بسم الله الرحمن الرحيم

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Fibroblast Gross Factor-23 and Carotid Artery Stiffness in Hemodialysis Patient

Thesis

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By

Salwa Yasser MohamMed Ali
(M.B.B.C.h.,)

Under Supervision Of

Prof. Dr. Hisham Mohamed Atef Abu Al-Layl
Professor of Internal Medicine and Nephrology Faculty of Medicine- Ain Shams University

Dr. Khaled Gouda Abdel Wahab
Lecturer of Internal Medicine and Nephrology Ain Shams University- Faculty of Medicine

Faculty of Medicine
Ain Shams University
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Salwa Yasser Mohammed Ali

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List of Abbreviations

Abb.	Full term
ABI	*Ankle - brachial index*
AC	*Arterial compliance*
ACEIs	*Angiotensin Converting Enzyme Inhibitors*
AD	*Aortic distensibility*
ADHR	*Autosomal dominant hypophosphatemic rickets*
AIx	*Augmentation index*
ARBs	*Angiotensin 2 Receptor Antagonists*
ARHR	*Autosomal recessive hypophosphatemic rickets*
CAD	*Coronary artery disease*
CaSRs	*Calcium-sensing receptors*
CCIMT	*Common carotid intima media thickness*
Chr 12p13	*Chromosome 12p13*
CKD	*Chronic Kidney Disease*
CKD-MBD	*Chronic Kidney disease – mineral bone disorder*
CTA	*Computed tomographic angiography*
CVD	*Cardiovascular Disease*
CYP24A1	*Cytochrome p450 subfamily A member (Protein coding)*
CYP27B1	*Cytochrome p450 subfamily B member (Protein coding)*
DMP-1	*Dentin matrixprotein-1*
eGFR	*Estimated glomerular filtration rate*
ELISA	*Enzyme-Linked Immunosorbent Assay*
ESRD	*End-stage Renal Disease*
FD	*Fibrous dysplasia*
FGF	*Fibroblast growthfactor*
FGF-23	*Fibroblast growth factor 23*
FGF23-R	*Fibroblast growth factor 23-receptor*
GFR	*Glomerular Filtration Rate*

List of Abbreviations (Cont...)

Abb.	Full term
HRP	*Horseradish Peroxidase*
IMT	*Intima media thickness*
iPTH	*Intact Parathyroid Hormone Serum Levels*
KD	*Kilo Dalton*
LL37	*The only human member of cathelicidin family of antimicrobial peptides*
LRNc	*Lipid rich necrotic core*
MEPE	*Matrix Extracellular Phosphoglycoprotein*
MRI	*Magnetic resonance imaging*
mRNA	*Messenger Ribonucleic Acid*
PCR	*Polymerase chain reaction*
PET	*Positron emission tomography*
PP	*Pulse pressure*
PWV	*pulse wave velocity*
S.Ca	*Corrected Serum Calcium*
S.Creat.	*Serum Creatinine*
S.Po4	*Serum Phosphorous*
SAC	*Systemic arterial compliance*
TCD	*Trans cranial Doppler*
TIO	*Tumor induced osteomalacia*
URR	*Urea Reduction Rate*
VC	*Vascular calcification*
VDRs	*Vitamin D receptors*
XLH	*X -linked hypophosphatemia*

ABSTRACT

Background: FGF23 is a free circulating hormone secreted by osteocytes affecting mainly phosphate metabolism as it inhibits its renal tubular reabsorption by suppressing the expression of luminal sodium-phosphate co –transporters (Na Pi).

Aim of the Work: Aim of study is to verify the usefulness of FGF23 as a marker for diagnosis of arterial stiffness in CKD patients on regular hemodialysis (3 sessions per week, 4 hours each).

Patients and Methods: The present study enrolled 30 living end stage renal disease patients on regular hemodialysis randomly slected from hemodialysis unit at Ain Shams university hospitals after exclusion of patients of known cardiovascular disease or ischemic heart disease,also patients of age below 18 years and above 50 years were excluded as well as patients having arterio venous fistulas on both arms. All patients were subjected to complete medical history taking, including (Age, Sex, Etiology of chronic kidney disease, drugs and duration of dialysis), and detailed clinical examination was done.

Results: In this study patients have elevated serum levels of FGF-23 ranging from 100 up to 700 pg/ml. when the normal refrence range is 18-108 pg/ml. Also our study result revealed a statistical significance of negative correlation between FGF-23 and diabetes mellitus duration, serum phosphorous, corrected calcium and estimated glomerular filtration rate as well. The current study shows statistical correlation of positive significance between FGF-23 and hypertension duration where, common carotid artery intima media thickness as well as present plaques in common carotid artery. Moreover there is no statistical significant correlation between FGF-23 and pulse pressure.

Conclusion: FGF23 serum levels are markedly elevated in chronic kidney disease CKD and among patients on regular hemodialysis causing arterial stiffness.

Keywords: Fibroblast Gross Factor-23; Carotid Artery Stiffness; Hemodialysis

INTRODUCTION

Fibroblast growth factor 23 (FGF-23) is a circulating osteocyte derived hormone that is often seen in elevated serum concentrations in patients with advanced chronic kidney disease (CKD) ***(Gutierrez et al., 2005).***

Fibroblast growth factor 23 (FGF-23) plays a key role in regulating serum phosphorous concentration by promoting phosphorous excretion and inhibiting 1 alpha hydroxylase in the renal proximal tubule ***(Burnett et al., 2006).***

FGF-23 requires its co-receptor which is a Klotho-receptor to bind to target tissue and exert its biological effects and most studies have showed that there is no expression of Klotho-receptor in human vascular cells as the one done by ***(Scialla et al., 2013 and Lindberg et al., 2013).***

However, there is a study suggested that, the expression of Fibroblast growth factor-23 (FGF-23) may be induced by vitamin D.receptor activator in human aortic smooth muscle cells as demonstrated by ***(Lim et al., 2012).***

Elevated serum Fibroblast growth factor-23 (FGF-23) is associated with cardiovascular disease (CVD), yet the mechanism remain uncertain Since, FGF-23 is integral in regulating phosphorous and vitamin D. metabolism, not only it responds to increased serum phosphorous, but it may also induce arterial calcification and stiffness as demonstrated by

several studies like the one done by ***(Jeffry et al., 2014)*** and also there are many previous studies like those done by ***(Nasrallah et al., 2010 and Desfardins et al., 2012)*** that, have observed associations of elevated serum Fibroblast growth factor 23 (FGF-23) with arterial calcification and stiffness.

However the study done by ***(Scialla et al., 2013)*** revealed that Fibroblast growth factor-23 FGF23 is not associated with and does not induce arterial calcification.

Multiple community- based studies have demonstrated associations between measures of increased arterial stiffness ***(Peralta et al., 2012)*** and high ankle - brachial index (ABI) ***(OH et al., 2006)*** with increased cardiovascular morbidity and mortality, as well as incident hypertension, coronary heart disease, stroke, heart failure and kidney function decline

Aim of the Work

Aim of study is to verify the usefulness of FGF23 as a marker for diagnosis of arterial stiffness in CKD patients on regular hemodialysis (3 sessions per week, 4 hours each).