

The Correlation Between Serum Testosterone Level and Sarcopenia in Egyptian Male Patients With Liver Cirrhosis

Thesis

*Submitted for Partial Fulfillment of Master Degree
in Internal Medicine*

By

Sara Mohamed Abd El-Kader Khalil

M.B. B.Ch

Supervisors

Prof. Dr. Mansour Nasef Mohamed

Professor of Internal Medicine

Faculty of Medicine – Ain Shams University

Prof. Dr. Wesam Ahmed Ibrahim Mohamed

Professor of Internal Medicine

Faculty of Medicine – Ain Shams University

Dr. Ahmed ElSaady Mohamed Khaial

Assistant Professor of Internal Medicine

Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
2017



العلاقة بين معدل هرمون التستوستيرون في الدم و تآكل العضلات في المرضى المصريين الذكور المصابين بتليف الكبد

رسالة

توطئة للحصول على درجة الماجستير في أمراض الباطنة

مقدمة من

الطبيبة / سارة محمد عبدالقادر خليل

بكالوريوس الطب والجراحة

تحت إشراف

الأستاذ الدكتور / منصور ناصف محمد

أستاذ الباطنة العامة

كلية الطب - جامعة عين شمس

الأستاذ الدكتور / وسام أحمد إبراهيم محمد

أستاذ الباطنة العامة

كلية الطب - جامعة عين شمس

الدكتور / أحمد السعدي محمد خيال

أستاذ مساعد الباطنة العامة

كلية الطب - جامعة عين شمس

كلية الطب

جامعة عين شمس

٢٠١٧

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(سُبْحَانَكَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ

لَا يُلْمُ لَنَا الْعِلْمُ الْحَكِيمُ)

صدق الله العظيم

سورة البقرة - مدنية - الآية ٣٢



Acknowledgment

First of all, I would like to raise my greatest gratitude and thanks to "ALLAH" who gave me strength and help to accomplish this work,

*I would like to express my sincere thanks, respect, gratefulness and appreciation to **Prof. Dr. Mansour Nasef Mohamed**, Professor of Internal Medicine Faculty of Medicine – Ain Shams University, for his generous assistance, close supervision, constructive criticism, and expertise. I am greatly thankful for his valuable advice, continuous encouragement, indispensable guidance and great effort he has devoted in his supervision of this work. I am very privileged and honored to have him as my supervisor.*

*I am deeply grateful to **Prof. Dr. Wesam Ahmed Ibrahim Mohamed**, Professor of Internal Medicine Faculty of Medicine – Ain Shams University, for the enthusiastic cooperation, worthy remarks, great advices and support he provided me during supervision of this work. Without his assistance, I would not have been able to start and reach the production of this work indeed.*

*I am deeply thankful to **Dr. Ahmed ElSaady Mohamed Khaial**, Assistant Professor of Internal Medicine Faculty of Medicine – Ain Shams University for his great help, outstanding support, active participation and guidance.*

Sara Mohamed Abd El-Kader Khalil



*"To my dear **Father** for his help and to my beloved **Mother** and my **sisters** for their care and support*

*And to my dear **husband** who was and still supporting me in all my hard times and to my beautiful daughter, **Isabel***

*To my Godfather, **Lofty** and soul of my uncle, **Essam** and all my family and friends*

The Correlation Between Serum Testosterone Level and Sarcopenia in Egyptian Male Patients with Liver Cirrhosis

Prof Dr: Mansour Nasef Mohamed: professor of internal medicine.

prof Dr :Wesam Ahmed Ibrahim Mohamed:professor of internal medicine.

Dr: Ahmed ElSaady Mohamed Khaial:

Assistant professor of internal medicine. **Sara Mohamed Abd El-Kader**

Khalil: M.B.,B.CH

Department of Internal Medicine, Faculty of Medicine – Ain Shams University

ABSTRACT

Background: Cirrhosis results from different mechanisms of liver injury that lead to necroinflammation and fibrogenesis; histologically it is characterised by diffuse nodular regeneration surrounded by dense fibrotic septa with subsequent parenchymal extinction and collapse of liver structures, together causing pronounced distortion of hepatic vascular architecture. Androgen are important anabolic hormones produced in the testes, with effects on muscle, hematopoiesis, metabolism and sexual function, low circulating testosterone levels in men are associated with anaemia, osteoporosis, the extent of androgen deficiency increase in parallel with worsening severity of liver failure, low serum testosterone has been reported in up to 90% of men with cirrhosis. Sarcopenia is defined as muscle mass two standard deviations below the young healthy adult men, although Sarcopenia associated with wit aging, it can also be present as a result of chronic disease including cirrhosis. **Aim Of The Work:** The aim of this study is to detect the correlation between serum testosterone level and Sarcopenia in Egyptian male patients with liver cirrhosis

Patient and Methods: This study will be conducted on 40 patients with liver cirrhosis and 20 healthy subjects without evidence of any liver disease as controls. Patients and controls will be selected from inpatient and outpatient clinic of GIT Department, Ain Shams University hospital and the Hepatology Department, Al haram Specialized Hospital.

Result: In the current study, the group of cirrhotic patient reported decrease in the serum free & total testosterone than healthy controls, also this group of cirrhotic patients reported presence of Sarcopenia

Conclusion: there was a direct significant correlation between serum testosterone level and Sarcopenia in Egyptian male patients with liver cirrhosis

Keywords: Chronic liver diseases - hepatitis C virus - Sarcopenia - serum Testosterone

List of Contents

Title	Page No.
List of Tables	9
List of Figures	11
List of Abbreviations	13
Introduction	16
Aim of the Work.....	18
Review of Literature	
▪ Liver Cirrhosis	19
▪ Sarcopenia.....	35
▪ Sarcopenia in Cirrhosis.....	65
▪ Testosterone	87
Patients and Methods	110
Results	118
Discussion	144
Summary	150
Conclusion.....	155
References	157
Arabic summary	

List of Tables

Table No.	Title	Page No.
Table (1):	Etiologies of hepatic cirrhosis.....	21
Table (2):	Child-Pugh Score	33
Table (3):	The etiology of sarcopenia and its consequences.	40
Table (4):	Measures techniques for sarcopenia_.....	46
Table (5):	EWGSOP stages of sarcopenia.....	47
Table (6):	Measurements of the various components of sarcopenia (EWGSOP).	49
Table (7):	Summary of treatments options.	64
Table (8):	Studies investigating the prognostic impact of sarcopenia in cirrhosis.	80
Table (9):	The Child-Pugh score	114
Table (10):	Comparison between study groups regarding demographic characteristics.	119
Table (11):	Comparison between study groups regarding clinical presentation (2/1).	120
Table (12):	Comparison between study groups regarding clinical presentation (2/2).	121
Table (13):	Comparison between study groups regarding ultrasongraphy findings.	122
Table (14):	Comparison between study groups regarding Hb, PLT and TLC.	123
Table (15):	Comparison between study groups regarding ALT, AST and total bilirubin.....	124
Table (16):	Comparison between study groups regarding INR, albumin and Na.	126
Table (17):	Comparison between study groups regarding free and total testosterone.....	127
Table (18):	Comparison between study groups regarding SMI.	129
Table (19):	Correlation between Free testesterone and other variables.	131

List of Tables cont...

Table No.	Title	Page No.
Table (20):	Correlation between total testosterone and other variables.	133
Table (21):	Correlation between SMI and other variables.	135
Table (22):	Diagnostic performance of free testosterone and SMI in differentiation between child grades.	136
Table (23):	Diagnostic characteristics of free testosterone and SMI in differentiating CLD from control Characters	139
Table (24):	Diagnostic characteristics of free testosterone and SMI in differentiating child-A from control.	140
Table (25):	Diagnostic characteristics of free testosterone and SMI in differentiating child-B from child-A.	141
Table (26):	Diagnostic characteristics of free & total testosterone and SMI in differentiating child-C from child-B.	142

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Clinical stages of cirrhosis according to clinical features: yearly rates of progression and death	32
Figure (2):	Causes of sarcopenia.....	40
Figure (3):	The relationship between androgen levels and the development of sarcopenia.	42
Figure (4):	ACE inhibitors in the treatment of sarcopenia.	61
Figure (5):	Comprehensive approach to primary and secondary sarcopenia treatment.....	63
Figure (6):	Pathophysiology mechanisms of primary sarcopenia and treatment.....	64
Figure (7):	Overview of the causes of sarcopenia in cirrhosis	72
Figure (8):	Muscle regulation and potential therapeutic strategies.....	86
Figure (9):	Adult testosterone effects	93
Figure (10):	Biosynthesis of testosterone.....	95
Figure (11):	Regulation of testosterone.....	96
Figure (12):	Some nutrients and their affection on testosterone level.....	98
Figure (13):	Comparison between study groups regarding free testosterone.	128
Figure (14):	Comparison between study groups regarding total testosterone.....	128
Figure (15):	Comparison between study groups regarding SMI.	130
Figure (16):	Comparison between study groups regarding sarcopenia.	130
Figure (17):	Correlation between Free testosterone and SMI in child-A	132

List of Figures

Fig. No.	Title	Page No.
Figure (18):	ROC curve for free testosterone and SMI in differentiation between child grades (A: child-A from control, B: child-B from child-A, C: child-C from child-B).....	137
Figure (19):	ROC curve for free testosterone and SMI in differentiation between CLD and control.	138
Figure (20):	Diagnostic characteristics of free testosterone in differentiating study groups.....	143
Figure (21):	Diagnostic characteristics of SMI in differentiating study groups.	143

List of Abbreviations

Abb.	Full term
<i>AFP</i>	<i>Alpha fetoprotein</i>
<i>AKI</i>	<i>Acute kidney injury</i>
<i>ALM</i>	<i>Appendicular lean mass</i>
<i>APLM</i>	<i>Appendicular lean mass</i>
<i>BCAAs</i>	<i>Branched chain amino acids</i>
<i>BCLC</i>	<i>Barcelona-Clinic Liver Cancer</i>
<i>BMI</i>	<i>Body mass index</i>
<i>CDC</i>	<i>Centers for Disease Control</i>
<i>CLDs</i>	<i>Chronic liver diseases</i>
<i>CSA</i>	<i>Cross-sectional area</i>
<i>CSPH</i>	<i>Clinically significant portal hypertension</i>
<i>CT</i>	<i>Computerized tomography</i>
<i>CVD</i>	<i>Cardio-vascular disease</i>
<i>DHT</i>	<i>5α-dihydrotestosterone</i>
<i>DXA</i>	<i>dual energy X-ray absorptiometry</i>
<i>FFI</i>	<i>Fried Frailty Index</i>
<i>FOXO</i>	<i>Forkhead box transcription factor</i>
<i>GH</i>	<i>Growth hormone</i>
<i>GnRH</i>	<i>Gonadotropin-releasing hormone</i>
<i>HCC</i>	<i>Hepatocellular carcinoma</i>
<i>HCV</i>	<i>Hepatitis C virus</i>
<i>HE</i>	<i>Hepatic encephalopathy</i>
<i>HREs</i>	<i>Hormone response elements</i>
<i>HRS</i>	<i>Hepatorenal syndrome</i>
<i>HRT</i>	<i>Hormone replacement therapy</i>
<i>HVPG</i>	<i>Hepatic venous pressure gradient</i>
<i>IGF-1</i>	<i>Insulin-like growth factor</i>

List of Abbreviations cont...

Abb.	Full term
<i>IGSOP</i>	<i>International Group on Sarcopenia in Older People</i>
<i>MELD</i>	<i>Model for End Stage Liver Disease</i>
<i>MRI</i>	<i>Magnetic resonance imaging</i>
<i>mTOR</i>	<i>Mammalian target of rapamycin</i>
<i>NGF</i>	<i>Nerve growth factor</i>
<i>PKB</i>	<i>Protein kinase B</i>
<i>PMN</i>	<i>Polymorphonuclear leucocytes</i>
<i>PPG</i>	<i>Portal pressure gradient</i>
<i>RDA</i>	<i>Recommended dietary allowance</i>
<i>SBP</i>	<i>Spontaneous Bacterial Peritonitis</i>
<i>SHBG</i>	<i>Sex hormone-binding globulin</i>
<i>SMI</i>	<i>Skeletal Muscle Index</i>
<i>SPBB</i>	<i>Short Physical Performance Battery</i>
<i>SPSS</i>	<i>Statistical Package for Social Sciences</i>
<i>TRT</i>	<i>Testosterone replacement therapy</i>
<i>TUG</i>	<i>Timed up and go test</i>

