# A COMPARATIVE STUDY OF PREVALENCE OF HEPATITIS B AMONG HIV POSITIVE AND HIV NEGATIVE PREGNANT WOMEN IN KENYATTA NATIONAL HOSPITAL, NAIROBI, KENYA

INVESTIGATOR: DR. MARGARET KAMENE KILONZO

M.MED OBSTETRICS AND GYNAECOLOGY STUDENT

UNIVERSITY OF NAIROBI

REG. NO.H58/62976/2010

A DISSERTATION SUBMITTED AS PART OF FULFILMENT FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE IN OBSTETRICS AND GYNAECOLOGY, UNIVERSITY OF NAIROBI

## CERTIFICATE OF SUPERVISION

This is to certify that this dissertation has been written by Dr. Margaret Kamene Kilonzo under my supervision and has been submitted with my approval as a University supervisor.

**Professor Koigi Kamau**

Associate Professor of Obstetrics and Gynaecology
Consultant Obstetrician and Gynaecologist
Department of Obstetrics and Gynaecology
University of Nairobi

Signed……..Date……...

1. **Dr. Guyo Jaldesa**
   Consultant Obstetrician and Gynaecologist
   Senior Lecturer, Department of Obstetrics and Gynaecology
   University of Nairobi

   Signed……Date……

## DECLARATION

I declare that this dissertation is my original work and it has not been presented for the award of a degree at any other university.

**Dr. Margaret Kamene Kilonzo**

Master of Medicine in Obstetrics and Gynaecology Student

Department of Obstetrics and Gynaecology

College of Health Sciences, School Of Medicine

University of Nairobi

Registration Number H58/62976/2010

MBChB

University of Nairobi

Signed…….. Date…….....

**CERTIFICATE OF AUTHENTICITY**

This is to certify that this dissertation is the original work of Dr Margaret Kamene Kilonzo MMed. student registration number H58/62976/2010, Department of Obstetrics and Gynaecology, College of Health Sciences, University of Nairobi, supervised by Professor Koigi Kamau and Dr G. Jaldesa. It has not been presented in any other university for award of a degree.

Signed……

Date…….

**Professor Zahida Qureshi**

Associate Professor of Obstetrics and Gynaecology,

Consultant Obstetrician and Gynaecologist

Chairlady, Department Of Obstetrics and Gynaecology

University Of Nairobi

**ACKNOWLEDGEMENT**

I thank God for enabling me to undertake this study. I am also very grateful to the following for their support and contribution to this study.

1. My supervisors Prof. Koigi Kamau and Dr. Guyo Jaldesa for their guidance throughout the study.
2. The Partners in Prevention (PrEP) study for processing, storage and running of the HBsAg ELISA.
3. My lecturers in the department of Obstetrics and Gynaecology for their inputs/critique.
4. The nurses and laboratory technicians in clinic 18 especially sister Mutonga and laboratory technician Mr Mburu for their assistance in data collection.
5. My family for their unending moral and financial support.
6. My statistician Mr Kenneth Mutai
7. My colleagues for their critiquing of the proposal and dissertation drafts.

**TABLE OF CONTENTS**

## LIST OF ABBREVIATIONS

| | |
|---|---|
| AIDS | Acquired Immune Deficiency syndrome |
| ANC | Antenatal clinic |
| ART | Antiretroviral therapy |
| ARV | Antiretroviral |
| AZT | Zidovudine |
| 3TC | Lamivudine |
| DNA | Deoxyribonucleic acid |
| EFV | Efavirenz |
| ELISA | Enzyme Linked Immunosorbent Assay |
| ERC | Ethics and Research Committee |
| FTC | Emtricitabine |
| HAART | Highly active anti-retroviral therapy |
| HBcAb | Hepatitis B core antibody |
| HBeAg | Hepatitis B e antigen |
| HBIG | Hepatitis B Immune Globulin |
| HBsAg | Hepatitis B surface antigen |
| HBV | Hepatitis B virus |
| HIV | Human immunodeficiency virus |
| KDHS | Kenya Demographic and Health Survey |
| KEPI | Kenya Expanded Program on Immunization |
| KNH | Kenyatta National Hospital |
| MTCT | Mother to Child Transmission |
| NVP | Nevirapine |
| PMTCT | Prevention of mother to child transmission (of HIV) |

| | |
|---|---|
| TDF | Tenofovir Disoproxil Fumarate |
| UNAIDS | The Joint United Nations Program on HIV/AIDS |
| UON | University of Nairobi |
| WHO | World Health Organization |

## ABSTRACT

**Back ground:**

HIV is a major health burden in the world and especially in Africa including Kenya where the prevalence of HIV among adults aged 15-64 is 5.6% to 6.3% and 8% among women aged 15-49 years. The burden of hepatitis B infection is also high although there is no adequate data in relation to pregnancy yet it is an important cause of morbidity and mortality. HIV and HBV have common risk factors and modes of transmission. Some antiretroviral drugs have activity against both HIV and HBV. Hepatitis B vaccine for adults at high risk of infection such as HIV positive pregnant women can lower the prevalence of HBV among these at risk groups by preventing new infections. HIV/HBV co-infection increases the risk of HBV chronic carriage, progression and mother to child transmission hence the need to study the prevalence of co-infection and rationalize the need for screening for HBV among the HIV positive patients.

**Objective:** To compare the prevalence of hepatitis B as measured by hepatitis B surface antigen (HBsAg) seropositivity among HIV infected pregnant women to that among HIV negative pregnant women attending antenatal clinic (ANC) in Kenyatta National Hospital (KNH)

**Setting:** The Kenyatta National Hospital antenatal clinic.

**Study Design:** This was a comparative cross-sectional study.

**Sample size:** A total of 286 pregnant women aged 18-49years were recruited; 144 were HIV negative and 142 were HIV positive.

**Method:** Consecutive recruitment of participants for each subgroup was done until the sample size was attained. All mothers who agreed to participate gave informed written consent, their HIV status was recorded from their antenatal file, and socio-demographic data was then obtained by administration of a questionnaire. A blood sample was then drawn for HBsAg ELISA. HBsAg tests were done at the University of Nairobi Department of Obstetrics and Gynaecology laboratory. Data collection was done between 23$^{rd}$ January, 2013 and 26$^{th}$ June, 2013.

**Main Outcome measures:** The main outcome measures were HIV status, HBsAg status, socio-demographic data (age, education level, parity, employment status) and HBV vaccination status.

**Results:** 12 of the 286 study participants tested positive for HBsAg; 8 of these were HIV negative. HBsAg seropositivity was more prevalent among the HIV negative mothers (5.6%) compared to the HIV positive mothers (2.8%). This difference in Hepatitis B prevalence was not statistically significant (p=0.248). There was no association between the age, marital status, parity, education level or form of employment with HBsAg seropositivity among both the HIV negative and HIV positive women. Only 1.4% of mothers in this study had been immunized against hepatitis B. HBV immunization rates were similar for the HIV negative and HIV positive mothers.

**Conclusion:** The prevalence of Hepatitis B mono-infection and HIV/HBV co-infection in pregnant women in KNH is of intermediate endemicity and has no association with socio-demographic characteristics while the HBV vaccination rates are very low.

**Recommendations:** Universal screening of pregnant women as is recommended by the World Health Organization is essential to reduce this prevalence to less than 2%. Counselling of all pregnant women on hepatitis B risk factors, modes of transmission and availability of passive-active immunization of neonates of HBsAg positive mothers should be done to increase awareness. A larger study of the prevalence of hepatitis B among newly diagnosed HIV positive women who are yet to start ARVs is needed to avoid the prophylactic and therapeutic effect of ARVs on HBsAg seropositivity

## INTRODUCTION

HIV and HBV are among the leading causes of deaths due to infectious diseases worldwide with 34 million and 2 billion persons estimated to be HIV and HBV infected respectively. Both are endemic in sub-Saharan Africa. Globally, about 350 million persons have chronic HBV infection. HBV is the leading cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma [1-6]. HBV and HIV share common risk factors and transmission routes. Risk factors include high risk sexual behaviour such as multiple sexual partners and men having sex with men, injection drug abuse, and vertical transmission[1]. While HIV in pregnancy has been widely studied in our set up, hepatitis B and its co-infection with HIV in pregnant women as well as the provision of hepatitis B vaccination for persons at high risk (including HIV positive women) of infection with hepatitis B have been overlooked.

In Kenya, the prevalence of HIV among Kenyan women aged 15-49 years, was 8% in 2008-2009.[7] A survey done in 2012 estimated that 5.6% of adults aged 15-64 were infected with HIV[8]. Studies also estimated that 9.3% of pregnant women were HBsAg positive in 2002.[9,10] The prevalence of hepatitis B and HIV/HBV co-infection in pregnancy in Africa is 6.3% to 25%[11-18] and 0.7% to 11.6% [19-26] respectively. HIV and hepatitis B co-infection has been studied in non-pregnant persons in Kenya[28-29]. Hepatitis B infection in pregnancy has serious implications including the risk of mother to child transmission, more so in the HIV/HBV co-infected mothers[30-35]. Co-infection with HIV and hepatitis B increases the risk of becoming a chronic HBV carrier as well the risk of perinatal transmission of HBV, and accelerates HBV-related liver damage. It also has impact on the choice of antiretroviral (ARV) drugs as there are ARVs with dual action against HIV and hepatitis B. HBV associated liver damage is complicated by hepatotoxicity associated with ARVs[36-42]. HBV has also been associated with adverse pregnancy outcomes[43-47].

Maternal factors such as high maternal viraemia of both viruses and HBeAg positivity for HBV infected mothers increase the risk of perinatal transmission of HIV and hepatitis B[48-56]. Primary prevention of hepatitis B is possible by vaccinating at risk groups including HIV positive women and all neonates at birth[4, 5, 55, 57]. Screening and treatment of both HIV and HBV reduces the maternal viraemia of both and is known to significantly reduce perinatal transmission in addition to improving maternal health and slowing the progression of both infections[57-59]. Universal

screening of pregnant women for HIV is done on a voluntary basis in Kenya and all pregnant women have access to free HIV testing. The public health institutions in Kenya are not yet screening pregnant women or vaccinating HIV positive reproductive age women and pregnant women against hepatitis B.

The serious impact of HBV infection and HBV/HIV co-infection in pregnancy make it important to establish their prevalence to guide integration of preventive and treatment efforts including health education, vaccination of HIV positive persons for HBV, screening for HBsAg and effective ARVs for both infections and passive active immunization of the new-born for HBV.

## LITERATURE REVIEW

### EPIDEMIOLOGY

HIV and HBV infections are global pandemics[1-5]. Thirty four million people were estimated to be living with HIV at the end of 2011 and majority of them were living in sub-Saharan Africa while 1.6 million were Kenyans[6]. The prevalence of HIV among women aged 15-49 years in Kenya in 2008-09 was 8%[7] while that among adults aged 15 to 64 years in 2012 was 5.6%[8].

The World Health Organization estimates that 240 million persons were chronic HBV carriers worldwide by July 2013 and up to 0.6 million people die annually of HBV-related liver disease [5]. Sub-Saharan Africa is among the areas of high HBV endemicity with HBV prevalence above 8% [1, 3]. HBV prevalence of 5.3% to 25% has been reported in pregnant women in Africa[9-18]. In Nigeria, the HBsAg sero-prevalence in pregnant women was reported to be 5% in 2008-2009 to 17.2% in 2012 [11, 12] while it was found to be 25% in Harare in 1996[13]. A study in Mali in May 2008 to December 2009 found the prevalence of hepatitis B in pregnant women to be 8%[14]. In Central Africa, HBsAg prevalence of 6.5% was found in pregnant women in Brazzaville, Congo in a study done on 292 pregnant women in 1993[15]. Closer to home, the HBV prevalence in pregnant women was 5.3% in Ethiopia in 2004, 5.6% Sudan in 2006 and 6.3% Tanzania in 1999[16-18].

In Kenya, the HBsAg prevalence among pregnant women is 9.3%. Okoth et al, in a multicentre hospital based cross-sectional study of 2241 women attending antenatal clinic (ANC) in KNH

and eight hospitals from five provinces in Kenya in June 2001 to June 2002, found the HBsAg prevalence to be 9.3%. Okoth et al also found that there were significant differences in HBV prevalence between various geographic areas with 3% HBsAg prevalence reported at Coast Provincial General Hospital, 4.3% in Nyeri Provincial General Hospital, 7.7% in KNH, 12.3% in Isiolo District Hospital and 15.3% and 17.8% in Lopiding AMREF static facility and Moi Teaching and Referral Hospital respectively. Okoth et al did not include the HIV status of the women screened for HBsAg in his study. The prevalence of HIV in reproductive age women in Kenya in 2003 as per the 2003 KDHS was 8.7%. The average 9.3% prevalence of HBsAg seropositivity reported by Okoth et al was in agreement with the findings of Murugu N.M in pregnant women in Machakos District Hospital in 1984[9, 10].

Globally, 5-10% of HIV infected persons are co-infected with hepatitis B[1, 5]. HIV/HBV co-infection in pregnancy has been studied around the world and a prevalence of 1.5% and 4.9% reported in America and Europe respectively[20, 21] while in Africa it has been estimated to be 0.7% -11.6% [22-26].

Rouet et al conducted a retrospective survey on blood samples of 501 HIV positive and 501 HIV negative pregnant women collected between September 1995 and November 1998 during a clinical trial to investigate means of mother to child transmission of HIV in Abidjan, Cote d'Ivoire and found similar prevalence of HBV among the HIV positive women (9%) and HIV negative women (8%) [21]. A cross sectional study of toxoplasma gondii, hepatitis C, and hepatitis B seroprevalence and co-infection among HIV positive and HIV negative pregnant women in Burkina Faso which included 129 HIV negative and 207 HIV positive pregnant women in Saint Camille Medical centre in Ouagadougou in Burkina Faso in 2004 – 2005 reported an overall prevalence of HBV in pregnant women of 9.8%. The prevalence of HBsAg seropositivity was higher in HIV positive women (11.6%) than in HIV negative women (7%) [23]. Christy et al did a multicentre cross- sectional study on 1120 pregnant women attending ANC in Anambra state in Nigeria in July 2002 to July 2003 and found the prevalence of HBsAg seropositivity was 9.3% and significant infection rates for HIV, HBV, and HIV/HBV co-infection were associated with age groups 16-20 years and 21-30 years. Widowed/divorced women had the highest HBV/HIV co-infection rates followed closely by the unmarried [24]. A cross sectional study of prevalence and immune status of HIV/HBV co-infected pregnant women in two hospitals in Nigeria in 2008 by

Lar et al found the prevalence of HBsAg seropositiviy among HIV positive pregnant women to be 11.8%. It also found occupation and educational level were significantly associated with HBsAg seropositivity in HIV positive pregnant women. The highest HIV/HBV co-infection reported among housewives and business ladies and those with at least secondary education[25]. A more recent study of 959 pregnant women attending ANC in Yaoundé, Cameroon between March 2011 and June 2012 found the prevalence of hepatitis B in pregnant women to be 7.7% and the prevalence of HIV/HBV co-infection to be 0.74%. However, the prevalence of hepatitis B among the HIV positive women in their study was 8.8% (7/80). The Cameroon study did not find any association of age, marital status, parity and education level with the HBsAg status[26]. A retrospective survey conducted on samples collected between July 2001 and February 2004 from pregnant women who were enrolled in a study of prevention of mother to child transmission of HIV estimated the prevalence of HIV/HBV co-infection in pregnant women to 2.4% and 4.9% in Rwanda and Uganda respectively. These samples were taken before initiation of ARVs[27].There are no available published data on HIV/HBV co-infection in pregnant women in Kenya but the prevalence of HIV/HBV co-infection in a group of non-pregnant HIV positive patients seeking care in Aga Khan University Hospital in 2006 was reported to be 6.1%[28]. A study of prevalence of HBV markers in patients with AIDs in Kenya found markers of past exposure to HBV in 78% of the participants [29].

## THE NATURAL HISTORY OF HEPATITIS B VIRUS INFECTION

HIV and HBV share risk factors and modes of transmission[4, 5]. The three main modes of transmission are by sexual contact, perinatal transmission and horizontal transmission mainly in early childhood by close contact with an infected person and sharing contaminated items. Following acute HBV infection, less than 10% of children aged below 5 years and 30%-50% of persons aged above 5 years are asymptomatic[4]. Symptoms of HBV infection include nausea, vomiting, malaise, jaundice, fever, dark urine and clay coloured stools[4, 5, 30]. Acute hepatitis in pregnancy presents in a similar way as in the non-pregnant state and may be confused with other causes of liver disease in pregnancy such as intrahepatic cholestasis, acute fatty liver of pregnancy and the haemolysis, elevated liver enzyme and low platelet (HELLP) syndrome[33]. Fulminant hepatitis, liver failure and death occur in 0.5% - 2% of acutely infected persons[2, 4]. Up to 90% of HBV infections acquired in the perinatal period, 25% - 35% of those acquired at ages

1-5years, and 2%-5% of HBV infections in immune-competent adults progress to chronic HBV infection. Liver cirrhosis and primary hepatocellular carcinoma develop in 25% - 30% and 5% - 10% of chronically infected persons in 30 - 40 years[4, 32-37] respectively.

## IMPACT OF HIV ON HBV DISEASE PROGRESSION

HIV/HBV co-infected persons have a 21% - 41% risk of progression to chronic HBV infection compared with 5% risk of progression to chronic infection in the HBV mono-infected immune-competent adult. The risk of becoming a chronic carrier increases with lower nadir CD4 count at the time of HBV infection[38]. HIV/HBV co-infected persons also have higher levels of HBV replication with higher HBV DNA levels as well as persistence of HBeAg seropositivity[31]. Co-infection also results in higher HBV associated liver morbidity, faster progression to cirrhosis, and more frequent flares of hepatic transaminases which occur with immune reconstitution syndrome or due to interruption of ART[39]. In addition, co-infection of HIV and HBV has been shown to result in a faster emergence of lamivudine resistance[4, 40]. When Lamivudine-resistant HBV is present, continued therapy with lamivudine results in development of more mutations which can compromise the use of other anti-HBV agents[41]. Studies have differed on whether HBV infection has any impact on progression to AIDS in HIV infected individuals or on HIV viral and immunological responses to HAART [42].

## IMPACT OF HBV INFECTION ON PREGNANCY OUTCOME AND OF PREGNANCY ON HBV DISEASE

Infection with hepatitis B in the first trimester is not known to be teratogenic to the fetus[31]. Treatment for hepatitis B less than a year before pregnancy is risk for severe hepatitis flares when antivirals are withdrawn[43]. An increased incidence of gestational diabetes mellitus, lower Apgar scores at five minutes, preterm labour and preterm birth have been reported in HBV infected mothers[44, 45]. However, some studies did not find HBV to be associated with adverse pregnancy outcomes[46]. Flares of hepatitis can occur following delivery and these are thought to be due to reactivation of the immune system. Close monitoring is therefore recommended in chronic HBV carriers after delivery[46].

## PERINATAL TRANSMISSION OF HBV

High maternal HBV viraemia, high HBV DNA, and HBeAg positivity have been shown to increase the risk of perinatal transmission of HBV[47-49]. Studies have shown that 70% - 90% of infants born to HBsAg positive, HBeAg positive mothers, and 5 - 20% of new-borns of HBsAg positive, HBeAg negative mothers are infected with HBV in the perinatal period when no interventions are taken[4, 31, 50]. Most of these infections occur at birth due to contact with maternal blood and vaginal secretions. In utero (Trans placental) HBV transmission occurs in 10% - 16% of infants of HBV carrier mothers when no interventions are taken[30, 31]. In utero HBV infection is thought to occur through placental breach as in threatened preterm labour, placental infection or through ascend of infected vaginal fluids into the uterus[51]. Amniocentesis in hepatitis B carrier mothers rarely causes in utero HBV infection[52]. Studies have also shown that 5 - 10% of infants of HBsAg positive HBeAg positive mothers acquire HBV infection despite passive active vaccination at birth. Breastfeeding does not pose additional risk of HBV infection to infants of HBsAg positive mothers[53, 54]. Infants of HBV carrier mothers are at high risk of HBV infection after delivery due to continued contact with an infected household contact.

## SCREENING AND MANAGEMENT OF HBV, HIV/HBV CO-INFECTION IN PREGNANCY

All pregnant women should be screened for HBV and HIV infections on the first antenatal visit[4, 34]. Liver function tests especially alanine aminotransferase, a full blood count as a low platelet count is an indicator of hepatic fibrosis, imaging such as an abdominal ultrasonography to look for features of fibrosis should be carried out in HBsAg positive mothers. HBcAb and HBeAg testing should also be done[31].

Treatment of chronic hepatitis B mono-infection in pregnancy is mainly supportive[31, 34]. HBV DNA levels are estimated in the late second trimester and if above $10^6$ log copies per millilitre ARVs are started for PMTCT of HBV[4, 55]. Lamivudine (3TC), emtricitabine (FTC) and telbivudine monotherapy have been shown to be effective for prevention of mother child transmission of hepatitis B. Tenofovir is considered a better choice due to its efficacy and less likelihood of resistance as well as a better safety profile in pregnancy. Lamivudine and telbivudine have been reported to have a higher incidence of ARV resistance with long term therapy. Mothers with advanced HBV associated liver disease but DNA levels less than $10^6$ log copies/mL are started on antiviral therapy to slow disease progression but not for prevention of perinatal transmission[31]. ARV monotherapy is not recommended in HIV positive mothers.

Interferons are contraindicated in pregnancy due to potential anti-proliferative effect on the foetus [4, 34].

HIV/HBV Co-infected mothers should be started on HAART effective for the treatment of both HIV and HBV. The preferred first line of treatment is TDF + (3TC or FTC) + EFV while the alternative first line is the use of 3 nucleoside reverse transcriptase inhibitors (NRTIs): AZT + (3TC or FTC) + TDF. There is a high risk of developing lamivudine resistance 3TC is used without combination with a second ARV effective against HBV. Up to 90% of patients on lamivudine monotherapy for hepatitis B treatment will develop lamivudine resistance in 4 years. Co-infected patients requiring change to second line due to HIV treatment failure or development of resistance but whose HBV DNA is well suppressed, should retain TDF +(3TC or FTC) in addition to the second line HAART[4, 31,34]. The 2011 national guidelines for antiretroviral drug therapy in Kenya recommend the use of the combination of 3TC + TDF + FTC for HIV/HBV co-infection[36]. In KNH the ARV protocol for HIV infected mothers is to give AZT + 3TC + NVP for mothers with CD4 count less than 250 cells per microliter, AZT + 3TC + EFV for mothers with CD4 counts of 250 cells/microliter to 350cells per microliter and above. AZT + 3TC + TDF is started if a mother with a CD4 count of 250 or more is in the first trimester.

PREVENTION OF MOTHER TO CHILD TRANSMISSION OF HEPATITIS B

Primary prevention by ensuring that pregnant women are hepatitis B free would eliminate vertical transmission of hepatitis B. Health education of pregnant women and the general public including women of reproductive age on the risk factors, modes of transmission, consequences of infection with hepatitis B, the need for screening, the availability of a safe and effective vaccine against hepatitis B for those at high risk of hepatitis B infection and passive- active immunization of new-borns as well as follow-up and treatment of those infected is therefore essential. Vaccination against hepatitis B for at risk groups and sexual partners and household contacts of those who are HBsAg positive, and ensuring that blood and blood products are safe are also important in primary prevention[5].

In 2001, Kenya, in line with the recommendations of the global advisory group of the Expanded Programme on Immunization which were endorsed by the WHO in 1992 incorporated hepatitis B vaccine into the KEPI schedule. The hepatitis B vaccine is given in combination with

Diphtheria, Pertussis and Tetanus, Haemophilus influenza type b at ages 6 weeks, 10 weeks and 14 weeks in Kenya[55, 56]. At birth dose of hepatitis is not given in the public hospitals in Kenya. According to KDHS 2008-09, only 77% of children were fully immunized[7]. No catch up immunization was instituted for adults or at risk groups in Kenya. There are no available reports on hepatitis B vaccination rates or policy for vaccination of pregnant women at high risk of hepatitis B infection. Pregnant women in Kenya are at significant risk of being HBsAg positive with the prevalence of hepatitis B among the pregnant women being as high as 9.3%[10] and therefore HBV screening would be essential until the cohort of vaccinated infants reaches reproductive age.

The Centres for Disease Control (CDC) recommended the vaccination of all adults receiving care in HIV/AIDS counselling, testing and treatment centres in 2006[57]. The WHO guideline on the management of hepatitis B and HIV co-infection in Europe (2011 revision) also recommends the vaccination of all HBsAg negative HIV positive persons against hepatitis B. There is paucity of published work on the coverage of hepatitis B vaccination in pregnant women and adults irrespective of their HIV status in Africa but a study in Cameroon in 2011 to 2012 found that only 2.7% of pregnant women had ever been vaccinated against hepatitis B[26]. In non-pregnant HIV positive patients attending Aga Khan University Hospital, Kenya in 2006-07, 18% of study participants had been vaccinated against hepatitis B. Lack of hepatitis B vaccination was found to be associated with risk of HIV/HBV co-infection[28]. In the United States, the overall hepatitis B vaccination coverage among adults aged 19 years to 49 years in 2011 was reported to be 35.9%[58]. The hepatitis B vaccine has been shown to be safe in pregnancy with no risks to the foetus. Pregnant women at high risk of infection with hepatitis B should be vaccinated[59].

Screening and intervention for mothers found to be HBsAg positive is essential in preventing perinatal transmission of hepatitis B. Lamivudine has been shown to reduce mother to child transmission of HBV when used in the third trimester especially when HBV DNA is more than $10^7$ log copies per milliter[60.] HAART is given to HIV/HBV co-infected mothers at diagnosis to achieve maximal suppression of replication of both viruses to reduce MTCT[4, 31]. Delivery by elective Caesarean section has been reported to lower the rate of vertical transmission of HBV infection especially in mothers with high HBV DNA levels[61]. Passive-active immunization of new-borns of HBsAg positive mothers by administration of HBIG and HBV vaccine within 12

hours of birth reduces perinatal transmission to 5-10% for infants of HBsAg positive HBeAg positive mothers and to less than 5% for infants whose mothers are HBsAg positive but HBeAg negative[62-64]. Mutations of the hepatitis B surface antigen gene are known to cause failure of HBIG and HBV vaccine and may account for some cases of perinatal infection with HBV despite passive-active immunization against hepatitis B[32]. High perinatal maternal HBV DNA levels have also been associated with failure of neonatal HBV vaccination.[65] Other causes of Hepatitis B vaccine failure include polymorphisms of the cytokines critical for immune response to HBV[66] and failure to adhere to the immunization protocol. Babies infected in utero are not protected by HBIG and HBV vaccination at birth[67].

## RATIONALE

HIV and HBV are global pandemics with serious public health implications. The pregnant women are a special group in that they can transmit both HIV and hepatitis B to their unborn child and neonate and they are often started on HAART regardless of their CD4 count or clinical stage of HIV disease, usually for PMTCT of HIV. HAART started without regard to HBV status in co-infected patients may not include ARVs that cover both HBV and HIV and this may lead to emergence of HBV resistance in addition to continued HBV replication, higher HBV DNA levels and more HBeAg seropositivity and therefore a higher risk of HBV MTCT. Such treatment would also constitute a missed opportunity for PMTCT of HBV. The public health sector in Kenya does not screen pregnant women for HBV because it has not been given the importance it may deserve, general lack of knowledge regarding HBV in terms of modes of transmission and the impact of HBV infection, and due to financial constraints in the health sector. The hepatitis B vaccination rates among the pregnant women in our set up including that among the HIV positive pregnant women who are a high risk group is unknown. Establishing whether the HBV vaccination rates are different between the HIV negative and HIV positive mothers is also useful in determining whether it is the cause of difference in prevalence of hepatitis B between the two groups of mothers if any does exist. There are no published data on HIV/HBV co-infection in pregnant women in Kenya. By determining and comparing the prevalence of HBsAg and hepatitis B vaccination rates among HIV negative and HIV positive mothers, this study will provide an estimate of the burden of HBV in both groups. This information can contribute to formulation of policies on prevention and management of HBV in pregnant women in Kenya. In particular, this would be more important in relation to HIV/HBV co-infected mothers. The overall result of such interventions would be a well mother and baby.

## CONCEPTUAL FRAMEWORK

### NARRATIVE

HIV and HBV are serious infections that share risk factors and routes of transmission. HIV promotes replication of HBV after acute HBV infection resulting in high HBV DNA viral loads. HIV infected persons are also less likely to clear HBV infection after acute infection. HIV and HBV co-infection has been shown to accelerate HBV-related liver disease and mortality. HIV/HBV co-infected mothers are more likely to transmit the HBV to their neonates due to high HBV DNA viral loads and persistence of the HBeAg. Perinatal transmission of HBV results in higher rates of chronic HBV infections and therefore increased risk of premature death from sequelae of chronic HBV infection.

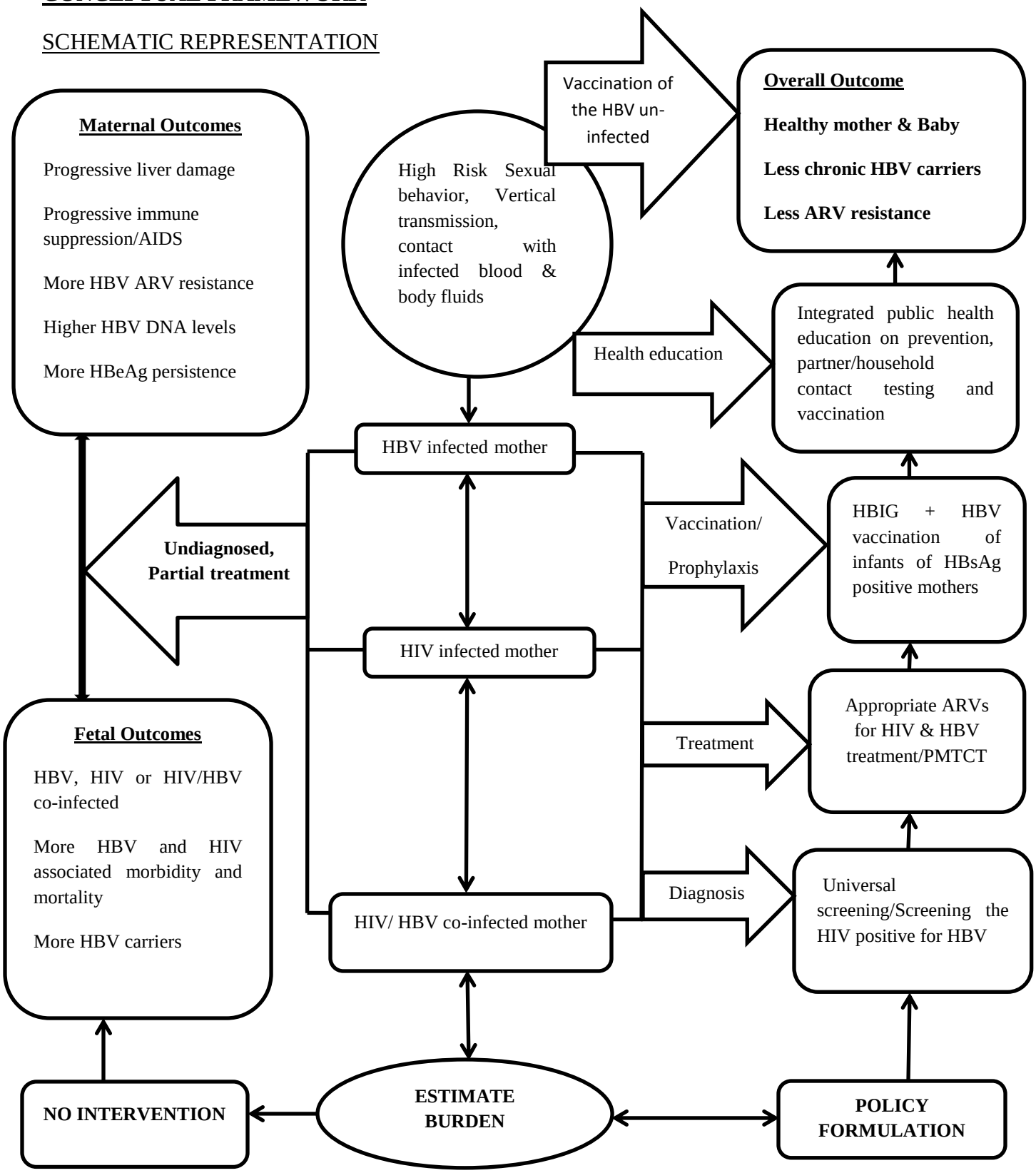
Vaccination of mothers at high risk of hepatitis B infection including the HIV negative mothers at high risk such as those with a HBsAg sexual partner/household contact would curb mother to child transmission of hepatitis B. Screening of pregnant women for HIV and HBV infections and initiation of appropriate ARVs for both reduces progression of both in addition to reducing perinatal transmission and reducing emergence of resistance to ARVs by avoiding partial treatment and sudden stoppage of dually active drugs. Passive active immunization of neonates of HBsAg positive mothers by administration of HBIG and HBV vaccination within 12 hours of birth is highly effective for prevention of perinatal transmission of HBV.

Integration of HIV/HBV preventative measures such as health messages on risk factors, routes of transmission, effects of infection, importance of screening and treatment should be done for efficiency and to ease the financial burden. Guidelines targeting these key areas of intervention to prevent, diagnose and institute appropriate treatment for HBV infection and HBV/HIV co-infection in pregnancy are lacking in the public sector in Kenya. An estimate of the burden of HBV infection in the HIV positive and HIV negative pregnant women and the HBV vaccination rate would promote policy formulation to address these issues resulting in a better overall outcome of mothers infected or co-infected with HBV and HIV and reduced perinatal transmission of both.

This framework is presented schematically on the next page

## CONCEPTUAL FRAMEWORK

SCHEMATIC REPRESENTATION



**RESEARCH QUESTION:**

Does HIV infection predispose to hepatitis B infection in pregnant women in Kenyatta National hospital?

**HYPOTHESIS**

**Null hypothesis:**

There is no difference in the prevalence of hepatitis B and its relation to socio-demographic characteristics between HIV positive and HIV negative pregnant women in KNH

**OBJECTIVES**

**MAIN OBJECTIVE**

To compare the prevalence of HBsAg seropositivity and hepatitis B vaccination rates among HIV positive and HIV negative women attending antenatal clinic at KNH.

**SPECIFIC OBJECTIVES**

1.) To determine and compare the prevalence of hepatitis B in HIV positive and HIV negative women attending antenatal clinic in KNH.
2.) To correlate the prevalence of hepatitis B with the socio-demographic characteristics of the HIV positive and HIV negative pregnant women attending antenatal clinic in KNH.
3.) To compare the HBV vaccination rate between the HIV positive and HIV negative pregnant women attending antenatal clinic in KNH.

**METHODOLOGY**:

**Study Design**:

This was a comparative cross-sectional study of the prevalence of hepatitis B by HBsAg seropositivity and its association with the socio-demographic factors and immunization against hepatitis B among 144 HIV positive and 142 HIV negative pregnant women who were attending ANC in KNH between 23rd January 2013 and 26th June 2013. This design was chosen due to its

ability to estimate the prevalence of HBsAg, compare the proportion of HBsAg seropositivity between the HIV positive and HIV negative groups as well as allow a descriptive analysis of the socio-demographic characteristics of the HIV positive and HIV negative women in relation to the prevalence of HBsAg.

**Study Site and Setting**:

The study was carried out at the Kenyatta National Hospital Antenatal clinic. The KNH is a national referral and teaching hospital. The antenatal clients include a majority of self-referred women and patients referred from lower level facilities throughout the country. The clients are mainly from low and middle income earners from Nairobi and its environs. The antenatal clinic serves a large volume of clients with 130-150 women seen on each clinic day for three days a week. Less than one percent of the women who attend ANC in KNH are below the age of 18years. On average 1500 women, including 20-25 HIV positive women, are seen in the clinic each month. The clinic is run by Professors of Obstetrics and Gynaecology and consultant Obstetrician/Gynaecologists and lecturers in the department of Obstetrics and Gynaecology, University of Nairobi and KNH assisted by post graduate students in Obstetrics and Gynaecology and midwives. Also in attendance are undergraduate students from the University of Nairobi, and midlevel college students from Kenya Medical Training College in KNH. A booking clinic is run every Monday during which new clinic attendants are enrolled, antenatal profiles requested and appointments for next visit given. The new clients are scheduled for follow up in either the Tuesday, Wednesday or Thursday clinics for subsequent clinic visits after the booking visit.

HIV testing is offered routinely in KNH to all pregnant women on the first antenatal visit and subsequently on each visit for mothers who decline testing on the first visit or were not screened on the first visit. Couple counselling and testing for HIV is offered for all mothers who are able to bring their spouses/partners to the clinic. The HIV tests are done using Determine and UniGold rapid test kits by qualified HIV counsellors. Mothers who test HIV positive are worked up for initiation of HAART for PMTCT. Baseline tests that are done include a total blood count, serum creatinine, alanine aminotransferase (ALT) and a CD4 count. Mothers who have CD4 count of 250 -350 cells per microliter or more are started on AZT + 3TC + TDF if in first trimester, AZT + 3TC + EFV if beyond the first trimester and AZT + 3TC + NVP if CD4 count

is less than 250. HAART is usually continued for life after initiation in pregnancy. Mothers are advised for delivery by elective caesarean section if a viral loads done at 36 weeks gestation is above 1000 copies per microliter of blood. Mothers with viral load below 1000 copies per microliter are delivered by caesarean section for other obstetric indications. Mothers are enrolled in a high risk clinic for follow up after delivery and eventually discharged to a comprehensive care centre for follow up and management of HIV.

No routine HBV testing is done in the KNH antenatal clinic, even for mothers who are HIV positive. HBsAg and other HBV markers are however available on request by the clinician for diagnostic purposes for mothers suspected to have HBV infection such as those with jaundice. Mothers who have been screened for hepatitis B and already know that they are HBsAg positive at the time of being seen in the KNH ANC are counselled on the need for passive–active immunization of their new born at birth, need for partner and household contact screening and immunization against hepatitis B. The paediatrician reviews all infants of HBsAg mothers at birth and prescribes passive-active immunization which is then offered if available. Mothers are informed and referred to the private sector for passive immunization of their new-borns when this is not available in KNH. KNH does not have a protocol on HBV vaccination, screening, or management in terms of ARVs in place for pregnant women irrespective of their HIV status. ARVs are not started for HBV treatment or PMTCT of HBV in HIV negative mothers in KNH. There is no protocol in place for initiation or adjustment of regimen for mothers who are HIV positive and known to be HBsAg positive in KNH. The national antiretroviral drug therapy guideline, however, does recommend the use of a regimen with 3TC and TDF for HIV/HBV co-infected patients.

KNH was considered a suitable site for this study due the availability of large numbers of HIV negative and HIV positive mothers most of who are screened for HIV, as well as accessibility to quality laboratory services at the University of Nairobi in KNH. It also had appropriate personnel including Obstetricians, physicians and gastro-enterologists and neonatologists at hand to manage mothers and neonates depending on the HBsAg test results.

**Study Population**:

The study population was the pregnant women attending antenatal clinic in KNH who fit the eligibility criteria outlined below.

***Inclusion criteria:***

1.) Confirmed pregnancy at any gestational age.
2.) Already screened for HIV and HIV status indicated in the antenatal record/file.
3.) Women aged 18 years and above ( > 18 obviated need for parental consent)
4.) Irrespective of whether HBsAg status is already known.
5.) Women willing to participate in the study who gave a written consent to participate.

***Exclusion criteria:***

1.) Women who were tested for HIV but unwilling to participate in the study.

**Sample size:**

The prevalence of HBsAg seropositivity in pregnancy in Kenya has been estimated to be 9.3%[10]. Using this prevalence the minimum sample size was 130. This was multiplied by two to cater for the design effect. It was then adjusted for non-response of 10% giving a total of 286. A minimum sample size of 286 participants with an equal number of participants for both the HIV positive and HIV negative subgroups was targeted.

144 HIV negative and 142 HIV positive participants were recruited into the study. This sample size was calculated as below.

$\mathbf{n=Z^2pq/\ d^2}$ (Cochran formula 1963)

**Where**

**n** = required sample size
**Z =** confidence level at 95% (standard value of 1.96)
**p =** estimated prevalence of HBsAg seropositivity
**d =** margin of error at 5% (standard value of 0.05)
**q** = 1-**p**

**Sampling procedure**

Women who fit the inclusion criteria were recruited into the study by the principal researcher and assistant by consecutive sampling procedure. The entry point was the antenatal clinic (clinic 18) reception office where all mothers attending ANC on each clinic day report on arrival for their files to be retrieved for consultation for the day. All files for each clinic day were checked for mothers who had been tested for HIV and their status indicated irrespective of whether they were on ARVs or the ARV regimen they were on. The files of all HIV positive mothers attending ANC on each clinic day were identified in the reception office. An equivalent number of files of HIV negative mothers attending clinic on the same day were then picked consecutively. The mothers whose files had been selected in the reception office were then approached and requested to participate in the study. This was done on each clinic day until the sample sizes were attained. No matching was done for age, parity, and marital status, and education level, form of employment or HBV vaccination status.

This method was chosen as it allowed recruitment of all HIV positive mothers attending ANC during the study period and thus made it possible to attain the sample size for both groups of pregnant women during the limited period of data collection.

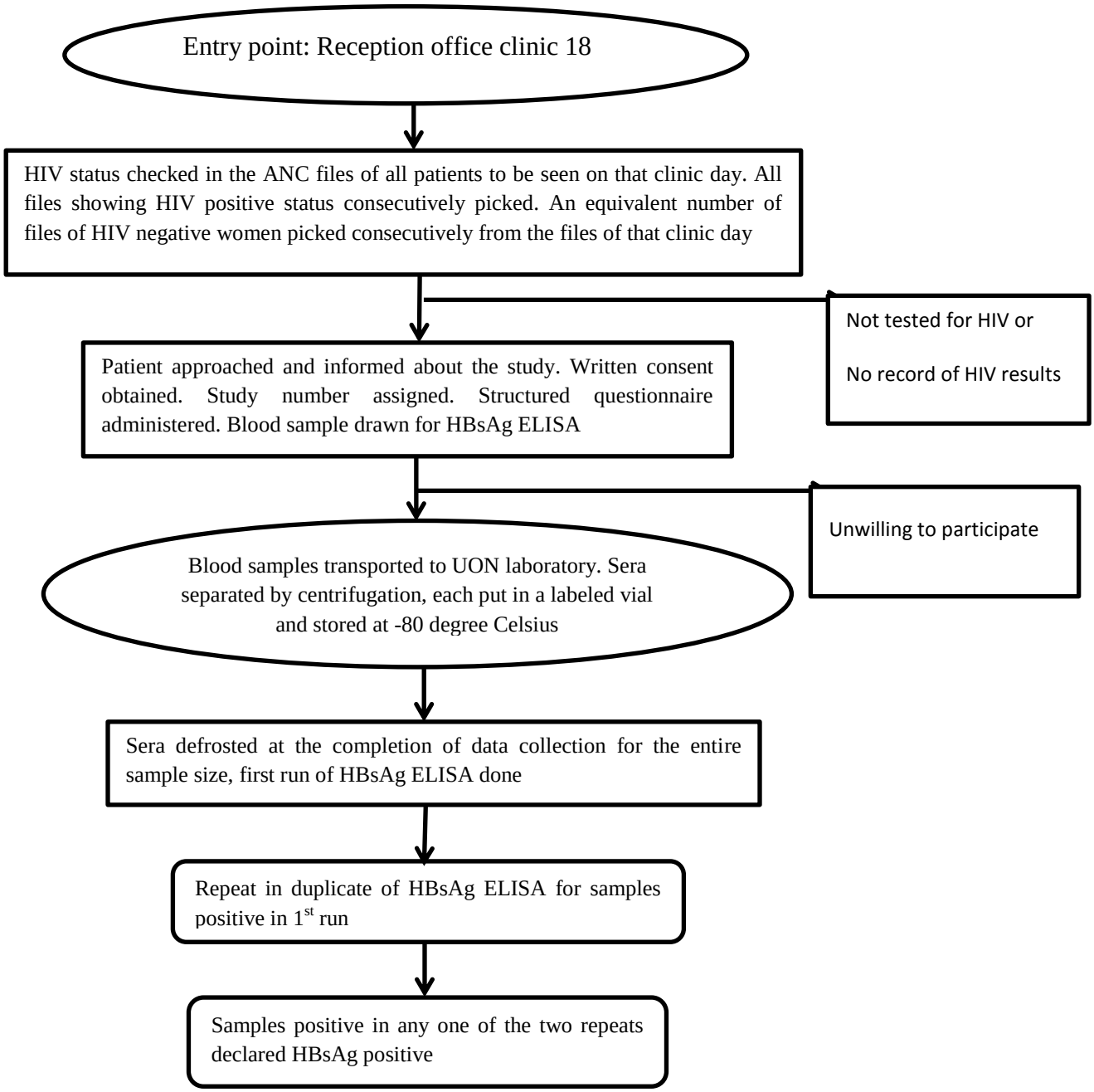
**DATA COLLECTION**

Each participant's antenatal file was rechecked to confirm that she had been tested for HIV and the HIV results indicated in her file. Consecutive recruitment of all HIV positive mothers and an equivalent number of HIV negative mothers was done on each clinic day until the sample size was attained. None of the women approached to participate in the study declined. After introducing themselves, the research assistant or principal investigator then informed each patient whose file had been selected by the sampling procedure about the research and asked her to participate on a voluntary basis. Upon agreeing to participate, the participant gave a written consent (appendix I, II) and was assigned a study number then interviewed in a private room in the clinic using a structured coded questionnaire (appendix III). The HIV status was entered in the structured questionnaire from the antenatal file. A laboratory request form (appendix IV) was filled out for each participant after the interview then four millilitres of venous blood was drawn aseptically from a peripheral vein and put in a 4ml plain vacutainer for HBsAg assay by ELISA

method. All HIV positive mothers attending antenatal clinic during the study period were voluntarily recruited into the study. Blood samples were placed on a test tube rack and transported to the University of Nairobi Obstetrics and Gynaecology laboratory in KNH within three hours of collection of collection. The study flow is as shown in figure 1 below;

**Figure 1**

**STUDY FLOW**



**Infection Control Measures**

Single use of clean medical examination gloves was done by the research personnel (principal investigator or assistant) for each venepuncture. The research personnel also washed hands before each venepuncture. Surgical spirit and cotton wool swabs were used to clean the skin before venepuncture. Sterile single use syringe and needle were used for venepuncture and were not recapped after use. Used needles were placed in a clearly labelled safe sharps box for safe disposal by incineration with other sharps from the hospital. Blood samples were put in vacutainers, placed in a test tube rack in a safe room under the watch of the research assistant and transported to the laboratory within 3 hours of collection. Used gloves and swabs were disposed in a safe bin with red paper liner for safe disposal with other hospital wastes contaminated by body fluids. In the laboratory the specimens were handled by a qualified laboratory technician to avoid cross-contamination.

**Laboratory and Laboratory Methods**

The HBsAg ELISA tests were done at the University of Nairobi Department of Obstetrics and Gynaecology laboratory using the standard procedure utilized there using the Human reagent. The research laboratory assistant was recruited from among the laboratory technicians involved in HBsAg testing in that laboratory. In the laboratory, samples were spun at 1500 rounds per minute for 15 minutes to separate serum from other blood components. The sera were then placed in 2ml cryovials and stored at minus 80 degrees Celsius until testing was done. Samples were defrosted at the time of running the tests.

Procedure

1. Hepatitis template form was prepared to include all samples to be run
2. The hepatitis B surface antigen ELISA Human reagent surface antigen was left to warm at room temperature.
3. 25 microliters of the diluent was placed in each well
4. 75 microliters of each sample and controls were put in each of the wells starting with the samples and incubated for an hour.

5. 50 microliters of conjugate was then put into all the wells and incubated at 37 degree Celsius for 30 minutes.
6. These were then washed 5 times with a buffer.
7. 100 microliters of substrate was then added into all the wells and incubated for 30minutes.
8. The reaction was then stopped with sulphuric acid.
9. The plate was then read using 450/620 wavelength.

Samples positive in the first run were repeated in duplicate and those that were positive in at least one of the retests were declared HBsAg positive.

**Quality Control Measures**

The study questionnaire was pretested by administration to the nurses running the antenatal clinic to ascertain clarity, ease of use and time taken to fill it out. Samples were handled by a qualified laboratory technician to avoid cross contamination. Each questionnaire was rechecked by the principal researcher/research assistant to ascertain completeness and clarification made where needed while the study participant was still present at the point of interview. Each complete hepatitis B Human reagent HBsAg ELISA test kit runs 96 tests and comes with negative control (Normal human serum free of Hepatitis B markers ) and Positive control (Diluted HBsAg positive human serum, inactivated).These controls are used to ascertain quality and 36 of the 96 tests were run on these controls.

Samples testing positive in the first run were repeated in duplicate and declared positive if at least one of the repeat tests in the second run was above the cut off optical density.

**Data Variables**

The main outcome measures were:-

1. HIV status (negative or positive)
2. Socio-demographic data( age, parity, education level, from of employment)
3. HBsAg (positive or negative)

4. HBV vaccination status(Vaccinated, Not vaccinated, don't know if vaccinated)

## DATA MANAGEMENT AND ANALYSIS

Data from the questionnaire was cleaned, coded and entered into Microsoft Excel data sheet. Data analysis was done using SPSS version 17.0. Baseline characteristics such as age, marital status, employment, education, and parity and HIV status were summarized into percentages. Prevalence of HBsAg seropositivity was calculated and presented as a proportion with 95% confidence interval. Baseline characteristics were associated with HBsAg seropositivity using Chi square test and Fisher's exact test in cases of small numbers. All statistical tests were performed at 5% level of significance (95% confidence interval). The findings were presented using tables and a graph.

## ETHICAL CONSIDERATIONS

This study had no major ethical issues. The proposal was reviewed by the KNH and University of Nairobi Ethics and Research Committee (KNH/UON ERC) and approval was given prior to data collection. The following measures were instituted to safeguard the rights and safety of the study participants:

1. The principal investigator/ research assistant introduced themselves to each participant and informed her of the nature and purpose of the study.
2. Participation in the study was on voluntary basis.
3. Pregnant women who opted out of the study received the same quality of care usually offered in the KNH ANC as those who agreed to participate in the study.
4. Informed written consent was obtained from all mothers who agreed to participate in the study.
5. HBsAg testing was free of charge. No form of payment was given for participation in the study.
6. Information on the researcher and the KNH/UON ERC and their telephone numbers were availed to the participants for questions, additional information and complaints.

7. Blood samples were drawn in aseptic manner and were only screened for HBsAg.
8. All interviews and HBsAg test result disclosures were conducted in private and confidentiality was maintained throughout the study.
9. Participants who tested positive for HBsAg were contacted, counselled on their HBsAg status, then on the need for
    a.) HBIG in addition to HBV vaccine at birth for their neonates. HBsAg results slip was issued to the mothers to carry to labour ward at onset of labour so that the neonate can receive appropriate care.
    b.) ARV regimen review to ascertain coverage of both HIV and HBV for those on HAART and that this would be done in the KNH ANC.
    c.) Partner and household contact screening for hepatitis B and immunization if HBsAg negative and that this services are available in KNH on request by clinician in the outpatient and immunization clinic.
    d.) Referred on a voluntary basis for appropriate management and follow up in the KNH medical outpatient clinic by the physicians.

**STUDY LIMITATIONS**

1. This was a hospital based study and therefore it only reflects Hepatitis B prevalence among antenatal clinic attendants and thus the results may not be generalizable to the general population.
2. This study included all HIV positive women including those who were already on ARVs, the women 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 lower the prevalence of HBsAg seropositivity among the HIV positive group.

## RESULTS

A total of 286 women who fit the eligibility criteria were enrolled into the study between 23rd January 2013 and 26th June 2013; 144 were HIV negative while 142 were HIV positive. The baseline characteristics and hepatitis B immunization status of the study participants are shown in table 1 below.

**Table 1: Socio-Demographic characteristics and hepatitis B immunization status of pregnant women attending ANC in KNH**

| Variable | Overall ( HIV +/-) n =286 (%) | HIV status | | P value |
|---|---|---|---|---|
| | | HIV Positive (n=142) n (%) | HIV Negative (n=144) n (%) | |
| **Age** | | | | |
| <20 | 2 (0.7) | 0 (0.0) | 2 (1.4) | 0.152 |
| 20-24 | 54 (18.9) | 21 (14.8) | 33 (22.9) | |
| 25-29 | 96 (33.6) | 48 (33.8) | 48 (33.3) | |
| 30-34 | 93 (32.5) | 48 (33.8) | 45 (31.3) | |
| >=35 | 41 (14.3) | 25 (17.6) | 16 (11.1) | |
| **Marital status** | | | | |
| Married | 239 (83.6) | 106 (74.6) | 133 (92.4) | <0.001 |
| Widowed/separated | 4 (1.4) | 4 (2.8) | 0 (0.0) | |
| Single | 43 (15.0) | 32 (22.5) | 11 (7.6) | |
| **Education** | | | | |
| None | 1 (0.3) | 0 (0.0) | 1 (0.7) | 0.211 |
| Primary | 39 (13.6) | 24 (16.9) | 15 (10.4) | |
| Secondary | 100 (35.0) | 51 (35.9) | 49 (34.0) | |
| College/university | 146 (51.0) | 67 (47.2) | 79 (54.9) | |
| **Parity** | | | | |
| Para 1or Primigravid | 168 (58.7) | 96 (67.6) | 72 (50.0) | 0.002 |
| Two and more | 118 (41.3) | 46 (32.4) | 72 (50.0) | |
| **Employment** | | | | |
| Unemployed | 60 (21.0) | 24 (16.9) | 36 (25.0) | 0.351 |
| Casual worker | 22 (7.7) | 10 (7.0) | 12 (8.3) | |
| Self employed | 119 (41.6) | 63 (44.4) | 56 (38.9) | |
| Permanent employment | 85 (29.7) | 45 (31.7) | 40 (27.8) | |
| **HBV immunization** | | | | |
| Yes | 4 (1.4) | 2 (1.4) | 2 (1.4) | 0.855 |
| No | 240 (83.9) | 121 (85.2) | 119 (82.6) | |
| Don't know | 42 (14.7) | 19 (13.4) | 23 (16.0) | |

Table 1 on the previous page shows that only 1.4% of the study participants were below the age of 20. Majority, 66% , were aged 25 to 34 years. The women were mainly married (83.6%). It also shows that the HIV positive women were significantly more likely to be single or separated (p-value = <0.001) and to be of lower parity (p value = 0.002) compared to the HIV negative women. Literacy level was high with only one participant (0.3%) reporting never having had formal education while 51% had college level of education. Unemployment rate was 21%. Majority (41.6%), were self- employed and 29.7% in permanent employment. There was no significant difference between the HIV positive and negative women in terms of education and employment levels (p=0.211 and 0.351 respectively). The rate of vaccination against HBV was very low at 1.4% among both HIV negative and HIV positive mothers.

**Table 2: Prevalence of hepatitis B among HIV positive and HIV negative pregnant women attending ANC in KNH**

| **Variable** | **HIV status** | | **OR (95% CI)** | **P value** |
|---|---|---|---|---|
| | **Positive (n=142)** | **Negative (n=144)** | | |
| **HBsAg results** | | | | |
| Positive | 4 (2.8%) | 8 (5.6%) | 0.5 (0.1-1.7) | 0.248 |
| Negative | 138 (97.2%) | 136 (94.4%) | 1.0 | |

Table 2 shows that the prevalence of hepatitis B as measured by HBsAg seropositivity in HIV negative pregnant women attending ANC in KNH was 5.6% (8/144) while that among HIV positive pregnant women was 2.8% (4/142). There was no statistically significant difference in HBV prevalence in HIV negative and HIV positive mothers 95% CI: 0.1-1.7, p-value=0.248

**Table 3: Hepatitis B surface antigen seropositivity by socio-demographic characteristics in HIV positive and HIV negative pregnant women in KNH**

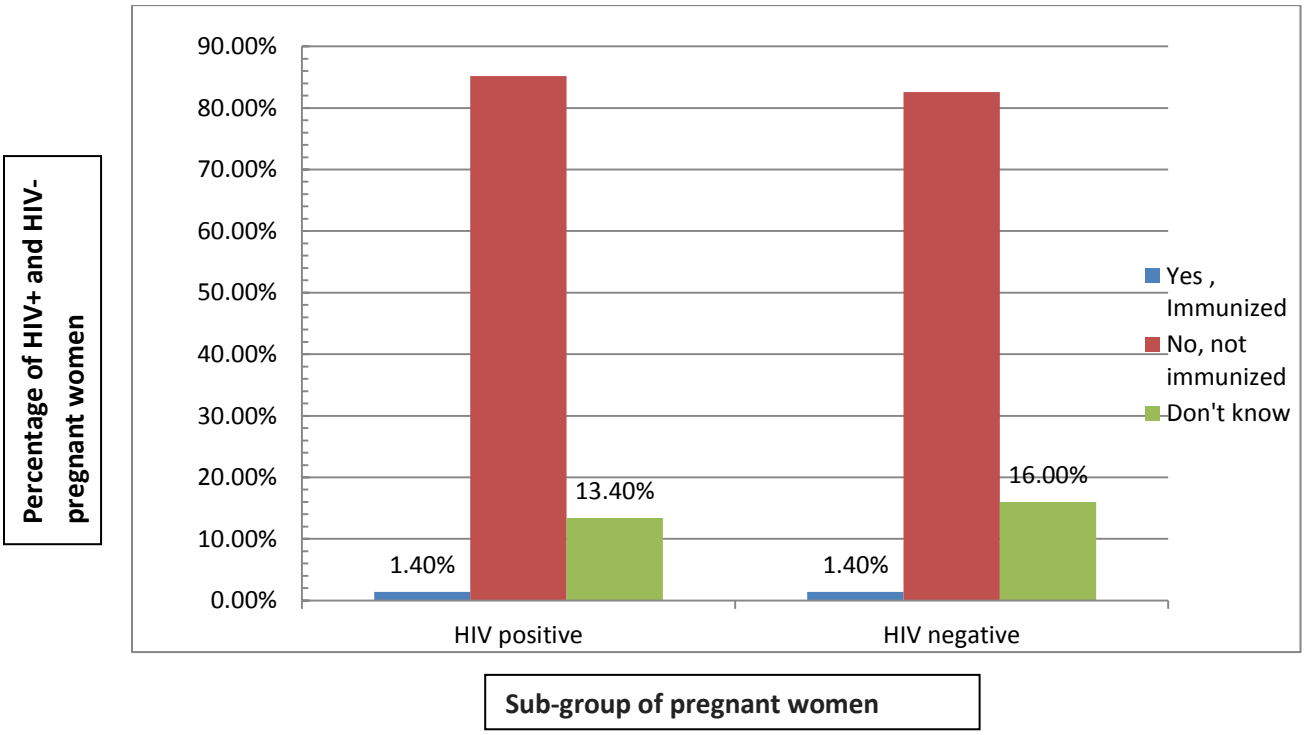
| Variable | HIV +ve n=142 (%) | | | HIV-ve n=144 (%) | | |
|---|---|---|---|---|---|---|
| | HBsAg positive(n=4) n(%) | HBsAg negative(n=138) n(%) | p-value | HBsAg positive(n=8) n(%) | HBsAg negative(n=136) n(%) | p-value |
| **Age (Years)** | | | | | | |
| <20 | 0 | 0 | 0.356 | 0 (0.0) | 2 (1.5) | 1.000 |
| 20-29 | 3 (75.0) | 66 (47.8) | | 5 (62.5) | 76 (55.9) | |
| >30 | 1 (25.0) | 72 (52.2) | | 3 (37.5) | 58 (42.6) | |
| **Marital status** | | | | | | |
| Married | 4 (100.0) | 102 (73.9) | 0.572 | 8 (100.0) | 125 (91.9) | 1.000 |
| Unmarried | 0 (0.0) | 36 (26.1) | | 0 (0.0) | 11 (8.1) | |
| **Education** | | | | | | |
| None | 0 (0.0) | 0 (0.0) | 1.000 | 0 (0.0) | 1 (0.7) | 0.497 |
| Primary/Secondary | 2 (50.0) | 73 (52.9) | | 5 (62.5) | 59 (43.4) | |
| Tertiary | 2 (50.0) | 65 (47.1) | | 3 (37.5) | 76 (55.9) | |
| **Parity** | | | | | | |
| 0-1 | 2 (50.0) | 94 (68.1) | 0.595 | 4 (50.0) | 68 (50.0) | 1.000 |
| ≥2 | 2 (50.0) | 44 (31.9) | | 4 (50.0) | 68 (50.0) | |
| **Employment** | | | | | | |
| Informal | 3 (75.0) | 94 (68.1) | 1.000 | 8 (100.0) | 96 (70.6) | 0.106 |
| Formal | 1 (25.0) | 44 (31.9) | | 0 (0.0) | 40 (29.4) | |

Table 3 shows that none of the socio-demographic characteristics studied including age, parity, education level and form of employment were found to be associated with hepatitis B seropositivity among both HIV negative and HIV positive mothers in KNH. All the p-values were > 0.05

**Immunization against HBV among pregnant women in KNH ANC**

HBV immunization rate was very low at 1.4% among both study groups. None of the HBsAg positive women had ever been vaccinated against HBV while 4 of those HBsAg negative had been immunized. However, the difference was not statistically significant (p=0.744). The HBV immunization rates were similar for the HIV negative and HIV positive women in this study with only 2 women in each group having been vaccinated for HBV. These similar rates of vaccination against hepatitis B suggest that the hepatitis vaccination status did not influence the small difference in prevalence of hepatitis B between the HIV negative and HIV positive pregnant women.

**Figure 2: Immunization against hepatitis B among HIV positive and HIV negative pregnant women attending ANC in KNH**




HBV Immunization rates were low and similar for the HIV negative (2/142: 1.4%) and HIV positive (2/144: 1.4%) pregnant women in this study. 16% and 13.4% of HIV negative and HIV positive mothers respectively did not know whether they had been vaccinated against hepatitis B. These findings are shown in figure 2 above.

## DISCUSSION

Determining and comparing the prevalence of hepatitis B infection and hepatitis B vaccination rates among HIV negative and HIV positive pregnant women is essential to inform the integration of prevention and treatment interventions for these two public health problems.

The hepatitis B prevalence as determined by HBsAg seropositivity in this study was 5.6% among the HIV negative pregnant women and 2.8% among the HIV positive women in KNH. This prevalence puts HBsAg prevalence in Kenya among the intermediate endemicity zones according to the WHO which classifies regions of hepatitis B endemicity by the prevalence of HBsAg in a population as highly endemic if HBsAg seropositivity prevalence is ≥8%, intermediate endemicity in regions with HBsAg prevalence of 2% to 7%, and low endemicity when the HBsAg prevalence is less than 2%[2].

This prevalence of HBV of 5.6% would suggest a lower HBV prevalence compared to the 9.3% reported by Murugu N M and Okoth F et al[9, 10]. Okoth F et al, in a multicentre cross-sectional study on 2241 pregnant women including 300 women sampled in KNH in 2001 reported the prevalence of HBsAg seropositivity in pregnant women in Kenyatta National hospital to be 7.7% and 9.3% in Kenya[10]. Murugu N M had reported hepatitis B prevalence of 9.3% in pregnant women in Machakos in 1984[9]. However, Okoth et al also found the prevalence of HBsAg to be highly varied between the various geographic regions with the Coast and Nyeri Provincial General Hospitals HBsAg prevalence in pregnant women standing at 3% and 4.3% respectively while Isiolo District hospital and Moi Teaching and referral hospital had high prevalence of 12.3% and 17.8%[10] respectively. Kenyatta National hospital attends to a fairly cosmopolitan population from each of the geographical regions but mostly resident in Nairobi. Both Okoth et al and Murugu recruited pregnant women irrespective of their HIV status and therefore the comparison of the prevalence of HBV in our study with their findings is done with that background information. The prevalence of hepatitis B in the two sub groups in our study is lower than that reported by Murugu and Okoth et al.

This lower HBV prevalence may be an actual reduction in the prevalence of HBsAg seropositivity in pregnant women in KNH or it may be attributable to the small number of study participants. Okoth et al reported HBsAg seropositivity in 23/298 women in KNH in 2001 giving

a HBsAg prevalence of 7.7% 95% confidence interval 5.0- 11.4[10]. Therefore the confidence interval of this study of 95% confidence interval of prevalence of 2.1 – 6.6 overlaps with that used by Okoth et al. A true reduction in HBsAg prevalence can possibly be accounted for by the public health interventions such as public health education on safe sex, the dangers of having multiple sexual partners and avoidance of contact with blood and body fluids of other persons, which have been put in place to curb the spread of HIV. Kenyans are well informed about these risks of HIV transmission as well as prevention of transmission of HIV as is evidenced by the 2008-09 KDHS which estimated that 75% of women knew that the chance of getting HIV can be reduced by using condoms while 92% of women interviewed knew limiting sex to one faithful partner reduces chances of getting HIV[7]. These interventions have seen the prevalence of HIV among reproductive age women decrease from 8.8% in 2003 to 8% in 2008-09 and that among adults decrease from 6.3% in 2008-09 to 5.6% in 2012[7, 8]. HIV and HBV share risk factors, modes of transmission and even antiviral treatment[2] and therefore prevention of the spread of HIV generally prevents the spread of HBV as well.

The HBV prevalence found in this study is however, similar to that reported in other East African countries with a prevalence of 5.3% in Ethiopia in 2004 (Fisseha et al), 5.6% in Sudan in 2006 (Rasha et al), and 6.3% in Tanzania in 1999 (Menendez et al)[16-18]. Higher prevalence of HBV prevalence among pregnant women has been reported in by Brett MacLean et al in Mali[14]. Cultural practices that predispose to infection with HBV such as female genital mutilation and traditional scarification account for most of the regional differences in HBV prevalence[10]**.** The risk factors for hepatitis B infection were not assessed our study.

Majority of the women in this study were aged between 25 years and 34 years irrespective of the HIV status. HIV positive women were more likely to be single, widowed or separated than the HIV negative women. This could not be explained within this study but it is in congruence with the findings of the KAIS 2012 by NASCOP which found a higher prevalence of HIV among widowed women and men[8] suggesting that samples of HIV positive women will likely have more unmarried women. The HIV positive women were also more likely to be of lower parity. This could not be accounted for in this study. It may be due to continued counselling for family planning in the comprehensive care centres. Literacy and employment levels were high among the clinic attendants in this study. This is explained by the fact that at the time of the study clinic

attendants needed to pay to receive services and therefore mainly employed women were able to access services in this clinic.

There was no association between age, parity, education level or form of employment with HBsAg seropositivity. These findings echo those of Fisseha et al in Ethiopia[17]. In a cross-sectional study of 209 pregnant women attending antenatal care at Debre –Tabor Hospital carried out between January and March 2004, Fisseha et al reported an overall HBsAg prevalence of 5.3% with no statistically significant difference in HBsAg prevalence among the various age groups. In his study the age group 16-22 had the highest HBsAg prevalence of 7.59% followed closely by age group 23-28 years at 6.25%. Similar findings were reported in Sudan by Rasha et al[18]. Murugu N M. also found no association between parity and hepatitis B seropositivity in pregnant women in Machakos[9]. Educational level was not found to have any association with HBsAg seropositivity in this study. In contrast, in Niger, Buseri F et al found a higher HBsAg seropositivity among pregnant women with no formal education and those of age group 20-24years[11]. Lar et al found a higher HBsAg seropositivity among pregnant women with at least secondary education in Nigeria in 2008 and found that housewives and business ladies were significantly more likely to be HBsAg positive[25]. This difference in association of HBsAg seropositivity with education may be due to the differences in the populations sampled as only one pregnant woman reported not having had formal education in our study.

There was no statistically significant difference in HBsAg seropositivity between the HIV positive and HIV negative pregnant women in this study (OR (95% CI) 0.5(0.1-1.7) p-value = 0.248). There were no available published reports on the prevalence of HBsAg seropositivity in HIV positive pregnant women in Kenya for comparison purposes. HIV HBV co-infection rate of 6.1% was reported in a group of non-pregnant HIV positive patients attending care in Aga Khan University Hospital in Nairobi in 2006[28]. The lower HBsAg seropositivity in the HIV positive women compared to the HIV negative women in our study could be due to the fact that these women are repeatedly counselled on infection prevention specifically safe sex and avoidance of contact with blood and body fluids. HAART may also play a role in preventing new HBV infections in the HIV positive women on treatment with ARVs with anti-HBV activity. This study enrolled HIV positive women regardless of whether they were on ARVs or not and did not assess the ARV regimen of those already on HAART. Our study may also have been

underpowered to detect a significant difference in hepatitis B prevalence between the two study groups due to the large number of patients who would have been required for a larger power.

The prevalence of HBV in HIV positive pregnant women is similar to what Pirillo et al reported in Kigali, Rwanda (2.4%) and Kampala, Uganda (4.9%) in 2001- 2004.[27] This similarity may be due to similarity of the urban populations sampled or it may imply similar modes of transmission of hepatitis B in the three regions which also have similar healthcare policies.

Rouet et al found the prevalence of HBV among HIV negative pregnant women in Abidjan, Cote d'Ivoire was 8% and that among HIV positive women was 9.8% in 1995 to 1998. This difference was not statistically significant[21]. However, hepatitis B was of high endemicity there among both HIV positive and HIV pregnant women in compared to the findings in KNH in this study. In Burkina Faso, an overall HBV prevalence in pregnant women of 9.8% was found. The HBsAg prevalence was higher in HIV positive women at 11.6% than in HIV negative women at 7%. This difference was not statistically significant. Since higher prevalence of hepatitis B in pregnant women has been reported in this two regions, and the fact that cultural practices of West Africa and Kenya differ may explain this difference in the prevalence of HBV in HIV positive pregnant women.

In this study, there was no association between age, parity, education and employment status and HBsAg seropositivity among the HIV positive women. In contrast, in Nigeria significant infection rates for HIV, HBV, and HIV/HBV co-infection were associated with age groups 16-20years and 21-30 years. The prevalence rates were inversely associated with increase in educational status while HBV/HIV co-infection rates were highest among widowed/divorced groups followed closely by the unmarried (Christy et al, 2002-03) [24]. In this study all the women who tested HBsAg positive were married but there was no association between marital status and HBsAg seropositivity.

The rate of immunization against hepatitis B was only 1.4% among all pregnant women in this study with similar immunization rates among the HIV positive and HIV negative women. This hepatitis B vaccination rate among pregnant women in KNH is lower than the 2.7% rate reported in pregnant women in Yaoundé, Cameroon in 2011 to 2012 by Fomulu et al[26]. Countries which have higher levels of HBV vaccination among groups at high risk of hepatitis B such as the

United States of American have been able to achieve much lower hepatitis B prevalence[59]. This very low HBV vaccination rate in addition to large numbers of women who did not know their HBV vaccination status suggest a lack of awareness or knowledge of hepatitis B infection, and in the background of an intermediate endemicity of hepatitis B in pregnant women emphasizes the need for education of pregnant women on hepatitis B during antenatal care as well as routine antenatal screening of all pregnant women for hepatitis B. This HBV vaccination rate is also well below the rate of hepatitis B vaccination in adults aged 19-49 years in the United States of America which was estimated to be 35.9% in 2011[59]. The lack of a policy on hepatitis B vaccination for adults including those who are HIV positive in the public sector in Kenya is partially liable for the low hepatitis B vaccination rates among pregnant women. This gap needs to be addressed in our set up until the cohort of children vaccinated against hepatitis B under the KEPI programme reaches reproductive age.

Majority of the HBsAg positive women had not been immunized against hepatitis B and the remaining did not know whether they had been immunized against hepatitis B. Kenya incorporated the HBV vaccine in the KEPI schedule in 2001 and no catch up immunization program was instituted for non- immunized persons aged over 12 months and therefore, it is unlikely that women who reported not knowing their HBV immunization status had been immunized as the HBV vaccine is available at a fee at immunization clinics and the private sector which mainly serve travellers[57].

None of the 4 study participants who had been vaccinated against hepatitis B tested positive for hepatitis B. This study did not find an association between HBV immunization status and HBsAg seropositivity. Reena et al surveyed non pregnant HIV positive patients in Aga Khan University Hospital and only 18% had had hepatitis B vaccination. Their study also found that none of those who had been vaccinated against hepatitis B was HBsAg positive and lack of hepatitis B vaccination was significantly associated with the risk of hepatitis B infection[28]. This is consistent with the reported 95% efficacy of the HBV vaccination against infection with HBV[4, 58].

## CONCLUSION

The prevalence of hepatitis B in pregnant women attending antenatal clinic in KNH is of intermediate endemicity with no statistically significant difference in HBV prevalence between the HIV positive and HIV negative women. There is no association between the age, marital status, parity, educational level or form of employment with HBsAg seropositivity among both HIV negative and HIV positive women in Kenyatta National Hospital. The number of pregnant women who have ever been immunized against hepatitis B in Kenyatta National Hospital is very low at 1.4%.

## RECOMMENDATIONS

1. In view of the intermediate endemicity of HBsAg seropositivity and low HBV immunization rates among both HIV positive and HIV negative pregnant women in KNH, all pregnant women should be screened for HBV during the antenatal period.
2. Hepatitis B vaccination should be given to all pregnant women at high risk of hepatitis B infection until the cohort of children vaccinated at birth reaches reproductive age.
3. There is need for a larger study of newly diagnosed HIV positive pregnant women before initiation of HAART to avoid the prophylactic and therapeutic effect of ARVs against HBV which may have influenced HBV prevalence in this group.
4. All pregnant women should be counselled on prevention of hepatitis B infection irrespective of their HIV status.

## REFERENCES


1. Miriam J. Alter. Epidemiology of viral hepatitis and HIV co-infection. Journal of hepatology 2006 ; vol 44, supplement 1,p56-59
2. Francis J. Mahoney. Update on diagnosis, management and prevention of HBV infection. Clinical Microbiology Reviews 1999; 12(2):351
3. Elisabetta Franco, Barbara Bagnata , Maria Giulia Marino et al. Epidemiology and prevention of hepatitis B in developing countries. World J. Hepatol 2012 march 27; 4(3): 74-80
4. WHO: Management of hepatitis B and HIV co-infection. Clinical protocol for the World Health Organization European Region 2011 revision. www.euro.who.int/documents/e/9579.pdf. Accessed 28/7/2012 10.40 pm.
5. WHO: Fact sheet on hepatitis B: http://www.who.int/mediacentre/factsheets/fs204/en/ Accessed April 22, 2012
6. Joint United Nations Program on HIV/AIDS (UNAIDS). World AIDS Day Report 2011. http://www.unaids.org/en/ (Article accessed on April 24, 2012 2pm)
7. The Kenya National Bureau of Statistics (KNBS) and ICF Macro.2010. Kenya Demographic and Health Survey 2008-09. Calverton, Maryland: KNBS and ICF Macro.
8. National AIDS and STI Control Programme, Ministry of Health, Kenya. September 2013. Kenya AIDS Indicator Survey 2012: Preliminary Report. Nairobi Kenya Available at http://www.nascop.or.ke
9. Murugu N. M. The prevalence of hepatitis B surface antigen in pregnant women in Machakos. University of Nairobi MMed. Dissertation1984
10. Okoth F., Mbuthia J., Gatheru Z. et al. Seroprevalence of hepatitis B markers in pregnant women in Kenya. East African Medical Journal 2006; 83(9): 485-93.
11. Buseri F. I., Seiyaboh E., Jeremiah Z. A. Surveying infections among pregnant women in the Niger Delta, Nigeria. J Global Infect. Diseases 2010;2:203- 211
12. J. A. Ndako, G. O. N. Echeonwu, O. O. Nwankiti et al. Hepatitis B seroprevalence among pregnant females in Northern Nigeria. Research Journal of Medical Sciences 2012; 6(3): 129-133

13. Madzime S., Adem M., Mahomed K. et al. Hepatitis B virus among pregnant women delivering at Harare Maternity Hospital, Zimbabwe 1996 to 1997. Cent. Afr. J. Med. 1999: 13(8): 195-198
14. Brett MacLean, Rosanna F. H., Edward B., et al. Seroprevalence of hepatitis B surface antigen among pregnant women attending the Hospital for Women and Children in Koutiala, Mali. South African Medical Journal 2012; 102(1):47-9
15. Itoua-Ngaporo A., Sapaulou M. V., Ibara J. R., et al. Prevalence of hepatitis B viral markers in a population of pregnant women in Brazaville (Congo). J Gynecol Obstet Biol Reprod (Paris). 1995;24(5):534-6
16. Menendez C., Sanchez-Tapias J. M., Kahigwa E. et al. Prevalence and mother to child transmission of hepatitis viruses B, C and E in Southern Tanzania. Journal of Medical Virology 1999; 58:215-220
17. Fisseha Walle, Daniel Asrat, Atnaf Alem, Enyew Tadesse et al. Prevalence of HBsAg among pregnant women attending antenatal care at Debre-Tabor Hospital, North West Ethiopia. Ethiopia J. Health science. 2008; 17: 1
18. Rasha M Alsheikh, Ahmed A. Daak, Mohamed A. Elsheikh et al. Hepatitis B and hepatitis C in pregnant Sudanese women. Virology Journal Oct 2007;4:104
19. Santiago-Munoz P., Roberts S., Sheffield J. et al. Prevalence of hepatitis B and hepatitis C in pregnant women who are infected with HIV. American Journal of Obstetrics and Gynecology 2005; 193: 1270-1273.
20. Landes M., Newell M. L., Barlow P. et al. Hepatitis B or hepatitis C co-infection in HIV-infected pregnant women in Europe. HIV Med 2008;9:526-534
21. Rouet F., Chaix M. L., Inwoley A. et al. Hepatitis B and Hepatitis C prevalence and viraemia in HIV positive and HIV negative pregnant women in Abidjan, Cote d'voire. The ANRS study 1236. Journal of medical virology 2004;74:34-40
22. C. Chasela, P. Wall, E. Teshale et al. Prevalence of HBV and occult HBV infections among pregnant women co-infected with HIV-1 in Lilongwe, Malawi: The Breast feeding, Antiretroviral and Nutrition (BAN) study. doi: 10.1016/j.hep.2013.10.029
23. Simpore J., Savado A., Ilboudo D. et al. Toxoplasma gondii Hepatitis C and hepatitis B seroprevalence and co-infection among HIV positive and HIV negative women in Burkina Faso. Journal of medical virology 2006; 78: 730-733

24. Christy Nkiru Ezegbudo, Dennis Edo Agboulabor, Gilbert Obiora Nuobu et al. The seroprevalence of HBsAg and HIV among pregnant women in Anambra State, Nigeria. H Shiraz E-Medical Journal 2004;5:2
25. Lar P. M., Pam P. K., Christopher P. B., Gwamzhi L., and Mawak J. D. Prevalence and immune status of HIV/HBV co-infected pregnant women. Afr. J. CLN. Exper microbial 14(3): 120-126
26. Fomulu N. J., Frederick L. M., Tirimiro J. N. et al. Prevalence, correlates and pattern of hepatitis B among clinic attenders in Yaoundé-Cameroon: Is perinatal transmission of HBV neglected in Cameroon? BMC Pregnancy and Childbirth. 2013; 13: 158
27. Pirillo M. F., Bassani L., Germinario E. A., et al. Seroprevalence of hepatitis B virus and hepatitis C in HIV- infected pregnant women in Uganda and Rwanda. J. Med Virol, 2007; 79(12):1797-1801
28. Reena S. H, Karuru J., Mark N. et al. HIV hepatitis B and hepatitis C co-infection in Kenya. AIDS. 2008; 22(10): 1221-1222
29. Ogutu E. O., Amayo E. O., Okoth F., Lule G. N. The prevalence of HBsAg, antiHBs and anti-HBc in patients with AIDS. East African Medical Journal 1990; 65 (5): 355-8
30. Erol R. Norwitz, S. Amulkaran, I. M. Symonds, A. Fowlie (eds.): Oxford American Handbook of Obstetrics and Gynecology, Oxford University press 2007 Chapter 4- Infectious diseases in pregnancy.
31. Ronald D Wilcox. Hepatitis B co-infection in pregnancy. HIV Clinician, Winter 2010; 22 (1): 5-6
32. Bodsworth N. J., Cooper D. A., and Donovan B. The influence of HIV-1 infection on the development of the hepatitis B carrier state. Journal of infectious diseases. 1991; 163:1138-1140
33. Behrouz Navabakhsh, Narges Mehrabi, Arezoo Estakhri et al. Hepatitis B Virus Infection during pregnancy: Transmission and prevention. Middle East Journal of Digestive Diseases 2011; 3: 2
34. American College of Obstetricians and Gynaecologists. Viral hepatitis in pregnancy. Washington (DC): American College of Obstetricians and Gynaecologists; 2007. Oct. (ACOG Practice bulletin; no. 86).

35. Tram T. Tran. Hepatitis B Virus in pregnancy. Clinical Liver Disease. Special Issue: Hepatitis B 2013; (2):issue 1 29-33
36. National AIDs and STI control programme. National Guidelines for antiretroviral drug therapy in Kenya. 4th edition, Nairobi, Kenya 2011. Available at : http://www.nascop.or.ke accessed 12th December 2012, 2pm
37. Ching Lung Lai, Vlad Ratziu, Man-Fung Yuen et al. Viral hepatitis B. Lancet 2003; 362(9401): 2089-94.
38. Hadler S. C., Judson F. N., O'Malley P. M., et al. Outcome of hepatitis B virus infection in homosexual men and its relation to prior human immunodeficiency virus infection. J Infectious Diseases 1991; 163:454-9.
39. Chloe L. Thio, C. L. Seaberg, E.C. Skolasky et al. HIV, Hepatitis B virus and risk of liver related mortality in the multicentre cohort study (MACS). Lancet,2002; 360: 1921-1926
40. Scott E. Kellerman, Debra L. Hanson, A. D. McNaghten et al. Prevalence of chronic hepatitis B and Incidence of acute hepatitis B infection in HIV infected persons. Journal of Infectious diseases 2003:188
41. Chloe L Thio. Virology and clinical sequelae of drug-resistant HBV in HIV-HBV co-infected patients on HAART. Antivir Ther. 2010;15(3 Pt B): 487-491
42. Sinicco A., Raiteri R., Sciandra M., et al. Co-infection and super-infection of hepatitis B virus in patients infected with human immunodeficiency virus: no evidence of faster progression to AIDS. Scand J Infect Dis1997; 29:111-5
43. Kim H. Y., Choi J. Y., Park C. H., et al. Outcome after discontinuing antiviral agents during pregnancy in women infected with hepatitis B virus. J Clin Virol.2013;56(4):299-305
44. Tse K. Y., Ho L. F., Lao T., et al. The impact of hepatitis B surface antigen carrier status on pregnancy outcomes: a case control study. J. Hepatol 2005 Nov;43 (5):771-5
45. Azar Aghamohammadi, Maryan Noortajaer. Maternal HBsAg carrier and pregnancy outcome. Australian Journal of Basic and Applied Sciences, 5 (3); 607-610, 2011
46. Pastorek J. G 2nd. , Miller J. M. Jr., Summers PR. The effect of hepatitis B antigenemia on pregnancy outcome. Am J Obstet Gynecol. 1988 Mar; 158(3pt1):486-9

47. M. J. Ter Borg, W. F. Leemans, R. A. De Man., et al. Exacerbation of chronic hepatitis B infection after delivery. Journal of Viral hepatitis 2008; 15(1) 37-41
48. Burk R. D., Hwang L. Y., Ho G. Y., et al. Outcome of perinatal hepatitis B exposure is dependent on maternal viral load. J. Infect Diseases 1994; 170: 1418-23.
49. Greenfield, Osidiana V., Karayiannis P. et al. Transmission of hepatitis B virus in Kenya; Its relation to the presence of serum HBV DNA and anti-HBe in the mother. Journal of Medical Virology 19:135-142
50. Beasly R. P., Trepo C., Stevens C. S. et al. The 'e' antigen and vertical transmission of HBsAg. American Journal of Medical Virology 9:57-68
51. Zhang S. L., F. Yue, G. Q. Bai et al. Mechanism of intrauterine infection of hepatitis B virus. World J Gastroenteral 2004;10(3):437-438
52. J M. Alexander., R. Ramus., G. Jackson., et al. Risk of hepatitis B transmission after amniocentesis in chronic hepatitis B carriers. Infect. Diseases in Obstet and Gynaecol 7: 283-286; 1999
53. Beasly R. P., Stevens C. E., Shiao I. S., Meng H.C. Evidence against breast feeding as a mechanism for vertical transmission of hepatitis B. Lancet 1975; 2:740
54. Hill J. B., Sheffield J. S., Kim M. J., et al. Risk of hepatitis B transmission of breast fed infants of chronic hepatitis B carriers. Obstet. Gynaecol 2002;99:1049
55. F. Guido, Carine D., M. Jeffery et al. Hepatitis B vaccination in Africa; mission accomplished? The South Afr. J Epidemiol and Infect Diseases 2008; 23(1): 24-28
56. Immunization schedule for Kenya. Available at www.gavialliance.org/country/Kenya/documents/cmyps/Comprehensive-multi-year-plan-for-211-2015. Accessed 24th October 2012
57. The Centres for Disease Control. Hepatitis B vaccination recommendations for Adults. Available at: http://www.cdc.gov/hepatitis/HBV/vaccadults.htm. Accessed 24 October 2012
58. Walter W. W., Peng-Jun Lu, Stacie G. et al. Non-influenza Vaccination Coverage among adults- United States, 2011. Available at http://www.cdc/gov/mmwr accessed 26th October 2013.

59. Advisory Committee on Immunization Practices: Guidance for vaccine Recommendations in Pregnant and breastfeeding women. Available at www.cdc.gov/vaccines/pubs/preg-guide.htm, accessed 29/12/2013 10pm
60. Shi Z., Yang Y., Ma L., et al. Lamivudine in late pregnancy to interrupt in utero transmission of hepatitis B virus: a systematic review and meta-analysis. Obstet Gynaecol 2010; 116: 147-59
61. Pan C. Q., Zou H. B., Chen Y., et al. Caesarean section reduces perinatal transmission of HBV infection from hepatitis B surface antigen positive women to their infants. Clin Gastro-enterol Hepatol. 2013 April 27. 1991;163:1138-1140
62. Wong V. C., Ip H. M., Reesink H. W., et al. Prevention of HBsAg carrier state in newborn infants of mothers who are chronic carriers of HBsAg and HBeAg by administration of Hepatitis B vaccine and hepatitis B immunoglobulin. Double blind randomized placebo-controlled study. Lancet. 1984 28: 1(8383) 921-926.
63. Lee C., Gong Y., Brok J., et al. Effect of hepatitis B immunization in new-born infants of mothers positive for hepatitis B surface antigen; systematic review and meta-analysis. BMJ 2006; 332:328-36.
64. Beasly R. P., Hwang L. Y., Lee G. C. et al. Prevention of perinatally transmitted HBV infection. HBIG and HBV vaccine. Lancet 1983;2(8359):1099-102
65. Riwha C., Pia M. G., Salko W. S. et al. Failure of neonatal hepatitis B vaccination, the role of HBV-DNA in hepatitis B carrier mothers and HLA antigens in neonates. Journal of Hepatol. 1994; 20(4): 483-6
66. Wang C., Tang J., Song W., et al. HLA and cytokine gene polymorphisms are independently associated with responses to hepatitis B vaccination. Hepatology 2004; 39:978-988.
67. Tang J. R., Hsu H. Y., Lin H. H., et al. Hepatitis B surface antigenemia at birth: A long term follow up study. Journal of paediatrics 1998. 133:374-7

## RESEARCH BUDGET

| Item | Unit price(KSH) | Quantity | Estimated cost(KSH) |
|---|---|---|---|
| Laboratory tests/reagents | 45, 000 | 1 | 45, 000 |
| Personnel ( research assistant) | | 1 | 20, 000 |
| Lab technician | | 1 | 20, 000 |
| Statistician | | 1 | 30, 000 |
| Vacutainers | 21 | 300 | 6,300 |
| Syringes 5ml | 500/box | 20 | 10, 000 |
| 21 gauge needles | 20 | 300 | 6, 000 |
| Cotton wool (swabs) | 500 | 1 roll | 500 |
| Surgical spirit | 500 | 1 | 500 |
| Clean gloves | 850 | 6 boxes | 5, 100 |
| Stationery | | | 5, 000 |
| Laboratory consumables | | | 11,000 |
| Miscellaneous | | | 1,000 |
| Total | | | 160,400 |

**PROJECT TIMELINES**

| **PROJECT MONTHS** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Proposal presentation | | | | | | | | | | | | | | | | | | | | | | | | |
| Proposal Correction | | | | | | | | | | | | | | | | | | | | | | | | |
| Data instrument/testing | | | | | | | | | | | | | | | | | | | | | | | | |
| Oral presentation | | | | | | | | | | | | | | | | | | | | | | | | |
| 1st Supervisors review | | | | | | | | | | | | | | | | | | | | | | | | |
| Handed to ethics | | | | | | | | | | | | | | | | | | | | | | | | |
| Ethical comments | | | | | | | | | | | | | | | | | | | | | | | | |
| 2nd Supervisors review | | | | | | | | | | | | | | | | | | | | | | | | |
| 2nd Ethics review | | | | | | | | | | | | | | | | | | | | | | | | |
| Data collection | | | | | | | | | | | | | | | | | | | | | | | | |
| Data analysis | | | | | | | | | | | | | | | | | | | | | | | | |
| Data presentation | | | | | | | | | | | | | | | | | | | | | | | | |
| Poster presentation | | | | | | | | | | | | | | | | | | | | | | | | |
| Final marking | | | | | | | | | | | | | | | | | | | | | | | | |

**APPENDIX I**

Study Number…… Date……

**University of Nairobi**

**The Hepatitis B In Pregnancy Prevalence Study Participation Consent Form.**

**Investigator:** Dr Margaret Kilonzo, MBChB. Postgraduate student in Obstetrics and Gynecology, University Of Nairobi. This study will be supervised by Prof.Koigi Kamau and Dr. Guyo Jaldesa both of the department of Obstetrics and Gynecology, University of Nairobi.

**Purpose of study**

I am carrying out a study as part of the requirement for postgraduate qualification. My objectives are to determine whether Hepatitis B infection is more common among HIV infected pregnant mothers compared to the HIV negative pregnant mothers in Kenyatta National Hospital. The findings of this study are hoped to guide policy making on screening of pregnant women for hepatitis B in the public sector in Kenya. I therefore request your participation in this study. The risks, benefits and additional information you may need are outlined below. Feel free to ask for clarifications and more information.

**Participants' information on Hepatitis B**

Hepatitis B is a viral infection which is common in our set up. Majority of people infected with hepatitis B are able to spontaneously clear the infection while a small percentage become chronically infected and are at risk of liver damage from the infection and may be a source of infection to others including to the unborn baby more so if they also HIV infected.

Hepatitis B is preventable by vaccination and avoiding contact with contaminated blood and body fluids. Immunization of babies born to Hepatitis B infected mothers at birth minimizes chances of Hepatitis B infection. Starting the HIV infected mother on appropriate antiretroviral drugs (ARVs) treats both HIV and Hepatitis B and slows disease progression.

Hepatitis B surface antigen (HBsAg) test is one of the Hepatitis B screening tests and will be done in this research. Knowing ones hepatitis B status is essential for every pregnant woman due to the risk of transmission to the unborn baby.

**Ethical Issues**

I bring to your attention the following ethical issues to guide your participation.

1. Participation in this study is voluntary.
2. This test is free. No payments will be required for the test to be done.
3. You may withdraw from the study at any time and there are no consequences for your decision to withdraw.
4. All information you provide including details on your demographic characteristics and your test results will be treated as confidential. Only the investigator and the Kenyatta National Hospital/ University of Nairobi Ethics and research committee will have access to information about you. This information about you will be identified by a study number and will not be linked to your name in any records. Your name will not be used in any published report.
5. Blood drawn from you will only be tested for hepatitis B surface antigen.
6. If you test positive for hepatitis B surface antigen, you will be offered appropriate advice on need for treatment, prevention of infection to your baby and family. You will be given extra counseling as needed to allay anxiety and help you get appropriate services.
7. The study protocol has been reviewed by the KNH/ UoN research and ethics committee.

**Benefits**

Knowing your hepatitis B surface antigen status.

There will be no monetary or other personal benefits for participating in this study.

**Side Effects/risks**

You may get anxious or worried about knowing your hepatitis B surface antigen status and what to do if the test results turn out positive. You will be advised on the best way forward depending on your test results.

Some discomfort is expected from the prick to obtain a blood sample for hepatitis B testing.

**Procedure**

Once you have read through the above and have opted to participate in this study, you will be expected to:-

1. Give an informed written consent.
2. You will be assigned a study number
3. You will then be interviewed by a research assistant/nurse for socio-demographic details.
4. 4 millimeters of venous blood will then be drawn from your antecubital area for hepatitis B testing.
5. Your test results will be disclosed to you during your next antenatal clinic visit in a confidential manner in a private room where you can discuss your concerns with the research personnel.
6. If you are not willing to participate in this study you will still receive similar routine antenatal care in the KNH clinic like the mothers who choose to be part of this study.

.

For further information, questions and clarification, kindly contact me on **0721588928.**

The KNH/UoN Ethics and Research Board can be reached on email: **uonknh_ erc@uonbi.ac.ke** or phone number **020-2726300 Extension 44355**

I, the undersigned, do hereby consent to participate in this study whose nature, purpose and objectives have been fully explained to me. I am aware that participation is voluntary and that there are no consequences of withdrawing from the study. I have been informed that all data provided will be used for the purposes of the study only.

Signed……Study No.……date……

I,……..declare that I have adequately explained to participant the purpose of the of the study, procedures, risks and benefits. I have given the participant time to ask questions and seek clarification regarding the study.

Signed……date…….

**APPENDIX II:**

**Nambari ya Uchunguzi……**

**Tarehe……**

**CHETI CHA KUKUBALI/KUKATAA KUSHIRIKI KATIKA UCHUNGUZI WA HEPATITIS B KWA WAJAWAZITO.**

Mimi ni Daktari Margaret Kilonzo, mwanafunzi wa masomo ya juu katika idara ya afya ya kina mama katika Chuo Kikuu cha Nairobi.

Nafanya utafiti kuhusu homa ya ini ya aina ya B (hepatitis B infection) katika wajawazito walio na virusi vya ukimwi na wasio na virusi hivyo katika hospitali ya Kenyatta**.** Matokeo ya uchunguzi huu yanatarajiwa kutumika kutengeneza miundo msingi ya kuwapima waja wazito kama wana virusi vya hepatitis B kwenye hospitali zetu za uma hasa walio na virusi vya ukimwi. Wasimamizi wa uchunguzi huu ni Prof. Koigi Kamau na Daktari Guyo Jaldesa wa chuo kikuu cha Nairobi. Tunakuuliza ushiriki katika uchunguzi huu.

**Ugonjwa wa Hepatitis B ni nini?**

Homa ya ini ya aina ya B ama hepatitis B kwa Kiingereza ni ugonjwa wa ini unaosababishwa na Virusi vya Hepatitis B na ambao unapatikana sana hapa kwetu. Mara nyingi watu wanapopata hepatitis B wanapona bila matibabu yoyote, lakini watu wachache hubaki na virusi hivi kwa muda mrefu au kwa maisha yao bila kupona. Ugonjwa huu huharibu ini na unaweza kupitishwa kwa mtoto kabla ya kuzaliwa iwapo mama anao wakati wa mimba. Pia unaweza kupitishwa kwa watu wengine kwa jamii kwa njia ya kugusa au kuguswa na damu, mate,au jasho ya aliye na virusi vya hepatitis B. Pia upitishwa kwa njia ya kufanya mapenzi bila kinga. Hepatitis B inaweza Kuzuiwa kwa kujikinga kutokana na Kugusa au kuguswa na damu, mate, jaso iliyo na virusi, chanjo ya hepatitis B kwa watu wote na chanjo ya kukinga watoto wanapozaliwa na mama aliye na hepatitis. Kuanzisha walio na virusi vya ukimwi na hepatitis B madawa yanayotibu virusi hivi viwili huwa kuna manufaa ya kuzuia kuendelea kwa ugonjwa haraka na pia umkinga mtoto kabla hajazaliwa.

**Maslahi ya mshiriki**

Itakuwa vizuri kujua yafuatayo kukusaidia kuamua kama utashiriki kwenye uchunguzi huu.

Kushiriki kwa uchunguzi ni hiari yako au ni  kwa mapenzi yako.

1. Kipimo cha hepatitis B ni bure, hakuna utakacholipa.
2. Unaweza kujiondosha kwenye utafiti huu wakati wowote bila matatizo yoyote.
3. Taarifa tutakayopata kwako na matokea yako ya hepatitis B yatawekwa siri. Matokea hayo yatatambuliwa kwa nambari ya uchunguzi peke yake, jina lako halitawekwa kwa matokea au kuchapishwa.
4. Damu utakayotolewa itapimwa hepatitis B peke yake.
5. Iwapo baada ya kupimwa utakuwa una hepatitis B, utaelezewa jinsi ya kumkinga mtoto wako ambaye hajazaliwa na jamii yako wasipate virusi vya hepatitis B, na kama utahitaji matibabu au la. Utapewa mawaidha zaidi iwapo yatahijika ili kuondosha wasiwasi.
6. Uchunguzi huu umeithinishwa na kamati ya uchunguzi na maadili ya Kenyatta National Hospital (KNH/UoN research and Ethics Board).

**Faida ya Kushiriki**

Faida kuu ya kushiriki itakuwa kujua zaidi kuhusu hepatitis B na kujua kama una virusi vya hepatitis B. Hakuna malipo utakayopata kwa kushiriki kwa uchunguzi huu.

**Madhara**

Shida ambayo inatarajiwa ni kupatwa na wasiwasi kuhusu kujua kama una virusi vya hepatitis B au la. Pia utaweza kuona haya kidogo kuulizwa maswali kuhusu kazi huifanyayo na mimba ulizowahi kupata. Utahisi uchungu kidogo wakati wa kutolewa damu ya kupima Hepatitis B. Hakuna madhara zaidi yanayotarajiwa.

**Utahitajika**

Kusoma na kuelewa cheti hiki kisha kama utaamua kushiriki:-

- Utie sahihi kibali cha kukubali kushiriki.
- Utaulizwa maswali machache na msaidizi wa uchunguzi ambaye atakuwa muuguzi kuhusu umri, mimba ulizowahi kupata, kiwango cha masomo, kama umepata chanjo ya hepatitis B, na kazi unayofanya.

- Utatolewa milimita 4 za damu mkononi kupima kama una virusi vya hepatis B.
- Matokeo ya kipimo hiki utapewa utakaporudi kliniki tena na mzungumzie matokeo hayo pamoja na unachohitaji kufanya huhusu matokeo hayo.

Kwa maswali au maelezo zaidi, wasiliana nami kwa nambari **0721 588 928.**

Unaweza kuwasiliana na Jopo la usimamizi wa maadili ya uchunguzi wa kisayanzi la Hospitali kuu ya Kenyatta na Chuo kikuu cha Nairobi kwa barua pepe:- **uonknh_ erc@uonbi.ac.ke** au kwa nambari ya simu **020-2726300 Extension 44355.**

**Cheti cha Kukubali cha mshiriki**

Nimeelezewa sababu,uzuri na madhara ya uchunguzi huu na kwamba hakuna malipo yoyote na ninaweza kujitoa kwa uchunguzi huu wakati wowote. Nakubali kushiriki kwenye uchunguzi huu kwa hiari yangu.

Sahihi…….Nambari ya uchunguzi…….. Tarehe……

Nimemweleza mshiriki kuhusu uchunguzi huu, faida zake na madhara yake na kwamba kushiriki ni hiari na hakuna malipo yoyote.

Sahihi…….. Tarehe……

**APPENDIX III**

**QUESTIONNAIRE**

**THE HBsAg SEROPREVALENCE IN PREGNANCY STUDY**

**Study number……...**

**Date of interview……..……**

**Sub-group A (HIV Positive)** ☐

**Sub-group B (HIV Negative)** ☐

**Please answer the questions below by circling one appropriate response.**

1. What is your age in years?
   a.) <20
   b.) 20-<25
   c.) 25-<30
   d.) 30-<35
   e.) ≥35
2. What is your marital status
   a.) Married
   b.) Widowed/Separated
   c.) Single
3. What is the highest educational level that you have attained?
   a.) None
   b.) Primary
   c.) Secondary
   d.) College/University
4. How many children/pregnancies have you had?
   a.) Para 1/ Primigravida
   b.) Two to four
   c.) Five
   d.) More than five
5. Are you employed?
   a.) Unemployed
   b.) Casual worker
   c.) Self employed
   d.) Permanent/ Long-term employment.
6. Have you ever been immunized against hepatitis B?
   a.) Yes
   b.) No
   c.) Don't know
7. If Yes in 6 above, when
   a.) Within the last 5 years
   b.) >5-10 years ago
   c.) In childhood
   d.) Don't know.
8. HBsAg test results
   a.) Positive
   b.) Negative

**APPENDIX IV**

**LABORATORY REQUEST FORM**

**THE HBsAg SEROPREVALENCE IN PREGNANCY STUDY**

**Date _____**

**Study Number _____**

**Sub-group_____**

HBsAg (ELISA) Results:

a.) Negative

b.) Positive

Reported By_____

Signed _____ Date_____