



**Assessment of Nutritional State in HCV
Chronic Liver Disease Before and After
Treatment with Direct Acting Antivirals
Therapy in Egyptian Patients**

Thesis

*Submitted for partial fulfillment of master degree in internal
medicine*

Presented by

Ahmed Abdulaziz EL-Moursi EL-Sayed
M.B., B.Ch

Supervised by

Prof. Dr. Essam Mohamed Baioumy Helal

Professor of Internal Medicine

Faculty of Medicine, Ain Shams University

Prof. Dr. Amal Shawky Bakir

Professor of Internal Medicine

Faculty of Medicine, Ain Shams University

Dr. Hany Haroun Kaisar

Assistant Professor of Internal Medicine

Faculty of Medicine, Ain Shams University

Dr. Mohamed Hassan Ahmed Fouad

Lecturer of Internal Medicine

Faculty of Medicine, Ain Shams University

Faculty of Medicine

Ain Shams University

2018



**تقييم الحالة التغذوية في مرضى الكبد الفيروسي (ج) المزمن قبل وبعد
العلاج بالعلاج المباشر المضاد للفيروسات في المرضى المصريين**

رسالة

توطئة للحصول علي درجة الماجستير في الباطنة العامة

مقدمة من

□ أحمد عبد العزيز المرسى السيد/الطبيب

بكالوريوس الطب و الجراحة

تحت إشراف

□ أ.د/ عصام محمد بيومى هلال

أستاذ الباطنة العامة

كلية الطب- جامعة عين شمس

□ أ.د/ آمال شوقي بكير

أستاذ الباطنة العامة

كلية الطب- جامعة عين شمس

□ أ.د/ هاني هارون قيصر

أستاذ مساعد الباطنة العامة

كلية الطب- جامعة عين شمس

□ أ.د/ محمد حسن أحمد فؤاد

مدرس الباطنة العامة

كلية الطب- جامعة عين شمس

كلية الطب

جامعة عين شمس

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢



*First and foremost thanks to **ALLAH**, the Most Merciful.*

*I wish to express my deep appreciation and sincere gratitude to my dear professors **Prof Dr. Essam Mohamed Baioumy Helal, Prof Dr. Amal Shawky Bakir** Professors of Internal Medicine and gastroenterology, Ain Shams University, for their close supervision, valuable instructions, continuous help, patience, advices and guidance. They have generously devoted much of their time and effort for planning and supervision of this study. It was a great honor to me to work under their direct supervision.*

*I wish to express my great thanks and gratitude to **Dr. Mohamed Hassan Ahmed Fouad** Lecturer of Internal Medicine and gastroenterology, Ain Shams University, for his kind supervision, indispensable advice and great help in this work.*

Last and not least, I want to thank all my family, my colleagues, for their valuable help and support.

Finally, I would present all my appreciations to my patients without them, this work could not have been completed.

Contents

Subjects	Page
• List of Abbreviations	I
• List of tables	III
• List of Figures	V
• Introduction	1
• Aim of the Work.....	8
• Review of literature:	
Chapter 1: Epidemiology of Malnutrition in cirrhosis..	9
Chapter 2: Nutritional problems in liver disease.....	20
Chapter 3: Assessment of the nutritional state in patient with liver disease.....	26
Chapter 4: Effect of Treatment of HCV on Health- Related Quality of life (HRQOL).....	35
• Patients And Methods.....	39
• Results.....	50
• Discussion.....	71
• Conclusion	81
• Recommendations	83
• Summary	84
• References	87
• Arabic Summary	-

List of Abbreviations

(BT) ratios	: Branched-chain amino acid / tyrosine ratio
(I-SMI)	: Increased skeletal muscle index
AMAs	: Antimitochondrial antibodies
ANA	: Anti-nuclear antibodies
ASH	: Alcoholic steatohepatitis
ASMA	: Anti-smooth muscle antibodies
BCAA/ AAA	: Branched-chain amino acid / aromatic amino acid
BMI	: Body mass index
BTR	: Branched-chain amino acid to tyrosine ratio
CHC	: Chronic hepatitis C
DAAs	: Direct-acting antivirals
DAC	: Daclatasvir
GI	: Gastrointestinal
Hb	Hemoglobin
HbA1C	: Glycated hemoglobin
HCC	: Hepatocellular carcinoma
HCV	: Hepatitis C virus
HDL	: High density lipoproteins
HE	Hepatic encephalopathy
HGS	: Hand grip strength
HOMA-IR	: Homeostasis model assessment of insulin resistance
HRQOL	: Health- Related Quality of life
HRS	Hepatorenal syndrome
IBD	: Inflammatory bowel disease
IFN	: Interferon
INR	: International normal range
IR	: Insulin resistance
IV	Intravenous
LC1	: anti-liver cytosol
LDL	: Low density lipoproteins
LKM1	: Anti-liver kidney microsomes
LPS	: lipopolysaccharide
LSM	: Low Skeletal muscle mass
MAC	: Mid arm circumference
MELD	: Model for end-stage liver disease
NASH	: Non-alcoholic steatohepatitis
PAUS	: Pelvi-abdominal ultrasound
PBC	: Primary biliary cholangitis
PCR	: Polymerase chain reaction
PSC	: Primary sclerosing cholangitis

List of Abbreviations

RBV	: Ribavirin
SD	: Standard deviation
SGA	: Subjective global assessment
SIM	: Simprevir
SMI	: Skeletal muscle index
SML	: Skeletal muscle loss
SMM	: Skeletal muscle mass
SOF	: Sofosbuvir
SPSS	: Statistical program for social science
SVR	: Sustained virologic response
TC	: Total cholesterol
TG	: Triglycerides
TLR	: Toll-like receptor
TNF-α	: Tumor necrosis factor - alpha
tTG	: Tissue transglutaminase
TTT	: Treatment
UGI	Upper gastrointestinal
WHO	: World Health Organization

List of Tables

<i>Tab. No.</i>	<i>Subject</i>	<i>Page</i>
Table (1)	Prevalence of malnutrition in cirrhosis	14
Table (2)	Impact of malnutrition on complications of liver disease in cirrhosis	22
Table (3)	Characteristics of the studied subjects as a whole as regard the Age.	50
Table (4)		51
Table (5)	Characteristics of the studied subject's groups for age.	52
Table (6)	Characteristics of the studied subjects for the sex	53
Table (7)	Characteristics of the studied subjects for the BMI	54
Table (8)	Characteristics of the studied subjects as regard the treatment protocol	55
Table (9)	Characteristics of the studied subjects as regard the treatment group	56
Table (10)	Comparison between group B & C as regard weight before and after treatment with DAA's	57
Table (11)	Comparison between group B & C as regard BMI before and after treatment with DAA's:	59
Table (12)	Comparison between groups (B) & (C) as regard MAC before and after treatment with DAA's	60
Table (13)	Comparison between group(B) & group(C) as regard Hand Grip Assessment before and after treatment with DAA's	61
Table (14)	Comparison between group (B) & group (C) regarding serum albumin before and after treatment with DAA's	62
Table (15)	Comparison between group (B) & group (C) regarding total proteins before and after treatment with DAA's	64
Table (16)	Comparison between group (B) & group (C) regarding lipid profile before and after treatment with DAA's	65
Table (17)	Hb before and after treatment with RBV for both groups (C) and (B) patients	66

List of Tables

<i>Tab. No.</i>	<i>Subject</i>	<i>Page</i>
Table (18)	Comparison between different treatment regimen regarding hand grip strength assessment before and after treatment with DAA's	66
Table (19)	Comparison between different treatment regimen regarding HGS assessment before and after treatment with DAA's	68
Table (20)	Correlation between HGS assessment and different variables before treatment with DAA's	69
Table (21)	Correlation between HGS assessment and different variables after treatment with DAA's	69

List of Figures

Fig. No.	Subject	Page
Fig. (1)	Model Structure of HCV.	4
Fig. (2)	Regulation of skeletal muscle mass.	17
Fig. (3)	Diagnostic and therapeutic issues that link outcomes of liver diseases to nutrition	20
Fig. (4)	Nutritional and metabolic factors associated with health-related quality of life in patients with chronic hepatitis C	21
Fig. (5)	Increased intestinal permeability and dysbiosis are common features linking the liver to a number of nutritional/gastrointestinal (GI) diseases.	24
Fig. (6)	Hand Dynamometer	26
Fig. (7)	Characteristics of the studied subject's groups for age.	52
Fig. (8)	Characteristics of the studied subjects for the sex	53
Fig. (9)	Characteristics of the studied subjects for the BMI	54
Fig. (10)	Characteristics of the studied subjects as regard the treatment protocol	55
Fig. (11)	Characteristics of the studied subjects as regard the treatment group	56
Fig. (12a)	Comparison between group B & C as regard weight before and after treatment with DAA's	57
Fig. (12b)	Comparison between group B & C as regard weight before and after treatment with DAA's	58
Fig. (13)	Comparison between group B & C as regard BMI before and after treatment with DAA's:	59
Fig. (14)	Comparison between group B & C as regard MAC before and after treatment with DAA's	60
Fig. (15)	Comparison between group (B) & group (C) as regard Hand Grip Assessment before and after treatment with DAA's	61
Fig. (16a)	Comparison between group (B) & group (C) regarding serum albumin before and after treatment with DAA's	62
Table (16b)	Comparison between group (B) & group (C) regarding serum albumin before and after treatment with DAA's	63

List of Figures

<i>Fig. No.</i>	<i>Subject</i>	<i>Page</i>
Fig. (17)	Comparison between group (B) & group (C) regarding total proteins before and after treatment with DAA's	64
Fig. (18a)	Comparison between different treatment regimen regarding hand grip strength assessment before and after treatment with DAA's	67
Fig. (18b)	Comparison between different treatment regimen regarding hand grip strength assessment before and after treatment with DAA's	67

Abstract:

Egypt own the highest prevalence rate of HCV infection worldwide, so the government launched a national HCV treatment program targeted a prevalence of <2% by 2025.

Malnutrition in cirrhosis characterized by progressive loss of muscle mass with simultaneous occurrence of lipid compartments consumption to satisfy a higher energetic demand of the hypercatabolic state of the cirrhotic patients affecting their (HRQOL) as they became physically and mentally impacted by fatigue, depression and anxiety. It's evaluated by many tools e.g. Anthropometric tools including BMI, and MAC and Functional tests such as HGS which represent a reliable and easy-to-perform method that can predict sarcopenia in the cirrhotic patient with overall better sensitivity and specificity than other tools.

DAA therapy is a treatment that promises improved quality of life and a favorable prognosis in HCV- infected patients, as in contrast to interferon-based treatment, lead to a high viral eradication rate, less or mostly no side effects.

Inadequate nutrition worsens severity of liver disease and also affects the HRQOL. So, nutritional interventions are important beside DAAs.

INTRODUCTION

Viral hepatitis was estimated to be the 7th leading cause of mortality worldwide. In many cases, it is attributed to hepatitis C virus (HCV), which is the main causes of liver fibrosis, cirrhosis and cancer worldwide, however, Egypt own the highest prevalence rate in the world. (*Mohd, et al., 2013*).

It is widely accepted that the widespread of infection in Egypt was due to implementation of mass population antischistosomal treatment with “tartar emetic injections” (from 1950s to 1980s) beside the usual modes of transmission, such as IV drug usage, shared or reused needles, poorly sterilized surgical or dental equipment, and blood transfusions. (*Ahmed, et al., 2016*).

It is well known that there has been a spectrum of treatments to target the public health disaster represented by the hepatitis C problem in Egypt ranging from the use of PEGylated interferon to the recent use of direct acting antiviral drugs. (*Ahmed, et al., 2016*).

The era of recent direct-acting antivirals (DAAs) provides possibility of reducing disease burden and eliminating this blood-borne virus as a public health concern. (*World Health Organization, 2017*).

The prevalence of hepatitis C in Egypt has a historical and cultural context in response to that the public health measures encouraged by Egyptian health authorities and World Health Organization officials were serious in a period spanning over three decades in the latter half of the last century. (*Ahmed, et al., 2016*).

World Health Organization has recently formulated the “Global Health Sector Strategy on Viral Hepatitis”, Egyptian government following successful negotiations for 99% discounted DAA prices, it launched a national HCV treatment program aiming to treat over 250,000 chronically infected individuals per year, with the goal of achieving a national chronic infection prevalence of <2% by 2025. (*Silva. et al., 2018*).

About 180 million people worldwide are infected with (HCV) that causes both acute and chronic infection. Although the acute stage is largely asymptomatic with little visible symptoms, it's required 20-40 years harboring the infection to develop chronic hepatitis when noticeable symptoms or signs of the disease will occur (*Struthers, 2007*).

The Approximately 55–85% of infected individuals will develop chronic hepatitis C virus and about 15-30% of the chronically infected by HCV will develop cirrhosis (*Webster et al., 2015*), (*Ponziani, et al., 2017*).

HCV is a significant “precursor” for fibrosis, cirrhosis, and even hepatocellular carcinoma, but it is important to understand that this is only in chronic cases. Advanced liver disease and its complications such as ascites, HE, UGI bleeding , hepatopulmonary syndrome, HRS and hepatocellular carcinoma and “*sarcopenia*” , which is defined as progressive loss of muscle mass representing frequently unseen complication is also common, reflecting the poor nutritional status in cirrhotic cause significant morbidity and mortality, which definitely affect the Health- Related Quality of life (HRQOL) of the patients as they are physically and mentally impacted by fatigue, depression and anxiety (*Barboza, et al. ,2016*) (*Nitin, et al., 2016*) .

HCV is a hepatotropic RNA virus of the genus Hepacivirus in the Flaviviridae family. It's exists as an enveloped, positive-stranded RNA virus which is ~50 nm in size and is made up of ~9600 nucleotide bases covered by an icosahedral nucleocapsid which is further surrounded by a lipid bilayer and glycoproteins. (*Zhao, et al., 2014*).

HCV is grouped into 6 major genotypes that exhibit at least 30% variation in nucleotide sequence from one another. (Fig.1)