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The Diagnostic and prognostic value of Fibrinogen and D-dimer levels versus α-Fetoprotein level in Hepatocellular Carcinoma (HCC) in Egyptian patients

Thesis

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List of Abbreviations

Abb.	Full-term
AIH	Autoimmune hepatitis
AJCC	American Joint Committee on Cancer
BCLC	The Barcelona Clinic Liver Cancer system
BMI	Body mass index
CT	Computed tomography
DAA	Direct acting antiviral
DLC	Dioxin-like Compounds
EARN HCC	Egyptian Research Network for HCC
GWAS	Genome-wide association studies
HBV	Hepatitis B virus؛
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus؛
HFE	Hemochromatosis protein
HLA	Human leukocyte antigen؛
IDMC	Independent Data Monitoring Committee
IGF-1	Insulin-like growth factor-1
IL	Interleukin
IR	Insulin resistance
MOH	Ministry of Health
MRI	Magnetic resonance irradiation
NAFLD	Nonalcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NGO	Non-governmental organizations
OCs	Oral contraceptives
OS	Overall survival

List of Abbreviations (Continued)

Abb.	Full-term
O-toluidine	Ortho-Toluidine
PBB	Polybrominated biphenyls
PCB	Polychlorinated biphenyls
PCE	Perchlorethylene
PVC	Polyvinyl chloride
TCE	Trichloroethylene
TNM	Tumor-node-metastasis
VCM	Vinyl chloride monomer
WES	Wholeexome sequencing
WHO	World Health Organization

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INTRODUCTION

Hepatocellular carcinoma (HCC) is a globally prevalent deadly disease. The tumor occurs primarily on the background of chronic hepatitis viral infection and cirrhosis ***(Nakamoto, 2016).***

Radical therapies, including surgical resection, liver transplantation, and radiofrequency ablation, are the standard modalities used for the curative treatment of HCC; however, the application of these therapies is limited due to impaired liver function and advanced tumour stage of patients and a shortage of donors ***(Balogh et al., 2016).***

Many pathological conditions including thrombosis, inflammation, and trauma lead to the activation of coagulation factors and fibrinolysis ***(Allen et al., 2015).***

Coagulation and fibrinolysis markers have the potential to serve as predictors of disease and disease severity ***(Deng et al., 2016).***

An increasing body of evidence suggests the existence of a relationship between activation of coagulation and tumor angiogenesis, progression, and metastatic spread ***(Hao et al., 2015; Zhu et al., 2016).***

Aim of the Work

The aim of this study is to investigate their predictive and prognostic value versus α- Fetoprotein level in Egyptian patients with Hepatocellular carcinoma (HCC).

Chapter (I): Hepatocellular carcinoma

Hepatocellular carcinoma (HCC), the primary cancer of the liver, is derived from hepatocytes and occurs in more than approximately 80% of cases of liver cancer ***(Jemal, 2011).***

Epidemiology and disease burden in Egypt Hepatocellular carcinoma (HCC) represents the sixth most common cancer worldwide ***(Forner, 2018).***

In Egypt, it represents the fourth common cancer ***(Alemayohu et al., 2015).***

The reason for increased incidence could be attributed to:

Improvement in screening programs and diagnostic tools ***(El Serag, 2001)***

Increasing the incidence and complications of hepatitis C virus (HCV) ***(Salama et al., 2018)***

Which is the most important risk factor in developing liver cancer including HCC in Egypt ***(Salama et al., 2014).***

It was estimated to be responsible for nearly 9.1% of the total deaths in 2012 (746,000 deaths) ***(Rebelo et al., 2012).*** In Egypt, It is the most common cause of mortality and morbidity related cancer ***(Salama et al., 2014).***

Life expectancy of patients with HCC depends on the stage of the cancer at diagnosis. In advanced stage, some months are expected, however, when the diagnosis is early and effective treatment performed, five- year survival rate can be accomplished ***(Forner et al., 2012).*** If the diagnosis is performed at early stage, its treatment is limited and effective; whereas, at advanced when traditional chemotherapy has no satisfactory effect, poor prognosis is expected ***(Liu et al., 2015).*** At early stage of HCC, curative treatments such as surgical resection, liver transplant and local ablation can improve the survival of the patients.

Therefore, early detection and the adequate therapy are crucial to increase survival and improve the life quality of HCC patients. When classified as stage C (advanced stage) with the presence or absence of vascular invasion and preserved liver function, according to Barcelona Clinic Liver Cancer (BCLC) classification, the use of Sorafenib has been effective to improve these patients´ survival ***(Gomes et al., 2013; de Lope et al., 2012).***

Alpha-fetoprotein (AFP) has been used as a biomarker in HCC diagnosis by serum. However, AFP is not a precise marker since it provides low sensibility and specificity ***(Morimoto et al., 2012; Lok et al., 2010).*** Therefore, a biomarker that presents higher diagnostic accuracy and high reliability are needed. Recent studies