STUDY OF VERTICAL TRANSMISSION OF HEPATITIS B VIRUS INFECTION AND PREVALENCE OF HEPATITIS B SURFACE Ag AND ANTIBODY IN EGYPTIAN INFANTS AND CHILDREN.

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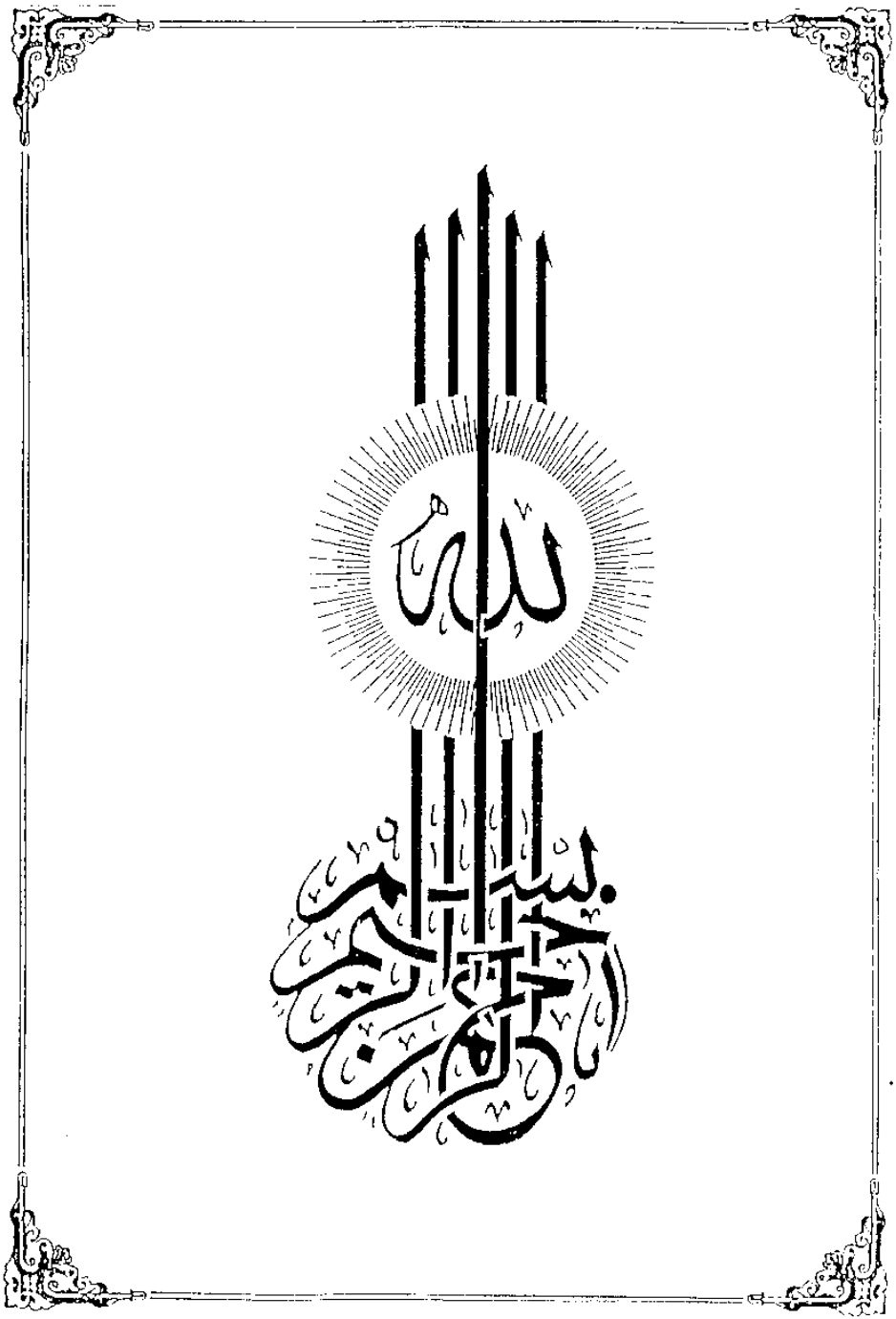

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INTRODUCTION

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Viral hepatitis is a major and serious public health problem in most parts of the world . It is a systemic infection predominatly affecting the liver and caused by a variety of viruses of widely different taxon . Hepatitis virus type A , B , C (non-A , non-B) and D (delta) are the most important causes of acute hepatitis .

Hepatitis B accounts for 18-70 % of all reported cases of viral hepatitis . The spectrum of infection ranges from inapparent anicteric (but symptomatic) , icteric , to fulminant . Many cases of hepatitis B are anicteric . Some of them remain chronically antigenemic , thus , constituting a carrier state . According to WHO , 1978 , there are about 200 million carriers of this virus mainly in tropical areas of the world . The majority are "healthy", some suffer various forms of chronic hepatitis , some will develop cirrhosis and primary liver cancer . The significance of this condition , especially as regards the infectivity of the carriers , still remains to be clarified .

Veritcal transmission , i . e infection passing from a mother to foetus or neonate , is probably a numerically important method of infection in counteries with high carrier rates . The infection is transmiting either transplacental or at the time of birth where there is a chance of maternal - foetal blood mixing , or during close contact afterwards (sherlock , 1981) . Antigenemia develops in the baby within three months of birth and tends to persist (Beasley et al . , 1977) . These infants will be subjected to chronic hepatitis B virus infection , and about 25 % of them may ultimately die of liver failure caused by chronic active hepatitis , cirrhosis , and possibly primary hepatocellular carcinoma (Krugman , 1985) .

Consequently , it is highly informative to study the prevalence of hepatitis B surface antigen (HBsAg) and antibody (anti-HBs) among those high risk groups of infants and children as well as the extent of infectivity among women in last trimester of pregnancy in Egypt .

REVIEW OF LITERATURES

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[1] HISTORICAL REVIEW

The first reference to epidemic jaundice has been ascribed to Hippocrates . Epidemic outbreaks of jaundice were noted as early as the eighth century A . D . in Europe , and by the nineteenth century the disease became known as infectious hepatitis . With the advent of gamma globulin prophylaxis and the introduction of vaccination programs against other infectious diseases (as yellow fever) another form of acute viral hepatitis , the homologous serum hepatitis was observed . A major advance in our understanding of hepatitis occured in the mid - 1940 s and early 1950 s when the clinical and epidemiological characteristics of two distinct forms of hepatitis (Type A and Type B) in man were described in extensive detail . The acquisition of Type A hepatitis was characterized by a short incubation period , predominantly orofecal route of transmission , and frequent epidemic outbreaks . Type B hepatitis was observed to have a long I . P , a parenteral route of transmission , and an endemic nature of occurance .

but antigenically unrelated to either types (Alter, et al., 1975 a) and it has been designated non-A , non-B hepatitis . At the present time , the non-A , non-B viral agents have not been identified .

More recently , Hepatitis D virus is a newly described , unique viral agent that may cause acute or chronic hepatitis (Krugman , 1985) .

[2] VIROLOGY

(A) Morphology and properties of hepatitis viruses:

i - Hepatitis A virus (HAV) :

The hepatitis A virus (HAV) is a small 27 nanometer (n m) cubically symmetrical RNA virus, Fig(1) , that belongs to the picorna virus class of enteroviruses (koff , 1980) .

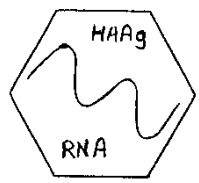

Fig (1) : Diagram of the hepatitis A virus shown as a hexa gonal body containing single stranded R N A .
Ref : Sherlock , 1981 . pp 250

Persons infected with HBV and who are serologically HBsAg positive are circulating all morphological forms associated with HBV of which 22 n m spheres constitute the bulk of antigenic mass and Dane particles only a small , but varrying proportion of this mass .

Only Dane particles is considered infectious . The other circulating morphologic forms (spheres and tubules) are not infective , although they possess antigenecity (Maynard , 1980) . This is because these spheres and tubules are devoid of any HBc Ag , D N A polymerase , or D N A .

Resistence of the HBV (Biophysical properties) :

Both HB V and HBs Ag are stable at - 20°c and their integrity is preserved after plasma fractionation . Heating at 60°c for 10 hours or boiling for one minute , inactivates HBV but not affect the antigenicity of HBs Ag . Soduim hypochlorite 0.1 % - 0.5 % destroys antigenicity (and the HB V) within 3 minutes in protein - deficient solutions (Hollinger & Stevens , 1982) .

The surface component of hepatitis D virus is hepatitis B surface antigen (HBs Ag) and its core component is 35 - 37 n m in diameter containing the R N A genome and delta antigen (Fig 3) . Recognition of this infection in the presence of HBs Ag is important because the prognostic implications are more sever (progressive liver disease) and the therapeutic approach different from normal H B V infection .

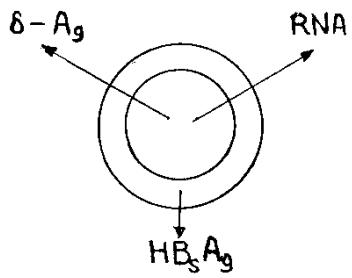

Fig 3 : Morphology of delta virus (Rizzetto,1985. pp3).

(B) Hepatitis B Antigens:

The following four antigens are known to be associated with H B V infection :-

i - Hepatitis B surface antigen (HBs Ag) :

In most individuals infected with H B V , HBs Ag was replicated in their liver and released to plasma and bile (Overby , 1983) . When serum is positive , most other body fluids can be demonstrated to have HBs Ag , which may represent leakage from blood due to haemorrhage , exudation or transduction . However ,

From the epidemiological point of view , only the ayw and adw - grouped specificities as well as ayr and adr are of interest (Maynard , 1980) . Although these sets appear to represent mutually exclusive subdeterminants , additional subtypes (x , n , t , q) forthcoming as newly described determinants are confirmed (Holland , 1975) .

These subtypes are of great use in providing additional epidemiologic markers in evaluating the transmission of HBV infection from one person to another since secondary cases have the same subtype as the index case . But correlation between subtypes and severity of hepatitis B infection or outcome has been established (Gerety, et al , 1975) .

Current work on HBs Ag subtypes is limited by the ability to find or produce antibodies to other than the group reactive determinant " a " . The other determinants appear to be less immunogenic than " a ".

ii - Hepatitis B core antigen (HBcAg) :

This antigen has been localized predominantly to the nucleus and infrequently to the cytoplasm of infected hepatocytes (Yamada & Nakane , 1977) . This antigen is specific to the liver and is not found in serum or other tissues (Murphy, et al., 1976) .

iV Delta antigen (δ antigen) :

Delta antigen (δ . Ag) , originally described by Rizzetto , et al . , 1977 in liver cell nuclei in Italian carriers of HBs Ag , was confirmed by Canese, et al ., 1979 and Ogra & Beutner , 1981 . Diagnosis is based on the finding of the delta antigen-antibody system . Antibody to delta antigen (IgM class) has been detected in sera of patients with persistent HBV infection, and may be correlated with progression to chronic hepatitis (Rizzetto, et al . , 1979) .

Delta antigen is immunologically distinct from the HBs Ag , HBe Ag and HBc Ag . Experimental transmission of delta antigen to chimpanzees has been reported (Rizzetto, et al . , 1980) . Rizzetto , 1985 reported that delta antigen , is the immunologic expression of a unique hepatitis B virus .

C - Immune response to HBV

The host reaction to HBV may depend on : immune response of the host , size of inoculum , the portal of entery , and the number of exposures (Thomas & Jewel , 1979) . It seems that the immune response of the host to the virus rather than the virus itself

(which is not directly cytopathic) may be the predominant factor in determining the pathogenesis of liver injury in HBV infection . This immune response to HBV is exeedingly complex and very variable and from this stems some of the variability in the resulting clinical manifestations of infection .

i - Humeral immune responses

The sequence of appearance of HBV related antibodies is : anti - HBc appears first , follows by anti - HBe and finally by anti - HBs Fig (5) .

a- Antibody to hepatitis B core antigen (anti-HBc):

Anti - HBc is the first measurable reading of humeral response in HBV infection and generally follows the detection of HBs Ag by 2 to 10 weeks (Irwin , et al . , 1977) . Anti - HBc is immunoglobulin belongs predominantly to I g M and I g G subclass (Brzoske , et al . , 1975) . The initial anti - HBc response consists mostly of Ig M antibody which then falls to undetectable levels , while only anti - HBc Ig G persists. (Hoofnagle, 1981) . However some chronic HBs Ag carriers may mentain moderate to low titers of anti - HBc Ig M (Kryger, et al . , 1981) .