شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

شبكة المعلومات الجامعية

بعض الوثائق الأصلية تالفة

بالرسالة صفحات لم ترد بالأصل

EVALUATION OF SOME OF THE DIAGNOSTIC MODALITIES IN HEPATOCELLULAR CARCINOMA

Thesis

Submitted to the Faculty of Medicine
University of Alexandria
In partial fulfillment of the
requirments of the degree of

Master of Intenal Medicine

By

Fairouz Amin Morsy Ahmed

(MBBch, Alex)

Faculty of Medicine

University of Alexandria

1998

SUPERVISORS

Prof. Dr. Ali Abdel-Moeity Soliman

Professor of Internal Medicine
Faculty of Medicine
Alexandria University

Prof. Dr. Ahmed Mohamed El-Gowhary

Professor of Internal Medicine
Faculty of Medicine
Alexandria University

Prof. Dr. Shadia Abu Seif Helmy

Professor of Radiology
Faculty of Medicine
Alexandria University

ACKNOWLEDGEMENT

At the Beginning, I would like to thank **God** *for helping me and standing beside me to bring this work into existence.*

I would like to express my gratitude to **Prof. Dr. Ali Abdel-Moeity Soliman**, *Professor of Internal Medicine, Faculty of Medicine, Alexandria University, for his valuable guidance and kind supervision of this work.*

Also, I wish to acknowledge the meticulous work of **Prof. Dr. Ahmed Mohamed El-Gowhary**, *Professor of Internal Medicine, Faculty of Medicine, Alexandria University who gave me great assistance and valuable advices for the completion of this work.*

Also, I would like to express my thanks and appreciation to **Prof. Dr. Shadia Abu Seif Helmy**, *Professor of Radiology, Faculty of Medicine, Alexandria University, for her great help, valuable assistance and correct guidance to bring this work into existence.*

Next, I wish to express my thanks to **Dr. Nagla Mashal**, *Ass. Professor of Internal Medicine, Alexandria University for her kind help and valuable advices.*

Last but not least, I would like to thank **Dr. Aiman Sakr** *Lecturer of Radiology, Institute of Graduate studies and research for his great assistance which helped me a lot to bring this work into existence.*

CONTENTS

INTRODUCTION

INTRODUCTION

Hepatocellular carcinoma is one of the most common primary cancers around the world, several prospective studies have been performed on the incidence of hepatocellular carcinoma.[1] The incidence rate vary widely throughout the world from < 4 per 100,000 in the UK, Canada and Australia to >100 per 100,000 in Mozambique and Taiwan.[2] In northern European countries the incidence is lower, three cases per 100,000 in comparison with southern European countries, in which the incidence is considered intermediate (6-10 cases per 100,000).[3,4,5]

The different geographical distribution seems to be related to the prevalence of factors that carry a risk for the disease namely viruses, chemicals, alcohol, oral contraceptive pills and cirrhosis.[5]

Viruses:

The possibility that viruses might be involved in the aetiology of HCC was suggested many years ago. The hypothesis was difficult to study in the absence of a candidate viruses, but the

situation has now changed dramatically, initially following the discovery of Australia antigen[6], and subsequently the explosion of knowledge of hepatitis B virus (HBV) resulting from the application of recombinant DNA technology.[7]

Hepatitis B virus is a 42 nm double shelled virus originally known as dane particle. The outer shell is the major coat protein of the virus, referred to as hepatitis B surface antigen (HBsAg). Detergent treatment of dane particles release an antigenically distinct core antigen (HBcAg) which is 27 nm spherical core.[8,9] The core contains another antigen called Lettle 'e' antigen (HBeAg) which is a protein subunit of the core.[10]

Hepatitis B virus multiplies only in hepatic parenchymal cells. The virologically most important property of HBV is its ability to cause the infected hepatocytes to produce not only multiple copies of the virus itself i.e. the viron, but also large number of associated particles. The latter are made up of the same proteins of (HBsAg) that coat the viron.[11]

DNA polymerase activity and endogenous DNA template are associated with the inner core of the dane particle. The DNA

template consists of double-stranded DNA with a molecular weight of approximately 1.6×10^6.[8]

Hepatitis B virus in Egypt:

HBV infection is recognised as one of the most important diseases with high prevalence rate in Egypt.[12] it reached 7.4% among industrial labourers and 4.5% among rural population in villages.[13]

In a study conducted in upper Egypt, the prevalence rate was 5.7% among inhabitants of rural areas.[12]

The presence of HBeAg in the serum is a marker of active viral replication, HBeAg disappears early in the acute illness usually 2-3 weeks before the clearance of HBsAg.[11] Anti-HBe appears in the serum as the HBeAg begins to disappear early during the coarse of acute illness and its presence signals the onset of resolution of acute hepatitis.[14]

The nucleoprotein core is separately replicated in the nucleus of hepatocytes[11], antibodies against it are the first antibodies detected after exposure to HBV.[15]

The lines of evidence associating HBV and HCC are; numerous, including the world-wide correlation between the incidence of HCC and the geographical distribution of HBsAg carriers.[16,17] i.e. in countries with high prevalence of HCC, anywhere, from 60-90 percent of cases are associated with HBV. In countries with low to intermediate HCC prevalence rates, as few as 1-50 percent of cases are associated with HBV.[18] Mothers of patients with HCC have a much higher HBsAg carrier frequency than fathers, implying possible perinatal transmission. In addition, numerous family clusters of concurrent HCC and HBsAg carrier state have been reported that their mothers are usually HBsAg positive.[19,20] Demonstration of the virus itself or its components are present within tumour tissue i.e. various viral proteins including HBsAg and HBcAg have been found in tumour tissue and hepatitis B viral DNA can be found within the chromosomes of HCC cells and in non-tumours tissue adjacent to HCC.[21] Moreover, replicative forms of HBV DNA can be found within these tissues.[22] HBV DNA is integrated into the cellular genome[23,24] at specific site(s) leads to activation of specific gene(s) responsible for carcinogenesis[25], also other possibilities for HBV-induced carcinogenesis are the unregulated expression of the HBV X gene product or the HBV polymerase, the former has transcriptional transactivating properties and the latter has reverse transcriptase

activity.[26-29] Hepatitis B virus is a cause of cirrhosis which is listed among the predisposing factors of HCC.[22] A series of prospective studies have shown that HBV carriers are at much higher risk of developing HCC than are age and sex matched but non-infected control subjects.[22] It has been suggested that hepatocyte necrosis plays a key role in both initiation and promotion of HBV-associated carcinogenesis. Thus patients with persistently active liver disease caused by a continuously high level of HBV replication and those with recurrent exacerbations associated with fluctuating levels of HBV replication may become prone to develop HCC.[30]

Unlike hepatitis B virus, hepatitis C virus has not proven to be integrated into cellular genome.[31,32] Hepatitis C virus (HCV) induces chronic hepatitis subsequently develop into liver cirrhosis that is characterized by multiple regenerative nodules of varying size. Although these regenerating nodules have been considered to be hyperplastic and not neoplastic, they are predominantly composed of monoclonal cells which are speculated to arise from accumulation of certain genetic alterations that are required for carcinogenesis. Thus they can be considered as precancerous lesions.[33] However, HCV may act by different mechanisms either by activation of cellular oncogenes or by causing necro-