# HEPATITIS B SURFACE ANTIGEN IN HEALTHY CARRIERS, CHRONIC HEPATITIS, LIVER CIRRHOSIS AND HEPATIC TUMOURS

THESIS

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Master Degree in Clinical Pathology

By

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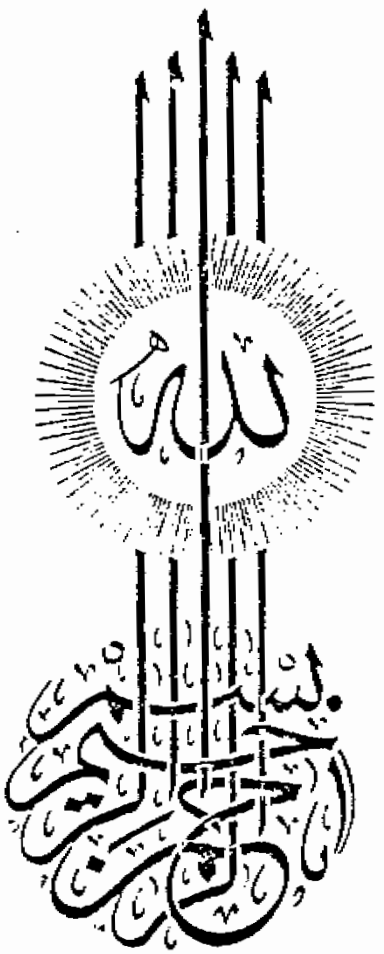

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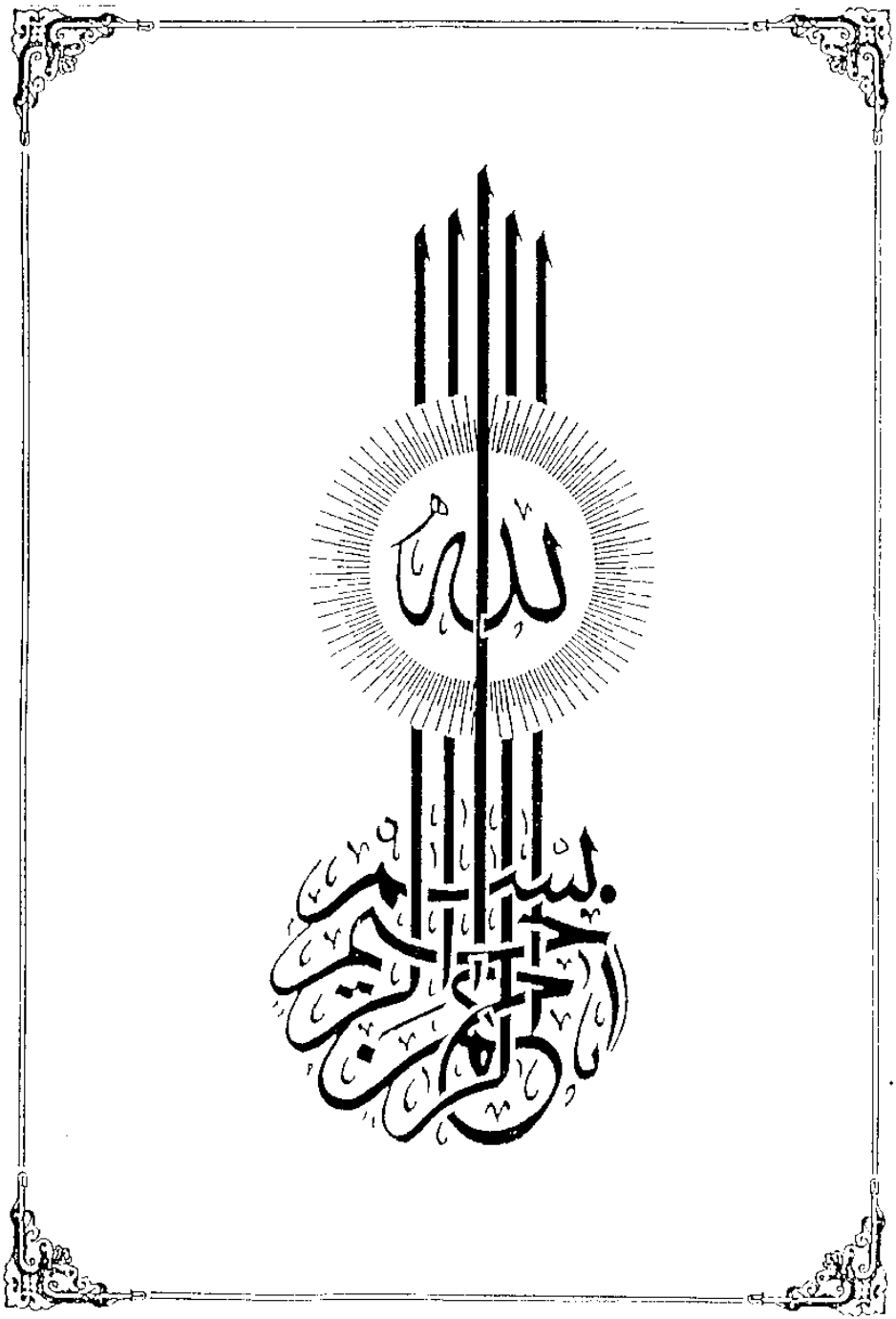

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## ABBREVIATION

| | |
|---|---|
| Anti.HAV | antibody to hepatitis A virus. |
| Anti.HBc IgG | IgG antibody to hepatitis B core antigen. |
| Anti.HBc IgM | IgM antibody to hepatitis B core antigen. |
| Anti. HBe | antibody to hepatitis Be antigen. |
| HBe Ag | hepatitis Be antigen. |
| HBs Ag | hepatitis B surface antigen. |
| HBV | hepatitis B virus. |
| HCC | hepatocellular carcinoma. |
| NANB | non-A, non-B hepatitis virus. |
| N/C | nuclear/cytoplasmic ratio. |

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# INTRODUCTION AND AIM OF WORK

Viral hepatitis is recognized as a major public health problem in all parts of the world because the currently available data indicate that persistent infection of liver with hepatitis B virus (HBV) is envolved in etiology and pathogenesis of nearly all hepatocellular carcinoma (HCC) in humans, (Blumberg et al., 1982).

Liaw et al., 1986 reported that asymptomatic carrier state, chronic hepatitis and hepatocellular carcinoma are successive sequelae of chronic hepatitis B virus infection but not necessarily linear sequential sequelae, because chronic hepatitis could progress directly to hepatocellular carcinoma.

Immunization of High risk population, and prevention of HBV infection early in life should prevent the development of chronic hepatitis therefore, should also prevent the development of HCC. At present three approach are being evaluated to prevent HBV infectione arly in life. One is administration of heigh- titer antibody to HBsAg (HBIG)

at birth. The second is immunization with an HBsAg vaccine, and the third is passive - active immunization, (Hann et al., 1982).

The aim of our study is to detect the incidence of HBsAg and the carriage rate in hepatocellular carcinoma, liver cirrhosis patients and in apparent healthy carriers.

# Review of Literature

## VIRAL HEPATITIS

The term human viral hepatitis refers to infections caused by four different viruses or groups of viruses, hepatitis A, hepatitis B, the more recently identified forms of hepatitis, non-A, non-B hepatitis which are caused by two viruses, epidemic non-A hepatitis (previously referred to as epidemic non-A, non-B hepatitis) and delta virus. Hepatitis A and hepatitis B can be differentiated by sensitive laboratory tests for specific antigens and antibodies and the virus have been characterized. Specific laboratory test are also available for the delta agent, a defective virus, which replicates in individuals infected with hepatitis B virus (Harrison, et al., 1986).

### Hepatitis A virus (HAV)

The disease is due to a small 27 n.m, cubically symmetrical, RNA entero virus (Feinstone, et al., 1973). The virus can be spread by intestinal-oral route and it is highly contagious (Krugman, et al., 1967). It has an incubation period of two to six weeks (Neefe, et al., 1974).

The virus can be identified in the stool of patients from about two weeks before until one week after the onset of jaundice by immune electron microscopy (Dienstag et al., 1977).

A serum antibody (anti-HAV) appears as the stool becomes negative for virus, this antibody persists for only two to six months (Deker et al., 1979). There is no cross immunity between HAV and HBV infection, as patients with infectious hepatitis were later proven to be immune to the same type, but not immune against the serum hepatitis (Krugman et al., 1967).

Serodiagnosis of HAV infection is based on the detection of serum anti-HAV can be widely performed by Radioimmunoassay and enzyme-linked immunoassay.

**Hepatitis B virus (HBV)**

HBV infections are of particular interest because of progression in a proportion of patients to chronic liver disease, cirrhosis and hepato cellular carcinoma and this will be discussed in details later on.

**Non-A, non-B hepatitis virus (NANB hepatitis)**

This is now the most common form of post-transfusion hepatitis in many areas of the world (Dienstag et al., 1977). Haemophiliacs receiving factor concentrates obtained from commercial sources are particularly at risk (Craske et al., 1975) NANB hepatitis occurs in renal dialysis (Galbraith et al., 1979), in renal transplant recipient (Dienstag et al., 1977).

It is now known to cause many epidemics and endemic viral hepatitis in tropical countries (Tong et al., 1981). It shares certain of the features of type B hepatitis in that it has a relatively long incubation period, usually extending beyond fifty days, and may be followed by a chronic carrier state (Tedder, 1981).

Diagnosis NANB hepatitis is usually done by serological exclusion of virus A and virus B, other small virus which cause hepatitis.

## Hepatitis delta virus

The Delta antigen was discovered in 1977 by Rizzeto and Co-workers in Turin Italy. Using direct immunofluorescence, they detected a new antigen in the nuclei of hepatocytes that was neither HBsAg, HBcAg or HBeAg. This antigen, which they named delta ( δ ), was found only in liver tissue from HBsAg-positive individuals, it was never found in patients with type A or non-A, non-B hepatitis or in individual with anti-HBs and/or anti-HBc as the sole HBV marker in the serum. The presence of delta antigen was usually associated with progressive liver disease, chronic active hepatitis or an active cirrhosis.

Hepatitis delta virus infection can occur in three situations:

a) Simultaneous acute delta and acut type B hepatitis (co-infection).
b) Acut delta infection superimposed upon chronic type B hepatitis (superinfection).
c) Chronic delta infection superimposed upon chronic type B hepatitis (chronic delta hepatitis) (Howard C and Thomas E, 1987).

Howard and Thomas, (1987) concluded that delta antigen was either a new serotype of HBV or a separate viral agent somehow intimately associated with HBV infection.

## Other viral causes of hepatitis

Hepatitis is frequently associated with other common viral infections such as cytomegalo virus, Epstein-Bar-virus and yellow fever virus. In addition there are a number of viruses that do not normally cause liver damage but nevertheless occasionally display increased hepato-tropism, resulting in jaundice and a clinical picture which may be primarily that of the systemic infection or of hepatitis. This group of viruses includes herpex simplex virus, entero viruses, particularly Coxsackie A and B virus and adeno virus (Howard C., 1984).

## Cytomegalo virus

This type is due to human herpes virus type V. Infection by this virus requires close contact and usually occurs in infants and childhood. Neonatal infection acquired in utero is dramatic, the infant may present