A Study on,
The role of fibroblast growth factor 23 in mineral homeostasis and vascular calcifications in patients with acute renal failure
Thesis

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by

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Abstract

This study was performed on 53 patients from Kasr El Aini University hospital , Internal Medicine and Nephrology Department.

The patients were divided into 3 groups:-Group 1:-17 patients with acute renal failure, Group 2:- 27 patients non-diabetic with CRF on regular hemodialysis for at least 6 months, Group 3:- 9 controls with normal renal functions.

Each patient was subjected to full history taking, full clinical examination and laboratory investigations including:-

(S.creatinine, Bl.urea, S.calcium, S.phosphorus, P.T.H, S.cholesterol, S.triglyceride, S.albumin , and F.G.F.23{fibroblast growth factor 23}) and non contrast CT abdomen and A.C.I. was measured.

FGF23 levels showed significant difference between the studied groups as in ARF=2498.8±1669.1,CRF=6030±4141.5 and controls=95.8±52.3 with significant P-value=0.0001.

Also ACI showed significant difference between the studied groups as in ARF=4.1±9.0,CRF=15.5±10.2 and controls=3.7±3.8 with significant P-value=0.001.

In multiple regression analysis showed ACI correlated with FGF 23 in ARF with significant P-value=0.014 and CRF with significant P-value=0.004.

We concluded that there is strong positive relationship between FGF23 and ACI. This positive correlation may open the gate for routine estimation of this agent as a surrogate marker of arterial calcification.

- **Key words: CRF – FGF 23 –ACI--PTH**

Dedications

I dedicate this work to my family, especially to
My dear ***father*** *who gave me support and*
to my loving ***mother*** *who always shows so much*
Care, aid and patience.

I dedicate this work also to all my dear professors
From whom I learned as well as for all my sincere
Friends who support me.

Lastly, my dedication and appreciation go to all
The wonderful patients I treated over the past
Years, who, despite illness found it in their
Hearts to pray selflessly for my
Good health.

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List of abbreviations

$1,25(OH)_2D$	**1,25-dihydroxyvitamin D**
ACC	**The American College of Cardiology**
ACEI	**Angiotensin Converting Enzyme Inhibitor.**
ACI	**aortic calcification index**
ADA	**The American Diabetes Association.**
ADHR	**Autosomal dominant hypophosphatemic rickets**
ADMA	**Asymmetrical diethylarginine**
AHA	**American Heart Association**
ANZ	**The Australia and New Zealand**
ARF	**Acute renal failure**
ARHR	**Autosomal recessive hypophosphatemic rickets**
AVG	**Arteriovenous grafts**
BMP	**Bone mo Bone morphogenetic protein**
CAC	**Coronary artery calcium**
C-ANCA	**Cytoplasmic antineutrophil cytoplasmic antibody.**
CKD	**Chronic kidney disease**
CORES	**Control de la Osteodistolia Renal en Sudamérica)**
CrCl	**Creatinine clearance**
CRF	**Chronic Chronic renal failure**
CRP	**C-reactive protein**
CV	**Cardio Vascular**
DDAH	**Dimethylarginine dimethylaminohydrolase**
DM	**Diabetes mellitus**
DMP1	**Dentin matrix protein 1**

EBCT	**Electron Beam Computed Tomography**
eNOS	**Endothelial NO synthase**
ESRD	**End stage renal disease**
FGF23	**Fibroblast growth factor 23**
FSGS	**Focal and segmental glomerulosclerosis**
GFR	**Glomerular filtration rate**
HbA1C	**Glycosylated Hemoglobin**
HD	**Hemodialysis**
HFTC	**Hyperphosphatemic familial tumoral calcinosis**
HIV	**Human Immunodeficiency Virus**
HOPE	**Heart out comes prevention evaluation**
HSMC	**Human smooth muscle cell**
HUS	**Hemolytic-uremic syndrome**
IL	**Interleukin**
IVUS	**Intravascular ultrasound**
K/DOQI	**The Kidney Disease Outcomes Quality Initiative**
LAV	**Left atrial volume**
LIFE	**Losartan Intervention For Endpoint reduction in hypertension**
LVH	**Left ventricular hypertrophy**
LVMI	**Left ventricular mass index**
MEPE	**Matrix extracellular phosphoglycoprotein**
MGP	**Matrix Gla protein**
MV	**Microvesicles**
MWFS	**Midwall fractional shortening**
NHANES III	**Third National Health and Nutrition Examination Survey**
NKF	**National Kidney Foundation**
NO	**Nitric oxide**
$O_{2}^{\cdot-}$	**Superoxide anion radical**
OPN	**Osteopontin**
P-ANCA	**Perinuclear pattern antineutrophil cytoplasmic antibody**
Phex	**Phosphate-regulating endopeptidase homolog, X-linked.**

PRMT	**protein methyltransferase**
PTH	**parathyroid hormone**
PTHrP	**Parathyroid hormone-related peptide**
PWV	**Pulse wave velocity**
RANK	**Receptor activator of NF alpha B**
RVR	**Renal vascular resistance**
SCT	**Spiral Computed Tomography**
sFRP4	**Secreted frizzled-related protein 4**
SIBLING	**Small integrin binding ligand N-linked glycoprotein**
TGF-β	**Transforming growth factor–β**
TIO	**Tumor-induced osteomalacia**
TmP	**Maximal tubular reabsorption of phosphate (TmP**
TNF	**Tumor necrosis factor**
TTP	**Thrombotic thrombocytopenic purpura**
US	**United STATES**
USRDS	**The United States Renal Data System**
VC	**Vascular calcification**
VSMC	**Vascular smooth muscle cell**
XLHR	**X-linked hypophosphatemic rickets**

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INTRODUCTION AND AIMS OF STUDY

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The kidney plays a major role in the regulatory system for bone and mineral metabolism.

In chronic kidney disease various abnormalities in this regulatory system occur ,including hyperparathyroidism and reduction in the 1 α hydroxylation of vitamin D these changes affect bone mineralization and may also increase the risk of metastatic calcification of soft tissue especially blood vessels (**Fukagawa et al.,2006**).

Fibroblast growth factor 23 (FGF23) is a recently discovered circulating factor that reduces serum phosphate levels, inhibits 1α hydroxylation of vitamin D and inhibits soft tissue calcification (**Razaqque et al., 2005**).

It was recently suggested that elevated levels of FGF23 in renal failure patients established on hemodialysis may have a protective role in prevention of vascular calcifications (**Inalia, et al 2006**) however, the interaction between FGF23,vitamin D and soft tissue calcification is not completely elucidated (**Razzaqque et al., 2005**).

The effect of FGF23 in ESRD patients, who not yet put on hemodialysis schedule and the extent of soft tissue calcification, are not yet clear (**Tanwaki et al., 2005**).