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Hepatitis B Virus Vaccination in Nigeria – A Review

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ABSTRACT

Effective vaccination against hepatitis B infection has not reduced or eradicated the dreaded disease in most part of the world including Nigeria: which is described as an endemic zone. Information used in this work was mainly from published work within and outside Nigeria. The prevalence of hepatitis B virus is still considerably high which is due to its transmission mainly during childhood, sexual promiscuity, unscreened blood transfusion and in part, quality of living. Vaccination, mass immunization and sensitization of the public remains a sure way to curb and eradicate hepatitis B virus. While utmost attention and care must be given to those that are already infected.

Keywords: Hepatitis B Virus; prevalence; vaccination; Nigeria

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1. INTRODUCTION

Hepatitis B surface antigen (HBsAg) was formerly called Australia antigen because it was first observed in the serum of an Australian aborigine in 1963 (Blumberg *et al*., 1967), Okochi and Murakami 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. These particles were designated as the hepatitis B virus (HBV) (Emechebe *et al*., 2009). Hepatitis B Virus, a major public health problem world wide is more prevalent in the developing countries (Emechebe *et al*., 2009). A staggering figure of 2 billion people are infected with HBV world-wide while some 280 million are chronic carriers, harboring the virus in their liver. A mortality rate of 2 million of these carriers die each year as a result of cirrhosis or primary liver cell cancer induced by the virus.

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 (Clement, 1990). About 5 - 10% of infected adults become chronic carries. The remainder eliminates the virus from their body . 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 (Zuckerman, 1999). West Africa is a region of high endemicity with an average carrier rate of 10 - 20% in the general population (Emechebe et al., 2009). Seventy to 95% of adults in the Sub-Saharan have at least one marker of HBV. About 40% of children in West Africa have been estimated to be infected by the age of two years while an estimated 90% by age ten . Chronic carrier rate is 20% in these children. A chronic carrier rate above 7% in a population is classified as hyper endemic (Kire, 1993).

2. RELATED LITERATURE

According to some investigations done in Nigeria, the HBV carriage rate is within the range of 9 to 39%- (Brook et al., 2004; Ukaeje et al., 2005) Hepatitis B virus (HBV) is a typical member of the *Hepadnaviridae* (hepatotropic DNA virus) family genus orthohepatodnavirus (Finlayson et al., 1999) It is the only hepadna virus causing infection in humans (Brooks et al., 2004). The virus can be cultivated by transferring it into a suitable primate as chimpanzee It is a resilient virus that can exist on almost any surface for about 1 month. 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 (Brooks et al., 2004). The virus particle, called Dane particle (virion), consists of an outer lipid envelope and an icosahedral nucleocapsid core composed of protein. The nucleocapsid encloses the viral DNA and a DNA polymerase that has reverse transcriptase activity similar to retroviruses (Locarnini, 2004).

The outer envelope contains embedded proteins which are involved in viral binding of, and entry into, susceptible cells. The virus is one of the smallest enveloped animal viruses with a virion diameter of 42 nm, but pleomorphic forms exist, including filamentous and spherical bodies lacking a core. These particles are not infectious and are composed of the lipid and protein that forms part of the surface of the virion, which is called the surface antigen (HBsAg), and is produced in excess during the life cycle of the virus (Howard, 1986). HBV virions are double-shelled particles, 40 to 42 nm in diameter (Dane *et al.,* 1970) with an outer lipoprotein envelope that contains three related envelope glycoproteins (or surface antigens) (Ganem, 1991). Within the envelope is the viral nucleocapsid, or core. The core contains the viral genome, a relaxed-circular, partially duplex DNA of 3.2 kb, and a polymerase that is responsible for the synthesis of viral DNA in infected cells (Summers *et al.,* 1975). DNA sequencing of many isolates of HBV has confirmed the existence of multiple viral genotypes, each with a characteristic geographic distribution (Kao, 2002).

The genome of HBV is made of circular DNA, but it is unusual because the DNA is not fully double-stranded. One end of the full length strand is linked to the viral DNA polymerase. The genome is 3020–3320 nucleotides long (for the full-length strand) and 1700–2800 nucleotides long (for the short length-strand) . The negative-sense (non-coding) is complementary to the viral mRNA. The viral DNA is found in the nucleus soon after infection of the cell. The partially double-stranded DNA is rendered fully double-stranded by completion of the (+) sense strand and removal of a protein molecule from the (−) sense strand and a short sequence of RNA from the (+) sense strand . The function of the protein coded for by gene X is not fully understood but it is associated with the development of liver cancer. It stimulates genes that promote cell growth and inactivates growth regulating molecules (Li *et al.,* 2010).

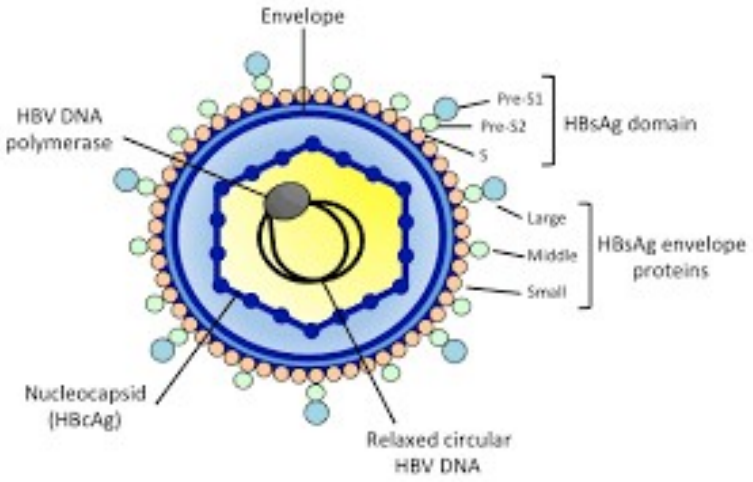

Fig. 1: Hepatitis B Struture

HBV infection contracted early in life may lead to chronic hepatitis, then to cirrhosis, and finally to HCC, usually after a period of 30 to 50 years. Once infected with HBV, males are more likely to remain persistently infected than women, who are more likely to be infected transiently and to develop anti-HBs. It is possible that in man, HBV is not carcinogenic by a direct viral mechanism. Instead, the role of HBV may be to cause chronic liver cell damage with associated host responses of inflammation and liver regeneration that continues for many years. This pathological process, especially when leading to cirrhosis, may be carcinogenic without involving a direct oncogenic action of the virus. No viral oncogene, insertional mutagenesis, or viral activation of oncogenic cellular genes has been demonstrated. (Mahoney and Kane, 1999).

HBV occurs worldwide: The highest rates of HBsAg carrier rates are found in developing countries with primitive or limited medical facilities. In areas of Africa and Asia, widespread infection may occur in infancy and childhood. The overall HBsAg carrier rates may be 10 to 15%. The prevalence is lowest in countries with the highest standards of living, such as Great Britain, Canada, United States, Scandinavia, and some other European Nations. In North America infection is most common in young adults. In the USA and Canada, serological evidence of previous infection varies depending on age and socioeconomic class. In developed countries, exposure to HBV may be common in certain high-risk groups. Adults infected with HBV usually acquire acute hepatitis B and recover, but 5 to 10% develop the chronic carrier state. Infected children rarely develop acute disease, but 25 to 90% become chronic carriers. About 25% of carriers will die from cirrhosis or primary liver cancer as adults

In Nigeria, chronic infection with HBV occurs in 90% of infants infected at birth, 30% of children infected at 1-5 years and 6% of persons infected above 5 years (CDC, 2003). Thus, there is an inverse relationship between chronic infection and age due to maturation of the immune system. In Akwa, Ezegbudo *et al*., (2004) found that the prevalence of HBsAg among pregnant women decreases with increasing social status. Mustapha *et al.,* (2004) and Seresena *et al.,* (2002) in Gombe and Jos respectively found that having multiple sex partners increased the carriage of HBsAg. Ola *et al.,* (1994) in Ibadan found that 57.1% of patients with primary liver cell carcinoma were positive for HBsAg. In Ibadan, Olubuyide *et al.,* (1997) 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 to lack of vaccination and infrequent application of universal precaution.

Hollinger and Liang (2001) recognized four major modes of transmission, which are transmission vis: From mother to child at birth (perinatal), by contact with an infected person (horizontal), by sexual contact, and by parenteral (blood-to-blood) exposure to blood or other infected fluids. HBV is stable on environmental surfaces for at least 7 days, and indirect inoculation of HBV can occur via inanimate objects like toothbrushes, baby bottles, toys, razors, eating utensils, hospital equipment and other objects, by contact with mucous membranes or open skin breaks. Infectious HBV can be present in blood without detectable HBsAg, so that the failure to detect antigen does not exclude the presence of infectious virus. (Tacket *et al.,* 1999).

3. THE RESERVOIR AND PREVALENCE OF HB

The natural reservoir for HBV is man while Closely related hepadnaviruses have been found in woodchucks and ducks, but they are not infectious for humans. (Ganem and Schneider, 2001). Most infections in Nigeria occur through horizontal transmission. (Multimer, 1994). Various studies in Nigeria showed that blood transfusion is an important source of HBV transmission . Although, CDC publications and a study in South Africa linked HBV transmission to tattoos and body piercings, most studies in Nigeria found no link between traditional practices like scarification, circumcision, ear piercing and HBV infection (Chukwuka *et al.,* 2003).

Higher HBsAg prevalence noted among prisoners and rural dwellers were attributed to overcrowding and clustering. Studies from North-central Nigeria indicates that unprotected sex is implicated in the transmission of HBV (Mustapha and Jibrin, 2004; Sirisena *et al.,* 2002).Acute hepatitis B viral is associated with acute viral hepatitis – an illness that begins with general ill-health, loss of appetite, nausea, vomiting, body aches, mild fever, and dark urine, and then progresses to development of jaundice. It has been noted that itchy skin has been an indication as a possible symptom of all hepatitis virus types. The illness lasts for a few weeks and then gradually improves in most affected people. A few people may have more severe liver disease (fulminant hepatic failure), and may die as a result. The infection may be entirely asymptomatic and may go unrecognized (Terrault *et al.,* 2005).

Chronic infection with hepatitis B virus either may be asymptomatic or may be associated with a chronic inflammation of the liver (chronic hepatitis), leading to cirrhosis over a period of several years . Hepatitis B virus has been linked to the development of membranous glomerulonephritis (MGN), (Gan *et al.,* 2005). Symptoms outside of the liver are present in 1–10% of HBV-infected people and include serum-sickness–like syndrome, acute necrotizing vasculitis (polyarteritis nodosa), membranous glomerulonephritis, and papular acrodermatitis of childhood (Gianotti–Crosti syndrome) . The serum-sickness–like syndrome occurs in the setting of acute hepatitis B, often preceding the onset of jaundice. The clinical features are fever, skin rash, and polyarteritis. The symptoms often subside shortly after the onset of jaundice, but can persist throughout the duration of acute hepatitis B (Liang, 2009).

4. DIAGNOSIS OF HB

Diagnosis of hepatitis is made by biochemical assessment of liver function. Initial laboratory evaluation should include: total and direct bilirubin, ALT, AST, alkaline phosphatase, prothrombin time, total protein, albumin, serum globulin, complete blood count, and coagulation studies. (Hollinger and Liang, 2001). Diagnosis is confirmed by demonstration in sera of specific antigens and/or antibodies. Three clinical useful antigen-antibody systems have been identified for hepatitis B: hepatitis B surface antigen (HBsAg) and antibody to HBsAg (anti-HBs), antibody (anti-HBc IgM and anti-HBc IgG) to hepatitis B core antigen (HBcAg), hepatitis B e antigen (HBeAg) and antibody to HBeAg (anti-HBe). Immunofluorescence studies, in situ hybridization, immunohistochemistry, and thin-section electron microscopy are used to examine pathological specimens for the presence of HBV-associated antigens or particles, providing information about the relationship between HBV DNA replication and HBV gene expression. Within the hepatocyte, HBsAg localizes in the cytoplasm, and HBcAg is seen in the nucleus and/or the cytoplasm. Detection of complete virions in the liver is uncommon. DNA hybridization techniques and RT-PCR assays have shown that almost all HBsAg/HBeAg-positive patients have detectable HBV DNA in their serum, whereas only about 65% of the HBsAg/anti-HBe-reactive patients are positive.

PCR tests have been developed to detect and measure the amount of HBV DNA, called the viral load, in clinical specimens. These tests are used to assess a person's infection status and to monitor treatment. Individuals with high viral loads, characteristically have ground glass hepatocytes on biopsy.

5. HB PREVENTION

There are three major ways in the prevention of Hepatitis B infection:

Vaccination
The hepatitis B vaccine is the mainstay of hepatitis B prevention. WHO recommends that all infants receive the hepatitis B vaccine as soon as possible after birth, preferably within 24 hours. The birth dose should be followed by 2 or 3 doses to complete the primary series. In most cases, one of the following two options is considered appropriate:

a 3-dose schedule of hepatitis B vaccine, with the first dose (monovalent) being given at birth and the second and third (monovalent or combined vaccine) given at the same time as the first and third doses of diphtheria, pertussis (whooping cough), and tetanus – (DTP) vaccine (WHO, 2015); or sFour doses, where a monovalent birth dose is followed by three monovalent or combined vaccine doses, usually given with other routine infant vaccines.
The complete vaccine series induces protective antibody levels in more than 95% of infants, children and young adults. Protection lasts at least 20 years and is probably lifelong. Thus, WHO does not recommend booster vaccination for persons who have completed the 3 dose vaccination schedule (WHO,2015). All children and adolescents younger than 18 years-old and not previously vaccinated should receive the vaccine if they live in countries where there is low or intermediate endemicity. Hepatitis B immunoglobulin (HBIG) reduces the risk of HBV transmission and is used in resource rich settings where pregnant women have high viral loads. A meta-analysis of the benefit of adding immunoglobulin to the vaccine for the prevention of HBV MTCT has shown that compared with placebo/no intervention, HBV vaccine plus HBIG significantly reduced hepatitis B occurrence (Emechebe *et al*., 2009). Even where women have access to birth dose vaccine and HBIG there remains a 5-10% failure rate. This occurs in women with high HBV viral loads. For these women, ART during pregnancy has been shown to significantly reduce the risk of MTCT. Where mothers do not need ART for their own health, therapy can be used during pregnancy with the primary aim of reducing the risk of MTCT of HBV.

Tenofovir, lamivudine and telbivudine are nucleotide inhibitors which act as chain termination in DNA elongation and can be administered from 28 weeks' gestation. Many of the early studies were performed using lamivudine and whilst the benefit of using this drug to reduce transmission was evident, it has been associated with the emergence of resistance because of its low genetic barrier. Tenofovir has a high barrier to resistance and has been used extensively in the setting of HIV. In studies of tenofovir in pregnancy, significant reductions in HBV viral load and risk of transmissions in treated mothers were reported.

There is no specific treatment for acute hepatitis B. Therefore, care is aimed at maintaining comfort and adequate nutritional balance, including replacement of fluids lost from vomiting and diarrhoea. Chronic hepatitis B infection can be treated with drugs, including oral antiviral agents.

Treatment can slow the progression of cirrhosis, reduce incidence of liver cancer and improve long term survival (WHO, 2015). Acute hepatitis B infection does not usually require treatment and most adults clear the infection spontaneously (Hollinger and Lau, 2006). Early antiviral treatment may be required in fewer than 1% of people, whose infection takes a very aggressive course (fulminant hepatitis) or who are immunocompromised. On the other hand, treatment of chronic infection may be necessary to reduce the risk of cirrhosis and liver cancer. Chronically infected individuals with persistently elevated serum alanine aminotransferase, a marker of liver damage, and HBV DNA levels are candidates for therapy. Treatment lasts from six months to a year, depending on medication and genotype (Alberti and Caporaso, 2011).

6. CONCLUSION

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 (Hudson et al., 1990). It was also noted that HBV infection is not a commonly perceived problem in Africa.This is because infections are often sub clinical and there is long interval before the consequences of chronic carriage manifest.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 (Emechebe et al., 2009).

A sure way to the reduction in HBV virus is education , sensitization of the populace. The same attention HIV/AIDS receive in Nigeria should be extended to people with HBV; thereby eradicating or reducing it to the barest minimum. Foundations should be set up to cater for patients suffering from HBV while local researches into ways to reduce and eliminate the disease should be embarked upon.

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