International STD Research & Reviews

7(1): 1-17, 2018; Article no.ISRR.36989
ISSN: 2347-5196, NLM ID: 101666147

Epidemiology of Hepatitis B Virus Infection in South-South, Nigeria: A Review

C. F. Umego[1], C. I. Mboto[1], E. N. Mbim[1], U. O. Edet[1,2*], U. E. George[3] and J. E. Tarh[4]

[1]Deparment of Microbiology, Faculty of Biological Sciences, University of Calabar, Calabar, Cross River State, Nigeria.
[2]Deparment of Microbiology, Faculty of Natural and Applied Sciences, Obong University, Obong Ntak, Etim Ekpo LGA, Akwa Ibom State, Nigeria.
[3]Department of Virology, College of Medicine, University of Ibadan, Ibadan, Oyo State, Nigeria.
[4]Department of Microbiology, Cross River University of Technology, Calabar, Cross River State, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Authors CFU, CIM, ENM and UOE managed the literature searches and wrote the first draft of the manuscript. All authors read, reviewed and approved the final manuscript.

Article Information

DOI: 10.9734/ISRR/2018/36989
Editor(s):
(1) Basavraj S. Nagoba, Professor, Department of Medical Education, MIMSR Medical College, India.
Reviewers:
(1) Thompson J. Akinbolaji, Yuma Regional Medical Center, USA.
(2) Essam A. El-Moselhy, Al-Azhar University, Egypt.
Complete Peer review History: http://www.sciencedomain.org/review-history/23075

Review Article

Received 26th September 2017
Accepted 16th January 2018
Published 8th February 2018

ABSTRACT

Hepatitis B virus (HBV) is a small enveloped DNA virus of the *Hepadnaviridae* family associated with infection of the liver, and a major public health problem globally. The virus preferentially infects the liver leading to hepatic complications such as hepatic carcinoma and liver cirrhosis. About two billion people globally have been estimated to be infected with hepatitis B virus and approximately 350-400 million others reportedly suffer from the chronic forms. An estimated two million of these carriers die each year as a result of complications. The mode of transmission of the disease is largely through unprotected sex, mother-to-child transmission (MTCT), contaminated blood and blood products and use of contaminated sharp objects or instruments. Africa is a high endemic area with 7–26% prevalence rate of HBsAg. Nigeria has been placed among the group of countries

**Corresponding author: Email: uwemedet27@gmail.com;*
Email: mbimelizabeth@gmail.com;

endemic for HBV infection with about 18 million infected. In recent years, the rates of prevalence of HBV have been increasing within the South-South part of the country. Serological and molecular techniques are currently employed not only in the diagnosis of this infection but also to assess the prognosis of the disease, guide therapy and monitor treatment responses. Treatment is highly supportive and two major groups of antiviral treatment licensed for the treatment of chronic HBV infection are pegylated interferon alpha and nucleoside or nucleotide analogues. Interrupting early transmission is key to breaking the cycle of ongoing HBV infection. In addition to active vaccination, the implementation of blood safety strategies including quality-assured screening of all donated blood and components used for transfusion may prevent transmission of HBV to a significant level.

Keywords: HBV; epidemiology; prevalence; South-South Nigeria.

1. INTRODUCTION

Inflammation of the liver has historically been regarded as hepatitis, and eleven viruses are associated with hepatitis in humans with nine being hepatotrophic and two, transient in nature [1]. The global distribution of infections with hepatotrophic viruses as well as their attendant morbidities and mortalities associated with these infections are becoming major health concerns. This is because about 2 million of carriers die globally each year as a result of cirrhosis or primary liver cell cancer [2]. Hepatitis B virus (HBV) infection pose a major public health challenge globally and has been reported by Ott et al. [2] to be more prevalent in the developing countries. Globally, it has been reported that about two billion people are infected with hepatitis B virus and approximately 350-400 million others suffer from the chronic form [3].

According to Zhu et al. [4], an estimated eighty percent of hepatocellular carcinoma is caused by hepatitis B virus; a leading cause of mortality in Africa and Asia. According to Emechebe et al. [5], an estimated 5-10% of infected adults become chronic carriers while the rest most often eliminate without sequalae, the virus from their body. They further added that an estimated one quarter of chronic carriers often die due to hepatic complications, a few remain life-long carriers while others at varying intervals clear the infections.

The mode of transmission of the disease is largely through unprotected sex, mother-to-child transmission (MTCT), contaminated blood and blood products and use of contaminated objects or instruments [6]. Maternal HBV transmission is a risk factor in the development of liver cirrhosis and hepatocellular carcinoma among young adults [7]. This means that infancy-related HBV infections that often result to chronic cases usually lead to liver cirrhosis and hepatocellular carcinoma; thus prompting the need for urgent prevention of mother to child transmission. According to Zenebe et al. [7], the probability of becoming a chronic HBV carrier is inversely related to age at the time of infection. Furthermore, neonatal HBV infection often leads to chronic carrier states and occurs in approximately 90% of infants born from mothers who are positive for hepatitis B surface antigen (HBsAg) and hepatitis B e-antigen (HBeAg).

In addition, the prevalence of HBV infection has been reported to vary according to ethnic groups, regions and countries with the most endemic areas being middle and low income countries [8]. As reported by Zenebe et al. [7], the prevalence of chronic HBV infection globally is clustered as low (<2%), intermediate (2-7%) and high (≥8%). Thus, sub-Saharan Africa including Nigeria has been reported as a region of high endemicity with an average carrier rate of 10-20% among the general population [5]. They further added that about 70-95% of adult carriers in sub-Saharan Africa possess at least one HBV marker.

HBV have been implicated with co-infections and management complications with human immunodeficiency virus (HIV), hepatitis C, tuberculosis, malaria, just to mention a few [5]. Co- infection of HBV with other infections has been reported by several researchers [9-10]. Hepatitis B co-infections with Hepatitis C virus and human immunodeficiency virus (HIV) are known to affect the progression, management, therapy and outcome of these infections [9]. According to Mengesha [10], the co-infections of HIV with hepatitis (B and C) is due to similar routes of transmission. They added that the coexistence of TB, HIV and viral hepatitis infections in the same patient poses a unique challenge to such a patient and clinicians. They further reported that most commonly available anti-TB and antiretroviral agents have associated risk of liver damage. Similarly, Lar et al. [11] reported that HIV/HBV co-infection is associated with increased liver related morbidity and

mortality. Ikpeme et al. [12] reported a prevalence rate of 6.02% in children co-infected with HIV/HBV in Uyo, South-South Nigeria. HBV co-infections with malaria also pose a public health concern as reported by Omalu et al. [13]. They equally added that co-endemic malaria and acute hepatitis B occur commonly in Africa. The reasons for these co-infections could be due to the geographical overlap of the endemicity of these infections.

The South-South region of Nigeria comprises the area covered by the natural delta of the Niger River, defined by its geology and hydrology. Its approximate northern boundaries are located close to the bifurcation of the Niger River at Aboh, while the western and eastern boundaries are around the Benin River and the Imo River, respectively. The area is approximately 25,900 square kilometers [14] and consists of six states; Akwa-Ibom, Bayelsa, Cross River, Delta, Edo, and Rivers (Fig. 4). The region is extremely important due to its oil reserves and biological diversity. The South-South region is extremely heterogeneous with respect to culture and ethnicity.

Some studies in Nigeria revealed HBV to be the most common cause of liver disease with carriage rate in the range of 9-39% [15-17]. Unfortunately, knowledge of the natural history, risk factors, modes of transmission and the degree of HBV exposure and other confounding variables among Nigerians in the South-South at risk is very limited. This review is therefore aimed at evaluating the epidemiology of Hepatitis B virus in South-South, Nigeria.

2. HISTORY AND ORIGIN OF HEPATITIS B VIRUS

Blumberg et al. [18] reported the discovery of hepatitis B surface antigen (HBsAg) also known as Australia antigen with its antibody; HBsAb in 1965. They added that the virus has an average incubation period of 90 days from time of exposure to onset of symptoms, but may vary from 6 weeks to 6 months. In addition, the virus preferentially infects the liver, although infection of other tissues has been reported [6]. Hepatitis B virus (HBV); a small enveloped DNA virus of the *Hepadnaviridae* family is one of the major hepatotrophic viruses and has been reported by Ahizechukwu et al. [6] to be double shelled. Infections caused by these species of viruses have been reported to be 50-100 times more infectious than HIV and 10 times more infectious than HCV [1]. Currently, eleven viruses have been implicated in the development of hepatitis of which two are herpes viruses (Cytomegalovirus and Epstein-Bar virus) and others (hepatotrophic viruses). Five of the nine hepatotrophic viruses including A, B, C, D and E viruses have been well characterized while TTV (Transmission Transfusion Virus) is yet to be accepted globally [1].

Hepatitis B virus is one of the most common human viral infections in the world. History has it that the virus originally infected birds back then when Dinosaurs still roamed the planet. As reported by Gerlich [19], Blumberg in 1967 while researching on the genetics of disease susceptibility postulated that people who received blood products from a large number of donors could have developed antibodies against polymorphic serum proteins. But with the work of Blumberg's colleague (Alter), who discovered a new antigen in several samples of huge serum collected most especially in Australian aborigines for whom the Australia (AuAg) was named, set the pace for more research in the area. Consistent with this discovery, Alfred Prince, a co-worker of Blumberg in 1967 while specifically looking at serum hepatitis antigen in the blood of hepatitis B patients discovered that the results of his research were similar to the AuAg earlier reported. Several researches further confirmed that Au/SH-Ag was actually a marker for acute or chronic hepatitis B with a few apparently healthy carriers [19]. In 1969, Blumberg and Millman developed the hepatitis B vaccine [18].

In 1971, it was reported by Hirsch et al. [20], that purified AuAg preparations would contain a reverse transcriptase like retroviruses. This research article though unconfirmed paved way for the detection of the HBV genome. In 1974, William et al. identified the viral DNA which he termed a product of an *endogenous DNA* polymerase activity [21]. According to Gerlich, [19], the cloning and sequencing of HBV DNA was reported almost at the same time by three different renowned researchers in 1978 [22-24].

In line with Robert Koch's postulates, in 1982, the dane particles was proven to be HBV by it's ability to infect an animal model as reported by Will et al. [25]. In 1986, the preS1 domain was characterized as a site for attachment of HBV to hepatic cells and after several years, the liver-specific *sodium-dependent taurocholate cotransporting polypeptide* (NTCP), an essential receptor for the preS1 attachment site of HBV

was identified. The receptor is only expressed in the intact liver, disappears within a few days in primary hepatocyte cultures and is absent in undifferentiated hepatoma cell cultures [19].

2.1 Biology of HBV

According to Inan and Tabak [26] and WHO [27], hepatitis B virus is made up of three different structures: the Dane (42 nm), filamentous (22 nm) and spherical (20 nm) particles which are often observed in serum of HBV-infected patients as presented in Figs. 1 and 2. All the three particles possessed a similar HBsAg on their surface. However, Inan and Tabak [26] added that the filamentous and spherical particles are non infectious because even though both possessed HBsAg and host-derived lipids, they are without HBV genomes. This further reveals that the Dane particle; a 42 nm sphere is the complete infectious HBV virion with its core region being small, partially double stranded, circular DNA molecule and viral DNA polymerase that is surrounded by nucleocapsid [27].

The HBV genome encodes four partially overlapped open reading frames (ORF): the *surface (preS1, preS2, S)*, *core (precore, core)*, *polymerase* and the '*x'* genes, respectively. High genetic variability is a characteristic feature of the HBV as the viral polymerase lacks proof-reading activity and uses an RNA intermediate during its replication [28]. On the other hand, the extreme overlapping of the open reading frames of the HBV genome limits the possibility of fixation of all these mutations. These opposite aspects render the substitution rate of HBV to an intermediate level between RNA and DNA viruses [29].

The nucleocapsid is composed of assembled core antigens (HBcAg) of hepatitis B and is covered with a lipid envelope containing HBsAg [25]. The lipid envelope rich in cholesterol is necessary for viral infectivity and during budding of the nucleocapsid from the endoplasmic reticulum, with the nucleocapsid inducing a condensed and ordered arrangement of three physiologically different surface glycol-proteins including small (S), middle (M) and large (L) on the membrane [26-27].

Chronic infections with HBV have been described as persistence of the HBsAg in the serum over a period of more than 6 months [26]. HBV genome found in the nucleocapsid structure consist of 3.2 kilobases in length and only relaxed partially double-stranded circular DNA (rcDNA) molecule with the nucleocapsid being formed through the composition of viral capsid proteins(240), containing single copy of viral genome DNA and polymerase enzymes that are attached covalently to the 5' end of the chain. According to Inan and Tabak [26] a unique feature of the HBV genome is its asymmetric structure of the chains with most cellular proteins being packed in the nucleocapsid structure. They further added that the genome possess overlapping and open reading frames (OFR) for X, P, C and S encoding four different proteins as presented in Fig. 3.

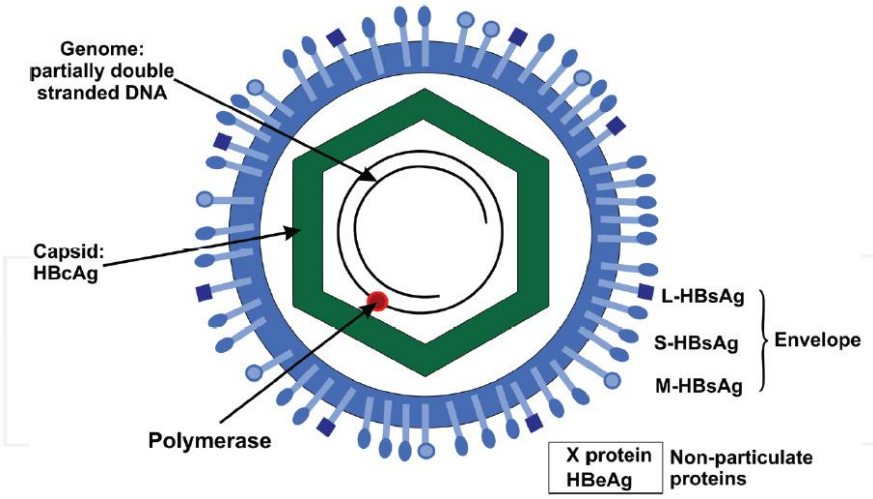

Fig. 1. Basic structure of the HBV genome [28]

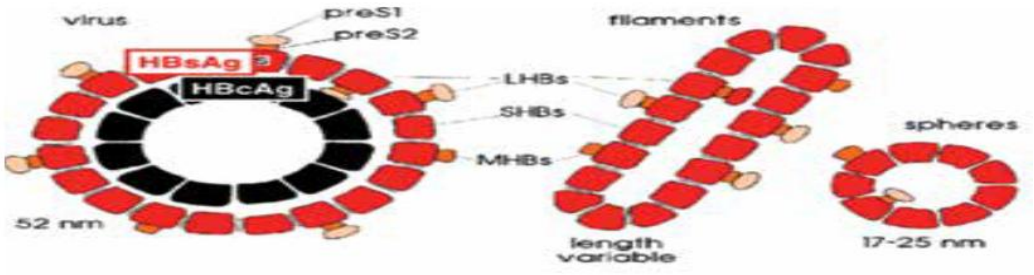

Fig. 2. Spherical, filamentous and HBV Dane HBsAg particles [19]

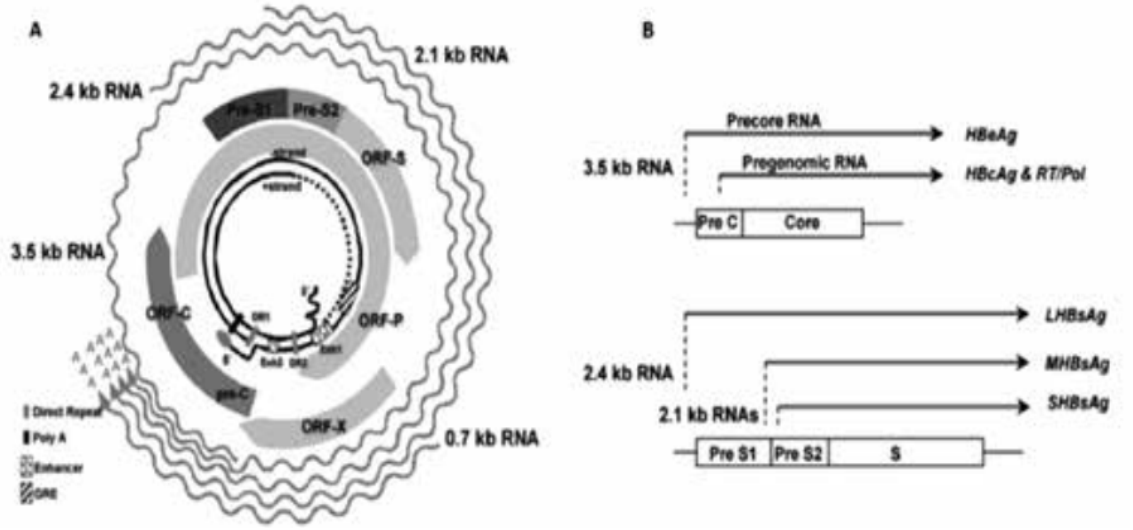

Fig. 3A. Organization of HBV genome and key regulatory elements, 3B. Transcripts and their related proteins of HBV [30]

Research has it that during replication, sub viral particles are excessively secreted compared to mature virions (Dane particle) because they act as evasins; enabling the development of chronic infections [31]. The C ORF region has been reported to contain core regions coding for structural core protein of nucleocapsid called HBcAg and soluble nucleocapsid protein known as HBeAg; with the core protein intrinsically self-binding, forming a capsid-like structure and C-terminal with RNA-binding activity [26]. The HBeAg secretion has been reported to cause secretion of pregenomic mRNA, core, and polymerase while acting as immune tolerant for the development of persistent infections. PORF region codes for polymerase; a large protein with four functional domains which act in encapsidation, reverse transcription, pregenomic RNA destruction and at initiation of negative-DNA chain synthesis. In addition, the XORF region encodes HBxAg protein due to other fXmRNA translation and has a role in HBV replication including inhibition of protein degradation, signalling, transcriptional activation and DNA repair [26].

2.2 Hepatitis B Viral Proteins

Seegar and Mason [31] reported that HBsAg is the prototype serological marker of HBV infection that characteristically appears after 1 to 10 weeks of an acute exposure to HBV but before the onset of visible symptoms or elevation of serum alanine aminotransferase (ALT). They further reported that the principal function of the hepatitis B surface protein as a virological structure is to enclose the viral components. HBsAg plays a major role in cell membrane attachment to initiate the infection process by binding to the hepatocyte plasma membrane [32].

Fig. 4. Map South- South Nigeria showing HBV prevalence rates

Fig. 5. Map of Nigeria showing HBV prevalence rates across the country

A report by CDC [33] described Hepatitis B core antigen (HBcAg) as the major constituent of the nucleocapsid, which is essential for viral replication. In addition, they reported that Anti-HBc (core antibody) develops in all HBV infections, and appears shortly after HBsAg in acute disease, and indicates HBV infection at some undefined time in the past. Anti-HBc only occurs after HBV infection and does not develop in persons whose immunity to HBV is from vaccine. However, it persists for life and is not a serologic marker for acute infection [33].

According to Liu et al. [34], Hepatitis B envelope antigen (HbeAg) is an accessory protein of HBV, not essential for replication *in vivo* but important for natural infection. This antigen has been used clinically as an index of viral replication, infectivity, severity of disease, and response to treatment. Hepatitis B X antigen (HBxAg), is a 17 kDa multifunctional, non-structural protein, comprised of 154 amino acids, which is conserved across all the mammalian infecting *Hepadnaviridae* [35] HBx protein promotes virus gene expression and replication by trans-activating the virus promoters and enhancer/promoter complexes [35].

2.3 HBV Replication/ Life Cycle

According to Inan & Tabak [26], Hepadnaviruses, including human hepatitis B virus (HBV), replicate through reverse transcription of an RNA intermediate, the pregenomic RNA (pgRNA). They also reported that the first step in HBV replication and life cycle is the reversible non-energy requiring binding to a host structure or cell surface. Hepatitis B virus infects and multiplies within the hepatocytes through several stages ranging from binding to cell receptors to the release of the virus particles [36]. In addition, Urban et al. [36] further reported that the binding of the virus particles to the hepatocytes involves non reversible and reversible specific attachment to the receptors - cell associated heparan sulfate proteoglycans and hepatocyte-specific preS1-receptor, respectively. The entry mechanisms into the cell are via two major mechanisms: endocytosis which leads to the release of nucleocapsids from the endocytic vesicles and fusion of the viral envelope with the plasma membrane [26]. Within the hepatocytes, the nucleocapsids is transported through the microtubules to the nucleus. The interaction of the accumulated capsids with the adaptor proteins of the nuclear pore complex degrade the viral nucleocapsids and ensure the release of the relaxed circular DNA (rcDNA) into the nucleoplasm though the mechanism via which the degradation occurs is not known [37].

It is reported that the rcDNA is repaired by the cellular enzymes through the removal of the viral polymerase and short RNA-primer used for the DNA plus strand synthesis from the 5'-end of the minus strand DNA. He added that the propagation of the viral DNA is enhanced by the formation of cccDNA which occurs via the ligation of both DNA strands. Production of viral RNAs for protein synthesis and viral replication is mediated by the host cell's transcription factors (CCAAT/enhancer-binding protein(C/EBP) and hepatocyte nuclear factors (HNF) as well as viral proteins (core, the regulatory X-protein) which also plays a vital role in gene expression. The major mRNA produced in this stage is processed, stabilized and exported by the host factor La RNA binding protein [36,38]. According to Levrero et al. [39], the translation process involves formation of viral core proteins and polymerase as well as subsequent formation of a complex of core proteins, polymerase and assembly of a nucleocapsid containing RNA. The RNA is then reversed transcripted to a plus strand DNA followed by maturation and release of the virons from the nucleus into the cytoplasm [36, 39].

2.4 Epidemiology of Hepatitis B Virus Infection

The prevalence of HBV infection has been reported to vary in different countries, regions and ethnic groups with the highly endemic areas in the world being East/South-east Asia, the Pacific, sub-Saharan Africa and parts of southern Europe. In North America, western and northern Europe, HBV infection has been reported to be rare with a prevalence rate of 0.1%.A report by the National Notifiable Disease Reporting (NNDR) system revealed that the prevalence of HBsAg in Canada is estimated to be 0.5–1.0% of the population [8]. In Europe, the HBsAg seroprevalence varies widely ranging from 0.3 to 12% [41]. The prevalence of HBV infection is categorized as low (< 2%), intermediate (2%-7%) and high (≥ 8%) endemicity [40]. The endemicity of HBV in Indonesia has been reported to range from 2.5-10% [2].Another report by WHO confirmed the findings of Ott et al. [2] agreeing that low endemicity areas include North America, Western and Northern Europe, Australia, and parts of South America. The carrier rate here is

less than 2% with less than 20% of the population infected with HBV [42].

Africa is considered a high endemic area with 7–26% prevalence of HBsAg, and Ott et al. [2], revealed that the highest endemic areas are in sub-Saharan Africa. However, Andre [43] revealed that infection in areas including Kenya, Zambia, Ivory Coast, Liberia and Sierra Leone Tunisia has an intermediate endemnicity. Meanwhile, in countries such as Egypt, Algeria and Morocco, low endemnicity has been reported [44]. According to Kiire [45], Africa has the second largest number of individuals with chronic HBV infection, approaching 58 million with over 90% of the population in some countries in western Africa including Senegal and Gambia being exposed to and become infected with HBV during their lives [46]. Hepatitis B virus infection has been reported to be hyper-endemic mostly in some sub-Saharan countries such as Nigeria, Gabon, Namibia, Burkina Faso and Cameroon [44]. They further revealed that the prevalence of HBsAg is higher in rural areas compared to urban areas. In addition, they observed a greater risk for males becoming HBV chronic carriers, with a male to female ratio ranging from 1:1 to 3:1 and increasing with age. In some unrelated studies in Senegal, Zambia, Ethiopia, Tanzania, Ghana, South Africa, Nigeria and Zimbabwe, the rates of HBeAg-positive cases found in HBsAg-positive pregnant women were 1.6% [47], 2.2% [48], 4.7% [49], 8.8% [50], 12.3% [51], 13.4% [52], 13.6% [53], and 17.1% [54], respectively.

3. DISTRIBUTION OF HEPATITIS B VIRUS INFECTION IN NIGERIA INCLUDING SOUTH-SOUTH

In Nigeria, the prevalence of HBV infection has been found to be high and this places the country among the group of countries endemic for HBV infection [55]. Gabriel and Austin [56] reported that about 18 million Nigerians are currently infected with hepatitis B virus. Between 2000 and 2013, Musa et al. [15] obtained a pooled prevalence of 13.6% for adults and 11.5% for children from a study they conducted in Nigeria. Similarly, some investigators found a high HBV prevalence of 25.7% among blood donors [57], 23.4% among surgeons [58] and infants 16.3% [59].

Pregnant women are generally considered low risk for HBV infection, however, rates as high as 11% was reported in Nigeria by Mbaawuaga et al. [60]. In Lagos, Southern Nigeria, the reported prevalence rates were 14%, 30% and 56% for HBV related hepatitis, liver cirrhosis and hepatocellular carcinoma, respectively [60]. Hepatitis B virus is the commonest cause of chronic liver disease in the southern part of the country. This agrees with Lesi [61] who revealed that 58.1% of patients with chronic liver disease were HBsAg positive.

In North Central Nigeria, the Federal Capital Territory was reported by Joyce and Chima [62] to have a prevalence rate of 7.3% among some residents of a staff quarters. Kwara and Niger states have high prevalence of 12.7% and 12.8%, respectively as reported by Ogunlaja et al. [63] and Ndams et al. [64] among pregnant women. Kogi, Plateau and Nassarawa states have an even higher prevalence of 14.0%, 14.5% and 17.1% among farmers, HIV infected patients and female sex workers [65,66,67], respectively. Benue state has the highest prevalence rate in the North central with a rate of 20.0% observed among blood donors [68].

In Kaduna, Kano and Sokoto states of North western Nigeria, the prevalence rates of 3.9% and 6% were observed among pregnant women and HIV positive patients [69-70]. Saidu et al. [71] observed a higher prevalence of 6.5% among pregnant women in Sokoto state [53] while in other states of the North west like Jigawa, Kastina, Kebbi and Zamfara there were no available data.

Ndako et al. [72] and Imaranezor et al. [73] observed prevalence rates of 5.3% and 6% among students in Gombe and Taraba states of the North eastern Nigeria while Isa et al. [74] observed a prevalence of 8% among children in Maiduguri, the capital of Borno state. In a population of Mubi town Yola state, Okoye and Samba [75] observed a prevalence of 9% meanwhile, neighbouring states like Bauchi and Yobe states have higher prevalence rates of 18% and 49% observed among blood donors and students as reported by Mojolagbe et al. [76] and El- Ishaq and Liman [77], respectively.

Studies conducted on pregnant women attending antenatal clinics in Ekiti, Lagos and Osun states in South western Nigeria by Awoleke et al. [78], Rabiu et al. [79] and Opaleye et al. [80] revealed prevalence rates of 4.0%, 6.08% and 7.1%, respectively. Shittu et al. [81] observed a prevalence of 7.4% among blood donors in Ondo state while Okonko et al. [82] and Anaedobe et

al. [83] observed prevalence rates of 8.0% and 8.3% in Ogun and Oyo states.

In South eastern Nigeria, 3.4%, 6.5% 7.1% and 7.6% prevalence rates were observed among pregnant women in Enugu, Ebonyi, Abia and Anambra states by Ikeako et al. [84], Nworie et al. [85], Onwuakor et al. [86] and Ezegbudo et al. [87]. A very high prevalence of 50.7% was noted among adults with clinical features of liver disease in Imo state confirming the fact that infection with HBV lead primarily to the development of liver cancer.

In South-south Nigeria, Obi et al. [88] recorded a prevalence of 4.6% in Portharcourt among pregnant women. In 2012, Mboto and Edet observed a prevalence of 4.7% among students of the University of Uyo in Akwa Ibom State while Utoo et al. [89] observed prevalence rates of 6.6% and 7.9% among pregnant women in Obudu, Cross River and Bayelsa states. Babatope et al. [90] reported an 8.3% among healthy looking adults in Edo state while in Delta state, Osazua and Erhunwunselmade [91] recorded a prevalence of 21.1% among blood donors in Delta state. Available studies revealed progressive increase in the prevalence rates of HBV in the South-South Nigeria and also the entire country. See Figs. 4 and 5.

3.1 Risk Factors of HBV

The age of the individual has been reported to be an influential risk factor in the development of diseases. Consistently, neonates and the elderly whose immune systems have been reported to be weak, enable the successful entry and establishment of most infections including hepatitis B virus. Old age, elevated alanine aminotransferase (ALT) levels and presence of HBeAg in the blood of individuals have been reported by McMahon [92] to be risk factors associated with the development of HBV infection. Peri-natal transmission of this disease according to Ansari [93] occur most frequently especially if the mother is a chronic hepatitis B surface antigen (HBsAg) carrier as well as if the mother contracted the acute form of the infection during late pregnancy, in the first postpartum. Ahizechukwu et al. [6] further revealed that vertical transmission of approximately 10% occurs in neonates whose mothers had acute HBV in the first trimester and virtually 80-90% in the third trimester. House-hold contact has been reported by Li et al. [94] to be one of the risk factors associated with HBV transmission. Dental procedures and surgical operations have been revealed by Janahi [95] as some of the major routes in which patients contract this disease.

Transmission of HBV infections has been reported by Ahizechukwu et al. [6] andZenebe et al. [7] to be largely through unprotected sex, permucosal or percutaneous contact with contaminated blood/blood products, use of contaminated objects or instruments, intravenous routes including the use of contaminated body piercing instruments in processes including manicure/pedicure, injection needles, acupuncture, tattooing and ear piercing, haemophiliacs, haemodialysis and healthcare workers. Sexual transmission has been reported as one of the major routes of transmission of this infection with the probability of one being infected through this mode depending solely on the act of unprotected sex with an infected partner [6]. Visitors to highly endemic areas, sexually active heterosexuals especially when having more than one sex partner within a period of six months as well as prisoners with long term sentences who are exposed to homosexual acts have also been reported by Janahi [95] to be the most at risk for hepatitis B infections.

3.2 Clinical Presentation of HBV

Some studies have revealed that hepatitis B virus infection could either be acute or chronic depending on factors including the duration of its incubation and persistence in the bloodstream as well as the age and immune status of the person involved [95]. Acute infections could either be asymptomatic or symptomatic with signs and symptoms appearing faster compared to the chronic form most often observed in adults. The incubation period of acute hepatitis B virus has been reported to range from one to three months and present symptoms including nausea, tiredness, fever, loss of appetite, diarrhoea, abdominal pain, aches and pains, dark urine and as well as jaundice [93]. In rare scenarios, acute liver failure which often leads to death has been reported in some patients with acute hepatitis [30,95].

In most cases, infection with HBV could be chronic (continued existence of HBsAg in blood for more than six months); causing chronic liver infection that often develop into cirrhosis and cancer of the liver [95]. According to Liang [30], most chronically infected persons exhibit mild liver diseases with short term morbidity whereas in others, infection may progress to cirrhosis and

hepatocellular carcinoma. Chronic infections have also been reported mostly among children [26]. McMahon [92] added that cirrhosis often become visible once depreciation of the immune system occurs, enabling the development of more apparent symptoms usually indicative of cirrhosis.

According to McMahon [92], the development of chronic hepatitis B infection occurs in three basic phases including; immune tolerant phase, the immune active phase and the inactive phase as presented in Table 1.

4. DIAGNOSIS OF HEPATITIS B INFECTIONS

The diagnosis of hepatitis B infection has taken a drastic turn in recent times due to the high morbidity associated with this infection. In line with this trend, serological and molecular techniques are currently employed not only in the diagnosis of this infection but also to assess the prognosis of the disease, guide therapy and monitor treatment responses [96]. Furthermore, the diagnosis of HBV is often based on clinical, laboratory and epidemiologic findings with HBsAg in serum or plasma being the most commonly assessed marker for detecting carriers or diagnosing acute HBV infections. This is because according to Krajden et al. [98], HBsAg is often secreted in excess and serves as a marker for active infection and infectivity but added that the presence of HBeAg in serum often depicts higher HBV replication levels, infectivity and a pointer of hepatic fibrosis. HBsAg as revealed by Seeger and Mason [31] may be detected as early as 1-2 weeks or 11-12 weeks later after exposure to HBV especially when sensitive assays are employed. However, Krajden et al. [97], added that the nature and the type of test to be performed on an individual should correlate with the person's risk factors, findings from previous tests as well as vaccination history.

Conventional methods including immunoassay (IA) according to Zhang et al. [98] only give a qualitative diagnosis of HBV infection usually via detection of HBsAg. The detection and quantification of viral antigens and of specific antibodies in body fluids according to Kidd-Ljunggren et al. [99], is often based on the use of sandwich enzyme immunoassays (EIAs) where recombinant antigens or antibodies are used to capture circulating antibodies or antigens, respectively, onto the wells of microtiter plates, microbeads or specific holders adapted to close automated devices [100].

Classical techniques for viral genome detection and quantification are now progressively being replaced by molecular techniques including real-time PCR assay [101]. Therefore, quantitative diagnosis of HBV will involve molecular techniques which may quantify viral loads before and after the initiation of treatment [102]. Molecular testing can detect and measure presence of minimal residual gene mutation or proteins associated with disease condition which cannot be done by conventional methods, thereby aiding in the accurate diagnosis of HBV infections [3,102]. This is because, these techniques possess the capacity of detecting loads in the samples up to lacs of virus copies that nullifies the chances of false positive or false negative results, thereby reducing chances of incorrect diagnosis [103]. Molecular techniques

Table 1. Developmental phases of chronic hepatitis B infection

Phases	Features
Inactive	Anti-HBe, Hepatic inflammation minimal or absent, ALT levels normal, HBV DNA ≤200 IU/mL and hepatic fibrosis may improve over time and HBsAg clearance may eventually occur.
Immune tolerant	ALT levels are normal, liver biopsy is normal or shows only minimal inflammation with no or minimal fibrosis, HBV DNA ≥ 200,000 IU/mL (≥ 1 million copies), after perinatal infection from HbeAg- positive mother and frequently in HBV genotype C infection.
Immune Active (Clearance)	HBeAg-positive chronic hepatitis B with elevated ALT levels and HBV DNA ≥20,000 IU/mL, Anti-HBe–positive chronic hepatitis B with elevated ALT and HBV DNA ≥2000 IU/mL and as well as hepatic inflammation with or without fibrosis on biopsy.

[Source: 92]

including those which are based on hybrid capture, tube based signal amplification, semi-automated quantitative polymerase chain reactions, or plate based branched DNA signal amplification with various detection ranges have been employed in the diagnosis of viral infections [97].

5. MANAGEMENT OF HBV

Currently, there is no specific acceptable therapy for acute HBV infections since treatment is supportive. However, two major groups of antiviral treatments have been licensed for the treatment of chronic HBV infection in most countries and they include: pegylated interferon alpha (IFNa, or PEG-IFNa) and nucleoside or nucleotide analogues such as adefovir, entecavir, lamivudine, tenofovir and telbivudine [97]. These antiviral agents have been reported to act via inhibition of the reverse transcriptase domain of viral polymerase. However, many more drugs are under clinical evaluation [94]. Furthermore, as revealed by Amado et al. [102], these antiviral drugs are recommended in patients with an elevated serum alanine aminotransferase activity (above the upper limit of normal), evidence of chronic hepatitis with or without cirrhosis and as well as HBV DNA titer above 2,000 IU/mL. In addition, Stéphane and Jean-Michel [104] added that combinations de-novo could be employed as first line treatment especially in patients with high HBV DNA levels who many not clear the infection on monotherapy. However, resistance has been reported in various degrees among the different drugs currently in use. Valsamakis [105] reported highest rate of resistance with lamivudine compared to other nucleoside /nucleotide reversed transcriptase inhibitors.

6. PREVENTION AND CONTROL OF HEPATITIS B VIRUS

As revealed by Andersson et al. [106], interrupting early transmission is key in breaking the cycle of ongoing HBV infections. As at 2012, 181 countries according to WHO had implemented universal HBV vaccination, with global coverage estimated to be greater than 79%, thus, leading to a remarkable reduction of chronic viral hepatitis B in high burden countries in East Asia. However, in sub-Saharan Africa, HBV vaccine coverage is not commensurate with the prevalence rates often reported in the region [107,108,109].

Though, WHO recommends HBV vaccination at birth, the first dose of mono-valent HBV vaccine superseded by the pentavalent vaccine DTP-HepB-Hib in many countries is given at about 6 weeks of age often in Africa. In the developed countries, the administration of hepatitis B immunoglobulin to infants born to mothers with high HBVviral loads in combination with birth dose vaccine has been considered as a standard of care to prevent HBV MTCT [107]. However, they further added that the cost and logistics of HBV diagnosis and administration of hepatitis B immunoglobulin are prohibitive among most women in sub-Saharan countries even when the administration of antiviral therapy from the second trimester of pregnancy has been proven to reduce maternal HBV viral load and decrease the risk of MTCT [107]. WHO [110] further revealed that booster vaccination for persons who have completed the three dose vaccination schedule is not recommended. This is because the complete vaccine series which is reported to induce protective antibody levels in more than 95% of infants, children and young adults provides protection that lasts at least 20 years or probably lifelong.

In addition to active vaccination, the implementation of blood safety strategies including quality-assured screening of all donated blood/components used for transfusion may prevent transmission of HBV to a significant level [110]. The World Health Organization further added that safe injection practices, eliminating unnecessary and unsafe injections could be effective strategies to preventing the transmission of HBV. Safer sex practices, including minimizing the number of partners and using barrier protective measures (condoms) has been adequately encouraged most especially in developed countries where awareness and education campaigns are effective [110]. However, such giant strides are yet to pull weight in developing countries.

The "*Global Health Sector Strategy on Viral Hepatitis, 2016-20* adopted by the World Health Assembly with strategies to highlight the critical role of Universal Health Coverage is in alignment with those of the Sustainable Development Goals. The common goal and vision is eliminating viral hepatitis as a public health problem. It is encapsulated in the global targets of reducing new viral hepatitis infections by 90% and deaths due to viral hepatitis by 65% by 2030 [42]. With this in mind, there is an urgent need for effective awareness and education campaigns

against the transmission and development of hepatitis B virus infection in sub Saharan Africa including South-South, Nigeria.

7. CONCLUSION

The prevalence of HBV infection varies in different regions and with increasing rates in recent years as is observed in the South-South, Nigeria. The prevalence here is rated intermediate to high which calls for immediate intervention. Mother to child transmission is one of the major routes of transmission of the virus probably due to lack of awareness of the viral infection, inadequate medical facilities which could facilitate proper screening of pregnant women who attend ante-natal clinics and limited vaccination coverage in the South-South Nigeria. Unprotected sex, contact with contaminated blood/blood products, use of contaminated body piercing instruments (in processes including manicure/pedicure, acupuncture, tattooing and ear piercing), haemophiliacs and healthcare workers are all implicated in the transmission of HBV. Continued existence of HBsAg in blood for more than six months causes chronic liver infection that often develop into cirrhosis and cancer of the liver with a high morbidity rate. Implementation of blood safety strategies including quality-assured screening of all donated blood/components used for transfusion, safer sex practices may prevent transmission of HBV to a significant level. Vaccination coverage should be constantly increased, particularly in endemic populations. Researches on dimensions of HBV variability, genotype and pathogenicity still have to be explored. Indication and monitoring of therapy including well-founded prevention rules should be further optimized.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Mboto C, Edet EJ. Prevalence and Risk Factors of Hepatitis B Virus Infection among Students in University of Uyo. International Journal of Modern Biology and Medicine. 2012;2:101-111.
2. Ott JJ, Stevens GA, Groeger J, Wiersma ST. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. Vaccine. 2012;30:2212-2219.
3. Portilho MM, Martins PP, Lampe E, Villar, LM. A comparison of molecular methods for hepatitis B virus (HBV) DNA detection from oral fluid samples. Journal of Medical Microbiology. 2012;61:844–851.
4. ZhuRX, Wai-Kay S, Ching-Lung L, Man-Fung Y. Epidemiology of Hepatocellular Carcinoma in the Asia-Pacific Region. Gut Liver. 2016;10:332–339.
5. Emechebe GO, Emodi IJ, Ikefuna AN, Ilechukwu GC, Igwe WC, Ejiofor OS, Ilechukwu CA. Hepatitis B virus infection in Nigeria - A review. Niger Medical Journal. 2009;50:18-22.
6. Ahizechukwu CN, Uzoamaka AE, Charles IO, Ifeanyichukwu UE. Prevalence, Correlates and Pattern of Hepatitis B Surface Antigen in Low Resource Setting. Virology Journal. 2011;8:12.
7. Zenebe Y, Mulu W, Yimer M, Abera B. Seroprevalence and risk factors of hepatitis B virus and human immunodeficiency virus infection among pregnant women in Bahir Dar city, Northwest Ethiopia: A cross sectional study. BMC Infectious Diseases. 2014;14:118.
8. Zhang J, Zou S, Giulivi A. Epidemiology of hepatitis B in Canada. Canadian Journal of Infectious Diseases and Medical Microbiology. 2001;12:345-350.
9. Ojide CK, Kalu EI, Ogbaini-Emevon E, Nwadike VU. Co-infections of hepatitis B and C with human immunodeficiency virus among adult patients attending human immunodeficiency virus outpatients clinic in Benin City, Nigeria. Niger J Clin Pract. 2015;18:516-21.
10. Mengesha E, Airgecho T, Negera E and Mulugeta Kebede M. Prevalence of triple viral infections of human immunodeficiency virus (HIV), hepatitis B and C among tuberculosis patients and associated risk factors: The case of West Arsi Zone, Ethiopia African Journal of Microbiology Research. 2015;9(26):1675–1683.
11. Lar PM, Pam VK, Christopher PB, Gwamzhi L, Mawak, JD. Prevalence and immune status of HIV/HBV co-infected

pregnant women. African journal of clinical and experimental microbiology. 2013;14(3):120-126.
12. Ikpeme E, Etukudo O, Ekrikpo U. Seroprevalence of HBV and HIV co-infection in children and outcomes following highly active antiretroviral therapy (HAART) in Uyo, South-South Nigeria. African Health Sciences. 2013; 13(4):955–961.
13. Omalu IC, Jibrin LC, Olayemi IK, Hassan IS, Mgbemena C, Mgbemena A, Adeniran LA. Seroprevalence of malaria and hepatitis B (HBsAg) with associated risk factors among pregnant women attending antenatal clinicin General Hospital Minna, North - Central Nigeria Annual Review & Research in Biology. 2012;2(4):83-88.
14. Arokoyu SB, Weje II. Spatial distribution of health facilities in the South- South, Nigeria. ARPN Journal of Science and Technology. 2015;5(2):61-67.
15. Fakunle YM, Abdulrahman MB, Whittle AC. Hepatitis B virus infection in children and adults in Northern Nigeria, a Preliminary Survey. Trans R Soc Trop Med Hyg. 1981;75:626-9.
16. Ukaeje CJ, Ogbu O, Inyama PU, Anyanwu GI, Njoku O. Prevalence of hepatitis B surface antigen among blood donors and human immunodeficiency virus infected patients in Jos, Nigeria. Mom do inst Oswaldo Cruz. 2005;100:13-6.
17. Musa BM, Bussell S, Borodo MM, Samaila AA, Femi OL. Prevalence of hepatitis B virus infection in Nigeria, 2000-2013: A systematic review and meta-analysis. *Nigerian* Journal of Clinical Practice. 2015;18:163-172.
18. Blumberg BS. Australia antigen and the biology of hepatitis B. Nobel Foundation. International Journal of Medicine and Biomedical Research. 1977;3:45-51.
19. Gerlich WH. Medical virology of hepatitis B: How it began and where we are now. Virology Journal. 2013;10:239.
20. Hirsch RC, Lavine JE, Chang LJ, Varmus HE, Ganem D. Polymerase gene products of hepatitis B viruses are required for genomic RNA packaging as well as for reverse transcription. Nature. 1990; 344(6266):552–555.
21. Robinson WS, Clayton DA, Greenman RL. DNA of a Human Hepatitis B Virus Candidate. Journal of Virology. 1974; 14(2):384–391.
22. Charnay P, Gervais M, Louise A, Galibert F, Tiollais P. Biosynthesis of hepatitis B virus surface antigen in *Escherichia coli.* Nature. 1980;893-895.
23. Valnezuela P, Medina A, Rutter WJ, Ammerer G, Hall BD. Synthesis and assembly of hepatitis B virus surface antigen particles. Nature. 1982;282:347-350.
24. Pasek M, Goto T, Gilbert W, Zink B, Schaller H, Mackay P, Leadbetter G, Murray K. Hepatitis B virus genes and their expression in E. coll. Nature. 1979;282:575-579.
25. Will H, Cattaneo R, Koch HG, Darai G, Schaller H, Schellekens H, vanErd PM, Deinhardt F. Cloned HBV DNA causes hepatitis in chimpanzees. Nature. 1982;299:740.s
26. Inan N, Tabak F. Hepatitis B virus: Biology and life cycle. Viral Hepatitis Journal. 2015;21:1-7.
27. World Health Organization. Department of Communicable Diseases surveillance. WHO/CDS/CSR/EPH/2002.12; 2002.
28. Trevor Graham Bell, Anna Kramvis. The Study of hepatitis B virus using bioinformatics, bioinformatics - Updated features and applications, Prof. Ibrokhim Abdurakhmonov (Ed.), InTech; 2016, DOI:10.5772/63076.
Available:https://www.intechopen.com/books/bioinformatics-updated-features-and-applications/the-study-of-hepatitis-b-virus-using-bioinformatics
29. Wai CT, Chu CJ, Hussain M, Lok AS. HBV genotype B is associated with better response to interferon therapy in HBe Ag(+) chronic hepatitis than genotype C. Hepatology. 2002;36(6):1425-1430.
30. Liang TJ. Hepatitis B: The virus and disease. Hepatology. 2009;49:13-21.
31. Seeger C, Mason WS. Molecular biology of hepatitis B virus infection. Virology. 2015;672–686.
32. Perz JF, Armstrong, G L, Farrington LA, Hutin YJ, Bell BP. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. Journal of Hepatology. 2006;45(4):529-538.
33. Center for Disease Control. Recommendation for identification and public health and management of persons

with chronic hepatitis B virus infection. MMWR. 2008;57.
34. Liu B,Wen X,zHuan C, Wei Y. Unraveling the complexity of hepatitis B virus: From molecular understanding to therapeutic strategy in 50 years. The International Journal of Biochemistry & Cell Biology. 2013;45:1987– 1996.
35. Keasler VV, Hodgson AJ, Madden CR, Slagle BL. Enhancement of hepatitis B virus replication by the regulatory X protein in vitro and in vivo. Journal Virol. 2007;81:2656–2662.
36. Urban S, Schulze A,,Dandri M, Petersen J. The replication cycle of hepatitis B virus. Journal of Hepatology. 2010;52(2): 282–284.
37. Kann M, Schmitz A, Rabe B. Intracellular transport of hepatitis B virus. World Journal of Gastroenterology. 2007; 13(1):39–47.
38. Beck J, Nassal M. Hepatitis B virus replication. World Journal Gastro-enterology. 2007;13(1):48-64.
39. Levrero M, Pollicino T, Petersen J, Belloni L, Raimondo G, Dandri M. Control of cccDNA function in hepatitis B virus infection. J. Hepatol. 2009;51:581–592.
40. Yoshihiko Y, Takako U, Maria IL, Yoshitake H. Hepatitis B virus infection in Indonesia. World Journal Gastro-enterology. 2015;21:10714–10720.
41. Custer B, Sullivan SD, Hazlet TK. Global epidemiology of hepatitis B virus. Journal of Clinical Gastroenterology. 2004;38: S158–S168.
42. World Health Organization. Hepatitis B Fact sheet; 2016.
43. André F. Hepatitis B epidemiology in Asia, the middle East and Africa. Vaccine. 2000;18:S20-S22.
44. Rosa BA, Sagnelli C, Alessio L, Adinolfi EL, Sagnelli E, Coppola N. Hepatitis B virus burden in developing countries. World Journal of Gastroenterology. 2015;21:11941-11953.
45. Kiire CF. African regional study group. Hepatitis B infection in sub-Saharan Africa. Vaccine. 1990;8:S107-S112.
46. Edmunds WJ, Medley GF, Nokes DJ. The transmission dynamics and control of hepatitis B virus in The Gambia. Statistics in Medicine. 1996;15: 2215-2233.
47. Diop-Ndiaye H, Touré-Kane C, Etard JF, Lô G, Diaw P, Ngom-Gueye NF, Gueye PM, Ba-Fall K, Ndiaye I, Sow PS, Delaporte E, Mboup S. Hepatitis B. C seroprevalence and delta viruses in HIV-1 Senegalese patients at HAART initiation (retrospective study). J Med Virol. 2008;80(8):1332-6.
48. Kapembwa KC, Goldman JD, Lakhi S, Banda Y, Bowa K, Vermund SH, Mulenga J, Chama D, Chi BH HIV, Hepatitis B, and Hepatitis C in Zambia. J Glob Infect Dis. 2011;3(3):269-74.
49. Kabato AA, Weldearegay GM. Prevalence and associated risk factors of Hepatitis B and Hepatitis C virus among volunteer blood donors in Arba Minch Blood Bank SNNPR, Ethiopia Journal of Medical Laboratory and Diagnosis. 2016;7(4):20-27.
50. Matee MIN, Magesa PM, Lyamuya EF. Seroprevalence of human immuno-deficiency virus, hepatitis B and C viruses and syphilis infection among blood donors at the Muhimbili National Hospital in Dar Es Salaam, Tanzania. BMC Public Health. 2006;30(6):21.
51. Ofori-Asensor R, Brhlikova P,Pollock AM. Prescribing indicators at primary health care centers within the WHO African region: A systematic analysis (1995–2015) BMC Public Health BMC 2016;16(724):1-14.
52. Attia KA, Eholié S, Messou E, Danel C, Polneau S, Chenal H, Anglaret X. Prevalence and virological profiles of hepatitis B infection in human immunodeficiency virus patients. World Journal of Hepatology. 2012;4(7):218–223
53. Musa BM, Bussel S, BorodoMM, Samaila AA, Femi OL. Prevalence of HBV infection in Nigeria 2000-2013: A symptomatic review and Meta analysis. Nigerian Journal of clinical practice. 2015; 18(2):163-172.
54. Mzingwane ML, Mamvura T. Hepatitis B Virus Seroprevalence and Serology Patterns in a Cohort of HIV Positive Individuals from Harare, Zimbabwe. Journal of Viruses; 2014. DOI:http://dx.doi.org/10.1155/2014/691953
55. Henrietta OA, Maryam A. Seroprevalence of hepatitis B virus serological markers among pregnant Nigerian women.Annals of African Medicine. 2016;15:20-27.
56. Gabriel UPI, Austin OI. Sero-epidemiology of hepatitis B surface antigenaemia among adult Nigerians with clinical features of liver diseases

attending a primary-care clinic in a resource-constrained setting of Eastern Nigeria. North American Journal of Medical Sciences. 2013;5:293–300.

57. Bada AS, Olatunji PO, Adewuyi JO, Iseniyi JO, Onile BA. Hepatitis B surface antigenaemia in Ilorin, Kwara State, Nigeria. The Central African Journal of Medicine. 1996;42:139-141.
58. Belo AC. Prevalence of hepatitis B virus markers in surgeons in Lagos, Nigeria. East African Medical Journal. 2000;77: 283 -285
59. Sadoh AE, Sadoh WE. Serological markers of hepatitis B infection in infants presenting for their first immunization. Nigerian Journal of Paediatrics. 2013;40: 248-253.
60. Mbaawuaga EM, Enenebeaku M, Okopi J. Hepatitis B virus (HBV) infection among pregnant women in Makurdi, Nigeria. African Journal of Biomedical Research. 2008;2:155-159.
61. Lesi OA, Kehinde MO, Omilabu SA. Prevalence of the hepatitis B "e" antigen in Nigerian patients with chronic liver disease. Nigerian Quarterly Journal of Hospital Medicine. 2004;14:1-4.
62. Joyce MT, Chima KE. Prevalence of hepatitis B surface antigen among residents of julius berger staff quarters, Kubwa. International Journal of Prevention and Treatment. 2015;4:29-33.
63. Ogunlaja OA, Bojuwoye MO, Fawole AA, Adesina AK, Olawumi HO, Ogunlaja IP. Prevalence of hepatitis B virus infection amongst parturients in the University of Ilorin Teaching Hospital Nigerian Journal of Gastroenterology and Hepatology Nigerian Journal of Gastroenterology and Hepatology. 2015;7(1):7-12.
64. Ndams IS, Joshua IA, Luka SA, Sadiq HO. Epidemiology of hepatitis B infection among pregnant women in Minna, Nigeria. Science World Journal. 2008; 3(3):5-8.
65. Sule, WF, Okonko IO, Ebute AJ, Donbraye E, Fadeyi A, Udeze AO, Alli JA. Farming and non-farming individuals attending Grimard Catholic Hospital, Anyigba, Kogi State, Nigeria were comparable in Hepatitis B surface antigen seroprevalence. Current Research Journal of Biological Sciences. 2010;2: 278-282.
66. Agbaji OO, Ladep NG, Agaba P, Badung BP, Danung ML, Imade G, Idoko JA. Murphy R, Kanki P. Prevalence and characteristics of hepatitis B surface antigenemia among HIV infected patients in Jos, Nigeria. Hungarian Medical Journal. 2008;2:77-82.
67. Forbi JC, Onyemauwa N, Gyar SD, Oyeleye AO, Entonu P, Agwale SM. High prevalence of hepatitis B virus among female sex workers in Nigeria. Revista do Instituto de Medicina Tropical de São Paulo. 2008;50:219-221.
68. Alao OO, Okwori E, Egwu C. Audu F. Seroprevalence of hepatitis B surface antigen among prospective blood donors in an urban area of Benue State. The Internet Journal of Hematology. 2009; 5:12.
69. Taura DW, Oyeyi TI, Hafsat MN. Prevalence of hepatitis B surface antigen (HbsAg) among HIV positive patients attending Aminu Kano Teaching Hospital, Kano. Nigeria International Int. J. Bio. Med. Health Sci. 2008;4(1):33-39.
70. Aba HO, Aminu M. Seroprevalence of hepatitis B virus serological markers among pregnant Nigerian women. Annals of African Medicine. 2016;15:20-27.
71. Saidu AY, Salihu Y, Umar AA, Muhammad BS, Abdullahi, I. Seroprevalence of Hepatitis B Surface Antigen among Pregnant Women Attending Ante-Natal Clinics in Sokoto Metropolis. 2015; 4(4):46-50.
72. Ndako JA, Yahaya A, Amira JO, Olaolu DT, Akande TA. Hepatitis B virus (HBV) infection among alcoholic consumers at a local community, North-East Nigeria. Journal of Natural Sciences Research. 2013;3(13):23-30.
73. Imarenezor EPK, Brown STC, Yakubu OE, Soken DC. Survey of hepatitis B and C among students of Federal University Wukari, Taraba State, Nigeria International Research Journal of Medicine and Medical Science. 2016;4(3):31-37.
74. Isa MA, Bello HS, Gulani A, Aliyu B, Aisha MA. Iliya H. Prevalence of hepatitis B virus infection among children attending Mohammed Shuwa memorial hospital Maiduguri, Borno state, Nigeria. International Journal of Advanced Research in Biological Sciences. 2015; 128–132.
75. okoye IC. Samba SA. Sero-Epidemic Survey of hepatitis B in a population of

Northern Nigeria. Animal Research International. 2006;3:485-488.
76. Majolagbe ON, Oladipo EK, Daniel LE. Prevalence and awareness of hepatitis b infection among blood donors in Abubakar Tafawa Balewa University Teaching Hospital (ATBUTH), Bauchi, Nigeria. 2014;11(2):955-960.
77. El Ishaq A, Liman FM. Prevalence of hepatitis B surface antigen among blood donors and patients attending general Hospital Potiskum. Extensive Journal of Applied Science. 2015;3:199-203.
78. Awoleke JO. Hepatitis B surface antigenaemia among pregnant women in atertiary health institution in Ekiti State, Nigeria. Tropical Journal of Obstetrics and Gynaecology. 2012;29(2):34-39.
79. Rabiu KA, Akinola OI, Adewunmi AO, Omololu OM, Ojo TO. Risk factors for hepatitis B virus infection among pregnant women in Lagos, Nigeria. Acta Obstetriciaet Gynecologica Scandinavica. 2010;8(8):1024-1028.
80. Opaleye OO, Salami S, Funmilayo F, Olowe OA, Ojurongbe O, Bolaji OS, Odewale G, Ojo, JA. Seroprevalence of hepatitis B surface antigen and antibody among pregnant women attending a tertiary health institution in Southwestern Nigeria. Journal of Dental and Medical Sciences. 2014;13:67-7.
81. Shittu MO, Saheed AS, Ajao KO, Adeniji TW, Christianah O. Seroprevalence of hepatitis B surface antigenemia and hepatitis C virus among intending blood donors at mother and child hospital, Akure, Nigeria. International Journal of Medicine and Medical Sciences. 2014;47: 1554-1557
82. Okonko OI, Soleye FA, Alli FA, Ojezele MO, Udeze AO, Nwanze JC, Adewale OG. Seroprevalence of Hbsag Antigenaemia among Patients in Abeokuta, South Western Nigeria. Global Journal of Medical Research. 2010;10: 40-49.
83. Anaedobe GC, Fowotade A, Omoruyi CE, Bakare R. Prevalence, sociodemographic features and risk factors of Hepatitis B virus infection among pregnant women in Southwestern Nigeria. The Pan African Medical Journal. 2015;20:406.
84. Ikeako LC, EzegwuiHU, Ajah LO, Dim CC, Okeke TC. Seroprevalence of human immunodeficiency virus, hepatitis B, hepatitis C, syphilis, and co-infections among antenatal women in a tertiary institution in South East, Nigeria. Annals of Medical Health. 2014;4:954-958.
85. Nworie O, Orji O, Jerry, Ekuma JO, Ukpabi N, Onu EN. Studies on the seroprevalence of hepatitis B virus infection among school children in Ohaukwu, Ebonyi State, Nigeria.World Applied Sciences Journal. 2015;33:1767-1772.
86. Onwuakor CE, Eze VC, Nwankwo IU, Iwu, JO. Seroprevalence of hepatitis B surface antigen (HBsAg) amongst pregnant women attending antenatal clinic at the federal medical centre Umuahia, Abia State, Nigeria. American Journal of Public Health Research. 2014;2:255-259.
87. Ezegbudo CN, Agbonlahor DE, Nwobu GO, Igwe CU, Agba MI, Okpala HO, Ikaraoha CI. The seroprevalence of hepatitis B surface antigen and human immunodeficiency virus among pregnant women in Anambra State, Nigeria.Shiraz E-Medical Journal. 2004;5:4-8.
88. Obi RK, Umeh SC, Okurede OH, Iroagba II. Prevalence of hepatitis B virus infection among pregnant women in an antenatal clinic in Port Harcourt, Nigeria. African Journal of Clinical and Experimental Microbiology. 2006;7:78-82.
89. Utoo B. Hepatitis B surface antigenemia (HBsAg) among pregnant women in southern Nigeria. African Health Sciences. 2013;13:1139–1143.
90. Babatope IO, Inyang NJ, Imhanrenezor K, Aghahowa A. Seroprevalence of Hepatitis (B and C) viruses among apparently healthy Adults in Ekpoma, Edo State, Nigeria. Special Viral Pathogens Journal. 2015;1:15-20.
91. Osazuwa F, Erhumwunselmade P. Remunerated or Non-remunerated Blood Donation: How do we ensure the safety of blood in Nigeria?.Continental Journal of Tropical Medicine. 2013;7:1-2.
92. McMahon BJ. The natural history of chronic hepatitis B virus infection. Hepatology. 2009;49:45-55.
93. Ansari AS, Khanani MR, Abidi SH, Shah F, Shahid A, Ali SH. Patterns of HIV infection among native and refugee Afghans. AIDS. 2011;25:1427–1430.
94. Li X, Zheng Y, Liau A, Biao C, Dongqing Y, Feng H, Xiaorong S, Fuyang G, Liu X, Shun L, Jing L. Hepatitis B virus infections and risk factors among the general

population in Anhui Province, China: an epidemiological study. BMC Public Health. 2012;12:272.
95. Janahi EM. Prevalence and Risk Factors of Hepatitis B Virus Infection in Bahrain, 2000 through 2010. PLoS ONE. 2014;9(2):e87599.
96. WHO. Department of communicable diseases surveillance and response. Hepatitis B. Available:http://www.who.int/csr/disease/hepatitis/HepatitisB_whocdscsrlyo2002_2.pdf
97. Krajden M, McNabb G, Petric M. The laboratory diagnosis of hepatitis B virus. The Canadian Journal of Infectious Diseases & Medical Microbiology. 2005;16:65–72.
98. Zhang HW, Yin JH, Li YT, Li CZ, Ren H, Gu CY, Cao, GW. Risk factors for acute hepatitis B and its progression to chronic hepatitis in Shanghai, China. Gut. 2008;57(12):1713–1720.
99. Kidd-Ljunggren K, Holmberg A, Bläckberg J, Lindqvist B. High levels of hepatitis B virus DNA in body fluids from chronic carriers. Journal Hosp. Infect. 2006; 64(4):352-7.
100. Culley S, Towers GJ, Selwood DL, Henriques R, Grove J. Infection counter: automated quantification of in vitro virus replication by fluorescence microscopy. Viruses. 2016;8(7):201. DOI: 10.3390/v8070201.
101. Monjezi R, Tan SW, Tey BT, Sieo CC, Tan WS. Detection of hepatitis B virus core antigen by phage display mediated TaqMan real-time immuno-PCR. Journal of Virological Methods. 2013;187(1):121-126.
102. Amado LA, Villar LM, De Paula, VS, De Almeida AJ, Gaspar, AMC. Detection of hepatitis A, B, and C virus-specific antibodies using oral fluid for epidemiological studies. Memorias do Instituto Oswaldo Cruz. 2006;101:149-155.
103. Thomas HC, Karayiannis P, Fowler MJ, Monjardino J. Clinical uses of hbv-dna assays. Elsevier Journal of Virological Methods. 1985;10:29l-294.
104. Chevaliez P, Jean-Michel P. Virological techniques for the diagnosisand monitoring of hepatitis B and C. Annals of Hepatology. 2009;8(1):7-12.
105. Valsamakis A. Molecular testing in the diagnosis and management of chronic hepatitis B. Clinical Microbiology Reviews. 2007;20:426-439.
106. Andersson MI, Rajbhandari R, Kew MC, Vento S, Preiser W, Hoepelman AI. Lesi, O. Mother-to- child transmission of hepatitis B virus in sub-Saharan Africa: time to act. The Lancet Global Health. 2015;3:e358-e359.
107. Stéphane C, Jean-Michel P. Techniques for the diagnosis and monitoring of hepatitis B and C. Annals of Hepatology. 2009;8:7-12.
108. Nelson NP, Easterbrook PJ, McMahon BJ. Epidemiology of hepatitis B virus infection and impact of vaccination on disease. Clinics in Liver Disease. 2016; 20(4):607-628.
109. Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horynia D, Degenhardt L. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: Results of systematic reviews. The Lancet. 2011;378:571-583.
110. WHO. Proposing a Global Health Sector Strategy for Viral Hepatitis 2016-2021 Available:http://apps.who.int/iris/bitstream/10665/246177/1/WHO-HIV-2016.06-eng.pdf?ua=1. Accessed 07-08-2017.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history/23075