Comparative study between different modalities of treatment of HCV in new era of Direct Acting Antiviral drugs (DAAs) in Aswan Governorate

Thesis

Submitted for Partial Fulfillment of Master Degree
in Tropical Medicine

By

Fawzy Madkor Mohammed Ismail
Diploma of Tropical Medicine
Ain Shams University, 2014

Under Supervision of

Prof.Dr. Eman Mohamed El-Gindy

Professor of Tropical Medicine
Faculty of Medicine – Ain Shams University

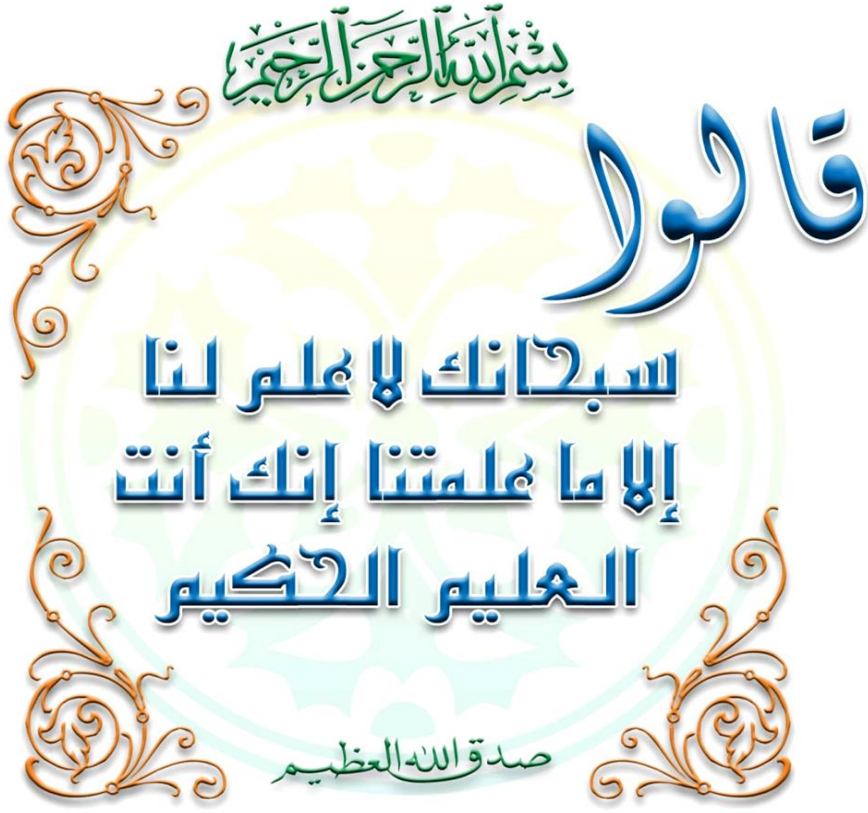
Prof.Dr. Ehab Fawzy Abdou Mostafa

Professor of Tropical Medicine
Faculty of Medicine – Assiut University

Dr. Iman Mohamed Fawzy Montasser

Assistant Professor of Tropical Medicine
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
2018



سورة البقرة الآية: ٣٢

Acknowledgments

*First and forever, thanks to **Allah**, Almighty for giving me the strength and faith to complete my thesis and for everything else.*

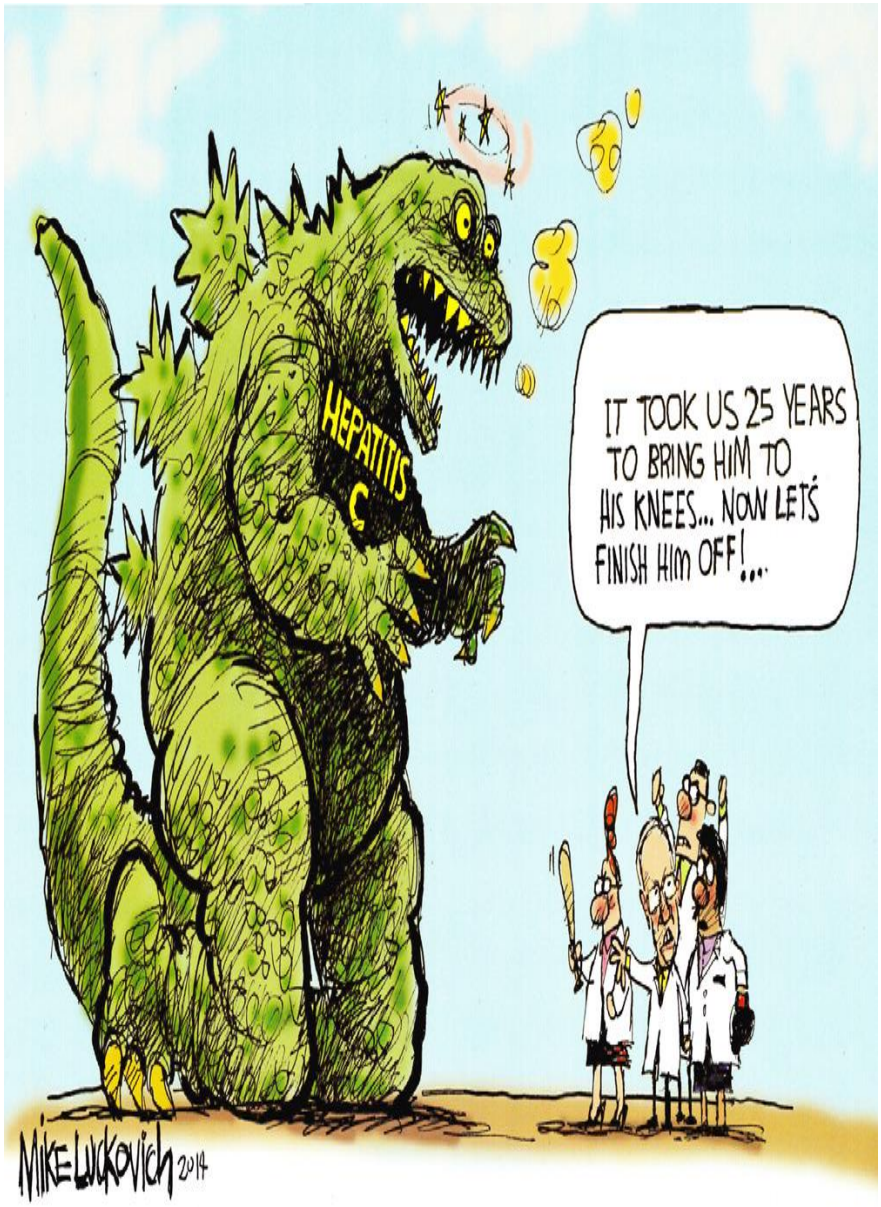
*My deepest thanks to **Professor Dr. Eman Mohamed El-Gindy,** Professor of Tropical Medicine, Faculty of Medicine, Ain Shams University, to whom I am indebted and who cared about every detail written down in this work. It was impossible for me to finish this work without her wise instructions, her guidance and her way of thinking.*

*My deepest thanks to **Professor Dr. Ehab Fawzy Abdou Mostafa,** Professor of Tropical Medicine, Faculty of Medicine, Assiut University, who helped me achieve my goal in this work with his meticulous supervision, valuable instructions, sincere efforts, fruitful encouragement, outstanding support and generous help. I doubt that I will ever be able to convey my appreciation.*

*Words will never be able to express my deepest gratitude and appreciation to **Professor Dr.Iman Fawzy Montasser**, Assistant professor of Tropical Medicine, Faculty of Medicine, Ain Shams University, for her strict supervision and revision of this work. She gave me much of her time, experience and support. Her valuable comments and effort were the causes to complete this work properly.*

Last but not least, allow me to send my deepest gratitude, my great appreciation and sincere thanks to my wife.

Fawzy Madkor Mohammed Ismail


HEPATITIS C
IT TOOK US 25 YEARS TO BRING HIM TO HIS KNEES... NOW LETS FINISH HIM OFF!...
MIKE LUCKOVICH 2014

List of Contents

List of Abbreviations

Abbrev.		Full-term
ACE	**:**	Angiotensin Converting Enzyme
AEs	**:**	Adverse events
AFP	**:**	Alpha fetoprotein
AHA	**:**	Autoimmune haemolytic anaemia
ALT	**:**	Alanine Aminotransferase
ANC	**:**	Absolute neutrophilic count
AST	**:**	Aspartat transaminase
BMI	**:**	Body mass index
C4	**:**	complement 4
CBC	**:**	Complete blood count
CGs	**:**	Cryoglobulins
CT	**:**	Computarized Tomography
CTP	**:**	Child Turcotte Pugh
D.bil	**:**	Direct bilirubin
DAAs	**:**	Direct Acting Antivirals
Dacl	**:**	Daclatasivir
DCV	**:**	Daclatasevir
DM	**:**	Diabetes mellitus
EHMs	**:**	Extrahepatic manifestations
EIAs	**:**	Enzyme-linked immunoassays
ESRD	**:**	End-stage renal disease
FDA	**:**	Food and Drug Administration
GN	**:**	Glomerulonephritis
GT	**:**	Genotype
Hb	**:**	Haemoglobin
HbA1c	**:**	Glycated haemoglobin
HBV	**:**	Hepatitis B virus
HCC	**:**	Hepato Cellular Carcinoma
HCV	**:**	Hepatitis C virus
HCWs	**:**	Health Care Workers
HIV	**:**	Human Immuno deficiency Virus
HLA	**:**	Human Leucocyte Antigen

HTN	**:**	Hypertention
IDU	**:**	intravenous drug use
INR	**:**	International normalized ratio
IRES	**:**	internal ribosome entry site
IU	**:**	International units
LDLr	**:**	Low Density Lipoprotein receptor
LPDs	**:**	Lymphoproliferative Disorders
MALT	**:**	Mucosal Associated Lymphoid Tissue lymphoma
MC	**:**	mixed cryoglobulinaemia
MRI	**:**	Magnetic Resonance Imaging
NHL	**:**	Non Hodjkin Lymphoma
NNPIs	**:**	Non-nucleoside polymerase inhibitors
NPIs	**:**	Nucleot(s)ide polymerase inhibitors
ORF	**:**	open reading frame
Peg INF	**:**	Pegylated interferon
Plt	**:**	Platelet
RBS	**:**	Random blood sugar
RBV	**:**	Ribavirin
RF	**:**	Rheumatoid factor
RT-PCR	**:**	reverse trans crepitase
SD	**:**	Standard deviation
SHEA	**:**	Society for Healthcare Epidemiology of America
SOF	**:**	Sofosbuvir
SVR	**:**	Sustained Virological Response
T.bil	**:**	Total bilirubin
TLC	**:**	Total leucocytic count
TMA	**:**	Transcription-mediated amplification
TSH	**:**	Thyroid stimulating hormone
U.S	**:**	United States
WHO	**:**	World Health Organization

List of Tables

Tables in Patients and Methods:

List of Figures

Figure No.	Title	Page No.

Figures in Review:

Figures in Results:

Abstract

Background: HCV infection is considered a national progressing problem that threatens the life of Egyptian people as Egypt has the highest prevalence of HCV infection in the world with prevalence rates of 14.7 % of the adult population. HCV infection causes chronic hepatic inflammation and severe liver diseases, such as liver cirrhosis and hepatocellular carcinoma. Currently, HCV is curable, unlike HIV and HBV. Gools of therapy are to eradicate HCV infection to prevent hepatic cirrhosis, decompensation of cirrhosis, HCC and death. End point of therapy: undetectable HCV RNA in a sensitive assay (<15 Iu /ml) 12 weeks (SVR12) and 24 weeks (SVR24) after the end of treatment. **Aim of the Work:** To assess the efficacy of DAAs in the treatment of HCV in Aswan Governorate; and to compare between the different combinations of DAAs ± ribavirin ±interferon which were available during the study period as regards efficacy and possible side effects in each treatment combination. Patients and Methods: This retrospective study was conducted between Aswan fever hospital, Aswan hospital health insurance &Tropical Medicine Department Ain Shams University. Study population: Patients with chronic hepatitis C who received treatment in the period from January 2015 to July 2016. Group I: Triple therapy (Sofosbuvir + Ribavirin + Interferon) for 3 months. Group II: Sofosbuvir + Ribavirin for 6 months. Group III: Sofosbuvir + Simeprevir for 3 months. Group IV: Sofosbuvir + daclatasvir ± Ribavirin for 3 months. **Results:** All patients achieved SVR. There were 18 cases out of 35 cases showing side effects, the main side effects were anaemia (14.3%), hyper bilirubinaemia (5.7%) and photonsensitivity (5.7%). **Conclusion:** This is a large real-life report of the use of very low-cost generic medications for treating HCV-G4 within the largest treatment programme worldwide. The use of entirely generic SOF DCV combination with or without generic RBV was well tolerated and associated with high response rate in patients with different stages of liver disease. This can be an example for other countries of similar limited resources for managing their patients with HCV.

Key words: HCV, direct acting antiviral drugs

Introduction

Hepatitis C is a disease with a significant global impact. According to the world Health Organization, there are about 150 million people chronically infected with the hepatitis C virus (HCV) corresponding to 2-2.5% of the world's total population ***(WHO, 2015).***

Chronic hepatitis C is the most common cause of chronic liver disease and cirrhosis and the most common indication for liver transplantation in the United States (U.S), Australia, and most of Europe ***(Wasely and Alter, 2000).*** It is the most common chronic blood borne disease ***(Alter, 1997)*** and it is a progressive disease, the rate of progression is highly variable.

HCV seroprevalence in Egypt 2008 was estimated to be 14.7 % ***(El –Zanty et al., 2009)***. Accordingly, Egypt has the highest HCV prevalence in the world ***(lavnchy, 2011)*** caused by extensive iatrogenic transmission during the era of parentral antischistosomal therapy mass compaigns ***(Frank et al., 2000)***. Currently, HCV is curable, un like HIV and HBV ***(Maragan ore et al., 2015).***

The goal of therapy is to cure HCV infection in order to prevent the complications of HCV-related liver and extrahepatic diseases, including hepatic necroinflammation, fibrosis, cirrhosis, decompensation of cirrhosis, HCC, severe

extrahepatic manifestations and death.The endpoint of therapy is an SVR, defined by undetectable HCV RNA in blood 12 weeks (SVR12) or 24 weeks (SVR24) after the end of therapy, as assessed by a sensitive molecular method with a lower limit of detection 615 IU/ml **(EASL, 2016)**.

Worldwide hepatitis C is the cause of 27% of cirrhosis cases and 25% of hepatocellular carcinoma **(*Malcolm* et al., 2010).** About 10–30% of those infected develop cirrhosis over 30 years **(*Wilkins* et al., 2010).** Cirrhosis is more common in those also infected with hepatitis B, schistosoma, or HIV, in alcoholics and in those of male gender ***(Wilkins* et al., 2010)**. In those with hepatitis C, excess alcohol increases the risk of developing cirrhosis 100-fold ***(Ray* and Thomas, 2009).**

Those who develop cirrhosis have a 20-fold greater risk of hepatocellular carcinoma.This transformation occurs at a rate of 1–3% per year ***(*Wilkins *et al., 2010).*** Being infected with hepatitis B in addition to hepatitis C increases this risk further ***(Forton et al., 2005).***