Association between Serum Asymetrical Dimethylarginine Level and Cardiac Functions in Chronic kidney Disease Patients

Thesis

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List of Abbreviations

Abb.	Full term
ACE-2	*Angiotension –converting enzyme 2*
ACE-I	*Angiotension –converting enzyme inhibitor*
ACR	*Albumin/creatinine ratio*
ADMA	*Asymetrical Dimethylarginine*
AF	*Atrial fibrillation*
AKI	*Acute Kidney disease*
ARBs	*Angiotensin receptors antagonist*
BMI	*Body mass index*
BP	*Blood pressure*
BUN	*Blood urea nitrogen*
BWT	*Body weight*
CBC	*Complete Blood Picture*
CKD	*Chronic kidney disease*
CKD-MBD	*Chronic kidney disease-mineral bone disorder*
COX2	*Cyclooxygenase 2*
CRP	*C-reactive protein*
CVD	*Cardiovascular disease*
DD	*Diastolic Dysfunction*
DDAH	*Dimethylarginine Dimethylaminohydrolase*
DHF	*Diastolic heart failure*
DM	*Diabetes mellitus*
DMSA	*Dimercaptuosuccinic acid*
DN	*Diabetic nephropathy*
e GFR	*Estimated glomerular filtration*
EF	*Ejection fraction*
ERK	*Extracellular signal-regulated kinases*
ESAs	*Erythropoietin –stimulating agents*
ESRD	*End stage renal disease*
ETRA	*Endothelin receptor antagonist*
FGF-23	*Fibroblastic growth factor 23*
GFR	*Glomerular filtration rate*
GN	*Glomerulonephritis*

List of Abbreviations **cont...**

Abb.	Full term
HD	*Hemodialysis*
HF	*Heart failure*
HTN	*Hypertension*
IGFs	*Insulin- like growth factors*
IVSD	*Inter ventricular septum diameter*
JAK	*Janus kinase*
LAD	*Left Atrial Diameter*
LVH	*Left Ventricular Hypertrophy*
LVMI	*Left Ventricular Mass Index*
NO	*Nitric oxide*
PI3K	*Phosphatidylinositol-3 kinase*
PRMTs	*Protein arginine N-methyltransferases*
PTH	*Parathyroid hormone*
RAAS	*Renin-Angiotensin –Aldosterone system*
RAS	*Renin –Angiotensin system*
RCT	*Randomized clinical trial*
ROD	*Renal osteodystrophy*
RRT	*Renal replacement therapy*
SHPT	*Secondary hyerparathyrodism*
STAT	*Signal transducer and activators of transcription*
TDI	*Tissue Doppler Imaging*
TNF	*Tumor necrosis factor*
UF	*Ultrafiltration*
US	*Ultrasonography*
VDR	*Vitamin D receptor*
VEGF	*Vascular endothelial growth factor*
VLDL	*Very low density lipoprotein*
VSMCs	*Vascular smooth muscle cells*

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Abstract

Background: Chronic kidney disease (CKD) is a major public health problem worldwide and is associated with a considerable increase in morbidity and mortality, cardiovascular disease is most common cause of death among chronic kidney disease patients.

Objectives: The aim of study was to determine the association between serum ADMA level and cardiac functions assessed by tissue Doppler imaging in chronic kidney disease patients.

Patients and methods: our study conducted on 90 patients from outpatient clinic or inpatient department of national institute of nephrology and urology. All patients were subjected to full history, full clinical examination, laboratory investigations including: serum urea, serum albumin, complete blood picture, serum electrolytes (calcium and phosphorus), PTH, serum ADMA, lipid profile and echocardiography and Tissue Doppler imaging.

Results: 90 patients were included in the study. Each group consisted of 30 patients stage 3, 4, and, 5 non-dialysis patients. Mean age of stage 3, stage 4, and stage 5 non-dialysis CKD patients were respectively 42.33 years, 39.77 years and 38.67 years. The mean levels of ADMA in stage 3, stage 4, and 5 were 12701 ng/mL, 14853 ng/mL, and18481 ng /mL respectively. Analysis of the differences between the groups showed significant differences in ADMA levels (p=0.037), as ADMA level increase with progression of disease.

Conclusion: Serum ADMA is negatively correlated with diastolic function among CKD patients,, Tissue Doppler imaging is more accurate than echocardiography to estimate diastolic function.

Key words: ADMA, Diastolic Dysfunction, Tissue Doppler imaging.

INTRODUCTION

Chronic kidney disease (CKD) has been considered one of the risk factors of cardiovascular disease, and even minor to moderate renal insufficiency has been reported to be associated with adverse cardiovascular events. Furthermore, in CKD patients, cardiovascular disease is the major cause of death, which cannot be entirely explained by the clustering of the traditional cardiovascular risk ***(Rahman et al., 2014).***

Asymmetric dimethylarginine (ADMA) is a naturally occurring modified amino acid in human blood. It inhibits the production of nitric oxide, a key regulator of the vascular tone, and may thereby contribute importantly to the process of atherosclerosis. ADMA has been shown to correlate with various measures of subclinical atherosclerosis, including carotid intima-media thickness and flow-mediated dilatation. Additionally, a growing number of studies suggest that high values of circulating ADMA concentration are associated with the incidence of cardiovascular disease (CVD) outcomes ***(Fliser et al., 2005).***

Nitric oxide deficiency may occur in patients with chronic kidney disease and may contribute to accelerate progression of chronic kidney disease, hypertension and cardiovascular complications. An increase of endogenous nitric oxide inhibitors like asymmetric dimethylarginine seems to play a major role in this process.. Asymmetric dimethylarginine

accumulation predicts both accelerated renal function loss and death in patients with chronic kidney disease and incident cardiovascular complications in CKD patients ***(Zoccali et al., 2001).***

According to studies, high ADMA levels predicted more accelerated course of renal function loss and promoted the development of renal damage due to the fact that it triggered glomerular hypertension, endothelial damage, salt accumulation, and cell senescence ***(Ravani et al., 2005).***

There are some possible molecular mechanisms of ADMA involvementin renal impairment ***(Matsuguma et al., 2006).***

AIM OF THE WORK

To evaluate the relationship between plasma asymmetric dimethyl arginine (ADMA) levels and the myocardial function assessed by tissue doppler imaging in the CKD population.

Chapter (1)

CHRONIC KIDNEY DISEASE (CKD)

Chronic kidney disease (CKD) is a type of kidney disease in which there is gradual loss of kidney function over a period of months to years. Initially there are generally no symptoms; later, symptoms may include leg swelling, feeling tired, vomiting, loss of appetite, and confusion. Complications include an increased risk of heart disease, high blood pressure, bone disease, and anemia ***(Liao, 2012).***

Signs and symptoms

CKD is initially without symptoms, and is usually detected on routine screening blood work by either an increase in serum creatinine, or protein in the urine. As the kidney function decreases***:***

- **Blood pressure** is increased due to fluid overload and production of vasoactive hormones created by the kidney via the renin–angiotensin system, increasing the risk of developing hypertension and heart failure**.**
- **Urea** accumulates, leading to azotemia and ultimately uremia (symptoms ranging from lethargy to pericarditis and encephalopathy). Due to its high systemic concentration, urea is excreted in eccrine sweat at high concentrations and crystallizes on skin as the sweat evaporates (uremic frost).