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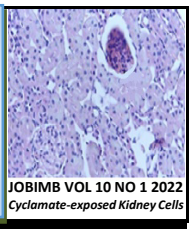


# Study of Hepatitis B core Antibody (HBcAb) among Pregnant women and their Newborn at Delivery at Umaru Shehu Ultra-Modern Hospital Maiduguri, Borno State Nigeria

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**ABSTRACT**

Hepatitis B virus infection (HBV) is a worldwide Health problem that has destroyed the lives of people that were predisposed to viral attack, with a significant public implication. The main objectives of this study are to determine the overall prevalence of Hepatitis B Core antibodies in mothers, the overall prevalence of Hepatitis B Core antibodies in their newborns, the prevalence according to the age of mothers, the prevalence according to the gender of the newborns and maternal transfer of HBcAb from the mother to their newborns. A total of 101 plasma were collected from pregnant women and their newborns in the delivery room from the maternity ward at the Umaru Shehu ultra-modern Hospital Maiduguri, Borno state, Nigeria. Pro-med gold Rapid Diagnostic test kits from the United State of America (USA) was used for the detection of Hepatitis B core antibody. Of the 101, mothers and 101 newborns that were assayed for, mothers within the age range of 17 – 40 years with mean ± SD age of 25.9 (±5.2) years, having an overall prevalence of 28.7% for HBcAb of the mothers observed from the result analysis of plasma from pregnant women attending an antenatal program at the Umaru Shehu ultra-modern Hospital Maiduguri, Borno state, Nigeria. Hepatitis B Virus remains a threat to be causing public Health Havoc Globally, this research has revealed that a significant proportion of 72 (71.3%) of the study population is at risk of being infected with HBV since they have no detectable marker of infection or immunity against the virus. Therefore, there is a need for regular and prompt screening of pregnant women for HBV infection and vaccination of those at risk.

## INTRODUCTION

Hepatitis B virus infection (HBV) is a worldwide Health problem that has destroyed the lives of people that were predisposed to viral attack, with a significant public implication. The World Health Organization (WHO) with various agents that reside in some part of Africa have estimated that about 1 million people are carriers of the deadly Virus, the morbidity rates show that the people are chronically infected with HBV and Nigeria is one among African Countries that remains endemic with viral strains [1]. According to reports, hepatitis B virus (HBV) infection is the most common cause of severe liver infection worldwide [2]. The disease has been recognized as an international health concern [3]. Acute and chronic forms of the infection exist, but most adults who contract an acute form of the infection will eventually get better [2, 4, 5]. Despite effective treatment, the chronic form is always fatal [1,5]. More than two billion people have been infected with HBV, and another 350

million have chronic infection, according to estimates [6–9]. The high endemicity of HBV infection in Nigeria indicates that approximately 75% of the population has been exposed to the virus at some point in their lives [10]. HBV antibodies were found in the cord blood of some recently delivered mothers, suggesting that the virus was transmitted from mother to child during pregnancy. Replicating primarily in hepatocytes, hepatitis B virus primarily disrupts liver function. NTCP is a receptor that is the cellular receptor [11,13].

The pre domain of the viral surface antigen mediates the binding of the virus to the host cell, which then undergoes endocytosis to take in the virus [10,14,15]. Although hepatocytes are the primary cell type that expresses HBV-pre-specific receptors, viral DNA and proteins have been found in extrahepatic sites [16,17], suggesting that HBV cellular receptors may exist on extrahepatic cells. The host immune response during HBV infection damages hepatocellular tissue and clears the virus. Most of the liver injuries associated with HBV infection are caused by the adaptive immune response, in particular virus-specific cytotoxic T lymphocytes (CTLs) [18,19], despite the fact that the innate immune response plays no significant role in these processes. When activated, CTLs eliminate HBV infection by killing infected cells and secreting antiviral cytokines, which are then used to remove HBV from healthy hepatocytes [20,21].

Most adults who contract acute hepatitis B recover without treatment [22]. Early antiviral treatment with lamivudine [18,22-26]. Used in the extremely rare cases of fulminant hepatitis or in those with compromised immune systems [9,18]. However, chronic infection treatment might be required to prevent cirrhosis and liver cancer. Those who have had HBV for an extended period of time and have high levels of HBV DNA in their blood as well as elevated levels of serum alanine aminotransferase, a marker of liver damage, are candidates for therapy [18,23,27]. Hepatitis B is typically spread through the following: It can be transmitted through sexual contact if the infected person's blood, saliva, sperm, or vaginal secretions are absorbed into the healthy partner's body during an unprotected sex session. Needles and syringes that have come into contact with infected blood are a major vector for the spread of the virus [18,28]. Needlestick injuries are a common cause of transmission among healthcare workers and others who come into contact with human blood. Hepatitis B can be passed from mother to child if the mother has it during pregnancy and gives it to her baby. However, vaccination is available to guard against the spread of infection in newborns [18,29]. The primary goal of this research is to find out how (i) commonplace the presence of Hepatitis B Core antibody is among pregnant women, (ii) the rate at which their newborns are exposed to the hepatitis B core antibody, (iii) the incidence rate as a function of maternal age (iv), birthrate distribution by gender and (v) transmission of HBcAb from mothers to their infants. Over the years, the mortality rate resulting from HBV has increased due to poor management [18,30]. Because of the replication of the HBV in the liver cell (Hepatocytes) [18,31-33].

## METHODOLOGY

### Study area and authorization approval

Samples were collected from pregnant women and their newborns (day olds) within different age groups between October 2020 to March 2021 at Umaru Shehu health care center Maiduguri, Borno state, Nigeria.

Ethical clearance (Authorization) for sample collection was approved by the Medical Director Umaru Shehu health care center Maiduguri, Borno State Nigeria.

### Case study

Cross-sectional study method was used as 101 samples were collected from both pregnant women and their newborns from the hospital laboratory, Obstetrics and Gynaecology unit of the Umaru Shehu health care center, Maiduguri, Borno state, Nigeria. The health is located in Bulukutu area close to Nigeria Air force Base Maiduguri Nigeria. With secondary health facilities, the only overpowered case is referred University of Maiduguri Teaching Hospital for expert management. The population under study were pregnant women attending antenatal treatment and newborns at delivery. The study was from October 2020 to April 2021. Pregnant women attending antenatal programs donate samples at the point of delivery.

### Sample size

Data collection was designed to obtain and record information such as Location, patient serial number, age, and date. The sample size was determined using the following simple formula according;.

$$n = Z^2 xP (1- P ) / e^2$$

Where n = Sample size
Z = statistics for a level of confidence
P = expected prevalence rate
e = Margin of error

The prevalence rate was gotten from surveillance of Hepatitis B Biomarkers Journal of Advances in Medicine and Medical Research published in 2019 written by [18].

P = 7.1% = 0.071 [18].
Z = 1.96
e = 0.05
$n = (1.96)^2 X 0.071 X ( 1 - 0.071) / ( 0.05)^2$
$= 3.8416 X 0.071 X 0.929 / 0.0025$
n = 101.

Pro-med gold Rapid Diagnostic test kits from United States of America (USA) Pro-med gold for HBV Infection Marker in whole blood (surface antigen, surface antibody, core antibody, envelope antibody) ( colloidal Gold ) and expiring date 6/2022. Intended use for the qualitative detection of the five hepatitis B Markers HBsAg, HBsAb, HBeAg, HBeAb, and HBcAb in human whole blood, for clinical diagnosis. The product uses the colloidal gold and membrane chromatography technology, and measures HbsAb, HBeAg in whole with dual- antibody sandwich method, and measures HBsAb and HBcAb with neutralization competitive inhibition method.

### Sampling

A total number of 101 pregnant women and their newborn attending the Umaru Shehu health care antenatal clinic between October to December 2020, were recruited into the study after obtaining their informed consent. 5 ml of venous blood was collected from individual subjects by venepuncture which was later poured into EDTA blood collection tubes, the blood samples were transported to the University of Maiduguri teaching hospital, after which the separated plasma was poured into a microvalves container and kept at -20 $^0$C until used.

**Serology**
This test was conducted in accordance with the manufacturer's instructions. The pouch was opened, and the testing device was taken out. For one minute, with the arrow pointing downward, a fresh serum specimen was dipped onto the test strip, with care taken to keep the marker line above the serum. Each strip was then laid out flat on the nonabsorbent testing bench next to its corresponding labeled sample tube. After a minute, the line bands on the test strips could be read to reveal the test results. The results were interpreted per the manual provided by the manufacturer.

Prior to conducting the test, we read the kit's instructions. The test board was reset, and the samples were stored in a temperature-controlled environment between 20 and 30 degrees Celsius. Immunochromatographic strips (Promed-gold Rapid Diagnostic, kits) were used to detect HBcAb instead of monoclonal antibody sandwiches for detecting HBsAg. Subjects' whole blood was collected through a small straw and dropped into 5 sample wells of the test board (25 Ul per well, or one drop), with the right side of the board remaining horizontal from the original packaging, left to right, corresponding to HBsAb. In less than 15 minutes, we were able to observe and record the outcome of the experiment. In about 15 to 20 minutes, the test line started showing faintly positive samples. If a decision took longer than 30 minutes to reach, it was nullified. In extreme conditions (over 30 degrees Celsius or high humidity), the tested paper from the original packaging was used within 1 hour.

**HBcAb (Competition method )**
Negative: two purple bar (control and test line) appears in the test line (T) zone.
Positive: Detecting (c) zone; only one purple bar in the control (C) zone.
Invalid: Detecting (C) and (T) zone; It was Observed that no purple bar in the (C) and (T) zone.

## RESULTS

There were 101, mothers and 101 newborns. The mothers were in the age range of 17 – 40 years with mean ± SD age of 25.9 (±5.2) years. The overall prevalence of 28.7% for HBcAb in the mothers was observed from the result analysis of 101 samples from pregnant women attending an antenatal program at the Umaru Shehu health care center Maiduguri, Borno state, Nigeria (**Table 1**). The distribution of HBcAb is presented in **Table 2**. 4(30.8)% of those within the age 11-20 years were positive while 19 (27.5)% who fell within the age of 21-30 were positive and 6 (31.6)% of those within the age of 31-40 were positive.

**Table 1**. Prevalence of Maternal HBcAb according to age.

| Age group (Years) | No tested | No. Positive | %Positive |
|---|---|---|---|
| 0-10 | 0 | 0 | 0 |
| 11-20 | 13 | 4 | 30.8 |
| 21-30 | 69 | 19 | 27.5 |
| 31-40 | 19 | 6 | 31.6 |
| Total | 101 | 29 | 28.7 |

Overall Prevalence= 29/101 × 100 =28.7%;
$X^2$ = 0.2491, df=2,p=0.8829 (NS)

**Table 2**. Seroprevalence of Hepatitis B core antibody in associated risk factors among pregnant women at delivery.

| Risk factors | Number tested | Number positive | $X^2$, df=1, p-value |
|---|---|---|---|
| | Yes 35 | 6(17.14)% | 0.707 > 0.05 |
| Blood transfusion | No 61 | 31(50.810)% | |
| History of surgery/dental procedure | Yes 11 | 2(18.18)% | 0.371 > 0.05 |
| | No 82 | 16(19.51)% | |
| | Yes 21 | 9(42.8)% | 0.577 > 0.05 |
| History circumcision | No 74 | 27(36.48)% | |
| | Yes 15 | 3(20.00)% | 0.306 > 0.05 |
| History of tribal mark | No 83 | | |
| | Yes 25 | 32(38.55)% | 0.433 > 0.05 |
| History of tattoo | No 76 | 3(12.00)% | |
| History of jaundice/ Hepatitis | Yes 27 | 16(21.05)% | 0.343 > 0.05 |
| | No 75 | 2 (7.40)% | |
| | Yes 7 | 17(22.66)% | 0.373 > 0.05 |
| History of STIs | No 86 | 1(14.28)% | |
| | Yes 23 | 7(8.13)% | 0.321 > 0.05 |
| Use of shapes | No 69 | 23(33.33)% | |

The 101 blood samples from the children were stratified into male and female and were presented in **Table 3**. 12 (32.4)% of males were positive and 12 (21.9)% of females were positive, making the overall prevalence of 25.7%. The overall prevalence of 25.7% for HBcAb in the children was observed from the result analysis of 101 samples collected in the delivery room from the maternity ward at the Umaru Shehu Ultra-modern Hospital Maiduguri, Borno state, Nigeria. The distribution of HBcAb is presented in **Table 4**. The results show that 2 (33.3)% of children at birth from the month of October 2020, were positive, 3 (18.8)% for the month of November 2020 were positive, 1 (4.2)% for the month of December 2020, were positive, 4 (44.4)% for the month of January 2021, were positive, 7 (29.3)% for the month of February 2021 were positive and 9 (40.9)% for the month of March 2021 were positive.

**Table 3**. Prevalence of HBcAb according to Gender of the newborns.

| Gender of babies | No. (%) tested | No. (%) positive |
|---|---|---|
| Male | 37 (36.6) | 12 (32.4) |
| Female | 64 (63.4) | 14 (21.9) |
| Total | 101 | 26 (25.7) |

Overall prevalence (positive) for children is 25.7%. Fisher exact test, p=0.1751 (NS)
Prevalence=26/101 × 100 =25.7% For male, prevalence =32.4% and for female, prevalence 21.9%

**Table 4**. The distribution of HBcAb.

| Month & year | No tested | No positive % |
|---|---|---|
| October 2020 | 10 | 2 (20.0) |
| November 2020 | 12 | 4 (33.3) |
| December 2020 | 24 | 8(33.3) |
| January 2021 | 9 | 1(11.1) |
| February 2021 | 24 | 5 (20.8) |
| March 2021 | 22 | 9(40.9) |
| Total | 101 | 29 (31.7) |

Prevalence =29/101 × 100 =28.7%;$X^2$ = 4.435, df=5,p=0.4886 (NS)

For the prevalence of HBc antibody (HBcAb) according to birth month/year of children, 2 (33.3%) children at birth from the month of October 2020 were positive, 3 (18.8)% for the month of November 2020 were positive, 1 (4.2)% for the month of December 2020, was positive, 4 (44.4)% for the month of January 2021, were positive, 7 (29.2)% for the month of February 2021 were positive and 9 (40.9)% for the month of March 2021 were positive (**Table 5**).

**Table 5**. Prevalence of HBc antibody (HBcAb) according to birth month/year of children.

| Month & year of Birth | No. tested | No.(%)positive |
|---|---|---|
| October 2020 | 10 | 3 (30.0) |
| November 2020 | 12 | 2 (16.7) |
| December 2020 | 24 | 1 (4.2) |
| January 2021 | 9 | 4 (44.4) |
| February 2021 | 24 | 7 (29.2) |
| March 2021 | 22 | 9 (40.9) |
| Total | 101 | 26 (25.7) |

Prevalence =26/101 × 100 =25.7%;$X^2$ = 10.90, df=5,p=0.0534 (NS)

**Maternal transfer of HBcAb from the mother to child**

Of the 29 mothers who had maternal antibodies, 26 (89.7%), transferred to their newborns, while 3 (10.3%) did not, this shows that the 3 newborns can be susceptible to HBV infection. 8 (27.6)% of Children who were positive and their mothers are positive, 18(25.0)% children who were positive and their mothers are negative, 12 (41.4)% children who were negative and their mothers are positive and 54 (75.0)% children who are negative and their mothers are negative. The overall prevalence of children who acquired HBcAb from their mothers respectively is 25.7%. 8(27.6)% of Children who were positive and their mothers are positive, 18(25.0)% of children who were positive and their mothers are negative, 12(41.4)% of children who were negative and their mothers are positive and 54(75.0)% children who are negative and their mothers are negative. The overall prevalence of children who acquired HBcAb from their mothers respectively is 25.7%.

**Table 6**. Maternal transfer of HBc antibodies to their newborns.

| (HBcAb) Children | Mother HBcAb | | Total |
|---|---|---|---|
| | Positive | Negative | |
| Positive | 8 | 18 | 26 |
| Negative | 21 | 54 | 75 |
| Total | 29 | 72 | 101 |
| Fisher exact | | P=0.4860 (NS) | |

## DISCUSSION

Testing of infected pregnant women and their newborns stands as an important instrument in disease detection, prompt diagnosis and intervention particularly at an early stage of disease [18,34,35]. From this study, the prevalence of HBcAb is 28.7% observed among pregnant women attending delivery at the Umaru Shehu health center Maiduguri, Borno state. The prevalence of HBcAb among pregnant women in this study is 28.7%. This is higher than 7.1% obtained in a previous study in Maiduguri [18,36,37], but less than 44.1% in southwestern Nigeria [38,39] and 45.6% reported in Maiduguri [18,40]. 72 (71.3%) of pregnant women obtained from this study were all negative for HBcAb, and this might be attributed to the immunization program administered to them in the antenatal unit of the Hospital or it may be due to a previous vaccination program administered to them even before the pregnancy [38,41,42]. Those who haven't been immunized against hepatitis B yet are at risk of contracting the disease. Public health concerns are elevated because 71.3% of vulnerable pregnant women (5 in the first trimester, 3 each in the second and third trimester) [18,43].

Since the micronutrients that allow the quick healing of HBV are developed by women during pregnancy, about 25.7% of neonates are affected by vertical transmission in the first and second trimesters, and 60-90% of children may be infected by vertical transmission in the third trimester [44,45]. WHO estimates that over 686 000 people worldwide succumb to hepatitis B-related diseases like cirrhosis and liver cancer every year [18,30,46].The risk of vertical transmission of the virus and the subsequent fatal consequences for the foetus is high, especially in the third trimester, if any of these women contract the virus and allow the infection to progress [1,47]. Symptoms of acute hepatitis B reveal its presence, and it remains in the body permanently [18,48]. Chronic Hepatitis B infection causes hepatocyte destruction [18,31], and the presence of anti-HBc indicates a history or current infection with HBV. Thus, these women without immunity were likely to have been exposed to chronic hepatitis B infection but had a lower risk of vertically transmitting the virus to their newborns [18,49,25].

In order to determine whether or not a patient was at risk for contracting hepatitis B virus, we administered a structured questionnaire that asked about the patient's history of blood transfusions, number of sexual partners, history of contact with people infected with the virus, history of tattoos or tribal markings, history of jaundice, history of STIs, history of using sharps, history of previous contact with an HBV infected person, history of vaccination against HBV, and current or previous employment The ethical committee at the Umaru Shehu health care center gave their blessing to this study. Analysis of Data STATA 11 package [18] was used to run the statistical calculations. Cross-tabulations were used to analyze the data and look for patterns in the data that might indicate a connection between the variables of interest.

The correlation between the groups was analyzed using the chi-square test. P 0.05 was chosen as the cutoff for statistical significance (providing 95 percent confidence interval). Only 28% of the female population was immune to HBc, suggesting that they likely had a chronic infection with a low risk of vertical transmission [18]. 25.7% of the children who acquired anti-HBc from their respective mothers who did not develop immunity to the virus are likely to have been infected and transferred the infection to their newborn prior to their initial exposure to HBV during the stage of early pregnancy, but later develop immunity against HBV and recovered from the HBV infection that has already been transferred to their children before recovery [18,50,51]. Treatment of chronic Hepatitis is attributed to two different strategies finite and infinite [52-54]. the study population is at risk of being infected with oral anti-HBV [55]. since they have no detectable marker of infection Nucleoside/ nucleotide (NUCs) [56,51]. Immunity against the virus [57-59]. Therefore, there is a need for regular and prompt screening of pregnant women for HBV infection and vaccination of those at risk [18,39].

About 8(27.5) % of the children that were positive for anti-HBc whose mothers were also positive for anti-HBc indicates that women who had anti-HBc were able to transfer the infection to their children through vertical transmissions [14,18,60-62]. 18 (25.0)% of mothers who were negative for anti-HBc and children who were positive for anti-HBc indicates that mothers are likely to have transferred the infection to their children and later develop immunity against HBV and later recovered [18,47]. And 12 (41.4)% of the children who were negative for anti-HBc and mothers who were positive for anti-HBc indicated that despite not having immunity against the virus and having chronic infection to HBV but had a reduced risk of vertical transmission [18,38,63]. 54(75.0%) of mothers who were negative of anti-HBc and children were negative indicates that women may be positive of anti-HBc. [64]. Anti-HBc positivity underestimates past exposure to HBV since subjects who clear the infection may gradually lose anti-HBc hence HBV genomic difference partake in the liver damage as its receptor bind to Hepatocytes [48,50,51,65-67]. Women who lose anti-HBc become negative

of anti-HBc and thus, cannot transfer the infection to their children [18,68].

## CONCLUSION

Pregnant women at the Umaru Shehu health care center in Maiduguri, Borno State, Nigeria, were analyzed for their HBcAb levels. It has also shown that 72 people (71.3% of the study population) are vulnerable to oral anti-HBV infection because they lack any evidence of immunity to the virus or any marker of infection (Nucleoside/Nucleotide (NUC)s). Pregnant women should be tested for HBV infection and vaccinated against the virus on a regular basis.

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## CONFLICT INTEREST

The authors have declared no conflict of interest.

## REFERENCE

1 World Health Organisation (WHO). Who encourages countries to act now to reduce deaths from viral hepatitis Online; 2006.World Health Organization (WHO).2016.
2 Hyun MH, Lee YS, Kim JH, Je JH, Yoo YJ, Yeon JE, Byun KS. Systematic review with meta-analysis: the efficacy and safety of tenofovir to prevent mother-to-child transmission of hepatitis B virus. Aliment Pharmacol Ther. 2017;45(12):1493-1505.
3 Chan SL, Wong VW, Qin S, Chan HL. Infection and Cancer: The Case of Hepatitis B. J Clin Oncol. 2016;34(1):83-90.
4 Schillie S, Murphy TV, Sawyer M, Ly K, Hughes E, Jiles R, et al.. CDC guidance for evaluating health-care personnel for hepatitis B virus protection and for administering postexposure management. MMWR. Recomm Rep. 2013;62(RR-10): 1-19.
5 Shepard CW, Simard EP, Finelli L, Fiore AE, Bell BP. Hepatitis B virus infection: epidemiology and vaccination. Epidemiol Rev. 2006;28:112-25.
6 Peters MG. Hepatitis B Virus Infection: What Is Current and New. Topic Antiviral Med. 2019;26(4):112-116.
7 Zuckerman AJ. Hepatitis Viruses. In Baron S, et al. (eds.). Baron's Medical Microbiology (4th ed.). University of Texas Medical Branch. ISBN 978-0-9631172-1-2. 1996
8 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;30:22129
9 Roche B, Samuel D. The difficulties of managing severe hepatitis B virus reactivation. Liver Int. 2011;31(Suppl 1):104-110.
10 Watashi K, Wakita T. Hepatitis B Virus and Hepatitis D Virus Entry, Species Specificity, and Tissue Tropism. Cold Spring Harb Perspect Med. 2015;5(8):a021378..
11 Bruss V. Hepatitis B virus morphogenesis. World J Gastroenterol. 2007;13(1): 65-73.
12 Ben Guarino. New strains of hepatitis B virus discovered in ancient human remains. The Washington Post. Retrieved 9 January 2018.
13 Willey JM, Sherwood LM, Woolverton CJ, Editors. Human diseases caused by viruses and prions, direct contact diseases: Viral hepatitis. In: Prescott's Microbiology. International Edition. Eight Edition. New York: The McGraw Hill companies.2011;919-921.
14 Hundie GB, Stalin Raj V, Gebre Michael D, Pas SD, Koopmans MP, Osterhaus AD, et al.. A novel hepatitis B virus subgenotype D10 circulating in Ethiopia. J Viral Hep. 2017;24(2):163-173.
15 Sangkomkamhang US, Lumbiganon P, Laopaiboon M. Hepatitis B vaccination during pregnancy for preventing infant infection. Cochrane Database Syst Rev. 2014;(11): CD007879.
16 Iannacone M, Sitia G, Ruggeri ZM, Guidotti LG. HBV pathogenesis in animal models: Recent advances on the role of platelets. J Hepatology. 2007;46(4):719-726
17 Ivanov AV, Valuev-Elliston VT, Tyurina DA, Ivanova ON, Kochetkov SN, Bartosch B, Isaguliants MG. Oxidative stress, a trigger of hepatitis C and B virus-induced liver carcinogenesis. Oncotarget. 2017;8(3):3895-3932.
18 Oyinloye, D.N. Bukbuk and F.A. Sanda. Surveillance of Hepatitis B Biomakers in Borno state, Nigeria. J Adv Med Med Res. 2018;28(10):1-8.
19 Villa E, Fattovich G, Mauro A, Pasino M. Natural history of chronic HBV infection: special emphasis on the prognostic implications of the inactive carrier state versus chronic hepatitis. Digest Liver Dis. 2011;43(Suppl 1):S8-14.
20 Liaw YF, Brunetto MR, Hadziyannis S. The natural history of chronic HBV infection and geographical differences. Antivir Ther. 2010;15:25-33.
21 T, Masuda G, Ajisawa A, Hiruma K, Tsuda F, Nishizawa T, Takahashi M, Okamoto H. Characterization of seven genotypes (A to E, G and H) of hepatitis B virus recovered from Japanese patients infected with human immunodeficiency virus type 1. J Medic Virol. 2005;76(1):24-32.
22 Schroth RJ, Hitchon CA, Uhanova J, Noreddin A, Taback SP, Moffatt ME, Zacharias JM. Hepatitis B vaccination for patients with chronic renal failure. Cochrane Database Syst Rev. 2004;2004(3):CD003775.
23 Bell SJ, Nguyen T. The management of hepatitis B. Aust Prescr. 2009;32(4):99-104.
24 Coffin CS, Mulrooney-Cousins PM, van Marle G, Roberts JP, Michalak TI, Terrault NA. Hepatitis B virus (HBV) quasispecies in hepatic and extrahepatic viral reservoirs in liver transplant recipients on prophylactic therapy. Liver Transpl. 2011;17(8):955-62.
25 Mastroianni CM, Lichtner M, Citton R, Del Borgo C, Rago A, Martini H, Cimino G, Vullo V. Current trends in management of hepatitis B virus reactivation in the biologic therapy era. World J Gastroenterol. 2011;17(34): 3881-7.
26 Pramoolsinsup C. Management of viral hepatitis B. J Gastroenterol Hepatol. 2002;17(Suppl):S125-45.
27 Terrault NA, Bzowej NH, Chang KM, Hwang JP, Jonas MM, Murad MH. AASLD guidelines for treatment of chronic hepatitis B. Hepatology. 2016;63(1):261-83.
28 Katz LH, Fraser A, Gafter-Gvili A, Leibovici L, Tur-Kaspa R. Lamivudine prevents reactivation of hepatitis B and reduces mortality in immunosuppressed patients: systematic review and meta-analysis. J. Viral Hepat. 2008;15(2):89-102.
29 Shi Z, Yang Y, Wang H, Ma L, Schreiber A, Li X, Sun W, Zhao X, Yang X, Zhang L, Lu W, Teng J, An Y. Breastfeeding of Newborns by Mothers Carrying Hepatitis B Virus: A Meta-analysis and Systematic Review. Arch Pediatr Adolesc Med. 2011;165 (9): 837-846.
30 GBD 2015 Mortality and Causes of Death, Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016;388(10053):1459-1544.
31 Zhong-Liao Fang, Caroline A Sabin, Bai-Qing Dong, Shao-Chao Wei, Qin-Yan Chen, Kong-Xiong Fang, Jin-Ye Yang, Xue-Yan Wang, Tim J Harrison. The association of HBV core promoter double mutations (A1762T and G1764A) with viral load differs between HBeAg positive and anti-HBe positive individuals: A longitudinal analysis. J Hepatol. 2008;50(2):273-280.
32 Lok AS, McMahon BJ. Chronic hepatitis B. Hepatology. 2007;45(2):507-39.
33 Tong S, Li J, Wands JR. Carboxypeptidase D is an avian hepatitis B virus receptor. J Virol. 1999;73(10):8696-8702.
34 GBD 2015 Disease and Injury Incidence and Prevalence, Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet.2016;388(10053):1545-1602.
35 GBD 2017 Disease and Injury Incidence and Prevalence, Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1789-1858.

36 -Lai CL, Yuen MF. The natural history and treatment of chronic hepatitis B: a critical evaluation of standard treatment criteria and end points. Ann Internal Medic. 2007;147(1):58-61.
37 Yan H, Zhong G, Xu G, He W, Jing Z, Gao Z, Huang Y, Qi Y, Peng B, Wang H, Fu L, Song M, Chen P, Gao W, Ren B, Sun Y, Cai T, Feng X, Sui J, Li W. Sodium taurocholate cotransporting polypeptide is a functional receptor for human hepatitis B and D virus. eLife. 2012;1: e00049.
38 Ifeorah, A. S. Bakarey, M. O. Adewumi, T. O. C. Faleye, A. Akere, C. E. Omoruyi, A. O. Ogunwale, C.C. Uttah, M. A. Oketade & J. A. Adeniji. Patterns of serologic markers of hepatitis B virus infection and the risk of transmission among pregnant women in southwestern Nigeria. J Immuno Immunochem. 2017;38(6):639-651.
39 Mühlemann B, Jones TC, Damgaard PB, Allentoft ME, Shevnina I, Logvin A, et al. Ancient hepatitis B viruses from the Bronze Age to the Medieval period. Nature. 2018;557(7705):418-423.
40 Taylor JM. Hepatitis delta virus. Virology. 2006;344(1):71-76.
41 Glebe D, Urban S. Viral and cellular determinants involved in hepadnaviral entry. World J Gastroenterol. 2007;13(1):22-38.
42 Liang TJ. Hepatitis B: the virus and disease. Hepatology. 2009;49(5 Suppl): S13-21.
43 Paraskevis, Dimitrios. Dating the Origin and Dispersal of Hepatitis B Virus Infection in Humans and Primates. Hepatology. 2013;(3): 908-16.
44 Nongo BH, Agida TE,Oghenebuk U, Tahir Y. Seroprevalence of hepatitis B virus among antenatal attendees at the University of Abuja Teaching Hospital, Nigeria. Ann Niger Medic. 2016;10(2):58-62.
45 Keats JJ, R Fonseca, M Chesi, R Schop, A Baker, WJ Chng, S Van Wier. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst Rev. 2019;14;3(3):CD004905.
46 Patterson Ross Z, Klunk J, Fornaciari G, Giuffra V, Duchêne S, Duggan AT, et al.. The paradox of HBV evolution as revealed from a 16th century mummy. PLOS Pathogens. 2018;14(1):e1006750.
47 Guerrieri F, Belloni L, D'Andrea D, Pediconi N, Le Pera L, Testoni B, et al. Genome-wide identification of direct HBx genomic targets. BMC Genomics. 2017;18(1):184.
48 Buti M, Rodriguez-Frias F, Jardi R, Esteban R. Hepatitis B virus genome variability and disease progression: the impact of pre-core mutants and HBV genotypes. J Clin Virol. 2005;34Suppl1:S79-82.
49 Bao-Ming Liu, Tong Li, Jie Xu, Xiao-Guang Li, Jian-Ping Dong, Ping Yan, Jing-Xian Yang, Ling Yan, Zhi-Yong Gao, Wen-Peng Li, Xie-Wen Sun, Yu-Hua Wang, Xiu JuanJiao, Chun-Sheng Hou, Hui Zhuang. Characterization of potential antiviral resistance mutations in hepatitis B virus reverse transcriptase sequences in treatment-naïve Chinese patients. Antivir Res. 2010;85(3):512-519.
50 Cao GW. Clinical relevance and public health significance of hepatitis B virus genomic variations. World J Gastroenterol. 2009;15(46): 5761-5769.
51 Davis, Jane. Molecular Epidemiology of Hepatitis B in the Indigenous People of Northern Australia. Gastroenterol Hepatol. 2013;(7):1234-1241.
52 Alberti A, Caporaso N. HBV therapy: guidelines and open issues. Digest Liver Dis. 2011;43(Suppl 1):S57-63.
53 J, Nassal M. Hepatitis B virus replication. World J Gastroenterol. 2007;13(1):48-64.
54 Bonacini, Maurizio, MD. Hepatitis B Reactivation. University of Southern California Department of Surgery. Archived from the original on 27 November 2008. Retrieved 24 January 2009
55 Chu CM, Liaw YF. Predictive factors for reactivation of hepatitis B following hepatitis B e antigen seroconversion in chronic hepatitis B. Gastroenterology. 133 (5): 1458-65. doi:10.1053/j.gastro.2007.08.039. PMID 17935720.
56 Magnius LO, Norder H. Subtypes, genotypes and molecular epidemiology of the hepatitis B virus as reflected by sequence variability of the S-gene. Intervirology. 1995;38(1–2):24–34.
57 Chen W, Gluud C. Vaccines for preventing hepatitis B in health-care workers. Cochrane Database Syst Rev. 2005;(2):CD000100.
58 Fairley CK, Read TR. Vaccination against sexually transmitted infections. Curr Opin Infect Dis. 2012;25(1):66-72.
59 Lee C, Gong Y, Brok J, Boxall EH, Gluud C. Hepatitis B immunisation for newborn infants of hepatitis B surface antigen-positive mothers. Cochrane Database Syst Rev. 2006;19;(2):CD004790..
60 Bonino F, Chiaberge E, Maran E, Piantino P. Serological markers of HBV infectivity. Ann Ist Super Sanita. 1987;24(2):217-23.
61 Eke AC, Eleje GU, Eke UA, Xia Y, Liu J. Hepatitis B immunoglobulin during pregnancy for prevention of mother-to-child transmission of hepatitis B virus. Cochrane Database Syst Rev. 2017;2(2):CD008545.
62 Henrietta Oneh Aba and Maryam Aminu. Seroprevalence of Hepatitis B virus serological markers among pregnant Nigerian women. Ann Afr Med. 2016;15(1):20-27.
63 Littlejohn M, Locarnini S, Yuen L. Origins and Evolution of Hepatitis B Virus and Hepatitis D Virus. Cold Spring Harb Perspect Med. 2016;6(1): a021360.
64 Kerkar N. Hepatitis B in children: complexities in management. Ped Transplant. 2005;9(5):685-691.
65 Buti M, Rodriguez-Frias F, Jardi R, Esteban R. Hepatitis B virus genome variability and disease progression: the impact of pre-core mutants and HBV genotypes. J Clin Virol. 2005;34Suppl 1:S79-82.
66 Balakrishnan L, Milavetz B. Epigenetic regulation of viral biological processes. Viruses. 2017;9(11):346.
67 Araujo, NM. Hepatitis B virus intergenotypic recombinants worldwide: An overview. Infect Genet Evol. 2015;36:500-510.
68 Gan SI, Devlin SM, Scott-Douglas NW, Burak KW. Lamivudine for the treatment of membranous glomerulopathy secondary to chronic hepatitis B infection. Can J Gastroenterol. 2005;19(10):625-629.