Response of Elderly Patients to Directly Acting Anti-Hepatitis C virus Treatment and Its Impact on their Quality Of Life

Thesis

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List of Abbreviations

Abb.	Full term
ACEI	*Angiotensin converting enzyme inhibitors*
BB	*Beta blockers*
CCB	*Calcium channel blockers*
CHC	*Chronic hepatitis c*
CLD	*Chronic liver disease*
CVS	*Cerebrovascular stroke*
DAAs	*Directly acting antiviral drugs*
EDHS	*Egyptian demographic health survey*
EGFR	*Estimated glomerular filtration rate*
EIA	*Enzyme immunosorbent assay*
ETR	*End of treatment response*
EVR	*End virologic response*
HCC	*Hepatocellular carcinoma*
HCV	*Hepatitis c virus*
HF	*Heart failure*
HIO	*Health insurance organization*
HRQOL	*Health related quality of life*
ISHD	*Ischemic heart disease*
NS	*Non structural*
PRO	*Patient reported outcomes*
RA	*Rheumatoid arthritis*
ROS	*Reactive oxygen species*
RVR	*Rapid virologic response*
SF	*Short form*
SLE	*Systemic lupus erythematosus*
SVR	*Sustained virologic response*
US	*United states*

INTRODUCTION

Hepatitis C virus (HCV) is a leading cause of liver disease worldwide, as 130–170 million patients are chronically infected and 350,000 patients die every year from HCV infection. The HCV prevalence varies widely among countries, and being highest in several African and Eastern Mediterranean countries. The incidence of new HCV infections may be decreasing in developed countries, but there is still a major reservoir of chronic infections. The most important mode of HCV transmission has been injecting drug use in developed countries with low prevalence and unsafe therapeutic injections in developing countries with moderate-high prevalence ***(Papatheodoridis et al., 2012).***

Hepatitis C virus infection is a major health and economic problem in Egypt. Studies have been conducted on the various aspects of HCV in Egypt in the last twenty years since HCV diagnostic assays became available. More than 20 years after the discovery of the HCV, it is now well established that HCV is of global importance affecting all countries, leading to a large global health problem that requires widespread active interventions for its prevention and control ***(Gomaa et al., 2017).***

Egypt has the highest prevalence of hepatitis C worldwide. Globally, roughly 1 person in 50 is infected with the HCV. In Egypt, a study in 2011found that about one person in seven of Egypt's 83 million populations tested positive for antibodies against HCV, indicating that these persons have

been infected with the virus at some time. However, nearly one person in ten carries its viral RNA and is therefore chronically infected. This represents a large viral reservoir that is fueling the spread of the disease among Egyptians, mainly through hospitals and clinics (medical and dental; private and public). A 2010 study estimated that more than half a million people are newly infected each year. However, the Egyptian Ministry of Health and Population (MOHP) puts the number at 100,000 per year ***(Yahia et al., 2011).***

The Egyptian program is the largest national HCV screening and treatment program in the world. With this screening program and the mass treatment effort that has been the largest in the world so far, Egypt is on a fast track to HCV elimination and has the potential to be the first country to achieve the WHO disease elimination targets. The introduction of DAAs in 2014 led to substantial uptake and scale-up with Egypt's program becoming the largest in the world treating more than 2 million HCV-infected patients. This represents more than half of those treated globally in the last four years ***(Kandeel et al., 2017).***

The major route of exposure to HCV appears to have been via widespread parenteral anti- schistosomal treatment (PAT), with more than 35 million injections given over a 20‐year period (1960–1980). Despite termination of this program and the implementation of measures designed to reduce hospital‐related infection, transmission continues ***(Lehman et al., 2009).***

Chronic hepatitis C was linked to the development of cirrhosis and hepatocellular carcinoma in many areas of the world ***(Gomaa et al., 2017).***

Multiple researches had revealed that infection with HCV significantly decreases quality of life (QOL), even in the absence of cirrhosis. Currently, there is no clear explanation for this reduction. Pathophysiological events resulting from infection may be contributing to decreased QOL in HCV-infected patients ***(Foster et al., 2009).***

Another issue which promises to become central during treatment of elderly with HCV infection is the possible drug-drug interactions between antiviral therapy and the multiple drugs frequently used by elderly patients because of multiple comorbidities ***(Vespasiani et al., 2015).***

The first studies on the effects of HCV infection on patients' quality of life, using the short form (SF-36) Health Survey, showed that patients were poly symptomatic and had diminished quality of life with significant decrease in all domains. The reduction in quality of life could not be related to the degree of liver inflammation or to the mode of acquisition of the infection. Hence, researchers conclude that chronic HCV infection gives rise to physical symptoms that reduce the quality of life of infected patients. Also, studies with matched controls demonstrated that work productivity is significantly impaired ***(Cardoso et al., 2017).***

The achievement of a sustained virological response is associated with an improvement of clinical outcomes, namely a reduction of all-cause mortality. The impact on PRO following successful HCV therapy is also significant; several studies with paired HRQoL assessments demonstrated an overall improvement of all domains of SF-36. Viral eradication leads to HRQoL improvement, regardless of fibrosis stage ***(European Association for The Study of The Liver " EASL", 2017).***

Direct-acting antivirals (DAA) are currently used for the treatment of chronic HCV. However, few studies describe the adverse effects (AE) associated with DAA therapy. The most frequently reported AE were fatigue (43%), headache (42%), neuropsychiatric symptoms (30%) and nausea (26%). Furthermore, hemoglobin < 12 mg/dL was the most frequent (38%) laboratory abnormality observed. Also loss of appetite, insomnia, shortness of breath, impaired concentration, itching, dizziness, diarrhea, also noted ***(Medeiros et al., 2017).***

AIM OF THE STUDY

The aim of the study is to report the response of elderly patient to Directly Acting Anti HCV treatment and its impact on quality of life of elderly patients.

DEMOGRAPHY AND MODE OF TRANSMISSION OF HEPATITIS C VIRUS

Hepatitis C virus (HCV) is a major health problem all over the world. In 2015, the worldwide prevalence of HCV infection was 1.0%, with the highest prevalence in the Eastern Mediterranean Region (2.3%) followed by the European one (1.5%). The annual mortality due to HCV-related complications is estimated to be approximately 700000 deaths ***(Omran et al., 2018).***

Seven HCV genotype strains have been known and classified according to the phylogenetic and sequence analyses of the whole viral genomes. Genotype strains differ at 30%-35% of the nucleotide sites. HCV genotype (4) is the predominant sort among chronically infected Egyptian patients ***(Elbedewy et al., 2015).***

The highest prevalence of HCV infection is present in Egypt, with 92.5% of patients infected with genotype (4), 3.6% patients with genotype 1, 3.2% patients with multiple genotypes, and < 1% patients with other genotypes ***(Smith et al., 2014).***

Egypt has the biggest number of HCV patients worldwide. The recently released Egyptian Demographic Health Survey [EDHS] tested a representative sample of the entire country for HCV antibody. The sample included both urban and rural populations and included all 27 governorates of Egypt. Over 11,000 individuals were tested. The overall prevalence positive for antibody to HCV was 14.7% ***(El-Zanaty and Way, 2009).***