

## Sero-Prevalence of Hepatitis B Virus Amongst Food Sellers In Benue State University Campus Makurdi

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Date of Submission: 25-12-2020

Date of Acceptance: 03-01-2021

### I. CHAPTER ONE

#### INTRODUCTION

Hepatitis B virus (HBV) infection is a serious global public health problem and is endemic in Africa, including Nigeria with the viral antigen initially called Australian antigen (Weinbaun et al., 2008; Andre, 2004; Dane et al., 1970). HBV is the prototype member of the Hepadnaviridae (hepatotropic DNA virus) family with virions which are double-stranded particles, measuring 40 to 42 nm in diameter with an outer lipoprotein envelope that contains three related envelope glycoproteins (or surface anti-gens) (Uyar et al., 2009; Hinnachi et al., 2009). The infection can be acute or chronic, while adults that acquire acute infection usually recover or can be managed by supportive therapy; the chronic type is ultimately fatal (Shepard et al., 2006). Diagnosis of HBV infection is usually through serological and

virological markers. Hepatitis B surface antigen (HBsAg) is the hallmark of HBV infection and is the first serological marker to appear in acute HBV infection, and persistence of HBsAg for more than 6 months suggests chronic HBV infection (Kao, 2008).

Globally, over 2 billion people are infected with the virus and over 350 million have chronic infection (Eke et al., 2011). Infection with this virus does not only leads to acute illnesses, but chronic illnesses like liver cirrhosis and hepatocellular carcinoma which accounts for more than 1 million deaths globally (Eke et al., 2011; El-Magrahe et al., 2010). The prevalence of hepatitis B virus infection is relatively high in Africa, having the second highest number of chronically HBV-infected individuals (Mbaawuaga et al., 2008).

Hepatitis B is a major global health problem; it is a potentially life-threatening liver

infection caused by Hepatitis B virus (HBV). Hepatitis B virus is 50 to 100 times more infectious than HIV. Recent statistics indicate that not less than 23 million Nigerians are estimated to be infected with the Hepatitis B virus (HBV), making Nigeria one of the countries with the highest incidence of HBV infection in the world (Alexander and Kowdley, 2006). Consequently, the global disease burden of HBV was considered substantial due to the high HBV related morbidity and mortality. Approximately 5.0% of the world's populations were reportedly seropositive for hepatitis B surface antigen (HBsAg). The global burden of hepatitis B remains enormous, due largely to lack of universal HBV vaccination (Sharmar et al., 2005).

Nigeria is classified among the group of countries endemic for HBV infection with a current infected population of 18 million (Ojo and Anibijuwon, 2009). Despite the existence of a safe and effective vaccine, Nigeria has remained a hyper-endemic area for HBV infection, with an estimated 12% of the population being chronic carriers (Jatua and Yabaya, 2009). Sero-prevalence studies on HBsAg in Nigeria have shown that the prevalence of the infection in pregnant women range from 2 to 15.8% (Ojo and Anibijuwon 2009; Ndams et al., 2008; Duncan et al., 1995; Candottiet al., 2007).

Hepatitis B (HBV) affects 240 million people globally, with the highest prevalence in East Asia and sub-Saharan Africa (SSA) and it is the 10th leading cause of death worldwide (WHO, 2016). Approximately 686,000 deaths per year are caused by chronic hepatitis and hepatocellular carcinoma. Sub-Saharan Africa also has the highest number of people living with HIV (PLWHIV) globally: 70% of the 36.7 million (United Nations Program on HIV/AIDS, 2016).

Hepatitis B virus is very infectious, and can easily be contracted at a much faster rate than HIV. Hepatitis B is becoming very common in most places despite the fact that vaccines are administered to people to help reduce the harm that could result from the virus. Hepatitis is easily transmitted among students at various levels, due to the nature of their environment and the kind of activities they engage in.

Food sellers form a major segment of the Benue State University labour market. The market is characterized by the presence of different sales personnel engaging in different kinds of trade. The food sellers feed majority of the student population, workers and even staff on Benue State University Campus. This signifies the importance of this category of people when it comes to health and

livelihood of the Benue State University population since infections and diseases might easily be transmitted from food sellers to customers if the right hygienic practices are not adopted. It is on this premise that this study is designed to investigate the seroprevalence of Hepatitis B virus among food sellers in Benue State University campus.

### 1.1 Aim

To determine the prevalence of Hepatitis B Virus amongst food sellers in Benue State University Campus.

### 1.2. Objectives

- i. To determine the rate of infection with hepatitis B virus amongst food sellers in Benue State University
- ii. To determine the relationship between sex, age and infection with Hepatitis B virus
- iii. To correlate Hepatitis B infection with some of the risk factors associated with the Virus.

## II. CHAPTER TWO

### LITERATURE REVIEW

#### 2.1. Hepatitis B Virus

Hepatitis B is an infectious disease caused by the hepatitis B virus (HBV) which affects the liver. It can cause both acute and chronic infections. Many people have no symptoms during the initial infection. Some develop a rapid onset of sickness with vomiting, yellowish skin, feeling tired, dark urine and abdominal pain. Often these symptoms last a few weeks and rarely does the initial infection result in death. It may take 30 to 180 days for symptoms to begin. In those who get infected around the time of birth 90% develop chronic hepatitis B while less than 10% of those infected after the age of five do. Most of those with chronic disease have no symptoms; however, cirrhosis and liver cancer may eventually develop. These complications result in the death of 15 to 25% of those with chronic disease (Chang, 2007).

The virus is transmitted by exposure to infectious blood or body fluids. Infection around the time of birth or from contact with other people's blood during childhood is the most frequent method by which hepatitis B is acquired in areas where the disease is common. In areas where the disease is rare, intravenous drug use and sexual intercourse are the most frequent routes of infection. Other risk factors include working in healthcare, blood transfusions, dialysis, living with an infected person, travel in countries where the infection rate is high, and living in an institution. Tattooing and acupuncture led to a significant

number of cases in the 1980s; however, this has become less common with improved sterility. The hepatitis B viruses cannot be spread by holding hands, sharing eating utensils, kissing, hugging, coughing, sneezing, or breastfeeding. The infection can be diagnosed 30 to 60 days after exposure. Diagnosis is typically by testing the blood for parts of the virus and for antibodies against the virus. It is one of five known hepatitis viruses: A, B, C, D, and E (Pungpaonget et al., 2007).

The infection has been preventable by vaccination since 1982. Vaccination is recommended by the World Health Organization in the first day of life if possible. Two or three more doses are required at a later time for full effect. This vaccine works about 95% of the time. About 180 countries gave the vaccine as part of national programs as of 2006. It is also recommended that all blood be tested for hepatitis B before transfusion and condoms be used to prevent infection. During an initial infection, care is based on the symptoms that a person has. In those who develop chronic disease antiviral medication such as tenofovir or interferon maybe useful, however these drugs are expensive. Liver transplantation is sometimes used for cirrhosis (Williams, 2006).

About a third of the world population has been infected at one point in their lives, including 240 million to 350 million who have chronic infections. Over 750,000 people die of hepatitis B each year. About 300,000 of these are due to liver cancer. The disease is now only common in East Asia and sub-Saharan Africa where between 5 and 10% of adults have chronic disease. Rates in Europe and North America are less than 1%. It was originally known as serum hepatitis. Research is looking to create foods that contain HBV vaccine. The disease may affect other great apes as well (Barker et al., 1996).

## 2.2. Signs and Symptoms of Hepatitis B Infection

Acute infection with hepatitis B virus is associated with acute viral hepatitis – an illness that begins with general ill-health, loss of appetite, nausea, vomiting, body aches, mild fever, and dark urine, and then progresses to development of jaundice. It has been noted that itchy skin has been an indication as a possible symptom of all hepatitis virus types. The illness lasts for a few weeks and then gradually improves in most affected people. A few people may have more severe liver disease (fulminant hepatic failure), and may die as a result. The infection may be entirely asymptomatic and may go unrecognized (Terrault et al., 2005).

Chronic infection with hepatitis B virus either may be asymptomatic or may be associated with a chronic inflammation of the liver (chronic hepatitis), leading to cirrhosis over a period of several years. This type of infection dramatically increases the incidence of hepatocellular carcinoma (liver cancer). Across Europe hepatitis B and C cause approximately 50% of hepatocellular carcinomas. Chronic carriers are encouraged to avoid consuming alcohol as it increases their risk for cirrhosis and liver cancer. Hepatitis B virus has been linked to the development of membranous glomerulonephritis (MGN) (Gan et al., 2005).

Symptoms outside of the liver are present in 1–10% of HBV-infected people and include serum-sickness-like syndrome, acute necrotizing vasculitis (polyarteritis nodosa), membranous glomerulonephritis, and papularacrodematitis of childhood (Gianotti–Crosti syndrome) (Dienstag, 1981). The serum-sickness-like syndrome occurs in the setting of acute hepatitis B, often preceding the onset of jaundice. The clinical features are fever, skin rash, and polyarteritis. The symptoms often subside shortly after the onset of jaundice, but can persist throughout the duration of acute hepatitis B. About 30–50% of people with acute necrotizing vasculitis (polyarteritis nodosa) are HBV carriers. HBV-associated nephropathy has been described in adults but is more common in children. Membranous glomerulonephritis is the most common form. Other immune-mediated hematological disorders, such as essential mixed cryoglobulinemia and aplastic anemia (Liang, 2009).

## 2.3. Transmission

Transmission of hepatitis B virus results from exposure to infectious blood or body fluids containing blood. It is 50 to 100 times more infectious than HIV. Possible forms of transmission include sexual contact, blood transfusions and transfusion with other human blood products, re-use of contaminated needles and syringes, and vertical transmission from mother to child (MTCT) during childbirth. Without intervention, a mother who is positive for HBsAg has a 20% risk of passing the infection to her offspring at the time of birth. This risk is as high as 90% if the mother is also positive for HBeAg. HBV can be transmitted between family members within households, possibly by contact of non-intact skin or mucous membrane with secretions or saliva containing HBV. However, at least 30% of reported hepatitis B among adults cannot be associated with an identifiable risk factor. Breastfeeding after proper

immunoprophylaxis does not appear to contribute to MTCT of HBV (Shapiro, 1993).

## 2.4. Biology of Hepatitis B Virus (Virology)

### 2.4.1. Structure

Hepatitis B virus (HBV) is a member of the hepadnavirus family. The virus particle (virion) consists of an outer lipid envelope and an icosahedral nucleocapsid core composed of protein. These virions are 30-42 nm in diameter. The nucleocapsid encloses the viral DNA and a DNA polymerase that has reverse transcriptase activity (Locarnini, 2004). The outer envelope contains embedded proteins that are involved in viral binding of, and entry into, susceptible cells. The virus is one of the smallest enveloped animal viruses, and the 42 nM virions, which are capable of infecting liver cells known as hepatocytes, are referred to as "Dane particles". In addition to the Dane particles, filamentous and spherical bodies lacking a core can be found in the serum of infected individuals. These particles are not infectious and are composed of the lipid and protein that forms part of the surface of the virion, which is called the surface antigens (HBsAg), and is produced in excess during the life cycle of the virus (Howard, 1986).

### 2.4.2. Genome

The genome of HBV is made of circular DNA, but it is unusual because the DNA is not fully double-stranded. One end of the full length strand is linked to the viral DNA polymerase. The

genome is 3020–3320 nucleotides long (for the full-length strand) and 1700–2800 nucleotides long (for the short length-strand). The negative-sense (non-coding) is complementary to the viral mRNA. The viral DNA is found in the nucleus soon after infection of the cell. The partially double-stranded DNA is rendered fully double-stranded by completion of the (+) sense strand and removal of a protein molecule from the (–) sense strand and a short sequence of RNA from the (+) sense strand. Non-coding bases are removed from the ends of the (–) sense strand and the ends are rejoined. There are four known genes encoded by the genome, called C, X, P, and S. The core protein is coded for by gene C (HBcAg), and its start codon is preceded by an upstream in-frame AUG start codon from which the pre-core protein is produced. HBeAg is produced by proteolytic processing of the pre-core protein. The DNA polymerase is encoded by gene P. Gene S is the gene that codes for the surface antigen (HBsAg). The HBsAg gene is one long open reading frame but contains three in frame "start" (ATG) codons that divide the gene into three sections, pre-S1, pre-S2, and S. Because of the multiple start codons, polypeptides of three different sizes called large, middle, and small (pre-S1 + pre-S2 + S, pre-S2 + S, or S) are produced. The function of the protein coded for by gene X is not fully understood but it is associated with the development of liver cancer. It stimulates genes that promote cell growth and inactivates growth regulating molecules (Liang, 2009).



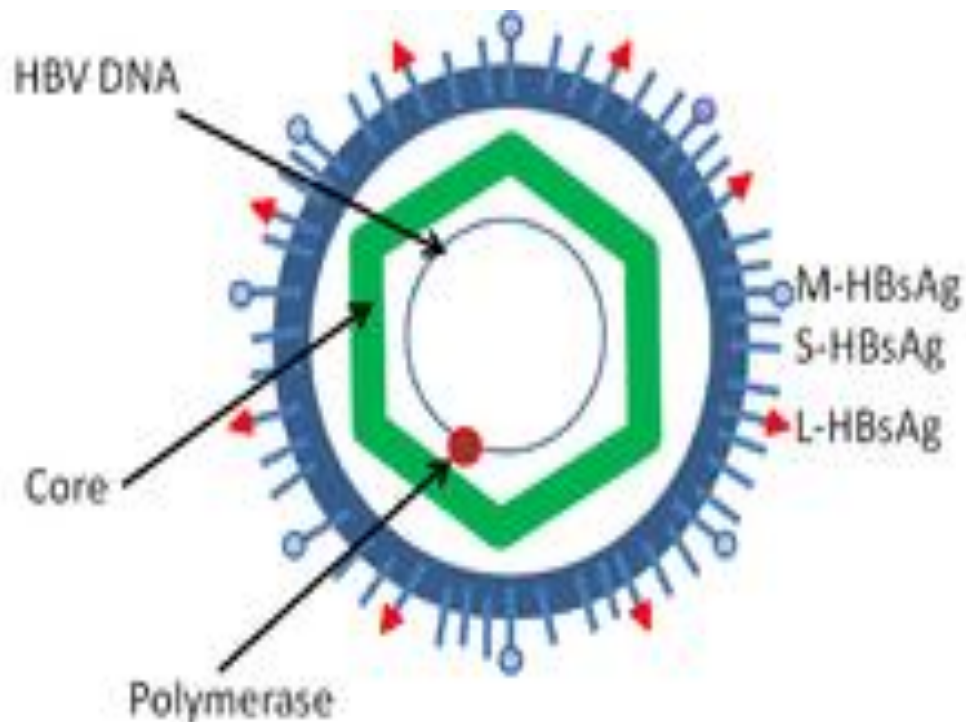


Plate 1: Structure of Hepatitis B Virus (CDC, 2014).



Plate 2: Electron Micrograph of Hepatitis B virus (CDC, 2014)

#### 2.4.3. Pathogenesis

The life cycle of hepatitis B virus is complex. Hepatitis B is one of a few known pararetroviruses: non-retroviruses that still use reverse transcription in their replication process.

The virus gains entry into the cell by binding to NTCP on the surface and being endocytosed. Because the virus multiplies via RNA made by a host enzyme, the viral genomic DNA has to be transferred to the cell nucleus by host proteins

called chaperones. The partially double stranded viral DNA is then made fully double stranded by viral polymerase and transformed into covalently closed circular DNA (cccDNA). This cccDNA serves as a template for transcription of four viral mRNAs by host RNA polymerase. The largest mRNA, (which is longer than the viral genome), is used to make the new copies of the genome and to make the capsid core protein and the viral DNA polymerase. These four viral transcripts undergo additional processing and go on to form progeny virions that are released from the cell or returned to the nucleus and re-cycled to produce even more copies. The long mRNA is then transported back to the cytoplasm where the virion P protein (the DNA polymerase) synthesizes DNA via its reverse transcriptase activity (Beck and Nassal, 2007).

#### 2.4.4. Serotypes and genotypes

The virus is divided into four major serotypes (adr, adw, ayr, ayw) based on antigenic epitopes presented on its envelope proteins, and into eight genotypes (A–H) according to overall nucleotide sequence variation of the genome. The genotypes have a distinct geographical distribution and are used in tracing the evolution and transmission of the virus. Differences between genotypes affect the disease severity, course and likelihood of complications, and response to treatment and possibly vaccination (Kramviset al., 2005).

Genotypes differ by at least 8% of their sequence and were first reported in 1988 when six were initially described (A–F). Two further types have since been described (G and H). Most genotypes are now divided into subgenotypes with distinct properties (Kramviset al., 2005).

#### 2.4.5. Mechanisms

Hepatitis B virus primarily interferes with the functions of the liver by replicating in hepatocytes. A functional receptor is NTCP. There is evidence that the receptor in the closely related duck hepatitis B virus is carboxypeptidase D. The virions bind to the host cell via the preS domain of the viral surface antigen and are subsequently internalized by endocytosis. HBV-preS-specific receptors are expressed primarily on hepatocytes; however, viral DNA and proteins have also been detected in extrahepatic sites, suggesting that cellular receptors for HBV may also exist on extrahepatic cells (Coffinet al., 2011).

During HBV infection, the host immune response causes both hepatocellular damage and viral clearance. Although the innate immune response does not play a significant role in these

processes, the adaptive immune response, in particular virus-specific cytotoxic T lymphocytes (CTLs), contributes to most of the liver injury associated with HBV infection. CTLs eliminate HBV infection by killing infected cells and producing antiviral cytokines, which are then used to purge HBV from viable hepatocytes. Although liver damage is initiated and mediated by the CTLs, antigen-nonspecific inflammatory cells can worsen CTL-induced immunopathology, and platelets activated at the site of infection may facilitate the accumulation of CTLs in the liver (Iannacone et al., 2007).

#### 2.5. Worldwide Epidemiology of Hepatitis B Infection

In 2004, an estimated 350 million individuals were infected worldwide. National and regional prevalence ranges from over 10% in Asia to under 0.5% in the United States and northern Europe. Routes of infection include vertical transmission (such as through childbirth), early life horizontal transmission (bites, lesions, and sanitary habits), and adult horizontal transmission (sexual contact, intravenous drug use) (Custer et al., 2004).

The primary method of transmission reflects the prevalence of chronic HBV infection in a given area. In low prevalence areas such as the continental United States and Western Europe, injection drug abuse and unprotected sex are the primary methods, although other factors may also be important. In moderate prevalence areas, which include Eastern Europe, Russia, and Japan, where 2–7% of the population is chronically infected, the disease is predominantly spread among children. In high-prevalence areas such as China and South East Asia, transmission during childbirth is most common, although in other areas of high endemicity such as Africa, transmission during childhood is a significant factor. The prevalence of chronic HBV infection in areas of high endemicity is at least 8% with 10–15% prevalence in Africa/Far East. As of 2010, China has 120 million infected people, followed by India and Indonesia with 40 million and 12 million, respectively. According to World Health Organization (WHO), an estimated 600,000 people die every year related to the infection. In the United States about 19,000 new cases occurred in 2011 down nearly 90% from 1990 (Custer et al., 2004).

#### 2.6. Epidemiology of Hepatitis B Virus Infection in Nigeria

Sub-Saharan Africa, Asia, the Pacific, the Amazon and southern part of eastern and central Europe are areas of high endemicity with the

prevalence rate of above 7%. Chronic infection varies from less than 1 % in USA and Western Europe to 5% in the Indian subcontinent and Middle East (WHO, 2014).

In Nigeria, Chronic infection with HBV occurs in 90% of infants infected at birth, 30% of children infected at 1-5yrs and 6% of persons infected above 5yrs (CDC, 2014). Thus there is inverse relationship between chronic infection and age due to maturation of the immune system. In Awka, Ezegbudo et al. (2004) found that the prevalence of HBsAg among pregnant women decreases with increasing social status. Mustapha et al., (2004) and Seresena et al (2002) in Gombe and Jos respectively found that having multiple sex partner increased the carriage of HBsAg. Ola et al., (1994) in Ibadan found that 57.1 % of patients with primary liver cell carcinoma were positive for HBs Ag. In Ibadan, Olubyide et al., (1997) found that a high (39 %) prevalence of HBsAg was associated with Surgeons and Dentists, with high potential of transmissibility. They speculated that it was due to lack of vaccination and infrequent application of universal precaution.

Multimer et al.(1994) found that blood transfusion clearly increased the risk of HBV infection as shown by significantly higher markers of HBV infection (HBsAg and anti HBc) in subjects who were transfused. Abiodun et al.(1985) in Benin observed that HBV infection increased with increasing units of blood transfused. Agumadu and Abiodun (2002) studying 213 children with sickle cell anaemia, showed that markers of HBV infection (HBsAg and anti HBc) increased with age. Amazigo and Chime(1990) in Eastern Nigeria found that HBsAg carriage and exposure rate to HBV were significantly higher in rural than in urban population. This was attributed to overcrowding and clustering. They also demonstrated that by 40yrs of age 87% of indigenous population of Eastern Nigeria has at least one HBV marker in their serum.

Some studies in Nigeria on HBV infection showed it occurred earlier in children SCA (Olatunji and Akanmua, 1982). The increasing surface antigenaemia with age has been demonstrated by several workers in Nigeria. Amazigo et al. (1990) found a significantly higher HBsAg prevalence among prisoners in eastern Nigeria, which was attributed to overcrowding and clustering. Recent studies on HBsAg prevalence in Jos (Ukaeje et al.(2005) and Gombe (Mustafa and Jibrin, 2004) among patients with human immune deficiency syndrome (HIV) showed a prevalence of 25.9% and 26.5% respectively. These high values

could be because HIV and HBV share similar modes of transmission and risk factors.

### 2.7. Transmission of Hepatitis B Virus in Nigeria

Transmission of HBV occurs when blood or body fluid of an infected person enters the body of a person who is not immune (CDC, 2003). Most studies in Nigeria found a low prevalence in infancy and an increasing rate with age. A figure of 2.8% has been documented as the rate of HBV transmission from Nigerian females to their offspring (Abdulsalami et al.(1986). Most infections in Nigeria occur through horizontal transmission. Various studies in Nigeria showed that blood transfusion is an important source HBV transmission (Multimer et al.1994). Although CDC publications (CDC, 2003) linked HBV transmission to tattoos and body cuttings/piercing, most studies in Nigeria found no link between traditional practices like, scarification, circumcision, ear piercing and HBV infection. Higher HBsAg prevalence noted among prisoners and rural dwellers were attributed to overcrowding and clustering (Amazigo, 1990). Studies from north-central Nigeria indicates that unprotected sex is implicated in the transmission of HBV (Mustafa and Jibrin, 2004; Sirisena et al.(2002).

### 2.8. Diagnosis of Hepatitis B Infection

The tests, called assays, for detection of hepatitis B virus infection involve serum or blood tests that detect either viral antigens (proteins produced by the virus) or antibodies produced by the host. Interpretation of these assays is complex (Bonino et al., 1987).

The hepatitis B surface antigen (HBsAg) is most frequently used to screen for the presence of this infection. It is the first detectable viral antigen to appear during infection. However, early in an infection, this antigen may not be present and it may be undetectable later in the infection as it is being cleared by the host. The infectious virion contains an inner "core particle" enclosing viral genome. The icosahedral core particle is made of 180 or 240 copies of core protein, alternatively known as hepatitis B core antigen, or HBcAg. During this 'window' in which the host remains infected but is successfully clearing the virus, IgM antibodies specific to the hepatitis B core antigen (anti-HBc IgM) may be the only serological evidence of disease. Therefore, most hepatitis B diagnostic panels contain HBsAg and total anti-HBc (both IgM and IgG) (Bonino et al.,1987).

Shortly after the appearance of the HBsAg, another antigen called hepatitis B e antigen

(HBeAg) will appear. Traditionally, the presence of HBeAg in a host's serum is associated with much higher rates of viral replication and enhanced infectivity; however, variants of the hepatitis B virus do not produce the 'e' antigen, so this rule does not always hold true. During the natural course of an infection, the HBeAg may be cleared, and antibodies to the 'e' antigen (anti-HBe) will arise immediately afterwards. This conversion is usually associated with a dramatic decline in viral replication.

If the host is able to clear the infection, eventually the HBsAg will become undetectable and will be followed by IgG antibodies to the hepatitis B surface antigen and core antigen (anti-HBs and anti HBc IgG). The time between the removal of the HBsAg and the appearance of anti-HBs is called the window period. A person negative for HBsAg but positive for anti-HBs either has cleared an infection or has been vaccinated previously (Locarnini, 2004).

Individuals who remain HBsAg positive for at least six months are considered to be hepatitis B carriers. Carriers of the virus may have chronic hepatitis B, which would be reflected by elevated serum alanine aminotransferase (ALT) levels and inflammation of the liver, if they are in the immune clearance phase of chronic infection. Carriers who have seroconverted to HBeAg negative status, in particular 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 (Locarnini, 2004).

PCR tests have been developed to detect and measure the amount of HBV DNA, called the viral load, in clinical specimens. These tests are used to assess a person's infection status and to monitor treatment. Individuals with high viral loads, characteristically have ground glass hepatocytes on biopsy (Zoulim, 2006).

## 2.9. Prevention of Hepatitis B Infection

Vaccines for the prevention of hepatitis B have been routinely recommended for infants since 1991 in the United States. Most vaccines are given in three doses over a course of months. A protective response to the vaccine is defined as an anti-HBs antibody concentration of at least 10 mIU/ml in the recipient's serum. The vaccine is more effective in children and 95 percent of those vaccinated have protective levels of antibody. This drops to around 90% at 40 years of age and to around 75 percent in those over 60 years. The protection afforded by vaccination is long lasting even after antibody levels fall below 10 mIU/ml.

Vaccination at birth is recommended for all infants of HBV infected mothers. A combination of hepatitis B immune globulin and an accelerated course of HBV vaccine prevents HBV transmission around the time of birth in 86% to 99% of cases (Schillie et al., 2013).

All those with a risk of exposure to body fluids such as blood should be vaccinated, if not already. Testing to verify effective immunization is recommended and further doses of vaccine are given to those who are not sufficiently immunized (Schillie et al., 2013).

In assisted reproductive technology, sperm washing is not necessary for males with hepatitis B to prevent transmission, unless the female partner has not been effectively vaccinated. In females with hepatitis B, the risk of transmission from mother to child with IVF is no different from the risk in spontaneous conception (LeFevre, 2014).

Those at high risk of infection should be tested as there is effective treatment for those who have the disease. Groups that screening is recommended for include those who have not been vaccinated and one of the following: people from areas of the world where hepatitis B occurs in more than 2%, those with HIV, intravenous drug users, men who have sex with men, and those who live with someone with hepatitis B (LeFevre, 2014).

## 2.10. Complications Resulting from Hepatitis B Infection

HBV is hepatotropic and has a profound effect on the liver. Majority of patients with acute, sub-acute symptoms and even sub clinical cases of HBV infection will clear the infection with temporary infiltration of liver by inflammatory cells. In fulminant hepatitis there is total destruction of liver parenchyma leaving only connective tissue septa. Persistent histologic changes in patients with HBV indicates development of chronic hepatitis (Finlayson et al., 1999). This manifests in two forms, chronic persistent hepatitis and chronic active hepatitis. Chronic persistent hepatitis is limiting, with minimal changes in lobular architecture while in the chronic active hepatitis there is piecemeal necrosis of hepatocytes. This disruption of lobular architecture leads to cirrhosis and often primary liver cell carcinoma which is a leading cause of death in sub-Saharan Africa (Kire, 1993). Presumably, persistent infection leads to rapid cell turnover, accumulation of errors in replication and instability in the host genome. A more direct role in tumorigenesis, with occasional viral insertion into host genome, may inactivate a tumour



suppressor gene or activate cellular proto oncogene (Lance et al., 1999).

In Ibadan, 57.1% of patients with primary liver cell carcinoma were infected with HBV (Olubuyide et al., (1997). Edington et al., (1976) had earlier reported similar trend in North-central Nigeria. Kaine et al. (1988) in Enugu found that cellular infiltration was more aggressive, particularly in the portal tracts in children with sickle cell disease who were positive for HBsAg HBV infection may be responsible for 20-40% prevalence of cirrhosis reported in patients with sickle cell disease (Barrette, 1968).

### 2.11. Control of HBV Infection

There are broadly three strategies for dealing with HBV infection in the developed countries, immunization for at risk population, antiviral drugs (lamivudine, adefovir and dipivoxil) and immunostimulatory therapy with alpha-interferon for those affected (Hepatitis B Immunization, 2003).

Immunization is the most effective means of controlling and HBV world-wide. The vaccine has an outstanding record of safety and efficacy, and it is 95% effective in preventing development of the chronic carrier state (WHO, 1998). In Africa, vertical transmission accounts for 1-5% of cases, while most children are infected with HBV between ages of 2-11 years through horizontal transmission, hence universal immunization at birth has been adopted. As cost effective measure it has been incorporated into WHO expanded programme on immunization (EPI) on global basis according to Yaounde declaration at the International conference on the control of HBV held in 1991 (Kire, 1993).

In addition to the above measures where it is feasible, HBV infection in Nigeria can be prevented or drastically reduced through health education of the general population on the various mode of transmission of HBV and preventive measures (Sirisena et al., (1994). Such measures include careful handling of blood and body fluid since they are potentially infectious. Also discouraging communal sharing of blade/sharp instruments used for shaving, barbing, manicure and body piercing/cutting and high level sexual networking (Sirisena, 1994; CDC, 2001). Prechewing of solid for children by an adult, especially those at risk for HBV infection should be discouraged because saliva is known to transmit HBV.

WHO recommends universal screening of blood and plasma for HBsAg by sensitive method before transfusion (Kire, 1993). Even when all blood donations are screened for HBsAg, donations

from volunteered non remunerated donors have been proved to be safest. About 2 out of 1000 units screened plasma donations, negative for HBsAg using a very sensitive test are still infectious because the sensitivity of the third generation test is not 100%. Addition of a low dose hepatitis B immunoglobulin to potentially infectious plasma appears to be reliable measure to eliminate the hepatitis B transmission. This is preferred to other methods for labile plasma derivatives. Where possible only donations from immunized donors with a detectable amount of anti-HBs should be collected either for transfusion or for preparation of plasma derivative. Pasteurization of plasma derivatives like albumin, factors iii and viii at 60°C for at least 10 hours is essential for the elimination of HBV Because of risks of blood transfusions, it should be given only when it is absolutely necessary as it was said that most blood transfusions were not necessary (Multidimer et al., 1994).

Babies born to HBsAg positive mother should be given hepatitis B immunoglobulin at birth and active immunization should commence immediately. Post exposure prophylaxis with hepatitis B immunoglobulin should be given promptly in all cases of suspected blood or body fluid inoculation as this could reduce HBV infection (Immunization action coalition, 2005).

In Nigeria most of these control measures, are poorly observed and safe blood for transfusion are not easily accessible. Socio-economic and living condition of most Nigerians encourage transmission of HBV (Amazigo and Chime, 1990).

### 2.12. Treatment of Hepatitis B Infection

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

Although none of the available drugs can clear the infection, they can stop the virus from replicating, thus minimizing liver damage. As of 2008, there are seven medications licensed for treatment of hepatitis B infection in the United

States. These include antiviral drugs lamivudine (Epivir), adefovir (Hepsera), tenofovir (Viread), telbivudine (Tyzeka) and entecavir (Baraclude), and the two immune system modulators interferon alpha-2a and PEGylated interferon alpha-2a (Pegasys). The World Health Organization recommended a combination of tenofovir and entecavir as first line agents. Those with current cirrhosis are in most need of treatment (Alberti and Caporaso, 2011).

The use of interferon, which requires injections daily or thrice weekly, has been supplanted by long-acting PEGylatedinterferon, which is injected only once weekly. However, some individuals are much more likely to respond than others, and this might be because of the genotype of the infecting virus or the person's heredity. The treatment reduces viral replication in the liver, thereby reducing the viral load (the amount of virus particles as measured in the blood). Response to treatment differs between the genotypes. Interferon treatment may produce an e antigen seroconversion rate of 37% in genotype A but only a 6% seroconversion in type D. Genotype B has similar seroconversion rates to type A while type C seroconverts only in 15% of cases. Sustained e antigen loss after treatment is ~45% in types A and B but only 25–30% in types C and D (Cao, 2009).

**2.10. Results from Previous Studies**

Studies done in Nigeria shows HBV carriage rate in the range of 9 to 39%. It has been estimated that 19 million people have been infected (About 1 out of 10 people). More than 3 million people are chronically infected 7.3- 24% (Average 13.4%) of the population has serological evidence

of current infection. Results further reveal that, over a 100,000 people will become infected each year and 5,000 will die each year from hepatitis and its complications. Approximately one health care worker dies each day from hepatitis. The psychological impact of hepatitis B virus infection does not only pose a threat to the nation but everybody is either infected or affected. An infected individual faces psychological issues ranging from increase in financial burden, unproductivity, loss of life and stigmatization. The individual may experience extreme stress, anger, depression, fear, confusion, guilt, hopelessness, anxiety, loss of status, difficulty in disclosure etc. The impact is very severe with consequent implications on the affected people and the nation as a whole.

In a study carried out by Maryam et al., 2013, 25 (12.5%) of the 200 samples analyzed were positive for Hepatitis B. the high prevalence obtained in the study suggests that hepatitis B is common among students in the campus and may be due to the mode of transmission which is basically via contact with bodily fluid (including saliva, semen, sweat, breastmilk, urine, vaginal secretions and faeces).

Another study by Mbawuuagaet al., 2014 in Benue state, Nigeria revealed a prevalence of 12% for serological patterns in pregnant women. A 6% prevalence rate was also revealed in a study conducted by Alegbeleyeet al., 2013 on the maternal and neonatal seroprevalence of hepatitis B surface antigen in a hospital based population in south-south, Nigeria. Of the 250 women tested for Hepatitis B, only 15 tested positive.

**Table 2.1: Prevalence of Hepatitis B infection in Nigeria**

Authors and Date	Prevalence	Location
Mbawuuaga et al.2014	12%	Benue
Chukwuka et al.2004	7.6%	Imo
Alikor and Erhabor (2007)	12.4%	Delta
Otegbayo et al.(2003)	21.3%	Oyo
Uneke et al.(2005)	15.1%	Plateau
Egah et al.(2007)	15.1%	Plateau
Nneka et al.(2007)	17.1%	Nassarawa
Alao et al.(2009)	20.0%	Benue
Buseri et al.(2009)	18.6%	Osun
Sule et al.(2010)	11.0%	Kogi
Umolu et al.(2005)	5.4%	Edo
Olokoba et al.(2009)	2.4%	Adamawa
Ejele and Ojule (2004)	1.6%	Rivers
Ugwuja and Ugwu (2010)	4.1%	Ebonyi

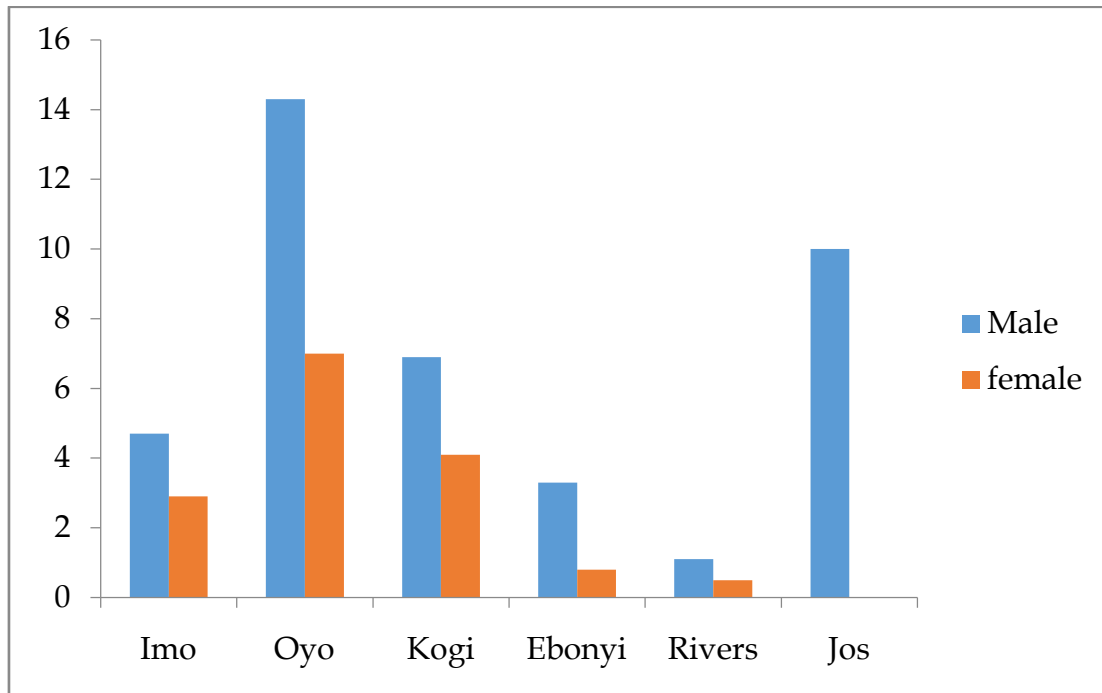


Figure 1: Sex Distribution of Hepatitis B in Nigeria

Source: Adopted from Table 1

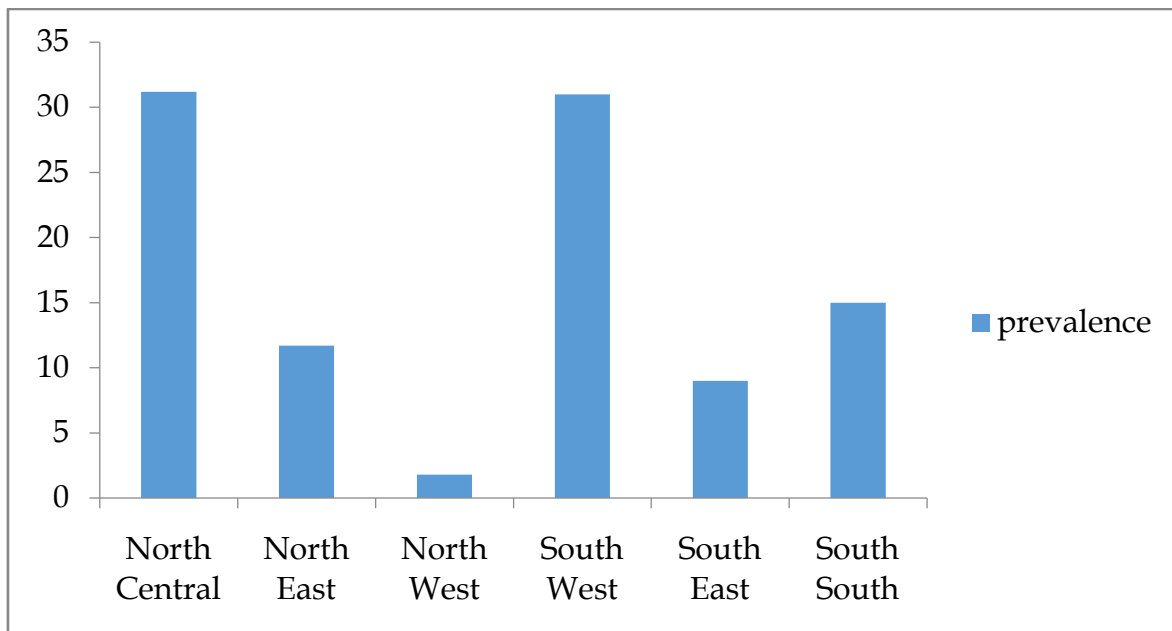


Figure 2: Regional Prevalence of Hepatitis B in Nigeria

(Adopted from Table 1)

### III. CHAPTER THREE

#### MATERIALS AND METHODS

##### 3.1. Study Area

This study was carried out in Makurdi, the capital of Benue state, Nigeria. The city is located in central Nigeria along the Benue River, on

latitude 07<sup>0</sup>43'N and Longitude 08<sup>0</sup>35'E and holds the base for the Nigerian Air Force.

Makurdi lies on the south bank of the Benue River. Founded about 1927 when the railroad from Portharcourt was extended to Jos and Kaduna. Makurdi has rapidly developed into a transportation and market centre. As of 2007, Makurdi had an estimated population of 500,797 (Ministry of Land and Survey, 2015).

The climatic condition in Makurdi is influenced by two air masses: the warm, moist south westerly air mass, and the warm, dry north-easterly air mass. The mean annual rainfall in Makurdi is about 1,290mm. Temperature in Makurdi is however, generally high throughout the year, with February and March as the hottest months. Temperature in Makurdi varies from a

daily of 40<sup>0</sup>C and a maximum of 22.5<sup>0</sup>C (Ministry of Land and Survey, 2015).

Makurdi and its environs are built on "Makurdi sand-stone" The sand stone are also overlain by shale units in some place especially the low-lying areas of Wadata. The soil here ranges from fine sand on the riverside to silt sand and even clay in some parts of the town. Thus, in rainy season, a slight rain only can render the untarred streets muddy.

Benue State University is one of the first state Universities in North Central Nigeria. It is located along Gboko-Makurdi road and is close to the famous Tactical Headquarters of the Nigerian Airforce Base in Makurdi. The University offers a host of courses and awards degrees ranging from Diploma to Doctor of Philosophy Degrees (PhD).

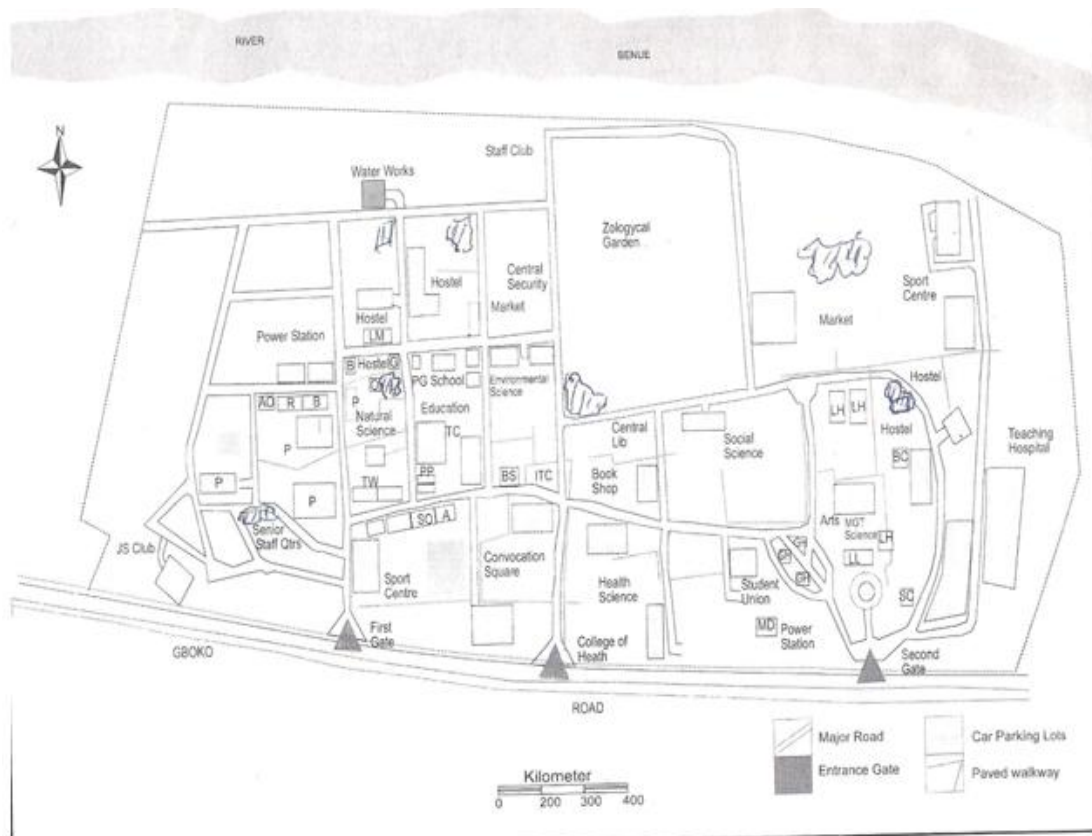


Fig 3.1: Map of Benue State University

Source: Benue State University Physical Planning Committee

### 3.2. Sample Size

A total of 345 blood samples were randomly collected from food vendors selling food

within and around Benue State University campus for examination during the study period. This



sample size was determined using the formula below as stated by Nianget al (2006).

$$n = \frac{z^2 p(1 - p)}{d^2}$$

Where

n = sample size

z = statistic for a level of confidence, in this case the level of confidence was 95% (1.96)

p = expected prevalence

d = precision at 5% (0.05)

Thus,

$$n = \frac{1.96^2 \times 0.34(1 - 0.34)}{0.05^2}$$

$$n = \frac{3.84 \times 0.34(0.66)}{0.05^2}$$

$$n = 243$$

### 3.3. Sample Collection

Verbal consent was obtained from the food sellers involved in the study. Questionnaires were administered to each seller that consents to the study so as to obtain socio-demographic data pertaining to the research.

Using the appropriate aseptic techniques for the collection of blood samples, 5ml of blood sample was collected from food sellers, appropriately labeled, and taken to the microbiology laboratory of the Department of Biological Sciences for examination.

### 3.4. Examination of Samples

The sera from collected blood samples were screened for hepatitis B surface antigens and Hepatitis C antibodies using Osytest Rapid Diagnostic test strips and Two Dot Rapid One Step Test strips. The results were read after 10 minutes and recorded.

### 3.5. Interpretation of Results

Based on the appearance of the coloured lines across the central window of the test assays. Results were recorded as positive, negative or invalid. Two lines, Control (C) and T (test) indicated positive test. Only one line in C indicated negative result. A pale coloured line in T was also considered positive. Invalid test was considered if no line appeared in C line region.

### 3.6. Data Analysis

The percentage prevalence (%) was calculated. Analysis of the results were done using chi-square ( $\chi^2$ ) to determine the relationship between prevalence of hepatitis and possible risk factors such as sex, age, location, alcoholism etc. A p-value less than 0.05 ( $p < 0.05$ ) was considered statistically significant.

## IV. CHAPTER FOUR

### RESULTS

This study revealed an overall prevalence of 4.50% for hepatitis B among food sellers in Benue State Univeristy, Makurdi. Sex distribution of Hepatis B infection among food sellers in Benue State University campuses also varied greatly with highest infection rates recorded by females (5.80%) than males (0.00%). Chi-square analysis however revealed that there is no significant relationship between prevalence of infections and sex as shown in table 1.

In terms of age, prevalence rates for hepatitis B infection was highest within the age group of 26-30 (11.6%) and least among age groups of 10-15, and 36 years and above. Age range of 16-20years however recorded a prevalence rate of 2.60% while age group of 26-30years recorded prevalence of 6.50% respectively. Statistically analysis however shows that there is no significant relationship between prevalence of infection and age as shown in table 2.

Single food sellers had highest prevalence of infection with prevalence rate of 5.20% among single people, 3.60% among married people and 0.0% amongst divorced food sellers. There was also no significant relationship between prevalence of infection and marital status.

Education also had no significant statistical relationship with prevalence of infections even though there were variations in prevalence rates with those with non-formal education having a prevalence of 9.1%, primary education (0.0%), secondary education (3.3%) and tertiary education (6.8%). Food sellers living within Kanshio however recorded highest prevalence of infections with 8.3% prevalence followed by Kanshio (6.2%) while other food sellers from other regions had prevalence rates of zero (table 5).

Results for prevalence of infections in relation to possible risk factors of infection are presented in table 6. The results show that there was no significant relationship between risk factors of infection and prevalence of infections amongst food sellers in Benue State University, Makurdi ( $P > 0.05$ ). Risk factors of piercings, immunization, blood transfusion and alcoholism all recorded least prevalence for those who gave a "No" option for this risk factors. Those who don't take alcohol also recorded highest prevalence rates for hepatitis infection indicating that alcohol consumption amongst food sellers in Benue State University has no association with hepatitis B infection.

**Table 1:**Prevalence of Hepatitis B In Relation To Sex among Food Sellers in Benue State University, Makurdi.

Sex	Total number tested	Number positive (%)
Male	44	0 (0.00)
Female	156	9(5.80)
<b>Total</b>	<b>200</b>	<b>9(4.50)</b>

$X^2=2.65$ ,  $P=0.103$ ,  $df=1$

**Table 2:**Prevalence of Hepatitis B In Relation To Age of FoodSellers in Benue State University, Makurdi.

Age	Total number tested	Number positive (%)
10-15	7	0(0.00)
16-20	38	1(2.60)
21-25	46	3(6.50)
26-30	43	5(11.6.)
31-35	14	0(0.00)
36-40	21	0(0.00)
Above 40	31	0(0.00)
<b>Total</b>	<b>200</b>	<b>9(4.50)</b>

$X^2=9.27$ ,  $P=0.159$ ,  $df=6$

**Table 3:**Prevalence of Hepatitis B In Relation To Marital status among Food Sellers in Benue State University, Makurdi.

Relationship	Total number tested	Number positive (%)
Single	115	6(5.20)
Married	83	3(3.60)
Divorced	2	0(0.00)
<b>Total</b>	<b>200</b>	<b>9(4.50)</b>

$X^2=0.383$  $P=0.83$ ,  $df=2$

**Table 4:**Prevalence of Hepatitis B In Relation To Education among Food Sellers in Benue State University, Makurdi.

Level	Total number tested	Number positive (%)
Non-formal	11	1(9.1)
Primary	26	0(0.00)
Secondary	90	3(3.3)
Tertiary	73	5(6.8)
<b>Total</b>	<b>200</b>	<b>9(4.50)</b>

$X^2=2.987$ ,  $P=0.394$ ,  $df=3$

**Table 5:**Prevalence of Hepatitis B In Relation To Residence among Food Sellers in Benue State University, Makurdi.

Residence	Total number tested	Number positive (%)
Wurukum	129	8(6.2)
High level	22	0(0.00)
North bank	19	0.(0.00)
Kanshio	12	1(8.3)
Modern market	11	0(0.0)
Wadata	7	0(0.00)
<b>Total</b>	<b>200</b>	<b>9(4.50)</b>

$X^2=4.06$ ,  $P=0.541$ ,  $df=5$

**Table 6:**Prevalence of Hepatitis B In Relation To Possible Risk factors among Food Sellers in Benue State University, Makurdi.

Risk Factor	Total	number	Number positive	p-value
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	tested	(%)	
Piercing			
Yes	4	0(0.00)	
No	196	9(4.60)	0.661
Immunization			
Yes	39	0(0.00.)	
No	161	9(5.6)	0.131
Blood transfusion			
Yes	18	0(0.00)	
No	182	9(4.9)	0.334
Alcoholism			
Don't take	114	7(6.1)	
Daily	18	0(0.00)	
Weekly	43	2(4.7)	
Monthly	25	0(0.00)	
<b>Total</b>	<b>200</b>	<b>9(4.5%)</b>	



Plate 4.1: HBsAg positive Strips



Plate 4.2: HBsAg Negative Strips

## V. CHAPTER FIVE

### Discussion, Conclusion And Recommendation

#### 5.1. Discussion

This study which examined the seroprevalence of hepatitis B among food sellers in Benue State revealed an overall prevalence of Hepatitis B to be 4.50%. This prevalence rate was formed by only females who recorded an individual prevalence rate of 5.80% when compared to males with zero prevalence as shown in table 1. An overall prevalence of 4.50 recorded in this study is lower than what was previously recorded by Obisike et al., (2018) in their study on prevalence of Hepatitis B among food vendors in Wurukum, Makurdi, Benue State. In his study, he reported an overall prevalence of 10.8%. The finding of this study also differed from the reports of Alao et al. (2008) who reported a prevalence rate of 30.0% in their study on Hepatitis B in Otukpo, Benue State, Nigeria and 12% prevalence reported by Mbawuuaga et al., (2014) in Benue State.

Differences in prevalence rates with respect to sex as observed in this study is in line with Obisike et al., (2018) who recorded that there was difference in the occurrence of hepatitis B among food sellers in Makurdi. The findings of Obisike et al. (2018) however differed from this

study in that their study recorded more hepatitis B positive males than females. The findings of this study also differ from the reports of Terwase et al. (2015) who recorded higher prevalence rates in males than females. Chi-square analysis however presented that; there was no significant relationship between sex and prevalence of hepatitis B infection. Differences observed between the results of this study and that of Obisike might be attributed to the differences in study population since Benue State University food sellers are mostly females who are not adequately equipped with knowledge on hepatitis B unlike Wurukum market which is dominated by mixed crowds with vast people from all shades of life.

Highest prevalence of infections was recorded by age group 21-25. This age group is characterized by people in the prime of their youth, energy and ability to move around in search of basic needs of life without stringent restrictions. This may be attributed in part to the high prevalence recorded in this age group. Age group above 30 years were however free of hepatitis B infection as shown in table 2. This is an indication to the fact that hepatitis infection among Benue State University food sellers is lowest amongst children and Adults above 30 years. This finding is



in agreement with Obiskike et al. (2018) who reported age group 20-29 to present higher prevalence rates for hepatitis B. It is also similar to Terwase et al.(2015) who reported that the young adult had higher prevalence than older age group. According to the reports of Obiskwe et al.(2018), high prevalence reported in the most dominant age group for hepatitis in this study poses a great risk to the people as this age group constitutes the main work force. Despite the differences recorded in prevalence rates of the various age groups examined, chi-square analysis shows that there was no significant association between age and infection rates.

Single persons recorded higher prevalence rates than other categories of people. This is representative in the 5.20% rate of hepatitis B infection recorded by this age group in comparison with the 3.60% recorded by married people and zero percent prevalence recorded by divorced food vendors. There was also no significant statistical relationship between marital status and prevalence of hepatitis B infection in Benue State University, Makurdi as  $P > 0.05$  (table 3).

In terms of Education, those who have tertiary forms of Education recorded the highest prevalence of infection for Hepatitis B. This finding differs markedly from the reports of Obisikwe et al.(2018) who reported that prevalence of hepatitis B infection is highest amongst those with no formal education. Statistical analysis however shows that there is no difference between infection with Hepatitis B and Educational background since  $P > 0.05$  (table 4).

Locational differences occurred between food sellers on Benue State University campus in relation to prevalence of Hepatitis B infection. It was observed from the study that Wurukum had the highest prevalence followed by Kanshio; the rest having a zero prevalence. There was also no significant relationship between location and prevalence of hepatitis amongst Food sellers on Benue State University campus as  $P > 0.05$ .

Various possible factors associated with hepatitis B infection were highlighted in this study. The findings however show that there was no significant difference between risk factors of piercings, immunization, Blood transfusion and alcoholism as  $P > 0.05$  for all the risk factors examined (table 5). This study therefore points to the fact that consumption of alcohol, piercing of body parts, blood transfusion or alcoholism does not affect the rate of infection with hepatitis B virus.

## 5.2. Conclusion

This study revealed an overall of prevalence hepatitis B amongst food sellers in Benue State University, Makurdi to be 4.9% which is relatively low when compared with results from retrospective studies. It also reveals that highest prevalence of Hepatitis B virus was observed among females than males indicating the dangers associated with transference of this infection to their families if right hygienic conditions are not employed and implemented.

Also, despite the fact that the prevalence of hepatitis B virus is low when compared to results from previous studies, the risk of infection is very high and spread of the virus in the future is possible if the students, staffs and workers who buy food from these food sellers are exposed to source of infections.

## 5.3. Recommendations

From this study, it is recommended that:

- Definite preventive measures should be adopted by food sellers to reduce the spread of the infection.
- Food sellers, Students and University workers should be conscious of their environment and prevent themselves from been exposed to sources of infection with Hepatitis B virus such as blood from cuts, saliva of patients and general body fluids.
- Food sellers should be vaccinated against Hepatitis B virus so as to ensure that their immune system is able to effectively defend them against Hepatitis B virus. By so doing, the risk of transmission and spread of the infection will be greatly reduced.
- Food sellers should undergo strict tests as part of their screening exercise before been allowed into the University to sell foods so as to screen Hepatitis B positive vendors, treat them and prevent spread of the disease to the general University population.
- Government should create more awareness about the virus and stress its high infectivity. By so doing, the community would be aware of the dangers that could be posed by the virus and as such prevent the spread of the disease between the outside the community and the students who relate continuously with themselves and food vendors.

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