Health Related Quality of Life and Response to Combined Anti-Viral Therapy in Chronic Hepatitis C Patients

Thesis submitted for partial fulfillment of M.D in Epidemiology

By

Heba Abdel Aziz Abdel Monem
Master degree in Epidemiology
National Hepatology and Tropical Medicine Research Institute
(N.H.T.M.R.I.)

Supervisors

Professor Dr. Aisha Abol Fotouh El-Gamal
Professor in the department of Community,
Environmental and Occupational medicine
Faculty of Medicine, Ain Shams University

Professor Dr. Mostafa El Hossainy
Professor in the department of Community,
Environmental and Occupational medicine
Faculty of Medicine, Ain Shams University

Professor Dr. Sameh Mohamed Seif El-Din
Professor in Tropical medicine department,
Head of the viral hepatitis treatment Centre
National Hepatology and Tropical Medicine Research Institute

Faculty of medicine
Ain Shams University
2019

ACKNOWLEDGEMENT

*First and foremost, I thank **Allah** for endowing me with health, patience, and knowledge to complete this work.*

*I dedicate my work to the soul of my **Dad** (RIP) and to my **Mom** and my **children** (**Yassin & Hunia**).*

*I would like to gratefully and sincerely thank **Prof. DR. Aisha Abo Al Fotouh** for her kindness and endless support.*

*I would like to give special thanks to **Prof. Dr. Mostafa El-Hossini**, for the patient guidance, encouragement and advice he has provided throughout my thesis.*

*I would like to extend my sincere gratitude to **Prof. Dr. Sameh Mohamed Saif**, for providing me valuable suggestion to complete this research.*

*I would like to thank the **National Hepatology and Tropical Medicine Research Institute** for their approval for conducting my research.*

*Finally, I am very grateful to all my **respondents** (patients) who agreed to be interviewed allowing me to get valuable information.*

Abstract

Background: Chronic hepatitis C virus infection is a major cause of chronic liver disease and death throughout the world. In addition to viral factors, several host factors also are implicated in modulating the effectiveness of IFN-therapy for the treatment of HCV infection. Likely, these host factors play an equally important role in modulating the efficacy of IFN- treatment. Therefore, an understanding of how these factors influence IFN- therapy may provide therapeutic targets to improve the efficacy of IFN-treatment several studies have shown an impaired health-related quality of life in patients with CHC compared to general population whereas treatment for this disease often induces similar symptoms as well.

Aim: to estimate the response rate to combined anti-viral therapy and

to determine the role of host factors in affecting response to combined anti-viral therapy such as host factors , viral factors, hepatic histopathology, also to measure the changes in the HRQoL of the patients after the treatment.

Methodology: 427 chronic HCV newly recruited patients to receive pegylated interferon and ribavirin for 48 weeks in the National Hepatology & Tropical medicine Research

Institute where all patients completed the SF-36 quality of life questionnaire before treatment and at the end of treatment then followed up for another six months to determine sustained virological response.

Results A total of 427 chronic HCV Egyptian patients with response rate 63.5%. Age is significantly true predictor for SVR (OR=0.975, 95% CI: 0.953- 0.998) while presence of diabetes was negative predictors for response (OR=3.239, 95% CI: 1.493- 7.027). Patients' HRQoL showed deterioration in all domains at the end of treatment compared to baseline measures with high statistical significance ($p < 0.001$). Non-responders showed more deterioration than patients with SVR especially in the perception of "mental health, social wellbeing, bodily pain, and general health".

Conclusion Sustained virological response rate between chronic hepatitis C patients receiving combined anti-viral therapy (interferon and ribavirin) was 63.5%. Age is significantly true predictor for SVR while diabetes was negative predictors for response. HRQoL of patients receiving combined anti-viral therapy (interferon and ribavirin) deteriorated during the course of treatment till the end of treatment.

Key words: *chronic hepatitis C, genotype 4, pegylated interferon, treatment response predictors, sustained virological response, Health-related quality of life*

Table of Content

LIST OF ABBREVIATIONS ..... *I*

LIST OF TABLES ..... *III*

LIST OF FIGURES ..... *VII*

PROTOCOL ..... *A*

INTRODUCTION *1*

AIM OF THE WORK *4*

REVIEW OF LITERATURE

- ***Chapter I: Hepatitis C*** *5*
- ***Chapter II: Health Related Quality of Life*** *35*

PATIENTS & METHODS *91*

RESULTS *100*

DISCUSSION *146*

CONCLUSION *167*

RECOMMENDATIONS *168*

LIMITATION OF STUDY *169*

ENGLISH SUMMARY *170*

REFERENCES *173*

APPENDIX *219*

ARABIC SUMMARY

LIST OF ABERRAVIATIONS

95% CI	*95% Confidence interval*
AFP	*Alfa-fetoprotein*
ALT	*Alanine Aminotransferase*
ARLD	*Alcohol Related Liver Disease*
AST	*Aspartate aminotransferase*
BMI	*Body Mass Index*
CDC	*Center for Disease Control*
CHC	*Chronic Hepatitis C*
CVH	*Chronic Viral Hepatitis*
DNA	*Deoxyribonucleic acid*
ETR	*End of treatment response*
HAV	*Hepatitis A virus*
HBV	*Hepatitis B virus*
HCC	*Hepatocellular Carcinoma*
HCV	*Hepatitis C Virus*
HEV	*Hepatitis E virus*
HIV	*Human Immunodeficiency virus*
HRQoL	*Health Related Quality of Life*
INF	*Interferon*
MOHP	*Ministry of Health and Population*
NAFLD	*Non-Alcoholic Fatty Liver Disease*

NHTMRI	*National Hepatology and Tropical Medicine Research Institute*
PCR	*Polymerase Chain Reaction*
PEG-IFN	*Pegylated Interferon*
QoL	*Quality of Life*
RCP	*Royal College of Physician*
RNA	*Ribonucleic acid*
SF-36	*Short-form 36*
SPSS	*Statistical Package for Social Science*
SVR	*Sustained Virological Response*
USDA	*United States Department of Agriculture*
WHO	*World Health Organization*

List of Tables

Review of Literature

Table 1
Recommendations for anti-HCV antibodies screening *7*

Table 2
Scoring systems used to evaluate stage of liver fibrosis..... *17*

Table 3
Definitions of therapeutic milestones for treatment of hepatitis C..... *25*

Table 4
Definition of patient response to hepatitis C therapy..... *26*

Table 5
Duration of treatment with simeprevir, pegylated interferon, and ribavirin..... *30*

Table 6
Adverse effects of hepatitis C treatment options..... *34*

Table 7
Standard international terminology used to describe virologic response in patients with chronic hepatitis C *75*

Table 8
Side effects combined Peg-IFN and RBV therapy..... *77*

Table 9
Uncommon Serious Adverse Events of Interferon and Ribavirin..... *78*

Results

Table 1
Baseline Characteristics of Patients Enrolled in the study *104*

Table 2
Distribution of study population according to the presence of other diseases *105*

Table 3
Distribution of study population according to liver pathology *105*

Table 4
Distribution of study population according to their biochemical results and virology *106*

Table 5
Distribution of study population according to their response to treatment *108*

Table 6
Relation between SVR and gender *109*

Table 7
Relation between SVR and Age *109*

Table 8
Relation between SVR and Duration of illness *110*

Table 9
Relation between SVR and diabetes *110*

Table 10
Relation between SVR and blood pressure *111*

Table 11
Relation between SVR and history of bilharziasis *111*

Table 12
Relation between SVR and smoking status *112*

Table 13
Relation between SVR and BMI *112*

Table 14
Relation between SVR and serum ALT more than normal *113*

Table 15
Relation between SVR and baseline PCR *113*

Table 16
Relation between SVR and activity score *114*

Table 17
Relation between SVR and fibrosis score *114*

Table 18
Predictive variables at baseline associated with SVR *116*

Table 19
Distribution of study population according to different HRQoL domains' score at baseline *118*

Table 20
Relation between response to treatment and different HRQoL domains at baseline *120*

Table 21
Relation between response to treatment and different HRQoL domains at end of treatment *121*

Table 22
Distribution of the study population according to the change in HRQoL domains before and after treatment *125*

Table 23
Comparison between health related quality of life before and after treatment *126*

Table 24
Relation between age and changes occurred in HRQoL domains before and after treatment *128*

Table 25
Relation between gender and changes occurred in HRQoL domains before and after treatment *131*

Table 26
Relation between employment and changes occurred in HRQoL domains before and after treatment *134*

Table 27
Relation between smoking and changes occurred in HRQoL domains before and after treatment *137*

Table 28
Relation between duration of illness and changes occurred in HRQoL domains before and after treatment *140*

Table 29
Relation between response to treatment and changes occurred in HRQoL domains before and after treatment *143*

List of Figures

Review of Literature

Fig. 1
Flow diagram of the hepatitis C virus transmission model *8*

Fig. 2
Development of chronic hepatitis C therapy *74*

Fig. 3
The relationship between disease- and treatment-related adverse events and HRQoL *81*

Subjects & Methods

Fig 1
Flow chart illustrating the course of treatment and follow up visits *98*

Results

Fig. 1
Distribution of study population according to their response to treatment *108*

Fig. 2
Relation between response to treatment and different HRQoL domains at end of treatment *122*

Fig. 3
Comparison between health related quality of life before and after treatment *127*

Health Related Quality of Life and Response to Combined Anti-Viral Therapy in Chronic Hepatitis C Patients

Thesis submitted for partial fulfillment of Ph.D in Epidemiology

By

Heba Abdel Aziz Abdel Moniem

Master degree in Epidemiology
National Hepatology and Tropical Medicine Research Institute
(N.H.T.M.R.I.)

Supervisors

Professor Dr. Aisha Abol Fotouh El-Gamal

Professor in the department of Community, Environmental and Occupational medicine
Faculty of Medicine, Ain Shams University

Professor Dr. Nanees Ahmed Ismail Gad

Professor in the department of Community, Environmental and Occupational medicine
Faculty of Medicine, Ain Shams University

Professor Dr. Sameh Mohamed Seif El-Din

Head of the Tropical medicine department,
Head of the viral hepatitis treatment Centre
National Hepatology and Tropical Medicine Research Institute

Faculty of medicine

Ain Shams University

2012

Chronic hepatitis C virus infection is a major cause of chronic liver disease and death throughout the world.[1]

More than 170 million people worldwide are chronically infected by the hepatitis C virus (HCV).[2] According to the WHO Report of 2002.[3] In 2001, chronic liver diseases were responsible for 1·4 million deaths, including 796 000 due to cirrhosis and 616 000 due to primary liver cancer. At least 20% of these deaths are probably attributable to HCV infection—more than 280 000 deaths. [4]

Egypt has a very high prevalence of HCV and a high morbidity and mortality from chronic liver disease, cirrhosis, and hepatocellular carcinoma.[5].

It is not a single disease, but rather a complex clinico-pathological syndrome with multiple causes, varying stages of necro-inflammatory and sclerosing liver damage, different prognoses and responses to treatment [6].

Egypt has higher rates of HCV than neighboring countries as well as other countries in the world with comparable socioeconomic conditions and hygienic