Study of Golgi Protein 73 (golph2) a Valuable Serum Marker for Hepatocellular Carcinoma

Protocol for Thesis

submitted for

Partial fulfillment of master degree in

Internal medicine

Presnted by

Marwa Mohamed Elhoseny Ahmed

M.B.B.CH

AIN Shams University

Under supervision of

Prof.Dr.Sayed Mohamed Shalaby

Professor of internal medicine

Faculty of medicine, Ain Shams University

Dr.Moataz Mohamed Sayed

Assistant Professor of internal medicine

faculty of medicine Ain Shams University

Dr.Wesam Ibrahim Ahmed

Lecturer of internal medicine

Faculty of medicine, Ain Shams University

2011

Acknowledgement

First and foremost, thanks for **ALLAH** for guiding and helping me to finish this work

I would like to express my deepest thanks and sincere gratitude to **Prof. Sayed Mohamed Shalaby ,** Professor of Internal Medicine, Ain Shams University, for his close supervision, valuable instructions, continuous help and sincere advice.

Words stand short to express my deep appreciation and sincere gratitude to **Prof. Moataz Mohamed Sayed ,** Professor of Internal Medicine, Faculty of Medicine, Ain Shams University, for his continuous guidance and pioneer advices that put me on the right way. It was a great honor to me to work under his supervision.

I wish to introduce my deep respect and thanks to **Dr. Wesam Ibrahim Ahmed,** Lecturer of Internal Medicine , Faculty of Medicine, Ain Shams University, for his valuable supervision, sincere advice and his immense effort in the practical part of this study.

I am much grateful to all my colleagues in Tropical Department and HCC clinic for their co-operation and support and also to all patients included in this study. In addition, I wish to thank **Dr. Abd Elasis** for his help and co-operation in producing statistics and data analysis. Also, I would like to thank **Dr. Mahmed Shoair** for his sincere help in producing the lab results

List of contents

List of Tables (Review of Literature- Subjects & Methods)

List of tables (Results)

List of figures (Review of literature)

List of figures (Results)

List of abbreviations

^{131}I	Iodine-131
5`-NPD	5`-Nucleotide phosphodiesterase
5-FC	5-.fluorocytosine
5-FU	5-fluorouracil
AASLD	American Association for the study of the liver disease
AAT	Alpha-1-antitrypsin
Ad	Adenoviral
AFB1	Aflatoxin B1
AFP	Alpha-fetoprotein
AFP L3	Lens culinaris agglutinin reactive alpha fetoprotein
AFPIC	Alpha-fetoprotein immunocomplexes
AFU	Alpha-L-fucosidase
AJCC	The American Joint Committee on Cancer
ALP	Alkaline phosphatase
ALT	Alanine transaminase
ANOVA	Analysis of Variance
AST	Aspartate transaminase
BCLC System	The Barcelona-Clinic- Liver-Cancer system
BCS	Budd-Chiari syndrome
BSA	Bovine Serum Albumin
CD	cytosine deaminase
CECT	Contrast enhanced helical computed tomography
CEUS	Contrast enhanced ultrasound
CgA	Chromogranin-A
CLD	Chronic liver disease
CLIP	The Cancer of the Liver Italian Program
CT	Computed tomography
CTAP	CT arterial portography
CTHA	CT during hepatic arteriography
CUPI	Chinese University Prognostic Index
DCP	Des-gamma carboxyprothrombin
DGCP	Des-γ-carboxy prothrombin

DNA	Dinucleic acid
DPR	The differential positive rate curve
EASL	European association for the study of the liver
EDTA	Ethylenediaminetetraacetic acid
ELISA	Enzyme-linked immunosorbent assay
FDA	Food and Drug Administration
FLR	Future liver remnant
FNAB	Fine needle aspiration biopsy
G6P	Glucose-6-phosphatase
GCV	Ganciclovir
GGT	Gamma-glutamyl transpeptidase
GP73	Golgi protein 73
GPC3	Glypican-3
H-ALP	HCC Specific Alkaline Phosphatase
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HFL	Hepatic focal lesion
HGF	Hepatocyte growth factor
HIFU	High intensity focused ultrasound
HMG CoA reductase	Hydroxy methyl glutaryl coenzyme A reductase
HS-GGT	Hepatoma-specific GGT
HSP	Heat shock protein
HSV	Herpes Simplex virus
HSV-tk	Herpes simplex virus thymidine kinase
hTERT	Human telomerase reverse transcriptase
HTN	Hypertension
ICG	Indocyanine Green
ICG R15(%)	Indocyanine Green retention rate at 15 minutes
IGF-II	Insulin like growth factor- II
IL-8	Interleukin-8
ILP	Interstitial laser photocoagulation
INR	International normalized ratio
IVC	Inferior vena cava
JIS Score	The Japan Integrated Staging score

LCA	Lens culinaris agglutinin
LCSGJ	The Liver Cancer Study Group of Japan
LDH	Lactate dehydrogenase
LITT	Laser induced thermotherapy
LT	Liver Transplantation
MAA	Macro-aggregated albumin
MCT	Microwave Coagulation Therapy
MDCT	Multidetector helical CT
MELD	The Model for End Stage Liver Disease
mJIS	The modified Japan Integrated Staging
MOVC	Membranous obstruction of the inferior vena cava
MPCT	Multiphasic helical CT
MRI	Magnetic resonance imaging
mRNA	Massenger Ribonucleic acid
NASH	Nonalcoholic steatohepatitis
OLT	Orthotopic liver transplantation
PAS	Periodic acid–Schiff
PAT	Parenteral anti-schistosomal treatment
PBC	Primary biliary cirrhosis
PBMCs	Peripheral blood mononuclear cells
PCT	Porphyria cutanea tarda
PDGFR	Platelet derived growth factor receptor
PEI	Percutaneous ethanol injection
PEIT	Percutaneous ethanol injection treatment
PIAF	Cisplatin/Interferon a2b/Doxorrubicin/Fluorouracil
PIVKA-II	Protein induced by vitamin K absence or antagonist II
PMCT	Percutaneous Microwave Coagulation
PS	The performance status score
PSC	Primary sclerosing Cholangitis
PSI	Percutaneous hot saline injection
PUO	Pyrexia of unknown origin
PVE	Portal vein embolism
PVT	Portal vein thrombosis
RCT	Randomized Controlled Trial

RFA	Radiofrequency ablation
RILD	Radiation induced liver disease
ROC	The receiver operating characteristic curve
RT-PCR	Reverse transcription polymerase chain reaction
SBP	spontaneous bacterial peritonitis
SCCA	Serum squamous cell carcinoma antigen
SCCAIC	Serum squamous cell carcinoma antigen immunocomplexes
SD	Standard Deviation
SELDI-TOF	Surface-enhanced laser desorption/ionization-time of flight mass spectrometry
sGPC3	soluble Glypican-3
SIRT	Selective internal radiation therapy
TACE	Transarterial chemoembolization
TGF-α	Transforming growth factor-α
TGF-β1	Transforming Growth Factor-beta 1
TNM Staging System	Tumor, Node and Metastases Staging System
UNOS	United Network of Organ Sharing
US	Ultrasonography
VEGF	Vascular endothelial growth factor
VEGFR	Vascular endothelial growth factor receptor
VSV	Vesicular Stomatitis virus
WHO	World Health Organization

Introduction

The incidence of hepatocellular carcinoma (HCC) varies widely according to Geographic location. The distribution of HCC also differs among groups within the same country these extreme differences in distribution of HCC are probably due to regional variation, in exposure to hepatitis and environmental pathogens ***(kuda et al., 2011)***

Hepatocellular carcinoma (HCC) is strongly associated with either chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection, and the third leading cause of cancer death worldwide. ***(SHariff et al., 2009)***

Hepatocellular carcinoma is primary malignancy of the Hepatocyte generally leading to death within 6-20 month. Hepatocellular carcinoma frequently arises in the setting of cirrhosis appearing 20-30 years following the initial insult to the liver. How ever, 25%of patients have no history or risk factors for the development of cirrhosis. ***(Jemal et al., 2009)***

The use of serological markers in patients at the highest risk for developing HCC can thus decrease the cancer-related mortality and reduce medical costs. ***(Benowtz, 2007)***

Alfa-fetoprotein (AFP) has been only standard serum marker for the detection of HCC for the last 40 years, even

though its sensitivity of 39-65% is not very satisfactory. Identification of better early diagnostic biomarker is crucial. Recent studies have identified Golgi protein73. (G p 73, also named golgiphosphoprotein2 (golph2)) ***(Marrero et al., 2005)***

Golgi protein73 a potential novel HCC serum marker Gp73 is a 400 amino acid its mRNA was first identified in a search for up regulated hepatic genes in a patient with syncytial giant cell hepatitis **(*Kladney et al ., 2000)***

AIM OF the Work

The aim of this study was to determined value of serum GP73 in diagnosis of HCC in high risk patient (cirrhotic patient).