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PREVALENCE AND FACTORS ASSOCIATED WITH HEPATITIS B INFECTION AMONG PATIENTS ATTENDING SPECIAL TREATMENT CENTRE (CASINO CLINIC) NAIROBI COUNTY, KENYA

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Prevalence and Factors Associated with Hepatitis B Infection among Patients Attending Special Treatment Centre (Casino Clinic) Nairobi County, Kenya

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other university.

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This thesis has been submitted for examination with our approval as university supervisors:

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DEDICATION

I dedicate this work to my family members; my lovely wife and my children for their unfailing love, support and encouragement during this period of study.

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ACRONYMNS AND ABBREVIATIONS

ALT	Alanine aminotransferase
ARVs	Anti-retroviral drugs
CBD	Central Business District
CDC	Centre for Diseases control
CHB	Chronic Hepatitis B
CSW	Commercial Sex Workers
CTL	Cytotoxic T-lymphocytes
DNA	Deoxyribonucleic acid
ELISA	Enzyme linked immunosorbent assay
EPI	Expanded programme immunization
FSW	Female Sex Workers
H_2SO_4	Sulphuric acid
HAART	Highly active antiretroviral therapy
HBc-Ab	Hepatitis B Core Antibody
HBeAg	Hepatitis B e Antigen
HBsAb	Hepatitis B Surface Antibody
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B Virus

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HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IFNa	Interferon alpha
IFNa	Interferon alpha
IgG	Immunoglobulin G
IgM	Immunoglobulin M
KEMRI	Kenya Medical Research Institute
LC	Liver Cancer
mRNA	Messager ribonucleic acid
MSM	Men who have sex with Men
Nm	Nanometers
OHBV	Occult hepatitis B virus
OHBVI	Occult Hepatitis B virus infection
OP	Outpatient

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OR	Odds Ratio
PCR	Polymerase chain reaction
RNA	Ribonucleic acid
RNA	Ribonucleic Acid
SD	Standard Deviation
SERU	Scientific Ethical Review Unit
SPSS	Software package for social sciences
SRBC	Sensitized sheep red blood cells
SSC	Scientific steering committee
STC	Special treatment Centre
STD	Sexually Transmitted Diseases
TLV-1	T-Lymphotropic virus
TMB	Tetramethylbenzidine
UK	United Kingdom
UL	Microliter

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USA	United State of America
VCT	Voluntary counselling and Testing Unit

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DEFINITION OF TERMS

Fulminant hepatitis: decompensated stage of liver cirrhosis

Hepatitis endemic areas: regions with prevalence of hepatitis B surface antigen above 8%

Hepatitis: refers to the inflammation of the liver, which is characterized by onset of jaundice.

Horizontal transmission: Through sex contacts or injecting of drugs

Icteric patients: These are patients with obstructive jaundice

Perinatal transmission: One way to transmit hepatitis B virus (HBV) is from mother to infant during birth

Vertical transmission: when an infected mother transmits the virus to the neonatal during birth

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ABSTRACT

Hepatitis B virus is one of the most common infectious disease in the world, infecting two billion people, 350 million of them being chronically infected. It is primarily transmitted through contact with body fluids of the infected person. The aim of the study was to determine prevalence and factors associated with hepatitis B virus infection among patients attending Special Treatment Centre clinic in Nairobi. The blood samples were taken for serological analysis of hepatitis B proteins. The samples were transported to KEMRI where they were screened for Hepatitis B surface antigen (HBsAg), hepatitis B antibodies and antibody to the HBV core protein (HBcAb) using commercially available kits. A total of 200 adults; 80 males and 120 females aged 18-60 years with a mean age of 32.77, SD=8.638 and a median of 31 years participated in the study. In general, 9.5% (95% CI 7.3–12.4) of the respondents were positive for hepatitis B surface antigen while 26.5% (23.4-29.5) respondents were positive for Hepatitis B surface antibody. The prevalence of HBsAg among males and females was 10% (8/80) and 9.2% (11/120) respectively. A multivariate analysis of risk factors showed that multiple sex partners (p=0.001), presence of genital ulcers (p=0.001) and not using condom (p=0.0013) were associated with HBV infection. None of the study participant reported having been vaccinated against hepatitis B virus. Data on socio-demographic characteristics, information on sexual behavior, and clinical characteristics were collected using a semi structured interviewer administered questionnaire. This current study has revealed that HBV infection is also endemic among patients attending special treatment Centre. Therefore, this study group constitute a target population for further HBV prevention and treatment through provision of condom, early treatment of genital ulcer, health education on consistent condom utilization and need for having one sex partner. Routine immunization with hepatitis B (HB) vaccine is strongly recommended for the prevention of HBV infection in individuals at risk for STIs.

CHAPTER ONE

INTRODUCTION

1.1 Background

Globally, sexually transmitted infections (STIs) are among major causes of serious preventable conditions, such as liver cancer, infertility, pelvic inflammatory disease, ectopic pregnancy and congenital infection. STIs cause significant morbidity and mortality through their impact on sexual, reproductive and child health **(**Bezold *et al.,* 2017). Some of the known STIs are caused by; viral, parasitic and bacterial pathogens that are transmissible sexually.

Hepatitis B is among the sexually transmitted viral disease in the world. Hepatitis is an inflammatory condition of the liver which can be caused by viruses, toxic substances, or immunological abnormalities. Evidence indicating that hepatitis B can be transmitted through sexual route dates back from the early seventies, where the virus was isolated from saliva, semen (Frimpong, 2010) and vaginal secretions (Stanberry & Rosenthal, 2012). This disease being sexually transmitted disease poses a serious public health problem with a large number of cases, disease progression and a variety of social and economic impacts on more severely affected countries (Fattovich *et al.,* 2015). Sexually transmitted infections such as hepatitis B are usually concentrated in core groups, such as sex workers, who have a high number of partners and receive poor health care (Sopheab *et al.*, 2018).

Hepatitis B Virus is classified second among the carcinogens causing malignancy after tobacco (Kew, 2010). It is estimated that two billion people worldwide are infected with HBV, of which 350 million people have chronic infection and at least one million of them die each year from cirrhosis or hepatocellular carcinoma (Fattovich *et al.,* 2015). Out of two billion individuals infected worldwide, 65 million are found in Africa. Sub-Saharan Africa is ranked as a high endemic region with more than 50 million people believed to be chronic carriers of the HBV (Mcmahon, 2009). It's estimated that 250,000 deaths occur due to HBV infection annually in Sub-Saharan Africa (Mphalele, 2013). Kenya is categorized as a high

endemic area for HBV due to its high prevalence of above 8%. Despite of the fact that HBV vaccine is available in the health care systems, HBV infections are transient, approximately 5 to 10% of infected adults and more than 90% of infected neonates fail to clear the virus and develop a lifelong persistent infection, which may progress to chronic hepatitis, cirrhosis, and primary hepatocellular carcinoma (Liang, 2009; Block *et al.,* 2012).

High concentration of Hepatitis B virus is found in blood serum; moderate concentration is found in semen, vaginal secretions, and saliva and low concentration of the virus is found in sweat, tears, urine, and breast milk (Yatich, 2015). The most common routes of transmission of this virus vary depending on its endemicity (But *et al.,* 2018). In low endemic areas sexual intercourse is the most common route of transmission (Te *et al.,* 2010). Broad epidemiological studies on sexual transmission of HBV have been conducted in low endemic countries of the North America and West Europe. A descriptive study among sex workers carried out in Benin City of Nigeria showed that 14.1% of them were HBV infected (Azage *et al.,* 2014**).** This is because in endemic countries 80% of the population may already have been infected before reaching a sexual active age (Hoffmann *et al.*, 2018).

Drugs for the treatment of viral hepatitis that are available in the market are expensive, thus making them unaffordable by the low income earners. Assessing treatment offered by the global viral hepatitis Programme for the vast number of people with chronic HBV infection living in the developing world is far from becoming a reality. Safe and effective vaccine against HBV infection has been available from 1982 in Kenya (Kenya National Hepatitis guidelines, 2014). The implementations of mass immunization Programme, which was recommended by WHO from 1991, has dramatically decreased the incidence of HBV infection among infants, children, and adolescents in many countries (Thun *et al.,* 2010). A large number of persons are infected with HBV after the implementation of the hepatitis vaccine. In Kenya, infant vaccination was adopted in 2002, though the same has not been rolled out to other populations thus, leaving them at risk of contracting HBV infection.

Researchers in Kenya have shown that, HBsAg carrier rates among asymptomatic blood donors to range between 5-30% (Mutuma *et al.,* 2011). The prevalence of HBsAg among chronic liver disease patients in Kenya has been found to be 4.1% (Ochwoto *et al.,* 2013). This study was carried out to establish the prevalence and associated risk factors associated with hepatitis B infection among STI patients in Nairobi.

1.2 Statement of the Problem

Chronic Hepatitis B (CHB) and Hepatocellular Carcinoma (HCC) remain one of the major public health problems worldwide (WHO, 2017), despite of the existence of a stable vaccine for HBV. HCC is the sixth most common cancer in the world (Mahgoab, 2011). Chronic HBV accounts for majority of liver related morbidity and mortality in the world (Chang *et al.,* 2010). Globally, there are two billion people infected and over 350 chronically infected with hepatitis B virus. Hepatitis B cases are on the rise here in Kenya (The East African newspaper, 2017). The disease can easily be transmitted through blood transfusion, sexual intercourse and from mother to child. Eighty percent (80%) of African population lives in high endemic area. Like many other viral infection, HBV infection has not been researched comprehensibly in Kenya. If proper attention is not given to the virus, prevalence of HBV may rise to more 50% (KEMRI press release, 2014). Despite of the long history of the diseases in Kenya, very little has been done in terms of enhancing awareness to curb it except introduction of vaccination in Expanded Programme of Immunization (EPI), blood screening and sterilization of equipment's. Approximately 60% to 80% of liver cancer cases in the country are due to chronic infection with hepatitis B virus. In order to control the spread of HBV it's important to screen and vaccinate high risk groups like sex workers. The extent of HBV has been studied and documented in most risk groups thus little is known of this viral infection among the STD patients who are recognized as a high risk group too. The economic costs of the failure to control the transmission of infection include increased requirement for medical care, higher levels of dependency and the loss of productive labor force, placing heavy burdens on already over stretched health, social services and national economy (Buseri *et al*., 2018). As a result of the

complications related to this infection and the fact that the HBV and Human Immunodeficiency Virus (HIV) have a shared mode of transmission, there is need to find the magnitude of HBV infection among this risk group which could be in the increase also as the HIV epidemic.

1.3 Justification of the Study

Hepatitis B transmission has been found primarily among un vaccinated persons with risk behaviors for Hepatitis B transmission, including having multiple sex partners of people with chronic Hepatitis B infection (Daniel *et al.,* 2009). Kenya is classified by WHO as endemic for HBV (Ndungu *et al.,* 2013) and has also surpassed the prevalence of HIV by three fold (KEMRI press release, 2014). HBV infected individuals are at risk of infecting others via sex with consequence of developing fulminant hepatitis and liver cancer in the long run. Therefore, populations, such as the homeless, sex workers, and prisoners, have a higher prevalence of HBV infection than the general population (Villar *et al.,* 2011).

Serious sequelae may occur due to the absence of effective treatment for hepatitis viruses. Lack of data on the prevalence of these viruses and their risk factors would increase the incidence rate of these viruses. The high cost of the treatment of complications due to infection by these agents adds to the burdens of the devastated health sector. The Special Treatment Centre (STC-Casino) was chosen for this study because it's the only public health care Centre providing specialized STD treatment in Nairobi and its environs. Most of the patients attending the clinic are sex workers. There was a need to get a clear picture of the HBV infection in this era of HIV. The fact that the virus is highly prevalent in Kenya and its ability to be transmitted sexually; there was also a need for establishing the prevalence and sero epidemiology of HBV infection among this high risk group which is not available. Accurate information regarding the magnitude of HBV infection and seroprevalence in our population is crucial in order to undertake prevention efforts that would have an overall impact on the economy. Loss of young people through the diseases can undermine the growing economy; hence it is important that risks are minimized. This study has provided data on the magnitude of HBV infection, associated risk

factors and has found intervention strategies to prevent infected people from developing hepatocellular carcinoma and other viral hepatitis complications.

1.4 Research Questions

i. What is the prevalence of Hepatitis B infection among patients attending Special Treatment Centre in Nairobi?
ii. What are the individual level factors associated with HBV infection among patients attending the Special Treatment Centre in Nairobi?
iii. What is the proportion of individuals having immunity against Hepatitis B among Special Treatment Centre patients in Nairobi?

1.5 Objectives of the Study

1.5.1. Broad Objective

To determine prevalence and associated factors of Hepatitis B infection among patients attending the Special Treatment Centre in Nairobi, Kenya

1.5.2. Specific Objectives

i. To determine the prevalence of Hepatitis B infection among patients attending the Special Treatment Centre in Nairobi.
ii. To determine the individual- level factors associated with HBV infection among patients attending the Special Treatment Centre to Hepatitis B infection.
iii. To determine the proportion of individuals having immunity against Hepatitis B infection among Special Treatment Centre patients in Nairobi

CHAPTER TWO

LITERATURE REVIEW

2.1 Global burden of Hepatitis B Virus

Hepatitis refers to the inflammation of the liver, which is characterized by onset of jaundice. Viruses, among other causes, are the major cause of acute, sporadic or chronic hepatitis. There are a number of viruses that cause hepatitis among them those designated Hepatitis A-E (Kurbano *et al.,* 2010). Of all the Hepatitis the most prevalent and worldwide spread is Hepatitis B virus (HBV).

The burden of HBV infection continues to increase globally despite widespread awareness of preventive measures, including the availability of a safe and effective vaccine (Van *et al*., 2013). Over 240 million people are chronically infected with HBV in the world (WHO, 2014). It is reported that at least 600,000 individuals die from HBV related diseases such as chronic hepatitis B (CHB), liver cirrhosis (LC), and hepatocellular carcinoma (HCC) liver cancer annually in the whole world (Mustafa, 2014). The disease is 50 to 100 times more infectious than the deadly human immunodeficiency virus (HIV) and can remain on an untreated part of the body for close to seven days (Hepatitis Foundation International, 2016). The prevalence of HBsAg positivity in the Far and middle East, Africa and parts of South America ranges between 8 to 15% (Alvarado-Mora *et al.,* 2013). High prevalence areas have a prevalence of chronic hepatitis B infection that is equal to or greater than eight (8%); this include countries from North America, South America, Sub-Saharan Africa and most Asian countries (Alvarado-Mora *et al.,* 2013). Intermediate prevalence areas, shares a prevalence rate which ranges between 2% and 7% and include countries from South America, North Africa, Western Europe, Eastern Europe and the Indian subcontinent. Low prevalence areas are estimated to have a prevalence of chronic infection less than (2%) which includes most of the North American countries, Australia and most of Western Europe including the United Kingdom (UK). Hepatitis B virus prevalence in the serum, varies from <1% to >10% depending on the geographic region, with the highest prevalence in sub-Saharan Africa and Southeast Asia (Kravis *et al.,* 2011). In Sub-Saharan Africa the

prevalence of chronic HBV infection ranges between 7– 26% (Ott *et al*., 2012). It has been estimated that HBsAg carrier rates in the sub Saharan Africa ranges from 9.6% in South Africa to 20.6% in the Democratic Republic of Congo (DRC), while HBV infection rates range from 56.2% in Kenya to 91% in Senegal. In Namibia and Nigeria, the prevalence is 35% and 75% respectively (Ajayi *et al.,* 2015).

Hepatitis B transmission route varies according to the prevalence rate of the virus. Countries with very high prevalence rate usually have vertical transmission as the main route of transmission which is mostly found during childhood. Countries with intermediate prevalence rates normally have horizontal transmission as its major route where the disease is transmitted through sexual contact or through injecting of drugs. In countries with low prevalence rates such as the United Kingdom, the epidemic is mostly acquired during adulthood through sexual intercourse or injecting of drugs. According to a previous research chronic hepatitis infection can be treated in high income countries with the combination of Lamivudine, Terofavir and entecavir. Persons with severe liver cases are given liver transplants as well as surgery and chemotherapy to prolong their lives (WHO *et al.,* 2015). These options are unfortunately unavailable to those in low income countries due to the expensive nature of these treatments. Hence the only option for them is to stick to the saying that, "prevention is better than cure "through the use of vaccine. The WHO (2018) reported that hepatitis B vaccine has an excellent record of safety and effectiveness with over one billion doses used worldwide since 1982 and that it has a 95% capacity to prevent children and adults from contracting chronic infection if they are not already infected with the disease. Completion of the hepatitis B vaccination series is the safest and the most effective way of protecting against hepatitis B. The World Health Organization 2013 has targeted hepatitis B as one of eight infectious diseases that should be controlled through vaccination efforts. For the purpose of propagating this agenda, WHO in 1991 instructed all countries to incorporate hepatitis B vaccination into their national vaccination programs. Only 164 countries had implemented the directive as of 2006, with most countries coming from East and South East Asia, the Pacific, Islands, Australia, Western Europe and the Middle East (Mitchell *et al.,* 2010).

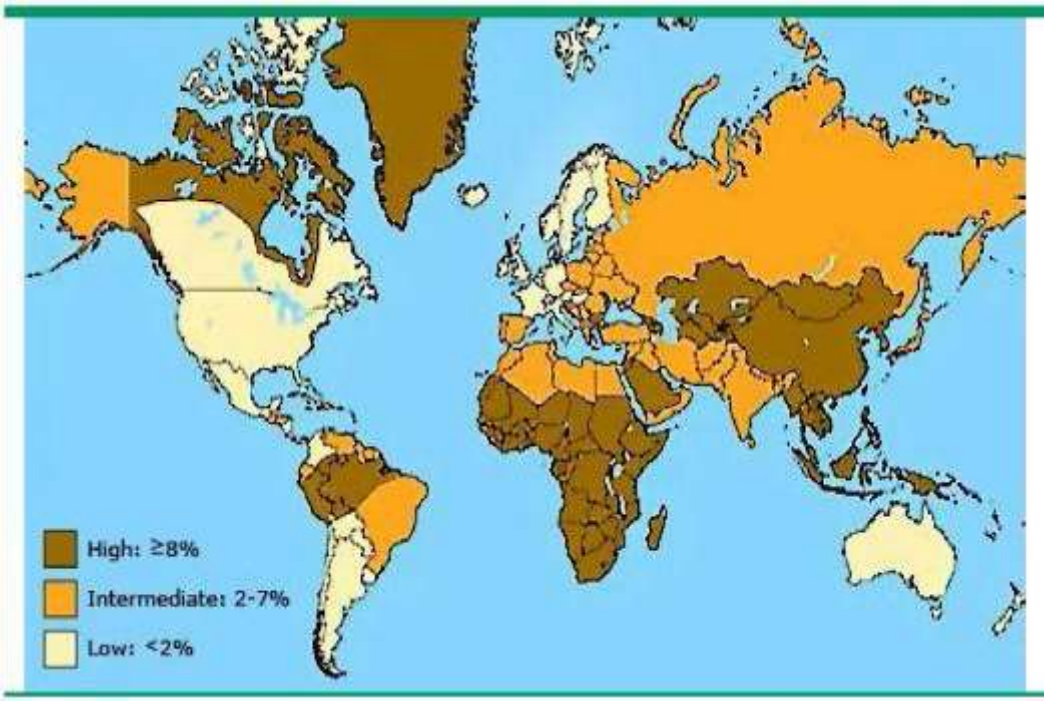

Figure 2.1: World map showing prevalence of chronic infection with Hepatitis B Virus (CDC, 2013)

2.2 Burden of Hepatitis Virus in Kenya

Studies in Kenya have shown a prevalence rate of HBsAg of 8.8% among the general population but values in urban areas range from 8 to 30% (Mutuma *et al.*, 2011). In one of the studies, 34% of those positive for HBsAg were children aged between 5 and 10 years (Fitzsimons *et al.*, 2013). A study done on circulating HIV-1 sub types among voluntary blood donors confected with HBV, Hepatitis C Virus (HCV), syphilis and Human T-Lymphotropic Virus 1 (TLV-1) in Western Kenya, showed the prevalence of HBV to be 2.5% (Ellington *et al.*, 2011). In another study done in Kisumu district hospital the prevalence of HB infection among all patients screened to be at 47% (Muriuki *et al.*, 2013). In Kenya, the prevalence of HBV among blood donors has overtaken the prevalence of HIV by three fold (KEMRI press release, 2014). The prevalence of HBV varies with the study population as observed by a prevalence of 11% and 18% among medical students in Kenya and Uganda respectively (Kramvis *et al.*, 2011). Among HIV-infected icteric patients, a

prevalence of 53% was observed (Muriuki *et al.,* 2013) and 26.2% among icteric patients in a general medical ward (Ellington *et al.,* 2011). A prevalence of 4.3% was found among urban residents and 3 to 11.9% in a rural population (Muriuki *et al.,* 2013). A prevalence of 12.2% was observed among HIV-infected outpatients. Among hemodialysis patients in Kenya, seroprevalence of 8% and 5% for HBV and HCV respectively was observed (Gasin *et al.*, 2012).

2.3 Natural history of HBV infection

2.3.1 Acute infection

Hepatitis B virus infection can lead to a self-limiting acute disease primarily affecting the liver which will clear within six months of infection. HBV has an incubation period of 90 to 150 days following which, markers of infection such as HBsAg and HBV DNA become detectable using the currently available commercial assays. Patients will normally have an elevated alanine aminotransferase (ALT) level. ALT is a liver enzyme released in the bloodstream during an episode of inflammation in the liver. The serological profile of acute, resolving hepatitis B infection is shown in Figure 2.3. Patients with an acute infection will show varied symptoms, ranging from nausea and vomiting to rashes and will often progress to jaundice (Previsani & Lavanchy, 2012).

About 1% of acute cases develop into fulminant hepatitis which is often fatal in adults (Previsani & Lavanchy, 2012). There is no specified treatment for acute HBV infection unless patients are suffering from fulminant hepatitis B or protracted severe acute hepatitis B (Lok & McMahon, 2014). In 95% of adults and only 10% of newborns, HBsAg will clear within three months with the development of protective anti-HBs antibodies. Since hepatitis B is currently rampant among Kenyan populations its paramount for its prevalence and immunity to be checked

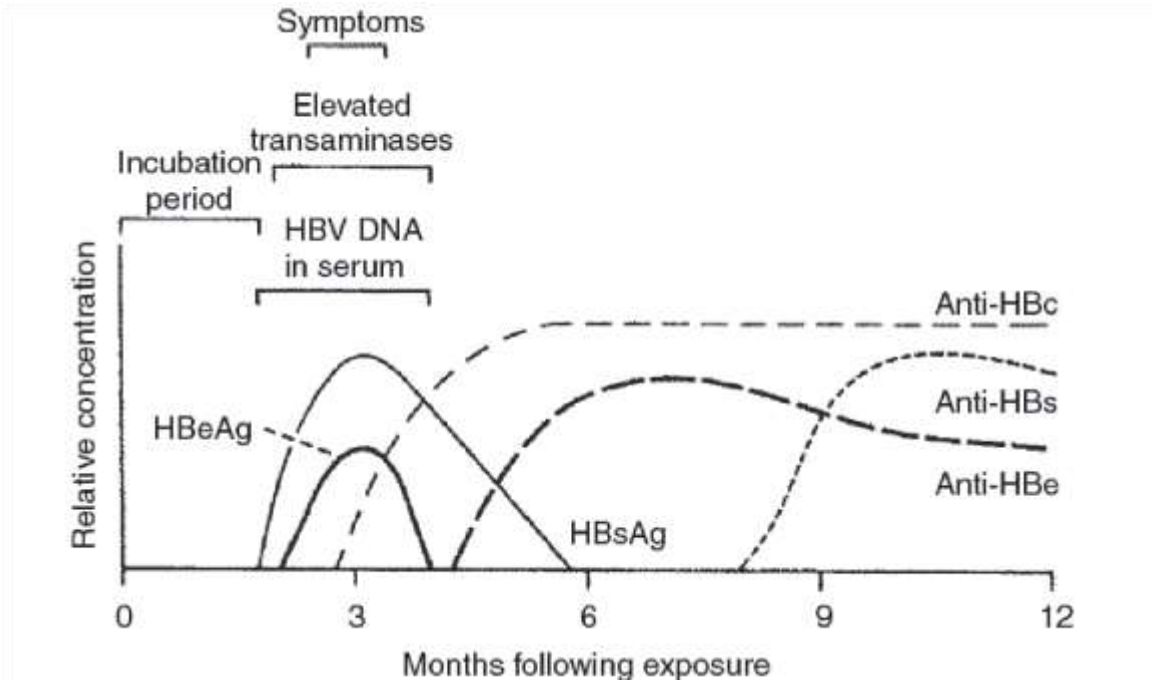

Figure 2.2: Serological profile of acute, resolving hepatitis B infection (Source Harrison, Dusheiko & Zuckerman, 2012)

2.3.2 Chronic infection

The most severe consequences of HBV infection are seen in chronically-infected patients who may develop cirrhosis and liver cancer decades after the initial infection. Chronic HBV infection is defined as HBsAg positivity for more than six months.

Age at infection is an important risk factor for development of chronicity. Vertical transmission from HBeAg-positive mothers has a 90% risk of resulting in a chronic infection (Pan *et al.*, 2012). This has been attributed to the immaturity of the infants' immune systems (Hadziyannis, 2011). Horizontal transmission before the age of five years has a reduced risk of chronicity of 10-30% (Pan *et al.*, 2012) and in adults, the risk of chronicity is less than 5% (Lok & McMahon 2014).

Chronic HBV infection is progressive and can be divided into four phases (illustrated in Figure 2.5) although not every patient will experience all stages in a particular order (Dandri & Locarnini 2012).

2.3.2.1 Immune tolerant phase

The first is the immune tolerant phase, which occurs mostly in infants who are infected vertically and in whom it may last for decades (Fattovich *et al*., 2008). Older children and adults may experience the immune tolerant phase transiently (Fattovich *et al*. 2015; Yim and Lok, 2016). During this stage, the virus is not cleared by the immune system of the patients. As a result, the patient has high viral loads (>20 000 IU/ml), high levels of HBeAg and HBsAg (Dandri &Locarnini, 2012), but normal or mildly elevated levels of liver enzymes (ALT and aspartate aminotransferase) with minimal liver damage (Fattovich *et al.,* 2015).

2.3.2.2 Immune clearance/HBeAg-positive chronic hepatitis B

During the immune clearance phase, immune tolerance to HBV is lost and the virus is cleared by the immune system (Fattovich *et al.* 2015; Yim & Lok 2016). Typically, in this phase, inflammation of the liver, elevated ALT levels and fluctuating HBV DNA levels (>20 000 IU/ml) are observed (Dandri & Locarnini, 2012; Fattovich *et al., 2015*).

Eventually, in most patients, this stage will result in the clearance of HBeAg and the appearance of antibody to hepatitis B e antigen (antiHBe) marking the transition to the next phase (Fattovich *et al.,* 2015). Some patients however, will periodically show fluctuating levels of DNA replication and flares in liver enzyme levels (Yim & Lok, 2016). The duration of this phase and the severity of the liver enzyme flares have been described as risk factors for cirrhosis and HCC (Dandri & Locarnini 2012; Yim & Lok, 2016).

2.3.2.3 Immune control phase

The following phase is the inactive HBsAg carrier state characterised by the absence of HBeAg, presence of antiHBe, a persistently low or undetectable level of HBV

DNA (<2000 IU/ml has been suggested) and normal ALT levels (Fattovich *et al. 2015*). If the patient remains in this phase, the outcome of the chronic infection is benign, with no resulting hepatic decompensation (Yim & Lok 2016).

2.4 Life cycle of HBV

Hepatitis B virus virion binds on the hepatocytes receptors where viral nucleoside enters the human cell through a mechanism referred to as endocytosis (Grove *et al.*, 2011). Hepatitis Virus multiplies via RNA made by a host enzyme, thus the viral genomic DNA is transferred to the cell nucleus by host proteins called chaperones. The partially double stranded viral DNA is then made fully double stranded and transformed into covalently closed circular DNA that serves as a template for transcription of four viral mRNAs. The largest viral mRNA is then used to make the new copies of the genome, the capsid core protein and the viral DNA polymerase. The four viral transcripts then undergo additional processing to form progeny virion that can either be released from the cell or returned to the nucleus and re-cycled to produce even more copies (Beck *et al.*, 2011). The long viral mRNA is then transported back to the cytoplasm of the host where the virion protein synthesizes DNA through the activity of its reverse transcriptase.

Hepatitis B virus interferes with the functions of the liver by replicating in liver cells, called hepatocytes. The virion binds to the host cell through the preS domain of the viral surface antigen where they are finally internalized by endocytosis. During HBV infection, the host immune response causes both hepatocellular damage and viral clearance. 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 (Bruss *et al.*, 2014).

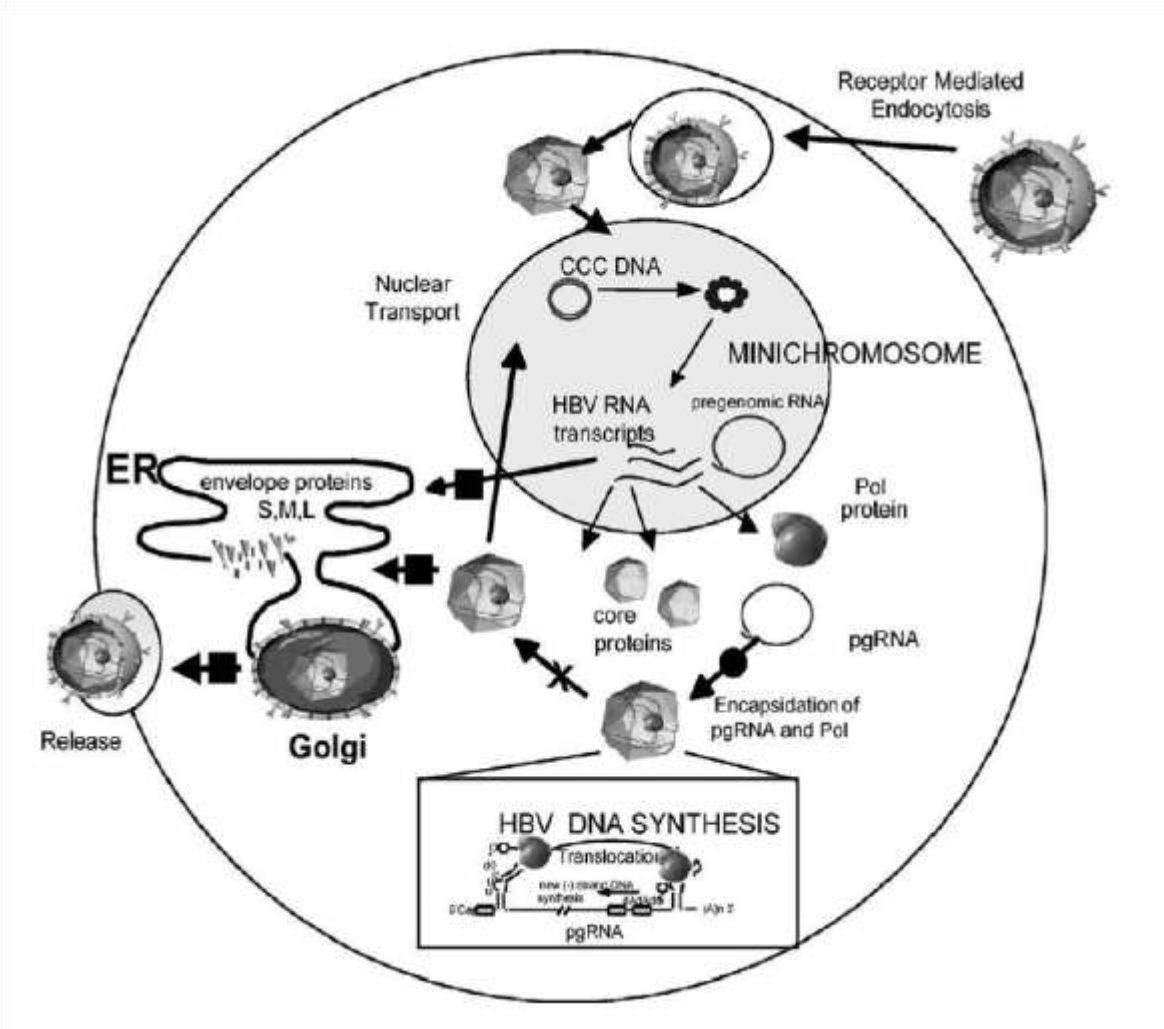

Figure 2.3: HBV life cycle HBV infection, replication, encapsulation and release from hepatocytes (Seeger *et al*., 2015)

2.5 Modes of HBV transmission

Hepatitis B virus infection can be transmitted at three stage in life; during birth, childhood, and in adult life (Pan *et al.*, 2012). The main modes of transmission are; mother to child (perinatal), child to child (horizontal), sexual and parenteral. The role of each of these modes varies across the globe. Transmission can be classified as being either vertical or horizontal. Horizontal transmission occurs during adolescence or childhood, throughout sexual exposure, needle prick (both accidental or through intravenous drug use), and blood transfusion (Elhafiz, 2015). Therefore, any person with renown history of sexually transmitted diseases (STDs), multiple sexual partners or an injecting drug user stands a higher chance of being infected with HBV (Ross *et al.*, 2012).

Exposure to blood is also by means of open wounds in households and other close contacts and multiple transfusions in hemophiliacs (Brewer, 2011). A vertical transmission occurs when an infected mother transmits the virus directly to the neonatal during child birth. Such transmissions are usually possible when the expectant mother suffers an acute infection of hepatitis B during pregnancy or if she is a chronic carrier during that period. The mode of this vertical transmission is not clear cut, but indications are that, infection might occur through a placenta cutting during childbirth. Majority of countries in South East Asia, the Western Pacific and Africa have high endemicity of HBV (Otts *et al.*, 2012). In these settings the major mode of HBV transmission has been identified as vertical, where by mothers directly transmit virus to their infants during prenatal periods or where infected siblings, playmates, other members of different households transmit the virus to their younger ones (Shimakawa, 2015). A part from the above mentioned major modes of transmission, tattooing and body piercing tools have been recently discovered to have contributed significantly to the spread of the disease. The commonly associated risk factors are sexual misconduct, tattooing, body-piercing, drug use or injection. In low developed countries, the use of crude methods during injections such as reused unsterilized or improperly sterilized needles and syringes are estimated to cause millions of cases of hepatitis B and C as well as HIV and other blood borne diseases globally (Gasim & Adam, 2013).

2.6 Clinical manifestation of hepatitis B virus infection

Hepatitis B infection may develop from acute, chronic, liver cirrhosis to liver cancer depending with the immune system of an individual. Acute viral hepatitis is an illness that begins with general weakness of the body, loss of appetite, nausea, vomiting, body aches, mild fever, and dark urine, itchy skin and then progresses to development of jaundice. This stage of infection may last for a few weeks and then gradually clear in most infected people. A few people develop fulminant hepatitis and may die.

Acute HBV infection may be entirely asymptomatic and may go unrecognized in most infected persons (Trigg *et al.*, 2011). Chronic hepatitis B infection may either be asymptomatic or may be associated with a chronic inflammation of the liver, leading to cirrhosis over a period of several years and finally progressing to liver cancer (Hepatocellular carcinoma). Cirrhosis results in liver cell necrosis and fiber (scar) tissue overgrowth. Although most carriers will not develop liver complications from chronic hepatitis B, 15-40% will develop serious sequelae during their lifetime (Akol, 2014). When liver cirrhosis progresses, the liver itself become hardened and shrink while the surface becomes uneven. Clinically, there are two stages in liver cirrhosis, compensated and decompensated (Miguel, 2014). In the compensated stage, disease progression is stealthy and shows very few noticeable symptoms. During this stage, the most common symptoms could be fatigue, anorexia, over-frequent thirst, thick coating on the tongue, nausea, stomach broadness, and dull pains in the liver area. As liver functions further deteriorate and the portal vein pressure increases, these symptoms may worsen. New symptoms and physical signs such as spider moles, liver palms, liver shrinkage, jaundice, edema, ascites, and low grade fever could start to show and at this point, the cirrhosis starts to enter the de-compensated stage.

The de-compensated stage of cirrhosis is the late stage of the chronic liver diseases and many complications may arise (Oyakhire, 2010**).** Complications in this stage are ascites, gastric bleeding, spontaneous peritonitis, hepatic-renal dysfunction, encephalopathy, and hepatocellular carcinoma (Hyung & Hyun, 2013).

2.7 Diagnosis and Roles of HBV markers

Diagnosis is based on clinical, laboratory, and epidemiologic findings. HBV infection cannot be differentiated on the basis of clinical symptoms alone. Conclusive status of infection depends on specific serologic test. The Serologic markers for HBV infection vary depending on whether the infection is in acute or chronic stage.

Hepatitis B virus replicates in the liver cells where it produces antigens that are detected in blood. These antigens serve as a marker of active infection and infectivity. The pattern of the antigens provides clues on the stages of HBV infection. HBsAg first appears during the late stages of the incubation period and is easily detectable by Polymerase Chain Reaction (PCR); reverse passive immuno-agglutination method (example Kemri hepcell Kit) and radioimmune assay or enzyme immunoassay. Presence of these antigens in blood circulation seizes once an immune response is mounted. These markers include; HBsAg and HBV DNA which are the first detectable markers of acute infection, appearing during incubation period, prodromal and acute disease (Carey *et al.,* 2016). HBsAg appears after infection and disappears one to two months after jaundice (Carey *et al.,* 2016). During convalescence it falls to undetectable levels. The persistence of HBV for more than 6 months is an indication of carrier state, risk for chronic hepatitis and HCC (Zhang *et al.,* 2013).

Antibodies to HBsAg replace HBsAg as the acute infection resolves, and this indicates immunity in almost 80% of cases after the acute infection (Dosanjh *et al.,* 2011). AntiHBs will also appear in serum after HBV vaccination. Some individuals lose these antibodies acquired after acute HBV infection and may become susceptible to HBV (Liaw *et al.,* 2009). HBsAg, derived from pre-core protein, is considered a marker of HBV replication and infectivity. HBV core antigen cannot be detected in the serum, but antibodies against it can, first immunoglobulin M and later immunoglobulin G (Carey *et al.,* 2016).

The antigen persists during the acute phase of the disease and sharply decreases when antibody to the surface antigen becomes detectable. Antibody of the IgM class

to the core antigen is found in the serum after the onset of the clinical symptoms and slowly declines after recovery. Its persistence at high titer suggests continuation of the infection. Core antibody of the IgG class persists for many years in the body of an infected person where they provide evidence of past infection.

Table 2.1: HBV serologic markers and their Significance (CDC, 2010**)**

Marker	**Significance**
HBsAg	Antigen indicating infection
HBV DNA	Indicating active viral replication
Anti-HBc	Appears after the onset of symptoms of acute HBV infection. Indicating previous or ongoing infection in an undefined time frame
HBeAg	Correlating with HBV replication and infectivity
Anti-HBs	Indicates immunity

2.8 Hepatitis B virus and its associated Risk factors

A previous study reported high prevalence of HBV markers in subjects practicing risky sexual behavior, like STD patients and commercial sex workers (Lama *et al*., 2010). In Africa, HBV infections are traditionally thought to occur in children through close contact with household contacts and ritual scarification with exposure to HBV occurring before the age of sexual debut (Panga, 2012). Sexual transmission in adulthood was found to be the most likely risk factor for the transmission of HBV among adult in Rakai, Uganda (WHO, 2018). In a study conducted among TB patients results suggested that younger age of sexual initiation and multiple sex partners are significant risk factors for the acquisition of HBV (Lima *et al.,* 2009). A study done in Barcelona showed that there was a higher prevalence among intravenous drug users of 22.5%, whereas among the non-intravenous drug users the

prevalence was 7.4% (Vallejo *et al.,* 2012). Other factors reported to be associated with acquisition of HBV include increasing age, male gender, low level of education and history of previous surgery, multiple sexual partners, HIV infection, and non-use of condoms (Bwogi *et al.,* 2009). Among pregnant women high parity, polygamy, multiple sexual partners and previous history of sexually transmitted disease were shown to be among the significant risk factors for HBV infection in Nigeria (Ferreira *et al.,* 2009). Marital status, previous history of jaundice, history of blood transfusion and age were found to have no association with HBV transmission (Nagu *et al.,* 2018) and Since HIV and HBV share the modes of HIV transmission, it is plausible that HBV and HIV co-infection can occur, and this has been documented. Co-infection in Tanzania among HIV infected patients was found to be 17.3% among patients attending the Care and Treatment Centre at the Mombili National Hospital.

Hepatitis B infection is predominantly acquired at an early age in developing countries, which includes vertical transmission from mother to child, perinatal transmission, and horizontal transmission from child to child. However, HBV can also be transmitted sexually heterosexual and homosexual, accounts for a majority of the transmission occurring in adult life (Urbanus *et al.,* 2009). Vertical transmission is the most common mode of transmission worldwide (Te & Jensen, 2010). High levels of virus in serum (HBV DNA and HBeAg positivity) have been associated with increased risk of transmission by needle stick exposure and by vertical routes (Franco *et al.,* 2012).

There are a number of sub populations at risk of contracting HBV (Jayaraman *et al.,* 2010) who includes; infants born to infected mothers, young children in day-care or residential settings with other children in endemic areas, sexually active heterosexuals, men who have sex with men (MSM), sexual or household contacts of infected persons, health care workers, patients and employees in hemodialysis centers, drug injectors with unsterile needles and persons living in regions or travelling to regions with endemic hepatitis B. Sexual route of transmission is probably the single most important mode of HBV transmission in areas of the world where the prevalence of infection is low, such as North America (El-Serag, 2012).

From 1980 to 1985 homosexuals were particularly at high risk of getting infection, accounting for 20% of all reported cases of HBV infection (Te *et al.,* 2010).

2.9 Treatment of Hepatitis B infection

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 (Levy *et al.*, 2011). 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. Chronic hepatitis B is therefore easily managed rather than treated.

Treatment for HBV infection is usually supportive therapy, unless the hepatitis becomes chronic. An acute hepatitis B infection does not necessarily require therapy as 90-95% of acute HBV infection in adults resolves the infection and develop immunity (Yu *et al.,* 2011). Children are at higher risk for chronic infection. Up to 90% of infected children will fail to clear the virus and proceed to develop chronic infection which may finally lead to fulminant hepatitis. A chronic HBV infection does not resolve and may be life threatening at some stages. Chronic hepatitis B infection may require treatment to avoid the increased risk of progressing to liver cirrhosis and hepatocellular carcinoma. HBV complications dependents on the HBV viral load in patient's serum (Caligiuri *et al.,* 2016).

Treatment of HBV infection depends on different parameters (Satia *et al.*, 2012). Some of the factors that play a role in Hepatitis eradication includes; the genotype of hepatitis, mutation of viral genome and the viral load in the serum in addition to host factors like immune status, age, intake of alcohol and others (Yu *et al.*, 2011). If someone has chronic hepatitis they may need the help of antiviral medications. For those who don't have chronic hepatitis B, rest is recommended, as well as avoiding

fatty food and substances that are toxic to the liver such as alcohol and acetaminophen.

A patient in chronic hepatitis B stage requires antiviral medications so as to help stop the damage to the liver that can result from chronic infection. If the damage to the liver becomes severe, a liver transplant may be required as a person cannot live without a functioning liver. Drugs used by clinicians in the treatment of chronic HBV include interferon, lamivudine, Adefovir dipivoxil, telbivudine entecavir, and tenofovir. Interferon, treatment which requires injections daily or thrice weekly, has been supplanted by long-acting PEGylatedinterferon, which is injected only once weekly (Dienstage *et al.*, 2010). Some individuals respond to the treatments than others, and this might be because of the genotype of the infecting virus or the person's heredity.

Response to treatment differs between the genotypes. Early antiviral treatment may be required in less than 1% of persons infected with fulminant hepatitis. Treatment of chronically infected persons is paramount because it reduces the risk of developing cirrhosis and liver cancer. Chronically infected persons with persistently elevated serum alanine aminotransferase, which is a marker of liver damage, and HBV DNA levels are candidates for therapy (Lai *et al.*, 2017). Hepatitis B treatment lasts from six months to a year, depending on the drug used and genotype (Albert *et al.*, 2013). In Kenya, clinicians base hepatitis B treatments on viral load levels.

None of the available drugs in the market has been known to clear the infection; they can only stop the virus from replicating, thus minimizing liver damage. Some of the general management strategies for HBV recommended by medical experts include;

A) Avoidance of:

- Heavy alcohol consumption.
- Unprotected sexual intercourse with partners who are not vaccinated.
- Sharing of shavers or tooth brushes
- Donation of blood or organs

B) Screening of family members and sexual partners for HBV infection and vaccination of those who are sero-negative
C) Patient education and long-term follow-up with regular testing of liver biochemistry and surveillance of hepatocellular carcinoma in high risk groups

2.10 Hepatitis B Virus prevention strategies

Even though HBV has become a major source of health concern worldwide, on the other hand, it is the only STD that can be prevented by vaccination (Xu *et al.,* 2009). 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 by the use of 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 (Buseri & Jeremiah, 2009). 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.,* 2015). 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.*, 2015).

CHAPTER THREE

MATERIALS AND METHODS

3.1 Study site

This study was carried out at Special Treatment Centre (STC), located off River Road behind Kampala Coach Bus terminus Nairobi Central Business District (CBD) area. This health facility is under the management of Nairobi County Government. It lies at an attitude of 36°50′ East and latitude 1°17′ South. The health facility has been specially established to offer subsidized health services to individuals with sexually transmitted infections (STIs). The Clinic clients include a majority of self-referred individuals and patients referred from lower level facilities throughout the county. It serves mainly commercial sex workers (CSWs) and other vulnerable subjects in the County from all walks of life. The clinic offers a range of STI care and treatment; provides free condoms, Voluntary Counseling and Testing unit (VCT), family planning and other related services. About 500 both new and old patients are attended/treated on a daily basis. The facility is meant to serve residents of Nairobi and its environs.

3.2 Study design

This was a hospital based descriptive cross-sectional study which followed a quantitative approach. Study participants completed a self-administered questionnaire which was the main data collection tool to assess socio-demographic, sexual behavior as well as clinical characteristic. Blood samples were collected from study participants to test for Hepatitis B Virus, Hepatitis B Surface Antigen assay, Hepatitis B Surface Antibody assay as well as Anti-HBC assay.

3.3 Study population

The study population comprised both males and females attending Special Treatment Centre (STC) in Nairobi County Kenya between August to December 2014.

3.3.1 Inclusion criteria

- Males and females aged 18 years and above who were seeking treatment at the STI Special treatment centre
- Males and females who gave a written consent

3.3.2 Exclusion criteria

- Men and women who were too ill to participate
- Men and women who decline to give a written consent

3.4 Sampling Technique

3.4.1 Sample size determination

The sample size was determined using Cochran, 1977 formular.

$n= z^2pq/d^2$ Where, z = the standard number deviate at the confidence level.

Standard Error (1.96) Confidence interval at 95%

p = assumed prevalence of Hepatitis B Virus. The assumed prevalence of HBsAg was chosen to be 30% according to Mutuma *et al*., 2011 in a study among Kenyans of various ages.

q=1-p (the proportion of population without characteristics)

d=Confidence interval at 95% (allowable error of 0.05)

$\frac{1.96^2 \times 0.3 \times 0.7}{0.05^2}$= 323 study participants

Since the target population is < 10,000**:** Finite population correction factor was used to arrive at the sample size. FPC = Nn/ N +n-1 n = 323x500/500+323-1 n =196 study participants

The minimum study participants that were required for this study was 196,

However, a total of 200 samples were used in this study to increase precision.

3.4.2 Sampling procedure

Special Treatment Centre- Casino in Nairobi was purposely selected since it's only public facility offering specialized Sexually Transmitted Diseases treatment in Nairobi county and its environs. To attain 200 study participant simple random sampling was used. The respondents respondent were picked using generated computer random numbers. Potential respondents were approached individually and those willing to participate were invited for an interview.

3.4.3 Study Variables

3.4.3.1 The dependent variables

The dependent variable was the status for Hepatitis B virus surface Antigen among study participants.

3.4.3.2 The independent variables

The independent variables were;

- Age
- Level of education and occupation
- Religion
- History of sexual life (involvement in sex, number of sexual partners, participating in commercial sex, use of protection).
- History of injecting drugs

3.5 Data collection methods

3.5.1 Questionnaire

Individuals who consented to participate were subjected to a face to face interview by the assistant researcher officer or investigator where pre-test counselling was done, after the questionnaire was administered to obtain information on demographic characteristics (age, sex, occupation, level of education and marital status), sexual behavior, social factors associated with the disease infection and their knowledge about the disease under study (Appendix II). After this a mark w was put on their clinic attendance cards to avoid repeat inclusions during their subsequent visits.

3.5.2 Blood Sample collection

Participants were asked to consent to blood withdrawal. After this a venipuncture was performed where five (5) mls of blood was collected from each patient with sterile vacutainer needle directly into a universal sterile tube. The vacutainer tube for each patient was labeled using his/her hospital outpatient (OP) number which was later matched with the one indicated on the questionnaire.

3.5.3 Blood sample transportation

The collected blood was stored at 2-8^{0}C fridge (Medicool- Sanyo, Japan) at the study site before they were transported to KEMRI, within 8 hours. At KEMRI, the blood samples were coded with laboratory numbers. They were then centrifuged (Hatachi-Japan) at 2200g for 10 minutes at room temperature. The obtained serum was aliquorted into two tubes of 300□l each. One tube was kept at 4^{0}C fridge (Medicool-Sanyo, Japan) for serological purposes. The other aliquot was stored at -80 ^{0}C (Biomedical Freezer, Sanyo- Japan) as a backup sample.

3.5.4 Test for Hepatitis B Markers

3.5.4.1 Hepatitis B surface antigen detection by KEMRI Hepcell^{R}

The freeze-dried KEMRI Hepcell^{R} reagent was reconstituted in 2, 5ul of the diluent for 100 test screening patterns. Screening procedure involved preparing a microplate (10 x 12 or 8 x 12 wells), for a purpose of using 4-wells in a row for each individual test serum and an additional row for the positive control. Twenty-five milliliters of the diluent were then added using a dropper into 4-wells in a row. Using the micro diluter, 25ml of the test serum was picked and added into the first well. Serially, the mixture was diluted up to the 4thwell before being discarded. Twenty-five milliliters of well-mixed Hepcell reagent (reconstituted, sensitized SRBC) was added into the last well in the dilution series (1:16). The content was then mixed thoroughly on a plate mixer or by tapping the corners of the microplate. The mixture was incubated at room temperature (20-30^{0}C) for 1-2 hours and the test was read on a white background. Agglutination in the last well was regarded as a clear positive screening result for HBsAg. Samples showing agglutination in the 4th (last) well were also regarded as HBsAg screening test positive. Those showing no agglutination but a clear button of cells in the 4th well were regarded as negative for HBsAg. Tests that had weak reacting results were repeated using the same kit. All positive samples were subjected to confirmation, were two rows and six wells were used. In each well of the first row 25 µl of Hepcell diluent was dispensed. Corresponding rows of the second row were dispensed with equal volumes of inhibition buffer. Twenty- Five microliters of sample were then added into each of the first wells of the two rows and serially diluted to the sixth wells. Sensitized cells were added to the last four wells of the rows and the microplate incubated at room temperature for two hours. The number of rows with haemagglutination in the second row were counted and subtracted from that of the first row. Where the difference was equal to two or more, the sample was termed as a true positive sample. Where the difference was less than two the sample was reported as negative.

3.5.4.2 Hepatitis B core antibody detection Assay

A volume of 200 ul of Sample diluent was put into all the wells of the micro titer plate except in well 1A. Ten microliter of controls or serum samples was pipe pipetted into the appropriate wells. Micro plate sealer was then applied and the plate incubated at 37 C for one hour.

The plate was then washed five times with Wash Buffer to remove unbound HBsAg. 200 ul of Antibody Conjugate was then added to all wells again in except 1A. Cover seal was used to cover the plate and incubate at 37^0 C for 1 hour. Test wells and controls were then filled substrate and then all the wells were washed five times with Wash Buffer. Add 200 ul of Substrate Solution was then added into all the wells including 1A. The plate was incubated at room temperature for 30 minutes in the dark. 50 ul of 4N sulfuric acid (H_2SO_4) was then added to all wells including 1A and their action was read at 492 nm in the ELISA reader.

3.5.4.3 Hepatitis B surface antibody detection Assay

The strip holder was fitted with the required number of Monolisa strips, a volume of 25 ul of specimen diluent was added into the assigned wells, then 100mls of undiluted sample or control; then the mixer was incubated at 37^0C for 60 minutes, a volume of 50ul of the conjugate was added into each well and then incubated the strips at 37ºC for 60 minutes. The microplate was then washed six times with phosphate buffer solution; a volume of 100ul TMB substrate was added into each well and the strips incubated at 15^0C for 30 minutes in the dark. The reaction was stopped by adding 100ul 1mol/1 sulphuric acid to each well. Then the solution absorbance was read at 450 nm within 15 minutes. Results were then interpreted according to the manufacturer's instruction.

3.6 Data management

All completed questionnaires were double checked, numbered, filed and kept safely in a cabinet. The cabinet was under lock and key and only the study research

personnel were able to access the Questionnaires. Data was entered in MS Excel application. Data verification and validation was performed by rechecking all data entries with the original data forms to achieve a clean dataset was then exported to Statistical Package for Social Science (SPSS) for analysis. A back up of these data was done regularly to avoid any loss or tampering. Compact discs (CD) and flash discs were used to back up the generated **data.**

3.7 Data analysis

The data obtained was entered in Microsoft Excel spread sheets, then cross checked and transferred to SPSS windows version 20 (SPSS; Atlanta GA, USA) for analysis. To minimize error data cleaning and validation was done. Data were tested for normality prior to analysis, and where necessary log-transformed to achieve normality. The seroprevalence of HBsAg and anti-HBV was expressed in percentages for the entire study group. Descriptive analysis was carried out by calculating mean, standard deviation, 95% confidence interval and frequencies of different variables using Epi Info software version

3.3.2 (CDC, Atlanta, GA, USA, 2005). Pearson's chi squire (X^2) was used to assess any association between hepatitis and various exposures. where the condations of chi square were not met, Fishers exact probability was used. Logistic regression test was used to determine the relationships between the predictor variables (associated risk factors for HBV infection found to be statistically significant) and the outcome variable (HBsAg) at multivariate level. Associated risk factor variables with $p<0.05$ were considered as having significant association with hepatitis B Virus.

3.8 Ethical considerations

This study was reviewed and approved by the Scientific and Ethical Review Unit (SERU) of the Kenya Medical Research Institute (KEMRI) and referenced as SSC Protocol No. 2421 prior to commencement of study. Permission to carry out the study at the STI clinic was sort from the Director of medical services in the County of Nairobi. Anonymity was maintained by coding rather than using participant's name in the questionnaire. Written informed consent was obtained from the

participants (Appendix IV). The purpose, risks and benefits and subject's rights were explained to participants. Participation was voluntary. Information was kept confidential at all steps of the study. Finally, permission to draw blood was sought from the respective study subjects.

CHAPTER FOUR

RESULTS

This study was conducted between August to December 2014 among patients attending Special treatment Centre in Nairobi county.

4.1 Patients-level factors

4.1.1 Socio-demographic characteristics of respondents

Majority of the respondents were females 119 (59.5%). The range of respondents age was 18-60 years with the mean age being 32.8 years, Standard Deviation (SD) 8.6 years and median age was 31 years. Most of the study participants were in age group 25-34 years 86 (43%) and least age group was 55 to 60 years 3 (1%). Study participants were either Christians or Muslims, a higher number 194 (97%) being Christians. A large proportion of the respondents were self-employed 101 (50.5%). Most of study participants 134 (67%) reported to be married and least 5 (2.5%) were cohabiting. A high proportion of the respondent 97 (48.5%) respondents had attained secondary education in comparison to only 2 (1%) with no education. Majority of the study participants 150 (75%) were living in permanent houses (Table 4.1).

Table 4.1: Socio-demographic characteristics of the patients

Variable	Frequency (n=200)	Percentage (%)	95% Confidence Interval	
			Lower	Upper
Age category				
15-24	35	17.5	12.1	26.0
25-34	86	43	33.4	54.7
35-44	57	28.5	19.8	36.0
45-54	19	9.5	3.4	13.9
55 -60	3	1.5	0.6	4.7
Sex				
Male	81	40.5	29.3	55.1
Female	1I9	59.5	40.0	67.5
Religion				
Christian	194	97	93.3	99.2
Muslim	6	3	0.7	3.2
Occupation				
Unemployed	56	28	21.3	34.1
Formal employee	38	19	13.5	25.0
Self employed	101	50.5	41.9	56.7
Student	5	2.5	0.6	4.9
Marital Status				
Married	134	67	58.7	75.2
Single	47	23.5	19.4	30.5
Cohabiting	5	2.5	0.7	5.2
Widowed	7	3.5	0.6	5.8
Divorced	7	3.5	0.6	5.8
Education Level				
No education	2	1	0.6	3.9
Primary education	61	30.5	24.6	36.7
Secondary education	97	48.5	38.2	45.3
Tertiary education	40	20	16.3	25.6
Housing				
Temporary	5	2.5	0.8	5.1
Semi- permanent	45	22.5	17.3	29.6
Permanent	150	75	60.1	82.1

4.1.2 Sexual behaviors of study participants

More than half 114 (57.0%) of the study respondent reported having more than one sexual partners. Majority 158 (79.0%) had engaged in sex for more than six months. A high proportion of study participants 109 (54.5%) reported not having used condom during sexual intercourse, 92 (46.0%) reporting to be using sometimes. Majority of the respondents 176 (88.0%) used vaginal as mode of sex penetration. Only, 40 (20%) reported to have bought or sold sex while 159 (79.5%) reported to

have been infected with sexually transmitted disease at one point of their life. Majority 199 (99.5%) of the respondents didn't have history of injecting themselves with drugs while a small number 5(2.5%) reported to have practiced tattooing (Table 4.2).

Table 4.2: Sexual characteristics of the patients

Variable	**Frequency (n=200)**	**Percentage (%)**	**95% Confider Interval**	
			Lower	**Upper**
Number of sexual partners				
One	69	34.5	27.6	40.5
Two	2	1.0	0.6	4.7
More than two	114	57.0	40.2	65.9
None	15	7.5	2.4	12.7
Period of sex engagement				
1-6 months	158	79.0	60.3	86.4
>6months	27	13.5	7.2	18.7
Not applicable	15	7.5	3.0	11.2
Condom use in vaginal sex				
Yes	76	38.0	30.7	45.4
No	109	54.5	43.1	60.2
Not applicable	15	7.5	2.9	13.1
Frequency of condom use				
Sometimes	13	6.5	2.2	10.1
Rarely	92	46.0	39.8	55.1
Often	6	3.0	0.9	7.3
Not applicable	89	44.5	34.6	55.8
Ever bought/sold sex				
Yes	40	20	15.3	24.7
No	160	80	73.2	88.5
Mode of sexual penetration				
Vaginal	176	88	78.4	93.7
Vaginal Oral	9	4.5	1.1	6.7
Not applicable	15	7.5	3.1	10.7
History of practicing tattooing				
Yes	5	2.5	0.8	5.1
No	95	97.5	94.3	98.9
History of drug injection				
Yes	1	0.5	0.2	2.1
No	199	99.5	98.0	99.8

4.1.3 Clinical characteristics of study respondents

A high proportion 147 (73.5%) reported having never been admitted in a health facility. Only 4 (2.0%) who had received blood transfusion. Majority 196 (98%) had not been vaccinated against Hepatitis B Virus. **(Table 4.3)**

Table 4.3: Clinical characteristics of the patients

	Frequency (n=200)	**Percentage (%)**	**95%Confidence Interval**	
Variable			**Lower**	**Upper**
History of health facility admission				
Yes	53	26.5	20.5	32.7
No	147	73.5	62.8	83.0
Ever received blood transfusion				
Yes	4	2.0	0.6	5.4
No	196	98	94.7	99.3
Vaccination against Hepatitis B				
Yes	4	2.0	0.7	4.6
No	196	98	94.0	99.1
History of Sexually Transmitted Disease				
No	41	20.5	14.6	27.8
Yes	159	79.5	68.6	89.2
Presence of genital ulcers				
No	68	34.0	28.6	40.8
Yes	132	66.0	62.3	70.7

4.2 Sero-prevalence markers of HBV infection (HBsAg) among the study respondents

Out of 200 individuals 19 (9.5% 95 % CI 7.3-12.4) were positive while 181 (90.5% 95% CI 86.3-95.2) were negative using KEMRI Hepcell^{R} (**Fig 4.1)**

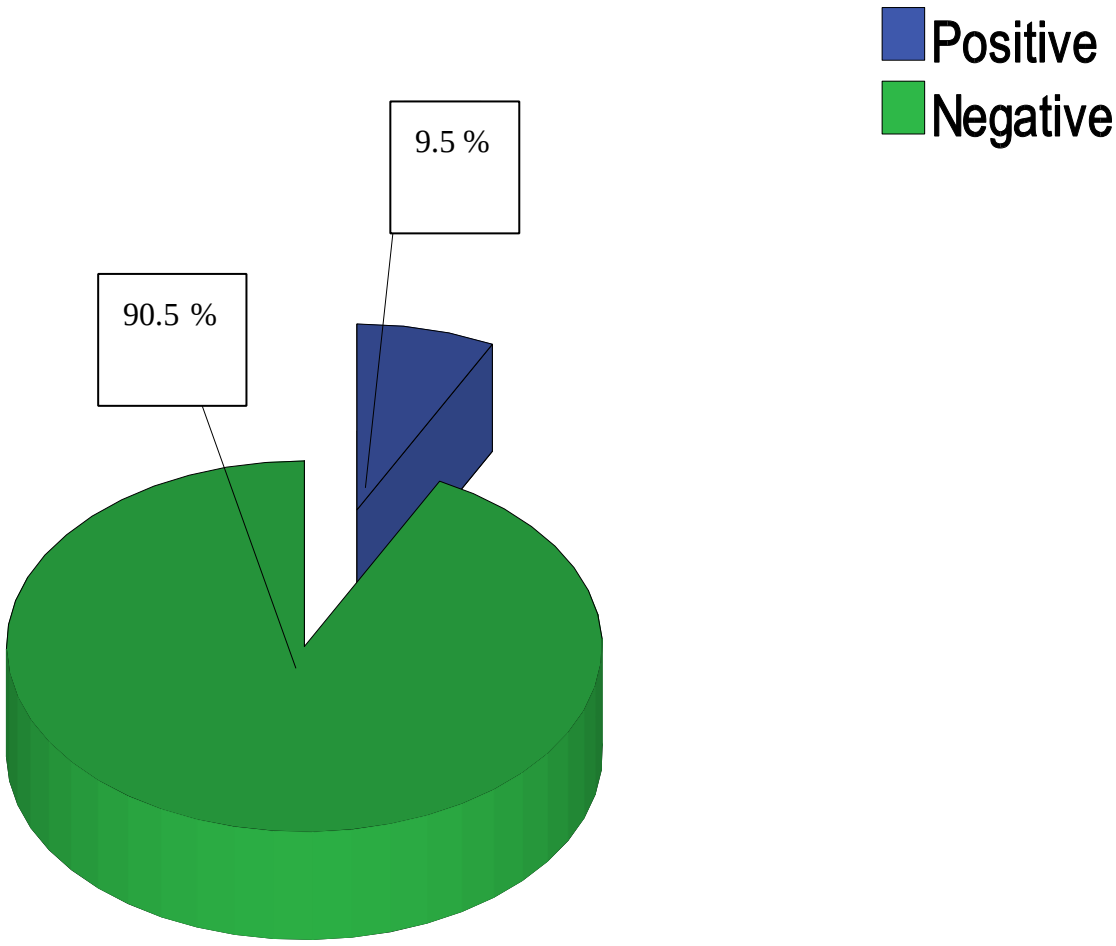

Figure 4.1: The sero-prevalence of HBV antigen markers of the patients

4.3 Sero-prevalence of HBV (HBsAb) immunity among the respondents

Immunity profile among study participant as per Hepatitis B virus antibody test using ELISA was found to be 53 (26.5%) while those who were not protected accounted for 147 (73.5%) **(Fig 4.2).**

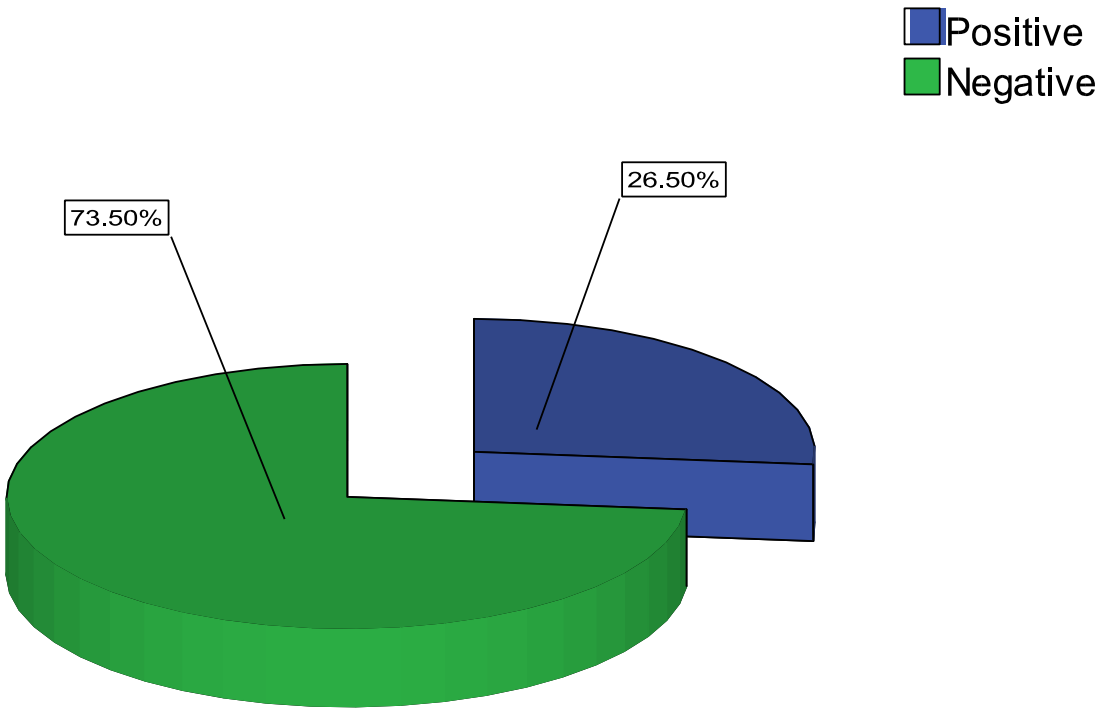

Figure 4.2: The sero-prevalence of HBV antibody markers of patients

4.4 Hepatitis B core antibody detection using ELISA

Majority of study participants 130 (65.0%) were found to be negative for Hepatitis B core antibody using Elisa while those positive for HBcAb were 70(35%) (Fig 4.3)

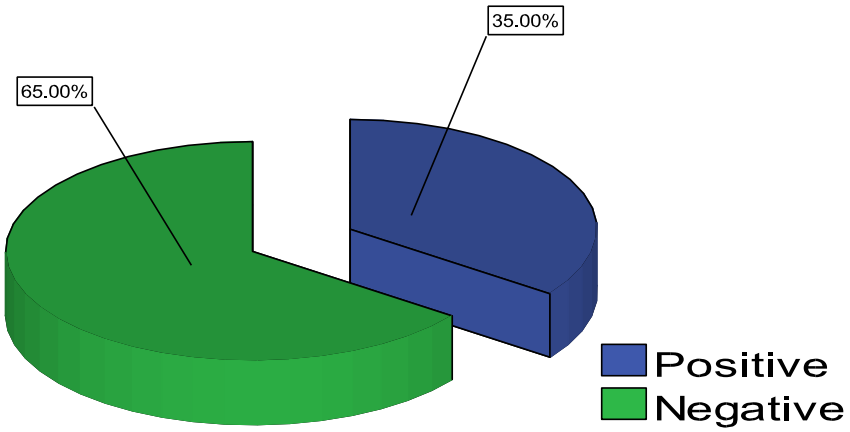

Figure 4.3: The sero-prevalence of HBV core antibody markers of patients

4.5 Association between patients -level factors and Hepatitis B infection among study respondents

4.5.1 Association of Hepatitis B infection and Socio-demographic characteristics

The chi-square test of association was used in bivariate analysis to find associations between having Hepatitis B infection and socio-demographic characteristics. Age (χ^2=32.748; $P < 0.05$, df=5), gender ($\chi^2 = 1.011$; $P > 0.05$, df= 2), Marital status (Fishers Exact=2.443; $P < 0.0043$) and Level of education (Fishers Exact =2.093; $P = 0.004$) were significantly associated with Hepatitis B infection ($P = 0.05$). Gender (χ^2=1.011., $P > 0.05$, df=1), Occupation (χ^2=0.630; $P > 0.05$, df=4) and Housing (Fishers exact = 0.534; $P = 0.340$) was not statistically significant with Hepatitis B infection. The Socio-demographic factors associated with exposure to HBsAg were also determined by comparing the proportion of HBsAg detection for study participants by their socio-demographic characteristics. Highest prevalence of more than half 52.6% was found among, those aged 25-34. It was also noted that females formed the highest proportion of 57.9%. In regard to marital status, the married were more prone to HBV infection with prevalence of 68.4% in comparison to those who were single as well as those who were cohabiting. Those who were self-employed had a higher prevalence of 47.4%. In terms of housing; the most affected were those who were living in permanent houses 78.9% (Table 4.4).

Table 4.4: Association between socio-demographic variables and Hepatitis B infection at STI clinic from August to November 2014

Variables	Positive (n=15)	Negative (n=185)	Fishers Exact test	P-value
Marital Status				
Married	11	123	2.341	**0.0043****
Single	3	44		
Cohabiting	1	4		
Divorced	0	7		
Gender				
Male	8	73	1.011*	0.061**
Female	7	112		
Age category				
15-24	3	32	32.748*	**0.0017****
25-34	6	83		
35-44	3	51		
45-54	1	18		
Above 55	2	1		
Education Level				
No education	0	2	2.093	0.0045**
Primary	5	56		
Secondary	9	88		
Tertiary	1	39		
Occupation				
Unemployed	4	52	0.700	0.166
Employed	8	35		
Self employed	8	52		
Housing				
Temporary	0	5	0.534	0.34
Semi-Permanent	4	41		
Permanent	11	39		

***Significant P≤0.05 * x^2 values*

4.5.2 Association of Hepatitis B infection and sexual behaviours

Selected sexual behaviours of the study participants were subjected to bivariate analysis using Chi-square test of association. Number of sex partners (χ^2=10.034; p <0.05, df=3), was found to be statistically significant. History of having bought or sold sex was also found to be associated with HBV infection among the study participants (χ2=1.802; *p* =0.05, df=1). Intravenous drugs injection (χ^2=3.854; P < 0.05 df=1) had a significant association with Hepatitis B infection. Duration of

engaging in sex (χ^2=3.365; p >0.05, df=2), use of condom (χ^2=4.534; p >0.05, df=2), Mode of sexual penetration (χ^2=2.211; p >0.05, df=2) were not significantly associated with Hepatitis B infection

Table 4.5: Association between Potential sex behaviors with Hepatitis B Infection

Variable	Positive n=15	Negative n=185	Fishers Exact test	p-value
No. of sex partners				
One	2	67	9.034*	**0.0016***
Two	1	1		
> two	12	102		
None				
Duration of engaging in sex				
1-6 months	4	23	3.365	0.269
>6 months	11	147		
Not applicable	0	15		
Mode of sexual penetration				
Vaginal	15	161	2.211	0.331
Vaginal oral	0	9		
Not applicable	0	15		
Use of condom				
Yes	3	73	4.523*	**0.042***
No	12	97		
Frequency of condom use				
Sometimes	12	80	7.803	**0.050**
Rarely	0	11		
Often	0	6		
Not applicable	3	88		
Sold/bought sex				
Yes	5	35	1.802*	**0.026***
No	10	150		
History of Sexually Transmitted Disease	3	38	0.002	0.960
Yes				
No	12	147		
Have you injected drugs				
Yes	0	1	3.800	0.130
No	15	184		
Ever practiced tattooing				0.543
Yes	1	4	1.155	0.283
No	14	181		

***Significant P ≤ 0.05 * x^2 values*

4.5.3 Association of Hepatitis B infection and clinical characteristics

Presence of genital ulcers (χ^2=4.534; p <0.05, df=1) was found to have a significant association with Hepatitis B infection. Having been hospitalized (χ^2=1.517; p >0.05 df=1), receiving blood transfusion (χ^2=0.331; p >0.05, df=1) and having been vaccinated (χ^2=1.802; p >0.05 df=1) against HBV had no significant association with Hepatitis B infection (Figure 4.6)

Table 4.6: Association between clinical characteristics of study participants with Hepatitis B Infection

Variable	Positive n=15	Negative n=185	Fishers Exact Test	p-value
History of hospitalisation				
Yes	6	47	1.517*	0.218
No	9	138		
Vaccinated against HBV				
Yes	1	3	1.802	0.179
No	14	182		
History of blood transfusion				
Yes	0	4	0.331	0.565
No	15	181		
Presence of genital ulcers				
Yes	7	44	4.534	0.0058*
No	8	141		

***Significant P≤0.05 *x^2 values*

4.6 Independent factors associated with HBV infection at multivariate analysis

The factors that were found to be statistically significant at bivariate level underwent binary logistic regression to determine the factors that contributed independently to HBsAg infection. The number of sexual partners, intravenous drug injection and history of having genital ulcers were found to be statistically significant in

explaining the outcome of interest at multivariate level since p-values is less than the set p-value of 0.05 as it is Table 4.7.

4.7 Multivariate regression analysis of significant factors associated with hepatitis B serologic markers

In the multivariate analyses and after adjustment of the odds ratio, serologic evidence of HBsAg was more likely to occur in those who were not using condoms, with multiple sex partners and also with genital ulcers.

Table 4.7: Adjusted Logistic Regression analysis of the associated risk factors for HBV positivity amongst patients with independent variables

	Crude			Adjusted		
Predictive logistic regression model	**OR**	**95% CI**	***P***	**OR**	**95% CI**	**p-value**
Not using condoms	**1.07**	1.02-1.09	<0.001	1.65	1.0-1.84	<0.0013*
Age	2.23	1.61-2.65	<0.001	1.59	1.21-2.03	0.021
Gender	3.22	2.81-3.56	<0.002	3.01	2.82-3.21	0.026
Maritual status	3.34	3.02-3.50	<0.005	3.25	3.16-3.42	0.034
Educational level	6.63	5.91-6.85	0.0043	7.21	6.84-8.02	0.179
Ever sold sex	2.62	1.82-2.92	<0.026	2.72	2.36-2.95	0.062
Multiple sex partners	0.65	0.23-0.92	<0.001	1.47	0.64-1.85	0.0012*
Genetal users	3.81	3.22-4.33	<0.005	1.37	0.82-2.35	0.0010*

**Significant P≤0.05*

CHAPTER FIVE

DISCUSSION, CONCLUSIONS AND RECOMMENDATIONS

5.1 Discussion

5.1.1 Prevalence of hepatitis B surface antigen

Efforts to reduce transmission of HBV through infant immunization and blood donor screening have been promoted in Kenya; however, HBV infection in our study was found to be 9.5% among the enrolled participants, therefore the prevalence remains to be high as reported by Muriuki *et al.* (2013) among HIV patients in Nairobi. The results were consistent with also other studies performed among hospital in-patients and blood donors

(Harania *et al*, 2010; Grasim *et al.,* 2012) among patients undergoing dialysis in Khartoum who found a prevalence of 6% and 8% respectively. However, the prevalence was much higher than results among blood donors in western Kenya of 2.5% (Brewer *et al.,* 2011), HBV prevalence among general population of 8-15% reported in Kenya (WHO, 2016; Gasim *et al*., 2013) rate of (4.7%) among female expectant mothers in African countries and a rate of 3.8% reported among the general population in Kenya and informal urban settlements residents 13.3%.

Also results from our study were not in agreement of 11% among blood donors (Matte *et al.,* 2008 and 17.3% Nagu *et al.,* 2018). However, the prevalence of anti-HBs in the former study was in agreement with present study as both found a prevalence of 26.5% despite different populations studied. In a survey aimed at determining the seroprevalence of viral hepatitis B and C in females who engaged in illegal sex behavior in Isfahan, Iran showed that HBsAg was detected in only 1participant (1.1%), anti-HBc in 4 (4.4%), antiHBs in 60 (65.9%), and HCV-Ab in 9 (9.9%). Evidence of vaccination was seen in 54 subjects (59.3%) (Kassaian *et al*., 2011). This study was significantly different from the present study because the prevalence of HBsAg was extremely low as compared to the present study that recorded 9.5% incidence. The prevalence in our study seems to be related to the

prevalence of HIV in our country which shares the same mode of transmission. However, the prevalence of anti-HBs was found to be high 65.9% as compared to the present study that revealed 26.5%. Similarly, this could mean that the study subjects were once exposed through natural infection and later sero converted. Antibodies against hepatitis B infection were also detected in immunized individuals. In most cases, when the patient recovers from HB infection, he or she mounts HBsAbs in his body.

Lack of hepatitis B vaccination among the study participants may also be a reflection of low hepatitis B vaccine utilization in the general population. Possible reasons for lack of immunization against HBV could include; lack of awareness, high cost and unavailability of an effective vaccine in Kenya before the year 2000.

The study results indicated that age 25-34 had the highest number of HBV infection. The results of this study differ with data from Hepatitis B cancer studies which shows age 40-59 years as the most HBV – HCC infected group (Wong *et al.*, 2012). This could have been as a result of difference in the study population (the population under study had no symptoms of HBV infection whereas the population under comparison was chronically infected). This could also have been as a result of the age bracket having the highest number of participants (86) than any other group. Therefore, it is pertinent to note that most infection of HBV is married persons aged between 25- 34 years. These findings were in consistent with Khan *et al*., 2011 were young adults were found to be infected than the children and the old persons. These couples stay with their families and share most household with their loved ones. Since HBV is 100 times more infectious than HIV (WHO, 2018) and that majority of people become infected or HBV carriers without knowing it, this poses a threat of clustered infection within household due to horizontal transmissions.

This was different from the work of Nwokediuko, (2010) who reported a high prevalence in males 79.2% than in females 20.8 %. This could have been as a result of difference in the study populations. Chronic infection is also slightly more common in men than in women, a pattern observed in other sub-Saharan African countries (Kim *et al.*, 2015). Similar results were reported in studies concerning

HBV infection: in Ethiopia 4.9% in males and 3.3% in females (Tessema *et al* 2011), Pakistan 72% in males and 28% in females (Almad *et al* 2016). Various reasons have been given for higher HBV prevalence in males than female, that include, their life style such as drinking habits, polygamy or multiple sex partners among males (Queen *et al.,* 2009). However, if this explanation was to apply to this study, then there could be similar trends in STDs such as HIV. Other than lifestyle, some researchers have focused on androgens and oestrogens and the findings show strong evidence for the difference in gender and HBV infection.

For instance, Theve *et al*., 2010 found out that male sex hormone influence hepatitis B virus in male young mice. Males were significantly more infected with HBV compared to female. Such results have been observed in many other studies (Page *et al*., 2009; Harania *et al.,* 2010).

Increased seroprevalence of HBsAg was not limited to any particular age group but was more common among STI patients of 25-34-year age group. The first peak of HBV infection in this study population, appears to occur age group 15-24, followed by the peak at the age group 25-34. This finding is in agreement with Tessema *et al.*, 2010 in which higher prevalence of HBsAg was observed among the youths in the age groups of 26-36 years and 36-45 years compared to age group of greater than 45 years. Our results were similar to Pennap *et al*. (2011), were the highest prevalence of infection was 25% among participants aged 31-35 years. The results from the studies done by Buseri *et al.*, 2009 which found, the highest rate of HBsAg positivity (29.8%) was in the 22–32 year-old. This was in agreement with the current study. The higher prevalence rate of HBV among this age group indicates that most of these participants may have been infected at earlier stage of their life. On the other hand, they may acquire HB infection through sex thus horizontal spread of the infection. The HBV infection usually occurs during infancy and childhood by horizontal transmission among children (Tagny *et al*., 2010). HBsAg is highly endemic in Sab Saharan region with HBsAg carrier rates of 9-20%, with 56-98% of the adult population showing evidence of past exposure to HBV infection.

5.1.2 Factors associated with HBV infection

This study was designed to assess among other factors, socio-demographic, sexual behavior, clinical characteristics and Hepatitis B infection among study participants. This has revealed that the highest proportion (59.5%) of the study participants were in the age group 25-34 years, 67% were married whereas majority (48.5%) had secondary education. In terms of occupation 50.5% were self-employed with most of them 75% living in permanent houses.

Regarding the sex distribution of HBV infection there were more female 60% patients than males 40%. This is inconsistent with other studies (Senn *et al.,* 2010; Prosser, 2017). This similarity may be attributed to the fact that women have the habit of seeking medical care than men (Klein *et al.,* 2015).

Regarding the factors associated with HBV infection in people attending STI clinic, the results of this study are consistent with the national and International literature, in which higher prevalence of HBV were described in older male individuals with multiple sex partners practice. The association between older age groups and HBV is a well-known and widely observed fact resulting from the increased risk of exposure with time and the greater vaccination coverage in younger populations (Alter *et al*, 2013; Oliveira *et al.,* 2014).

The association between genital ulcers and HBV infection found in the current study (OR=1.37, $p<0.0001$) is similar to findings from other studies (Arisbud *et al* 2014, Kwon *et al*. 2011). There is considerable variation in mode of transmission and prevalence rate between geographic areas and populations (Kwon *et al*., 2011). Horizontal transmission of HBV infection occurred mainly by exposure to blood transfusion (Bruseri *et al.,* 2018), Sexual depravity (Kwon *et al*., 2011), tattooing (Kwon *et al*., 2011), surgical procedures, needle stick, intravenous drug use and history of sexually transmitted diseases (Lee *et al*.,2016). Sex especially among the married couple may play a significant role in the transmission of HBV infection. In our study majority of HBV positive study subjects were married 67% (male and female) which may have crucial role in spreading of HBV infection.

After bivariate analysis, being married (p =0.0016) was found to be a risk factor for HBV infection. This is not surprising considering that HBV is a sexually transmitted infection. In a study in India, 90% of women being treated for STI had only one lifetime partner, and 14% were HBV -positive. In Kisumu, Kenya and Ndola, Zambia, adolescent married girls' aged 15-19 years were found to have higher prevalence of HBV infection than non-married sexually active girls of the same age, demonstrating that marriage can increase risk of HBV infection (Te *et al.,* 2010). Injecting drug use and anal sex have been documented as risk factors for HBV infection in FSWs (Chen *et al.,* 2013). In this study, multiple sexual activity was statistically associated with positive HBV (P-value=0.0047). Similar finding has been observed in (Brazil harania *et al*, 2010, Bahir Dar city Satterwhite, 2013). Since HBV is a sexually transmitted disease, it is not surprising that increased exposure to sexual activity is associated with increased HBV prevalence. The modes of acquiring HBV infection includes; sexual activity, multiple partners being one of the main risk factor among others in developed countries (Chen *et al*., 2013).

Presence of genital ulcers (p <0.0001) among the study participants was found to be significantly associated with HBV positive status, habit of practicing tattooing, prior presence of STDs and having been transfused with donated blood, were not statistically significant during multivariate analysis.

Several studies have been conducted across the globe to determine the epidemiology and risk factors for HBV. Moreover, in a study conducted by Atto *et al*., 2010, univariate analysis for risk factors associated with HBV infections revealed that history of tuberculosis (p = 0.0091) was found to be significantly associated with HBV incidence.

With regard to history of blood transfusion, no association was found in acquisition of HBV and HCV infection. This might be explained by the currently implemented screening for potential blood borne pathogens in blood banks. Other risk factors for hepatitis B viral infection considered in this study include level of education, whether one was vaccinated, practiced tattooing and having been transfused with donated blood. In some low prevalence areas like in Canada Western Europe, New

Zealand, sexual and percutaneous transmission during adulthood are the main routes of transmission but they were difficult to be identified (Sinha *et al.,* 2012).

It has been revealed that there are more than 30 independent risk factors including tooth brushes, baby bottles, toys, eating utensils, razors sharing, blood feeding insects, hemodialysis, breast feeding, acupuncture which are implicated in the transmission of HBV infection (Seeger *et al.,* 2015) but these risk factors were not considered in the present study.

5.1.3 Immune status of hepatitis B infection

This study was also not in agreement with; a Japanese study by (Koibuchi, *et al.*, 2011; Risbud *et al.,* 2014), STD clinic attendees study in Pune, India where the prevalences of HBsAg and HBAb were 0.6% and 23.4% and 3.6% and 26.5 % respectively. The discrepancy may be due to difference in the study populations in different geographical locations. However, the prevalence of anti-HBs in the former study was in agreement with our study as both reported a prevalence of 26.5% despite being in different geographical locations. For instance, in a Japanese study by Zhang *et al.,* (2012), revealed the prevalence of HBsAg and HBAb was 0.6 and 23.4% respectively in the CSW group and 0.4 and 71.8% in the control group. The present study was not in agreement with this study since the prevalence of HBsAg and HBsAb was 9.5% and 26.5% respectively.

5.2. Study Limitations

- The study only reflects Hepatitis B prevalence among STD clinic attendants, thus the **results** may not be generalizable to the general population.
- Risk of behaviors were self-reported and possibly they were subject to bias from recall and socially desirable responding. Assurance of responses to be kept confidential minimized this limitation
- This study did not consider checking the number of persons already on antiretroviral drugs (ARVs) due to trauma that goes with HIV. The participants on ARVs with dual activity against hepatitis B and HIV may have some prophylaxis against hepatitis B infection or may have cleared

hepatitis B infection due to HAART and thus may have lowered the prevalence of HBsAg sero-positivity among the study population

5.3 Conclusions

1. HBV is highly prevalent among STI positive patients a characteristic which may confound treatment and management of STI cases
2. The existence of many factors that were found to be associated with Hepatitis B infection (such as multiple sex partners, genital ulcers and not using condoms during vaginal intercourse), exposes STI positive patients to contracting HBV.
3. The fact that the majority (73.5%) were not protected against hepatitis B infection, is an indication of being more susceptible to HBV.

5.4 Recommendations

1. Ministry of Health should put in place policy guidelines as measures to have infected patients access medication early enough so as to avoid the disease from progressing to cirrhosis and eventually liver cancer.
2. MOH and research institutions such as KEMRI, should enhance screen on all STD infected patients for HBV.
3. MOH should further develop practical health education and promotional strategies for prevention and management of HB infection
4. A properly designed intervention strategy that will lead to reduction of Hepatitis infection in this vulnerable population (which serves as a reservoir from person to person transmission) needs to be put in place.
5. Introduction of catch-up vaccination services for older age groups and immunization campaign for this risk group need to be started, in order to improve herd immunity in the general population.
6. Future cohort studies to be carried out to determine the circulating genotypes in this sub population is highly recommended.

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APPENDICES

Appendix I: Informed consent form

Introduction

My name is James Murithi Gikunda working for Kenya Medical Research Institute. I am carrying out a study to determine the prevalence and risk factors of Hepatitis B among Sexually Transmitted Disease attendees in Nairobi for the award of a Masters degree and help policy makers in the control and management of hepatitis B.

Hepatitis B causes liver cancer at its advanced stage. It can be transmitted through sex, blood and blood products and other body fluids. The disease accounts for more than 1 million deaths annually. The disease is a significant cause of morbidity and socio economic losses in many parts of the country.

Research Procedures:

If you agree to be a participant in this study you will be ask to fill a questionnaire with questions about yourself. Some of them may be embarrassing or uncomfortable to you. I kindly ask you to answer as accurately as possible. Then I will take 3 milliliters of blood during the procedure. I will use sterile and disposable instruments that are clean and safe.

The blood taken from you will be transported to the KEMRI laboratories for analysis of HBsAg and antibodies. In order to ensure complete confidentiality of the test results, no names will be attached to the blood samples, but an identification number assigned to you will be used to label the sample and questionnaire.

Voluntariness:

Your participation in this study is completely voluntary. You are free to choose whether or not to participate in this study. You are also free to withdraw from the study at any time you wish to do so.

Potential Risks:

During this procedure there will be no long-lasting effect. However, you may feel a brief moment of pain or fear during the draw of blood, embarrassment from the question asked and psychological risk such as anxiety as you wait to get hepatitis result.

Potential Benefits:

There will be no direct clinical OR any monetary benefits; neither will you incur any costs. Knowledge will be gained that may benefit others. The study will benefit your community since by assisting the PI to gain knowledge; the government will understand the magnitude and interventions needed in the control and prevention of the disease.

Whom to contact:

You are encouraged to ask any questions to clarify any issues at any time during your participation in the study. In case of any complaints you can contact KEMRI/Ethical Review committee on **020-2722541, 0722-205901 OR 0733-400003. Email; era@kemri.org**

May I now ask if you would like to participate in the study?

I understand the above details about the study and the basis of participation have been explained to me and **I agree** to take part in the study that I am free to choose to be part of the study. I also understand that if I do not want to go on with the study, I can withdraw at any time. I give my consent for my blood to be tested for Hepatitis B markers.

Please sign here or put your right hand thumb mark if you agree:

Signature/ Thumb mark----------

Date ----------

Appendix II: Fomu ya Ridhaa

Utangulizi

Jina langu ni James Murithi Gikunda. Mimi ninfanya utafiti huu ili niweze kuamua mambo hatari yanayo husiana na uambukizaji wa homa ya manjano miongoni mwa waliohudhuria hospitali inayoushika na magojwa ya zinaa katika mkoa wa Nairobi. Matokeo ya utafiti huu yatatumika kwa ajili ya tuzo ya shahada ya Masters na kuzaidia

serikari kuweka mikakati ya kuzuia and kutibu ugonjwa huu.

Homa ya maini inasababisha saratani ya maini. Ugonjwa huu huambukizwa kwa njia ya ngono, mgonjwa anapopewa damu iliyo na chemi chemi ya virusi na kutoka kwa mama aliye na ugonjwa kwenda kwa mtoto. Saratani ya maini inaua zaidi ya watu milioni moja kila mwaka ulimwenguni kote. Haya maradhi usababisha hasara za kiuchumi na kijamii katika maeneo mengi ya nchi kwa kuwa wahadhiriwa huwa hawawezi kufanya kazi.

Utaratibu:

Kama utakubali kushiliki katika utafiti huu, utauliswa maswali kuhusu wewe. Bahadhi ya hayo maswali yanaweza kuwa ya haibu. Utaratibu utakaotumika utakuwa kuteka damu kidogo kutoka kwa mkono wako, bifaa vitakavyo tumika viko safi na havina athari zozote. Damu itapelekwa KEMRI kupima ugonjwa wa langi ya manjano. Habari yoyote utakayotoa wakati wa utafiti itawekwa madhubuti ya siri. Jina lako halitaonekana kwenye hati yoyote ya utafiti na badala yake, utapewa namba ya utambulisho.

Matokeo ya utafiti huu yatasambazwa kwa serikali na washikadau wengine kama vile Wizara ya Afya, yauma, KEMRI nawengineo, ambao watatengeneza miradi

mbalimbali itakayolenga kupunguza maambukizi nakuboresha huduma za walioathirika katika jamii hii, nanyingine hapo baadaye.

Kujitolea

Ushiriki wako katika utafiti huu ni kwa hiari yako. Wewe ni huru kuchagua kama au kushiriki katika utafiti huu. Wewe ni pia huru kuondoka kutoka utafiti wakati wowote unataka kufanya hivyo.

Faida:

Hautapata usaidizi wakimatiabu, kifedha, napia hutatumia pesa zako mwenyewe katika utafiti huu.Utafiti huu utasaidia jamii yako kwa sababu tukifahamu matatizo ya jamii hii, tutaweza kushaurina kutengeneza miradi mbalimbali ya kupunguza athari za homa ya manjano.

Mapungufu:

Utasikia maumivu kidogo ama uwoga wa kati unachomwasindano, lakini hutapata maumivu ya muda mrefu. Unaweza kuona aibu kutokana na maswali yanayouliswa na kuwa na wasiwasi unapongojea majibu ya kipimo cha homa ya manjano.

Mawasiliano

Waweza kuuliza kufafanuliwa masuala yoyote wakati wowote katika ushiriki wako katika utafiti huu. Kama unahitaji habari zaidi juu ya utafiti, utapiga nambali ya simu KEMRI/Ethical Review committee on **020-2722541, 0722-205901 OR 0733-400003.**

Email; era@kemri.org

Napenda kukuuliza ridhaa yako ya ushiriki wako katika zoezi la utoaji damu

Nimeelewa maelezo ya hapo juu yanayo husu utafiti huu, na ninakubali kushiriki katika zoezi hili. Naelewa kuwa ushiriki wangu ni wahiari, na pia kama sitakubali ananayo muda wowote na ruhusiwa kujitoa katika zoezi hili. Natoa ridhaa damu yangu itumike katika upimaji wa chemichemi za vinavyosababisha homa ya manjano.

Sahihi/dole gumba…… Tarehe……..

Appendix III: Questionnaire

INTERVIEW TO DETERMINE THE RISK FACTORS ASSOCIATED WITH HEPATITIS B INFECTION AMONG STD CLINIC ATTENDEES.

A. SOCIAL DEMOGRAPHIC CHARACTERISTICS

1. Age: …….
2. Gender : Male ( ) Female ( )
3. Marital status : Married ( ) Single ( )

   Cohabiting ( ) Widowed ( ) Divorced ( )

4. Religion : Christian ( ) Muslim ( )

   Others (Specify) …….

5. Level of education:

   No education ( ) Primary education ( )

   Secondary education ( ) Tertiary education ( )

6. Occupation: Student ( ) Formal employment ( ) Unemployed ( ) Self-employed ( )

   Others (specify) ……

7. Housing:

   Permanent ( ) Temporary ( )

   Semi-permanent ( )

   Others (specify) …….

B. SEXUAL BEHAVIOUR

i) How many sex partners do you have? One ( ) Many ( ) ii) How long have you been having sex with these partners? (1-5months) (more than 6 months) iii) Ever sold sex/bought sex? Yes( ) No( ) iv) Do you use condom when having sex? Yes( ) No( )

v) Have you had a Sexually Transmitted Disease before? Yes( ) No( ) vi) Do you have genetal ulcers yes ( ) No ( ) vii) What type of sexual penetration do you practice?

Oral ( ) Vaginal ( )

Others (specify)……..

OTHER INFORMATION

1. Have you used intravenous drugs in the last 6 months? Yes( ) No( )

   If yes, did you share needles with any person? Yes ( ) No ( )
2. When was the last time you were admitted to a hospital? Never( ) < 2 months( ) 2-6 months ( ) 6-9months( ) 9-12momths( )
3. Have you ever been transfused with donated blood while admitted? Yes (

) No ( )
4. Have you ever lived with a person known to have hepatitis B infection? Yes( ) No( )

MAHOJIANO KUAMUA MAMBO HATARI YANAOHUSISHWA NA KUAMBUKIZWA KWA HOMA YA MANJANO MIONGONI MWA WALIOHUDHURIA KLINIKI YA MAGONJWA YA ZINAA.

SEHEMU YA A: HABARI ZA KIBINAFSI

1. Umri: .....
2. Jinsia: Mme ( ) Mke ( )
3. Hadhi ya ndoa: Niko katika ndoa( ) sijaolewa ( )

   Mjane ( ) Talaka ( )

4. Dini: Mkristo ( ) mhisilam ( )

Wengine (taja) .....

5.Kiwango cha elimu: Hakuna elimu ( ) Elimu ya msingi ( )

Elimu ya sekondari ( ) Elimu ya juu ( )

Nyingine (taja).....

6. Kazi:

Mfanyakazi wa afya ( ) Waliojiajiri ( )

Ajira ( )

Njingine (taja) .

7. Makazi:

Nyumba ya mawe ( ) Nyumba ya mabati ( )

Nyumba ya matope ( )

SEHEMU YA B: TABIA ZA KIMAPENZI

Uko na wapenzi wangapi unaoshiriki nao kingono? Mmoja ( ) Wengi( )

i) Umekuwa ukifanya ngono nao kwa muda gani? (miezi 1-5 iliopita) (zaidi ya miezi 6

iliopita)

ii) umewahi kuuza au kulipia ngono? Ndiyo( ) La ( )

iii) Je, unatumia kondomu wakati wa ngono? Ndiyo( ) La( )

iv) Je, umewaipata ugonjwa wowote wa zinaa? Ndiyo ( ) Hapana ( ) vi) Je,

umewaipata vidoda katika sehemu zako za siri? Ndio ( ) La ( )

vii) Umekua ukitumia njia gani kufanya ngono?

Mdomo () Uke ( )

Nyingine (taja)

SEHEMU C:TAARIFA NYINGINE MUHIMU

1. Je, umetumia dawa zozote za kujindunga kwa sindano katika kipindi cha miezi 6

iliopita?

Ndiyo ( ) La( )

Kama ni ndio, ulitumia sindano moja na mtu mwingine? Ndio( ) La( )

2. Je,ulilazwa lini hospitalini mara ya mwisho? Miezi 2 iliyopita ( ) Miezi 6-9 iliopita( )

Miezi 9-12 iliopita ( ) Sijawahi kulazwa( ).

3. Je, uliwekwadamu ulipokuwa umelazwa hospitali? Ndio( ) La( )
4. Umewahi ishi na mtu anayeugua ugonjwa wa homa ya manjano? Ndiyo( ) La( )

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Director, CVR
NAIROBI

REF: SSC No. 2421 (Revised) – Prevalence and risk factors of Hepatitis B virus infection among sexually transmitted diseases clinic attendees in Nairobi, Kenya

Thank you for your letter received on 23rd November, 2012 responding to the comments raised by the KEMRI SSC.

I am pleased to inform you that your protocol now has formal scientific approval from SSC.

The SSC however, advises that work on the proposed study can only start after ERC approval

Sammy Njenga, PhD
SECRETARY, SSC

CENTRE FOR VIRUS RESEARCH
27 NOV 2012
P.O. Box 54628 - NAIROBI

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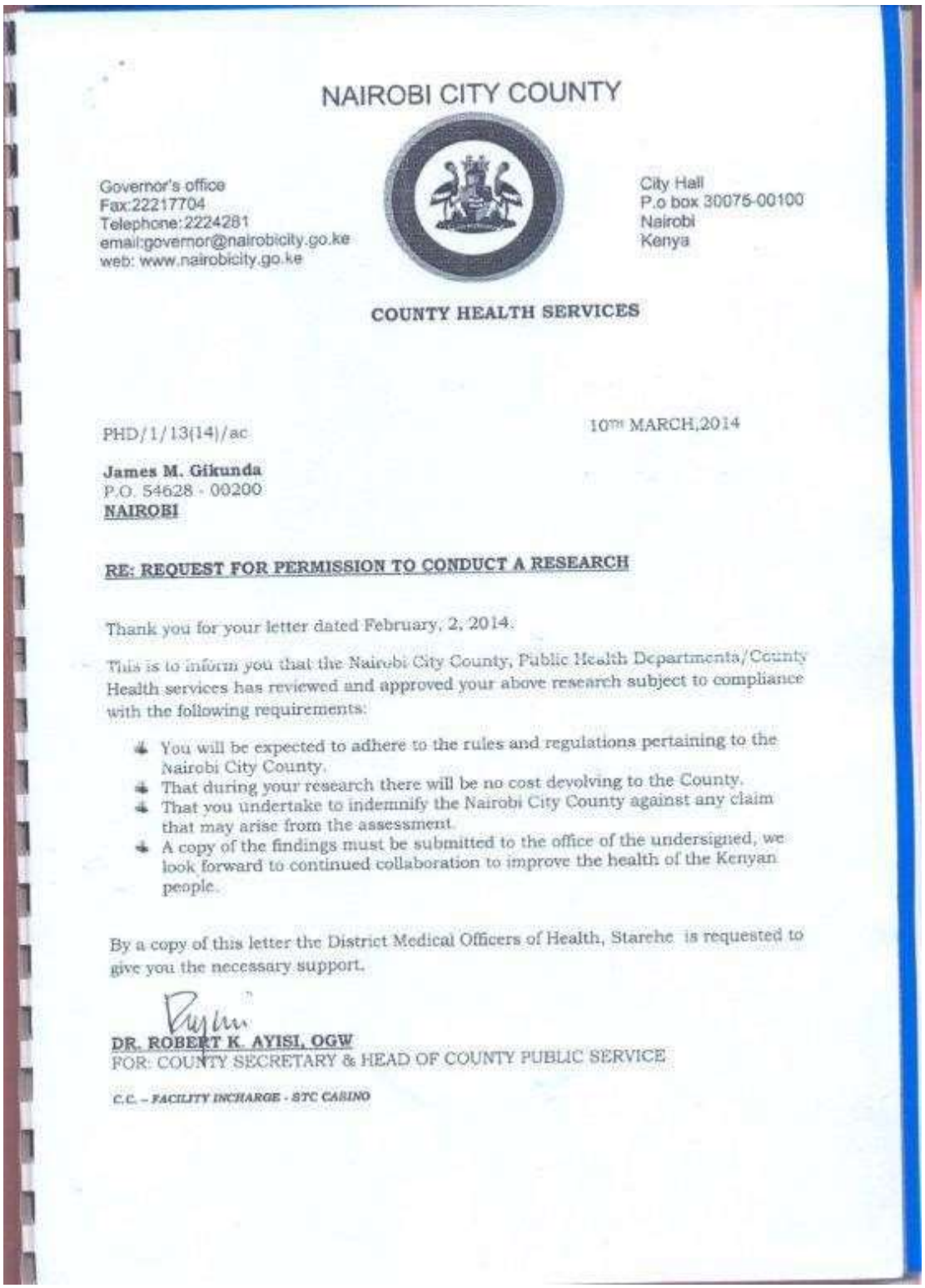
Appendix IV: KEMRI SSC Approval

Appendix V: Permission Letter for the Resersch



NAIROBI CITY COUNTY

Governor's office
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web: www.nairobicity.go.ke

City Hall
P.o box 30075-00100
Nairobi
Kenya

COUNTY HEALTH SERVICES

PHD/1/13(14)/ac

10TH MARCH,2014

James M. Gikunda
P.O. 54628 - 00200
NAIROBI

RE: REQUEST FOR PERMISSION TO CONDUCT A RESEARCH

Thank you for your letter dated February, 2, 2014.

This is to inform you that the Nairobi City County, Public Health Departments/County Health services has reviewed and approved your above research subject to compliance with the following requirements:

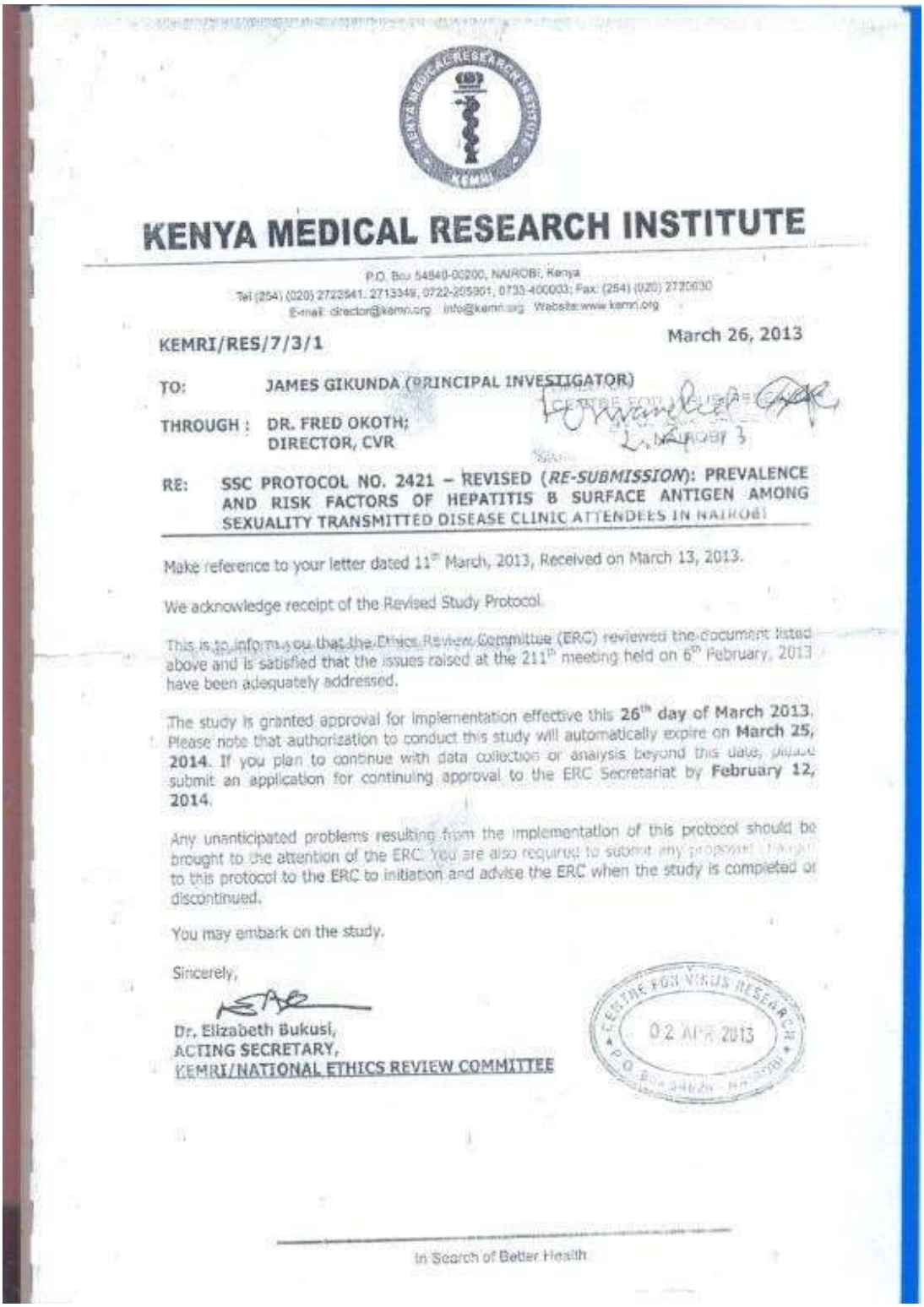
- You will be expected to adhere to the rules and regulations pertaining to the Nairobi City County.
- That during your research there will be no cost devolving to the County.
- That you undertake to indemnify the Nairobi City County against any claim that may arise from the assessment.
- A copy of the findings must be submitted to the office of the undersigned, we look forward to continued collaboration to improve the health of the Kenyan people.

By a copy of this letter the District Medical Officers of Health, Starehe is requested to give you the necessary support.

DR. ROBERT K. AYISI, OGW
FOR: COUNTY SECRETARY & HEAD OF COUNTY PUBLIC SERVICE

C.C. – FACILITY INCHARGE - STC CASINO

Appendix VI: KEMRI/ERC Approval



KENYA MEDICAL RESEARCH INSTITUTE

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Tel (254) (020) 2722541, 2713349, 0722-205901, 0733-400003; Fax: (254) (020) 2720030
E-mail: director@kemri.org info@kemri.org Website:www.kemri.org

KEMRI/RES/7/3/1 March 26, 2013

TO: JAMES GIKUNDA (PRINCIPAL INVESTIGATOR)

THROUGH : DR. FRED OKOTH;
DIRECTOR, CVR

RE: SSC PROTOCOL NO. 2421 – REVISED (*RE-SUBMISSION*): PREVALENCE AND RISK FACTORS OF HEPATITIS B SURFACE ANTIGEN AMONG SEXUALITY TRANSMITTED DISEASE CLINIC ATTENDEES IN NAIROBI

Make reference to your letter dated 11th March, 2013, Received on March 13, 2013.

We acknowledge receipt of the Revised Study Protocol.

This is to inform you that the Ethics Review Committee (ERC) reviewed the document listed above and is satisfied that the issues raised at the 211th meeting held on 6th February, 2013 have been adequately addressed.

The study is granted approval for implementation effective this **26th day of March 2013.** Please note that authorization to conduct this study will automatically expire on **March 25, 2014.** If you plan to continue with data collection or analysis beyond this date, please submit an application for continuing approval to the ERC Secretariat by **February 12, 2014.**

Any unanticipated problems resulting from the implementation of this protocol should be brought to the attention of the ERC. You are also required to submit any proposed changes to this protocol to the ERC to initiation and advise the ERC when the study is completed or discontinued.

You may embark on the study.

Sincerely,

Dr. Elizabeth Bukusi,
ACTING SECRETARY,
KEMRI/NATIONAL ETHICS REVIEW COMMITTEE

CENTRE FOR VIRUS RESEARCH
02 APR 2013
P.O. Box 54840 NAIROBI

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