

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

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

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List of Contents

<i>Subject</i>	<i>Page No.</i>
List of Abbreviations	i
List of Tables	iii
List of Figures	vii
Introduction	1
Aim of the Work	3
Review of Literature	
Epidemiology	4
HCV Transmission.....	9
HCV genotypes	13
Natural History and complications of HCV	20
Diagnosis and Treatment of HCV infection	30
Patients and Methods	56
Discussion	94
Summary and Conclusion.....	102
Recommendations.....	105
References.....	106
Arabic Summary.....	—

List of Abbreviations

<i>Abbrev.</i>	<i>Full-term</i>
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 Hodgkin 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

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
------------------	--------------	-----------------

Tables in Review:

Table (1):	Geographical distribution of HCV subtypes	19
-------------------	--	----

Tables in Patients and Methods:

Table (1):	Follow up tests of group I.....	60
Table (2):	Follow up tests of group II	60
Table (3):	Follow up tests of group III.....	61
Table (4):	Follow up tests of group IV	61

Tables in Patients and Methods:

Table (1):	Comparison between the four groups regarding demographic data of patients:.....	62
Table (2):	Initial evaluation before treatment for the different groups	63
Table (3):	The different types of commercial IFN used in Triple therapy	64
Table (4):	Initial laboratory investigations before treatment for group I.	65
Table (5):	Follow up laboratory investigations at one week, two weeks, eight weeks of treatment for group 1.	66
Table (6):	Follow up laboratory investigations at 4 weeks, 12 weeks, 24 weeks for group I.	67
Table (7):	HCV PCR at 4 weeks, 12 weeks (EOT) and 24 weeks (SVR12)	68
Table (8):	Response to treatment and side effects of group I.....	68
Table (9):	Initial laboratory investigations before treatment for group II.....	70
Table (10):	Follow up laboratory investigations at 4 weeks, 12 weeks, 24 weeks and 36 weeks of treatment.	71
Table (11):	HCV PCR after 4 weeks, 12 weeks, 24 weeks (EOT), 36 (SVR12) weeks.....	72
Table (12):	The response to treatment and side effects among patients in group 2:.....	72

Table (13): Initial laboratory investigations before treatment:	74
Table (14): Follow up laboratory investigations at 4 weeks, 12 weeks, 24 weeks of treatment:	75
Table (15): HCV PCR at 4 weeks, 12 weeks (EOT) and 24 weeks (SVR12)	76
Table (16): The response to treatment and side effects among patients in group III.....	77
Table (17): Initial laboratory investigations before treatment:	79
Table (18): Follow up laboratory investigations at 4 weeks, 12 weeks, 24 weeks of treatment:	80
Table (19): HCV PCR at 4 weeks, 12 weeks (EOT)and 24 weeks (SVR).....	81
Table (20): The response to treatment and side effects	81
Table (21): Comparison between patients of the four groups regarding laboratory tests before treatment.....	82
Table (22): Comparison between the different regimens regarding laboratory tests at 12 weeks.....	83
Table (23): Comparison between the different regimens regarding laboratory tests at 24 weeks:.....	84
Table (24): Comparison between the different regimens regarding response to treatment.....	85

Table (25): Comparison between cirrhotic (n=57) and non –cirrhotic(n=83) patients as regards type of treatment and end of treatment response.....	87
Table (26): Comparison between naïve and experienced patients as regards type of treatment and end of treatment response.	89
Table (27): Comparison between responders and relapsers as regards pre-treatment parameters in group 1.....	91
Table (28): Comparison between responders and relapsers as regards pre-treatment parameters in group II.	92
Table (29): Comparison between responders and relapsers as regards pre-treatment parameters in group III.....	93

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
-------------------	--------------	-----------------

Figures in Review:

Figure (1):	Prevalence of HCV seropositivity in Egypt	7
Figure (2):	HCV antibody prevalence by age, sex, and urban/rural area	8
Figure (3):	Model structure of HCV and proteins encoded by HCV genome	14
Figure (4):	HCV receptors for cell entry	15
Figure (5):	Life cycle of HCV	17

Figures in Results:

Figure (1):	Response to treatment in Group I	69
Figure (2):	Response to treatment in Group II	73
Figure (3):	Response to treatment in Group III	78
Figure (4):	Comparison between different drug regimens regarding response to treatment.	86
Figure (5):	Comparison between cirrhotic and non-cirrhotic patients regarding response to treatment	88
Figure (6):	Comparison between naïve and experienced patients regarding response to treatment	90

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. Goals 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 photosensitivity (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 (*lavnychy, 2011*) caused by extensive iatrogenic transmission during the era of parenteral antischistosomal therapy mass campaigns (*Frank et al., 2000*). Currently, HCV is curable, unlike 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**).