# DETECTION OF HEPATITIS B VIRUS FROM INMATES IN SELECTED CORRECTIONAL FACILITIES IN NIGER STATE

**BY**

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# FEDERAL UNIVERSITY OF TECHNOLOGY, MINNA

**JULY, 2021**

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**M. TECH, MEDICAL MICROBIOLOGY**

# A DISSERTATION SUBMITTED TO THE POSTGRADUATE SCHOOL FEDERAL UNIVERSITY OF TECHNOLOGY, MINNA, NIGERIA

**IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF THE MASTERS OF TECHNOLOGY DEGREE IN MEDICAL MICROBIOLOGY**

# JULY, 2021

# DECLARATION

I hereby declare that this Dissertation titled ―Detection of Hepatitis B Virus from Inmates in selected correctional facilities in Niger State‖ is a collection of my research work and it has not been presented for any qualification anywhere. All citations and sources of information (published or unpublished) are duly acknowledged.

………………………..

Ojodu, Abimbola Basirat Signature/Date

M.TECH/SLS/2017/7393

Federal University of Technology Minna, Nigeria

# CERTIFICATION

This Dissertation entitled ―Detection of Hepatitis B Virus from Inmates in selected correctional facilities in Niger State‖ by Ojodu, Abimbola Basirat (M.TECH/SLS/2017/7393) meets the regulations governing the award of the Degree of Masters of Technology of the Federal University of Technology, Minna and it is approved for its contribution to scientific knowledge and literary presentation.

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Dean, Postgraduate School Signature & Date

# DEDICATION

This study is dedicated to Almighty Allah, the Lord of unquestionable majesty; the Supreme Creator who taught man by pen

# ACKNOWLEDGEMENTS

My ultimate acknowledgement goes to the Almighty Allah for His guidance and protection from the beginning of my life up to this moment. Glory is to Allah, the knower of the unknown who taught man what he knows not.

My humble and undiluted regards goes to my able supervisor and mentor, Prof. M. Galadima for his guidance and motivation from the beginning to the completion of the program. It is indeed a rare privilege to have benefited from his wealth of experience, knowledge and understanding. The successful completion of the research is a product of his dogged commitment to the supervision. I have gained a lot not only from his professionalism but also from his good mentorship. I must say sincerely that his attitude gave me a better appreciation of the popular saying ―the more you know the more humble you become‖. It worth mentioning that working under his supervision has impacted positively on my academic proficiencies and my relationship with my colleagues.

I also express my thanks to the Heads of Department and the PG Coordinator, Dr. N. U. Adabara and Dr. J. D. Bala respectively for their numerous contributions to the success of this M.Tech program. To all Lecturers of the Department of Microbiology, FUTMinna, I say ―a very big thank you‖ for their support and constructive criticism during presentation. Indeed, their constructive criticism played significant role in making the research a success.

My appreciations also go to my family members for their support and prayers throughout the program. To my parents Mr and Mrs Ojodu, for their upbringing prayer for the progress in all my endeavors, I pray Allah forgive you both and make paradise your abode. To my precious spouse, Engr. I. M. Animashaun, I say a very big thank you for your understanding and cooperation. To

my precious sprout; Nasir, Maryam, Aisha, Khadija and Fatima, your lively compassion, companionship and prayer are well appreciated and acknowledged.

I have the rare opportunity to appreciate my colleagues for their cooperation and regular calls and messages on the need for timely completion of the program. My appreciation will not be complete without acknowledging my colleagues at Shamras Diagnostic Center, Minna, I say thank you all for your support throughout the program.

# ABSTRACT

Research has shown high transmission of hepatitis B virus (HBV) among inmates in correctional facilities in the developed world, but the data base for the developing countries is still lacking information on same. The aim of this study was to determine the prevalence of Hepatitis B virus infection in inmates of selected correctional facilities in Niger state. Blood samples were collected from inmates in three correctional facilities namely Bida, Kontagora and Minna. A total of 344 inmates consented to giving their blood samples for the test. Questionnaires were administered to get their Bio-data and 5ml of blood sample was collected from each person. The plasma was separated and tested for hepatitis B surface antigen (HBsAg) using rapid chromatographic immunoassay test (ICT). The negative samples were further screened using enzyme linked immunosorbent assay (ELISA). All the HBsAg positive samples either by ICT or ELISA were subjected to further test using 5-panel (HBsAg, HBsAb, HBeAg, HBeAb and HBcAb) HBV test card. Out of the 344 samples collected, 75 (22%) were positive by ICT for HBsAg. ELISA gave an overall prevalence rate of 25% (87/344) as additional 12 samples were positive. TThe result of the 5-panel showed that HBsAg, HBsAb, HBeAg, HBeAb and HBcAb were present in 87, 19, 20, 47 and 68 plasma respectively. This implies that 87 persons were infected, 19 had immunity against the virus, 20 had active viral replication, 47 with no viral replication and 68 with onset of acute infection. The HBV infection was highest in the age bracket 21-30 years (29.7%) and lowest in 61-70% (0%). There was no statistically significant difference between the viral infection and locations. However, out of the associated risk factors, sharing of objects showed statistically significant association with the high prevalence of the HBV. This study showed the prevalence of HBV among inmates. As such, there is need for constant screening of the inmates for effective prevention measure and proper clinical management strategy.

# TABLE OF CONTENTS

Title page ii

[Declaration iii](#_TOC_250081)

[Certification iv](#_TOC_250080)

[Dedication v](#_TOC_250079)

Acknowledgement vi

[Abstract viii](#_TOC_250078)

[Table of Contents ix](#_TOC_250077)

List of Figures xiv

List of Tables xv

[CHAPTER ONE 1](#_TOC_250076)

* 1. [INTRODUCTION 1](#_TOC_250075)
  2. [Background to the study 1](#_TOC_250074)
  3. [Statement of the Research Problem 2](#_TOC_250073)
  4. [Justification for the Study 3](#_TOC_250072)
  5. Aim and Objectives 3

[CHAPTER TWO](#_TOC_250071)

1. [0 LITERATURE REVIEW 5](#_TOC_250070)
   1. [The Hepatitis B Virus 5](#_TOC_250069)
   2. [Origin and History of Hepatitis B Virus 6](#_TOC_250068)
   3. [Biology of the Hepatitis B Virus 8](#_TOC_250067)
   4. [General population 12](#_TOC_250066)
      1. Indigenous populations 13
   5. [Inmates 13](#_TOC_250065)
      1. [The correctional facility environment 13](#_TOC_250064)
   6. [Epidemiology of Hepatitis B Virus Infection 14](#_TOC_250063)
      1. [Natural history of CHB infection 14](#_TOC_250062)
      2. [Complications of chronic HBV infection 17](#_TOC_250061)
   7. [Epidemiology 17](#_TOC_250060)
      1. [Epidemiology across the globe 17](#_TOC_250059)
      2. [Epidemiology in Nigeria 20](#_TOC_250058)
   8. [Serological Markers 25](#_TOC_250057)
      1. [Interpretation of Hepatitis B Serologic Test Results 27](#_TOC_250056)
         1. Hepatitis B surface antigen (HBsAg) 27
         2. Hepatitis B surface antibody (anti-HBs 28
         3. Total hepatitis B core antibody (anti-HBc) 28
         4. IgM antibody to hepatitis B core antigen (IgM anti-HBc) 28
   9. Root of transmission and care 31
      1. [Lifestyle advice 31](#_TOC_250055)
      2. Routes of transmission worldwide 31
      3. Low rates of diagnosis 31
   10. [Approaches to screening 34](#_TOC_250054)
       1. [Population- or community-based screening (including antenatal) 34](#_TOC_250053)
       2. [Health-care facilities 34](#_TOC_250052)
       3. Targeted risk factor-based screening 34
   11. [Progression of Chronic Hepatitis B (CHB) 34](#_TOC_250051)
   12. [Diagnosis and monitoring of hepatitis B 36](#_TOC_250050)
       1. [Cascade—acute hepatitis B 36](#_TOC_250049)
       2. [Resolved HBV infection 37](#_TOC_250048)
   13. [Treatment 38](#_TOC_250047)
       1. [Available treatments 38](#_TOC_250046)
       2. NUC therapy 39
       3. [Interferon therapy 39](#_TOC_250045)
          1. [Genotype and prediction of treatment success 40](#_TOC_250044)
       4. [Treatment in children 40](#_TOC_250043)
       5. [Pregnancy 40](#_TOC_250042)
       6. [Treatment of acute HBV 41](#_TOC_250041)
       7. [Future developments 41](#_TOC_250040)
   14. [Prevention of HBV infection 41](#_TOC_250039)
       1. [Vaccination 41](#_TOC_250038)
       2. [HBV vaccination programmes 42](#_TOC_250037)

[CHAPTER THREE 44](#_TOC_250036)

1. MATERIALS AND METHOD 44
   1. [Study Area 44](#_TOC_250035)
   2. [Methods 45](#_TOC_250034)
      1. [Study Design 45](#_TOC_250033)
      2. [Study Population 45](#_TOC_250032)
      3. [Sample size 46](#_TOC_250031)
      4. [Ethical Clearance 46](#_TOC_250030)
      5. [Inclusion Criteria 46](#_TOC_250029)
   3. [Laboratory Analysis 47](#_TOC_250028)
      1. [Rapid chromatographic Immunoassay Test Principle 47](#_TOC_250027)
      2. [ELISA Test Principle 47](#_TOC_250026)
         1. [Materials and Reagents preparation 48](#_TOC_250025)
         2. [Preparations of the Reagents 48](#_TOC_250024)
      3. [Storage and Stability 49](#_TOC_250023)
      4. [Samples Collection and Transportation 49](#_TOC_250022)

[3.3.5. Assay of Plasma Samples Procedure 50](#_TOC_250021)

[3.3.6 Interpretations of ELISA Result 51](#_TOC_250020)

* 1. [Serological Marker Test Principle 52](#_TOC_250019)
     1. Diagnostic Kit for HBV Infection Marker 52
     2. [Result Determination 52](#_TOC_250018)
  2. [Statistical Analysis 53](#_TOC_250017)

CHAPTHER FOUR 54

* 1. [RESULTS AND DISCUSSION 54](#_TOC_250016)
  2. [Results 54](#_TOC_250015)
     1. [Overall Prevalence rate in the Correctional facilities 54](#_TOC_250014)
     2. [Prevalence of HBV infection based on locations of correctional facilities 55](#_TOC_250013)
     3. [Prevalence of HBV infection based on age of inmates 56](#_TOC_250012)
     4. [Prevalence of HBV infection based on gender of inmates 57](#_TOC_250011)
     5. [Prevalence of HBV infection based on Educational level of inmates 57](#_TOC_250010)
     6. [Prevalence of HBV infection based on duration of stay of inmates 58](#_TOC_250009)
     7. [Prevalence of HBV infection based on marital status of inmates 58](#_TOC_250008)
  3. [,8 Hepatitis B Serological Markers 59](#_TOC_250007)

[4.1.9 Infection with HBV among inmates and some associated risk factors 61](#_TOC_250006)

* 1. [Discussion of Results 62](#_TOC_250005)

[CHAPTER FIVE 68](#_TOC_250004)

* 1. [CONCLUSION AND RECOMMENDATIONS 68](#_TOC_250003)
  2. [Conclusion 68](#_TOC_250002)
  3. [Recommendations 69](#_TOC_250001)

[REFERENCES 70](#_TOC_250000)

APPENDICES 81

|  |  |  |
| --- | --- | --- |
|  | **LIST OF FIGURES** |  |
| Figure 2.1 | Basic structure of the HBV genome | page 9 |
| 2. 2 | Spherical, filamentous and HBV Dane HBsAg particles | 9 |
| 2.3 | Genomic organization of HBV with key regulatory elements | 11 |
| 2.4 | The transcription start sites of various HBV transcripts and the | 11 |
|  | proteins they encode |  |
| 2.5 | Prevalence rate across Africa | 19 |
| 2.6 | Acute HBV infection | 25 |
| 2.7 | Chronic HBV infection (HBeAg positive) | 25 |
| 2.8 | Chronic HBV infection (HBeAg negative) | 26 |
| 2.9 | Risk of progression in patients with HBV-related cirrhosis | 36 |
| 3.1 | Map of the study area | 44 |
| 4.1 | Percentage of negative to positive samples | 54 |
| 4.2 | Sample population and the affected inmates in each location | 55 |
| 4.3 | Hepatitis B biomarkers in Inmate from Correctional facilities | 60 |

|  |  |  |
| --- | --- | --- |
|  | **LIST OF TABLES** |  |
| Table |  | page |
| 2.1 | Summary of prevalence across risk groups and nation | 19 |
| 2.2 | Hepatitis B biomarkers among the general population across | 12 |
|  | the six geographical zone of Nigeria |  |
| 2.3 | Interpretation of Hepatitis B Serological markers | 29 |
| 2.4 | Serological markers and the interpretation of possible combination | 30 |
| 2.5 | Phases of HBV infection | 33 |
| 2.6 | Progression of Chronic Hepatitis B | 35 |
| 3.1 | Dilution of concentration wash buffer | 49 |
| 4.1 | Sensitivity of ICT and ELISA methods | 54 |
| 4.2 | Prevalence of HBV infection based on locations | 56 |
| 4.3 | Prevalence of HBV infection based on age of inmates | 56 |
| 4.4 | Prevalence of HBV infection based on gender of inmates | 57 |
| 4.5 | Prevalence of HBV based on Educational level of inmates | 67 |
| 4.6 | Prevalence of HBV infection based on duration of stay of inmates | 58 |
| 4.7 | Prevalence of HBV infection based on marital status of inmates | 59 |
| 4.8 | Overall percentage positive of Hepatitis B biomarkers among Inmates | 60 |
| 4.9 | Infection with HBV among inmates and some associated risk factors | 61 |

# CHAPTER ONE

# INTRODUCTION

# Background to the Study

Hepatitis B is a blood borne virus (BBV) which spreads through body fluids, mainly the blood (Liang, 2010). Early symptoms of the infection may include loss of appetite, vomiting, loss of weight, tiredness, dark urine, right upper abdominal pain and yellowing of skin (jaundice) (Connor *et al.,*2006). If the virus is not combated at the early stage, the system of the host may be further deteriorated showing some symptoms such as fluid retention, bruising and prolonged bleeding (Ayiku, 2015). This infection could later result into acute and chronic necroinflammatory liver diseases (Liang, 2010).

Till recent time, Hepatitis B virus is a major public health concern worldwide, due to its high chronicity rate in liver disease morbidity and mortality in spite of the accessibility of the populace to the effective vaccination (Almasio *et al.,* 2011). On the global scene, the virus accounts for over 360 million cases of chronic hepatitis and claim the lives of about 620,000 persons per year (WHO, 2013). More than 8% of the populations in the Sub-Sahara Africa are infected with the virus with about 44% of cirrhotic liver disease and 47% of hepatocellular carcinoma cases are linked to it (Musa *et al.,* 2015). The virus is contracted through a number of means which include; body fluids (saliva and blood), HBV contaminated equipment, venereal transmission, mother to child transmission, and intravenous drug use (Dana *et al.,* 2013).

Research has shown that Intravenous Drug Users (IDUs) are at high risk for HBV infection as with other blood-borne pathogens (such as hepatitis C and human immunodeficiency virus) (Dana *et al.,* 2013). It is a common knowledge that correctional facilities often comprise of

inmate who are IDUs and those who are not but relate freely with them. Hence, transmission of blood-borne diseases among inmates are higher than the general population due to high presence of IDUs with high-risk addiction-related behaviors, having past history of multiple sexual partners and homosexuality, life style of the inmates and limited educational opportunities (Dana *et al.,* 2013; Tavakkoli *et al., 2008*). The health implication of this on the larger society is highly detrimental as they become potential reservoirs of infection to the non-incarcerated and uninfected individuals upon regaining their freedom (Adoga *et al*., 2009).

It is worth mentioning that in the developed worlds, which have citizens with high level of literacy and Governments which provide highly effective recombinant vaccine for the viruses, HBV is still a source of threat to them, talk more of the developing nation (such as Nigeria) where majority of the populace are having misconceptions or bias mind towards the vaccine and where vaccination programs receive less attention from government (Cutt *et al.,* 2013; Rainey *et al.,* 2011)*.* This account for the reason why the risk of contracting the virus in Nigeria is significantly high as it creates room for exposure of about 75% of the population to the virus (Musa *et al.,* 2015).

HBV is not like AIDS at its early stage as its infection can be prevented through vaccination and 95% of adults newly infected with the virus get cleared of the virus naturally and become immune for life (Ishikawa, 2012). However, once it gets chronic, it becomes incurable; treatment will only be aimed at suppressing HBV replication and retard the progression of liver disease before the development of cirrhosis and hepatocellular carcinoma (D‟Souza and Foster, 2004).

# Statement of the Research Problem

Though, a number of studies have been conducted on hepatitis B virus in some parts of developing nations, including Nigeria (Moses *et al.,* 2009; Musa *et al.,* 2015; Alkali *et al.,*2017), no work seems to have been documented on transmission of HBV within correctional facilities particularly in Niger state. Evidences has shown high transmission of HBV among inmates in the correctional facilities (Haber *et al*., 1999; Taylor *et al*., 2002; Adjei *et al.*, 2006; Ayiku, 2015, Alkali *et al*., 201**7**), however, no periodic national survey on the virus is conducted. The inmates are at high risk of contracting HBV due to over congestion, high risk behavior, correctional facility life style and limited education and awareness of the inmate and probable intra- correctional facility spread (Adjei *et al.*, 2006; Kassaian *et al*., 2012).

# Justification for the Study

The risk of free intermingling, unprotected sex and injecting drug use, commonly known with inmates do not stop at correctional facilities as that is continued after the release of inmate from the facilities. These make inmates who have become reservoir for virus (such as hepatitis B virus) to be sources of threat not only to their families but also to the society at large (Jack, 2011). Hence, understanding the prevalence rate of hepatitis B virus in such correctional facilities will aid in recommending appropriate method to prevent its further transmission among the inmate, the staff of the facility and to the outer world.

# Aim and objectives of the Study

This study aimed at the detection of Hepatitis B Virus from inmates in three selected correctional facilities in Niger State.

The objectives of the study were to:

* + 1. determine hepatitis B surface antigen among inmates;
    2. determine the level of significance between the rapid chromatographic test (ICT) and the ELISA;
    3. determine HBV infection serological markers; surface antigen (HBsAg), surface antibody (HBsAb,), envelope antigen (HBeAg), envelope antibody, (HBeAb) and core antibody (HBcAb);
    4. determine risk factors that are of high significance.

# CHAPTER TWO

# 2.0 LITERATURE REVIEW

# 2.1. The Hepatitis B Virus

Hepatitis B virus (HBV) infection is a main cause of morbidity and mortality globally. The World Health Organisation (WHO) has claimed that about two (2) billion people across the globe have contracted the disease and that three hundred and fifty (350) million of these are chronically infected (Umego *et al.,* 2018). Among those who have been chronically infected, it is likely that 65 million people will die from liver disease caused by the HBV infection (Aspinall *et al*., 2011). In Africa and Asia, about eighty percent of hepatocellular carcinoma is caused by hepatitis B virus; a leading cause of mortality (Zhu *et al.,* 2016). Approximately, 5-10% of infected adults become chronic carriers while the remaining most often eliminate the virus from their body system without *sequalae* (Emechebe *et al.,* 2009).

About 25% of the chronically infected individuals often die of hepatic complications; a few remain life-long carriers while others at varying intervals clear the infections (Emechebe *et al.,* 2009).Hepatitis B is an infection of the liver transmitted via percutaneous or permucosal exposure to infected blood or body fluids and has an incubation period ranging from 40 to 160 days (average 60–90 days) (Salisbury *et al.,* 2006). Transmission can occur vertically from infected mother to child, horizontally (e.g. child-to-child transmission within a household), sexually or parenterally (e.g. via injecting drug use, sharps injury or contaminated blood products).

The majority of acute HBV infections are asymptomatic. In adults, 30% will present with jaundice and hepatitis and 0.1–0.5% develops fulminant liver failure (Kao, 2008). During acute

infection, hepatitis B surface antigen (HBsAg) and hepatitis B envelope-antigen (HBeAg) can be detected in the serum and there are high levels of IgM antibodies to the viral core antigen (IgM anti-HBc). A successful host immune response to the virus leads first to clearance of HBeAg (and appearance of antibody to HBeAg) and subsequent clearance of HBsAg (and appearance of antibody to HBsAg). The appearance of antibodies to HBsAg indicates recovery from acute infection (Raimondo *et al.,* 2003). The persistence of HBsAg for .6 months from its first detection denotes chronic hepatitis B (CHB) infection. The likelihood of developing CHB varies with the age at which the infection is acquired, the risk being lowest in adults (5%) and greatest in neonates whose mothers are HBeAg positive (90%) (Aspinall *et al.,* 2011). The principal mode of HBV transmission also varies geographically. In low prevalence areas such as Northern Europe and North America, HBV infection is primarily acquired in adulthood through sexual contact or injecting drug use, whereas in high prevalence areas, HBV infection is most commonly acquired perinatally or in early childhood (Aspinall *et al.,* 2011).

# Origin and History of Hepatitis B Virus

The hepatitis B surface antigen (HBsAg) also known as Australia antigen with its antibody; HBsAb was discovered in 1965 (Blumberg*,* 1977). 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 (Blumberg*,* 1977). The virus mostly infects the liver, although infection of other tissues has been documented (Ahizechukwu *et al.,* 2011). Hepatitis B virus (HBV) is said to be 50-100 times more infectious than HIV and 10 times more infectious than HCV (Mboto and Edet, 2012). Presently, 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 globally accepted (Mboto and Edet, 2012).

Claim has been laid to the birds which has now gone into extinction has the origin of the virus (Umego *et al.,* 2018). Blumberg in 1967 however, postulated that people who received blood products from a large number of donors could have developed antibodies against polymorphic serum proteins (Gerlich, 2013). However, the work of Alter (Blumberg‘s colleague), fault the claim of Blumberg through the discovery of a new antigen in several samples of huge serum collected most especially in Australian aborigines for whom the Australia (AuAg) was named (Gerlich, 2013). 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 (Umego *et al.,* 2018). Several researches further confirmed that Au/SH-Ag was actually a marker for acute or chronic hepatitis B with a few apparently healthy carriers (Gerlich, 2013). In 1969, Blumberg and Millman developed the hepatitis B vaccine (Blumberg, 1977).

Two years after the development of the vaccine, it was realised that purified AuAg preparations would contain a reverse transcriptase like retroviruses (Hirsch *et al.,* 1990). 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 (Umego *et al.,* 2018). The cloning and sequencing of HBV DNA was reported almost at the same time by three different renowned researchers in 1978 (Gerlich, 2013). In line with Robert Koch‘s postulates, in 1982, the ―dane particles‖ was proven to be HBV by its ability to infect an animal model (Will *et al.,* 1982). In 1986, the preS1 domain was characterized as a site for attachment of HBV to hepatic cells. After a number of 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 (Gerlich, 2013).

# Biology of the Hepatitis B Virus

HBV is a hepadnavirus from a family of enveloped DNA viruses, its genome is composed of a circular partially double stranded DNA and made up of three different structures: the dane (42 nm), filamentous (22 nm) and spherical (20 nm) particles which are often noticed in serum of the infected patients (Figs. 2.1 and 2.2) (Umego *et al*., 2018, Mohammed and Eldaif, 2014). Out of the three particles (dane, filamentous and spherical) only the dane is infectious as it contains the HBV genomes which is lacking in the other two. Hence, Dane particle is the complete infectious HBV virion with its core region being small, partially double stranded, circular DNA molecule and viral DNA (Umego *et al.,* 2018)

Structurally it consists of a nucleocapsid core (HBcAg), and surrounded by an outer lipoprotein coat (envelope) which contains the surface antigen (HBsAg) (Aspinall *et al.,* 2011). The hepatitis B surface antigen (HBsAg) is an immunologically distinct soluble protein manufactured by the viral particle, which is secreted into circulation by binding to smooth endoplasmic reticulum within cells. Due to the fact that HBeAg is secreted into the serum of the host or infected individuals, it becomes an easily measured marker for active HBV replication in chronic infections (Ayiku, 2015).

The initial stage of its life cycle involves the binding of the HBV virion to a receptor at the surface of the liver cells known as hepatocyte which forms 70% of the liver (Seeger and Mason, 2000). The viral nucleocapsid enters the cell by a receptor mediated endocytosis which is

followed by uncoating of the envelope (Scaglioni *et al.*, 1996). The nucleocapsid then delivers the viral genome into the nucleus (Scaglioni *et al.*, 1996).

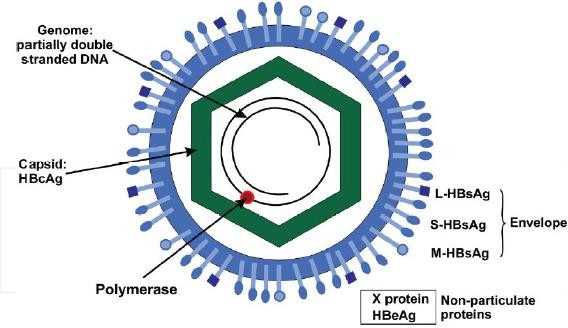


Fig. 2.1. Basic structure of the HBV genome Source: Umego *et al.* (2018)

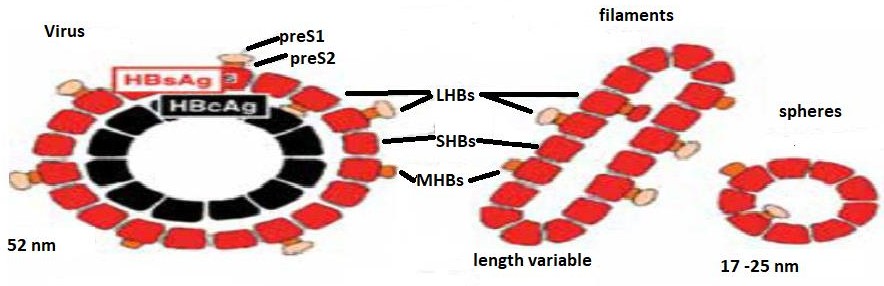


Fig. 2.2. Spherical, filamentous and HBV Dane HBsAg particles Source: Gerlich (2013)

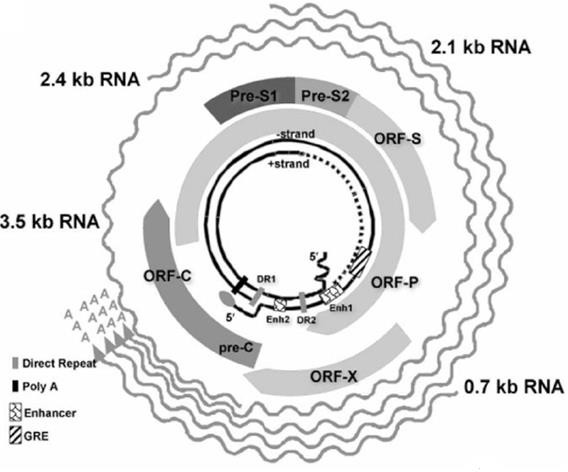
Here the second-strand DNA is fully synthesized by an endogenous polymerase to complete the double strand and this serves as a template for transcribing four viral RNAs (Ayiku, 2015).

These RNAs are polyadenylated, conveyed to the cytoplasm and then translated into the envelope (S-small, M- medium, L- large), the nucleocapsid and pre core antigen (C, pre-C), polymerase (P), and transcriptional transactivating proteins (X) and all form the various structural components of the virion (Beck and Nassal, 2007).

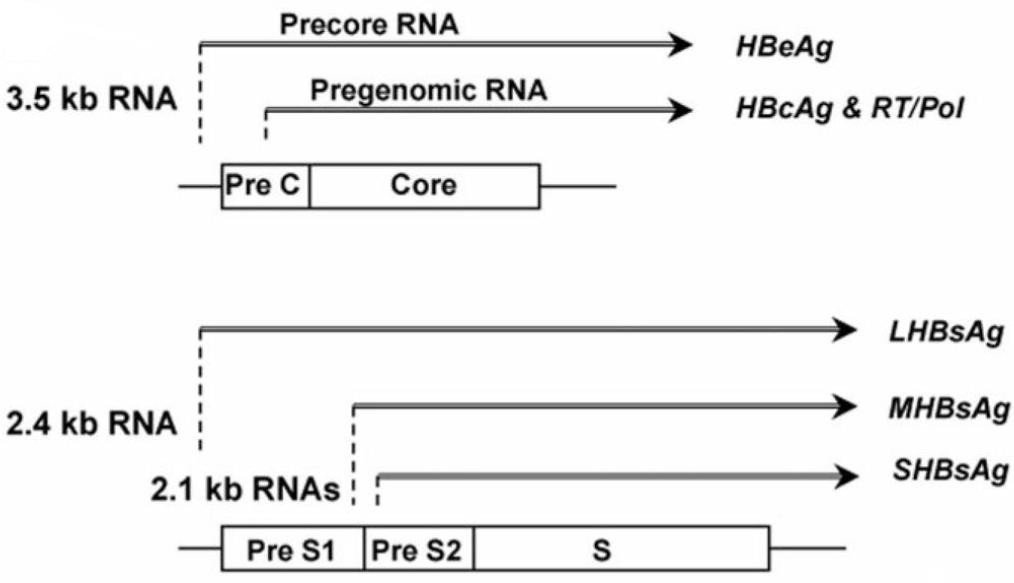
Hepatitis B viral DNA encodes four partially overlapping open reading frames (ORFs): that is the *surface (preS1, preS2, S)*, *core (precore, core)*, *polymerase* and the '*x'* genes, respectively. The *S* ORF codes for the viral surface envelope proteins (HBsAg), the *C* ORF encodes the HBcAg or HBeAg, the *P* ORF encodes the polymerase (pol) which is functionally divided into three domains (the terminal protein domain, the reverse transcriptase (RT) domain and H domain) and the HBV *X* ORF encodes the HBxAg (Liang, 2010). The *S* ORF can be structurally and functionally divided into the pre-S1, pre-S2, and S regions. All the aforementioned three envelope proteins contain HBsAg, which is heterogeneous antigenically resulting in 4 major subtypes (adw, ayw, adr and ayr) and their distribution varies geographically (Mohammed and Eldaif, 2014). The S protein is quantitatively the most essential component in the empty viral particles as well as in the complete virion because its hydrophilic region may be involved in attachment and development of the core particle during maturation of the virion. The S gene is coded for by a highly conserved region and from many related studies the S gene is the subgenomic region that has been found to be commonly used for HBV genotyping (Ayiku, 2015, Liang, 2010).

Chronic infections with HBV have been termed as persistence of the HBsAg in the serum over a duration of 6 months (Inan and Tabak, 2015). 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. A unique feature of the HBV genome is its asymmetric structure of the chains with most cellular proteins being packed in the nucleocapsid structure (Inan and Tabak, 2015). The genome possess overlapping and open reading frames (OFR) for X, P, C and S encoding four different proteins as shown in Figures 2. 3 and 2.4.



**FIGURE 2.3:** Genomic organization of HBV with key regulatory elements Source: Liang (2010)



**FIGURE 2.4:** The transcription start sites of various HBV transcripts and the proteins they encode.

Source: Liang (2010)

Worldwide, there are an estimated 250 million chronically infected persons, particularly in low- and middle-income countries (LMICs). Universal hepatitis B immunization programmes that target infants, with the first dose at birth, have been highly effective in reducing the incidence and prevalence of hepatitis B in many endemic countries. However, these programmes will not have an impact on HBV-related deaths until several decades after their introduction. The major complications of CHB are cirrhosis and hepatocellular carcinoma (HCC). Between 20% and 30% of those who become chronically infected will develop these complications, and an estimated 650 000 people will die annually due to CHB. The risk of developing chronic HBV infection decreases with age at infection, from about 90% when infected perinatally up to 6 months of age to 20–60% between the ages of 6 months and 5 years. Of those who acquire HBV as children 25% will develop primary liver cancer or cirrhosis as adults.

# General Population

The prevalence of HBV infection varies geographically and can be categorized into areas of high (8%), intermediate (2–7%) and low (<2%) endemicity (Umego *et al.,* 2018)

1. **High endemicity (>8%):** Any area with prevalence rate of greater or equal to 8% is considered high endemicity..
2. **Intermediate endemicity (2–5%):** Any region having an prevalence value of between 2–5% is considered intermediate endemicity region.
3. **Low endemicity:** Endemicity of a region is considered to be low if the value is below 2%.

Countries in the Americas, such as Mexico, Guatemala, and the USA had mostly low endemicity levels (HBsAg prevalence <2%), ranging from 0.01% (95% CI 0.01–0.01) in the UK to 10.32% (8.56–12.38) in Kyrgyzstan. Overall, the South-East Asia Region had low endemicity levels but on country level, HBsAg prevalence below 2% was only noted in India, Indonesia and Nepal.

The Eastern Mediterranean Region was of lower–intermediate endemicity (2·00–4·99%), but Djibouti, Somalia and Sudan showed a higher prevalence of HBsAg than other countries in the region. Most countries in Africa were of higher–intermediate endemicity (HBsAg prevalence 5– 7·99%), or highly endemic for HBV (HBsAg prevalence ≥8%n (Figure 2.5). The Western Pacific Region was also a high–intermediate endemicity region (5–7.99%), especially in the Pacific Island States such as the Solomon Islands

* + 1. **Indigenous populations:** In some settings, indigenous populations are also disproportionately affected by viral hepatitis infection, along with a number of other health problems. Contributing factors to these disparities may include higher rates of injecting risk behaviours among indigenous people who inject drugs and higher rates of incarceration

# Inmates

The prevalence of HBV in correctional facilities is often significantly higher than in the general population. Globally, the prevalence of HIV, STIs, hepatitis B and C and tuberculosis in correctional facility populations is estimated to be two to ten times higher than in the general population, and in some settings, 50 times higher (Ayiku,, 2015). People in correctional facilities and closed settings may be at particular risk for HBV, HCV and HIV infection for a number of reasons. Most commonly, this is due to sharing of needles and syringes and other injecting equipment; often because prevention hardware such as clean needles and syringes are not accessible to inmates (Ayiku, 2015).

# The Correctional facility environment

Correctional institutions serve as a measure of a society‘s humanity and are important components of the safety and stability of its environment (UN, 2012). The correctional facility environment comprises of the interactions between physical, psychological, and social factors

therefore measuring the properties of the correctional facility environment requires the psychological and structural approach. One way of attaining such information as suggested by many researchers may be through the perceptions of the various factions of the organization such as correctional facility officers, inmates, health care personnel and all other correctional facility staff (Awolutugu, 2013). The environments vary from facility to facility and most of these facilities are designed from a security and functional angle rather than care and reform although studies over the years to date have shown that a hospitable physical environment is an important factor that can promote health and well-being of inmates (WHO, 2007).

# Epidemiology of Hepatitis B Virus Infection

# Natural history of CHB infection

The natural history of CHB can be divided into five phases. Not all patients experience every phase, and the duration of each phase can be highly variable. Reversion or reactivation between different phases can occur seemingly without warning, and therefore, clinical management can be challenging (McMahon, 2010). The five phases are summarized below

**Phase 1**: immune tolerant phase

The ‗immune tolerant phase‘ is typically the first phase of infection and is characterized by host immune tolerance despite active HBV replication. The lack of host immune response means that liver histology and alanine aminotransferase (ALT) levels are usually normal. Active HBV replication releases HBV DNA, HBeAg and HBsAg, which are detectable in the serum (Liaw and Chu, 2009). The immune response is limited to anti-HBc antibody production (initially IgM and then IgG), but this does not act to neutralize infection.

**Phase 2**: HBeAg-positive CHB (immune reactive phase)

The ‗HBeAg-positive CHB phase‘ starts once the host mounts an immune response to the viral infected hepatocytes. Serum ALT is raised (higher levels indicating a more vigorous response and therefore more hepatocyte damage), and chronic active hepatitis is visible on liver ultrasound (USS) or biopsy (Liaw and Chu, 2009). During this phase, the immune response reduces (but does not eliminate) HBV replication and begins to clear HBeAg and HBsAg (which occurs at a rate of 10–15% and 0.5–1% per year, respectively) (Giacchino and Cappelli, 2010) The immune response to HBVtends to be episodic, with flares of ALT up to five times the normal limit and flares of anti-HBc IgM production, which may be confused with acute HBV infection. Active hepatitis occurring during this phase may lead to cirrhosis, in some cases complicated by hepatic decomposition and hepatocellular carcinoma (HCC) (Liaw and Chu, 2009). If patients clear HBeAg, they pass into the ‗low replicative phase‘, although their infection may subsequently reactivate (Liaw and Chu, 2009; Takkenberg *et al.,* 2010).

**Phase 3**: Low replicative phase patients in the low replicative phase have minimal HBV replication and HBV DNA is low or undetectable. HBeAg is negative, but HBsAg remains positive. Previously known as the ‗Inactive Carrier State‘, this term is now thought to be misleading, given the ongoing risk of reactivation to active disease. Around 10% of patients in this phase will reactivate at some point to HBeAg-positive CHB and 10–20% will reactivate to

‗HBeAg-negative CHB‘ (McMahon *et al.,* 2001).

**Phase 4**: HBeAg-negative CHB occurs due to a variant of the HBV virus that is unable to produce HBeAg. This is due to a mutation in the precore or core promoter region of the genome, although the virus is still actively replicating. HBeAg-negative CHB may occur following

periods in the low replicative or HBeAg-positive CHB phases and normally represents a later stage in disease progression (Aspinall *et al.,* 2011).

**Phase 5**: HBsAg-negative phase progression to clearance of both HBsAg and HBeAg is known as the ‗HBsAg-negative phase‘. HBV viral replication may persist but is unlikely to be detectable in serum (Kao, 2008). Once in the HBsAg-negative phase, there is an improved outcome and a reduced risk of liver complications, although HBV may reactivate in individuals receiving immunosuppressive therapy and still represents a risk for organ donation (Cooke *et al.,* 2010).

HBV infection following vertical transmission in neonates infected by mother to child transmission (MTCT), the risk of developing CHB depends on the HBeAg status of the mother. Neonates whose mothers were HBeAg positive during the perinatal period have a 90% chance of developing chronic infection, whereas this risk is 15% in neonates with HBeAg-negative mothers (McMahon, 2010). Neonatal vaccination can be effective in reducing the risk of MTCT and is discussed below. Both the immune tolerant phase and the HBeAg-positive CHB phase are prolonged in individuals infected in the neonatal period, with HBeAg clearance typically occurring during the third or fourth decade (Giacchino and Cappelli, 2010). This longer course of infection increases the risk of developing HBV-related liver complications. HBV infection in childhood (horizontal transmission) children infected between 1 and 5 years of age have a 20– 50% chance of developing chronic infection. The immune tolerance phase in these children is usually fairly short, with features of immune response to HBV sometimes present by the time of the first clinic review, and nearly always by adolescence or early adulthood (Giacchino and Cappelli, 2010). HBV infection in adulthood individuals infected in later childhood or adulthood

has a 5% risk of developing chronic infection. Progression through the phases of infection is very rapid, and the immune tolerant phase is sometimes absent (Kao, 2008; Liaw and Chu, 2009).

# Complications of chronic HBV infection

Patients with CHB are at increased risk of cirrhosis, hepatic decompensation and HCC (Liaw, 2009). Longitudinal studies of patients with CHB indicate that, after diagnosis, the 5years cumulative incidence of cirrhosis is from 8 to 20%, and once cirrhosis has developed, the annual risk of HCC is 2–5% (EASL, 2009). It has been estimated that HBV infection is responsible for 50–80% of HCC cases worldwide (Venook *et al.,* 2010). Table 2 shows the risk of liver complications in relation to the various phases of CHB infection. The risk of cirrhosis is highest in those with chronic active hepatitis (HBeAg-positive CHB or HBeAg-negative CHB), whereas the risk in those who remain in the low replicative or HBsAg-negative phase approaches that of the background uninfected population. The majority of cases of HCC occur in individuals who have already developed cirrhosis, although recent studies have shown that HCC can still occur in the low replicative and the HBsAg-negative phases in patients with seemingly normal liver architecture (Liaw, 2009; Chu and Liaw, 2009). The risk of cirrhosis and HCC is increased in males, older age, family history of HCC, high viral load, persistently raised ALT, co-infection with HCV or HIV and HBV Genotypes C and F (Kao, 2008; Liaw, 2009).

# Epidemiology

# Epidemiology across the globe

HBV infection is widespread, with a prevalence >8% in parts of sub-Saharan Africa such as West Africa—particularly, Burkina Faso, Ivory Coast, Gambia, Ghana, Guinea, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, Togo—Southern Sudan, Angola, Uganda and Somalia (Stasi *et al.,* 2017). An intermediate prevalence (2–7.99%) is present in some regions of

the eastern Mediterranean (e.g. Tunisia), Central Asia (e.g. Kazakhstan), Southeast Asia (e.g. Thailand, Bhutan and Bangladesh), China, parts of South America (e.g. Colombia) and in some European countries (e.g. Albania, Bulgaria, Romania and Turkey). A low prevalence is present (<2%) in some parts of North America (e.g. the United States, Canada and Mexico), in some European countries (e.g. Belgium, Czech Republic, Denmark, France) and in Australia (Schweitzer *et al.,* 2015). In the World Health Organization (WHO) European Region, approximately 13 million people are chronically infected with HBV, which leads to about 60,000 deaths a year from hepatitis B-related liver cancer and cirrhosis. Inmates in correctional facilities bear a greater burden of chronic viral infections and sexually transmitted diseases (Stasi *et al.,* 2016; Voller *et al.,* 2016) In general, high levels of viremia or infection, contracted at a young age, affect mostly males and are associated with an increased risk of death or developing hepatocellular carcinoma (Taylor *et al.,* 2009) The impact of screening programmes for viral hepatitis and HBV vaccination has significantly reduced viral hepatitis.

The rate of prevalence also varies from general population to homosexual, heterosexual and pregnant woman (WHO, 2017). In East Africa for instance, the prevalence rate among the general population is 8%, while the respective rate among the homosexual, heterosexual and pregnant woman were 9%, 6.5% and 4% (Table 2.1).

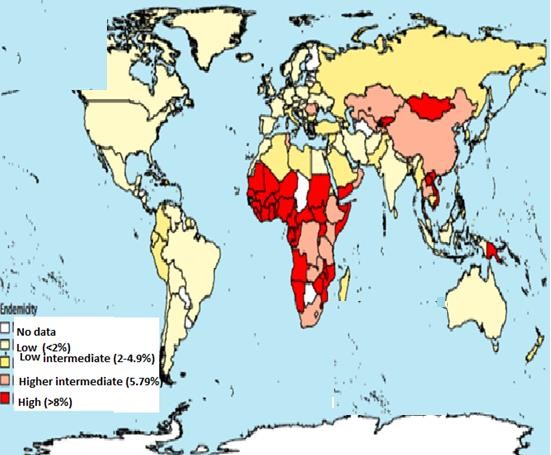
Africa has the second largest number of individuals with chronic HBV infection, approaching 58 million with over 90% of the population in some countries in western Africa including Senegal and Gambia being exposed to and become infected with HBV during their lives (WHO, 2017). The prevalence rate is as presented in Figure 2.5. 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.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Table 2.1**:**Summary of prevalence across risk groups and nation** | | | | |
|  | Gen. pop (%) | Homosexual  (%) | Heterosexual  (%) | Pregnant  (%) |
| East Africa | 8 | 9 | 6.5 | 4 |
| West, Central Africa | 11 | 22 | 12 | 9 |
| South Africa |  | 6.5 | 7 | 5 |
| Latin America | 1 | 9 | 3 | 0.5 |
| North America | 7 | 5 | 17 |  |
| South East Asia | 2 | 15 | 9 |  |
| Europe |  | 4 | 5 |  |
| East Asia |  | 12 | 5 |  |

Source: WHO (2017)

.



# FIGURE 2.5: Prevalence rate across Africa (WHO, 2017)

Umego *et al.,* (2018) has reported the prevalence rate found in HBsAg positive pregnant women in some unrelated studies in countries such as Senegal (1.6%), Zambia (2.2%), Ethiopia (4.7%), Tanzania (8.8%), Ghana (12.3%), South Africa (13.4%), Nigeria (13.6%) and Zimbabwe (17.1%). In the developed and developing countries alike, people at high risk for HBV include the following (Stasi *et al.*, 2017)

* + - 1. People who frequently require blood or blood products
      2. Dialysis patients
      3. Recipients of solid organ transplantations
      4. People interned in correctional facilities
      5. People who inject drugs
      6. People with household and sexual contact of people with chronic HBV infection
      7. People with multiple sexual partners
      8. Health care workers
      9. Travellers who have not completed their vaccination

# 2.7.2. Epidemiology in Nigeria

Research has shown that Nigeria with HBV prevalence of 13.6% can be classified as a highly endemic country (Henrietta and Maryam, 2016). Approximately eighteen million of the populace are said to be carriers of the virus in recent time (Gabriel and Austin, 2013). The percentage distribution of the adults and children over the entire populace between 2000 and 2013 were about 13.6% and 11.5% respectively (Musa *et al.,* 2015). A number of independent researchers have reported a high prevalence rate of 25.7%, 16.3%, 23.4% and 11% for blood donors, infants, surgeons and pregnant women respectively (Bada *et al.,* 1996; Belo, 2000; Mbaawuaga *et al*., 2008; Sadoh and Sadoh, 2013).

The data on hepatitis B prevalence on the general population in each state is rarely available, however, the prevalence rate among some particular groups (such as pregnant women and blood donor) in some states in each political zones (south west, south east, south-south, north central, north east and north west) of the country has been documented. The prevalence rate among pregnant women is generally considered low risk for HBV infection.

In the South west, the prevalence rate of the virus in pregnant women is 4.0%, 6.08% and 7.1%, in Ekiti, Lagos and Osun states respectively (Rabiu *et al.,* 2010; Awoleke, 2012, Opaleye *et al.,* 2014). Though, Osun state has the highest rate, the three state falls into the class of intermediate endemicity (2-7%). Among the blood donor, it has been reported that the prevalence rate is 8.0% and 8.3% for Ogun and Oyo states respectively (Okonko *et al.,* 2010; Anaedobe *et al.,* 2015). This indicated high endemicity (≥8%). The prevalence related hepatitis, liver cirrhosis and hepatocellular carcinoma. In another report, Lagos state was reported having prevalence rates of 14%, 30% and 56% for HBV related hepatitis, liver cirrhosis and hepatocellular carcinoma, respectively (Mbaawuaga *et al.,* 2008). Research has shown that Hepatitis B virus is the commonest cause of chronic liver disease in the southern part of the country as 58.1% of patients with chronic liver disease were HBsAg positive (Lesi, 2004).

In South-south Nigeria, pregnant women in Port Harcourt, Rivers state according to Obi *et al*. (2006) have a prevalence rate of 4.6%. The report by Utoo *et al.* (2013) claimed that the prevalence rates among pregnant women in Obudu, Cross River and Bayelsa states is 6.6% and 7.9% respectively.. A prevalence rate of 21.1% among blood donors was reported in Delta state (Osazua and Erhunwunselmade 2013). While PortHarcourt and Obuta can be categorized as intermediate endemicity, the values for Bayelsa signified the region is highly endemic as relates to HBV in blood donors.

In the South-east, independent researchers observed respective prevalence rates of 3.4%, 6.5% 7.1% and 7.6% for pregnant women in Enugu, Ebonyi, Abia and Anambra states (Ezegbudo *et al.,* 2004; Ikeako *et al.,* 2014; Onwuakor *et al.,* 2014; Nworie *et al.,* 2015). Like Lagos state, a similarly high prevalence rate was noted for Imo state where 50.7% of adults with clinical features of liver disease were confirmed to be carriers of HBV **(**Umego *et al*., 2018). This suggested that the virus to be responsible for higher percentage of liver cancer in the southern part of Nigeria.

In North Central Nigeria, the prevalence rate among the pregnant women in Kwara and Niger states was claimed to be 12.7% and 12.8%, respectively (Ndams *et al.,* 2008; Ogunlaja *et al.,* 2015). Benue state has a prevalence rate of 20.0% among blood donors (Alao *et al.,* 2009). Though, the figure indicated highest prevalence rate was observed in Benue, all the three sampled states fall into the class of high endemicity. In the North western region, Kaduna, Kano and Sokoto states, a prevalence rate of 3.9% was recorded (Taura *et al.,* 2008). In another report, prevalence rate in Sokoto was claimed to be 6.5% among pregnant women (Musa *et al.,* 2015). The values indicated the region fall into a class of intermediate endemicity.

In the North east, Bauchi State has a prevalent rate of 18% among the blood donors (Mojolagbe *et al.,* 2014). No data was available on pregnant women in the north east. However, there are data on children and students indicating prevalence rate of 8% among children in Maiduguri and 9% among general population of Mubi town Yola State (Okoye and Samba, 2006). Ndako *et al.* (2013) and Imaranezor *et al.* (2016) observed prevalence rates of 5.3% and 6% among students in Gombe and Taraba states while Isa *et al.* (2015) 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 observed a prevalence of 9% (Okoye and Samba, 2006). Yobe states has prevalence rate of 49% observed among students as reported by El- Ishaq and Liman (2015).

Aside the majorly targeted group (pregnant women and blood donors), prevalence rate for some other groups have been document. For instance, Kogi, Plateau and Nasarawa states have an a prevalence of 14.0%, 14.5% and 17.1% among farmers, HIV infected patients and female sex workers respectively (Umego *et al*., 2018). 6% of the patients with HIV in Kaduna, Kano and Sokoto states were also claimed to be carrier of HBV (Taura *et al.,* 2008; Aba and Aminu, 2016) In another report by Musa *et al*. (2015), the prevalence rate across certain categories, sub-group are as summarized below:

In another report by Musa *et al.* (2015) who conducted a research on the Nigerian population older than two (2) years of age of unknown human immunodeficiency virus status and resident in the community at the time of the survey. The results of his finding revealed that the prevalence of hepatitis B infection was 12.2% (CI = 10.3–14.5) depicting high level of hepatitis B endemicity in Nigeria. Prevalence however differs with subgroup. Olayinka *et al.* (2016) in a separate research reported difference prevalence rate. The values also indicated high prevalence in most of the subcategories

Olayinka *et al.* (2016) also reported Hepatitis B biomarkers among survey among the general population across the six geographical zone of Nigeria (Table 2.2). Of the participants, more than half, 527 (54.6%), had evidence of previous exposure to the HBV (HBcAb), 355 (36.8%) demonstrated the presence of protective antibodies (HBsAb) in their serum while 306 (31.7%) showed no serologic evidence of infection or vaccination. Seventy-six (7.9%) participants showed serologic evidence of being immune to HBV through vaccination. Only seven (23.3%) of those who reported having received up to three doses of HBV vaccine showed serologic

evidence of immunity due to vaccination; 279 (28.9%) of them showed serologic evidence of being immune to HBV through natural infection

# Table 2.2: Hepatitis B biomarkers among the general population across the six geographical zone of Nigeria (N = 965)

|  |  |  |
| --- | --- | --- |
| **Biomarker** | **Frequency** | **% (95% Cl)** |
| HBsAg | 118 | 12.2 (10.3-14.5) |
| HBsAb | 355 | 36.8 (34.5-40.7) |
| HBcAb | 527 | 54.6 (52.6 – 58.9) |
| HBsAb+ve and HBsAg  -ve and HBcAg -ve | 76 | 7.9 (16.1 – 24.1) |
| HBsAb+ve and HBsAg  -ve and HBcAg +ve | 249 | 25.8 (23.6 – 29.2) |
| HBsAb-ve and HBsAg  -ve and HBcAg -ve | 306 | 31.7 (29.5-35.4) |

Source: Olayinka *et al.* (2016)

# Serological Markers

Hepatitis B virus diagnosis is established by a specific serologic profile and this involves measurement of a number of HBV-specific antigens and host antibodies that react to these antigens (Mahoney, 1999). The interpretation of the results is often complex, and many possible outcomes based on the individual responses may exist. The outcomes of the serologic tests can determine whether a patient is prone to infection, has developed immunity due to recovery from a previous infection or vaccination, acutely infected, or chronically infected (Mast *et al.*, 2006). HBV incubation period may last for an average of 12 weeks (Mizukoshi *et al.*, 2015).

The clinical course of an HBV infection includes the incubation period (generally 4-12 weeks), acute illness (2 weeks -3 months) and recovery for individuals who resolve their function. Many HBV infections in adults are without the classical symptoms of jaundice. Individuals in whom HBsAg is present in their blood for more than six months are considered to be chronically infected with HBV. Serological profiles of acute and chronic HBV infections are presented in Figure 2.6, 2.7 and 2.8

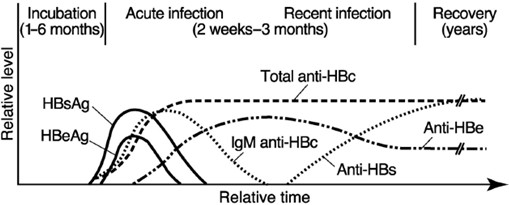


Figure 2.6 Acute HBV infection Source: Towell and Cowie (2012)

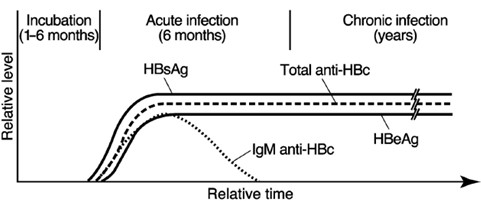


Fig 2.7 Chronic HBV infection (HBeAg positive) Source: Towell and Cowie (2012)

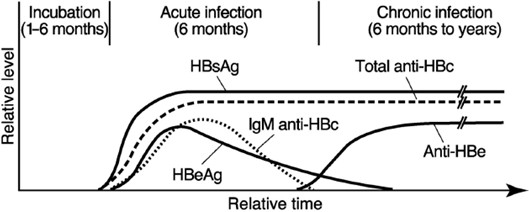


Fig 2.8 Chronic HBV infection (HBeAg negative) Source: Towell and Cowie (2012)

Screening for hepatitis B virus (HBV) infection involves measurement of distinct HBV-specific antigens and host antibodies that react to these antigens and these appear in a typical pattern (Weinbaum *et al.*, 2008). The first serologic marker to be detected is hepatitis B surface antigen (HBsAg). It can be detected in serum as early as 1 to 12 weeks after infection and HBeAg becomes evident shortly after (Liang, 2010). The presence of HBV DNA can also be detected by a serum assay for HBV DNA prior to the detection of HBsAg or HBeAg but it is generally not performed when it comes to diagnosing acute infection (Liang, 2010). The presence of HBeAg is an indication of infectivity or transmissibility unlike HBsAg which neither represents viral replication or infectivity [(www.c](http://www.cdc.gov/hepatitis))d[c.gov/hepatitis).](http://www.cdc.gov/hepatitis)) Nonetheless very limited data are available on the seroprevalence of HBeAg among Nigerian population and inmates in particular.

Antibodies to hepatitis B core antigen (anti-HBc IgM) appear just about the time that clinical symptoms develop (Towell and Cowie, 2012). Anti-HBc IgM in the serum decline to undetectable levels within 6 months, but antibodies to hepatitis B core antigen IgG class (anti- HBc IgG) persists indefinitely as a marker of previous HBV infection. For patients with resolved

HBV infection, the HBsAg disappears at about 3 to 6 months prior to the detection of antibodies to hepatitis B surface antigen (anti-HBs) (Gitlin, 1997). The presence of anti-HBs after an acute infection basically indicates recovery and protective immunity against re-infection (Center for Disease Control and Prevention (CDC), 2014). Also HBeAg disappears, antibodies to hepatitis B e antigen (anti-HBe) develop and these patients have persistence of anti-HBc (predominantly consisting of IgG) for life (Lee, 1997). Therefore presence of HBsAg beyond 6 months after infection and also the detection of HBsAg along with the absence of IgM anti-HBc in a single serum specimen is also indicative of chronic HBV infection (Towell and Cowie, 2012). Therefore chronic or persistent HBV infection with HBsAg and anti-HBc IgG generally persist for life. While the detection of anti-HBc IgM indicates recent, acute infection of less than 6 months duration, non-reactive anti-HBc IgM does not rule out chronic infection. The use of anti- HBc IgM to determine transmission may not be completely efficient in that inmates who were infected within the facility but have been infected for more than 6 months will go undetected and also recently infected inmates who have been in correctional facilities not more than 6 months who got infected just before incarceration will give a false picture. Therefore transmission within the correctional facilities will also depend on the duration of incarceration.

# Interpretation of Hepatitis B Serologic test results

* + - 1. **Hepatitis B surface antigen (HBsAg):** The interpretation of the hepatitis B serologic test results is shown in Table 2.3. A protein on the surface of hepatitis B virus; it can be detected in high levels in serum during acute or chronic hepatitis B virus infection. The presence of HBsAg indicates that the person is infectious. The body normally produces antibodies to HBsAg as part of the normal immune response to infection. HBsAg is the antigen used to make hepatitis B vaccine.
      2. **Hepatitis B surface antibody (anti-HBs):** The presence of anti-HBs is generally interpreted as indicating recovery and immunity from hepatitis B virus infection. Anti- HBs also develops in a person who has been successfully vaccinated against hepatitis B.
      3. **Total hepatitis B core antibody (anti-HBc):** Appears at the onset of symptoms in acute hepatitis B and persists for life. The presence of anti-HBc indicates previous or ongoing infection with hepatitis B virus in an undefined time frame.
      4. **IgM antibody to hepatitis B core antigen (IgM anti-HBc):** Positivity indicates recent infection with hepatitis B virus (< 6 month). Its presence indicates acute infection Hepatitis B serologic testing involves measurement of several hepatitis B virus (HBV)-specific antigens and antibodies. Different serologic ―markers‖ or combinations of markers are used to identify different phases of HBV infection and to determine whether a patient has acute or chronic HBV infection, is immune to HBV as a result of prior infection or vaccination, or is susceptible to infection. The interpretation of possible combinations of the biomarkers is presented in Table 2.4

# Table 2.3 Interpretation of Hepatitis B Serologic marker

|  |  |  |
| --- | --- | --- |
| Markers | Results | Interpretation |
| HBsAg | negative | Susceptible |
| anti-HBc | negative |  |
| anti-HBs | negative |  |
| HBsAg | negative | Immune due to natural infection |
| anti-HBc | positive |  |
| anti-HBs | positive |  |
| HBsAg | negative | Immune due to hepatitis B vaccination |
| anti-HBc | negative |  |
| anti-HBs | positive |  |
| HBsAg | positive | Acutely infected |
| anti-HBc | positive |  |
| IgM anti-HBc | positive |  |
| anti-HBs | negative |  |
| HBsAg | positive | Chronically infected |
| anti-HBc | positive |  |
| IgM anti-HBc | negative |  |
| anti-HBs | negative |  |
| HBsAg | negative | Interpretation unclear; four possibilities: |
| anti-HBc | positive | 1. Resolved infection (most common) |
| anti-HBs | negative | 2. False-positive anti-HBc, thus susceptible |
|  |  | 3. ―Low level‖ chronic infection |
|  |  | 4. Resolving acute infection |

**Source:** CDCP (2020)

# Table 2.4: Serological markers and the interpretation of possible combination

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **HBsAg** | **HBsAb** | **HBcAb** | **HBeAg** | **HBeAb** | **Interpretation** |
| 1. Detected | Not Detected | Detected | Detected | Not Detected | Either acute or chronic active HBV infection with ongoing high level  replication |
| 2. Detected | Not  Detected | Detected | Not  Detected | Detected | HBV carrier but usually  with low replicate as |
| 3. Not Detected | Detected | Detected | Not Detected | Detected | Probable resolved HBV infection. The presence of HBcAb indicates past  exposure to the virus |
| 4. Not Detected | Not Detected | Detected | Not Detected | Not Detected | A need to repeat test, false positive results or indicate patient has had HBV in the distant and have lost all the  serological markers |
| 5. Not Detected | Not  Detected | Detected | Not  Detected | Not  Detected | Immunity that is long  lasting |

Source: CDCP (2020)

# Routes of Transmission and Care

# Lifestyle advice

Smoking and excessive alcohol consumption are associated with a poorer prognosis in chronic HBV infection and patients should be offered lifestyle advice accordingly. Patients should be advised on the prevention of other blood-borne viruses, and vaccination against hepatitis A should be offered to those not already protected as a result of previous immunization or infection (Salisbury *et al.,* 2006). Ongoing review of patients in Phases 1–5 is required in order to monitor changes in disease phase or the development of liver complications (Table 2.5).

* + 1. **Routes of transmission worldwide:** In sub-Saharan Africa and east Asia, transmission predominantly occurs in infants and children by the perinatal and horizontal routes (i.e. resulting from close contact that is not parenteral, perinatal, or sexual in nature) whereas in more industrialized countries, rates of new infection and acute disease are highest among young adults and transmission predominantly occurs via injecting drug use and other high-risk behaviours. Worldwide, the majority of infections are acquired at birth or in early childhood.
    2. **Low rates of diagnosis:** Majority of people are unaware of their HBV infection, and therefore often present with advanced disease. At present, there is a massive burden of undiagnosed and untreated hepatitis B, with 89.5% of infected persons unaware of their status on global scale, though, the value varies greatly by region (WHO, 2020). By contrast, the estimated awareness of status among people living with HIV is within 84%, though the value also varies significantly with countries (UNAIDS, 2020).
* Based on still limited studies, overall <15% of the estimated 180 million who are chronically infected with HCV are aware of their diagnosis, based on data from higher- income setting – United States, Europe and China.
* And from a survey in the US, a similar proportion of those with chronic HBV infection are aware of their diagnosis.
* The proportion in low-income settings is even higher, with only a tiny fraction diagnosed and aware.

Table 2.5: Phases of HBV infection

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Phase of Infection | ALT |  | HBV DNA |  | HBeAg |  | HBsAg |  | Liver histology |  | Comment |  |
|  |  | 1. Immune tolerant | Normal |  | High |  | Positive |  | Positive |  | Normal or mild inflammation |  | May be short or absent in infection acquired during  adulthood |  |
|  |  | 2. HBe antigen- positive CHB (immune  reactive) | High |  | Moderate/h igh |  | Positive |  | Positive |  | Chronic inflammation |  | May last from weeks to several years |  |
|  |  | 3. Low replicative phase (Inactive carrier | Nor mal |  | Low/undet ectable |  | Negative |  | Positive |  | Depend on complications incurred in  previous phase |  | Reactivation into phase 2 or 4 possible |  |
|  |  | 4. HBe antigen- negative CHB | Periodicall y high |  | Moerate high/fluctu  ating |  | Negative |  | Positive |  | Chronic inflammation |  | Can be difficult to distinguish from phase 3 due to fluctuating  viral load |  |
|  |  | 5. HBsAg-negative phase (past infection) | Normal |  | Low/undet ectable |  | Negative |  | Positive |  | Depends on complication incurred in  previous phases |  | Immunosuppression may lead to reactivation |  |

Source: EASL (2009)

# Approaches to Screening

There are three key approaches to screening. The approaches are as follow:

# Population- or community-based screening (including antenatal)

This means that all members of the population have access to the screening programme under consideration. It may also include home-based testing (house to house); campaigns (e.g. HTC plus – malaria, safe water, non-communicable diseases e.g. diabetes and hypertension); outreach (mobile) in general and key populations; workplaces and schools; and health-care facility based screening.

# Health-care facilities

Testing could also be offered in special dedicated clinics, e.g. HIV, STI clinics. Screening at health-care facilities may include primary care settings, inpatient and outpatient settings, and may involve screening on the basis of clinical presentation or focus on only those with abnormal liver function tests, abnormal ultrasound scan, family history of liver disease or other clinical suspicion of liver function test.

* + 1. **Targeted risk factor-based screening.** This refers to screening of specific groups including key populations, who are generally at higher risk of being infected than the general population. This includes people who inject drugs (PWID), people in correctional facilities and other closed settings, migrant populations, some indigenous populations, MSM and sex workers, but may also include health-care workers. People attending services providing care and treatment for viral hepatitis or HIV can be encouraged to bring their partners to be tested.

# Progression of Chronic Hepatitis B (CHB)

CHB has a very variable course, ranging from silent subclinical infection to persistent hepatitis with progressive fibrosis leading to cirrhosis, liver failure and/or liver cancer. The determinants

of disease outcome are incompletely understood, but include viral, host, and environmental factors (Table 2.6), all of which interact (Feld and Janssen, 2015). Viral determinants of the prognosis have different significance depending on the stage of the disease. For example, serum HBV DNA titers are highest in the immune-tolerant phase of disease, despite the lack of hepatic inflammation or progressive fibrosis during this period (Peng *et al.,* 2012). In contrast, in HBeAg-negative CHB, the higher the HBV DNA level, the greater the risk of disease progression and hepatocellular carcinoma (HCC) (Peng *et al.,* 2012). The rates of progression to cirrhosis and HCC and associated mortality rates are shown in Fig. 2.9.

# Table 2.6: Progression of Chronic Hepatitis B

|  |  |  |
| --- | --- | --- |
| **Viral factors** | **Host factors** | **Environmental factors** |
| HBV genotype | Age | Aflatoxin |
| HBV DNA titer (varies with  phase) | Age at infection | Alcohol use |
| HBeAg status | Sex | Viral coinfections (HIV,  HCV, HDV) |
| Presence of pre-core or BCP  mutation | Ethnicity | Obesity |
| Presence of pre-S1 mutations | Family history of HCC | Iron overload |

BCP, basal core promoter; HBeAg, HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; HDV, hepatitis D virus; HIV, human immunodeficiency virus.

Source: Feld and Janssen (2015)

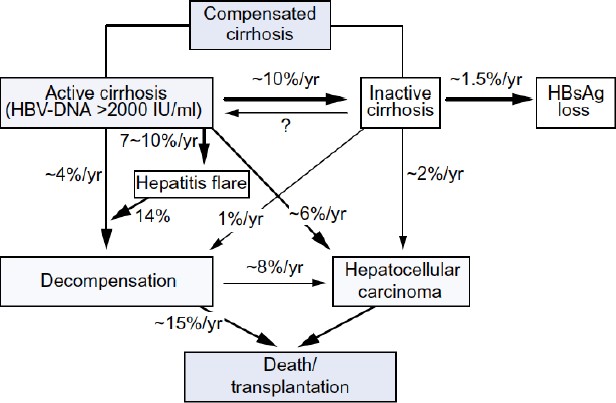


Fig. 2.9 Risk of progression in patients with HBV-related cirrhosis Source: Peng *et al.* (2012)

# Diagnosis and Monitoring of Hepatitis B

# Cascade—acute hepatitis B

The diagnosis of acute hepatitis B is based on the detection of HBsAg and anti-HBc (immunoglobulin M). During the initial phase of infection, markers of HBV replication such as HBeAg and HBV DNA are also present. Recovery is accompanied by the disappearance of detectable HBV DNA, HBeAg seroconversion to anti-HBe, and subsequent clearance of HBsAg and lastly appearance of anti-HBc (IgG) (Feld and Janssen, 2015). The course of acute HBV takes place within 3 months of the diagnosis-chronic HBV infection is characterized by persistence of plasma HBsAg for more than 6 months. Rarely, patients present during the

window period when HBsAg has already become negative but antibodies are not yet positive. In this setting, which is more common in patients with fulminant hepatitis B, in whom viral clearance tends to be more rapid, immunoglobulin M (IgM) HBeAb is the sole marker of acute HBV infection. The differential diagnosis of HBsAg-positive acute hepatitis includes exacerbations of CHB, which may occur at any time in any individual who is chronically infected (at these times, reversion back to anti-HBc IgM may occur). Acute hepatitis may occur following withdrawal from immunosuppressive therapy or through superinfection of a person chronically infected with hepatitis B with hepatitis C and/or D virus, or hepatitis A virus. Superimposed acute hepatitis due to drugs and other toxins administered to someone who has

―silent‖ CHB infection may also present as acute hepatitis. A precipitating factor is sometimes not identified (Feld and Janssen, 2015).

# Resolved HBV infection

Previous HBV infection is characterized by the presence of anti-HBs and IgG anti-HBc. Anti- HBs sometimes becomes undetectable after many years. (Anti-HBs is frequently undetectable if HBV infection occurred during childhood, as is seen in sub-Saharan Africa). Notably, although these individuals are referred to as having ―resolved HBV‖ infection, trace amounts of HBV DNA remain in their livers for years and possibly even lifelong (Feld and Janssen, 2015).. Immune control prevents viral expansion, but means that with severe immunosuppression (e.g., with advanced human immunodeficiency virus (HIV) coinfection, bone marrow transplantation, rituximab use, etc.), HBsAg may reappear (reverse seroconversion) or viral replication may be detectable in the liver even without the reappearance of serum HBV DNA. Immunity to HBV infection after vaccination is characterized by the presence of only anti-HBs (Feld and Janssen, 2015).

# Treatment

The goal of treatment is clearance of HBV DNA (and, if possible, clearance of HBeAg and HBsAg) to prevent the development of cirrhosis, liver failure and HCC (Jafri and Lok, 2010). Long-term treatment is often required, although some individuals maintain a low or undetectable HBV DNA level .6 months after stopping treatment, which is classed as a ‗sustained virological response‘ (SVR). Complete eradication of HBV infection does not occur, due to the persistence of HBV DNA within the nuclei of host hepatocytes (Di Marco and Craxi, 2009). Treatment should be considered for patients in either the HBeAg-positive CHB or the HBeAg-negative CHB phases and those with cirrhosis, irrespective of HBeAg status (Jafri and Lok, 2010). Treatment is not indicated for individuals in the immune tolerant phase, where liver damage has not yet occurred. The phase of infection or extent of liver damage may be difficult to assess, in which case a liver biopsy can be helpful. Patients and clinicians are often keen to avoid liver biopsy, and new non-invasive tests, including serum markers and transient elastography (fibroscanning), may avoid the need for biopsy in the future.

# Available treatments

There are currently seven drugs available for the treatment of CHB: five nucleotides analogues (NUCs) (lamivudine, adefovir, entecavir, tenofovir and telbivudine) and two interferon-based therapies (conventional interferon and pegylated interferon alpha). NUCs suppress viral replication by inhibiting HBV viral polymerase whereas interferon therapy works by enhancing the host immune response. The two main treatment strategies are finite therapy with interferon or NUC therapy (for those who maintain an SVR off treatment), or long-term therapy with one or more NUCs, for those with cirrhosis or who do not maintain an SVR (Di Marco and Craxi, 2009).

# Nucleotide analogues therapy

Nucleotide analogue therapy has a good side-effect and safety profile but there is a considerable risk of viral resistance (Liaw and Chu, 2009). Long term studies of lamivudine therapy have shown that treatment reduces the incidence of cirrhosis and HCC compared to untreated controls. However, long-term data on the effects of other NUCs are limited due to their relatively recent introduction into clinical practice (Liaw, 2009). The EASL currently recommends either entecavir or tenofovir as first-line monotherapy, given their antiviral potency (67–90% and 60– 88% have undetectable HBV DNA at 1 year respectively), and a much more favourable resistance profile compared with the previous first-line treatment, lamivudine (EASL, 2009). Lamivudine can still be used for the prevention of HBV reactivation in those undergoing immunosuppressive therapy (Carey and Harrison, 2009). Adefovir can be used (sometimes in tandem) in patients already on lamivudine who are showing signs of antiviral resistance (Carey and Harrison, 2009). Telbivudine has not been recommended in the UK for the treatment of chronic HBV due to unacceptably high levels of viral resistance (Aspinall *et al.,* 2011). There is currently a lack of evidence for the superiority of de novo combination NUC therapy over monotherapy in treatment naı¨ve patients. However, some experts recommend the use of de novo combination therapy in those with a high risk of viral resistance, or in patients with cirrhosis, for whom the development of resistance may have life-threatening consequences (EASL, 2009).

# Interferon therapy

The advantages of interferon therapy are the absence of viral resistance, the finite course of treatment (normally 48 weeks) and an increased chance of SVR and HBeAg and HBsAg clearance compared with those taking NUC therapy (Carey and Harrison, 2009) Long-term studies have demonstrated that interferon treatment is associated with a significant reduction in

the risk of cirrhosis and HCC, even in those who fail to clear HBeAg (Liaw, 2009) However, interferon has a poor side-effect profile (including persistent flu-like symptoms and psychiatric complications) compared with NUC therapy, requires subcutaneous injection and is not recommended for patients with decompensated cirrhosis. The use of interferon is therefore restricted to patients who are most likely to benefit; in particular, younger patients who have more potential years in which to develop complications from their CHB and thus have more to gain from achieving an SVR (Aspinall *et al.,* 2011).

# Genotype and prediction of treatment success

Genotypes A and B may be associated with a better response to interferon therapy, although the clinical trials that showed this association were not designed to look at the effect of genotype and may be confounded by ethnicity (Aspinall *et al.,* 2011). The success of NUC therapy does not appear to be associated with genotype (Raimondi *et al.,* 2010).

# Treatment in children

Treatment should be considered as soon as there is evidence of the immune reactive phase, regardless of the patient‘s age (Giacchino and Cappelli, 2010). Interferon therapy, lamivudine and adefovir are approved for use in children, but the newer antivirals (tenofovir and entecavir) have not yet been fully evaluated in younger children and are only recommended for individuals

.15 years of age (Giacchino and Cappelli, 2010). Treatment monitoring On-going review is recommended to monitor side-effects, alter treatment dosage and check adherence to the prescribed regimen. In compliant patients, a detectable HBV DNA following initial clearance (virological breakthrough) should raise the suspicion of viral resistance (EASL, 2009).

# Pregnancy

Treatment in women of childbearing age should take into account the likelihood of spontaneous reversion, the anticipated duration of treatment and the immediacy of pregnancy plans (Jafri and Lok, 2010). Treatment of pregnant women with antivirals is sometimes considered, but interferon therapy is contraindicated in pregnancy. The most recent EASL guidelines suggest testing the viral load in HBeAg positive mothers and considering the use of antivirals in the mother in the third trimester to reduce the viral load and vertical transmission (EASL, 2009). HBV infected women should be monitored closely after delivery as exacerbations of CHB may occur (Ter Borg *et al.,* 2008).

# Treatment of acute HBV

Most cases of acute HBV can be managed with supportive treatment, although there is some evidence that NUC therapy can improve prognosis in patients with severe or fulminant infection (EASL, 2009).

# Future developments

Valtorcitabine (a prodrug of telbivudine) and pradefovir (a prodrug of adefovir) are currently in Phase II clinical trials. However, there are no current developments that are likely to offer a significant improvement over existing regimens (Takkenberg *et al.,* 2010). The limited treatment options emphasize the importance of starting treatment at an appropriate time and encouraging patient compliance, in order to minimise the risk of antiviral resistance (Lai and Liaw, 2010).

# Prevention of HBV Infection

# Vaccination

Safe and effective hepatitis B vaccines containing inactivated HBsAg have been available since the early 1980s. The first vaccines were plasma derived; however, these have been replaced over

the years by vaccines manufactured in yeast or mammalian cells using recombinant DNA technology (Aspinall *et al.,* 2011). In general, the vaccine is administered using a three-dose schedule. Vaccine efficacy (defined as anti-HBs concentration of 10 mIU/ml) is greatest in infants, children and young adults—with protective antibody levels achieved in 95% of those vaccinated (Aspinall *et al.,* 2011). After the age of 40 years, the proportion of persons who have a protective antibody response following vaccination declines to 90% and to 75% in those vaccinated over the age of 60 years (Nguyen and Tran, 2009). Other factors associated with a reduced response to vaccination include immunosuppression, liver disease, renal failure, smoking and obesity (Aspinall *et al.,* 2011). Protection conferred by hepatitis B vaccination has been shown to be long lasting, with the risk of HBV infection significantly reduced even when anti-HBs concentrations decline to10 mIU/ml over time (WHO, 2009).

# HBV vaccination programmes

In 1992, the WHO recommended that all countries should introduce universal HBV vaccination into their routine immunization programmes (Aspinall *et al.,* 2011). The impact of universal infant HBV vaccination has been reported in a variety of countries and settings. In general, studies in high endemicity areas have shown a decline in the prevalence of CHB infections in children to 2%, and a reduction in the incidence of HCC in children and young adults has also been reported in some South East Asian countries where universal infant vaccination programmes have been in operation for up to 20 years (Chen, 2010).

In the USA, the number of newly acquired HBV infections has declined substantially since the introduction of a national immunization strategy which includes the universal vaccination of infants beginning at birth and the identification and vaccination of adults at increased risk of

infection (Nguyen and Tran, 2009). Between 1990 and 2007, the annual incidence of HBV infection in the USA declined by .80% overall, and by 98% in children, 15 years old (CDC, 2009). In Europe, studies in Italy and Bulgaria have demonstrated a dramatic decline in the incidence of acute HBV infections and the prevalence of CHB following the introduction of universal HBV vaccination programmes (Aspinall *et al.,* 2011). As of 2008, 177 of 193 WHO member states (92%) had integrated HBV vaccination into their national infant vaccination schedules (WHO, 2009). In Europe, 22 of 29 EU/EEA countries have implemented a universal infant or adolescent HBV vaccination programme. The remaining seven countries, including the UK, have adopted a selective vaccination programme targeting at-risk groups based on the local epidemiology of HBV infection (ECDC, 2010).

# CHAPTER THREE

* 1. **MATERIALS AND METHOD**

# Study Area

Niger state is situated in the North central part of Nigeria (Figure 3.1). The capital of the state is Minna, which is located on latitude 9.62, latitude 6.55 and it is situated at an altitude of 243 m above the sea level. The State has an estimated population of 3,950,249 based on the 2006 Census (State Bureau of Statistics, 2011). The state housed about 350 inmates. Correctional facilities s form part of the criminal justice system and it is estimated that over nine million people are in penal institutions worldwide, with 74, 000 incarcerated in Nigeria in about 250 correctional facilities (Alkali *et al.,* 2017).

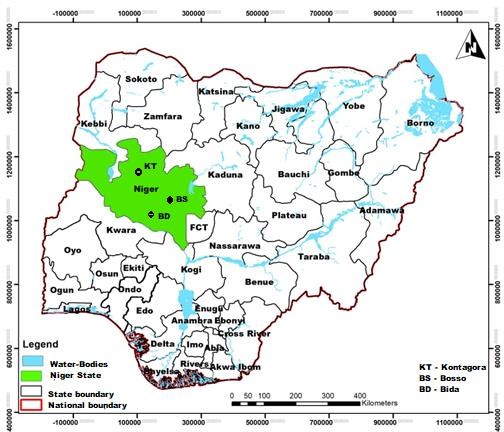


Figure 3.1: Study Area

Niger state has seven correctional facilities centers which are Minna Old Prison, Nigeria Prison Services, Bida, Kagara Prison, Lapai Prison, Agaie Prison, Kontagora Prison and Medium Security Prison Minna. However, the study was carried out in Minna old Prison, Nigeria Prison Services, Bida and Kontagora Prison. Niger State has three senatorial districts (Niger East, North and South) and the correctional facilities were built across the districts.

# Methods

# Study design

For the study on the detection of the prevalence of HBV in correctional facilities in Niger State, all the blood samples collected were carefully characterized using ICT and ELISA to detect HBsAg seropositive inmates from three correctional facilities in the state. All the HBV infected inmates were further tested with serological markers, since markers suggest the level of infections (chronic or acute) as well as evidence of being immune to HBV. Data such as duration of incarceration, risk behaviours, and nature of the prison environment obtained through a standardized questionnaire (Appendix A) were documented. These thus formed the cross- sectional study basis for this study.

# Study population

During the study, a random selection procedure was used in selecting correctional facilities within the state. The selection was first stratified by size of correctional facility and thereafter three (3) out of seven (7) available correctional facilities were deliberately selected. The selection was done in a way that each of the senatorial districts of the state was adequately represented. More so, the choice of the chosen correctional facilities was informed by the size of the inmates, hence, correctional facility with highest population was chosen. The three correctional facilities have about 500, out of which 344 consented to participate in the study. The

inmates involved in the study consist of a total of 328 male and 16 female. The study population comprised of HBV infected individuals in the three correctional facilities considered; the Minna Old Prison, Nigeria Prison Services, Bida and Kontagora.

# Sample size

Sample size estimation is fundamental in the design of a prevalence studies. To estimate the prevalence of HBV in the three correctional facilities, determination of sample size was done since it is not realistic to simply perform the diagnostic test on the whole population. In this study, sample size estimation was done using the equation reported in Arya *et al.* (2012).

𝑛 =

(𝑍2)𝑃(1 − 𝑃)

𝑑2

Where n = sample size,

z is the z statistic for the level of confidence and the value = +1.96;

P is the expected prevalence and based on the previous study the value = 30% and; d is the allowable error, which is 5%

𝑛 =

(1.962) \* 0.3 \* (1 − 0.3)

0.052

n = 323

# Ethical clearance

Approval was sought from the Ethical Committee of General Hospital, Minna (Appendix B) and correctional facility authority.

# Inclusion criteria

Inclusion criteria include inmates‘ willingness to give an informed consent to partake in the study. However, those who did not consent to partake were excluded. The consent form is shown in Appendix C.

# Laboratory Analysis

All the collected blood samples were first analysed using rapid immunochromatography kit after which the negative samples were further screened using ELISA. All the positive HBV positive samples were further tested with the serological markers. The analysis were done at General Hospital Minna and Center for Genetic Engineering, FUTMinna

# Rapid chromatographic immunoassay test principle

The HBsAg One Step Hepatitis B Surface Antigen Test Strip (Serum/Plasma) is a qualitative, lateral flow immunoassay for the detection of HBsAg in serum or plasma. The membrane is pre- coated with anti-HBsAg antibodies on the test line region of the strip. The mixture migrates upward on the membrane chromatographically by capillary action to react with anti-HBsAg antibodies on the membrane and generate a coloured line. The presence of this coloured line in the test region indicates positive result, while the absence indicates a negative result. To serve as a procedural control, a coloured line will always appear in the control line region indicating that proper volume of specimen has been added and membrane wicking has occurred. So, basically their mode of action is based on common principle of antibody present in the test serum or plasma reacting with the protein coated particle and migrating upward on a membrane chromatographically by capillary action to react with recombinant antigen present on the membrane thereby generating a colour line in the test region (Adeyemi *et al.,* 2013).

# ELISA test principle

The RecombiLISA HBsAg ELISA is a solid –phase enzyme-linked immunosorbent assay based on principle of antibody sandwich technique for the detection of HBsAg in human serum or plasma.

The RecombiLISA HBsAg ELISA Test is composed of two key options:

1. Solid microwells pre-coated with monoclonal antibodies against HBsAg
2. Liquid conjugate composed of polyclonal HBsAb conjugated with horseradish peroxide (HRP-HBsAb conjugate)

During the assay, the test specimen and HRP-HBsAb conjugate are incubated simultaneously in the anti-HBs antibody coated microwells. The HBsAg, if present in the specimen, bind to the anti-HBs antibody, as well as the HRP-HBsAb conjugate, and form a sandwich conjugate complex.

Any unbounded antigen or conjugate was then removed by washing. TMB substrate was then added to the microwells, and the presence of the conjugate complex was shown by the development of a blue color resulting from a reaction between the enzyme and the substrate. This reaction is then quenched upon addition of the stop solution, and the absorbance value for each microwell was determined using a spectrophotometer at 450/620-690nm.

# Materials and reagents preparation

The materials and reagents used for the analysis are as listed below;

* + - * 1. Pipettes capable of delivering 50micro-litre and 100microlitre with a precision better than 98.5%
        2. Microplate reader with a bandwidth of 10 nm or less and an optical density range of 0-2.5 or greater at 450 nm wavelength is acceptable.
        3. Absorbent paper for blotting the microwells.
        4. Timer
        5. Distilled or ionized water.

# Preparations of the reagents

All reagents including the controls were brought to room temperature (18-28 o C). The wash buffer was prepared and was warmed up (30x concentration) at 37 o C when the precipitants

became visible. The concentrated wash buffer was then diluted 30 fold with water as shown in Table 3.1. Each reagent was mixed before adding to the test wells

Table 3.1: Dilution of concentration wash buffer

|  |  |  |  |
| --- | --- | --- | --- |
| Plate | Dl water | Wash buffer(30X) | Final volume |
| 1 strip | 58 ml | 2 ml | 60 ml |
| 2 strips | 116 ml | 4 ml | 120 ml |
| 3 strips | 174 ml | 6 ml | 160 ml |
| 4 strips | 232 ml | 8 ml | 240 ml |

The number of microwells needed was determined and marked on the ELISA working sheet with the appropriate information. Positive and negative controls were run in duplicate to ensure accuracy.

# Storage and stability

All reagents except the concentrated wash buffer are ready to use as supplied. Store all components to 2-80C. Do not freeze. Avoid strong light. Ensure that the reagents are brought to room temperature before opening. Reseal the microwells after removing the desired number of wells. Place unused wells in the resealable plastic bag provided and return to 2-8 degree celcius. Once opened, the kit is stable for 8 weeks at 2-80C, or until the labeled expiration date, whichever is earlier.

# Samples Collection and Transportation

Five milliliters (5ml) of venous blood samples was collected from each subject using a sterile 5 ml Syringe and needle. The blood samples was collected and transferred into clean EDTA

samples bottles and transported to the lab where plasma was separated from cells within an hour. The plasma was transferred to red-top or serum-separator. The plasma were refrigerated for further use and parts of the specimen that will be stored longer than 24 hours was frozen at  – 20C. During sample collection, about 300 structured questionnaires on the general awareness of HBV infection were administered to the inmates.

# 3.3.5. Assay of Plasma Samples Procedure

The desired number of microwells was calculated. Wells were numbered including one Blank (e.g. A1), three Negative control (e.g. B1, C1, D1), and for two Positive control (e.g. E1, F1). Specimen was added to the microwells according to the designation on the ELISA Working sheet. No reagent was added to the blank well. 50 ul of HBsAg positive, negative control were added into the designated control wells, respectively. 50 ul of test specimens were added into each test wells respectively. 50 ul of the HRP-HBsAb conjugate were added to each well, except the blank well. The wells were gently mixed for 20 seconds and the plate was covered with a sealer.

oThe microwells were then incubated at C for 90 minutes. The microwells were then washed

37

manually by carefully removing the incubation mixture and depositing the solution into a waste container. Each of the microwells were then filled with 350 ul diluted wash buffer and mixed gently for 20 seconds. The wash solutions were then discarded completely. The procedure was repeated 4 more times. After completing the last wash step, the plate was tapped on the absorbent paper to remove residual liquid. 100ul of TMB substrate was added into each well. It was then

oincubated at C in dark for 20 minutes. The reaction was then stopped by adding 100ul of stop

37

Solution to each well. It was gently mixed for 30 seconds ensuring that all the blue color completely changes to a yellow colour. The microplate reader was then set to wavelength of

450nm. The absorbent (OD) of each well then measured against the Blank Well was added within 15 minutes after adding stop solution. A filter of 620-690 nm was used as a reference wavelength to optimize the assay result.

# Interpretations of ELISA Result

* + - 1. Setting up the cut-off value The cut-off value =0.08 + N

Where N: Mean OD of the negative control. Use 0.05 for calculation of the cut-off value if less than 0.05

* + - 1. Calculation of specimen OD ratio

OD ratio was calculated for each specimen by dividing the OD value by the cut-off value as follows:

Specimen OD ratio = specimen OD / cut-off value

* + - 1. Assay validation

The mean OD value of the HBsAg positive controls should be < 2.0

The mean OD value of the HBsAg negative controls should be < 0.10

* + - 1. Interpretation of result Specimen OD ratio Negative <1.00

Positive >1.00

* + - * 1. A negative result indicates that there is no detectable HBsAg in the specimen.
        2. Specimens with OD ratio > 1.00 are initially considered to be positive by the RecombiLISA HBsAg ELISA

# Serological Marker Test Principle

The product (micropoint rapid diagnostic test kit) uses the colloidal gold and membrane chromatography technology, and measures HBsAg, HBeAg and HbsAb in serum with dual- antigen sandwich method, and measures HBeAb and HBcAg with neutralization competitive inhibition method.

# Diagnostic kit for HBV serological marker

The procedure was carried out according to the manufacturer‘s instructions. All reagents were brought to room temperature (300 C) before use. Protective clothing and disposable gloves will be worn while handling the kit reagents and clinical specimen. After performing the test hands will be washed thoroughly. The plasma collected from the EDTA containers was used. The test device will be placed on a clean flat surface. Each test device will be numbered with a specimen‘s ID number. The right side of the test board was kept horizontal from the original package, from left to right, respectively corresponding to HBsAg, HBsAb, HBeAg, HBeAb, HbcAb. A small straw was used to take subject plasma, and add into 5 sample wells of the test boards by drops (70ul per well or 2 drops). The timer was set for 15minutes. The results was read in 15 minutes and interpreted. Quality control was carried out running one positive control and one negative control.

# Result determination

1. HBsAg, HBsAb, HBeAg (sandwich method)

Negative: only one purple bar (control line} in the control c zone. Posivtive: detecting T zone there are two purple bars in the control c zone Invalid: detecting T zone there is no purple bar in the control c zone.

1. HBeAb HBcAb (competition mode)

**Negative**: detecting T zone there are two purple bars in the control C zone

**Positive**: only one purple bar (control line) in the control c zone

(Weakly positive samples may appear a very thin response line at the test line)

**Invalid**: detecting T zone there is no purple part in the control c zone.

# Statistical Analysis

Data was analysed using Microsoft Excel. Comparative analysis was performed using the Student‘s t-test and Chi square test.

# CHAPTER FOUR

# RESULTS AND DISCUSSION

# Results

# Overall prevalence rate in the correctional facilities

A total of 344 inmates participated in the study. Out of the participants, there were 328 males (95.35%) and 16 females (4.65%). The participants fell in the age group 9-65 years. Rapid chromatographic immunoassay test (ICT) showed that HBsAg was present in 75 (22%) of the inmates. ELISA showed that additional 12 samples were positive making an overall prevalence rate of 25% (Table 4.1). The percentage of the positive to negative sample in the three correctional facilities is presented in Figure 4.1

Table 4.1: Sensitivity of ICT and ELISA methods

|  |  |  |
| --- | --- | --- |
| Method | Positive samples | % Positive |
| ICT | 75 | 22 |
| ELISA | 87 | 25 |

P= 0.0049

25.30%

Negative Positive

74.70%

Figure 4.1: Percentage of negative to positive samples

# Prevalence of HBV infection based on locations of correctional facilities

Figure 4.2 showed the sample population of each correctional facility with number of inmates who were infected with the virus. Out of the 201 inmates in Minna, 57 were found to be infected. In Kontagora, 17 out of the 70 inmates screened were infected. However, in Bida, 73 inmates were screened, out of which 13 were found to be positive.

The prevalence rate varied with locations. The highest prevalence rate (28.4%) was recorded in Minna old prison (Table 4.2) while the least was in Nigeria Prison Service, Bida (17.8%). Though, Minna old prison has the highest population and the highest prevalence rate, Median Security prison, Kontagora had the least population but not the least prevalence rate.

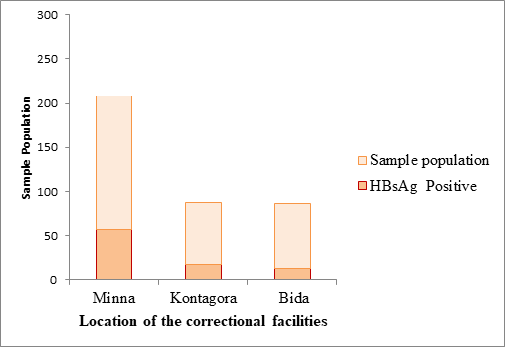


Fig. 4.2 Sample population and the number of infected inmates in each location

# Table 4.2: Percentage prevalence rate of HBV infection based on location

|  |  |  |  |
| --- | --- | --- | --- |
| **Correctional facility** | **Total**  **number** | **Number of**  **Positive** | **Positive**  **(%)** |
| Minna Old Prison | 201 | 57 | 28.4 |
| Medium Security prison, Kontagora | 70 | 17 | 24.3 |
| Nigeria Prison Service Bida | 73 | 13 | 17.8 |
| Total | 344 | 87 | 25.3 |

(X2 = 3.2, *df* = 2, P= 0.201)

# 4.1.3. Prevalence of HBV infection based on age of inmates

Table 4.3 shows the prevalence of HBV infection based on the age of inmates. The age groups of 21-30 with total participants of 155 had the highest prevalence rate (29.7%) followed by 31-40 year having prevalence rate of 26.4%.

# Table 4.3: Prevalence of HBV infection based on age of inmates

|  |  |  |  |
| --- | --- | --- | --- |
| Age group (year) | Total | No of positive | Positive (%) |
| 11 – 20 | 62 | 15 | 24.2 |
| 21 – 30 | 155 | 46 | 29.7 |
| 31 – 40 | 72 | 19 | 26.4 |
| 41 – 50 | 35 | 5 | 14.3 |
| 51 – 60 | 16 | 2 | 12.5 |
| 61 – 70 | 4 | 0 | 0 |
| Total | 344 | 87 | 25.3 |

(X2 = 6.65, *df*= 5, P= 0.248)

# Prevalence of HBV infection based on gender of inmates

Table 4.4 shows the prevalence of HBV infection based on gender. The total number of male screened were 328, out of which 83 were positive. On the other hand, the female were 16, having 4 of them being positive. The male and female inmates had prevalence rates of 25.3% and 25% respectively.

# Table 4.4: Prevalence of HBV infection based on gender of inmates

|  |  |  |  |
| --- | --- | --- | --- |
| Gender | Total | No of positive | Positive (%) |
| Male (M) | 328 | 83 | 25.3 |
| Female (F) | 16 | 4 | 25 |
| Total | 344 | 87 | 25.3 |

(X2 = 0.007, *df =* 1*,* P = 0.978)

# Prevalence of HBV infection based on Educational level of inmates

Table 4.5 shows the result of the prevalence of HBV based on the level of educational of inmates. Highest prevalence was recorded among the inmates with secondary school (32.6%) education followed by those who had primary school (28.6%) education.

# Table 4.5 Prevalence of HBV based on Educational level of inmates

|  |  |  |  |
| --- | --- | --- | --- |
| Level | Total | No of positive | Positive (%) |
| Primary | 28 | 8 | 28.6 |
| Secondary | 86 | 28 | 32.6 |
| Tertiary | 65 | 15 | 23.1 |
| No formal education | 165 | 36 | 10.5 |
| Total | 344 | 87 | 25 |

(X2 = 3.78, *df =* 3*,* P= 0.286)

# Prevalence of HBV infection based on duration of stay of inmates

Table 4.6 shows the prevalence rate of HBV infection among inmates based on the duration spent in the correctional facilities. The prevalence rate of those who had spent a year and below was 21%, while those who had spent between a year to two was 29.2%.

**Table: 4.6: Prevalence of HBV infection based on duration of stay of inmates**

|  |  |  |  |
| --- | --- | --- | --- |
| Duration  (years) | No screened | No of positive | Positive (%) |
| 0 – 1 | 214 | 45 | 21 |
| 1 to 2 | 48 | 14 | 29.2 |
| 2 to 3 | 24 | 9 | 37.5 |
| 3 to 4 | 13 | 8 | 61.5 |
| 4 to 5 | 9 | 6 | 66.7 |
| > 5 | 36 | 5 | 13.9 |
| Total | 344 | 87 | 25.3 |

(X2 = 24 *df = 5,* P= 0.00022)

# Prevalence of HBV infection based on marital status of inmates

Table 4.7 shows the prevalence based on marital status of inmates. The number of married inmates was higher as compared to the singles. No divorcee was in the facilities at the time of study and only one widow was present. The only widow screened tested negative. The prevalence rates in the singles and married inmates were 28.1% and 23.7% respectively.

# Table 4.7: Prevalence of HBV infection based on marital status of inmates

|  |  |  |  |
| --- | --- | --- | --- |
| Status | No screened | No of positive | Positive (%) |
| Single | 128 | 36 | 28.1 |
| Married | 215 | 51 | 23.7 |
| Widow | 1 | 0 | 0 |
| Divorce | 0 | 0 | 0 |
| Total | 344 | 87 | 25.3 |

(X2 = 1.16, *df =* 3*,* P= 0.559)

# Hepatitis B Serological Markers

The results of further tests done on the HBsAg positive samples using 5-panel test card are presented in Figure 4.3. In Minna, out of the 57 inmates that were HBsAg positive, Nine (9) of them had their HBsAb as positive, ten (10) had HBeAg as positive, HBeAb was positive in thirty

(30) and HBcAb was positive in forty two (42). The results showed that some of the samples had only HBsAg as positive, while the remaining serological markers were negative. Some of the samples have about three serological markers positives. For instance, five samples had HBsAg, HBcAb and HBeAg detected as positive which implied that either acute or chronic active HBV infection with ongoing high level replication had set in.

In Kontagora, Out of the 17 inmates that were HBsAg positive, HBsAb, HBeAg,, HBeAb, and HBcAb are detected in six (6), seven (7), nine (9) and fifteen (15) samples respectively. While at Bida, Out of the 13 inmates that were HBsAg positive, HBsAb, HBeAg,, HBeAb, and HBcAb were detected positive in four (4), three (3), eight (8) and eleven (11) samples respectively.

**No of positive**

Figure 4.3: Hepatitis B Serological Markers in Inmates from Correctional Facilities

60

50

40

30

HBsAg

HBsAB

HBeAg HBeAb HBcAb

20

10

0

Minna

Kontagora

**Serological** markers

Bida

The result of the biomarkers of the total inmates in the study area is presented in Table 4.8. Of the total inmates, the prevalence of hepatitis B infection (HBsAg) was 87 (25.3%) representing the level of hepatitis B endemicity in inmates in Niger state correctional facilities.

# Table 4.8: Overall percentage positive of Hepatitis B biomarkers among Inmates (N= 344)

|  |  |  |
| --- | --- | --- |
| **Biomarkers** | **No of Positive** | **% Positive** |
| HBsAg | 87 | 25.3 |
| HBsAb | 19 | 5.52 |
| HBeAg | 20 | 5.81 |
| HBeAb | 47 | 13.66 |
| HBcAb | 68 | 19.77 |

# Infection with HBV among inmates and some associated risk factors

Table 4.9 shows the HBV infection among inmates and some associated risk factors. Five associated risk factors were considered based on literature and the willingness of the inmates to respond to those factors. While 75 inmates have awareness about the HBV infection, 269 claimed ignorance of the disease. Out of 344 inmates, only 45 had knowledge on mode of transmission of the virus. Out of the 45, 13 were positive, while 74 of the remaining 299 that lack knowledge of its mode of transmission were also positive.

# Table 4.9: Infection with HBV among inmates and some associated risk factors

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Risk factor | Sample population | **No of Positive** | % **Positive** | P-value |
| Awareness | on HBV |  |  |  |
| Yes | 75 | 21 | 28 | 0.184 |
| No | 269 | 66 | 24.5 |  |
| Knowledge on | transmission mode |  |  |  |
| Yes | 45 | 13 | 28.9 | 0.145 |
| No | 299 | 74 | 24.7 |  |
| Intravenous | drug use |  |  |  |
| Yes | 225 | 70 | 31.1 | 0.2121 |
| No | 119 | 17 | 14.3 |  |
| Sharing of | objects |  |  |  |
| Yes | 267 | 72 | 26.9 | 0.028 |
| No | 77 | 15 | 19.5 |  |
| Multiple sex | partner |  |  |  |
| Yes | 105 | 54 | 51.4 | 0.482 |
| No | 149 | 33 | 22.15 |  |

P<0.01

# Discussion of Results

From the results of the prevalence rate in the correctional facilities, it was noted that the ELISA method detected more positive samples. The additional positive samples detected by ELISA were not unexpected as earlier researcher had asserted that though, ICT could be used for rapid decision, ELISA was more sensitive (Bibi *et al.,* 2014).

The prevalence rate recorded in this study can be classified as high based on the submission of the World Health Organisation (2010) that > 8% HBSAg positivity in a population is high. Analysis of this study (which is a study at a state level) when compared to the inmates in other states within Nigeria showed Niger state ranked high in prevalence rate of the virus. It is higher when compared to the prevalence rate (18%) in inmates in Bali correctional facility Taraba, Lagos correctional facilities (6.7%) and inmates in Nasarawa state correctional facility (23%) (Elijah and Ireebanije, 2014; Dada *et al.,* 2006; Adoga *et al.,* 2009). It is however less than 42.2% rate recorded in Sokoto correctional facility (Alkali *et al.,* 2017). When the results are compared to the prevalence of hepatitis B in inmates in Nigeria (23%), Africa (13.14%) and the world (5.17%) population, the rate was higher in Niger state (Moradi *et al*., 2018). The prevalence rate in the correctional facilities in this area of study when compared to the correctional facilities in some countries in Africa and the world, it shows the need for immediate measures to control the rate.

Though, the prevalence rate is almost the same with that of Ghanian correctional facilities (25.5%), a little higher than that of America correctional facilities (21.20 %), it is far higher than 4.5% found among inmates in Brazil, 3.4% found in Iranian correctional facilities and 6.5% in Greek inmates (Alasvand *et al.,* 2015; Silva *et al.,* 2017). It is however important to note that the rate of prevalence in this study is still within the hyper-endemic levels (10-40%) estimated for

Nigeria (Bello and Olabode, 2011). The result of the statistical analysis showed that there is a significant difference between ICT and ELISA (df = 1, P= 0.0049).

Considering the results of prevalence of HBV infection based on locations of correctional facilities, it could be inferred that the prevalence rate does not necessarily depend on population. The rate could be associated with differences in infection rate as regards to locality and the level of associated risk factors (Isa *et al.,* 2015). None of the three correctional facilities seems to have an institutionalized infection control measures against HBV infections as done in some countries. The percentage difference (10.6%) between the highest prevalence of Hepatitis B observed in Minna and the lowest prevalence observed in Bida was higher than prevalence reported elsewhere. Though, no literature is available that compare the percentage difference in prevalence rate between correctional facilities in Nigeria, Alasvand *et al.* (2015) reported percentage difference of 3.8% in a study conducted in correctional facilities in Iran. However, the result of the statistical analysis showed there is no statistical difference between sample locations (X2 = 3.2, *df* = 2, P= 0.201).

Based on the results of prevalence of HBV infection with respect to age of inmates, the highest prevalence rate observed in the age group 21-30 could be as a result of their high representation among the age groups in the correctional facilities and also due to the fact that they are within the reproductive age group as opined by Alkali *et al.* (2017). This age group noted in this research for the highest prevalence is in contrary to the earlier report which claimed higher prevalence rate exists in those above 40 years (Okonkwo *et al.*, 2012; Isah *et al.*, 2015). This could be as a result of the difference in the targeted population while Isa *et al.* (2015) examined the virus in the tertiary institution in North Western Nigeria Okonkwo *et al.* (2012) studied the virus in apparently healthy blood donors. However, the findings of this research is in agreement with

findings of Alkali *et al.* (2017) and Elijah and Ireebanije (2014) who reported that age group of between 20-29 had the highest prevalence rate in correctional facilities. The reason for high prevalence rate could be due to youthful exuberance. From the age of 21, the proportion of persons susceptible to the virus infection decreased with increasing age. This linear trend was also noted in the findings of Olayinka *et al.* (2016). The distribution of HBV infection according to age was not statistically significant (X2 = 6.65, *df*= 5, P= 0.248).

From the results of the prevalence rate based on gender, the higher prevalence rate noted in males could be attributed to the comparative higher number of male inmate which created crowdedness and probable transmission via a means such as body sweat. This result is in contrast with the report of Mustapha and Jibrin (2004) which showed that prevalence of HBV infection was higher in female than male. It however, agrees with the findings of Alkali *et al.* (2017) and Elijah and Ireebanije (2014) which showed higher prevalence of HBV infection among male inmates. There was no observed statistical difference in sex distribution of HBV infection among the inmates (X2 = 0.007, *df =* 1*,* P = 0.978).

Based on the results of prevalence of HBV infection with respect to level of education of inmates, the higher prevalence rate in secondary as compare to the primary could be as a result of relatively high number of inmates (86) with secondary as compare to the inmates (28) with primary. Youthful exuberance could also be responsible for the high prevalence rate among those with secondary education. The high prevalence in both could be attributed to their low level of education and lack of unawareness on HBV infection. Those that attended non formal education had the least rate of prevalence (10.5%). The least in this group could be associated with their mode of life and their religious ideology*.* More so, those with no formal education probably accept any type of job for living while those with formal education (particularly secondary) will

want to insist on white collar jobs which are not available; this could lead to frustration and various vices.

Among the groups with formal education, least prevalence was noted in those with tertiary education. This could be because they are careful enough and usually take necessary precautions when negotiating new sexual partners as opined by Alkali et al. (2017). The least prevalence recorded in those with ―no formal education‖ in this study and lesser prevalence in secondary as compare to those with primary agrees with the findings of Olayinka *et al.* (2016). Prevalence of HBV infection in correctional facilities based on their educational background was not significant (X2 = 3.78, *df =* 3*,* P= 0.286).

The results of the Prevalence of HBV infection based on duration of stay of inmates showed an increasing trend from a year up to five (5) years. This shows that there is high chance of contracting the virus as the period of incarceration increases. However, those with duration of stay above five (5) years, even with their high numbers (36), had the least prevalence rate (13.9%). The reason could be the type of seniority displayed in the correctional facility which allows them allocate some space to themselves. The increase in prevalence rate with year of incarceration has been reported in earlier studies (Alkali *et al.,* 2017; Dana *et al.,* 2013). There is a significant difference (X2 = 24 *df = 5,* P= 0.00022) in prevalence of HBV infection in correctional facilities based on their duration of stay in correctional facilities.

This result of the prevalence of HBV infection based on marital status of inmates suggests that the rate was higher in in the single as compared to the higher. This could be as a result of indiscriminate sexual activities. This finding is in disagreement with results of Alkali *et al*. (2017) who claimed high prevalence rate was among the married ones but affirm the claim of

Olayinka *et al.* (2016) that there was higher proportion of susceptible persons among single participants as compared to the married ones. The prevalence of HBV infection based on marital status was not statistically significant (X2 = 1.16, *df =* 3*,* P= 0.559).

From the results of the Hepatitis B Serological Markers, the obtained value for the HBsAb showed that; of the total carriers, 5.52% are having the presence of the protective antibodies in their serum, meaning they were developing immunity to the virus. This immunity is likely to be from the carrier‘s immune response as none of the inmate claimed to have received vaccine and vaccines are not administered to a known carrier. The overall HBeAg detected showed that the highly infectious individuals were 5.81%. The HBeAb indicated that 13.66% of the inmates were actively producing antibodies to suppress the HBV replication. The HBcAb results showed that 19.77% were experiencing onset of the acute hepatitis B which will persist for life; it may also imply ongoing HBV infection in those inmates.

From the results of the HBV infection among inmates and some associated risk factors, large majority of the inmates were not aware of the hepatitis B virus. However, the results of the screening showed that 28% of those who have awareness were positive while 24.5% of those who were not aware were also positive. There was no significant association between awareness and prevalence rate of HBV. There was also no significant association between knowledge of modes of transmission and HBV infection in the study areas. This is in agreement with the findings of Alkali *et al.* (2017) and Butler *et al.* (1997) who reported that in Australia there was poor knowledge of hepatitis risk factors among their study subjects*.* The association of intravenous drug use (IDU) with the prevalence of HBV infection was not significant. This could be as a result of restriction on IDU practice among the inmates in the study area. .

Out of the associated risk factors considered, result showed that ―sharing of objects‖ was associated with high prevalence rate of HBV infection in correctional facilities. This may be as a result of sharing of dress and sharp objects by the inmates. The result of this finding is in agreement with the reports of Ray and Hunter (2010) and Samuel *et al.* (2009) who reported significant association between the sharing of objects and infection with the HBV. The results of this study are in line with the findings of Abdul *et al.* (2010). The multiple sex partners and with HBV infection was also statistically insignificant.

# CHAPTER FIVE

# CONCLUSION AND RECOMMENDATIONS

# Conclusion

This study examined the prevalence of Hepatitis B virus infection in inmates of correctional facilities in Niger State. The overall prevalence rate of the HBV in the three correctional facilities was 25%. The infection was highest in the age bracket 21-30 years (29.7%).Through the serological markers, it was noted that 87 of the inmates were infected, 19 had immunity against the virus, 20 had active viral replication, 47 with no viral replication and 68 with onset of acute infection. The rapid chromatographic immunoassay test (ICT) method was cost effective and required lesser laboratory expertise, it is not as sensitive as the enzyme linked immunosorbent assay (ELISA) as there exist statistically significant difference between the two when assessing surface antigen of Hepatitis B (HBsAg). Also, both the duration of stay in correctional facilities and sharing of objects had statistical significant association with seropositivity of HBV and can thus be considered as important risk factors. By implication, HBeAg prevalence is influence by the unavailability of the common amenities such as dress and sharp object (such as razor). As such, there is a need for constant screening and vaccination of the negative inmates to avoid increasing rate of prevalence and placing the larger society at risk. Also, there is a need to create more awareness about HBV prevention and transmission especially by sharing of objects.

# Recommendations

The following recommendations are made based on the study:

* + 1. Based on the high prevalence of hepatitis B virus infection among inmates of the correctional facilities, it is recommended that a continuous monitoring and control of the HBV infection be put in place.
    2. The remaining correctional facilities (Kagara Prison, Lapai Prison, Agaie Prison, and Medium Security Prison Minna) which were not covered by this survey should be surveyed for the HBV infection.
    3. HBV immunization should be stepped up in the general population to prevent spread of the HBV infection.
    4. The inmates should be given adequate orientation on public health diseases and how to prevent their transmission.

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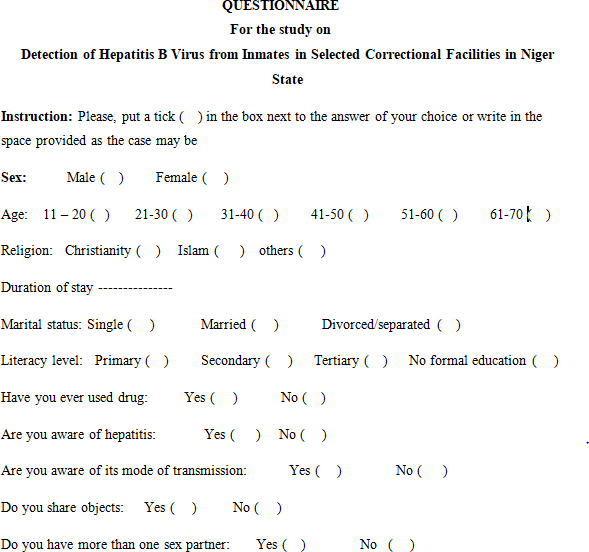
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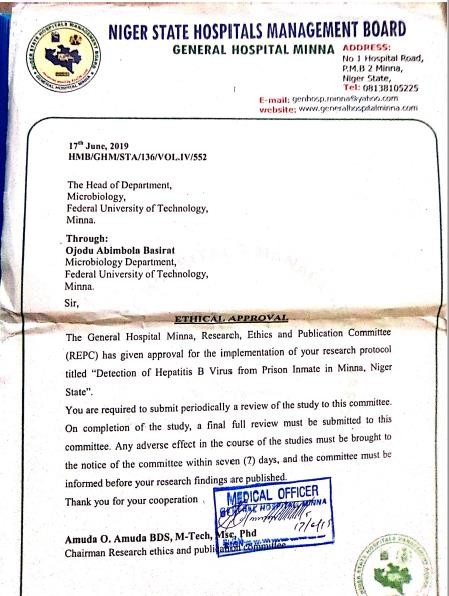
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Appendix A Questionnaire



Appendix B Ethical Approval



Appendix C

Consent Form

