Sofosbuvir/ledipasvir in treatment of HCV infected Egyptian patients with decompensated liver cirrhosis Child Pugh class (B)

Thesis

Submitted for the partial fulfillment of Master Degree
In Tropical Medicine

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2018

Acknowledgment

First and Foremost thanks to Allah, the most merciful and gracious.

I wish to express my deep appreciation and sincere gratitude to **Prof. Dr. Hassan Salaheldin Hamdy,** Head & Professor of Tropical Medicine, Ain Shams University, for planning, supervising this study and for his valuable instructions and continuous help.

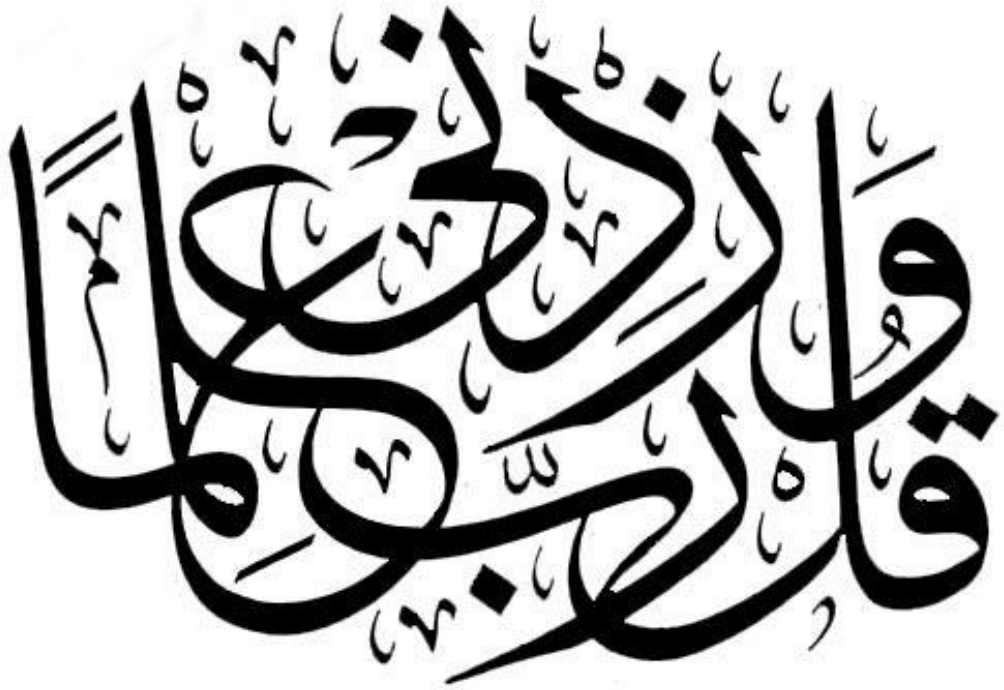
My deepest gratitude to **Dr. Mohamed Salaheldin Abd Elhamid,** Lecturer of Tropical medicine, Ain Shams University, for his generous time and fruitful help in achieving this successful work.

I have to proceed with thanking to **Lieutenant Colonel Dr. Ahmed Ghalwash,** Head & Consultant of Hepatology and Gastroenterology, Agouza Police hospital, who generously supervised my work in a supportive and educational way.

In addition, I would like to thank all my Professors and Colleagues for their support and guide at all times.

Finally but importantly, I would like to thank **my family** for their continuous encouragement.

Amr Mohamed Abbas – July 2018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List of abbreviations

AASLD: American Association for the Study of Liver Diseases.

AFP: Alpha Feto Protein.

ALT: Alanine aminotransferase.

ALP: Alkaline Phosphatase

AST: Aspartate aminotransferase.

CBC: Complete Blood Count.

Cmax: peak concentration

CT: Computed Tomography

CTP: Child Turcotte Pugh

CYP: Cytochrome p-450.

DAAs: Directly Acting Antivirals.

DHS: Demographic health survey

DNA: Deoxyribo nucleic acid.

EASL: European Association for the Study of Liver diseases.

eGFR: estimated glomerular filtration rate.

EIA: Enzyme Immune Assay.

FDA: Food and Drug Administration.

HB: Haemoglobin

HBsAg: Hepatitis B surface antigen.

HBcAb: Hepatitis B core antibody**.**

HBV: Hepatitis B Virus.

HCC: Hepatocellular carcinoma.

HCV: Hepatitis C Virus.

HE: Hepatic Encephalopathy

HIV: Human Immunodeficiency Virus.

IgG: Immunoglobulin G.

INR: International Normalised Ratio

Kpa: Kilo Pascal.

LC: Liver Cirrhosis

LDV/SOF: Ledipasvir/Sofosbuvir

LT: Liver Transplantation

MELD: Model for End-Stage Liver Disease

MSM: Men who have Sex with Men.

NAT: Nucleic Acid Test.

NHS: National Health Service

NS3: non-structural protein 3

NS5A: non-structural protein 5A

NS5B: non-structural protein 5B

PCR: Polymerase Chain Reaction.

PLT: Platelets

RIBA: recombinant immunoblot assay

RNA: Ribonucleic acid.

SVR: Sustained Viral Response.

TIPS: transjugular intrahepatic portosystemic shunt

UNOS: United Network for Organ Sharing

US: Ultrasonography.

WBC: White Blood Cells

WHO: World Health Organisation.

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Introduction:

Hepatitis C virus (HCV) infection is one of the main causes of chronic liver disease worldwide. The long-term impact of HCV infection is highly variable, from minimal changes to extensive fibrosis and cirrhosis with or without hepatocellular carcinoma (HCC).

Clinical care for patients with HCV-related liver disease has advanced considerably during the last two decades, due to an enhanced understanding of the pathophysiology of the disease, and because of developments in diagnostic procedures and improvements in therapy and prevention ***(Alessio A ,2014).***

It is estimated that approximately 130–210 million individuals, i.e. 3% of the world population, are chronically infected with HCV ***(Lavanchy, 2009).*** There are considerable regional differences. In some countries, e.g., Egypt, the prevalence is as high as 22% ***(Lozano et al., 2012).***

In Egypt some age groups suffer prevalence rates of up to 50%. As for the geographical distribution of anti-HCV in persons aged 10-50 years: the Nile Delta and Upper Egypt have rates of 28% and 26% respectively ***(Baatarkhuu et al ,2012).*** Liver mortality in Egypt reaches 40,000 per year, making 10% of total mortality, and comes second after heart diseases ***(El-Sayed, 2014).***

The annual infection rate in Egypt is more than 150,000 new cases every year; approximately 7 out of every 1000 acquire HCV infection every year. HCV genotype 4 is the predominant genotype being isolated from up to 91% of HCV infected persons in Egypt ***(Miller and Abu-Raddad, 2010).***

Most people infected with the virus are unaware of their infection and, for many who have been diagnosed treatment remains unavailable ***(Lemoine et al., 2013).*** Treatment is successful in the majority of persons treated, and treatment success rates among persons treated in low- and middle-income countries are similar to those in high-income countries ***(Ford et al., 2012)***. One third of those who become chronically infected are predicted to develop liver cirrhosis or hepatocellular carcinoma ***(Ly et al., 2012)***.

Six HCV genotypes, numbered 1–6, and a large number of subtypes have been described ***(Simmonds et al., 2005).***They originated from diverse areas in Africa and Asia, and some of them have spread widely throughout the world.

Evaluation of liver functions can be done by **the Child-Pugh score which consists of five parameters that assess the synthetic liver function** three of them are labs (i.e., total bilirubin level, serum albumin, and international normalized ratio, or INR) and two of which are based on clinical assessment (i.e., degree of ascites and degree of hepatic encephalopathy ***(Cheung and Andrew, 2013)***.

Treatment of HCV infected patient with child class B is challenging due to his liability to pass to decompensated child C class

& complicated with ascites , varices & other signs of liver cell failure ***(Lisa and Michael, 2015)*** **.**

Aim of Work:

This work aims to study;

Assessment of the safety & efficacy of sofosbuvir/ ledipasvir in infected naïve and experienced HCV Egyptian patients with decompensated liver disease.

Patients and Methods:

Patient Recruitment:

- **Study Design & Setting:** A prospective cohort study will be conducted in-cooperation between Tropical Medicine Department, Ain Shams university hospitals and EL-Agouza Police hospital.

- **Patients' population:**

100 patients with documented diagnosis of HCV infection (based on PCR results) with decompensated liver disease.

- **Inclusion Criteria:**

Patients with chronic hepatitis C infection that are fulfilling the following criteria will be enrolled in the study:

- HCV infection with detectable viremia: HCV RNA by polymerase chain reaction (Cobas Amplicor HCV Monitor v2.0 [Roche Diagnostics, Branchburg, New Jersey]; lower limit of quantitation [50 IU/mL]).

- Cirrhosis based on clinical, lab & imaging criteria.
- Decompensated liver disease (child B class).

♣ **Exclusion Criteria:**

1- Patients refusing to be enrolled in the study.

2- Other causes of chronic liver diseases.

3- Patients suffering from any other decompensated cardiac, chest & neurological diseases.

4- Patients with any malignancies.

5- HCC except after 3 months of its curative management.

6- Patients co infected with HBV & HCV or HIV & HCV

7- Patients with eGFR < 30 ml / min.

Methods:

All patients after signing informed consent will be subjected to the following:

I- Careful Full medical history taking

II-Thorough clinical examination with special stress on signs of liver cell failure; hepatomegaly, splenomegaly and/or ascites.

III-Laboratory investigations:

1- Routine liver function tests (ALT, AST, Alkaline Phosphatase, Total and direct bilirubin, albumin and prothrombin time).