Relationship Between Neutrophil Gelatinase Associated Lipocalin And Chronic Kidney Disease

THESIS

Submitted for partial fulfillment of master degree nephrology

By

Mohammed Hussein Mahmoud

Diploma of Internal Medicine

Supervised by

Prof. Dr. MAHMOUD ABD ELFATAH IBRAHEM

Professor of Internal Medicine and Nephrology

Faculty of medicine - Ain Shams University

Prof. Dr. OSAMA MAHMOUD MOHAMMED

Professor of Internal Medicine and Nephrology

Faculty of medicine - Ain Shams University

Dr. WALEED ANWAR ABD EL MOHSSEN

Lecturer of Internal Medicine and Nephrology

Faculty of medicine - Ain Shams University

Faculty of Medicine
Ain Shams University

2014

Acknowledgement

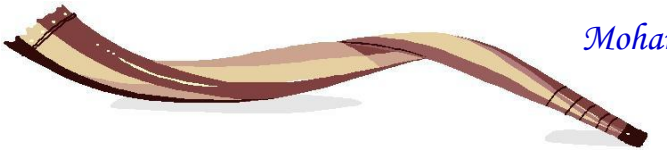
First of all thanks to Allah who guaranteed me the power to accomplish this work.

I feel greatly indebted to Prof. Dr. Mahmoud Abd El Fatah Ibrahem Professor of Internal Medicine & Nephrology ;Ain Shams University for his continuous support, kindness and wise supervision .

It is a pleasure to express my deep gratitude and thanks to Prof. Dr. Osama Mahmoud Mohamed Professor of Internal Medicine & Nephrology ; Ain Shams University for his fatherly guidance, kindness and continuous help to achieve this work.

I am also greatly indebted to Dr. Waleed Anwar Abdel-Mohssen Lecturer of Internal Medicine & Nephrology ; Ain Shams University for his careful and great support . He did not spare any effort in guiding me towards the best and his valuable advices.

I would like also to express my great thanks to all everyone who gave me all facilities and advice to perform this work.



Mohammed Hussein Mahmoud.

List of Contents

List of Abbreviation

Abbreviation	Item
ACE	Angiotensin Converting Enzyme.
AKI	Acute kidney Injury.
ARF	Acute Renal Failure.
BMI	Body Mass Index.
CAPD	Continuous Ambulatory Peritoneal Dialysis.
C-ANCA	Cytoplasmic Pattern Antineutrophil Cytoplasmic Antibody.
CKD	Chronic kidney Disease.
CrCl	Creatinine Clearance.
CRF	Chronic Renal Failure.
CRP	C-Reactive Protein.
DBP	Diastolic Blood Pressure.
ESR	Erythrocyte Sedimentation Rate.
ESRD	End Stage Renal Disease.
FE	Fractional Excretion.
GFR	Glomerular Filtration Rate.
GI	Gastrointestinal.
HbA1c	Glycated Hemoglobin.
HBV	Hepatitis B virus.
HCV	Hepatitis C virus.
HD	Hemodialysis.
HDL	High Density lipoproteins.
HIV	Human Immunodeficiency Virus.
HUS	Hemolytic Uremic Syndrome.
K/DOQI	The Kidney Diseases Outcomes Quality Initiative.
LDL	Low Density lipoprotein.
LIF	Leukemia Inhibitory Factor.
MDRD	Modification of Diet in Renal Disease.
MMP9	Matrix Metalloproteinase-9.
NGAL	Neutrophil Gelatinase Associated lipocalin.

NSAIDs	Non Steroidal Anti inflammatory Drugs.
P-ANCA	Perinuclear Pattern Antineutrophil Cytoplasmic Antibody.
PCI	Percutaneous Coronary Intervention.
PTH	Parathyroid Hormone.
RBC	Red Blood Cell.
SCr	Serum Creatinine.
sNGAL	Serum Neutrophil Gelatinase Associated lipocalin.
SBP	Systolic Blood Pressure.
TG	Triglycerides.
TLC	Total leucocytic Count.
TTP	Thrombotic Thrombocytopenic Purpura.
UCr	Urinary Creatinine.
uNGAL	Urinary Neutrophil Gelatinase Associated lipocalin.
USRDS	US Renal Data System.
VCUG	Voiding Cystourethrogram.
WBC	White Blood Cell.

List of Figures

List of Tables

Introduction& Aim of work

Introduction

(NGAL), a small 25-kDa protein belonging to the lipocalin family, one of the most promising biomarkers in the diagnostic field of (AKI) **(Bolignano D et al., 2008).**

This protein, initially found in activated neutrophils as an innate anti-bacterial factor, is released massively from kidney tubular cells after harmful experimental stimulations of various natures, activating specific iron-dependent pathways with the self defensive intent to contrast oxidative stress and cellular apoptosis **(Mori K et al., 2007).**

In patients undergoing treatments potentially detrimental to the kidney, such as contrast medium administration and cardiac surgery (**Hirsch R et al., 2007) *(*Mishra J *et al.,* 2003*)***, as well as in subjects with unstable nephropathies (**Trachtman H *et al.,* 2006)**, the increase in NGAL levels is a good predictor of a brief term onset of AKI, notably anticipating the resulting increase in serum creatinine levels and thus enabling the arrangement of preventive therapeutic measures in a timely manner. In parallel, recent studies have also reported altered NGAL levels in patients affected by some (CKD) associated conditions, such as autoimmune **(Brunner HI et al., 2006**), polycystic **(Bolignano D *et al.*,2007)** and proteinuric diseases, **(Ding H et al.,2007) (Bolignano D et al., 2008)**, suggesting the possibility that under these circumstances NGAL production from tubular cells may reflect the entity of active renal damage that underlies the chronic impairment condition **(Mori K et al.,2007).**

Aim of the work

In this research, we are trying to find out a way to follow up those patients with chronic kidney disease in different nephrology clinics and highlight the role of NGAL in assessment the severity of renal impairment.

Review of Literature

Chapter 1

Chronic Kidney Disease

The Kidney Diseases Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) defines chronic kidney disease (CKD) as either kidney damage or a decreased kidney glomerular filtration rate (GFR) of < 60 mL/min/1.73 m^2 for 3 or more months. Whatever the underlying etiology, the destruction of renal mass with irreversible sclerosis and loss of nephrons leads to progressive decline in GFR.

The K/DOQI definition and the classification of CKD allow better communication and intervention at the different stages **(K/DOQI clinical practice guidelines for chronic kidney diease 2002) (Coresh J et al., 2003) (Coresh J et al., 2005).**

The different stage of CKD forms a continuum in time; prior to February 2002, no uniform classification of the stages of CKD existed. At that time, K/DOQI published a classification of the stages of CKD, as shown in the following table (1).

Table (1): Clssification of chronic kidney disease.

Stage	Description	GFR(mL/min/1.73m^2)	Action
	At increased risk	90 (with CKD risk factors)	Screening CKD risk reduction.
1.	Kidney damage with normal GFR	90	Diagnosis and treatment. Treatment of comorbid conditions, slowing progression and reduction CVD risk.
2.	Kidney damage with mild decrease GFR	60-89	Estimating progression
3.	Moderate decrease GFR	30-59	Evaluating and treating complications.
4.	Severe decrease GFR	15-29	Preparation for kidney replacement therapy.
5.	Kidney Failure	<15 (or dialysis)	Replacement (if uremia present).

Epidemiology

The attention being paid globally to chronic kidney disease is attributable to five factors: the rapid increase in its prevalence, the enormous cost of treatment, recent data indicating that overt disease is the tip of an iceberg of covert disease, an appreciation of its major role in