# بسم الله الرحمن الرحيم


MONA MAGHRABY

# شبكة المعلومات الجامعية

# التوثيق الالكتروني والميكروفيلم

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# جامعة عين شمس

# التوثيق الإلكتروني والميكروفيلم

# قسم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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***MONA MAGHRABY***

# Assessment of the Value of Mean Platelet Volume, Des Gamma Carboxy Prothrombin and Alpha Feto Protein in Early Detection of HCC

A Thesis
Submitted for Partial Fulfillment of
master degree in **Internal Medicine**

By

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**Omnia Ahmed Ellaithy**

# List of Contents

# List of Tables

# List of Figures

# List of Figures (Cont…)

# List of Abbreviations

| Abb. | Full term |
|---|---|

*AFP* ..... *Alpha-fetoprotein*
*AFU* ..... *Alpha L-Fucosidase*
*AJCC* ..... *American Joint Committee on Cancer*
*ALT* ..... *Alanine aminotransferase*
*AST* ..... *Aspartate aminotransferase*
*BCLC* ..... *Barcelona Clinic Liver Cancer*
*CEUS* ..... *Contrast enhanced ultrasound*
*CLD* ..... *Chronic liver disease*
*CT* ..... *Computed Tomography*
*CUPI* ..... *Chinese University Prognostic Index*
*DAA* ..... *Direct-acting antivirals*
*DCP* ..... *Des-γ-carboxy prothrombin*
*DMSA* ..... *Dimercaptosuccinic acid*
*DWI* ..... *Diffusion-weighted*
*EPO* ..... *Erythropoietin*
*EUS* ..... *Endoscopic US*
*HBV* ..... *Hepatitis B virus*
*HCC* ..... *Hepatocellular carcinoma*
*HCV* ..... *hepatitis C virus*
*HSP* ..... *Heat shock protein*
*IGF-II* ..... *Insulin-like growth factor-II*
*IL 8* ..... *Interleukin-8*
*IOUS* ..... *Intra-operative US*
*IR* ..... *Insulin resistance*
*JIS* ..... *Japan Integrated Staging*
*LA* ..... *Laser ablation*

# List of Abbreviations (Cont…)

| Abb. | Full term |
|---|---|
| *MAGE* | *Melanoma antigen gene* |
| *MC* | *Milan criteria* |
| *MCT* | *Microwave coagulation therapy* |
| *MPC* | *Mean platelet component* |
| *MPV* | *Mean platelet volume* |
| *MR* | *Magnetic resonance* |
| *MRI* | *Magnetic resonance Imaging* |
| *PBC* | *Primary biliary cirrhosis* |
| *PEI* | *Percutaneous Ethanol injection* |
| *PET* | *Positron Emission Tomography* |
| *RFA* | *Radiofrequency Thermal Ablation* |
| *SCCA* | *Serum squamous cell carcinoma antigen* |
| *TACE* | *Transarterial chemoembolization* |
| *TAE* | *Transarterial embolization* |
| *TGF-β1* | *Transforming growth factor-beta 1* |
| *TNM* | *Tumor-Node-Metastasis Staging System* |
| *TNM* | *Tumor-Node-Metastasis Staging System* |
| *UICC* | *Union International Contre le Cancer* |
| *US* | *Role of Ultrasound* |
| *VEGF* | *Vascular endothelial growth factor* |
| *WHO* | *World Health Organization* |

# ABSTRACT

***Background:*** Hepatocellular carcinoma (HCC) is the most common primary malignant tumor of the liver. AFP is the gold standard tumor marker for HCC, mean platelet volume (MPV) is a parameter obtained from complete blood count (CBC) by automated analyzers, shown to be increased in multiple malignancies and inflammatory conditions. This cross sectional comparative study was designed to evaluate the diagnostic usefulness of MPV as a diagnostic marker in HCC patients due to cirrhosis.

***Aim of the Work:*** To determine the value of mean platelet volume, Des gamma Carboxy prothrombin and Alfa-feto protein in early detection of Hepatocelluler carcinoma

***Patients and Methods:*** 105 patients were enrolled in this study, they were divided into 3 equal groups **Group A:** Hepatocelluler carcinoma patients (HCC) **Group B:** Liver cirrhosis patients **Group C:** Healthy Control group each is 35 patients**.** MPV, AFP, DCP were evaluated in all groups. Ultrasound and Triphasic CT. were also done to Group A&B to confirm or exclude the diagnosis of HCC and in group C as they are candidates for LDLT donors.

***Results:*** Our results showed that regarding the diagnostic performance of the three tested tumor markers (AFP, MPV and DCP) in differentiating HCC from CLD groups that AFP had area under curve (AUC) of 0.719, Standard error (SE) of 0.061, Confidence interval (CI) of 0.599-0.839 and P value of 0.002 at a cut point of ≥40.0, MPV had area under curve (AUC) of 0.801, Standard error (SE) of 0.063, Confidence interval (CI) of 0.678−0.924 and P value of <0.001 at a cut point of ≥10.2, while DCP had area under curve (AUC) of 0.842, Standard error (SE) of 0.047, Confidence interval (CI) of 0.750−0.935 and P value of <0.001 at a cut point of ≥69.3 proving that DCP had the highest significant diagnostic performance in differentiating HCC from CLD groups also DCP≥ 69.3 had highest sensitivity(of 97.1%) and NPV(of 96.3%). AFP≥ 40.0 had highest specificity (of 91.4%) and PPV (of 86.4%).

***Conclusion:*** Measurement of MPV is non-invasive, cheap and quick, and may therefore serve as a predictor of HCC in patients with CLD. Low sensitivity and specificity, on the other hand, suggests that this may be an adjunctive parameter to some other markers like AFP. Further studies with larger samples are needed to determine the association of MPV with HCC. For a single test DCP had highest significant diagnostic performance in differentiating HCC from CLD groups. In detection of HCC testing AFP≥ 40.0 if positive considered positive. If negative, retest for DCP≥ 69.3 if positive considered positive, otherwise is negative. This although deceased specificity and Positive predictive value, it raised sensitivity and Negative Predictive Value to 100.0% when combining both AFP and DCP. The benefit of increasing the sensitivity is not to miss cases with HCC while the decreased specificity and PPV can be compensated by further imaging studies to eliminate the false positive cases.



***Keywords:*** Value of Mean Platelet Volume, Des Gamma Carboxy Prothrombin, Alpha Feto Protein, HCC

# INTRODUCTION

Primary liver cancer is the sixth most commonly diagnosed cancer and the fourth leading cause of cancer mortality worldwide, with an estimated 841,000 cases (9.3 cases per 100,000 person-years) and 782,000 deaths (8.5 deaths per 100,000 person-years) in 2018 **(Bray et al., 2018).**

HCC being often associated with liver cirrhosis masks symptoms of cancer progression and thus the clinical course of HCC is mostly asymptomatic **(Kurt et al., 2012).**

The incidence rate of HCC rises in accordance with increased rates of hepatitis C virus and hepatitis B virus infection **(El-Serag et al., 2010).** Aflatoxin exposure, heavy alcohol drinking, nonalcoholic fatty liver disease, and smoking also contribute to the occurrence and progression of HCC **(El-Serag et al., 2010).**

While the survival of patients with most malignancies has improved over the last decade, the prognosis of HCC remains poor, and most patients have a 5-years survival rate of less than 5% mainly because of the late diagnosis of more than two-thirds of patients diagnosed at advanced stages of disease **(Chen et al., 2009).** Although liver resection for early HCC could improve 5-year survival to 60–70% **(Forner et al., 2012).**

This worse outcome is due partly to the lack of an effective method for timely diagnosis, which leads to only 30–40% of HCC being suitable for potentially curative treatments at the time of diagnosis **(Llovet et al., 2008).**

Thus, surveillance of populations at-risk may detect tumors at an early stage when curative interventions can be implemented **(Lok et al., 2010).** Several studies reported a benefit of HCC surveillance on survival and guidelines from professional organizations recommend HCC surveillance for at-risk populations **(Lok et al., 2010).**

Two definitions of HCC were adopted as described previously, one for "definite" HCC and one for "presumed" HCC **(Lok et al., 2010)**

Definite HCC was defined by histologic confirmation or a new mass lesion on imaging with AFP levels increasing to >1,000 ng/mL **(Lok et al., 2010).**

Presumed HCC was defined as a new mass lesion on ultrasound in the absence of histology and AFP <1,000 ng/mL in conjunction with one of the following characteristics: a) 2 liver imaging studies showing a mass lesion with characteristics of HCC (arterial enhancement ± wash out), b) progressively enlarging lesion on ultrasound leading to death, or c) 1 additional imaging study showing a mass lesion with characteristics of HCC that either increased in size over time or was accompanied by AFP level >200 ng/mL and more than tripling of baseline value **(Lok et al., 2010).**

A major problem with HCC surveillance is the lack of reliable biomarkers. Alpha fetoprotein (AFP) is the most widely used biomarker for HCC surveillance; and was first introduced as a serological marker for HCC in the1960s **(Price et al., 2020).**