Relation Between Occult

Hepatitis B and Hepatocellular Carcinoma

Thesis

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Internal Medicine

By Akram Abd El-Aziz Yousef (M.B.B.ch)

Under Supervision Of
Prof. Dr. Amr Abd El-Kader Fatin
Professor of Internal Medicine
Gastroenterology and Hepatology
Faculty of Medicine - Ain Shams University

Dr. Hosam Eldin Abd El-Aziz Mahmoud

Assistant Professor of Gastroenterology and Hepatology

Faculty of Medicine - Ain Shams University

Dr. Amany Talat Kamal
Assistant Professor of Gastroenterology and Hepatology
Faculty of Medicine - Ain Shams University

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List of Abbreviations

ALT: Alanine transaminase

AST: Aspartate transaminase

ccDNA: Covalently closed circular deoxyribonucleic acid

CTL: Cytotoxic T lymphocytes

DC: Dendritic cells

HBV: Hepatitis B virus

HBcAb: Hepatitis B core antibody

HBcAg: Hepatitis B core antigen

HBeAb: Hepatitis Be antibody

HBeAg: Hepatitis B surface antibody

HBsAg: Hepatitis B surface antigen

HCV: Hepatitis C virus

HCC: Hepatocellular carcinoma

HIV: Human immune deficiency virus

IFN: Interferon

IL: Interleukin

NASH: Non alcoholic steatohepatitis

NK: Natural killer

PCR: Polymerase chain reaction

RNA: Ribonucleic acid

TNF: Tumor necrosis factor

U/S: Ultrasonography

WHO: World Health Organization

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Introduction

Hepatocellular carcinoma is the fifth commonest malignancy worldwide and one of the most challenging to treat (*Toh Han Chong*, *··•*).

HBV is considered to be the main causative factor of liver cancer, possibly accounting for 7.% of cases worldwide and \checkmark . % of cases in endemic areas (Qin Su et al., \checkmark ...).

The envelope protein of HBV, hepatitis B surface antigen (HBsAg), is the main marker for ongoing HBV infection (Damien Jeantet et al., **. ***).

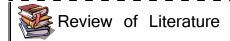
Occult hepatitis B virus (HBV) infection is generally defined as detection of HBV- DNA in the serum or liver tissue of patient who test negative for hepatitis B surface antigen (HBsAg) (Jorge A. Marreroa et al., **..***).

Lack of HBsAg may be due to rearrangements in HBV genome that interfere with gene expression or lead to Production of an antigenically modified S protein (*Irene Cacciola et al.*, 1999).

According to a study published in cancer journal, presence of occult hepatitis B infection increases the risk of liver cancer in patients with chronic hepatitis (Squadrito G et al., 7...1).

Aim of the Work

Detection of relation between occult hepatitis B and hepatocellular carcinoma in Egypt.



Hepatitis B Virus

Epidemiology of HBV

HBV worldwide:

Viral hepatitis with various forms of acute and chronic liver disease is with potential and ultimately fatal sequelae, causing a public health problem worldwide (*Poovorawan et al.*, *...*).

Hepatitis B is the most import-ant of several hepatitis viruses of man because of the number of cases of the disease and the frequent occurrence of persistent infection that may lead to cirrhosis and cancer of the liver (*Lee et al.*, **··**). HBV infection is the most common cause of chronic liver disease worldwide (*Pramoolsinsup*, **··***).

Roughly, one third of the world population has been infected with HBV (*Hilleman*, *...*).

Although hepatitis B is an ancient disease, most of the advances in our knowledge of its epidemiology, prevention, pathogenesis, natural history and treatment were made in the last r years (Lok, r · · ·).

HBV is the third most common disease after venereal diseases and chickenpox. It currently infects 'billion people in the world, of which 'o million are chronic carriers. At least 'million chronically infected individuals die each year due to HBV- related diseases, especially cirrhosis and liver cancer. The greatest concern about the diffusion of this virus is in endemic regions in central and southern Africa, South-East Asia and South America, where neonatal exposure results in high mortality rates (Gumina et al., '').

HBV in Egypt:

Hepatitis B is and will for some time be a major health problem in Egypt (Attia, 1991).

It is recommended to consolidate the Egyptian programme of infant hepatitis B vaccination, and to extend it to older children and high risk adult groups (El-Sayed et al., 1997).

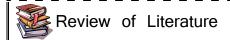
The prevalence of HBsAg carriers in Egypt varies widely with: age, sex, community (urban or rural), schistosomiasis and/or chronic liver disease, exposure to certain risk factors (Sherif et al., 1940).

Egypt was reported by *Andre*, *** to be an area of high prevalence for HBV however *Poynard*, *** reported it to be an In the early ^*s, carriage rate of *. *** and **. **.

were reported in Alexandria and Cairo by *Mailoum and colleagues* and *Shoeb* respectively and *El-Razky et al.* found that, among school children °-\° years from a rural village in Dakahlia, the exposure rate for HBV infection was '\'% with frequency of HBsAg of \(\frac{\chi}{\chi}\) by counterimmune electrophoresis, \(\frac{\gamma}{\chi}\) by reversed passive haemagglutination and \(\frac{\gamma}{\chi}\) by other tests .the frequency of HBsAb was \(\frac{\chi}{\chi}\). A carriage rate of \(\frac{\gamma}{\chi}\) was reported in two rural villages in the Nile Delta by HBsAg alone (*Emain*, \(\frac{\gamma}{\gamma}\)).

In the mid ^•s; higher prevalence was reported as follows; ^.^% in Lower Egypt and ``.'% in Upper Egypt with more prevalence in young adults and in males man females in both communities by *Sherif et al*.

The overall seroprevalence of HBV when HBsAg and/or HBcAb were assessed was found to increase progressively with age peaking in the £1-71 years old group at a rate of 77% which is an extraordinarily high seroprevalence rate (Darmsh et al., 1997). El-Sayed found it to be 71.1% collectively in all age groups in 1997 and 19.1% in 1997 (El-Sayed) 1997 and El-Sayed, 1997). There is the impression that HB carriage rate is decreased from 11.1% (Sherif et al., 1940) to 7.7% (Zakaria et al., 7111). In another study, HBV markers (presence of either anti-HBc and/or TIBsAg) were found to be prevalent in 75% of the



villagers in the northern Egyptian Nile Data (Kamel et al., 1992).

As for acute HBV infection, the prevalence of HBV in Egypt is not yet adequately estimated after the use of hepatitis B vaccine (Zakaria et al., """). However Orfi, """ stated that the prevelance of acute HBV infection was 17% in children """ years old and """ in adults > 12 years old. The most common age group infected by HBV ranged from """ years ("""). whereas the least infected age group was from """ years ("""). The most common risk factor for infection with acute HBV was accidental puncture in ("""1.1%), followed by dental procedures in (""1.1%) and surgical intervention in (""2.1%).

Geographical distribution:

Asia and Africa have previously been classified as areas of high endemecity for HBV but in some countries highly effective vaccination programmes have shifted this pattern towards intermediate or low endemicity. Thus, China is now the only country in Asia where HBV endemeicity is high. Countries with intermediate endemicity include India, Korea, Philippines, Taiwan and Thailand and those with low endemicity include Japan, Pakistan, Bangladesh, Singapore, Sri Lanka and Malaysia. Most countries in Africa have high HBV endemicity, with the exceptions of Tunisia and Moracco which have intermediate

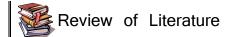
endemicity. In the middle east, Bahrain, Iran Israel and Kuwait are areas of low endemicity. Cyprus, Iraq and Emirates have intermediate endemicity. Egypt, Jordan, Oman, Palestine, Yemen and Saudi Arabia have high endemicity (Andre, **...).

Mode of transmission:

Hepatitis B is most commonly acquired during adult life either by sexual transmission or through intravenous drug use. Healthcare workers also have a risk of acquiring hepatitis B through needle sticks and cuts sustained during the care of patients. Because healthcare instructions require that healthworkers receive vaccination for hepatitis B, this mode of transmission is becoming loss common. infection through blood product transfusion is now rare because blood banks screen blood donors for hepatitis B, hepatitis C and HIV (*Lee*, 1997).

Familial clustering of hepatitis B virus infection in related to perinatal transmission, and is the main cause of familial type hepatocellular carcinoma (*Chen et al.*, **··**).

The latent period from the onset of infection to the diagnosis of hepatocellular carcinoma may range from '.- 'years (Tsukuma et al., 1997).



Structure:

HBV is the prototype member of hepadnaviridae family, which also infects ducks, ground squirrels and woodchucks (*Jack*, *··•*).

HBV virions are double-shelled particles, \mathfrak{t} to \mathfrak{t} nm in diameter with an outer lipoprotein envelope that contains three related envelope glycoproteins (or surface antigens). Within the envelope is the viral nucleocapsid are core. The core contains the viral genome (*Don Ganem et al.*, $\mathfrak{r} \cdots \mathfrak{t}$).