بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

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MONA MAGHRABY

Evaluation of the Role of Serum Vimentin as a Diagnostic Biomarker for Hepatocellular Carcinoma

Thesis

For Partial Fulfillment of Master Degree
in **Gastroenterology and Hepatology**

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M.B.B.Ch., 2014

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2021

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. Amira Ahmed Salem, Professor of Gastroenterology and Hepatology - Faculty of Medicine- Ain Shams University for her 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 Dr. Manal Sabry Mohamed, Assistant Professor of Gastroenterology and Hepatology, 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 Dr. Ahmed M. F. Mansour, Lecturer of Gastroenterology and Hepatology, Faculty of Medicine, Ain Shams University, for his great help, active participation and guidance.

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients participated in this study.

Yousef El Sayed Mohamed El Sayed

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List of Abbreviations

Abb.	Full term
18F-FDG	*18F-fluorodeoxyglucose*
AFB1	*Aflatoxin B1*
AFP	*Alpha-fetoprotein*
AFP-L3	*Alpha-fetoprotein*
ALT	*Alanine transaminase*
ANG-2	*Angiopoietin 2*
AST	*Aspartate transaminase*
BM	*Bone marrow*
BSA	*Bovine Serum Albumin*
CBC	*Complete Blood Count*
CEUS	*Contrast-enhanced US*
CLD	*Chronic liver disease*
CTCs	*Circulating tumor cells*
DCP	*Des-gamma-carboxy prothrombin*
ECM	*Extracellular matrix*
EMT	*Epithelial-to-mesenchymal transition*
GP73	*Golgi glycoprotein 73*
Gp-73	*Golgi protein 73*
HBV	*Hepatitis B virus*
HCC	*Hepatocellular carcinoma*
HCV	*Hepatitis C virus*
HGF	*Hepatic growth factor*
HRP	*Horseradish Peroxidase*
HSCs	*Hepatic stellate cells*
IF	*Intermediate filament*
IGF-1	*Insulin growth factor-1*
INR	*International randomized ratio*
LCA	*Lens culinaris agglutinin*
MRI	*Magnetic resonance imaging*

List of Abbreviations (Cont…)

Abb.	Full term
NAFLD	*Non-alcoholic fatty liver disease*
NASH	*Non-alcoholic steatohepatitis*
OPN	*Glypican-3 osteopontin*
PC	*Prothrombin concentration*
PET	*Positron emission tomography*
PME	*Premalignant environment*
PVTT	*Portal vein tumor thrombus*
ROS	*Reactive oxygen species*
SPSS	*Statistical Package for Social Sciences software*
TICs	*Tumor-initiating cells*
VEGF	*Vascular endothelial growth factor*

INTRODUCTION

Hepatocellular carcinoma (HCC) is a major unresolved medical issue, which is considered as the seventh most common cancer globally and the fourth leading cause of cancer deaths, with approximately 700,000 deaths per year **(Fitzmaurice et al., 2018).**

Multiple risk factors can trigger HCC development and progression, including viral hepatitis B and C infection, chronic alcohol consumption, metabolic disorders, and age **(Ghouri et al., 2017).**

The chief causes of HCC are liver fibrosis or cirrhosis from chronic viral infections. Because cases tend to arise from preceeding pathologies, biomarker surveillance in high-risk individuals is an indispensable tool for achieving earlier detection and improved outcomes of HCC **(Black and Mehta, 2018).**

A 2017 update of the AASLD guidelines recommends surveillance using ultrasonography, with or without α-fetoprotein (AFP), every six months **(Heimbach et al., 2018)**.

Surveillance strategies in patients at a higher risk of HCC have led to the diagnosis of the disease at much earlier stages. Patients in the early stages have a much higher chance of curative response with different treatment options. While surgery is the most effective treatment for liver tumors, about 80% of HCCs are

not curable at presentation, and therefore the patients die due to the delayed diagnosis **(Black and Mehta, 2018).**

Although numerous efforts have been made to discover more reliable biomarkers for the diagnosis of HCC such as AFP-L3, DCP and GP73, serum AFP remains the most commonly used biomarker **(Chaiteerakij et al., 2015).**

AFP is a glycoprotein, physiologically synthesized during the early stages of fetal liver development by the endodermal cells of the visceral yolk sac. The AFP expression by hepatocytes and endodermal cells of the yolk sac reduces after birth. The elevation of AFP can occur in hepatocyte regeneration, during hepato-carcinogenesis, and embryonic carcinomas **(Biondi et al., 2012).**

Serum concentrations of AFP have been shown to be the most useful tumor marker with regards to HCC but levels may be normal in up to 40% of patients, reducing its sensitivity. Moreover, it may be increased in patients with hepatitis and cirrhosis, compromising its specificity **(Lersritwimanmaen and Nimanong, 2018).**

It has recently been shown that most small HCC nodules do not increase AFP levels, decreasing the sensitivity of AFP for tumors smaller than 3 cm to just 25% **(Shu et al., 2017).**

Vimentin is classified as a type III intermediate filament (IF) protein. Its function is to maintain cellular integrity and

protect the cell against stress. It is the major cytoskeletal component of mesenchymal cells. It also plays a significant role in cell shape maintenance and in stabilizing cytoskeletal interactions **(Roggiani and Goulian, 2015).**

Vimentin expression in tumor cells has been recognized as a hallmark of epithelial- mesenchymal transition (EMT), and is associated with cell invasion and poor prognosis **(Satelli et al., 2017).**

Meng et al. (2018) reported that vimentin was involved in the process of EMT in HCC and that its down-regulation inhibits EMT.