The relationship between the acute viral hepatitis & erythrocyte sedimentation rate

Thesis

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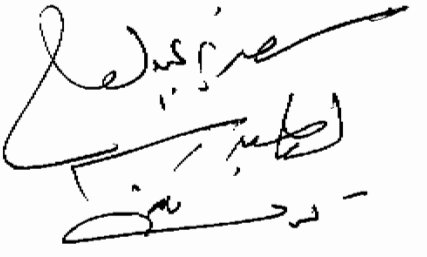

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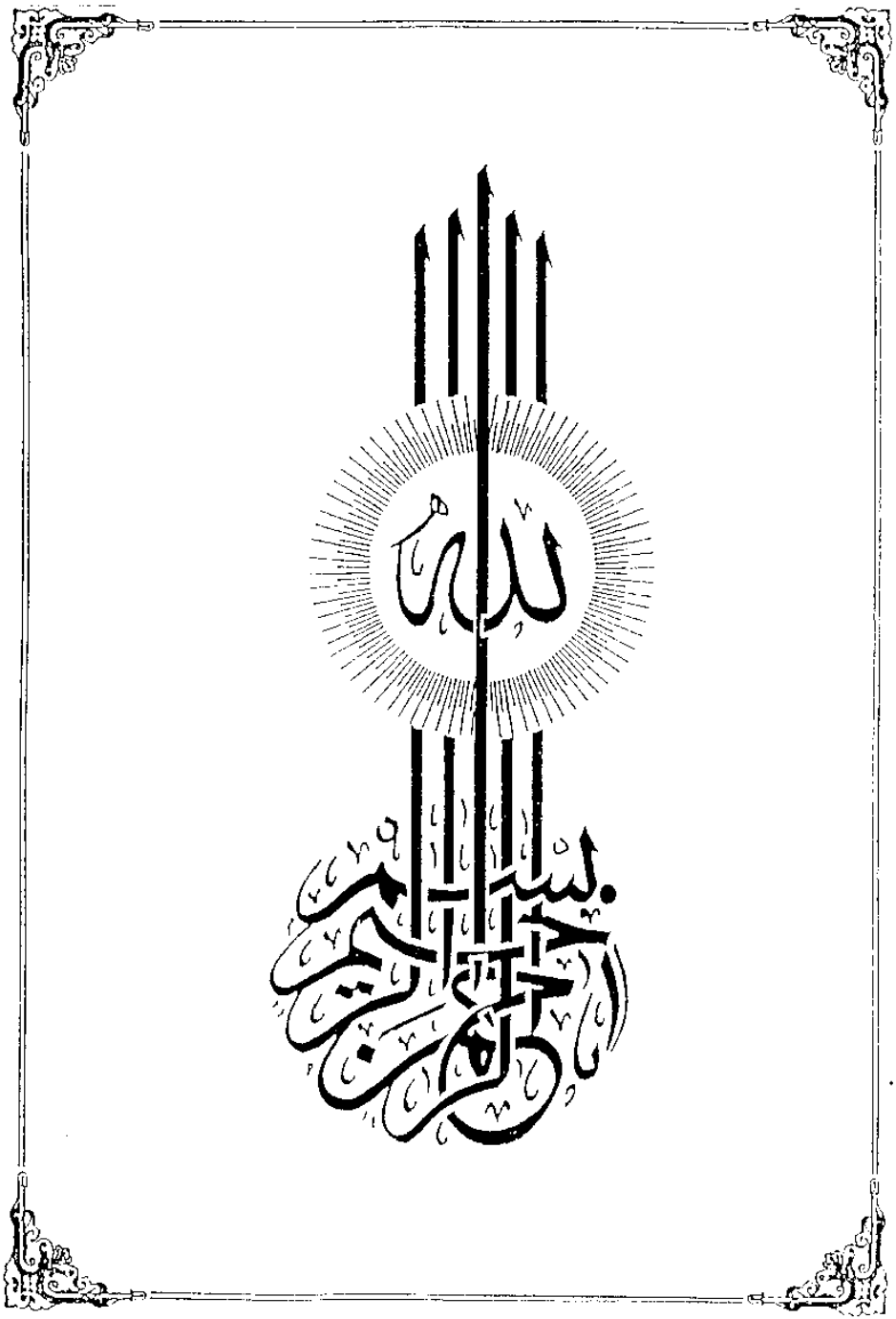

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CONTENTS

LIST OF ABBREVIATIONS

HA	hepatitis A
HAV	hepatitis A virus
HB	hepatitis B
HBV	hepatitis B virus
HNA-NB	hepatitis non-A non-B
HBAg	hepatitis B antigen
HBsAg	hepatitis B surface antigen
HBcAg	hepatitis B core antigen
SGPT ,ALT	Alanine aminotransferase
SGOT, AST	Aspartate aminotransferase
ELISA , EIA	Enzyme linked immunosorbent assay
ESR	Etythrocyte sedimentation rate
IGM	Immunoglobulin M
IGG	Immunoglobulin G

REVIEW OF LITERATURE

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HISTORICAL REVIEW

Viral hepatitis may be defined as a systemic viral infection in which hepatic cell necrosis and hepatic inflamation are responsible for a characteristic constellation of clinical, biochemical immunoserologic, and morphologic features (Zuckerman, 1979). The disease is produced by at least three (possibly four) viral agents with distinctive immunoserologic characteristics and specific epidemiologic attributes. The etiologically separate forms are called "hepatitis A", "hepatitis B", and "non-A, non-B viral hepatitis"(C) (Zuckerman, 1979).

An episodes of jaundice were described as early as the fifth century B.C. in Babylonia. The term "epidemic jaundice" was found in the writings of Hippocrates in Greece (Cockayne., 1912). In the 8th century A.D., Pepe Zacharias, Archbishop of Mainze, suggested that at least some forms of jaundice might be infectious. This was the earliest record of hepatitis in Western Europe. On the other hand, postvaccinal jaundice appeared in the 1930s and become so numerous in 1936 and 1937 that coincidence could no longer be invoked. The same occurrence was observed in Brazil during the late 1930s (Findlay 1937; Fox., 1942).

Later on when lyophilization was introduced, pools become much larger (hundreds of doners). The use of doners lead to much more widespread. As a result, post-transfusion jaundice became widely prevalent among battle casualties. In June 1945, 23 % of all cases of viral hepatitis in Army hospitals were plasma-associated (Sartwell., 1947). In 1947 MacCallum suggested that the virus that gave rise to serum hepatitis was called hepatitis B.

A new era in the history of viral hepatitis began with the discovery of "Australia antigen" by Blumberg and his colleagues in 1963, and it is reported two years later.

Australia antigen (lipoprotein antigen) was discovered in the serum of an Australian aborigine (laboratory animal). That antigen reacted with an antibody in the serum of two multiply transfused haemophilic patients. For that discovery, Blumberg was awarded Nobile Prize in 1977.

This antigen , now designated the hepatitis B surface antigen (HBsAg), and its associated particle were subsequently shown to comprise the surface material of the hepatitis B virus. Extension of these observations in the 1970s permitted the development of highly accurate methods for identification of hepatitis B infection. This resulted in extensive seroepidemiologic studies of this

infection. When this was achieved in the middle of the 1970s, non-A, non-B viral hepatitis was accepted as third etiologic entity.

Measurement of the rate of sedimentation of the red cells is frequently used as a non specific test which may indicate the presence of inflamation or occult disease. It confirm the presence of disease diagnosed by other means, or it may serve as a guide in following the course of a disease. The erythrocyte sedimentation rate (ESR) may significantly increased suggesting organic disease even when clinical and other laboratory studies are negative. Conversely a normal ESR is reassuring in a patient who believed to have no organic disease. However a normal ESR does not rule out the presence of organic disease.

Although the value of the ESR had provoked a controversy in the past, it can be very useful test in many clinical circumstances, when properly interpreted and applied (Lascari., 1972).

An accelerated ESR has been recognized in the acute phase of infectious hepatitis. Contrary to this Vahrman in 1978 has reported in type B hepatitis an ESR within normal limit or only slightly elevated.

MORPHOLOGY AND PROPERTIES OF HEPATITIS VIRUSES

HAV*

(1)Morphology:

In 1973 small 24 - 29 nm cubic virus particles were seen by immune electron microscopy in extracts of faeces obtained during the early acute phase of illness of adult volunteers infected with a strain of hepatitis A virus (Zuckerman, 1978).

In appearance, HAV resembles the RNA-containing picorna viruses and the DNA-containing paroviruses, (Purcell,1975). Both "full" particles and "empty "particles have been detected by electron microscopy. However, the two variants are antigenically indistinguishable and aggregate when mixed with serum containing antibody to the virus (WHO report, 1977).

(2) Biochemical Properties:

The biochemical nature of the HAV had not been widely studied owing to the difficulty of obtaining virus particles. However, attempts had been made to determine the type of nucleic acid of the virus by studying its staining characteristics when exposed to acridine orange. These studies suggested that the nucleic acid may be either

RNA or single stranded DNA (WHO Report, 1977).

It was recently shown that hepatitis A virus contains a linear genome of a single stranded RNA and polypeptides with similar molecular weights to the four major polypeptides of the enterovirus genus (Zuckerman, 1978; Siegl, 1982).

(3) Biophysical Properties:

In limited studies, HAV was shown to be relatively resistant to inactivation by ether, heating at 60° C for 1 hr. and acid at pH_3 , but was inactivated by formaldehyde solution (0.25 ml/l) at 37° C for 72 hours and by chlorine (1 mg/l) for 30 minutes.
Detergents or storage at 4° C , - 20° C , or - 70° C do not alter the morphology or destroy the infectivity of the virus. It can be destroyed by autoclaving, by boiling in water or by dry heat (Jawetz et al., 1974; Coulepis, 1982).

HBV:

(1) Morphology:

The circulating particles associated with hepatitis B virus fall into at least 3 distinct morphological categories (Anderson, 1975).Fig. 1,2.

1- The spherical are the most numerous of 18-21 nm.in diameter.

2- Tubular long forms are about the same diameter as the small spheres but variable in length from oval, or cigarshapes to long filaments.

3- Larger double-shelled particles discovered by Dane et al., 1970, are also found, but are present only in about 25 % of HBsAg positive sera (Cossart and field, 1970). The diameter of the outer shell of these Dane particles is about 42 nm, that of the inner shell is about 27 nm. Safouh, 1979 described Dane particles as being formed of an inner core 27 nm, 2 nm shell and an outer coat about 7 nm in thickness where the surface antigen is present.

(2) Biochemical Properties:

The outer shell of HBV was found to be lipoprotein in nature. Lipid content is mainly phosphatidyl choline, and sphingomyelin. The protein content is made of 2 major species of polypeptid chains of different molecular weights (25,000 and 30,000) (WHO Report, 1977).
The core consists of double stranded circular DNA and DNA polymerase. HBC antigen is present in the core (Krugman, 1980).

(3) Biophysical Properties:

HBV survives treatment by heating at 56° C for 6 hrs.(Gerin et al., 1969) freezing, thawing, but is partially

inactivated at 60° C for 10 hrs, and completely destroyed at 85° C for 1 hr (Krugman et al., 1970).

It is also resistant to digestion with proteolytic enzymes (Kim and Bissell, 1977), protein denaturants, treatment with ether, as well as to significant changes to ph.(Gerin et al., 1969). Its activity, however, is partially destroyed by powerful lipid solvents, suggesting that intact lipid in the particle is necessary for serologic activity (Barker et al., 1969).

Its antigenicity is also reduced by digestion with faeces and intestinal homogenates (Piazza et al., 1973), as well as certain bacteria (Mazzur et al., 1973). HBsAg is not destroyed by ultraviolet irradiation and viral infectivity may also resist such treatment (Jawets et al., 1974).

Hepatitis B antigens

HBsAg:

This is present on the surface of the small spheres, tubules and Dane particles.

Study of HBsAg showed that it is antigenically complex (Le bouvier, 1972). All hepatitis B surface antigens share a common (a) determinant. A number of other determinants, including pairs of determinants (d) and (y),(w)

and (r) have been described. Thus HBsAg main subtypes are adw, ayw, adr and ayr. These determinants remain constant with the passage of infection from one individual to another. Other variants related to a, w and r are also described. These subtypes have different geographic distribution and are of epidemiological rather than clinical value.

HBcAg:

It is present in the core of Dane particles and is rarely if ever found in the blood. It is demonstrated by electron microscopy and by immune histology in the nuclei of the liver cells (Stahl, 1982).

HBeAg:

It originates in the core and is associated with the presence of Dane particles and DNA polymerase. It is related to increased infectivity and chronicity of the disease (Zuckerman, 1979).

DNA polymerase

It appears in blood at or before the peak of hepatitis B surface antigenaemia.

Delta antigen:

It consists of a particle of 35 - 37 nm in diameter