بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

The role of hepcidin as a biomarker for iron status in patients with chronic kidney disease (stage IV and V) with negative virology

A Thesis

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in Internal Medicine

By

Ahmed Mahmoud Ibraheem
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Under Supervision of

Prof. Dr. Magdy Mohamed El Sharkawy
Professor of Internal Medicine and Nephrology
Faculty of Medicine, Ain Shams University

Prof. Dr. Heba Wahid Elsaid
Professor of Internal Medicine and Nephrology
Faculty of Medicine, Ain Shams University

Dr. Lina Essam Khedr
Lecturer of Internal Medicine and Nephrology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
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Ahmed Mahmoud Ibraheem

List of Contents

List of Abbreviations

Abbr.	Full-term
AA	**:** Amino-acid
CERA	**:** Continuous erythropoiesis receptor activator
CKD	**:** Chronic kidney disease
DMT1	**:** Divalent metal transporter 1
ER	**:** Endoplasmic reticulum
FGF-23	**:** Fibroblast growth factor-23
FPT	**:** Ferroprotein
GFR	**:** Glomerular filtration rate
HAMP	**:** Direct transcriptional suppression of hepcidin gene
HCV	**:** Hepatitis C virus
HO-1	**:** Haem oxygenase-1
IRE	**:** Iron-responsive elements
IRP	**:** Iron-regulatory proteins
IV	**:** Intravenous
KDIGO	**:** Kidney Disease: Improving Global Outcomes
Lrp1	**:** Lipoprotein receptor-related protein-1
NTBI	**:** Non-transferring bound iron
RBCs	**:** Red blood cells
rhEPO	**:** Recombinant human erythropoietin
SC	**:** Subcutaneous
SD	**:** Standard deviation

SPSS **:** Statistical package for social science

Tf **:** Transferrin

TfR **:** Transferrin receptors

TIBC **:** Total iron-binding capacity

α2M **:** α2-macroglobulin

List of Tables

List of Figures

Abstract

Background: Anemia is a severe complication of chronic kidney disease (CKD) that is seen in more than 80% of patients with impaired renal function. Hepcidin, an acute phase reactant protein produced in the liver, is a key regulator of iron homeostasis. **Aim of the Work:** to assess hepcidin level in 45 non-dialysis patients (CKD stage IV and V with negative virology) and its relation to iron parameters. **Patients and Methods:** A cross sectional study was conducted at Nasser Institute for Treatment and Research on 45 patients with chronic kidney disease stage IV and V. All patients included in this study were subjected to the following: Careful history taking, full clinical examination and proper laboratory investigations. **Results:** A statistically significant difference was found between CKD stage 4 and stage 5 according to Hb., iron, TIBC, Frerretin, serum and CRP. Also, there was a significant positive correlation of serum hepcidin with serum ferretin and hsCRP, while Hb and iron were significantly negatively correlated with hepcidin. We found statistically significant decrease in Hb level, serum Iron level, and TIBC in CKD stage 5 less than stage 4. We found statistically significant increase in Hepcidin level, serum ferritin, and hsCRP in CKD stage 5 more than stage 4. We found statistically significant Positive correlation between serum hepcidin with serum ferretin among patients with CKD stage 4 and 5. We found statistically significant Positive correlation between serum hepcidin with hsCRP among patients with CKD stage 4 and 5. **Conclusion:** Elevated hepcidin can predict the need for parenteral iron to overcome hepcidin-mediated iron-restricted erythropoiesis and need for relatively higher rhEPO doses to suppress hepcidin in CKD patients with negative viral markers.

Key words: hepcidin, iron status, chronic kidney disease, negative virology

Introduction

Anemia is a severe complication of chronic kidney disease (CKD) that is seen in more than 80% of patients with impaired renal function ***(Simon and Nakhoul, 2016).***

Although there are many mechanisms involved in the pathogenesis of anemia of renal disease, the primary cause is the inadequate production of erythropoietin by the damaged kidneys ***(Hasan et al., 2017).***

Adequate iron stores are essential for achieving maximum benefit from erythropoietic agents, such as recombinant human erythropoietin (rhEPO) or darbepoetin alfa. Decreased iron stores or decreased availability of iron are the most common reasons for resistance to the effect of these agents ***(Jelkmann, 2013).***

Hepcidin, an acute phase reactant protein produced in the liver, is a key regulator of iron homeostasis. Hepcidin inhibits intestinal iron absorption and iron release from macrophages and hepatocytes. Because hepcidin productions increased by inflammation, and high hepcidin concentrations limit iron availability for erythropoiesis, hepcidin likely plays a major role in the anemia of inflammation and rhEPO resistance ***(Singh, 2007).*** Serum levels of prohepcidin, the precursor molecule of hepcidin, were found lower in patients with chronic HCV infection ***(Ganz and Nemeth, 2012).***

Because of its renal elimination and regulation by inflammation, it is possible that progressive renal insufficiency leads to altered hepcidin metabolism, subsequently affecting enteric absorption of iron and the availability of iron stores ***(Ashby et al., 2017).***

Several studies have shown elevated hepcidin levels in CKD, and it is now considered to be the critical link between inflammation and anemia in CKD patients ***(Jairam et al., 2010).***

Treatment with agents that lower serum hepcidin levels or inhibit its actions may be an effective strategy for restoring normal iron homeostasis and improving anemia in CKD patients ***(Tsuchiya & Nitta, 2013).***

Aim of the Work

The aim of this work is to assess hepcidin level in non-dialysis patients (CKD stage IV & V) with negative virology and its relation to iron parameters.