COMPARATIVE ANALYSIS ON OCCURRENCE OF HEPATITIS B VIRUS AMONGST STUDENTS IN VARIOUS FACULTIES OF THE UNIVERSITY OF BENIN IN THE YEAR 2023

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CERTIFICATION

This is to certify that the project work titled "Comparative Analysis On Occurrence Of Hepatitis B Virus Amongst Students In Various Faculties Of The University Of Benin In The Year 2023" was carried out by **Abraham JOHNSON-OKIEMUTE** with Matriculation Number **LSC1806751** of the Department of Microbiology, Faculty of Life Sciences, University of Benin, Benin City.

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APPROVAL

This is to certify that this project work was accepted in partial fulfillment of the requirement of the award of Bachelor of Sciences (B.Sc.) degree in Microbiology, Faculty of Life Sciences, University of Benin, Benin City.

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Prof. (Mrs.) F.I. Akinnibosun **Date**

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DEDICATION

I humbly dedicate this work to the Almighty God, who has given me patience, wisdom, divine health, strength and grace until this point of my life. All glory and honor to Him.

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My utmost appreciation goes to God for His divine grace during the course of this research work and throughout the course of this program.

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ABSTRACT

Hepatitis B virus (HBV) infection is a global health disease. Early diagnosis can, however, improve outcomes in infected patients. Infections can be acute with a propensity to evolve into chronic diseases and their attendant life-threatening complications. The study aimed to determine the prevalence of HBV among University of Benin students and associated risk factors. Research methodology involved collection of blood sample from 93 students aged 16 to 59 years from different student using the systematic sampling technique. Ethical approval was obtained from the University of Benin Ethical Review Board, blood samples were collected from students and stored in a 5ml EDTA bottle. HBsAg was tested using the HBsAg rapid test kit. The test was carried out and interpreted according to the manufacturer's instructions. The questionnaire includes both closed and open-ended questions and will be sectionalized into socio-demographic characteristics, risk factors associated with HBV infection and vaccination history students and using systematic sampling technique. HBsAg was tested using the HBsAg test kit. Of the 328 students that were screened, 2 (0.6%) were positive. Study shows an apparent very low prevalence of University of Benin. The result of this research shows an apparent hesitancy towards vaccination and of a sharp instinct to not share sharp objects. Though it is lower than the countries recorded prevalence level, routine vaccination program and public enlightenment should be strengthened for further control of HBV.

CHAPTER ONE

INTRODUCTION

1.1 Background.

Hepatitis is a general term referring to inflammation of the liver, which may result from various causes (Ghabril, Chalasani and Björnsson, 2010) which can be infectious (i.e viral, bacterial, fungal, and parasitic organisms) and non infectious agents (e.g. alcohol, drugs, autoimmune diseases, and metabolic disorders) but viral hepatitis are the most common cause of hepatitis worldwide (Malaguarnera, Cataudella, Giordano, Nunnari, Chisarin and Malaguarnera, 2012). The most common causes of viral hepatitis are these hepatotropic viruses; Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D and Hepatitis E (Gallegos-Orozco, Rakela-Brödner, and Gross, 2010).

Hepatitis B virus is among the common viral infectious agents of public health importance globally.Hepatitis B is a common blood-borne viral infection with high mortality and morbidity rate. It is a serious global health problem. HBV causes acute and chronic liver diseases and is one of the reasons for the development of hepatocellular carcinoma (Eun J.R. *et al,* 2010). All age groups are almost equally at risk of being affected (Daw M.A. *et al,* 2014).

Hepatitis B virus is a hepadnavirus that has a circular genome of partially double-stranded DNA and replicates through an RNA intermediate form by reverse transcription, it was originally known as "serum hepatitis" (Bartenschlager, Junker-Niepmann, Schaller, 1990). The virus can remain viable for more than 7 days on environmental surfaces at room temperature. The average incubation period is 90 days from time of exposure to onset of symptoms, but may vary from 6 weeks to 6 months.

Nigeria is one of the countries in the HBV hyper-endemic zone. A meta-analysis of 46 Nigerian studies puts the average prevalence in the country as 13.6%(Musa *et a*l., 2015). HBV is infectious 50 to 100 times more than HIV. Unlike HIV, HBV can survive outside the body for at least 7 days and is an important occupational hazard for health workers (Aliu T.B. *et al,* 2022). About 2 billion people have been infected with the virus worldwide and about 350 million live with chronic HBV, referring to the virus as one of the most common human pathogens and a significant health concern worldwide and almost 75% in Asia. (Ogholikhan S. *et al,* 2016). The

virus is still the most significant transfusion transmissible infection, with a per-unit risk of 1:82,000 (Walia R., *et al,* 2016).

The early detection is important to resist the consequence of this virus. A various diagnostic tests are available to detect this virus. Among them, HBsAg is the most commonly used biological biomarker (Kramvis A. *et al,* 2022, Kim J. H. *et al,* 2020, Coffin C.S. *et al,* 2019, Deng R. *et al,* 2022). Evaluation of data on the prevalence of this transfusion transmitted infections(TTIs), that is HBV among healthy blood donors is actually an assessment of the occurrence of infections in the blood donor and concurrently for safe blood transfusion protocol. It also gives a glimpse of the epidemiology of this virus in the local society.

Nigeria, a tropical country, has been documented as highly endemic for HBV infection and about 75% of its population is likely to have been exposed to the virus at one time or the other in their lives (Sirisena et al., 2002). Currently about 18 million Nigerians are infected (Jombo et al., 2005). A prevalence rate of 4.3 % was reported from Port Harcourt (Akani et al., 2005), 5.7% from Ilorin (Agbede et al., 2007), 11.6% from Maiduguri (Harry et al., 1994) and 8.3% from Zaria (Jatau et al., 2009). A seroprevalence of 23.3% was reported among patients attending all clinics at the Aminu Kano Teaching Hospital (AKTH) (Nwokedi et al., 2006).

1.2 AIMS

The aim of this study is to assess trends in the prevalence of Hepatitis B Virus infection and its associated factors in a tertiary institution (University of Benin, Benin City, Edo State. Nigeria). These aims and objectives can be used to guide the design and implementation of a research study on Hepatitis B virus among students.

The specific objectives of this study include;

1. To determine the prevalence of Hepatitis B virus among students
2. To compare the prevalence of Hepatitis B virus among different group of students
3. To identify the risk factors associated with Hepatitis B virus infection among students
4. To assess the knowledge, attitude and practices of students regarding Hepatitis B virus
5. To identify gaps in knowledge and develop educational interventions to address these gaps

CHAPTER TWO

LITERATURE REVIEW

2.1 HEPATITIS

Hepatitis is defined as inflammation of the liver that can result from a variety of causes such as heavy alcohol use, autoimmune, drugs, or toxins. However, the most frequent cause of hepatitis is due to a viral infection and is referred to as viral hepatitis. In the United States, the most common types of viral hepatitis are Hepatitis A, Hepatitis B, and Hepatitis C. The other types of viral hepatitis are hepatitis D and E and are less frequently encountered (Zuckerman *et al.,* 1996). Based on the etiology of hepatitis, the severity can range from mild and self-limiting to severe illness requiring liver transplantation.

Hepatitis can be further classified into acute and chronic based on the duration of the inflammation/insult to the liver. If inflammation of the liver lasts for less than 6 months, then it is termed as acute hepatitis and if it lasts longer than 6 months it is termed as chronic hepatitis. Acute hepatitis is usually self-resolving but can cause fulminant liver failure depending on the etiology. In contrast, chronic hepatitis can cause liver damage that includes liver fibrosis, cirrhosis, hepatocellular carcinoma, and features of portal hypertension leading to significant morbidity and mortality (Dakhil *et al.,* 2009; Ryder *et al.,* 2001).

Most of the time, hepatitis results from hepatitis viruses A, B, C, D, and E. It is unclear whether the Hepatitis G virus is pathogenic in humans or not. Hepatitis A, B, C, and D are endemic to the United States with hepatitis A, B, and C viruses causing 90% of acute viral hepatitis in the United States and Hepatitis C being the most common cause of chronic hepatitis. Hepatitis A is an RNA virus from the Picornaviridae family. It is usually present in the highest concentration in the stool of infected individuals with the greatest viral load shedding occurring during the end of the incubation period.

The most common mode of transmission of hepatitis A is via the fecal-oral route from contact with food, water, or objects contaminated by fecal matter from an infected individual. It is more commonly encountered in developing countries where due to poverty and lack of sanitation, there is a higher chance of fecal-oral spread. International travel is the most significant risk factor identified from the cases reported in the United States. People who come in contact with infected individuals are also at risk, and the secondary infection rate for household contacts is about 20%,

which may also play a more prominent role in the maintenance of hepatitis A virus outbreaks (Koenig *et al.,* 2017; Basra *et al.,* 2011).

Hepatitis results in more than a million deaths a year, most of which occur indirectly from liver scarring or liver cancer. (Wang *et al.,* 2015) In the United States, hepatitis A is estimated to occur in about 2,500people a year and results in about 75deaths.The word is derived from the Greek hêpar (ἧπαρ), meaning "liver", and - itis (-ῖτις), meaning "inflammation".

2.2 SIGNS AND SYMPTOMS

Hepatitis has a broad spectrum of presentations that range from a complete lack of symptoms to severe liver failure (Dienstag *et al.,* 2015; Rutherford *et al.,* 2016; Khalili *et al.,* 2013). The acute form of hepatitis, generally caused by viral infection, is characterized by constitutional symptoms that are typically self limiting (Dienstag *et al.,* 2015; Rutherford *et al.,* 2016). Chronic hepatitis presents similarly, but can manifest signs and symptoms specific to liver dysfunction with long-standing inflammation and damage to the organ. (Khalili *et al.,* 2013; Dienstag *et al.,* 2015).

2.2.1 Acute Hepatitis

Acute viral hepatitis follows three distinct phases:

1. The initial prodromal phase (preceding symptoms) involves nonspecific and flu-like symptoms common to many acute viral infections. These include fatigue, nausea, vomiting, poor appetite, joint pain, and headaches (Dienstag *et al.,* 2015; Rutherford *et al.,* 2016). Fever, when present, is most common in cases of hepatitis A and E (Dienstag *et al.,* 2015). Late in this phase, people can experience liver-specific symptoms, including choluria (dark urine) and clay colored stools (Dienstag *et al.,* 2015; Rutherford *et al.,* 2016).

2. Yellowing of the skin and whites of the eyes follow the prodrome after about 1–2 weeks and can last for up to 4 weeks (Dienstag *et al.,* 2015; Rutherford *et al.,* 2016). The non-specific symptoms seen in the prodromal typically resolve by this time, but people will develop an enlarged liver and right upper abdominal pain or discomfort (Dienstag *et al.,* 2015). 10–20% of people will also experience an enlarged spleen, while some people will also experience a mild unintentional weight loss (Dienstag *et al.,* 2015; Khalili *et al.,* 2013).

3. The recovery phase is characterized by resolution of the clinical symptoms of hepatitis with persistent elevations in liver lab values and potentially a persistently enlarged liver (Dienstag *et al.,* 2015). All cases of hepatitis A and E are expected to fully resolve after 1–2 months (Dienstag *et al.,* 2015). Most hepatitis B cases are also selflimiting and will resolve in 3–4months. Few cases of hepatitis C will resolve completely (Dienstag *et al.,* 2015).

Both drug-induced hepatitis and autoimmune hepatitis can present very similarly to acute viral hepatitis, with slight variations in symptoms depending on the cause (Fontana *et al.,* 2014; Manns *et al.,* 2015). Cases of drug-induced hepatitis can manifest with systemic signs of an allergic reaction including rash, fever, serositis (inflammation of membranes lining certain organs), elevated eosinophils (a type of white blood cell), and suppression of bone marrow activity (Fontana *et al.,* 2014).

2.2.2 Fulminant Hepatitis

Fulminant hepatitis, or massive hepatic cell death, is a rare and life-threatening complication of acute hepatitis that can occur in cases of hepatitis B, D, and E, in addition to drug-induced and autoimmune hepatitis (Dienstag *et al.,* 2015; Fontana *et al.,* 2014; Manns *et al.,* 2015). The complication more frequently occurs in instances of hepatitis B, D and E co-infection at a rate of 2 20% and in pregnant women with hepatitis E at rate of 15–20% of cases (Dienstag et al., 2015; Rutherford et al., 2016). In addition to the signs of acute hepatitis, people can also demonstrate signs of coagulopathy (abnormal coagulation studies with easy bruising and bleeding) and encephalopathy (confusion, disorientation, and sleepiness) (Dienstag et al., 2015; Rutherford et al., 2016). Mortality due to fulminant hepatitis is typically the result of various complications including cerebraledema, gastrointestinal bleeding, sepsis, respiratory failure, or kidney failure (Dienstag *et al.,* 2015).

2.2.3 Chronic Hepatitis

Acute cases of hepatitis are seen to be resolved well within a six-month period. When hepatitis is continued for more than six months it is termed chronic hepatitis. (Munjal *et al.,* 2012). Chronic hepatitis is often asymptomatic early in its course and is detected only by liver laboratory studies for screening purposes or to evaluate nonspecific symptoms (Khalili *et al.,* 2013; Dienstag *et al.,*

2015). As the inflammation progresses, patients can develop constitutional symptoms similar to acute hepatitis, including fatigue, nausea, vomiting, poor appetite, and joint pain (Dienstag *et al.,* 2015). Jaundice can occur as well, but much later in the disease process and is typically a sign of advanced disease (Dienstag *et al.,* 2015).

Chronic hepatitis interferes with hormonal functions of the liver which can result in acne, hirsutism (abnormal hair growth) and amenorrhea (lack of menstrual period)in women (Dienstag *et al.,* 2015). Extensive damage and scarring of the liver over time defines cirrhosis, a condition in which the liver's ability to function is permanently impeded (Khalili *et al.,* 2013). This results in jaundice, weight loss, coagulopathy, ascites(abdominal fluid collection), and peripheral edema (leg swelling) (Dienstag *et al.,* 2015). Cirrhosis can lead to other life-threatening complications such as hepatic encephalopathy, esophageal varices, hepatorenal syndrome, and liver cancer (Khalili *et al.,* 2013).

2.3 RISK FACTORS

Causes of hepatitis can be divided into the following major categories: infectious, metabolic, ischemic, autoimmune, genetic, and other. Infectious agents include viruses, bacteria, and parasites. Metabolic causes include prescription medications, toxins (most notably alcohol), and nonalcoholic fatty liver disease. Autoimmune and genetic causes of hepatitis involve genetic predispositions and tend to affect characteristic populations.

2.3.1 Viral Hepatitis

Viral hepatitis is the most common type of hepatitis worldwide, especially in Asia and Africa (WHO, 2013). Viral hepatitis is caused by five different viruses (hepatitis A, B, C, D, and E) (Dienstag *et al.,* 2015). Hepatitis A and hepatitis E behave similarly: they are both transmitted by the fecal–oral route, are more common in developing countries, and are self-limiting illnesses that do not lead to chronic hepatitis (Dienstag *et al.,* 2015; CDC, 2016; WHO, 2023).

Hepatitis B, hepatitis C, and hepatitis D are transmitted when blood or mucous membranes are exposed to infected blood and body fluids, such as semen and vaginal secretions (Dienstag *et al.,* 2015). Viral particles have also been found in saliva and breast milk. Kissing, sharing utensils, and breastfeeding do not lead to transmission unless these fluids are introduced into open sores or cuts (CDC, 2010). Many families who do not have safe drinking water or live in unhygienic

homes have contracted hepatitis because saliva and blood droplets are often carried through the water and blood-borne illnesses spread quickly in unsanitary settings (WHO, 2023). Hepatitis B and C can present either acutely or chronically (Dienstag *et al.,* 2015). Hepatitis D is a defective virus that requires hepatitis B to replicate and is only found with hepatitis B co-infection (Dienstag *et al.,* 2015). In adults, hepatitis B infection is most commonly self-limiting, with less than 5% progressing to chronic state, and 20 to 30% of those chronically infected developing cirrhosis or liver cancer (WHO, 2023). Infection in infants and children frequently leads to chronic infection (WHO, 2023). Unlike hepatitis B, most cases of hepatitis C lead to chronic infection (CDC, 2016). Hepatitis C is the second most common cause of cirrhosis in the US (second to alcoholic hepatitis) (Friedman *et al.,* 2015). In the 1970s and 1980s, blood transfusions were a major factor in spreading hepatitis C virus (CDC, 2016). Since widespread screening of blood products for hepatitis C began in 1992, the risk of acquiring hepatitis C from a blood transfusion has decreased from approximately 10% in the 1970s to 1 in 2million currently (Dienstag *et al.,* 2015).

2.3.2 Parasitic Hepatitis

Parasites can also infect the liver and activate the immune response, resulting in symptoms of acute hepatitis with increased serum IgE (though chronic hepatitis is possible with chronic infections) (Harder *et al.,* 2008). Of the protozoans*, Trypanosoma cruzi, Leishmania species*, and the malaria-causing Plasmodium species all can cause liver inflammation (Harder *et al.,* 2008). Another protozoan, *Entamoeba histolytica*, causes hepatitis with distinct liver abscesses (Harder *et al.,* 2008). Of the worms, the cestode *Echinococcus granulosus*, also known as the dog tapeworm, infects the liver and forms characteristic hepatic hydatid cysts (Harder et al., 2008).

The liver flukes *Fasciola hepatica* and *Clonorchis sinensis* live in the bile ducts and cause progressive hepatitis and liver fibrosis (Harder *et al.,* 2008).

2.3.3 Bacterial Hepatitis

Bacterial infection of the liver commonly results in pyogenic liver abscesses, acute hepatitis, or granulomatous (or chronic) liver disease (Wisplinghoff *et al.,* 2008). Pyogenic abscesses commonly involve enteric bacteria such as *Escherichia coli and Klebsiella pneumonia* and are composed of multiple bacteria up to 50% of the time (Wisplinghoff *et al.,* 2008). Acute hepatitis

is caused *by Neisseria meningitidis, Neisseria gonorrhoeae, Bartonella henselae, Borrelia burgdorferi, Salmonella species, Brucella species* and *Campylobacter species (*Wisplinghoff *et al.,* 2008).

Chronic or granulomatous hepatitis is seen with infection from mycobacteria species, *Tropheryma whipplei, Treponema pallidum, Coxiella burnetii,* and *Rickettsia* species (Wisplinghoff *et al.,* 2008).

2.3.4 Alcoholic Hepatitis

Excessive alcohol consumption is a significant cause of hepatitis and is the most common cause of cirrhosis in the U.S (Friedman *et al.,* 2015). Alcoholic hepatitis is within the spectrum of alcoholic liver disease. This ranges in order of severity and reversibility from alcoholic steatosis (least severe, most reversible), alcoholic hepatitis, cirrhosis, and liver cancer (most severe, least reversible) (Friedman *et al.,* 2015). Hepatitis usually develops over years-long exposure to alcohol, occurring in 10 to 20% of alcoholics (Mailliard *et al.,* 2015). The most important risk factors for the development of alcoholic hepatitis are quantity and duration of alcohol intake (Malliard *et al.,* 2015).

2.3.4.1 Treatment

First-line treatment of alcoholic hepatitis is treatment of alcoholism (Mailliard *et al.,* 2015). For those who abstain completely from alcohol, reversal of liver disease and a longer life are possible; patients at every disease stage have been shown to benefit by prevention of additional liver injury (Mailliard *et al.,* 2015; Maneerat *et al.,* 2014). In addition to referral to psychotherapy and other treatment programs, treatment should include nutritional and psychosocial evaluation and treatment (Mailliard *et al.,* 2015; Maneerat *et al.,* 2014; Singh *et al.,* 2015).

2.3.5 Toxic and Drug-induced Hepatitis

Many chemical agents, including medications, industrial toxins, and herbal and dietary supplements, can cause hepatitis (Lee *et al.,* 2015; Malaguarnera *et al.,* 2012). The spectrum of drug induced liver injury varies from acute hepatitis to chronic hepatitis to acute liver failure (Lee *et al.,* 2015). Toxins and medications can cause liver injury through a variety of mechanisms, including direct cell damage, disruption of cell metabolism, and causing structural

changes (Lee *et al.,* 2003). Some drugs such as paraceutamol exhibit predictable dose dependent liver damage while others such as isoniazid cause idiosyncratic and unpredictable reactions that vary by person (Lee *et al.,* 2015). There are wide variations in the mechanisms of liver injury and latency period from exposure to development of clinical illness (Friedman *et al.,* 2015).

2.3.6 Non-alcoholic Fatty Liver Disease

Non-alcoholic hepatitis is within the spectrum of non-alcoholic liver disease (NALD), which ranges in severity and reversibility from non-alcoholic fatty liver disease (NAFLD) to non-alcoholic steatohepatitis (NASH) to cirrhosis to liver cancer, similar to the spectrum of alcoholic liver disease (Abdelmalek *et al.,* 2015). Non-alcoholic liver disease occurs in people with little or no history of alcohol use, and is instead strongly associated with metabolic syndrome, obesity, insulin resistance and diabetes, and hypertriglyceridemia (Friedman *et al.,* 2015). Over time, nonalcoholic fatty liver disease can progress to non-alcoholic steatohepatitis, which additionally involves liver cell death, liver inflammation and possible fibrosis (Friedman et al., 2015).

Factors accelerating progression from NAFLD to NASH are obesity, older age, non-African American ethnicity, female gender, diabetes mellitus, hypertension, higher ALT or AST level, higher AST/ALT ratio, low platelet count, and an ultrasound steatosis score (Friedman *et al.,* 2015).

2.3.7 Autoimmune

Autoimmune hepatitis is a chronic disease caused by an abnormal immune response against liver cells (NDDIC, 2010). The disease is thought to have a genetic predisposition as it is associated with certain human leukocyte antigens involved in the immune response (Teufel *et al.,* 2009). As in other autoimmune diseases, circulating auto-antibodies may be present and are helpful in diagnosis (Czaja *et al.,* 2016). Auto-antibodies found in patients with autoimmune hepatitis include the sensitive but less specific anti-nuclear antibody (ANA), smooth muscle antibody (SMA), and atypical perinuclear antineutrophil cytoplasmic antibody (p-ANCA) (Czaja *et al.,* 2016). Other auto-antibodies that are less common but more specific to autoimmune hepatitis are the antibodies against liver kidney microsome 1 (LKM1)and soluble liver antigen (SLA) (Czaja *et al.,* 2016).

Autoimmune hepatitis can also be triggered by drugs (such as nitrofurantoin, hydralazine, and methyldopa), after liver transplant, or by viruses (such as hepatitis A, Epstein-Barr virus, or measles) (Friedman *et al.,* 2015). Autoimmune hepatitis can present anywhere within the spectrum from asymptomatic to acute or chronic hepatitis to fulminant liver failure (Friedman *et al.,* 2013). Patients are asymptomatic 25–34% of the time, and the diagnosis is suspected on the basis of abnormal liver function tests (Czaja *et al.,* 2016).

As with other autoimmune diseases, autoimmune hepatitis usually affects young females (though it can affect patients of either sex of any age), and patients can exhibit classic signs and symptoms of autoimmunity such as fatigue, anemia, anorexia, amenorrhea, acne, arthritis, pleurisy, thyroiditis, ulcerative colitis, nephritis, and maculopapular rash (Friedman *et al.,* 2015). Autoimmune hepatitis increases the risk for cirrhosis, and the risk for liver cancer is increased by about 1% for each year of the disease (Friedman *et al.,* 2015). Many people with autoimmune hepatitis have other autoimmune diseases (Krawitt *et al.,* 2008). Autoimmune hepatitis is distinct from the other autoimmune diseases of the liver, primary biliary cirrhosis and primary sclerosing cholangitis, both of which can also lead to scarring, fibrosis, and cirrhosis of the liver (Friedman *et al.,* 2013; Czaja *et al.,* 2016).

2.3.7.1 Treatment

Autoimmune hepatitis is commonly treated by immune-suppressants such as the corticosteroids prednisone or prednisolone, the active version of prednisolone that does not require liver synthesis, either alone or in combination with azathioprine, and some have suggested the combination therapy is preferred to allow for lower doses of corticosteroids to reduce associated side effects, (Czaja *et al.,* 2016) although the result of treatment efficacy is comparative (Summerskill *et al.,* 1975). Treatment of autoimmune hepatitis consists of two phases; an initial and maintenance phase. The initial phase consists of higher doses of corticosteroids which are tapered down over a number of weeks to a lower dose. If used in combination, azathioprine is given during the initial phase as well. Once the initial phase has been completed, a maintenance phase that consists of lower dose corticosteroids, and in combination therapy, azathioprine until liver blood markers are normalized. Treatment results in 66–91% of patients achieving normal liver test values in two years, with the average being 22 months (Czaja *et al.,* 2016).

2.3.8 Genetic

Genetic causes of hepatitis include alpha-1-antitrypsin deficiency, hemochromatosis, and Wilson's disease (Friedman *et al.,* 2015). In alpha-1- antitrypsin deficiency, a co-dominant mutation in the gene for alpha-1- antitrypsin results in the abnormal accumulation of the mutant AAT protein within liver cells, leading to liver disease (Teckman *et al.,* 2013). Hemochromatosis and Wilson's disease are both autosomal recessive diseases involving abnormal storage of minerals (Friedman *et al.,* 2015). In hemochromatosis, excess amounts of iron accumulate in multiple body sites, including the liver, which can lead to cirrhosis (Friedman *et al.,* 2015). In Wilson's disease, excess amounts of copper accumulate in the liver and brain, causing cirrhosis and dementia (Friedman *et al.,* 2015). When the liver is involved, alpha-1-antitrypsin deficiency and Wilson's disease tend to present as hepatitis in the neonatal period or in childhood (Friedman *et al.,* 2015). Hemochromatosis typically presents in adulthood, with the onset of clinical disease usually after age 50 (Friedman *et al.,* 2015).

2.3.9 Ischemic Hepatitis

Ischemic hepatitis (also known as shock liver) results from reduced blood flow to the liver as in shock, heart failure, or vascular insufficiency (Medline Plus, 2012). The condition is most often associated with heart failure but can also be caused by shock or sepsis. Blood testing of a person with ischemic hepatitis will show very high levels of transaminase enzymes (AST and ALT). The condition usually resolves if the underlying cause is treated successfully. Ischemic hepatitis rarely causes permanent liver damage (Feldman *et al.,* 2010).

2.3.10 Other

Hepatitis can also occur in neonates and is attributable to a variety of causes, some of which are not typically seen in adults (Samyn *et al.,* 2015). Congenital or perinatal infection with the hepatitis viruses, toxoplasma, rubella, cytomegalovirus, and syphilis can cause neonatal hepatitis (Samyn *et al.,* 2015). Structural abnormalities such as biliary atresia and choledochal cysts can lead to cholestatic liver injury leading to neonatal hepatitis (Samyn *et al.,* 2015).

Metabolic diseases such as glycogen storage disorders and lysosomal storage disorders are also implicated (Samyn *et al.,* 2015). Neonatal hepatitis can be idiopathic, and in such cases, biopsy

often shows large multinucleated cells in the liver tissue (Roberts *et al.,* 2003). This disease is termed giant cell hepatitisand may be associated with viral infection, autoimmune disorders, and drug toxicity (Sokol *et al.,* 2012; Alexopoulou *et al.,* 2003).

2.4 MECHANISM

The specific mechanism varies and depends on the underlying cause of the hepatitis. Generally, there is an initial insult that causes liver injury and activation of an inflammatory response, which can become chronic, leading to progressive fibrosis and cirrhosis (Dienstag *et al.,* 2015)

2.4.1 Viral hepatitis

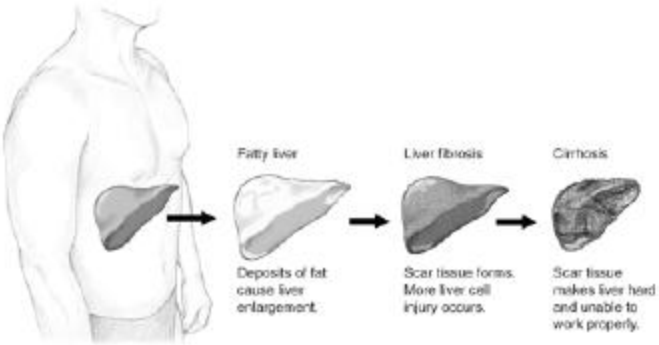

Fig 1: Stages of liver disease

The pathway by which hepatic viruses cause viral hepatitis is best understood in the case of hepatitis B and C (Dienstag *et al.,* 2015). The viruses do not directly activate apoptosis(cell death) (Dienstag *et al.,* 2015; Nakamoto *et al.,* 2003). Rather, infection of liver cells activates the innate and adaptive arms of the immune system leading to an inflammatory response which causes cellular damage and death, including viral induced apoptosis via the induction of the death receptor-mediated signaling pathway (Dienstag *et al.,* 2015; Nakamoto *et al.,* 2003; Lin *et al.,* 2017; Cao *et al.,* 2016).

Depending on the strength of the immune response, the types of immune cells involved and the ability of the virus to evade the body's defense, infection can either lead to clearance (acute disease) or persistence(chronic disease) of the virus (Dienstag *et al.,* 2015). The chronic presence of the virus within liver cells results in multiple waves of inflammation, injury and wound healing that over time lead to scarring or fibrosis and culminate in hepato-cellular carcinoma

(Nakamoto *et al.,*2003; Wong *et al.,* 2014). People with impaired immune response are at greater risk of developing chronic infection (Dienstag *et al.,* 2015). Natural killer cells are the primary drivers of the initial innate response and create a cytokine environment that results in the recruitment of CD4 T-helper and CD8cytotoxic T-cells. (Rehermann *et al.,*2015; Heim *et al.,* 2014). Type I interferons are the cytokines that drive the antiviral response (Heim *et al.,* 2015). In chronic Hepatitis B and C, natural killer cell function is impaired (Rehermann *et al.,* 2015).

2.4.2 Steatohepatitis

Steatohepatitis is seen in both alcoholic and non-alcoholic liver disease and is the culmination of a cascade of events that began with injury. In the case of nonalcoholic steatohepatitis, this cascade is initiated by changes in metabolism associated with obesity, insulin resistance, and lipid dysregulation (Hardy *et al.,* 2016; Yoon *et al.,* 2014). In alcoholic hepatitis, chronic excess alcohol use is the culprit (Chayanupatkul *et al.,* 2014). Though the inciting event may differ, the progression of events is similar and begins with accumulation of free fatty acids (FFA) and their breakdown products in the liver cells in a process called steatosis (Hardy *et al.,* 2016; Yoon *et al.,* 2014; Chayanupatkul *et al.,* 2014). This initially reversible process overwhelms the hepatocyte's ability to maintain lipid homeostasis leading to a toxic effect as fat molecules accumulate and are broken down in the setting of an oxidative stress response (Hardy *et al.,* 2016; Yoon *et al.,* 2014; Chayanupatkul *et al.,* 2014). Over time, this abnormal lipid deposition triggers the immune system via toll-like receptor 4(TLR4) resulting in the production of inflammatory cytokines such as TNF that cause liver cell injury and death (Hardy *et al.,* 2016; Yoon *et al.,* 2014; Chayanupatkul *et al.,* 2014). These events mark the transition to steatohepatitis and in the setting of chronic injury, fibrosis eventually develops setting up events that lead to cirrhosis and hepatocellular carcinoma (Hardy *et al.,* 2016). Microscopically, changes that can be seen include steatosis with large and swollen hepatocytes (ballooning), evidence of cellular injury and cell death (apoptosis, necrosis), evidence of inflammation in particular in zone 3 of the liver, variable degrees of fibrosis and Mallory bodies (Hardy *et al.,* 2016; Basra *et al.,* 2011; Haga *et al.,* 2015).

2.5 DIAGNOSIS

Diagnosis of hepatitis is made on the basis of some or all of the following: a person's signs and symptoms, medical history including sexual and substance use history, blood tests, imaging, and

liver biopsy (Friedman *et al.,* 2015). In general, for viral hepatitis and other acute causes of hepatitis, the person's blood tests and clinical picture are sufficient for diagnosis (Dienstag *et al.,* 2015; Friedman *et al.,* 2015). For other causes of hepatitis, especially chronic causes, blood tests may not be useful ([Friedman *et al.,* 2015). In this case, liver biopsy is the gold standard for establishing the diagnosis: histopathologic analysis is able to reveal the precise extent and pattern of inflammation and fibrosis (Friedman *et al.,* 2015). Biopsy is typically not the initial diagnostic test because it is invasive and is associated with a small but significant risk of bleeding that is increased in people with liver injury and cirrhosis (Grant *et al.,* 1999).

Blood testing includes liver enzymes, serology (i.e. for auto-antibodies), nucleic acid testing (i.e. for hepatitis virus DNA/RNA), blood chemistry, and complete blood count (Friedman *et al.,* 2015). Characteristic patterns of liver enzyme abnormalities can point to certain causes or stages of hepatitis (Green *et al.,* 2002; Pratt *et al.,* 2000). Generally, AST and ALT are elevated in most cases of hepatitis regardless of whether the person shows any symptoms (Friedman *et al.,* 2015) Unlike steatosis and cirrhosis, no imaging test is able to detect liver inflammation (i.e. hepatitis) or fibrosis (Friedman *et al.,* 2015). Liver biopsy is the only definitive diagnostic test that is able to assess inflammation and fibrosis of the liver (Friedman *et al.,* 2015).

2.5.1 Viral hepatitis

Viral hepatitis is primarily diagnosed through blood tests for levels of viral antigens (such as the hepatitis B surface or core antigen), anti-viral antibodies (such as the anti-hepatitis B surface antibody or anti-hepatitis A antibody), or viral DNA/RNA (Dienstag *et al.,* 2015; Friedman *et al.,* 2015). In early infection (i.e. within 1 week), IgM antibodies are found in the blood (Friedman *et al.,* 2015). In late infection and after recovery, IgG antibodies are present and remain in the body for up to years (Friedman *et al.,* 2015). Therefore, when a patient is positive for IgG antibody but negative for IgM antibody, he is considered immune from the virus via either prior infection and recovery or prior vaccination (Friedman *et al,* 2015). In the case of hepatitis B, blood tests exist for multiple virus antigens (which are different components of the virion particle) and antibodies (Villar *et al.,* 2015). The combination of antigen and antibody positivity can provide information about the stage of infection (acute or chronic), the degree of viral replication, and the infectivity of the virus (Villar *et al.,* 2015).

2.5.2 Alcoholic versus non-alcoholic

The most apparent distinguishing factor between alcoholic steatohepatitis (ASH) and nonalcoholic steatohepatitis (NASH) is a history of excessive alcohol use (Neuman *et al.,* 2014). Thus, in patients who have no or negligible alcohol use, the diagnosis is unlikely to be alcoholic hepatitis. In those who drink alcohol, the diagnosis may just as likely be alcoholic or nonalcoholic hepatitis especially if there is concurrent obesity, diabetes, and metabolic syndrome. Liver biopsies show identical findings in patients with ASH and NASH, specifically, the presence of polymorphonuclear infiltration, hepatocyte necrosis and apoptosis in the form of ballooning degeneration, Mallory bodies, and fibrosis around veins and sinuses (Friedman *et al.,* 2015).

2.6 HEPATITIS B VIRUS

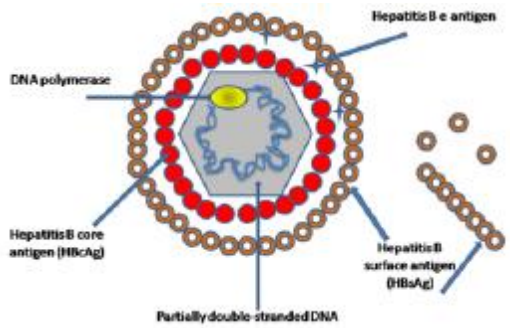

Fig 2.1: Structure of the Hepatitis B virus (Source: Dane et al.).

Hepatitis B virus is among the common viral infectious agents of public health importance globally. An estimated two billion people are infected worldwide with approximately 350 million others suffering the chronic form of the disease (WHO, 2009; Ott *et al.,* 2012). In Africa, more than 50 million people are chronically infected, with mortality risk of about 25%. The carrier rates of the virus in Sub-Sahara Africa range from 9% - 20% (Walana *et al.,* 2014). Hepatitis B virus (HBV) infection is a serious health problem worldwide. Once chronic infection is established, HBV may persist in the liver for lifetime (Jia *et al.,* 2007), which not only causes severe HBV-related sequalae such as cirrhosis and hepatocellular carcinoma but also constitutes the reservoir of the virus (Zou *et al.,* 2001).

The spectrum of the symptoms of HBV disease varies from sub-clinical hepatitis to icteric, hyper-acute, acute and sub-acute hepatitis during the primo-infection phase and from an asymptomatic carrier state to chronic hepatic cirrhosis and hepatocellular carcinoma during the

chronic phase. In the acute phase, the incubation period is 1-6 months (James *et al.,* 2012). Anicteric hepatitis is a predominant form of expression for this disease, at this phase most of the patients are asymptomatic. Patients with anicteric hepatitis have a greater tendency to develop chronic hepatitis. Icteric hepatitis B is associated with a prodromal period, during which a serum sickness-like syndrome can occur (Greenwood *et al.,* 2000).

The predominant routes of transmission is commonly through blood transfusion, blood products, body fluids (urine, semen, sweat, saliva, and tears), use of contaminated needles, vertical transmission (mother to child through infected birth canal), and sexual contact (Brooks *et al.,* 2007). Neonates born of chronically infected mothers have a 70–90% risk of the infection progressing to a chronic phase (Tong *et al.,* 2005). The demand for safe blood or blood products in life-saving interventions is critical to avoiding non curable infectious diseases (Walana *et al.,* 2014). Blood transfusions carry the risk of transfusion-transmitted infections such as hepatitis B. In order to measure their severity, the World Health Organization has recommended a pre-transfusion blood test. The residual risk of infection from HBV is higher than that of hepatitis C virus (HCV) in non-endemic countries (Kwon *et al.,* 2011).

2.6.1 HISTORICAL BACKGROUND

The hepatitis B virus was discovered in 1965 when Blumberg and co-workers found the hepatitis B surface antigen which was originally called the Australia antigen because it was found in serum from an Australian patient (Blumberg *et al.,* 1977). Dr Baruch Samuel Blumberg was awarded the 1976 Noble Prize in Physiology or Medicine for this discovery. The virus was fully described in the 1970s (Dane *et al.,* 1970). In recent times, the rapid and continuous discoveries of the viral disease around the whole world have improved our understanding of the complexity of this unusual virus. Although there has not been any substantial decrease in the overall prevalence of HBV, there is the hope that the next generation will see a decline in both the worldwide carrier rate and the incidence of new HBV infections if current HBV vaccinations are intensified (Batholomew, 2011).

2.6.2 DIAGNOSIS

The tests, or assays, for detection of hepatitis B virus infection involve serum or blood tests that detect either viral antigens (proteins) or antibodies produced by the host. Interpretation of these assays is complex (Bonino *et al.,* 1987). The first step in identifying patients with chronic HBV infection is to screen those with risk factors. Screening is focused on patients in high-risk groups, such as persons born in endemic areas, patients engaged in high-risk sexual behaviors, injection drug users, dialysis patients, HIV-infected and other immunosuppressed patients, pregnant women, and persons with occupational exposure, as well as family/household members and sexual contacts of HBV-infected persons.

The hepatitis B surface antigen (HBsAg) is most frequently used to screen for the presence of this infection. Testing for antibody to hepatitis B core (anti-HBc), and antibody to hepatitis B surface antigen (anti-HBs) indicate whether an individual has been previously exposed to HBV. The HBV DNA levels are not required for preliminary screening for the HBV-infection. The HBsAg is the first detectable viral antigen to appear during infection. However, the length of time within which detectable amount of HBsAg may persist in host depends on efficiency of host immune function at clearing the virus-infected hepatocytes and establishing enduring immunity (Lai *et al.,* 1991).

Individuals who remain HBsAg positive for at least six months are considered to be hepatitis B carriers (Lok and McMahon, 2007). Carriers of the virus may have chronic hepatitis B, which would be reflected by elevated serum alanine aminotransferase levels and inflammation of the liver, as revealed by biopsy. Carriers who have seroconverted to HBeAg negative status, particularly those who acquired the infection as adults, have very little viral multiplication and hence may be at little risk of long-term complications or of transmitting infection to others (Chu and Liaw, 2007). Additionally, polymerase chain reaction (PCR) tests have been developed to detect and measure the amount of viral nucleic acid in clinical specimens. These tests measure viral loads and are used to assess a person's infection status and to monitor treatment (Zoulim, 2007).

2.6.3 PATHOGENESIS, VIRUS AND HOST INTERACTION

Viral hepatitis, characterized by diffused inflammatory reaction, is associated with cell damage and death. It has been recently reported that HBV replication is associated with cell death, which is different from the widely accepted non-cytopathic characteristics of HBV (Philip *et al.,* 2006). The mechanism of cell damage is generally defined as the result of cytotoxic T-lymphocyte (CTL)- mediated immune responses to viral infection. Indeed, whatever the undesirable pathological effect that may result from the infection, it is only the consequence of the interaction of the virus with host factors. Generally, the hepatitis B virus interacts with the host hepatocytes at two levels (Kim *et al.,* 2007):

a) Virus protein interacting with host proteins (mainly transcriptional / signaling factors).

b) Virus genome interacting with host proteins (mainly transcriptional factors).

2.7 TRANSMISSION

HBV is highly contagious and is transmitted by percutaneous and permucosal exposure to infected blood and other body fluids (i.e. semen and vaginal fluid). The highest concentrations of the virus occur in blood and wound secretions (WHO, 2001). Moderate concentrations of HBV are found in semen and vaginal fluid, and lower concentrations occur in saliva. HBV is not spread by air, food, or water. Common modes of transmission include mother-to-infant, child to-child, unsafe injection practices and blood transfusions, and sexual contact. HBV may be detected in serum 30–60 days following infection, and may persist for widely variable periods of time. Perinatal transmission from HBsAg-positive mothers to their newborn infants (vertical) or transmission from one child to another (horizontal) is a major source of HBV infections in many countries where chronic HBV infection is highly endemic (WHO, 2001). Perinatal transmission usually happens at the time of birth; in-utero transmission is relatively rare, accounting for less than 2% of perinatal infections in most studies. There is no evidence that HBV can be spread by breastfeeding (Beasley *et al.,* 1975). The risk of perinatal transmission depends on the HBeAg serostatus of the mother. The risk of HBV infection approximately ranges from 70–90% for HBeAg-positive mothers to 5–20% for HBeAg negative mothers (Okada *et al.,* 1976; Beasley *et al.,* 1977). The spread of HBV from child to child usually happens in household settings but may also occur in child daycare centres and schools (WHO, 2001). The most probable pathways of child-to-child spread involve contact of skin sores, small breaks in the skin, or mucous

membranes with blood or skin sore secretions (Margolis *et al.,* 1997). HBV may also spread because of contact with saliva through bites or other breaks in the skin, and as a consequence of the premastication of food (MacQuarrie *et al.,* 1974; Scott *et al.,* 1980; Beasley & Hwang, 1983; Williams *et al.,* 1997). The virus may spread from inanimate objects such as shared towels or toothbrushes, because it can survive for at least 7 days outside the body, and can be found in high titres on objects, even in the absence of visible blood (Petersen *et al.,* 1976; Bond *et al.,* 1981; Martinson *et al.,* 1998). Among Gambian children aged 6 months to 5 years, a significant association was observed between HBV infection and the presence of bedbugs in each child's bed (Vall Mayans *et al.,* 1990). But controlling bedbugs by insecticide spraying of the child's dwelling did not have any effect on HBV infection (Vall Mayans *et al.,* 1994). Unsafe injection practices such as the re-use of a syringe or needle from patient to patient without sterilization are a common source of transmission of HBV in many developing countries (Kane *et al.,* 1999; Simonsen *et al.,* 1999).

In addition, unsatisfactory infection control practices, including the re-use of contaminated equipment for medical, cosmetic or dental procedures, failure to use appropriate disinfection and sterilization practices for equipment and environmental surfaces, and improper use of multidose medication vials, can also result in the transmission of HBV. Blood transfusion is also a common source of HBV transmission in countries where the blood supply is not screened for HBsAg. In addition, the injection of illicit drugs using shared needles is a common mode of HBV transmission in many developed countries. HBV is efficiently transmitted by sexual contact, which accounts for a high proportion of new infections among adolescents and adults in countries with low and intermediate endemicity of chronic HBV infection (Alter & Margolis, 1990). Risk factors for sexual transmission include multiple sexual partners, prostitution, and lack of protection in sexual activity (e.g. the use of condoms). In countries where HBV infection is highly endemic, sexual transmission does not account for a high percentage of cases because most persons have been infected since childhood.

2.8 STAGES OF HEPATITIS B VIRUS INFECTION

Remarkable progress has been made in the understanding of the three (3) main natural stages of the HBV infection in hosts: acute infection, chronic asymptomatic and chronic symptomatic stages according AASLD, 2007. However, not all HBV-infected patients go through all the three stages. The risk to develop liver–related complications, such as cirrhosis and hepatocellular carcinomas increases as patient progresses from acute to chronic stage of the infection. Indeed, most HBV infections end up at the acute stage (~ 90%) with a few progressing on to the chronic stage.

2.8.1 Acute HBV Infection

This is the initial stage of the infection and every HBV- infected patient goes through this, even though not all patients transit beyond this stage. Early phases of this stage of the infection are characterized serologically by the presence of HBsAg, high serum HBV DNA, HBeAg, and normal level of serum aminotransferase level (ALT), and minimal or insignificant inflammation on liver biopsy (Altiparmak *et al.,* 2005). A later phase, also called immunity phase, is marked by increased serum titres of anti-HBsAg IgG (HBsAb), anti-HBcAg IgG, lowered or disappearance of HBsAg and HBV DNA, normal liver histology. This is true for those who recover fully from the infection after attaining full and permanent immunity through exposure. The duration of either phase differs among patients but generally lasts between 5-8 months according to AASLD, 2007. However, those patients who fail to mobilize adequate immune response factors to combat the infection end up with the fate of living with the disease their entire lifetime. In this case, it is said the disease has become chronic. The physical signs and symptoms, such as jaundice, fever, dark-urine formation, nausea, among others, would occur, even though they will last shortly after which they get resolved following recovery. Generally, transition from the acute stage to the chronic stage depends on several factors including age, gender, viral genotype, and host immune competence.

2.8.2 Chronic HBV Infection

This occurs as a progression of the early phase of the acute HBV infection due to the host‘s failure to mount the necessary immune stimulus to ensure total viral clearance and consequent resolution of the disease. It is serologically marked by relative rise in serum anti- HBcAg IgG,

disappearance or lower titres of anti-HBsAg IgG, and either normal or significant liver damage as shown by ultrasonography (Krajden, 2005).

The serological presence of HBeAg is real in all stages of the disease. The presence of this antigen together with elevated viral load (HBV DNA > 10 3 copies/ml) and higher ALT (> 60 IU/l) is a strong indication of viral activity, replication, and infectivity (Krajden, 2005). Patients with such manifestations are put on retroviral. It is believed that seroconversion of HBeAg to HBeAb is accompanied with cessation of HBV replication and remission of liver disease. Several studies have shown that seroconversion with a marked reduction in HBV replication is associated with biochemical and histological remission of inflammatory activity in the majority of patients (McMahon, 2005).

2.8.3 Epidemiology of Infection

HBV is one of the most common infectious viruses worldwide. It is estimated that more than two billion people are infected. Approximately 360 million of these are chronically infected (Lee, 1997; Chen *et al.,* 2007; Dienstag, 2008). Approximately one million people die each year from HBV-related chronic liver disease, including liver cirrhosis and hepatocellular carcinoma (HCC) (Mahoney, 1999). HCC is one of the most common cancers in the world, and chronic HBV infection is responsible for 50–90% of HCC in high-risk areas (Chen *et al.,* 1997). The epidemiology of chronic HBV infection is distinct and diverse worldwide. Various seroprevalence studies conducted in different areas of world can easily be categorized into three distinct groups of higher, intermediate and lower endemicity (Hou *et al.,* 2005). In developing countries with larger population (South East Asia, Sub Sahara Africa, China, Indonesia, Nigeria and Amazon Basin), there is higher prevalence of endemicity with approximately 8% of population as chronic carrier of HBV. In aforementioned areas of world, 70% to 95% of population represents present or past serological markers against HBV. In another study, it has been reported that 60% of world population exist in high endemic zone of HBV infection (Colin *et al.,* 2006; Alter *et al.,* 2003; Margolis *et al.,* 1991).

The intermediate endemic zone of HBV infection, Middle East, Eastern and Southern Europe, South America and Japan exist. Among these populations the estimated infection is approximately 10-60% and the chronic carrier rate is 2-7%. In the region of intermediate

endemicity, majority of infection develop in adults but rate of chronic infection are higher in infants due to early childhood exposure to viral infection (Toukan, 1990). The seroprevalence of HBV infection has been reported 5% in India, while in Italy, Russia and Turkey the prevalence rate ranges from 3%-10% (Kurien *et al.,* 2005; Iashina *et al.,* 1992; Erden *et al.,* 2003; Da-Villa and Sepe, 1999).

Fig 2.2: Global epidemiology of HBV and prevalence of HBV carriers (Source: Murray et al., Medical Microbiology)

The HBV zone of lowest endemicity includes most developed countries such as Australia, North America and Northern and Western Europe. In aforementioned regions of world approximately 5-7% of population gets HBV infected with nearly 0.5% to 2.0% rate of chronic carriers. The most probable reasons of HBV infection in young adolescents could be exposure to high risk population groups, injection drug users, health care professionals, sex workers and unhealthy blood transfusion setups (McQuillan *et al.,* 1989).

2.8.4 PREVALENCE OF HEPATITIS B VIRUS IN NIGERIA

Nigeria, a tropical country, has been documented as highly endemic for HBV infection and about 75% of its population is likely to have been exposed to the virus at one time or the other in their lives (Sirisena *et al.,* 2002). Currently about 18 million Nigerians are infected (Jombo et al., 2005). A prevalence rate of 4.3 % was reported from Port Harcourt (Akani et al., 2005), 5.7% from Ilorin (Agbede *et al.,* 2007), 11.6% from Maiduguri (Harry et al., 1994) and 8.3% from

Zaria (Jatau *et al.,* 2009). A seroprevalence of 23.3% was reported among patients attending all clinics at the Aminu Kano Teaching Hospital (AKTH) (Nwokedi *et al.,* 2006).

2.8.4.1 Prevalence of Hepatitis B Virus Among Blood Donor

Mosley et al., suggested that anti-HBc screening of blood donations might prevent HBV transmission from HBsAg-negative blood donors that are positive for anti- HBc (Mosley *et al.,* 1995). The prevalence of OHB varies significantly between geographical regions as well as among various patient populations tested. Recent Evaluation of hepatitis B virus sero-positivity among 300 voluntary blood donors at a centralized blood service center in Nigeria by (Damulak *et al.,* 2013) revealed that Thirty-three (13.8%) of first-time donors were positive for hepatitis B markers while all retained donors were sero-negative. There were 32 (13.3%) sero- positive reactions to HBsAg and 3 (1.3%) reacted to HBeAg. In another study in Jos, Uneke and others reported a 14.3% HBsAg Seropositivity among their blood donors against a higher 25.9% among patients infected with HIV. They also noted higher infection rate of 44% in donors 51-60 years and 28% frequency within the age bracket of 31-40 years (Uneke *et al.,* 2005; Altiparmak *et al.,* 2012), while studying Seroprevalence of hepatitis B e antigen (HBe antigen) and B core antibodies among hepatitis B surface antigen positive blood donors at a Tertiary Centre in Nigeria found a seroprevalence of 8.2% (22 of 267) HBeAg, 4 of 267 (1.5%) were indeterminate while 241 (90.3%) of their subjects tested negative. Only 27 out of 267 donors (10.1%) tested positive to IgM anti-HBcore, 234(87.6%) tested negative, while 6(2.2%) were indeterminate. A higher percentage of 60.7% (162 of 267) tested positive to IgG anti- HBcore, while 39.3% (105 of 267) tested negative. They concluded that there is a low seroprevalence rate of HBeAg-positive chronic hepatitis and relatively high IgG anti-HBcore and IgM anti-HBcore rates in South West Nigeria (Altiparmak *et al.,* 2012).

Another study among blood donors, in North Central Nigeria, at the Bishop Murray Medical Centre in Makurdi, age group prevalence of HBV was reported at 11.90%, 13.05% and 6.53% within the age ranges of 18-22, 23-27 and 28-32 years respectively (Aernan *et al.,* 2011). Jeremiah and others reported a prevalence of 8.6% HBsAg in Maiduguri, Northeast Nigeria with anti HBc IgM in 18.4% suggesting that donors negative for HBsAg are not necessarily

uninfected with HBV and recommended the mandatory screening of HBc in donor blood (Jeremiah *et al.,* 2011).

In Southwest Nigeria Salawu and others reported the occurrence of other HBV markers in HBsAg negative blood donors and recommended the inclusion of routine testing of markers such as antibody to hepatitis B core (HBC) antigen in donor blood before transfusion (Salawu *et al.,* 2011). Japhet and his co-workers found an overall prevalence of transfusion transmissible infections of 32.6% in their study with 19.6% HBsAg positivity, 13.0% HBC antibody reaction and 8.9% hepatitis B envelop antigen (HBeAg) detection which marks infectivity of the virus and appears in blood after HBsAg (Japhet *et al.,* 2011).

In Benin City of Nigeria, Mutimer and others reported an overall 14% prevalence of TTIS. They concluded that screening of blood routinely may not reduce the incidence of HBV infections. Far in the North Eastern Nigeria, Harry and colleagues reported a high 22.0% HBsAg and 6.64% HBeAg among blood donors. They found only 11.6% and 1.39% of pregnant women subgroup of their study reactive for HBsAg and HBeAg respectively (Harry *et al.,* 1994).

2.8.4.2 Prevalence of Hepatitis B Virus among Pregnant Women

Adabara et al., evaluated the Prevalence of Hepatitis B Virus among Women Attending Antenatal Clinic in the General Hospital, Minna, Niger State, there results revealed that 13(6.5%) out of the 200 subjects investigated were found to be positive for hepatitis B infection(Adabara et al., 2012). On the basis of age, the distribution of HBV infection among the subjects revealed that the age group 20-29 has the highest rate of infection of 10.3% followed in descending order by 40-49 (4.5%), 30-39 (4.2%) and 10-19 (0.0%). The authors linked the prevalence of the virus to low level of awareness and the poor standard of living observed among the subjects (Eke *et al.,* 2011) carry out a cross-sectional study over a 3-month period (August-October 2009).

On Prevalence and pattern of hepatitis B among 480 women attending antenatal clinics in Nnewi, Nigeria was done by simple random sampling using computer generated random numbers. Of these, 40 tested positive to HBsAg, accounting for 8.3% of the sample population. The age of the subjects studied varied from 14 to 45 years (mean age - 24.3 years) while the mean parity was 2.18. The HIV/HBV co-infection rate was 4.2%. Agarry and Lekwot also

evaluated the prevalence of hepatitis B virus surface antigen (HBsAG) and hepatitis C (HCV) antibody amongst 200 pregnant women attending ante-natal clinic in Gwagwalada, Abuja. Of the 200 blood samples tested, 19 (9.5%) and 1 (0.5%) were positive for the presence of hepatitis B and C respectively. No mixed infection of both viruses was observed in the pregnant women tested (Agarry *et al.,* 2010; Ojo *et al.,* 2009). While studying the seroprevalence of hepatitis B virus (HBsAg) antibodies in pregnant women In Akure, Ondo State found that out of Eight hundred and sixty pregnant women. Only forty (4.7%) were positive while eight hundred and twenty (95.3%) were negative, indicating an overall prevalence of 4.7% (Ojo *et al.,* 2009).The prevalence of Hepatitis B Virus (HBV) carrier and infectivity status among three hundred (300) pregnant women in Makurdi were evaluated (Mbaawuaga *et al.,* 2014). Maternal HBV infectivity status was determined by testing all HBsAg positive samples for the presence of hepatitis B e antigen (HBeAg). Overall, 33 (11%) pregnant women were identified as carriers of HBV and 10 of the 33 (30.3%) pregnant women identified as HBV carriers tested positive for HBeAg. Hence, 3.3% of the entire study population was found to have high viral replication as well as high risk of transmitting HBV to their neonates.

2.8.4.3 Prevalence of Hepatitis B Virus Co-Infections with Other Disease

Recently Ejeliogu (Ejeliogu *et al.,* 2014), evaluated the Prevalence of Hepatitis B Virus Co-infected Nigerian Children (2 months to 15 years) with Human Immunodeficiency Virus. Out of 452 Children that were screened, three hundred and ninety-four (87.2%) were mono-infected with HIV while 58 (12.8%) were co-infected with HIV and HBV (HIV/HBV). Egah et al while studying seropositivity to hepatitis B, C and the human immunodeficiency viruses among clergy men in training, in a seminary in Jos, found a 15.5% hepatitis B surface antigen positive reaction among their subjects who were a low risk blood donor group. They also documented a crude transfusion transmissible infection prevalence of 22.1% and HIV/ HBV co-infection rate of 0.4% in their study (Egah *et al.,* 2007). In the year 2011 Omalu et al., evaluated the seroprevalence of Malaria and Hepatitis B (HBsAg) with Associated Risk Factors among Pregnant Women Attending Antenatal Clinic in General Hospital Minna, North-Central Nigeria. Out of the 269 pregnant women screened 216(80.30%) were positive for malaria, 22(8.18%) for hepatitis B and 21(7.81%) were co-infection of malaria and hepatitis B and 10 were negative, while non-

pregnant women had 51(51.00%), 8(8.00%) and 6(6.00%) for malaria, hepatitis B and co-infection of both out of 100 screened (Omalu *et al.,* 2012; Emmunuel *et al.,* 2014) found out that out of 1535 sampled individuals analyzed for Hepatitis B Virus (HBV), 1319 (85.9%) showed a serological evidence of exposure to HBV infection, some through natural infection (22.7%) and others (13.0%) through vaccination; 12% of the exposed were inferred to be currently infected and 91.2% chronically infected. Hepatitis delta virus (HDV) antigen was also detected in 2.7% of the HBsAg positive individuals; and was encountered more (6.7%) in those with acute hepatitis than those with chronic disease.

Jibrin & Mustapha (Jibrin *et al.,* 2004), screened, two hundred consecutively recruited HIV-infected individuals comprising 97 males and 103 females for HBsAg using ELISA. A total of Fifty-three of the patients tested positive for HBsAg giving an overall prevalence rate of 26.5% which was significantly higher ($p < 0.001$) than the 10.4% recorded among non-HIV-infected individuals. Co-infection rate in males (24.7%) did not differ significantly from that of females (28.2%). Co-infection was highest in the 40-49 years age group (41.6%), while no case of co-infection was recorded in the ≤ 19 years. Among the different occupational groups businessmen had the highest co-infection rate (44%) followed by long distance drivers (39.5%). In relation to marital status, divorcees/widows had the highest proportion of those with coinfection (53%) followed by those who were unmarried (32.5%) and those married (21.6%). The authors confirm the high prevalence rate of HBV co-infection in HIV-infected patients compared to the non-HIV-infected population. Therefore, there is a need to screen all HIV-infected patients for HBV infection. According to Taiwo et al. [Taiwo *et al.,* 2012] among patients in Lagos State University Teaching Hospital (LASUTH), Dual presence of HBsAg and anti-HCV was observed in 4(3.9%) of HIV infected patients, while 29(28.4%) and 15(14.7%) were repeatedly reactive for HBsAg and anti-HCV respectively. HIV negative blood donor controls have HBsAg and anti-HCV prevalence of (22) 6.0% and (3) 0.8% respectively. The prevalence of hepatitis co infection is higher among the male study patients 16(50%) than the female32 (45.7%). Salawu et al. [Salawu *et al.,* 2010] studied the Prevalence and trends of HBsAg, anti-HCV, anti-HIV and VDRL in blood donors in the last three and a half years in a tertiary health care facility in Ile-Ife, Nigeria. The screening records of all blood donors from January 2006 to June 2009were evaluated with respect to screening outcome for HBsAg, anti-HIV, anti-HCV and VDRL. Of the

total 14,500 donors bled, 7.50% were positive for HBsAg, 0.96% for anti- HIV, 0.86% for anti-HCV and 2.61% for VDRL. There was a gradual decline in the prevalence rate of HBsAg from 9.20% in 2006, to 8.37 in 2007 and 6.25% in 2008; with a rise in the first half of 2009 to 6.32%. Similarly, HIV prevalence declined from 1.44% in 2006 to 0.94% in 2007 and 0.66% in 2008 but rose to 0.96% in the first half of 2009. Ejeliogu et al. [Ejeliogu *et al.,* 2014], evaluated the prevalence of Hepatitis B Virus Co-infected Nigerian Children (2 months to 15 years) with Human Immunodeficiency Virus. Out of 452 Children that were screened, three hundred and ninety-four (87.2%) were mono-infected with HIV while 58 (12.8%) were co-infected with HIV and HBV (HIV/HBV). Jibrin & Mustapha [Jibrin *et al.,* 2004], screened, two hundred consecutively recruited HIV-infected individuals comprising 97 males and 103 females for HBsAg. A total of Fifty-three of the patients tested positive for HBsAg giving an overall prevalence rate of 26.5% Co-infection rate in males (24.7%) did not differ significantly from that of females (28.2%). Co-infection was highest in the 40-49 years age group (41.6%), while no case of co-infection was recorded in the ≤ 19 years. Among the different occupational groups businessmen had the highest co-infection rate (44%) followed by long distance drivers (39.5%). Similarly, Hamza et al. (2013) evaluated the prevalence of HIV-HBV- patients in Kano State and find out that 54/440 were HB-HIV coinfected [Nwokedi *et al.,* 2006], also evaluated the prevalence of HIV-HBV- patients in Kano State and find out that 211/300 were HB-HIV coinfected [Udeze et al., 2015], evaluated the prevalence rate of HB and C infections among HIV-infected patients accessing healthcare at HIV and AIDS section of University of Ilorin Teaching Hospital, Ilorin, Nigeria. Of the 356 HIV-infected participants, 114 (32.0%) and 14 (3.9%) were respectively positive for HBsAg and anti-HCV antibody.

2.8.4.4 Prevalence of Hepatitis B Virus among Healthy Individuals

James et al., 2011carried out a study to assess the sero-prevalence of hepatitis B surface antigen (HBsAg) and associated risk factors among students of a secondary school in Jagindi Tasha, Kaduna State, Nigeria. Out of One hundred and ninety (190) apparently healthy students that were screened for HBsAg, 35 (18.4%) were sero-positive. Subjects aged 13-15 years recorded 6.8% positivity and male subjects had 25.5% positivity compared to 10.9% positivity for females. Risk factors such as blood transfusion was 32.0% among male subjects compared to 30.0% in

females. Moses et al., (2010), evaluated the prevalence of Hepatitis B virus infections in apparently healthy urban Nigerians. Of the 1,891 participants, 957 (50.6 %) were males and 934 (49.4%) were females. Overall 114 (6.0%) were positive, of whom 71 (7.4%) were males and 43 (4.6%) females. Those aged 21–30 years had the highest infection rate, and males were more likely to be infected with the virus than females. According to Gambo et al. [Gambo *et al.,* 2012] out of 182 Fulani nomads in Toro, North-Eastern Nigeria the gender-specific seroprevalence of HBsAg was found to be in the ratio of about 2:1 male-female. Infection rate was found to be higher in those between 25 and 29 years (8.2%) followed by those the age group 30-37 years (6.0%). According to Olokoba et al., 2009, Five hundred and ninety-five consecutively recruited voluntary blood donors in Yola, Nigeria that were screened for hepatitis B and hepatitis C virus infections. Only 14 donors (male) each (2.4%) were positive for HBsAg and anti- HCV. The authors concluded that the seroprevalence of hepatitis B and C virus infection is low among voluntary blood donors in Yola, Nigeria [Odinachi *et al.,* 2014], evaluated the Prevalence of Hepatitis B surface Antigen among the Newly Admitted Students of University of Jos, Nigeria. Out of the 300 newly admitted students that were screened, 50 (16.7%) were seropositive to HBsAg. The prevalence of HBsAg was higher in males 34(11.33%) compared to 16(5.33%) in females. Age specific prevalence was significantly higher in the age bracket 25-29, with 16(28.57%) and the lowest was found in the age bracket 15 -19 years with 12(17.39%). In a study conducted by Ndako et al. [Ndako *et al.,* 2014], a total of 188 Health personnel, which constitutes Nurses, Doctors, Medical Laboratory Scientists, Technicians/Assistants, Pharmacists and Ward Assistance in Uyo Metropolis, were screened for HBV surface antigen (HBsAg). Out of the one hundred and Eighty-eight (188) respondents screened. Thirty-two (32) representing 17.0% were found to be seropositive, female subjects recorded (17.3%) prevalence compared to (16.7%) recorded by the Male subjects. Frank et al., 2004 carried out epidemiology study of HBV infection among 124 unvaccinated Dutch missionaries and family members who lived in a rural area of Nigeria. Antibodies to hepatitis B core antigen were found in 5 (9.8%) of 51 adults (incidence rate, 1.7 per 1000 person-months at risk [PMAR]) and 9 (12.3%) of 73 children (incidence rate, 2.8 per 1000 PMAR).

2.8.5 PREVENTION AND TREATMENT OF HEPATITIS B

Even though HBV has become a major source of health concern worldwide, we should also be reminded by the good news that it is the only STD that can be prevented by vaccination (CDC, 2005).The prevention of HBV globally has become one of the topmost priorities of major political actors and decision makers in recent years. The disease is prevented using safe and effective vaccine which became available in 1982 through funding and implementation of hepatitis B immunization programs. Measures for HBV prevention have been geared towards avoidance of unsafe blood exposure or blocking of transmission before the advent of the vaccine. Unsafe blood transfusion has been a major force in the transmission of HBV globally [Wang *et al.,* 1960]. The enactment of a law for the donation and management of blood in blood banks across the world has aggressively fought this channel of HBV transmission. This notwithstanding, current researches have showed that blood transfusion is regaining its position as one of the major risk factors for HBV transmission globally. This finding is attributed to the presence of occult HBV infection (OHBVI) among blood donors [Shang *et al.,* 2007]. It is also worth mentioning that the global acceptance of the auto-disposable syringes (ADS) has considerably reduced the incidence of HBV infections that occur due to unsafe injections. Also, as a result of the extensive use of invasive medical procedures, iatrogenic HBV infections are no longer frequent. There have also been speculations that dental care operations which are capable of causing oral mucous membrane injuries is becoming a major route to HBV transmission if steps are not taken to prevent it [Zhang *et al.,* 2008]. HBV per se does not have a permanent treatment therefore, the surest antidote to the global epidemic is prevention. There has not been any universal agreement on drugs used for the temporary treatment of the HBV in the world even though two therapeutic agents such as interferon alpha (IFNa) and lamivudine are currently used by many countries for the treatment of the disease. Interferon-alpha is a potent cytokine with antiviral and immune-modulating actions which is produced in response to viral infection [Sen *et al.,* 1993]. Temporary treatment of the disease is therefore aimed at suppressing viral replication, reducing the risk of progressing to advanced liver disease or inflammation of the liver and the development of complications such as liver failure or liver cancer [Adabara *et al.,* 2012; Amira, 2011; Ataallah *et al.,* 2011; Bonino *et al.,* 1987; CDC, 2005; Chu *et al.,* 2007; Colin *et al.,* 2006].

Chronic hepatitis B is therefore easily managed rather than treated. Some of the general management strategies for HBV recommended by medical experts include the avoidance of:

1. Heavy alcohol consumption.
2. Unprotected sexual intercourse with partners who are not vaccinated.
3. Sharing of needles or other items that potentially contain blood such as shavers or toothbrushes.
4. Donation of blood or organs.
5. Screening of family members and sexual partners for HBV infection and vaccination of those who are sero-negative [Conjeevaram *et al.,* 2001; Elgouhari *et al.,* 2008; Frank *et al.,* 2004; Hajrullah *et al.,* 2009; *Howard et al.,* 1986; Huang *et al.,* 2006; James *et al.,* 2011; Juergen *et al.,* 2007; Kim *et al.,* 2007; Lai *et al.,* 1991].

6. Patient education and long-term follow-up with regular testing of liver biochemistry and surveillance of hepatocellular carcinoma in high risk groups [Batholomew, 2011;Lavanchy, 2002; Locarnini, 2004; *Lok et al.,* 2007; McMahon *et al.,* 2007, Milich *et al.,* 2003].

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study settings

This study will be conducted in the University of Benin, Benin City, Edo State, Nigeria(6.3998° N, 5.6099° E). Both are male and female students. The university serves students in Edo State as well as neighboring States.. The choice of a University selection is based on pragmatic factors, including the availability of researchers in Benin City.

3.2 Study design

The study will use a cross-sectional design, collecting data on both outcome variables and covariates at one point in time.

3.3 Sample size determination

A representative sample size will be determined using the formula below:

$$n = \frac{3.84\pi (1-\pi)}{w^2}$$

Where n=estimated sample size; π=prevalence of HBV among University of Benin students in the federal University of Benin, Benin city; estimated at 13.7% (Dan Nwafor *et al.,* 2021); w= precision of estimate.

Therefore, with a prevalence of 13.7 (0.137) and wanting to estimate our sample size to within 3% (w=0.03) with 95% certainty, the estimated sample size for this study is 504. To account for a non-response rate of 15%, the sample size is increased to 630 (i.e., 315 UNIBEN students in Benin City).

3.3.1 Inclusion and exclusion criteria

All students who gave oral informed consent and willingness to participate in the study will be eligible to participate in the study. However, students (regardless of age) who are less than two

months in the University prior to the commencement of study data collection will be excluded from this study.

3.4 Sampling technique

A simple random sampling technique will be used in this study. Using students size per department, the estimated sample size for each prison will be randomly selected for the study. In the case of refusal, the randomisation process will be repeated until the sample size for a school is attained.

3.5 Ethical considerations

Ethical approval will be obtained from the University of Benin Ethical Review Board.

3.6 Data and sample collection

Five millilitres of blood will be aseptically collected from each student by venipuncture of the cubital vein using sterile disposable vacutainer blood collection needles and bottles. Samples will be placed in plain tubes, and the sera will be separated into sample vials and stored at -20°C until analysis. Serum samples will be analysed for the presence of HBsAg using a rapid lateral flow chromatographic immunoassay kit. The test was carried out and interpreted according to the manufacturer's instructions. Positive samples were confirmed using the Enzyme-Linked Immunosorbent assay technique (ELISA).

A pretested structured interviewer-administered questionnaire adapted from the national Hepatitis survey will be used for data collection. The questionnaire includes both closed and open-ended questions and will be sectionalised into socio-demographic characteristics, risk factors associated with HBV infection and vaccination history. The laboratory test results for participants will be anonymously linked to their questionnaire information through unique identifiers.

3.6.1 Data analysis

Multivariate analysis will be performed on factors significantly associated with HBV seropositivity for possible confounding and effect modification—chi-square tests for a significant relationship between the dependent and independent variables. HBV serological

marker patterns were interpreted using the WHO HBV markers algorithm. P-values were considered significant at < 0.05, and odds ratios were reported with a 95% confidence interval. A positive HBsAg test will be considered evidence of HBV infection (chronic carrier state or infection) and used to calculate the prevalence.

CHAPTER FOUR

RESULTS

Table 4.1: shows the result of the rapid diagnostic tests outcome for HBV and the percentage occurrence of students positive or negative to HBV. From the results garnered, it is observed that out of the 328 students tested, 326 (99.4%) of the students tested negative to HBV while only 2 (0.6%) students were positive to HBV.

Table 4.2: shows the socio-demographic characteristics and percentage frequency of students who are positive and those negative from the different faculties surveyed, the age category of the students, sex, level of study, state of residence, blood group, etc. in relation to HBV positivity and the risk factors.

Figure 3: shows age bracket of people who are most prone to H. pylori. It is observed that people who are most infected are the adolescents of the age 15 years to 27years. The infection is more rampart among immediate adults of the age 20years while adults between 28years to 40years are less prone to it. It is also observed that from age 45-60years the infection tends to diminish.

Table 4.1: Rapid diagnostic test outcome for HBV test

RDT HBV test	Frequency (%)
Negative	326 (99.4))
Positive	2 (0.6)
Total	328 (100.0)

Table 4.2: Socio-demographic characteristics of the study participants in relation to HBV positivity and risk factors

Characteristic	Negative (n=326)	Positive (n=2)
Mean (SD) age, year	21.6 (4.0)	23.0 (1.4)
Age category, year		
16-20	131 (40.2)	2 (100.0)
21-25	165 (50.6)	-
26-59	24 (7.4)	-
Missing	6 (1.8)	-
Sex		
Female	174 (53.4)	1 (50.0)
Male	152 (46.6)	1 (50.0)
Level of study		
100 level	110 (33.7)	-
200 level	59 (18.1)	1 (50.0)
300 level	60 (18.4)	-
400 level	**77 (23.6)**	1-
500-600 level	19 (5.8)	1 (50.0)
Missing	1 (0.3)	-
Tribal mark		
No	215 (66.0)	1 (50.0)
Yes	42 (12.9)	1 (50.0)

TABLE 4.2 continued

Missing	69 (21.2)	-
Use of local manicure (Aboki)		
No	311 (95.4)	2 (100.0)
Yes	15 (4.6)	-
Ownership of personal clipper		
No	251 (77.0)	2 (100.0)
Yes	75 (23 (23.0)	-
Sharing of sharp object		
No	257 (78.8)	2 (100.0)
Yes	69 (21.2)	-
Piercing on the body (other than earrings)		
No	302 (92.6)	2 (100.0)
Yes	24 (7.4)	-
Tattoo on the body		
No	317 (97.2)	2 (100.0)
Yes	9 (2.8)	-
Alcohol intake		
No	242 (74.2)	2 (100.0)
Yes	84 (25.8)	-
Blood transfusion		
No	320 (98.2)	1 (50.0)
Yes	6 (1.8)	1 (50.0)
Sexually active		
No	143 (43.9)	1 (50.0)
Yes	114 (35.0)	1 (50.0)
Prefer not to say	69 (21.2)	-
Previous Hepatitis B test		
No	312 (95.7)	2 (100.0)

Yes	14 (4.3)	-
No	201 (61.7)	2 (100.0)
Yes	7 (2.2)	-
Not sure	118 (36.2)	-

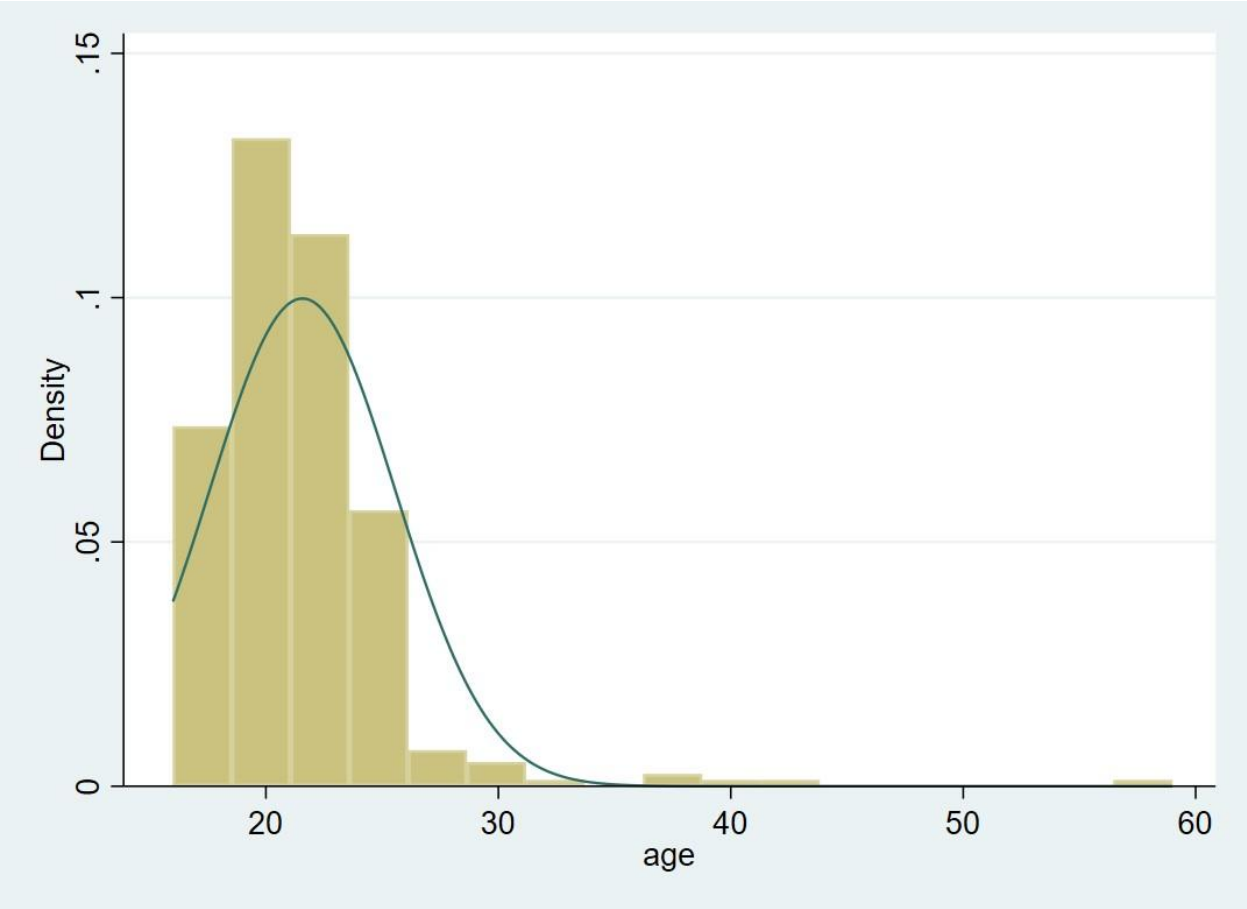

Figure 3: A graph showing the density and age distribution of student infected with HBV

CHAPTER FIVE

DISCUSSION

This study showed that the students have poor knowledge and lack of awareness about hepatitis B, its routes of transmission, risk factors, and modes of preventions. Similarly, most of the students about 30 of them(50.0%) were not vaccinated against hepatitis B, which makes them vulnerable to the disease. Interestingly, the main reason for not being vaccinated is the lack of motivation. However, the survey also shows that most of the students (92%) were aware of hepatitis.

Furthermore, our study revealed that common risk factors for hepatitis B infection among our participants were presence of tribal marks, sharing of sharp objects, syringes, having multiple sexual partners, and circumcision, which is performed traditionally on all Nigerian males and is one of the oldest surgical procedures carried out in home settings by traditional "circumcisionists," with some regions still practicing group circumcision (Osifo et al., 2009: Abdur-Rahman et al., 2012).

This factor may therefore suggest why the prevalence of HBV was higher in males although not statistically significant but similar to Uganda and other sub-Saharan African countries, where chronic HBV infections have been found to be more common in males (Bwogi et al., 2009), (Kiire et al., 1990), (Martinson et al., 1998), (Burnett et al., 2005). However in Vilibic's study and a similar study done in Cambodia, sex was not associated with HBV seropositivity (Vilibić-Cavlek et al., 2014) (Yamada et al., 2014).

The present study demonstrates surprising results and raises issues about the high number of students that are not vaccinated or not sure about their vaccination status. According to a recent study on medical students by Al-Ghamdi, anti-HBs levels were significantly low in many students after their primary immunization. Therefore, testing medical students for anti-HBs levels may be warranted as they represent a high-risk population (Al Ghamdi et al., 2013).

Another important issue also rises about the students' knowledge about this life-threatening infection and the need of further HBV education. Therefore, it is highly recommended that the University of Benin makes reforms to its educational curriculum to promote awareness among

the students. One important realization from this study is that education is necessary. As students play an important role in dissemination of knowledge and raising awareness among their communities, more educational efforts should be exerted on the students themselves for the importance of viral hepatitis, and Uniben must participate more in national/regional/international meetings about hepatitis in order to contribute to the prevention of viral hepatitis. Furthermore, educational initiatives should also be focused toward avoiding infection and seeking care in case of exposure to infected body fluids.

Another suggestion for a new initiative could be providing free HBV vaccines to all the nonvaccinated students to encourage universal vaccinations for all students upon their entry. Future studies may be directed at measuring the hepatitis B antibody titers and evaluating the response to the hepatitis B vaccine amongst students.

CONCLUSION

Hepatitis B virus (HBV) is still a worldwide health concern. Hepatitis B virus (HBV) is a hepatotropic virus with the potential to cause a persistent infection, ultimately leading to cirrhosis and hepatocellular carcinoma. Over the past four decades, the basic principles of HBV gene expression and replication as well as the viral and host determinants governing infection outcome have been largely uncovered. While divergent factors are involved in its pathogenesis, it is now clear that HBV RNAs, principally templates for viral proteins and viral DNAs, have diverse biological functions involved in HBV pathogenesis. These functions include viral replication, hepatic fibrosis and hepatocarcinogenesis.

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Appendices

DEMOGRAPHIC DATA

Questionnaire

Prevalence of HBV and HCV amongst undergraduate students

Date_____

14. Do you have tribal marks/ scarification? Yes No

15. Have you ever had a blood oath? Yes No

16. Do you patronize local manicure/pedicure vendors? Yes No

17. Do you use a personal clippers for shaving or hair cut? Yes No

18. Do you share personal belongings with others e.g., toothbrush, towel? Yes No

19. Do you share sharp objects e.g., Needles Razor blades clippers? Yes No

20. Do you have body piercing? Yes No

21. Do you have Tattoo on your body? Yes No

22. Do you share needles with partners? Yes No

23. Are you sexually active? No Yes

If yes to question 23:

- How many sexual partners have you had so far? _____
- Have you had sexual intercourse with someone who is not your regular partner within the last 6 months? Yes No Not sure
- Do you use condom when having sex? Always No Sometimes
- Your sexual partners are? Male only Female only Both
- Have you ever experienced painful urination and discharge? Yes No Don't know

- Have you ever had sex while under the influence of illicit drugs or alcohol Yes No

24. Do you take alcohol? Yes No

25.Do you smoke weed, Igbo, colos, tramadol and cocaine? Yes No

26. Have you ever received a blood transfusion? Yes No

27. Have you ever been tested for Hepatitis B? Yes No

28. If yes what was your result? Negative Positive

29. Have you ever been tested for Hepatitis C

30. If yes what was your result? Negative Positive

31. Have you ever received hepatitis B vaccine?

Yes No Not Sure

32. If yes, which year did you receive the vaccine (year)? ……

33. How many doses of the vaccine did you receive?

One dose Two doses Three doses More than 3 doses Not sure

Result

HBV _____

HCV_____

Informed Consent Form A study on the prevalence of Hepatitis B and its associated Factors Among University Students in Benin City, Nigeria

Hello! My name is_____ ___. I would like to invite you to take part in this study about Hepatitis B among university students in Benin City. Hepatitis B virus is the causative agent for Hepatitis B. This is part of our undergraduate final-year project. You are invited to take part in this study but taking part in this study is voluntary. Study Procedures If you take part in this study, we will ask you a few questions concerning yourself, including questions related to your faculty and department of study. In addition, we will take blood, about 2 ml, to do a rapid diagnostic test for the bacterium. You will get the result on the spot. The interview and test will take about 30-40 minutes. Confidentiality The information will be collected on paper. The information is stored securely and can only be accessed by approved study staff. The interview will take place in private. Everything you tell us is strictly confidential. Your identifying information will never be used in any reports. All information reported from this study will not be able to be linked to you. Potential Risks None is expected, other than the time you will spend in participating in the collection of data for the study. Potential Benefits You may or may not benefit by taking part in this study. If you take part in this study, you may help other students in the future as we would have identified the students most at risk of developing Hepatitis B, and will improve our understanding of how to implement interventions targeting the health condition overall. However, as a token of appreciation for your time, we shall provide light refreshments. Costs to Participate It will not cost you anything to take part in this study other than your time. Confidentiality and Access to your Health Information Access to the information you provide will be limited to persons involved with this study and will be protected in a secure place. Efforts will be made to protect your information and your answers to the interview questions. A unique number will be used instead of your name to identify your personal information and the answers you give. Only study staff can use this number to link your responses to you. Any answers included in the final report will not have your name or personal information on it. Contacting us If you have additional questions or any concerns, please contact the project supervisor: Dr. Kelly Elimian Department of Microbiology, Faculty of Life Sciences Phone: 08056679826 /08155465671 Do you want to ask me anything about the study? 2 Consent Statement I have read this form and/or someone has read it to me. I was encouraged to ask questions and given

time to ask questions. Any questions that I had have been answered satisfactorily. I agree to voluntarily take part in the study. I know that after choosing to take part in the study, I may withdraw at any time. I have been offered a copy of this consent form. 1. Do you agree to participate in the study? ‘YES’ means that you agree to do the interview. ‘NO’ means that you will NOT do the interview. _____Yes _____No Participant signature _____ Date: ___/___/___ DD/MM/YYYY Printed name of participant _____ Participant ID number _____ Signature of person obtaining consent_____ _____ Date: ___/___/___ DD/MM/YYYY