# Fibroblast Gross Factor-23 and Arterial Stiffness in Hemodialysis Patient

#### Thesis

Submitted for partial fulfillment for Master Degree in Internal Medicine

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## Aeknowledgment |

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## **Contents**

<b>Subjects</b> P	age
List of Abbreviations	I
List of Tables	
List of Figures	
• Introduction	
Aim of the Study	3
• Review of literature	
Chapter (1): Fibroblast Growth Factor 23 (FG	GF23)4
Chapter (2): Chronic Kidney Disease (CKD)	17
Chapter (3): Arterial Stiffness	33
Patients and Methods	48
• Results	61
• Discussion	77
• Summary	86
• Conclusion	90
Recommendations	92
• References	93
Arabic summary	

## List of Abbreviations

**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

**CaSRs** : Calcium-sensing receptors

**CAD** Coronary artery disease

**CCIMT**: Common carotid intima media thickness

**Chr** : Chromosome 12p13

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 1

(Protein coding)

CYP27B1 : Cytochrome p450 subfamily B member 1

(Protein coding)

#### 🕏 List of Aberrations 🗷

**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

**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

#### E List of Aberrations &

**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

## **List of Tables**

Table	Title	Page
1	Stages of CKD by GFR and albuminuria	18
	category	
2	Demographic data	61
3	Etiology of chronic kidney disease (CKD).	62
4	Demographic data	63
5	Renal function and hemoglobin level and	64
	other lab investigations results.	
6	Serum levels of Fibroblast Growth Factor -	65
	23 (FGF-23) (Pg/l)	
7	Showing the percentage of present to absent	66
	plaques in Common Carotid artery.	
8	Showing the relation between Fibroblast	67
	Growth Factor-23 (FGF-23) and absence or	
	presence of Plaques in the common carotid	
	artery.	
9	Showing the range and mean together with	69
	standard deviation of FGF23, pulse pressure	
	and common carotid artery intima media	
	thickness.	
10	The relation Between Fibroblast Growth	70
	Factor-23 (FGF -23) and parameters of	
	arterial stiffness together with dialysis	
	parameters.	

## 🕏 List of Tables 🗷

Table	Title	Page
11	Demographic data.	71
12	The relation between Fibroblast Growth	72
	Factor-23 (FGF -23) and dialysis	
	parameters.	

## List of Figures

Fig.	Title	Page
1	The FGF-23 bone–kidney axis	7
2	Spectrum of FGF23 level in CKD	12
3	The causes and consequences of arterial	35
	stiffness.	
4	Logiq 7 ultrasound	56
5	Normal view of common carotid artery.	58
6	Showing present pleques at common carotid	59
	artery bulb.	
7	Showing intime media thickness of 1.2 mm	59
	of common carotid artery.	
8	Showing the female to male ratio.	61
9	Etiology of CKD of participants in our	62
	study, as shown hypertension followed by	
	diabetes mellitus are the commonest cause	
	for CKD among participants.	
10	Showing percentage of serum levels of	65
	Fibroblast Growth Factor -23 (FGF-23)	
	among participants in our study so 36.7% of	
	them had a (FGF-23) level between 300-400	
	(pg/l).	
11	Showing that more than half of the	66
	participants had plaques in their common	
	carotid artery.	

## 🕏 List of Figures 🗷

Fig.	Title	Page
12	Showing that >65%OF patients had serum	67
	FGF-23 level OF300-400 Pg/l.	
13	Showing that as the level of FGF (23)	68
	increases the more present plaques.	
14	Scatter gram of the correlation between	70
	Fibroblast Growth Factor-23 (FGF -23)	
	serum levels and serum calcium levels	
	(negative correlation)	
15	Scatter gram of the correlation between	71
	Fibroblast Growth Factor-23 (FGF -23) and	
	Hypertension duration (positive	
	correlation).	
16	Scatter gram of the correlation between	72
	Fibroblast Growth Factor-23 (FGF -23)	
	serum levels and Diabetes Mellitus	
	durations (negative correlation).	
17	Scatter gram of the correlation between	73
	Fibroblast Growth Factor-23 (FGF -23)	
	serum levels and serum phosphorous levels	
	(negative correlation).	
18	Scatter gram of the correlation between	73
	Fibroblast Growth Factor-23 (FGF-23)	
	serum levels and serum urea before dialysis	
	(positive correlation).	

## 🕏 List of Figures 🗷

Fig.	Title	Page
19	Scatter gram of correlation between	74
	Fibroblast Growth Factor-23 (FGF -23)	
	serum levels and serum urea after dialysis	
	(positive correlation).	
20	Scatter gram of the correlation between	74
	Fibroblast Growth Factor-23 (FGF -23)	
	serum levels and estimated glomerular	
	filtration rate (negative correlation).	
21	Scatter gram of the correlation between	75
	Fibroblast Growth Factor-23 (FGF -23)	
	serum levels and common carotid intimal	
	thickness (positive correlation).	
22	Showing that as hypertension duration is	75
	increased the more present plaques among	
	participants (positive correlation).	
23	Showing that the number of patients with	76
	present plaques is more than in absent	
	plaques and is directly proportional to	
	serum urea level before and after dialysis.	
24	Showing positive correlation between	76
	present plaques and common carotid intimal	
	thickness.	

## 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 Study

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).