# Assessment of cardiac functions before and after treatment of Egyptian chronic hepatitis C patients using directly acting antivirals

## Thesis

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in Internal Medicine


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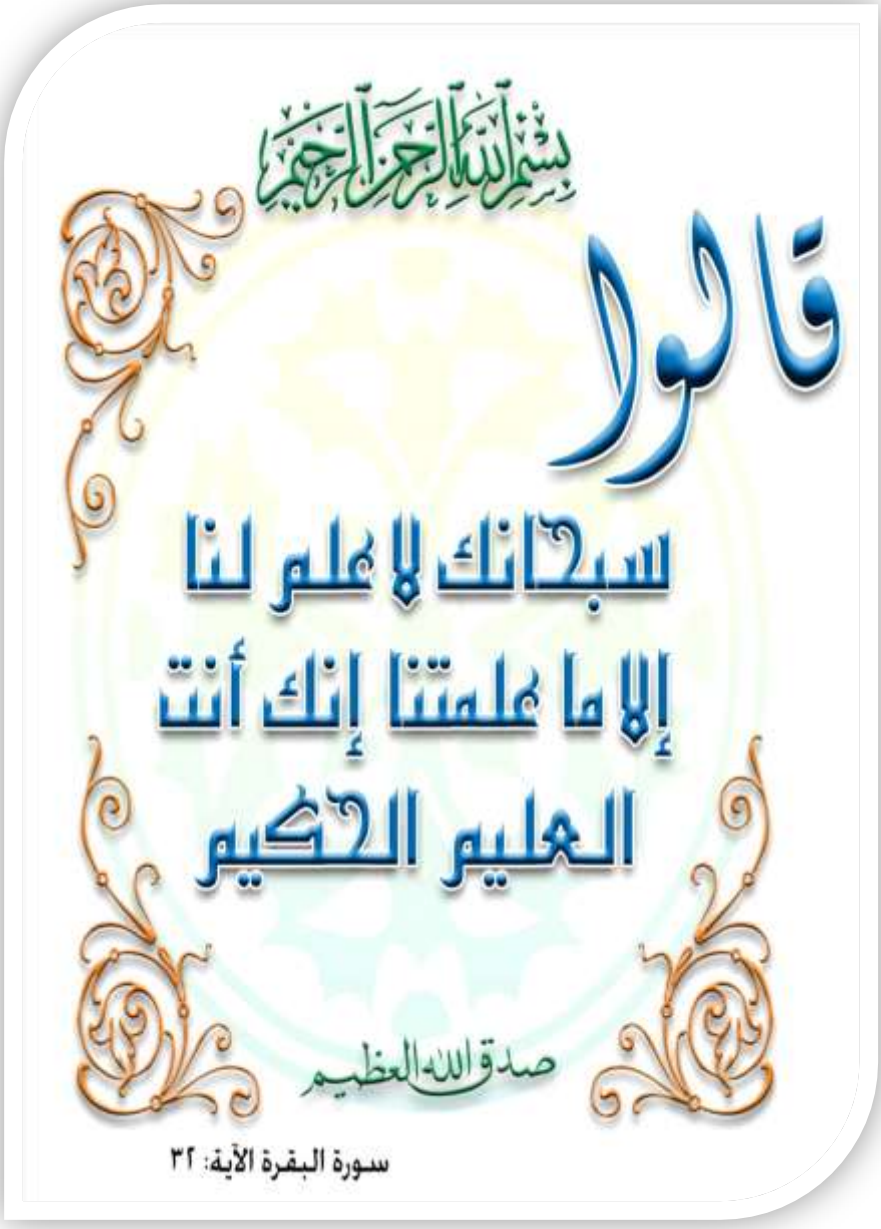
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*Mohamed Gamal Talkhan*

# List of Contents

# List of Abbreviations

| Abbr. | | Full-term |
|---|---|---|
| **a.a** | **:** | Amino acid |
| **AASLD** | : | American Association for the Study of Liver Diseases |
| **AFP** | **:** | Alpha-Feto Protein |
| **ALT** | **:** | Alanine Aminotransferase |
| **AST** | : | Aspartate Aminotransferase |
| **ART** | **:** | Anti-retroviral therapy |
| **BCLC** | **:** | Barcelona-Clinic Liver Cancer |
| **BMI** | : | Body Mass Index |
| **CBP** | **:** | Childbearing period |
| **CCM** | **:** | Cirrhotic cardiomyopathy |
| **CD34** | **:** | Cluster of Differentiation 34 |
| **CDC** | **:** | Centers for Disease Control |
| **CK7** | **:** | Cytokeratin 7 |
| **CKD** | **:** | Chronic Kidney Disease |
| **CLIP** | **:** | Cancer of the Liver Italian Program |
| **CMR** | **:** | Cardiovascular diseases |
| **CVD** | **:** | Cardiovascular Magnetic Resonance |
| **DAAs** | **:** | Direct Acting Antivirals |
| **DAC** | **:** | Daclatasvir |
| **DDIs** | **:** | Drug-drug interactions |
| **DM** | **:** | Diabetes Mellitus |
| **DSV** | **:** | Dasabuvir |
| **DT** | : | Deceleration time |
| **EASL** | **:** | European Association for the Study of the Liver |
| **EBR** | **:** | Elbasvir |
| **ECOG** | **:** | Eastern Cooperative Oncology Group |
| **EF** | **:** | Ejection fraction |
| **EDHS** | **:** | Egyptian Demographic Health Survey |
| **eGFR** | **:** | Estimated glomerular filtration rate |
| **EHIS** | **:** | Egyptian Health Issues Survey |
| **EIA** | **:** | Enzyme immunoassay |

| | | |
|---|---|---|
| **ER** | **:** | Endoplasmic Reticulum |
| **ESCRT** | **:** | Endosomal-Sorting Complex Required for Transport |
| **FDA** | **:** | Food and Drug Administration |
| **FE** | **:** | Fisher Exact |
| **GLE** | **:** | Glecaprevir |
| **GZR** | **:** | Grazoprevir |
| **HCC** | **:** | Hepatocellular Carcinoma |
| **HBV** | **:** | Hepatitis B virus |
| **HCV** | **:** | Hepatitis C virus |
| **HF** | **:** | Heart failure |
| **HIV** | **:** | human immunodeficiency virus |
| **HSP-70** | **:** | Heat shock protein 70 |
| **HTN** | : | Hypertension |
| **IDSA** | **:** | Infectious Diseases Society of America |
| **IFN** | **:** | Interferon |
| **IL28B** | **:** | Interleukin 28B |
| **INR** | **:** | International normalized ratio |
| **IRES** | **:** | Internal ribosome entry site |
| **ISDR** | **:** | Interferon Sensitivity Determining Region |
| **KDa** | **:** | Kilodalton |
| **LDLT** | **:** | Living Donor Liver Transplant |
| **LDs** | **:** | Lipid Droplets |
| **LDV** | **:** | Ledipasvir |
| **LRT** | **:** | Locoregional therapy |
| **LVEDD** | **:** | Left ventricular end diastolic diameter |
| **LVESD** | **:** | Left ventricular end systolic diameter |
| **LVEDV** | **:** | Left ventricular end diastolic Volume |
| **LVESV** | **:** | Left ventricular end systolic Volume |
| | | |
| **MC** | **:** | Monte Carlo |
| **MELD** | **:** | Model for End-stage liver Disease |
| **MPAP** | **:** | Mean pulmonary arterial pressure |
| **MSM** | **:** | men who have sex with men |
| **NAT** | **:** | nucleic acid testing |
| **NNPIs** | **:** | Non-nucleoside polymerase inhibitors |
| **NPI** | **:** | Nucleotide polymerase inhibitors |

| | | |
|---|---|---|
| **NT-Pro BNP** | **:** | N terminal pro hormone brain natriuretic peptide |
| **NTRs** | **:** | Non-Translated Regions |
| **NS** | **:** | Non-strtuctural |
| **OCLN** | **:** | Occludin |
| **OBV** | **:** | Ombitasvir |
| **OPTN** | **:** | Organ Procurement and Transplantation Network |
| **ORF** | **:** | Open Reading Frame |
| **OST** | **:** | opioid substitution therapy |
| **PAH** | **:** | Pulmonary arterial hypertension |
| **PCR** | **:** | Polymerase chain reaction |
| **PEI** | **:** | Percutaneous ethanol injection |
| **PIB** | **:** | Pibrentasvir |
| **PTV** | **:** | Paritaprevir |
| **PWID** | **:** | People who inject drugs |
| **RBV** | **:** | Ribavirin |
| **RCT** | **:** | Randomized control trial |
| **RDTs** | **:** | Rapid diagnostic tests |
| **RFA** | **:** | Radiofrequency Ablation |
| **ROS** | **:** | Reactive Oxygen Species |
| **SD** | **:** | Standard deviation |
| **SIM** | **:** | Simeprevir |
| **SOF** | **:** | Sofosbuvir |
| **SRB 1** | **:** | Scavenger Receptor B1 |
| **SVR** | **:** | Sustained Virological Response |
| **TACE** | **:** | Transcatheter arterial chemoembolization |
| **TAPSE** | **:** | Tricuspid Annular Plane Systolic Excursion |
| **TDI** | **:** | Trans doppler imaging |
| **TGF-beta.** | **:** | Transforming Growth Factor beta |
| **TNM** | **:** | Tumor, node, and metastases |
| **VEL** | **:** | Velpatasvir |
| **VIP** | **:** | Vasoactive Intestinal peptide |
| **VOX** | **:** | voxilaprevir. |
| **WHO** | **:** | World Health Organization |

# List of Tables

# List of Figures

# Abstract

**Introduction:** Hepatitis C virus (HCV) infection is one of the main causes of chronic liver diseases worldwide. HCV infection has been associated with numerous extra-hepatic manifestations. Also, up to 50 percent of patients with advanced cirrhosis have features of cardiac dysfunction. Treatment for chronic HCV infection is evolving from interferon-based therapy to directacting antiviral agents. **aims & Methods:** The aim of the study is to assess the effect of treatment of naïve Egyptians chronic hepatitis C patients on cardiac functions using direct acting antivirals. This study is a prospective cohort study that was conducted on 90 treatment-naïve adult patients with chronic hepatitis C infection. **results:** Assessment of LV systolic functions using EF % revealed no significant difference between the studied groups regarding EF before and after treatment ( P value 0.266 ,0.169 respectively) Change in EF was significantly higher in non-cirrhotic group (P value 0.024) . EF significantly increased in non-cirrhotic group after treatment( P value 0.003 ). Assessment of diastolic function using E/A ratio revealed no significant difference between the studied groups regarding E/A ratio before and after treatment(P value 0.752, 0.881 respectively ) . E/A ratio was non-significantly changed in both groups(P value 0.202, 0.108 respectively ) . Assessment of mean pulmonary artery pressure (MPAP) revealed No significant difference between the studied groups regarding MPAP before and after treatment (P value 0.466, 0.923 respectively ) **conclusion**: Treatment of chronic HCV infection using DAAs (Sofosbuvir, Daclatasvir, Ribavirin) has no clinicaly significant effect on cardiac functions.However, some sort of sub-clinical myocardial affection can occur for further analytical studies.

# Introduction

Hepatitis C virus (HCV) infection is one of the main causes of chronic liver diseases worldwide. The long-term impact of HCV infection is highly variable, ranging from minimal histological changes to extensive fibrosis and cirrhosis with or without hepatocellular carcinoma (HCC). Cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules ***(Messina et al., 2015).***

HCV infection has been associated with numerous extra-hepatic manifestations. They are lichen planus, oral cancer, porphyria cutanea tarda, membranous glomerulonepritis, etc. In addition, auto immune diseases like autoimmune thyroiditis and mixed cryoglobulinemia are also found. Although HCV is primarily a hepatotropic virus, has tropism for other tissues besides the liver. It has been isolated from the myocardium of patients with myocarditis and cardiomyopathy hence, its inclusion among the cardiotropic viruses ***(Sanchez and Bergasa, 2008).***

Also, up to 50 percent of patients with advanced cirrhosis have features of cardiac dysfunction. The term "cirrhotic cardiomyopathy" has been used to describe such patients, who are characterized as having normal to increased cardiac output and contractility at rest, but a blunted response to pharmacologic,

physiologic, or pathologic stress. Patients may also have electrophysiological abnormalities. It is thought to be related to both portal hypertension and cirrhosis. Cardiomyopathy can occur from any cause of cirrhosis, although patients with alcoholism or hemochromatosis may have additional contributing causes to cardiac dysfunction ***(Zardi et al., 2010).***

Treatment for chronic HCV infection is evolving from interferon (IFN)-based therapy to direct-acting antiviral (DAA) agents. Previous interferon-based anti-HCV therapies were mostly not tolerated by patients with advanced heart failure (HF), and had limited elimination efficacy ***(Petta et al., 2016).***

With the introduction of novel interferon-free highly efficient and well tolerated anti-HCV combination therapies, the issue of causal relationship between HCV infection and cardiac disease may finally be resolved since these new highly anti-HCV-specific drugs lack the complex unspecific side-effects upon cardiac functions which have always confounded interpretation of treatment results **(Kohli et al., 2014).**

However, new regimens comprised of DAAs that target different steps in the HCV life cycle are in development and some have received breakthrough therapy status by the U.S. Food and Drug Administration (FDA). Also, recent retrospective studies, case reports and post marketing reports