

Non-Response and Cost Effectiveness Analysis of Interferon Therapies in Management of Chronic Hepatitis C Patients

Thesis submitted for the partial fulfillment of M.D. degree in Public Health

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دراسة مقدمة من الطيبة : ريتا رأفت جاد
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ACKNOWLEDGMENTS

Deep thanks to God for everything

I wish to express my thanks and deep gratitude to Dr. Mostafa kamal Mohamed, Professor of Community, Environmental and Occupational Medicine, faculty of Medicine, Ain Shams University for his close supervision, expert advice and valuable scientific advises that greatly enriched this work.

I am sincerely indebted to the kindness of Dr. Mohamed Fawzy Montasser, Professor of Tropical Medicine, faculty of Medicine, Ain Shams University for his encouragement and support.

I am deeply grateful to Dr. Aisha Aboul Fotouh, Professor of Community, Environmental and Occupational Medicine, faculty of Medicine, Ain Shams University for her keen and continuous support, valuable suggestions and kind supervision.

Also, I wish to express my sincere thanks to Dr. Gamal Esmat, Professor of Tropical Medicine, faculty of Medicine, Cairo University for his encouragement and assistance

I wish to express my sincere gratitude to Dr. Moustafa el Housseiny, Assistant professor of Community, Environmental and Occupational Medicine, faculty of Medicine, Ain Shams University, for his continuous expert advise and sincere contribution to this work.

I wish to extend my deep thanks to the study participants, to the team members of the Hepatitis C Surveillance and Treatment Project at the National Hepatology and Tropical Medicine Research Institute; Department of Community, Environmental and Occupational Medicine, Ain Shams university specially Dr.Iman Bakr and Dr.Sahar Dewedar; the Unit of Emerging Infectious Diseases of Pasteur Institute specially Dr.Arnaud Fontanet. Without their help, this work would not have been possible.

At last and not the least, I would like to express my sincere gratitude to my husband, my mother and all my family for always being there for me.

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List of Abbreviations

95% CI	95% Confidence interval
AFP	Alfa-fetoprotein
ALT	Alanine Aminotransferase
BMI	Body Mass Index
CAPMAS	Central Agency for Public Mobilization and Statistics
CBA	Cost-benefit analysis
CDC	Center for Disease Control and Prevention
CEA	Cost-effectiveness analysis
CMV	Cytomegalovirus
CUA	Cost-utility analysis
DALYs	Disability-adjusted life years
DNA	Deoxyribonucleic acid
EBV	Ebstein Barr Virus
EIA	Enzyme Immunoassay
ETR	End of treatment response
EVR	Early virologic response
FV	Future value
GDP	Gross domestic product

HAI	Histological Activity Index
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C virus
HDV	Hepatitis D virus
HENCORE	Hepatitis C European Network for Cooperative Research
HEV	Hepatitis E virus
HIO	Health Insurance Organization
HIV	Human Immunodeficiency virus
ICER	Incremental Cost-effectiveness Ratio
IFN	Interferon
IQR	Interquartile range
IU	International Units
IVDU	Intravenous Drug Users
MOHP	Ministry Of Health and Population
MU	Million Units
NANB Hepatitis	Non A non B Hepatitis
NGO	Non-governmental organization

NHA	National health accounts
NHANESIII	Third National Health and Nutrition Examination Survey
NHS	National health system
NHTMRI	National Hepatology and Tropical Medicine Research Institute
NICE	National Institute of Health and Clinical Excellence
NIH	National Institute of Health
NPV	Negative predictive value
OLT	Orthotopic Liver transplantation
OR	Odds ratio
PCR	Polymerase Chain Reaction
PEG-IFN	Pegylated Interferon
PHC	Primary Health Care
PPV	Positive predictive value
PV	Present value
QALY	Quality-adjusted life years
RCT	Randomized controlled trial
RNA	Ribonucleic acid
ROC	Recipient Operator Characteristic
SF-36	Short-form 36

SVR	Sustained virological response
ULN	Upper limit of normal
VAS	Visual Analog Scale
VHRL	Viral Hepatitis Reference Laboratory
WHO	World Health Organization
WTP	Willingness to pay

Introduction

The prevalence of hepatitis C virus (HCV) infection is approximately 2.2% worldwide (The Global Burden of Hepatitis C Working Group, 2004); it infects about 170 million people worldwide and is responsible for approximately 20% of cases of acute hepatitis and 50% of cases of chronic hepatitis (WHO, 1999). The morbidity and mortality related to chronic hepatitis C is a major public health issue in Egypt where HCV prevalence nationwide is estimated around 12%. Interestingly, genotype 4 represents over 90% of cases in Egypt (MOHP, 1999).

Interferon alpha/ribavirin combination therapy is the standard treatment for patients with chronic hepatitis C; the sustained virological response or SVR (defined as negative HCV-RNA 6 months after the end of therapy) has been around 40% (El Zayadi et al, 1999) and has been as low as 0% in patients with genotype 4 (Al Faleh et al, 2000). With the introduction of pegylated interferon, a failure to eradicate infection occurs in around 20%.

of patients infected by genotype 2 or 3, and in around 50% of patients with genotype 1 (Pawlotsky, 2003).

In spite of these combined interferon and ribavirin regimens, the rate of SVR remains suboptimal. The growing evidence suggested that the treatment response of chronic hepatitis C are determined by a dynamic relationship among viral factors (including the pretreatment viral level, viral genotype), patient factors (including age, gender, race, HLA alleles and the body mass index (BMI) (Bressler et al, 2003), and interferon regimens (including type, dose, frequency and duration of treatment, and combination of interferon with other anti HCV agents) (Hu et al, 2001).

Studies have shown that predictors of SVR could differ by genotype. For example, low baseline HCV level and low baseline Gamma-GT levels were significantly associated with SVR in genotype 1-, 2- and 3-infected patients but not in genotype 2- and 3-infected patients (Berg et al, 2003). In another study, race was associated with SVR only in genotype 1 but not in genotype 2 and 3: black patients had significantly lower SVR than white patients (Brau et al, 2006).