بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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MONA MAGHRABY

A Diagnostic Value of Serum Level Cyclase-Associated Plasma Protein 2 Versus Alpha Fetoproteins as a novel Biomarker for Detection of Hepato-Cellular Carcinoma in Egyptian Patients with Liver Cirrhosis

Thesis

Submitted For Partial Fulfillment of Master Degree in Hepatology & Gastroentrology

By

Milad Emad Milad

M.B.B.Ch.,

Faculty of Medicine – Ain Shams University (2014)

Under supervision of

Prof. Dr. Mohamed Abd Elmoghny Moustafa

Professor of Internal Medicine (Hepatology & Gastroenterology)

Faculty of Medicine - Ain Shams University

Prof. Dr. Zainab Ahmed Ahmed Ali- Eldin

Professor of Internal medicine (Hepatology & Gastroenterology)

Faculty of Medicine - Ain Shams University

Prof. Dr. Nevine Ibrahim Musa

Professor of Internal Medicine (Hepatology & Gastroenterology)

Faculty of Medicine - Ain Shams University

Faculty of Medicine

Ain Shams University

2020

بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to ALLAH, the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to Prof. Dr. Mohamed Abd Elmoghny Moustafa, Professor of Internal Medicine (Hepatology & Gastroenterology) Faculty of Medicine - Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.

I am also delighted to express my deepest gratitude and thanks to Prof. Dr. Zainab Ahmed Ahmed Ali- Eldin, Professor of Internal Medicine (Hepatology & Gastroenterology) Faculty of Medicine - Ain Shams University, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.

I am deeply thankful to Prof. Dr. Nevine Ibrahim Musa, Professor of Internal Medicine (Hepatology & Gastroenterology) Faculty of Medicine - Ain Shams University, for her great help, active participation and guidance.

Milad Emad

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List of Abbreviations

Abb.	Full term
99mTc	Technetium-99m
AFP	Anti-alpha-fetoprotein
ALT	Alanine aminotransferase
APRI	Platelet ratio
AST	Aspartate aminotransferase
AST	Aspartate aminotransferase
BCLC	Barcelona Clinic Liver Cancer
CAP	Cyclase-associated protein family
CT	Computed tomographic
DKK1	Dickkopf-1
E2	Estradiol
ELF	European Liver Fibrosis panel
ELISA	Enzyme-linked immune sorbent assay
EPO	Erythropoietin
FDG	Fluorine-18 fluorodeoxyglucose
FSH	Follicle stimulating hormone
GGT	γ-glutamyl transpeptidase
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HH	Hereditary hemochromatosis
HNE	Hydroxynonenal
HOA	Hypertrophic osteoarthropathy
HRP	Horseradish peroxidase
INR	International normalized ratio
LC	Liver cirrhosis
LH	Luteinizing hormone
MELD	Model for End-stage Liver Disease

List of Abbreviations Cont...

Abb.	Full term
MMPs	Matrix metalloproteinases
MRA	Magnetic resonance angiography
MRI	Magnetic resonance imaging
NASH	Nonalcoholic steatohepatitis
OD	Optical density
PCT	Porphyria cutanea tarda
PDGF	Platelet-derived growth factor
PET	Positron emission tomography
PGA	Apolipoprotein-A1
SHASTA	Serum Hyaluronic Acid level with serum AST and Albumin level
SUV	Standardized uptake values
TIMP-1	Tissue inhibitor of metalloproteinase-1
ULN	Upper limit of normal

ABSTRACT

Background: HCC is the third deadliest and fifth most common cancer worldwide, despite the widespread use of surveillance programs in at risk populations, more than half of HCC cases are diagnosed late, and curative therapies such as surgical resection, radiofrequency ablation or TACE are possible in less than 30% of patients.

Objective: To assess the value of plasma cyclase-associated protein 2 level in diagnosis of hepatocellular carcinoma among the Egyptian patients with chronic hepatitis c virus.

Patients and Methods: This study has been carried out in the department of Internal Medicine and Gastroenterology in Ain Shams University Hospitals and Manshiet El-Bakry general hospital, Department of Gastrohepatology. This study evaluate the significance of Plasma CAP2 level as a new diagnostic marker for HCC patients with post hepatitis C liver cirrhosis where (80) persons, divided into three groups; Group A included (30) patients with post hepatitis C liver cirrhosis without HCC, Group B included (40) patients with post hepatitis C liver cirrhosis and HCC, and Group C included (10) healthy subjects as a control group.

Results: In this study CAP2 was **significantly higher** in HCC group than in cirrhotic and control groups ($p<0.001$) with mean levels (30.7±12.4), (14.4±7.6), and (6.9±4.3) ng/ml respectively although in HCC patients with negative or low AFP levels. This finding could imply the role of CAP2 in diagnosing early and AFP negative HCC patients.

Conclusion: CAP2 is significantly elevated in HCC group than in cirrhotic and control groups with better sensitivity and specificity than AFP at cut off values ≥15.9 ng/ml and ≥53.2 ng/ml respectively. Such results support using of CAP2 as a better diagnostic marker for HCC. AFP and CAP-2 were higher in multiple lesions than in single lesions, but the differences were significant only in CAP-2 with ≥27.3 ng/ml in differentiating multiple from solitary lesions Considering the HCC if both of them were positive decreased sensitivity but had perfect specificity.

Keywords: Hepatocellular carcinoma, hepatitis B virus, hepatitis C virus, nonalcoholic steatohepatitis

INTRODUCTION

Hepatocellular carcinoma (HCC) is the dominant form of primary liver cancer and is histologically and etiologically distinct from other forms of primary liver cancer ***(Yu et al., 2008).***

Approximately 70%–90% of patients with HCC have an established background of chronic liver disease and cirrhosis, with major risk factors for developing cirrhosis including chronic infection with hepatitis B virus (HBV), hepatitis C virus (HCV), alcoholic liver disease, and nonalcoholic steatohepatitis (NASH) ***(El-Serag & Rudolph, 2007).***

Additional risk factors for developing HCC include intake of aflatoxin-contaminated food, diabetes, obesity, certain hereditary conditions such as hemochromatosis, and some metabolic disorders ***(Montalto et al., 2002).***

HCC one of the human cancers in that the causative agent is often not clear. There are multiple etiologic factors affecting HCC, all of which vary by geographic location, have a direct impact on the characteristics of these patients, and influence the disease course, making HCC an extremely complex condition associated with a poor prognosis ***(Venook et al., 2010).***

HCC carcinogenesis is a complex process that can involve various modifications to a number of molecular

pathways as well as genetic alterations, and ultimately leads to malignant transformation and HCC disease progression ***(Shekih et al., 2008).***

In molecular biology, the Cyclase-associated protein family (CAP) is a family of highly conserved actin binding proteins present in a wide range of organisms and mammals. CAPs are multifunctional proteins that contain several structural domains. CAP is involved in species-specific signaling pathways ***(Deeks et al., 2007).***

CAPs family includes CAP1 and CAP2. They are firstly identified in yeast and mediate the cAMP-dependent pathway which is necessary for many different cell responses as the increase in heart rate, cortisol secretion, and breakdown of glycogen and fat ***(Effendi et al., 2003).***

It has been recently reported that CAP2 (cyclase-associated protein 2) is up-regulated in HCC patients and its expression correlates to the multistage development of HCC, CAP2 is also closely associated with cellular invasion and metastasis of HCC. In addition, CAP2 can be detected in tumor cells invading the stromal area in liver tissue ***(Chuma et al., 2013).***

AIM OF THE WORK

The aim of this study is to assess the value of plasma cyclase-associated protein 2 level in diagnosis of hepatocellular carcinoma among the Egyptian patients with chronic hepatitis c virus.