شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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HANAA ALY

Effect of direct acting anti-viral drugs on myostatin level among CRF Egyptian patients with chronic HCV infection and its correlation with sarcopenia

Thesis Submitted For Partial Fulfillment of Master Degree
In Internal Medicine

By

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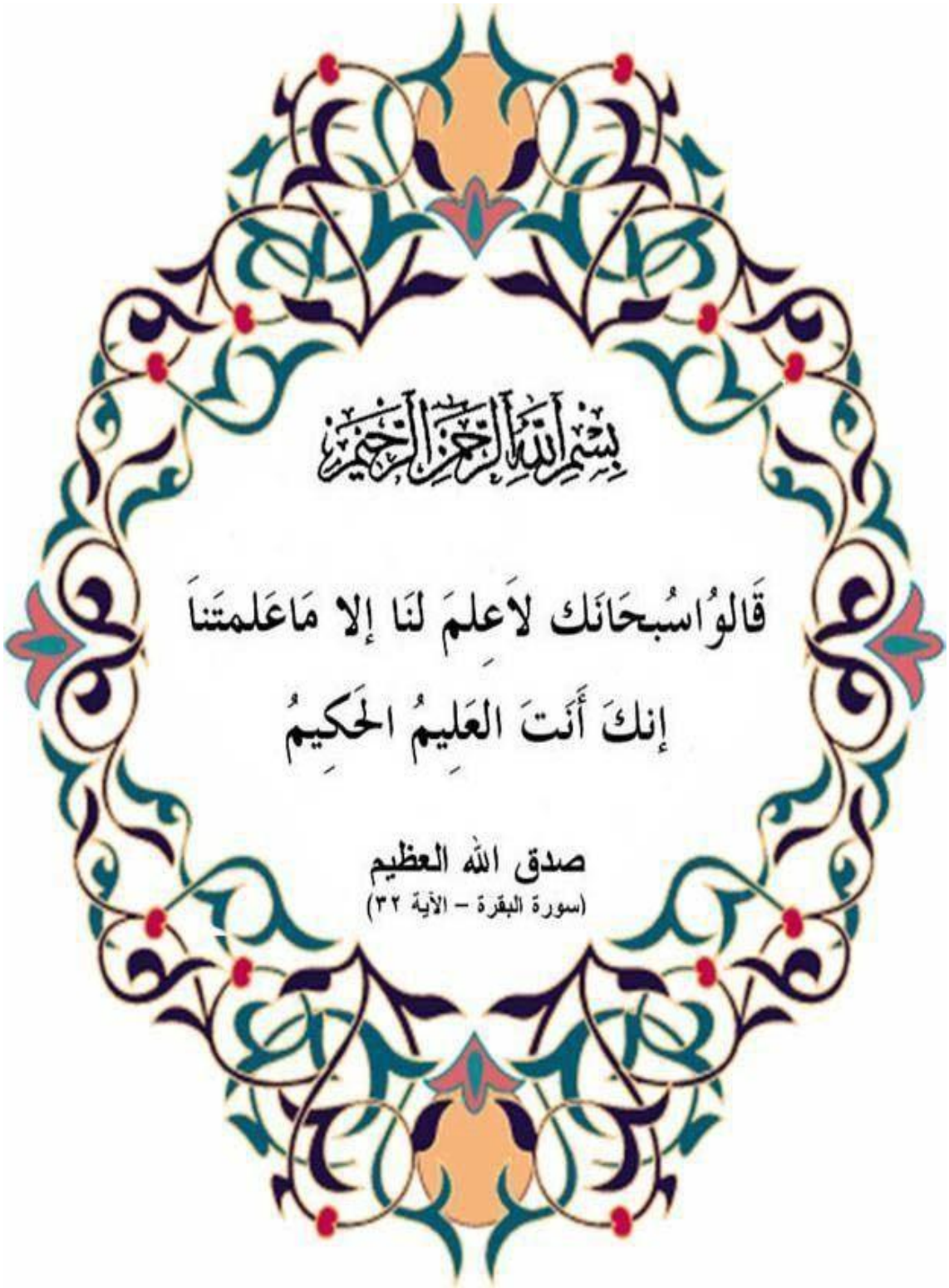
بسم الله الرحمن الرحيم
قَالوُاسُبحَانَك لاَعلمَ لنَا إلا مَاعَلمتَناَ
إنكَ أَنتَ العَلِيمُ الحَكِيمُ
صدق الله العظيم
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Wessam Abd el ElahElgezery

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LIST OF ABBREVIATIONS

Abb	**Full Term**
ActRIIB	activin type IIB receptor
ADAMTS	and degraded by matrix metalloproteinases, serine proteases, the adamalysin
AGE	advanced glycosylation end
ALK4	activin-like kinase 4
ALT	alanine aminotransferase
AST	aspartate transaminase
BIA	Bioimpedance analysis
BMD	bone mineral density
BMI	body mass index
BMP	bone morpogenetic protein
BUN	Blood urea nitrogen
CKD	Chronic kidney disease
CRF	Chronic renal failure
CryoVas	cryoglobulinemia vasculitis
CT	Computed tomography
DAA	direct-acting antiviral
DOPPS	Dialysis Outcomes and Practice Patterns Study
DXA	dual-energy X-ray absorptiometry
ECG	Echocardiogram
eGFR	Estimated glomerular filteration rate
ESDR	end-stage renal disease
ESKD	end stage kidney disease
EWGSOP	European Working Group on Sarcopenia in Older People
GASP	GDF-associated serum protein
GDF	growth and differentiation factor
GFR	glomerular fltration rate
GH	growth hormone
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	Hepatitis C virus
ICD	International Classification of Diseases
IFN	Interferon
IgA	Immunoglobulins
IGF	insulin-like growth factor

IL	Interlukin
KDIGO	Kidney Disease Improving Global Outcomes
KDOQI	Kidney Foundation Kidney Disease Outcomes Quality Initiative
KT	kidney transplant
KTR	kidney transplant recipients
MPGN	membranoproliferative glomerulonephritis
mTOR	mammalian target of rapamycin
NS5B	non-structural protein 5B
PegIFN	pegylated IFN
pQCT	Peripheral quantitative CT
PTH	parathyroid hormone
ROS	reactive oxygen species
RR	relative risk
SARC-F	A sarcopenia screening questionnaire
SMI	skeletal muscle mass index
SOF	Sofosbuvir
SPPB	Short Physical Performance Battery
SVR	sustained virological response
TE	Transient Elastography

ABSTRACT

Background: Chronic kidney disease (CKD) is a progressive condition that might negatively affect musculoskeletal health. Secondary sarcopenia due to chronic kidney disease may be accompanied with elevated fall risk and mobility limitations. The loss of muscle mass, in addition to the impact of poor body composition on muscle strength and mobility status are necessary for classification and staging of sarcopenia.

Aim of the Work: The main aim of this study was to assess the effect of direct anti-viral drugs on myostatin level and its correlation with sarcopenia in CRF patient with chronic HCV.

Patients and Methods: This was a case control study was conducted at gastroenterology outpatients' clinics and internal medicine and nephrology department Ain Shams university hospital and om elmasryeen general hospital including 50 chronic renal failure patients with chronic HCV infection and normal persons; they were divided into: Group A: 20 chronic HCV patient received direct acting anti-viral drugs. Group B: 20 chronic HCV patients didn't receive direct acting anti-viral drugs. Group C: 10 normal persons without chronic renal failure or hepatitis C virus. The duration of the study ranged from 6-12 months.

Results: There was no statistically significant difference between the studied groups as regard demographic data, there was high statistically significant difference between the studied groups as regard weight, lean body mass and BMI, there was high statistically significant difference between the studied groups as regard Hb, there was high statistically significant difference between the studied groups as regard history of ALT and AST and significant difference between the two studied groups as regards Alpha fetoprotein, there was high statistically significant difference between the studied groups as regard history of BUN and significant difference between the two studied groups as regards Creatinine, there was statistically significant difference between the studied groups as regard Serum myostatin.

Conclusion: The serum myostatin level was significantly lower in chronic HCV patients didn't receive direct acting anti-viral drugs than those who received direct acting anti-viral drugs and control groups.

Keywords: Direct acting anti-viral drugs, myostatin level, CRF, Chronic HCV infection, Sarcopenia

INTRODUCTION

Chronic kidney disease (CKD) is a progressive condition that might negatively affect musculoskeletal health. Secondary sarcopenia due to CKD may be accompanied with elevated fall risk and mobility limitations **(Hernand et al, 2018)**

Sarcopenia is a clinical disease entity defined by skeletal muscle mass depletion and muscle strength weakness. This disease has received significant attention from clinicians recently because of its significant deleterious influence on outcomes **(Cruz-Jentoft AJ et al., 2014)**

Myostatin is a cytokine belonging to the transforming growth factor beta family, and its functional role was first elucidated in 1997.21 Myostatin is a negative regulator of muscle protein synthesis, and is associated with the development of sarcopenia **(Yamada et al., 2016)**

HCV infection is an escalating global health issue. HCV is endemic in many countries and is a growing burden for society and health-care systems. The inexorable increases in long-term sequelae such as cirrhosis and hepatocellular carcinoma (HCC) are a particular problem **(Gre Belly et al., 2011)**

The rapid development of direct-acting antiviral (DAA) therapies for HCV infection has resulted in considerable optimism among clinicians who treat patients with HCV, with the realistic hope that therapeutic interventions will soon be more effective, better tolerated and shorter in duration than current therapie **(Dore , G et al ., 2012)**.

*Aim Of The Wor*k

In This study we aimed toassess the effect of direct anti-viral drugs on myoststin level and its correlation with sarcopenia in CRF patient with chronic HCV

Chapter (1)

Chronic kidney disease

The defnition and classifcation of chronic kidney disease (CKD) have evolved over time, but current international guidelines defne this condition as decreased kidney function shown by glomerular fltration rate (GFR) of less than 60 mL/min per 1·73 m², or markers of kidney damage, or both, of at least 3 months duration, regardless of the underlying cause. Diabetes and hypertension are the main causes of CKD in all high-income and middle-income countries, and also in many low-income countries. Incidence, prevalence, and progression of CKD also vary within countries by ethnicity and social determinants of health, possibly through epigenetic influence. Many people are asymptomatic or have nonspecifc symptoms such as lethargy, itch, or loss of appetite. Diagnosis is commonly made after chance fndings from screening tests (urinary dipstick or blood tests), or when symptoms become severe **(Webster et al., 2017).**

The best available indicator of overall kidney function is GFR, which is measured either via exogenous markers (eg, DTPA, iohexol), or estimated using equations. Presence of proteinuria is associated with increased risk of progression of CKD and death. Kidney biopsy samples can show defnitive evidence of CKD, through common changes such as glomerular sclerosis, tubular atrophy, and interstitial fbrosis. Complications include anaemia due to reduced production of erythropoietin by the kidney; reduced red blood cell survival and iron defciency; and mineral bone disease caused by disturbed vitamin D, calcium, and phosphate metabolism **(Vart et al., 2016).**