Hepatitis B Virus Infection in Nigeria – A Review

G O Emechebe[+], I J Emodi[*], A N Ikefuna[*], G C Ilechukwu[*],
W C Igwe[**], Ejiofor OS[#], CA Ilechukwu[# #].

SUMMARY

Background: Hepatitis B virus infection is a pandemic and chronic infection may lead to chronic liver diseases which are often lethal. This review was done to assess the status of hepatitis B virus infection in Nigeria.

Materials and Method: Source of information was mainly from published works in Nigeria and elsewhere. The information was extracted over period of 5months from May to December 2007.

Result: Since over 30years when pioneer works were done in Nigeria to the recent times the prevalence of hepatitis B virus infection has remained very high. In Nigeria, the transmission of hepatitis B virus occurs mainly during childhood and all the risk factors (like blood transfusion, sexual promiscuity, lower socioecomic status etc) implicated elsewhere in the spread of the virus in the general population also play role in Nigeria.

Conclusion: Reduction in the of hepatitis B virus infection could be achieved by public enlightenment campaign, mass immunization of the children and adults at risk while antiviral drugs and immunostimulatory therapy should be provided for those already infected.

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INTRODUCTION

Historically, hepatitis B surface antigen (HBsAg) was formerly called Australia antigen because it was first described in the serum of an Australian aborigine in 1963.[1,2] Okochi and Murakami [2] in 1968, discovered that the Australian antigen was related to type B hepatitis while Dane found virus-like particles in the serum of patients suffering from type B hepatitis in 1973.[1,3] These particles were designated as the hepatitis B virus (HBV).[4]

Hepatitis B Virus, a major public health problem world-wide is more prevalent in the developing countries.[4,5] More than 2 billion people are infected with HBV world-wide while some 280 million are chronic carriers, harboring the virus in their liver.[6] About 2 million of these carriers die each year as a result of cirrhosis or primary liver cell cancer induced by the virus.[6] This virus is responsible for 80% of all cases of primary liver cancer, which is one of leading causes of death in Asia and Africa.[6]

About 5 – 10% of infected adults become chronic carries. The remainder eliminates the virus from their body without sequale.[6] About a quarter of chronic carriers will die from hepatic complications of chronic infection, some remain lifelong carriers while others will clear the infection after varying intervals.[7] Sub-Saharan Africa is considered to be a region of high endemicity with an average carrier rate of 10 – 20% in the general population.[4] Seventy to 95% of adults in the Sub-Saharan have at least one marker of HBV.[8] In west Africa, it has been estimated that 40% of children will be infected by age two years and above 90% by age of ten years.[8] Chronic carrier rate is 20% in these children.[8] A chronic carrier rate above 7% in a population is classified as hyper endemic.[8] Studies done in Nigeria showed HBV carriage rate in the range of 9 to 39%.[10-14]

BIOLOGY OF HBV

The Hepatitis B Virus

The HBV belongs to the family hepadnaviridae and genus orthohepatodnavirus.[15] It is the only hepadna virus causing infection in humans.[16] It cannot yet be grown in an artificial medium but can be transmitted to certain primate such as the chimpanzee in which it is able to replicate.[16] It is a resilient virus that can exist on almost any surface for about 1 month.[17] Sodium hypochlorite 0.5% (1: 10 house hold bleach), destroys the HBV antigenicity within 3 minutes but the virus is stable at minus 20 degree centigrade for about 20years.[15]

HBV infected cells produce multiple types of virus related particles.[18] Electron microscopy of partially purified preparations of HBV shows three types of particles.[32,18]

(a.) Double shelled particles with diameter of 42-47 nanometer (Known as Dane particles, after their discoverer).

(b.) Spheres of about 22nm diameter, usually present in a 10,000 to 100,000 fold excess over Dane particles.

(c.) Relative to complete virus there are smaller quantity of filaments of 20nm diameter and variable length often measuring about 200nm,

All these forms have a common antigen on their surfaces termed hepatic B surface antigen (HBsAg), which is present in large quantity in serum of the infected host.[17] These viral particles in circulation allow for easy antigen detection.[18] The particles containing HBsAg are antigenically complex. Each contains a

From: [+]Department of Paediatrics, Imo state University Teaching Hospital Orlu. *Department of Paediatrics, University of Nigeria Teaching Hospital Enugu. **Department of Paediatrics, Nnamdi Azikiwe University Teaching Hospital Nnewi. [#] Amaku General Hospital, Awka [##]Institute of Child Health, University of Nigeria Teaching Hospital, Enugu.

Correspondence: **G. O. Emechebe,** Department of Paediatrics, Imo State University Teaching Hospital Orlu.
E-mail nnabuike20g@yahoo.com

group specific antigen, a, in addition to two pairs of naturally exclusive sub determinants, adw, ayw, adr and ayr,[15,18] These sub types have geographical predilection, For example in the United States of America adw is the predominant subtype, while in Africa it is adr.[15] There is no difference in the pathogenicity between subtypes because cross immunity exists among them due to universal presence of the "a'' determinant.[18] Antibody to "a" determinant are used in the diagnostic assay kit for HBsAg detection.[19]

The complete virus or Dane Particles is the infectious viron of HBV.[18] Its outer shell is a lipoprotein envelope containing the viral surface glycoprotein.[20] The inner core particle(hepatitis B core Antigen) or nucleocapsid has a diameter of 25 – 27nm and its major structural protein is the C protein.[16] Within the core is the viral DNA, a protein kinase and a polymerase known to be centrally involved in genomic replication.[18] The core also contains non particulate soluble antigen (HBeAg) derived from HBcAg by proteoltic self cleavage.[20,21] The viral DNA is a double stranded circular molecule. This molecule has an unusual structure in that its two DNA are not perfectly symmetrical.[18]

Replication of HBV occurs predominantly in liver but also occurs in lymphocytes, spleen, kidney and pancreas.[16] HBsAg is a product of S gene of the HBV genome and the prime constituent hepatitis B particle forms.[15] It is manufactured in the cytoplasm of infected hepatocytes in high quantities, the excess that did not combine with DNA to produce viral particles spill into the serum as 22nm diameter spheres and filaments.[15,18] Carriage of HBsAg is considered to be chronic when the patient has been HBsAg positive for 6 months or more.[22]

The spheres and filaments are exclusively of HBsAg and host derived lipids, approximately 30% by weight. These particles lack nucleic acid and hence are non infectious. Nonetheless, in pure form these particles are highly immunogenic and induce a neutralizing anti-HBs antibody response.[18] Prior to the development of recombinant HBsAg preparations, 20nm spheres as prepared from the serum of HBV carriers, served as HBV vaccine.[15]

Epidemiology

Sub-Saharan Africa, Asia, the Pacific, the Amazon and southern part of eastern and central Europe are areas of high endemicity with the prevalence rate of above 7%.[4] Chronic infection varies from less than 1% in USA and western Europe to 5% in the Indian subcontinent and middle east.[4]

Chronic infection with HBV occurs in 90% of infants infected at birth, 30% of children infected at 1-5yrs and 6% of persons infected above 5yrs.[23] Thus there is inverse relationship between chronic infection and age due to maturation of the immune system. In Awka, Ezegbudo et al[10] found that the prevalence of HBsAg among pregnant women decreases with increasing social status. Mustapha *et al*[24] and Seresena *et al*[25] in Gombe and Jos respectively found that having multiple sex partner increased the carriage of HBsAg. Ola *et al*[26] in Ibadan found that 57.1% of patients with primary liver cell carcinoma were positive for HBsAg. In Ibadan, Olubyide *et al*[27] found that a high (39 %) prevalence of HBsAg was associated with Surgeons and Dentists, with high potential of transmissibility. They speculated that it was due lack of vaccination and infrequent application of universal precaution.

In Benin, Obiaya *et al*[28] in their study noted that blood transfusion was hazardous in view of the high prevalence of HBsAg in donor blood. Multimer et al [29] found that blood transfusion clearly increased the risk of HBV infection as shown by significantly higher markers of HBV infection (HBsAg and anti HBc) in subjects who were transfused. Abiodun *et al*[30] in Benin observed that HBV infection increased with increasing units of blood transfused. Agumadu and colleagues[31] studying 213 children with sickle cell anaemia, showed that markers of HBV infection (HBsAg and anti HBc) increased with age. Amazigo *et al*[32] in Eastern Nigeria found that HBsAg carriage and exposure rate to HBV were significantly higher in rural than in urban population. This was attributed to overcrowding and clustering. They also demonstrated that by 40yrs of age 87% of indigenous population of Eastern Nigeria has at least one HBV marker their serum.

Most of studies in Nigeria on HBsAg did not find significant differences between males and females subjects.[33,34] Some studies in Nigeria on HBV infection showed it occurred earlier in children SCA.[14,35] The increasing surface antigenaemia with age has been demonstrated by several workers in Nigeria.[31,32,34,36] Amazigo *et al*[32] found a significantly higher HBsAg prevalence among prisoners in eastern Nigeria, which was attributed to overcrowding and clustering. Recent studies on HBsAg prevalence in Jos[12] and Gombe[24] among patients with human immune deficiency syndrome (HIV) showed a prevalence of 25.9% and 26.5% respectively. These high values could be because HIV and HBV share similar modes of transmission and risk factors.

Transmission of HBV

Transmission of HBV occurs when blood or body fluid of an infected person enters the body of a person who is not immune.[16,23,37] HBV could be transmitted through the following ways. Studies in Nigeria have confirmed some of the routes outlined above. Most studies in Nigeria found a low prevalence in infancy and an increasing rate with age.[4,32,34] A figure of 2.8% has been documented as the rate HBV transmission from Nigerian females to their offspring.[38] Most infections in Nigeria occur through horizontal transmission.[29,32]

Various studies in Nigeria showed that blood transfusion is an important source HBV transmission.[28,29,39] Although CDC publications[23] and a study in South Africa[40] linked HBV transmission to tattoos and body cuttings/piercing, most studies in Nigeria found no link between traditional practices like, scarification, circumcision,ear piercing and HBV infection.[41,42] Higher HBsAg prevalence noted among prisoners and rural dwellers were attributed overcrowding and clustering.[32] Studies from north-central Nigeria indicates that unprotected sex is implicated in the transmission of HBV.[24,25]

Table I Mode of Transmission of Hepatitis B Virus Infection

- Vertical transmission as in mother to child mainly during and after birth accounting for 1-5% infections in Africa.[8]
- Use of unsterilized needles and syringes for injections.[23]
- Transfusion of infected blood and blood products.[23]
- Close body contact with patients with active infection or carriers especially those with skin lesions like impetigo, scabies and cuts that enable transfer of blood and body fluid.[23,37]
- Unprotected sex with infected persons and human bites.[1, 13,23]
- Sharing of tooth brushes, razors, needles. nail and hair clippers.[23]

Complications of HBV infection

HBV is hepatotropic and has a profound effect on the liver. Majority of patients with acute, sub acute symptoms and even sub clinical cases of HBV infection will clear the infection with temporary infiltration of liver by inflammatory cells.[43] In fulminant hepatitis there is total destruction of liver parenchyma leaving only connective tissue septa.[44] Persistent histologic changes in patients with HBV indicates development of chronic hepatitis.[16] This manifests in two forms, chronic persistent hepatitis and chronic active hepatitis.[44] Chronic persistent hepatitis is limiting, with minimal changes in lobular architecture while in the chronic active hepatitis there is piecemeal necrosis of hepatocytes.[45] This disruption of lobular architecture leads to cirrhosis and often primary liver cell carcinoma[46] which is a leading cause of death in sub-Saharan Africa.[8] Presumably, persistent infection leads to rapid cell turnover, accumulation of errors in replication and instability in the host genome.[46] A more direct role in tumourigenesis, with occasional viral insertion into host genome, may inactivate a tumour suppressor gene or activate cellular proto encogene.[46]

In Ibadan 57.1% of patients with primary liver cell carcinoma were infected with HBV.[27] Edington et al[48] had earlier reported similar trend in North-central Nigeria. Kaine et al[47] in Enugu found that cellular infiltration was more aggressive, particularly in the portal tracts in children with sickle cell disease who were positive for HBsAg HBV infection may be responsible for 20-40% prevalence of cirrhosis reported in patients with sickle cell disease.[49]

Control of HBV infection

There are broadly three strategies for dealing with HBV infection in the developed countries, immunization for at risk population, antiviral drugs (lamivudine, adeforvir and dipivoxil) and immunostimulatory therapy with alpha-interferon for those affected.[50]

Immunization is the most effective means of controlling and HBV world-wide.[8] The vaccine has an outstanding record of safety and efficacy, and it is 95% effective in preventing development of the chronic carrier state.[51] In Africa, vertical transmission accounts for 1 – 5% of cases,[52] while most children are infected with HBV between ages of 2-11years through horizontal transmission, hence universal immunization at birth has been adopted.[21,52] As cost effective measure it has been incorporated into WHO expanded programme on immunization (EPI) on global basis according to Yaounde declaration at the International conference on the control of HBV held in 1991.[8]

In addition to the above measures where it is feasible, HBV infection in Nigeria can be prevented or drastically reduced through health education of the general population on the various mode of transmission of HBV and preventive measures.[25] Such measures include careful handling of blood and body fluid since they are potentially infectious. Also discouraging communal sharing of blade/sharp instruments used for shaving, barbing, manicure and body piercing/cutting and high level sexual networking.[37,25,17,21] Prechewing of solid for children by an adult, especially those at risk for HBV infection should be discouraged because saliva is known to transmit HBV.[53]

WHO recommends universal screening of blood and plasma for HBsAg by sensitive method before transfusion.[8] Even when all blood donations are screened for HBsAg, donations from volunteered non remunerated donors have been proved to be safest.[54] About 2 out of 1000 units screened plasma donations, negative for HBsAg using a very sensitive test are still infectious because the sensitivity of the third generation test is not 100%.[40] Addition of a low dose hepatitis B immunoglobulin to potentially infectious plasma appears to be reliable measure to eliminate the hepatitis B transmission. This is preferred to other methods for labile plasma derivatives.[54] Where possible only donations from immunized donors with a detectable amount of anti-HBs should be collected either for transfusion or for preparation of plasma derivative. Pasteurization of plasma derivatives like albumin, factors iii and viii at 60^0C for at least 10hours is essential for the elimination of HBV.[54] Because of risks of blood transfusions, it should be given only when it is absolutely necessary as it was said that most blood transfusions were not necessary.[28, 54]

Babies born to HBsAg positive mother should be given hepatitis B immunoglobulin at birth and active immunization should commence immediately.[53] Post exposure prophylaxis with hepatitis B immunoglobulin should be given promptly in all cases of suspected blood or body fluid inoculation as this could reduce HBV infection.[53]

In Nigeria most of these control measures, are poorly observed [25,27] safe blood for transfusion are not easily accessible. [29,30] Socio-economic and living condition of most Nigerians encourage transmission of HBV.[32]

Table 2: Summary of control of HBV infection

- Universal immunization of children and adults at risk.
- Health education of the public to discard various habits and practices that encourages the transmission of HBV.
- Practice safe sex.
- Avoid sharing body cutting instruments.
- Universal screening of blood and blood products.
- Post exposure prophylaxis with HBV immunoglobulin and for babies born to HBsAg positive mothers.
- Improve socio-economic status of the citizens.

CONCLUSION

From earlier studies done over 30years to more recent studies done in different populations in Nigeria, the prevalence of HBsAg has not decreased, in some studies it appeared to have increased, with range of 7-30% being reported.[13,24,55,56]

However the observed higher values in some of the recent studies were attributed to the use of more sensitive third generation HBsAg assay methods.

The persistent high value in Nigeria could be attributed in part to, the fact that, though WHO adopted HBV immunization as part of EPI in 1991 it was not until 2003 that it was incorporated into NPI and it was mostly not available until recently.[6,57] It was also noted that HBV infection is not a commonly perceived problem in Africa.[58] This is because infections are often sub clinical and there is long interval before the consequences of chronic carriage manifest.[58] This perception imparted negatively on health education directed at HBV. But education on HBV risk factor modification could be incorporated into the AIDS intervention programme as an alternative. This is because the problems associated with AIDS is being better appreciated and both share risk factors and mode of transmission.[58]

To quickly reduce prevalence of this deadly disease in Nigeria, nationwide campaign should be done on national immunization days as is the case with polio immunization to quickly vaccinate children that missed opportunity.

As was done for people infected with Human Immune Deficiency virus (provision of antiretroviral drugs), governments and non governmental organizations should make available antiviral drugs (lamivudine, adefovir and dipivoxil) and immunostimulatory drug like alpha-interferon for those already infected with HBV. These drugs will reduce viral replication and viral load over time thereby reducing the transmission of HBV and hence morbidity and mortality associated with it.

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