

شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو

بسم الله الرحمن الرحيم





HANAA ALY



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكرونيله



شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



HANAA ALY



شبكة المعلومات الجامعية التوثيق الإلكترونى والميكروفيلم

جامعة عين شمس التوثيق الإلكتروني والميكروفيلم قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها على هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



HANAA ALY





Serum Clusterin Level as a diagnostic and prognostic marker for Hepatocellular Carcinoma.

Thesis

Submitted for partial fulfillment of the Master Degree

In Gastroenterology

By Aml Salah Mohamed Ahmed

M.B.B.C.H Cairo University

Under supervision of

Prof. Dr. Hatem Abdellatif Mohammed

Professor of Internal Medicine, Gastroenterology Faculty of Medicine – Ain Shams University

Ass.prof. Dr. Eslam Safwat Mohammed

Assistant Professor of Internal Medicine, Gastroenterology Faculty of Medicine – Ain Shams University

Ass.Prof. Dr.Hany Samir Rasmy

Assistant professor of Internal Medicine, Gastroenterology Faculty of Medicine – Ain Shams University

> Faculty of Medicine Ain Shams University 2021





مستوى الكلوسترين بالمصل كمؤشر حيوي لتشخيص والتنبؤ بسير سرطان الكبد

أطروحة

مقدمة لنيل درجة الماجستير في أمراض الجهاز الهضمي

مقدمة من الطالبة أمل صلاح محمد أحمد بكالوريوس الطب والجراحة – جامعة القاهرة

تحت إشراف

أ.د: حاتم عبد اللطيف محمد

أستاذ أمراض الباطنة العامة والجهاز الهضمي كلية الطب – جامعة عين شمس

أ.د: اسلام صفوت محمد

أستاذ مساعد أمراض الباطنة العامة والجهاز الهضمي كلية الطب - جامعة عين شمس

أ.د : هاني سمير رسمي

أستاذ مساعد أمراض الباطنة العامة والجهاز الهضمي كلية الطب - جامعة عين شمس

كلية الطب جامعة عين شمس ٢٠٢١

Aeknowledgement

work, until it has reached its end, as a part of his generous help, throughout my life.

Really I can hardly find the words to express my gratitude to **Prof. Dr. Hatem Abdellatif Mohammed** Professor of Internal Medicine, Gastroenterology, Faculty of Medicine – Ain Shams University, for his supervision, continuous help, encouragement throughout this work and tremendous effort he has done in the meticulous revision of the whole work. It is a great honor to work under his guidance and supervision.

I would like also to express my sincere appreciation and gratitude to **Dr. Eslam Safwat Mohammed**, assistant Professor of Internal Medicine, Gastroenterology, Faculty of Medicine – Ain Shams University, for his continuous directions and support throughout the whole work.

I cannot forget the great help of **Dr. Dr. Hany Samir Rasmy** Assistant professor of Internal Medicine, Gastroenterology, Faculty of Medicine – Ain Shams University, for his invaluable efforts, tireless guidance and for his patience and support to get this work into light.

Last but not least, I dedicate this work to my family, whom without their sincere emotional support, pushing me forward this work would not have ever been completed.

Aml Salah Mhammed

List of Contents

Title Pa	ge	
Acknowledgment		
List of Abbreviations.		
List of Tables	viii	
List of Figures	xi	
Introduction	1	
Aim of the Work	4	
Review of Literature		
Hepatocellular Carcinoma	5	
• Clusterin	39	
Patients and methods	56	
Results	61	
Discussion	84	
Summary	95	
Conclusion	97	
Recommendation	98	
References	99	
Arabic summary	1	

List of Abbreviations

A1ATD : Alpha 1 antitrypsin deficiency

AASLD : American Association for the Study of Liver

Diseases

AFP : Alpha Fetoprotein

ALT : Alanine aminoTranferase
AST : Aspartate aminotransferase
BCLC : Barcelona clinic liver cancer
CD : Cluster of Differentiation
CECT : Contrast enhanced CT

CEMRI : Contrast enhanced magnetic resonance imaging

CEUS : Contrast Enhanced Ultrasound

CK : Cytokeratins

CRP : C- Reacive Protein
CT : Computed tomography

CTLA-4 : Cytotoxic T-lymphocyte-associated protein 4

CTP : Child-Turcotte –pugh classification.
DCP : Des-gamma-carboxyprothrombin

DM : Diabetes Mellitus

EASL : European Association for Study of Liver

EASL-EORTC : European Association for the Study of the Liver,

European Organisation for Research and Treatment

of Cancer

ELISA : Enzyme-Linked Immunosorbent Assay ERK : Extracellular signal-Regulated Kinases

ESLC : Egyptian Society of Liver Cancer.

EUS : Endoscopic US

FDA : Food And Drug Administration

Hb : Haemoglobin

HBeAg : Hepatitis B envelope antigen

HBV : Hepatitis B virus

HCC : Hepatocellular Carcinoma

HCV : Hepatitis C virusHCV-Ab : Hepatitis C antibodyHFL : Hepatic Focal Lesion

HGF : Hepatocyte growth factor

List of Abbreviations cont...

HGF/SF : Hepatocyte Growth Factor/ scatter factor

HIV : Human Immune Deficiency

HSP-70 : Heat Shock Protein 70 IDU : Intravenous drug use

IGF-II : Insulin-like growth factor-II
 IGFR : Insulin Growth Factor Receptor
 INR : International Normalized ratio
 JNK : Jun N-terminal kinases consist

KLCSG-NCC: Korean Liver Cancer Study G, National Cancer

Center

LC : Liver Cirrhosis

LT : Liver transplantation M : Metastasis classification

MAPK : Mitogen-Activated Protein Kinases

MC : Milan criteria

MDCT : Multi Detector CT

MELD : Model for End Stage Liver Disease

MiRNAs : MicroRNAs

MRI : Magnetic resonance imaging

MWA : Micro wave ablationN : Node Classification

NAFLD : Nonalcoholic fatty liver disease NASH : Non-Alcoholic steato Hepatitis

NO : Nitric oxide

PAI : Percutaneous acetic acid injection PBMCs : Peripheral blood mononuclear cells

PCR : Polymerase chain reac

PDGF : Platelet-derived growth factor

PEIT : Percutaneous ethanol injection Therapy

PLT : Platelet

PVT : Portal vein thrombosis

List of Abbreviations cont..

RFA : Radiofrequency ablation

ROC : Receiver operating characteristic

RT-PCR : Reverse transcription –polymerase chain reaction

SEER : Surveillance Epidemiology End Result SIRT : Selective internal radiation therapy

Selective internal radiation therapy
 TACE : Transarterial chemoembolisation
 TGF-β1 : Transforming growth factor-beta 1

TLC : Total leucocyte count

TNM : Tumor, node, metastasis staging VEGF : Vascular endothelial growth factor

WBC : White Blood Cells

WHO : World health organization

List of Tables

Table	Title	Page
1	American Joint Committee on Cancer (AJCC) staging system for Hepatocellular carcinoma (HCC).	28
2	Child-Pugh classification of chronic liver disease	57
3	Comparison between LC only group (group A) and LC with HCC groups (group B) regarding demographic characteristics:	61
4	Comparison between LC only group (group A) and LC with HCC groups (group B) regarding MELD & Child Score	62
5	Comparison between LC only group (group A) and LC with HCC groups (group B) regarding basal CBC	62
6	Comparison between LC only group (group A) and LC with HCC groups (group B) regarding Biochemical Parameters	63
7	Comparison between LC only group (group A) and LC with HCC groups (group B) and regarding Ultrasound Parameters	64
8	Comparison between LC only group (group A) and LC with HCC groups (group B) regarding basal Clusterin Level	64
9	Comparison between LC only group (group A) and LC with HCC groups (group B) regarding basal AFP Level	65
10	Distribution of HCC Group regarding type of intervention	66
11	Distribution of HCC Group regarding Lesion Number and diameter , Grading and	67

vi

Table	Title	Page
	Recurrence	
12	Comparison between basline AFP and different parameters among LC only group (group A) and LC with HCC groups (group B)	67
13	Comparison between basline Clusterin and different parameters among LC only group (group A) LC with HCC groups (group B)	70
14	Correlations of Basal AFP among HCC groups and LC groups regarding Different Parameters	72
15	Correlations of Basal Clusterin among HCC groups and LC groups regarding different parameters	73
16	Comparison between before and after locoregional treatment regarding different biochemical parameters among group B	74
17	Comparison between before and after locoregional treatment regarding AFP & Clusterin level	75
18	Comparison regarding baseline AFP and Clusterin before intervention Among Group B in relation to their mRecist grade	77
19	Comparison regarding baseline AFP and Clusterin After intervention Among Group B in relation to their mRecist grade	78
20	Comparison regarding Change in AFP & Clusterin level Before and After intervention Among Group B in relation to their mRecist grade	78
21	Diagnostic preference of AFP & Clusterin level in differentiating HCC group from LC gtoup	79

vii

Table	Title	Page
22	Diagnostic preference of Clusterin level in	80
	diagnosing progression of HCC after	
	intervention according to mRecist Grading	
23	diagnostic preference of AFP and Custerin	81
	level in differentiating progressive disease	
	(PD) from complete response (CR) after	
	intervention of HCC	

List of Figures

Fig.	Title	Page
1	Diagnostic algorithm for suspected HCC	17
2	Updated BCLC staging system and treatment strategy	30
3	Structure of <i>CLU</i> gene and transcription products	40
4	CLU structure	41
5	Reported sites of conventional CLU (sCLU) localization and function	43
6	Main mechanism of sCLU action	45
7	Comparison between LC only group (group A) and LC with HCC groups (group B) regarding basal Clusterin Level	65
8	Comparison between HCC groups and LC group regarding AFP	66
9	Correlation between basal AFP and lesion size	69
10	Correlation between basal AFP and different BCLC stages	69
11	Correlation between basal Clusterin and different mRecist score grades	71
12	Correlation between basal Clusterin and presence of recurrence after intervention	72
13(A-B)	comparison between AFP level in Group B before and after intervention	75
14(A-B)	comparison between Clusterin level in group B before and after intervention	76
15	ROC curve for basal Clusterin in diagnosing HCC	79
16	ROC curve for basal AFP in diagnosing HCC	79

Fig.	Title	Page
17	Roc Curve for Clusterin level between PD and CR+PR	81
18	ROC curve for Clusterin level in prediction of HCC group response to intervention	82
19	ROC curve for AFP level in prediction of HCC group response to intervention	82
20	Correlation between AFp and BCLC score	90