

**Evaluation of the Role of Alpha-Fetoprotein (AFP)
Levels in Chronic Viral Hepatitis C Patients,
Without Hepatocellular Carcinoma (HCC)**

Thesis

Submitted for Partial fulfillment of
Master Degree in Tropical Medicine

By

Ahmed "Mohamed Essam" Ismail Mahmoud
M.B.,B.Ch. - Sohag University

Supervised by

Professor / Hisham Khalil Dabbous

*Professor of Tropical medicine
Faculty of Medicine, Ain-Shams University*

Doctor / Runia Fouad EL-Folly

*Assistant Professor of Tropical Medicine
Faculty of Medicine, Ain-Shams University*

Doctor / Adham Mohamed Hamdan EL-Nakeeb

*M.D., Tropical Medicine (Ain Shams University)
Head of Hepatology & Gastroenterology Department
Sohag Cardiology and Hepato-Gastroenterology Center
Specialized Medical Centers, Ministry of Health*

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**Faculty of Medicine
Ain-Shams University
2009**



For ALLAH

To my Father

To my Wife

To my Mother

To my Kids

To my Sisters

To all of my family

Ahmed Essam



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LIST OF ABBREVIATIONS

AFP	: alpha-fetoprotein
ALF	: acute liver failure
ALT	: alanine aminotransferase
ANA	: antinuclear antibody
ANOVA	: analysis of variance
ARFP	: alternate reading frame protein
AST	: aspartate aminotransferase
bm-JIS	: biomarker combined-Japan integrated staging
CBC	: complete blood count
CD	: cluster of differentiation
CHC	: chronic hepatitis C
DAA	: direct-acting antivirals
DCP	: des-gamma-carboxy prothrombin
DM	: diabetes mellitus
DNA	: deoxyribonucleic acid
E-PHA	: erythroagglutinating phytohemagglutinin
EVR	: early virologic response
G-CSF	: granulocyte colony-stimulating factor
GGT	: gamma-glutamyl transferase or transpeptidase
GP	: glycoprotein
HCC	: hepatocellular carcinoma
HCV	: hepatitis C virus
HIV	: human immunodeficiency virus
HP	: hepatocyte proliferation
IEF	: isoelectric focusing
IFN	: interferon
IL	: interleukin
INR	: international randomization ratio
IRF-9	: interferon-regulatory factor-9
ISRE	: interferon-stimulated response elements
LDL	: low density lipoprotein
LT	: liver transplantation

LIST OF ABBREVIATIONS (Cont...)

MC	: mixed cryoglobulinemia
MPGN	: membranoproliferative glomerulonephritis
NI	: nucleoside inhibitors
NK	: natural killer
NNI	: non-nucleoside inhibitors
NS	: nonstructural
PAMPs	: pathogen-associated molecular patterns
PAT	: parenteral antischistosomal therapy
PBMC	: peripheral blood mononuclear cells
PCR	: polymerase chain reaction
PEG-INF	: pegylated interferon
PIs	: protease inhibitors
RCTs	: randomized controlled trials
RdRp	: RNA dependent RNA polymerase
RNA	: ribonucleic acid
ROC	: Receiver operating characteristic
RT	: reverse transcription
RVR	: rapid virologic response
SD	: standard deviation
STDs	: sexual transmitted diseases
SVR	: sustained virologic response
SVR12	: SVR obtained after 12 weeks
Th1	: type 1 CD4 ⁺ helper T
TNF	: tumor necrosis factor
TSH	: thyroid-stimulating hormone
TTD	: total tumor diameter
TTV	: total tumor volume
TVR	: telaprevir
US	: Ultrasonography
WHO	: World Health Organization

INTRODUCTION

The World Health Organization has declared hepatitis C a global health problem, with approximately 3% of the world's population (roughly 170-200 million people) infected with HCV. Hepatitis C virus (HCV) infection is the second viral cause for chronic liver disease (CLD) in the world (*Alavian, 2014*). In the US, approximately 3 million people are chronically infected, many of whom are still undiagnosed. In Egypt the situation is quite worse (*Mohamed, 2004*).

In 2008, The Egyptian Demographic Health Survey estimated HCV prevalence among the 15–59 years age group to be 14.7% (*El-Zanaty and Way, 2009*). Accordingly, Egypt has the highest prevalence of hepatitis C virus (HCV) in the world, estimated nationally at 14.7%. (*Mohamoud et al., 2013*).

More than 70% of acute HCV infections become chronic, and 20% of chronic hepatitis C (CHC) patients may develop liver cirrhosis within 20 years, with or without hepatic decompensation or hepatocellular carcinoma (HCC). CHC is associated with an increased risk of HCC, especially in liver cirrhosis patients (*Lee et al., 2008*).

HCV is known to be a human carcinogen based on sufficient evidence from studies in humans. Numerous cohort and case-control studies conducted in populations differing by race or ethnicity and in various geographical locations have

demonstrated that chronic HCV infection causes a malignant tumor of the liver (HCC) (*Neelima et al., 2000*).

Hepatocellular carcinoma (HCC) is one of the most frequent malignant tumors worldwide, with increasing incidence (*Tanaka et al., 2006*).

In the United States, HCC incidence and mortality rates continue to increase, particularly among middle-aged black, Hispanic, and white men (*Altekruse et al., 2009*).

Geographic variation in HCC incidence in Egypt has not been studied. Some reports have made simple comparisons between upper and lower Egypt as well as between urban and rural populations with respect to presumed exposures. However, the results were unsatisfactory (*Ezzat et al., 2005, Sayed et al., 2005 and El-Zayadi et al., 2001*).

Asymptomatic patients diagnosed with HCC through screening programs are more likely to be candidates for curative treatment and to have improved short- and medium-term survival (*Wong et al., 2000 and Yuen et al., 2000*).

In order to screen HCC in Egyptian patients with cirrhosis of all etiologies, 4-month intervals both serum alpha-fetoprotein (AFP>200ng) and liver ultrasound (US) are recommended (*Esmat et al., 2009*).

Alpha-fetoprotein (AFP) is a foetal glycoprotein which has been widely used as a serum marker for diagnosing

hepatocellular carcinoma (HCC); however, elevated serum AFP levels have also been documented in non-HCC patients with chronic liver disease (*Chen et al., 2007*).

AFP plays a limited role in the diagnosis of HCC, compared to imaging techniques. Increased detection of small lesions at presentation reflects increased awareness of the condition (*El-Zayadi et al., 2005*).

While elevations in AFP are commonly seen in persons with chronic hepatitis C, elevated levels have been shown to be more commonly associated with chronic liver disease and fibrosis than HCC and the value of measuring AFP in HCV has been called into question (*Di Bisceglie et al., 2005*).

Elevated serum AFP is not uncommonly seen in patients with CHC, but not HCC, and the incidence has ranged from 10% to 43% (*Chen et al., 2007*).

Previous reports examining the relationship between the elevated AFP levels and the outcome in HCV have primarily included patients from clinic-based studies who have undergone liver biopsy or been diagnosed with HCC and some studies have followed patients prospectively (*Hu et al., 2004*).

AIM OF THE WORK

The aim of this work was to evaluate the clinical significance of Alpha- Fetoprotein (AFP) levels in chronic hepatitis C patients without hepatocellular carcinoma (HCC).