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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٩٥٪ CI	٩٥٪ 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	Ribonucleiac acid
ROC	Recipient Operator Characteristic
SF-٣٦	Short-form ٣٦

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 ٢,٢٪ worldwide (The Global Burden of Hepatitis C Working Group, ٢٠٠٤); it infects about ١٧٠ million people worldwide and is responsible for approximately ٢٠٪ of cases of acute hepatitis and ٧٠٪ of cases of chronic hepatitis (WHO, ١٩٩٩). The morbidity and mortality related to chronic hepatitis C is a major public health issue in Egypt where HCV prevalence nationwide is estimated around ١٢٪. Interestingly, genotype ٤ represents over ٩٠٪ of cases in Egypt (MOHP, ١٩٩٩).

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 ٦ months after the end of therapy) has been around ٤٠٪ (El Zayadi et al, ١٩٩٩) and has been as low as ٥٪ in patients with genotype ٤ (Al Faleh et al, ٢٠٠٠). With the introduction of pegylated interferon, a failure to eradicate infection occurs in around ٢٠٪

of patients infected by genotype ٢ or ٣, and in around ٥٥٪ of patients with genotype ١ (Pawlotsky, ٢٠٠٣).

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, ٢٠٠٣), and interferon regimens (including type, dose, frequency and duration of treatment, and combination of interferon with other anti HCV agents) (Hu et al, ٢٠٠١).

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 ١-,٤- and ٦-infected patients but not in genotype ٢- and ٣-infected patients (Berg et al, ٢٠٠٣). In another study, race was associated with SVR only in genotype ١ but not in genotype ٢ and ٣: black patients had significantly lower SVR than white patients (Brau et al, ٢٠٠٦).