blood pressure
TG	Serum triglycerides
TNF-α	Tumor necrosis factor alpha
URR	Urea Reduction Ratio
VCAM-1	Vascular cell adhesion molecule-1
VLDL	Very low-density lipoprotein

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Introduction

Nowadays, chronic kidney disease (CKD) is recognized as a worldwide health problem with high morbidity and mortality rates, putting a significant burden on the global resources. The prevalence of CKD in the western countries is near 13%. Recent data estimate the number of patients that have end-stage renal disease (ESRD) to be more than 2 million patients all over the world ***(Sathyan et al., 2017).***

In Egypt, the estimated annual incidence of ESRD is around 74 per million and the total prevalence of patients on dialysis is 264 per million ***(Ahmed et al., 2010).***

According to KDIGO and KDOQI guidelines, CKD is defined as a heterogeneous group of disorders characterized by alterations in kidney structure and function, lasting for three months or more. The term "end-stage renal disease" refers to chronic kidney failure treated with either dialysis or transplantation ***(National Kidney Foundation, 2002)***.

CKD is recognized as an independent risk factor for numerous adverse health outcomes including cardiovascular disease (CVD) which is the most common

cause of morbidity and mortality in ESRD patients. In the western countries, data showed that CVD are responsible for hospitalizations and deaths in 40% and 50% of ESRD patients respectively. Most of CKD patients die due to CVD even before developing ESRD and beginning dialysis ***(Hamad et al., 2012)***.

CVD manifestations in CKD patients are classified as myocardial (left ventricular hypertrophy and dilated cardiomyopathy) and vascular (vascular calcification, arteriosclerosis and atherosclerosis) ***(Sarnak, 2003).***

Atherosclerosis is the most common risk factor for CVD. It begins years before the development of any clinical manifestations. It is considered as a complex inflammatory fibroproliferative response developing due to accumulation of the atherogenic lipoproteins in the arterial intima ***(Weber and Noels, 2011).***

The first structural change that can be detected in atherosclerosis is an increase in intima-media thickness (IMT) of the artery. Studies have shown that hemodialysis (HD) patients have advanced changes in the walls of their arteries, that present as increased IMT of the carotid and femoral arteries ***(Amann et al., 2003).***

Carotid intima-media thickness (CIMT) is a widely available, safe, and reproducible measure when performed by trained and certified sonographers with standardized equipment. IMT was measured for the first time by Pignoli using B-mode ultrasound in 1986. CIMT is measured by obtaining longitudinal images of the carotid arterial walls using duplex ultrasound ***(Naqvi and Lee, 2014)***.

In many studies, CIMT was proven to predict the existence of CVD. Increased CIMT was discovered to be a marker of diffuse atherosclerosis and so, increased CIMT may determine individuals at high risk for coronary artery disease (CAD). As a result of these numerous studies, CIMT was introduced as a golden parameter in detection of atherosclerosis even in its early stages ***(O'Leary and Polak, 2002)***.

One of the other traditional parameters that is well known in detection of atherosclerosis is the lipid profile. It consists of a group of biochemical tests which are used in prediction, diagnosis and treatment of lipid-related disorders including atherosclerosis ***(Weber and Noels, 2011).***

There is a lot of evidence that the concentrations of lipids {total cholesterol and triglycerides (TG)} and their

associated blood transporting lipoproteins {Low density lipoprotein cholesterol (LDL-c), high density lipoprotein cholesterol (HDL-c) and very low-density lipoprotein cholesterol (VLDL-c)} are related with the occurrence of atherosclerosis and CVD ***(Cummings, 2003)***.

For example, a strong association was found between the risk of atherosclerosis, high levels of LDL-c and low levels of HDL-c. Additionally, a lot of work has been done on the relationship between TG and HDL-c, and it was found that the ratio of TG to HDL-c is a strong predictor of CVD ***(Gaziano et al., 1997, Igweh et al., 2005)***.

The atherogenic index of plasma (AIP), calculated as {log (TG/HDL-c)}, has recently started to gain attention as a significant indicator of the risk of atherosclerosis and CVD. It is even more suitable and statistically reliable than lipid concentrations in CVD risk prediction ***(Cai et al., 2017).***

The association of TGs and HDL-c in this simple ratio theoretically reflects the balance between risk and protective lipoprotein forces, and both TGs and HDL-c are widely measured and available ***(Acay et al., 2014)***.

In this study, we are trying to discover the correlation between CIMT and AIP in hemodialysis

patients in particular which could result, if found positive, in using AIP as an easy to apply, inexpensive and most importantly a non-invasive test for diagnosis of subclinical atherosclerosis in this particular group of patients so as to proceed in prevention of atherosclerosis or in deceleration of its progression, thus decreasing CV morbidity and mortality.

Aim of the Work

The aim of this study is to detect the correlation between atherogenic index of plasma and carotid intima-media thickness as an indicator of subclinical atherosclerosis in haemodialysis patients.