PREVALENCE OF HEPATITIS B VIRUS, HIV AND HBV COINFECTION AND ASSOCIATED FACTORS IN PREGNANT WOMEN ATTENDING ANTENATAL CARE AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA

BY

DR. VICTOR K.P. SICHONE BSc. HB, MBChB

Dissertation submitted to the University of Zambia in partial fulfilment of the requirements for the award of degree of Master of Medicine in Obstetrics and Gynaecology

THE UNIVERSITY OF ZAMBIA

LUSAKA

2019

DECLARATION

I declare that this dissertation herein presented for the degree of Master of Medicine in Obstetrics and Gynaecology has not been previously submitted either wholly or in part for any other degree at this or any other university nor is it being currently submitted for any other degree.

I further hereby state that this dissertation is entirely the result of my own personal effort. The various sources to which I am indebted have been clearly indicated in the acknowledgements and reference list.

SIGNED_____

DR. VICTOR K.P. SICHONE

COPYRIGHT

Dr. Victor K.P. Sichone

2019

CERTIFICATE OF APPROVAL

This dissertation of Dr Victor K.P. Sichone has been approved as fulfilling part of the requirements for the award of the degree of Master of Medicine (obstetrics and gynaecology) by the University of Zambia.

Name Examiner 1: ……..Signature: ……. Date: …….

Name Examiner 2: ……...Signature: …….. Date: …….

Name Examiner 3: ……Signature: ……. Date: …….

Chairperson
Board of
Examiners: …….Signature: ……..Date: ……..

Supervisor: …….Signature: …… Date: …….

ABSTRACT

Human Immunodeficiency virus (HIV) and Hepatitis B virus (HBV) are a global public health problem which share common risk factors and modes of transmission. Perinatal transmission is the major route of HBV transmission in endemic areas. Without vaccination, the newborn infant has 10 - 20% risks of developing chronic hepatitis B if the mother is positive for HBsAg, and 90%, if also positive for the HBeAg. The burden of HBV infection in pregnant women at the University Teaching Hospital (UTH) is not known. Hence this study explored the prevalence of HBV infection in HIV positive and HIV negative pregnant women and associated factors.

This was a comparative cross-sectional study. A total of 316 pregnant women aged 16-46years were recruited including 158 HIV negative and 158 HIV positive. Recruitment of consenting participants for each subgroup in a 1:1 ratio was done from the antenatal ward until the sample size was attained. A structured questionnaire was administered for socio-demographic data to women with a known HIV status recorded on their antenatal cards. Blood for HBsAg screening were also collected. Data collection was done between 15th Dec 2016 and 30th May, 2017.

Of the 316 study participants 11(3.5%) tested positive for HBsAg showing intermediate endemicity. There was no statistical difference in the prevalence of HBV in the HIV negative and HIV positive pregnant women (3.8% and 3.2% respectively, P=0.76. Similarly, there was no association between the age, marital status, parity, residence, religion, education level or form of employment with HBV infection. However, HIV antiretroviral treatment seems to have a protective effect on acquisition of HBV infection [OR = 0.09, CI = 0.01 – 0.63, P = 0.02]

Given that no significant differences in the prevalence of HBV in the HIV positive and HIV negative were found, all pregnant women regardless of their HIV status or socio-demographic factors should routinely be screened for Hepatitis B as is recommended by the WHO. Policy makers should make available the Hepatitis B vaccine and Immunoglobulin for infants whose mothers test positive for HBsAg especially those that are also positive for HBeAg. All pregnant women should be counseled on hepatitis B concurrently as the HIV counseling is taking place to increase awareness. All HIV positive women should be encouraged to take antiretroviral drugs as it seems to have a protective effect on the acquisition of HBV infection. A large multi-centre study is, however, necessary to explore this association.

Key words: Hepatitis B, Hepatitis C, HIV, Pregnancy

DEDICATION

I dedicate this dissertation to all the women who accepted to participate in the study and my two children; Alicia and Suwilanji Sichone for the many times spent away from them because of my studies.

ACKNOWLEDGEMENTS

I am graciously thankful and will forever remain indebted to the following people without whom this dissertation would not have been made possible.

1. Prof. Bellington Vwalika: My supervisor, for the unwavering support, encouragement and guidance.
2. The nurse midwives: Mrs. Fydes Katenga Malupande and Mrs. Majorie Muyunda from the UTH, for tirelessly helping with data collection and making sure results for HBsAg were made available.
3. Mr. Raymond Muyovwe: my good friend of many years for helping with data entry and cleaning
4. Mr. Adrian Kalima Mulele for the wonderful work and guidance during data analysis.
5. Dr. Andrew Kumwenda and Dr. Davies Sasa for the technical support and guidance rendered
6. All the women who participated in the study.

CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

ABBREVIATIONS AND ACRONYMS

AIDS	Acquired Immuno-deficiency Virus
AOR	Adjusted odds ratio
ALT	Alanine aminotransferase
cART	Combined Anti-retroviral Therapy
CI	Confidence Interval
HBV	Hepatitis B virus
HBsAg	Hepatitis B surface Antigen
HBeAg	Hepatitis B e Antigen
HIV	Human Immune Deficiency Virus
OR	Odds ratio
SPSS	Statistical Package for Social Sciences
USA	United States of America
UTH	University Teaching Hospital
WHO	World Health Organization

CHAPTER ONE: STUDY BACKGROUND

1.1 Introduction

HIV and Hepatitis B virus (HBV) are a global public health problem, especially in the sub-Saharan Africa where they are known to be endemic (Kourtis et al, 2012). It is estimated that about 2 billion people worldwide have been infected by HBV at some time in their lifetime. Of these, 240 million remain chronically infected becoming carriers of hepatitis B infection, and more than 10% of these are said to live in the sub-Saharan Africa and East Asia (WHO, 2002, 2015). The major complications of chronic HBV infection are cirrhosis and hepatocellular carcinoma (WHO, 2015). HBV infected women like those who are HIV positive risk infecting their babies during pregnancy, delivery and puerperium with a consequence of developing fulminant hepatitis B infection especially if the woman is HBsAg positive and more so if the HBeAg is also positive (Xu, et al. 2002). HBV is said to be about 50-100 times more infectious than HIV and 10 times more than hepatitis C virus (Alter, 2006). Without vaccination, the risk that the newborn infant will develop hepatitis B is 10 to 20% if the mother is positive for HBsAg, and as high as 90% if she is also positive for the HBeAg (WHO, 2002). Zhang, et al (2014) in their study of the effects of hepatitis B immunization on prevention of mother –to-infant transmission of hepatitis B virus and immune response of infants towards hepatitis B vaccine, showed that hepatitis B immunoglobulin (HBIG) plus hepatitis B vaccine (HB vaccine) can effectively prevent mother to infant transmission of HBV and no breakthrough infection was observed in infants born to HBeAg- negative mothers who received HB vaccine with or without HBIG after birth.

According to Kumar, et al. (2010), the prevalence of chronic HBV infection ranges widely from 0.1–2% in low-prevalence areas like North America, Western Europe, Australia, and New Zealand to 10–20% in high prevalence areas like South East Asia, China, and sub-Saharan Africa. Intermediate-prevalence areas include; Japan, Central Asia, the Middle East, Central America, and South America. Kumar, et al. (2010), also noted that the mode of transmission differs among these geographic areas with; mother-to-child transmission predominating in high-prevalence areas, while horizontal transmission, particularly in early childhood, accounts for most cases of

chronic HBV infection in intermediate-prevalence areas. Unprotected sexual intercourse and intravenous drug use in adults are the major routes of spread in low-prevalence areas. In the United States of America, Euler, et al. (2003), noted that acute hepatitis B occurs in approximately 1 in 1000 pregnancies and that the prevalence of HBsAg among pregnant women in urban areas varies by race and ethnicity. The highest rate was 5.79% for Asian Americans, 0.97% for African Americans, 0.6% for whites and 0.14% for Hispanics. Studies done in Africa showed that the prevalence of HBV infection in pregnant women was between 3% and 13% showing intermediate or high endemicity. In Ethiopia, Zenebe et al. (2014) found 3.8% prevalence of HBV infection. In South Africa, Thumbiran, et al. (2014) reported a 5.3% HBV prevalence and Ahmed, et al. (1998) in Malawi, found a 13% prevalence. In Zambia, there was paucity of data as regards the prevalence of HBV more especially in the pregnant women population. Many people are unaware of their HBV infection and thus present for care with advanced disease. The paucity of data seems to be partly due to limited access to routine screening and treatment availability. Most of the studies done were in the non-pregnant and HIV infected adult population. A more recent study by Kapembwa, et al. (2009), at the University Teaching Hospital (UTH) found that 9.9% of the HIV infected adults had active HBV infection. A study done by Oshitani, et al. (1996) in their study of prevalence of hepatitis B antigens in human immunodeficiency virus type 1 seropositive and seronegative pregnant women in Zambia conducted in five rural district hospitals and 3 urban health centres found the prevalence of Hepatitis B surface antigen positivity in pregnant women at 6.5%. Another study by Siame, (2006) looked at the prevalence of HBV and HCV co-infections among 97 HIV positive pregnant women admitted to labour ward in Kitwe. The study found the prevalence of HBV at 9.3%.

This study aimed at determining the prevalence of HBV and HBV/HIV coinfection and associated factors in pregnant women attending antenatal care at the University Teaching Hospital.

1.2 Problem statement

Zambia lies within the sub-Saharan Africa were HIV and HBV are said to be endemic (Kourtis et al, 2012, WHO 2002). A lot is known about HIV, but there is paucity of data on studies looking at the prevalence of HBV and its co-infection with HIV especially in pregnant women in Zambia. At present no study has been done as

regards the prevalence of HBV infection in pregnant women at UTH despite knowing that mother to infant is the most important mode of HBV transmission globally (WHO, 2015). HBV is also known to be more infectious than HIV (Alter, 2006). Paucity of data on the prevalence maybe responsible for the unavailability of HB vaccine and HBIG needed to effectively prevent mother to infant transmission of HBV. Without vaccination, 90% of children born to HBV infected pregnant women develop chronic hepatitis B, and 25% will later die from chronic liver disease or liver cancer (WHO, 2002).

Knowing the prevalence of HBV and its coinfection with HIV in pregnant women in Zambia may help direct the policy makers to advocate for routine antenatal HBV screening. This would then allow allocation of resources to HBV infected women and ensure provision of the birth dose vaccines to exposed babies according to WHO recommendation. Zhang, et al (2014), in a study conducted in 15 centres in China, showed that hepatitis B immunoglobulin (HBIG) plus hepatitis B vaccine (HB vaccine) given to infants born to HBeAg positive mothers immediately after birth can effectively prevent mother to infant transmission of HBV. They also observed no breakthrough HBV infection in infants born to HBeAg- negative mothers who received HB vaccine with or without HBIG after birth.

1.3 Research question

What are the factors associated with HBV and HBV/HIV coinfection among women

1.4 Objectives

1.4.1 General objective

The study aimed at exploring the prevalence of hepatitis B in HIV positive and HIV negative pregnant women attending antenatal at the University Teaching Hospital, Lusaka, Zambia and associated factors.

1.4.2. Specific Objectives

1. To determine the overall prevalence of HBV in pregnant women attending antenatal at UTH

2. To compare the prevalence of HBV in the HIV positive and HIV negative pregnant women

3. To determine the socio- demographic factors associated with HBV and HBV/HIV coinfection

1.5 Variable Definitions

1. HIV status: being HIV negative or positive

2. Socio-demographic data

- Age: age as of last birthday
- Parity: number of pregnancies that went beyond viability regardless of outcome
- Residence: place of residence (rural, urban, low, medium or high density population)
- Religion: Christian, Hindu or Muslims and others.
- Education level: highest level of education attained
- Employment status: whether or not in formal or informal employment

3. HBsAg status: being sero-positive or negative for HBV

4. HBV vaccination status: whether or not has received the hepatitis B vaccine.

1.6 Organisation of Dissertation

The dissertation is organized as follows:

- The front part contains the Title, Declarations, Abstract, Acknowledgements, Tables of Contents, including list of Tables, Figures and Appendices and the Abbreviations
- Chapter 1 contains the Study Background which concludes with the problem statement, research question, objectives and variable definitions.
- Chapter 2 contains the Literature Review and includes a summary of the relevant epidemiology of HIV/HBV in pregnancy and its impact.
- Chapter 3 is the Research Methodology and includes a complete methodology, data collection and analysis plan and ethical considerations.
- Chapter 4 summarises all the relevant results
- Chapter 5 is a summary of the interpretation of the results
- Chapter 6 lists the Conclusions and Recommendations
- The last parts include the References and Appendices

CHAPTER TWO: LITERATURE REVIEW

HIV and HBV are both a major global health problem (WHO, 2015). The major burden of HBV is the sequelae of its chronic infection such as cirrhosis and hepatocellular carcinoma (WHO, 2015). HIV and HBV share common modes of transmission. According to WHO, 2015, perinatal transmission is the major route of HBV transmission in many parts of the world, and an important factor maintaining the reservoir of the infection in some regions, particularly in China and South-East Asia. This mode of transmission can be minimized by vaccination. In the absence of prophylaxis, a large population of viraemic mothers, especially those who are seropositive for HBeAg, transmit the infection to their infants at the time of, or shortly after birth. This risk of perinatal transmission is also increased if the mother has acute hepatitis B in the second or third trimester of pregnancy or within two months of delivery (WHO, 2015). According to WHO, (2015) universal hepatitis B immunization programmes that target infants, with the first dose at birth have been highly effective in reducing the incidence and prevalence of hepatitis B in many endemic countries. WHO and society for Maternal-Fetal medicine (SMFM) recommends administration of HBV vaccine and immunoglobulin to infants born to mothers who are HBsAg positive or those with unknown or undocumented status regardless of whether maternal antiviral therapy has been given during the pregnancy, within twelve hours of birth (WHO, 2002, Am J Obstet Gynecol. 2016).

2.1 Epidemiology of HBV in pregnancy

According to Kumar, et al. (2010), worldwide the prevalence of HBV has been classified as low prevalence (0.1-2%), intermediate (2-10%) or high prevalence regions (10-20%). Low prevalence regions include; North America, Western Europe, Australia, and New Zealand. High prevalence areas are South East Asia, China, and sub-Saharan Africa. Japan, Central Asia, the Middle East, Central America, and South America are intermediate-prevalence areas. Kumar, et al. (2010), also observed that the mode of transmission of HBV differs among these geographic areas; mother-to-child transmission predominates in high-prevalence areas, whereas horizontal transmission, particularly in early childhood, accounts for most cases of chronic HBV infection in intermediate-prevalence areas. Unprotected sexual intercourse and

intravenous drug use in adults are the major routes of spread in low-prevalence areas (Kumar, et al. 2010).

In the United States, Euler, et al. (2003), noted that acute hepatitis B occurred in approximately 1 in 1000 pregnancies and that the prevalence of HBsAg among pregnant women in urban areas varied by race and ethnicity. The highest rate was 5.79% for Asian Americans, 0.97% for African Americans, 0.6% for whites and 0.14% for Hispanics. In Europe, a systematic review conducted by Hahné, et al. (2013), found that HBsAg prevalence in the general population ranged from 0.1%-5.6% by country. Another study in Europe by Landes, et al. (2008), found the prevalence at 4.9% and noted that HBsAg positivity was associated with African origin.

In Africa, a number of studies have looked at the prevalence of hepatitis B virus infection and its coinfection with HIV in the pregnant and non-pregnant populations. Barth, et al. (2010) in a systematic review and meta-analysis of sixty studies of Hepatitis B/C and HIV in sub-Saharan Africa found that among HIV-infected individuals, mean HBsAg prevalence rate were 15%. They concluded that many HIV-positive individuals in sub-Saharan Africa are HBV co-infected and HIV is associated with a higher prevalence of HBV in this region. A systematic review of data on epidemiology and risk factors of maternal HBV infection in Arab and African countries by Gasim, et al. (2013), showed that the serology of hepatitis B varied greatly among countries; with different viral genotype patterns and that the variation in prevalence could be explained by the different risk factors involved. The risk factors for the transmission of HBV identified included; sexual contact, perinatal infection, blood and its derivatives, haemodialysis, intravenous and percutaneous drug use, occupational, habitual, and social behaviour. In South Africa, Thumbiran, et al. (2014) reported a 5.3% HBV and a 3.1% HBV/HIV co-infection prevalence in pregnant women. Ahmed, et al. (1998) in Malawi, found a 13% prevalence of HBV. In Yaoundé, Cameroon, a study on the prevalence, correlates and pattern of HBV among pregnant women by Fomulu et al. (2013), found the HBV prevalence at 7.7% and of these 28% were positive for HBeAg showing high infectivity and hence increased risk of perinatal transmission. The HBV/HIV coinfection in the same study was at 0 .74%. In Ethiopia, Zenebe et al. (2014) found 3.8% prevalence of HBV infection, and HIV/HBV co-infection of 19.0%. A study in Nigeria by Ajayi, (2013)

which tested a total of 1105 pregnant women found 7.5% were positive for HIV and 6.9% for HBsAg and 0.8% coinfected with both HIV and HBV. Elsheikh, (2007), in Sudan found 5.6% of pregnant women were positive for HBsAg irrespective of their age, parity and socio-demographic characteristics. Simpore, et al. (2006) in Burkina Faso found the prevalence of HBV in pregnant women was 9.8%.

In Zambia, Oshitani, et al. (1996), in their study of prevalence of hepatitis B antigens in human immunodeficiency virus type 1 seropositive and seronegative pregnant women in Zambia, conducted in three urban health centres in Lusaka and Five district hospitals in various provinces found no significant difference in hepatitis B prevalence between HIV positive and HIV negative pregnant women (7.1% vs. 5.4%; p=0.23). They also noted that HIV infected women were more likely to test positive for hepatitis B e antigen (HBeAg) than HIV –negative women (25% vs. 12.3%; p=0.05), suggesting more HBV replication in HIV infected people. Oshitani, et al. (1996), also found that HBsAg positivity was 6.5% and HBeAg was present in 16.1% of the HBV-infected women in a study of 2098 pregnant women. They also noted that HBsAg positivity ranged from 3.3% to 13.6% among the sites, with higher prevalence in the rural district hospitals than urban health centres in Lusaka. Siame, (2006) found the prevalence of HBV at 9.3% among 97 HIV positive pregnant women admitted to labour ward in Kitwe. A more recent study on the prevalence of HBV in Zambia was by Kapembwa, et al. (2009) which found that 9.9% of the HIV infected adults at the University Teaching Hospital had active HBV infection. Mwambungu, Siulapwa, Mampi (2015) found the seroprevalence of HBV among blood donors at Lewanika General Hospital in Mongu at 6.74%.

2.2 HIV/HBV in pregnancy

From the studies noted above, the prevalence of HBV/HIV co-infection in Africa ranges from 0.74 to 19%. A Systematic Review and Meta-analysis of HIV and the Risk of Hepatitis B Co-infection in Sub-Saharan Africa conducted by Mangani, (2010), found that HIV infection is associated with a small increase in the prevalence rates of HBV infection and significantly higher prevalence rates of markers of active HBV disease. Andersson, et al. (2013) showed a trend toward loss of immune control of HBV in HIV-infected women. From the study, in HIV infected women 3.4% of samples containing HBsAg, 18.9% were positive for HBeAg. In contrast, 2.9% of samples from HIV-negative women containing HBsAg only 17.1% were positive for

HBeAg. Thio, et al. (2002), noted a higher mortality from HBV in HIV/HBV co-infected individuals compared to HIV or HBV mono infection. Gilson, et al. (1997) described a higher incidence of lamivudine resistance and faster progression to cirrhosis in the HIV/HBV co-infected.

2.3 Impact of HBV on pregnancy and outcomes

Different studies have described divergent views on the impact of HBV on pregnancy outcomes. Reddick, et al. (2011) noted no association of viral hepatitis with IUGR or pre-eclampsia however, they noted an increased risk for complications during pregnancy such as antepartum haemorrhage and gestational diabetes mellitus. Reddick, et al. (2011), also observed that hepatitis in pregnancy was not associated with an increase in abortion rate, stillbirth or congenital malformation. Terrault, et al. (2007) said there was no worsening of maternal liver disease during pregnancy in women infected with HBV. Tse, (2005), noted an increase in gestational diabetes and low Apgar scores in HBV infected pregnant women. However, Levy M and Koren G, (1991), noted that prematurity seemed to be increased if hepatitis was acquired in the last trimester of pregnancy.

2.4 Impact of pregnancy on HBV

Soderstorm, (2003), described an overall increase of the median HBV DNA levels in late pregnancy and early postpartum. This is attributed to the depressed immune response against HBV following the physiological changes of pregnancy aimed at preventing fetal rejection. The study also noted an increase of post-partum ALT in both HBeAg positive and negative women.

2.5 Perinatal transmission of HBV

According to Gambarin, (2007), there is a less than 10% risk of transmission during pregnancy. However this is increased if there is acute HBV infection during the third trimester i.e. high maternal replication (HBeAg positive or high HBV DNA), and the presence of HBV in the placenta. Gambarin, (2007) also noted that, at the time of delivery the risk of transmission is more than 90% if HBeAg is positive and 30% if only HBsAg is positive. Breastfeeding is not associated with increased risk of transmission as was noted by Beasley, et al. (1975). HBV transmission is prevented by postnatal vaccination. Ranger et al. 2004 noted that, without vaccination the risk is more than 90%. If passive immunisation (HBV vaccine only) is done, the risk is 28% and when both passive and active immunization (HBV vaccine and HBIG) is done the risk is reduced to less 5%.

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Study design

This was a comparative cross sectional study.

3.2 Study setting

University Teaching Hospital, department of Obstetrics and Gynaecology, now called Women and Newborn Hospital. The UTH is the largest health institution in Zambia. It serves as a referral hospital for nearly all patients in the country.

3.3 Target population

All pregnant women attending antenatal at UTH

3.4 Study Population

Pregnant women, who attended antenatal at UTH, had a known HIV status and met the eligibility criteria.

3.5 Inclusion criteria

Pregnant women with a known HIV status

3.6 Exclusion criteria

Pregnant women who did not give consent

3.7 Study period

Data was collected over a six month period (i.e. from 2nd December 2016 to 31st May, 2017).

3.8 Participant recruitment

Study participants were recruited from the antenatal ward.

3.9 Sampling procedure and sample size

The sample size was calculated using OpenEpi version 3, a free, web based, open source, operating system-independent series of programs for use in epidemiology, biostatistics, public health, and medicine that provides a number of epidemiologic and statistical tools for summary data (According to Sullivan, Dean and Soe, 2009). Using this tool and 6.5% as the prevalence of Hepatitis B in pregnant women, a total sample of 316 women was calculated. To provide a 1:1 comparison, 158 HIV negative and 158 HIV positive pregnant women meeting the eligibility criteria were randomly selected. The degree of certainty (confidence) chosen for this study was 95% (with a cut off value of the appropriate probability distribution of 1.96) and the margin of error at 5%.

3.10 Data collection

Women who fitted the inclusion criteria were initially recruited into the study using block randomisation sampling method. However, with the introduction of the first level hospitals around Lusaka, numbers for HIV positive pregnant women coming for antenatal clinic at UTH reduced. A convenient sampling method was then employed. Recruitment was done in the antenatal clinic. On each clinic day, files for mothers who had been tested for HIV and their status indicated on the antenatal card were identified. Five files were then picked at random from among the available cards and the mothers were then approached and requested to participate in the study. An equivalent number of files of HIV negative mothers attending antenatal on the same day was also picked in a similar manner. A questionnaire was administered to collect socio-demographic factors and blood for HBV screening was collected and sent to the laboratory. Some of the sampled files had their HBsAg status already indicated on their cards as it was becoming routine to screen every patient for HBV infection at UTH. This was done until the sample size was attained. No matching was done for age, parity, marital status, level of education, form of employment or HBV vaccination status.

Participants who had blood collected for HBsAg screening had their results reviewed during their routine return visits at 2 to 4 weeks after enrolling in the study. Mothers who tested positive for HBV infection were appropriately referred to hepatitis experts for further management.

3.11 Data analysis

While the process of data collection was going on, checking for data accuracy was being done at the end of each week. Double entry of data in excel was done to minimize typing errors. Statistical Package for Social Sciences (SPSS) version 23.0 was used for statistical analyses. Descriptive statistics were computed for the various variables that were created. To produce graphical output both SPSS and MS Excel were utilized. For Independent samples, the T-test was used to compare mean values between groups. The Pearson's chi-squared test was used to study associations between categorical variables. The Fisher's exact test was used when one or more of the cells had an expected frequency of five or less. Some variable categories with less frequency were collapsed together accordingly. The relationship between study variables and presence of HBV and HBV/HIV coinfection was examined using

logistic regression. The selection for entry into the logistic regression model was considered at level $p<0.20$ or known clinical significance.

3.12 Ethical considerations

Ethical approval for study was obtained from the University of Zambia Biomedical Research Ethics Committee (**REF.No.013-09-16).** Permission to conduct the study was sought from the University Teaching Hospital management through the head of department of Obstetrics and Gynaecology Each participant was fully informed about the study and participation was completely voluntary. The importance of the study in adding to the existing body of knowledge and also increasing awareness of HBV among mothers at the UTH was fully explained to all the participants. The participants were assured of confidentiality. The study participants were also informed that it would not be possible to publicly identify any individual who participated in the study or even associate them with their responses after the study. No data that personally identified individuals was collected. The two research assistants involved in the study were informed of the need to maintain confidentiality on the data collected. All eligible participants were requested to sign or fingerprint a written consent form for participation. Each patient had the right to decline participation. Patients were informed that those who did not sign or finger print the written consent forms would not be interviewed and that their refusal/inability to participate would not have any negative consequences on them. No compensation was given to participants. For HBV-infected mothers with chronic infection, consultation with the infectious disease experts was sought and appropriate referral made. All the documents relating to the study were kept by the researcher

3.13 Study limitation

The results of this study cannot be generalized to the whole province or whole country as it was a hospital based study.

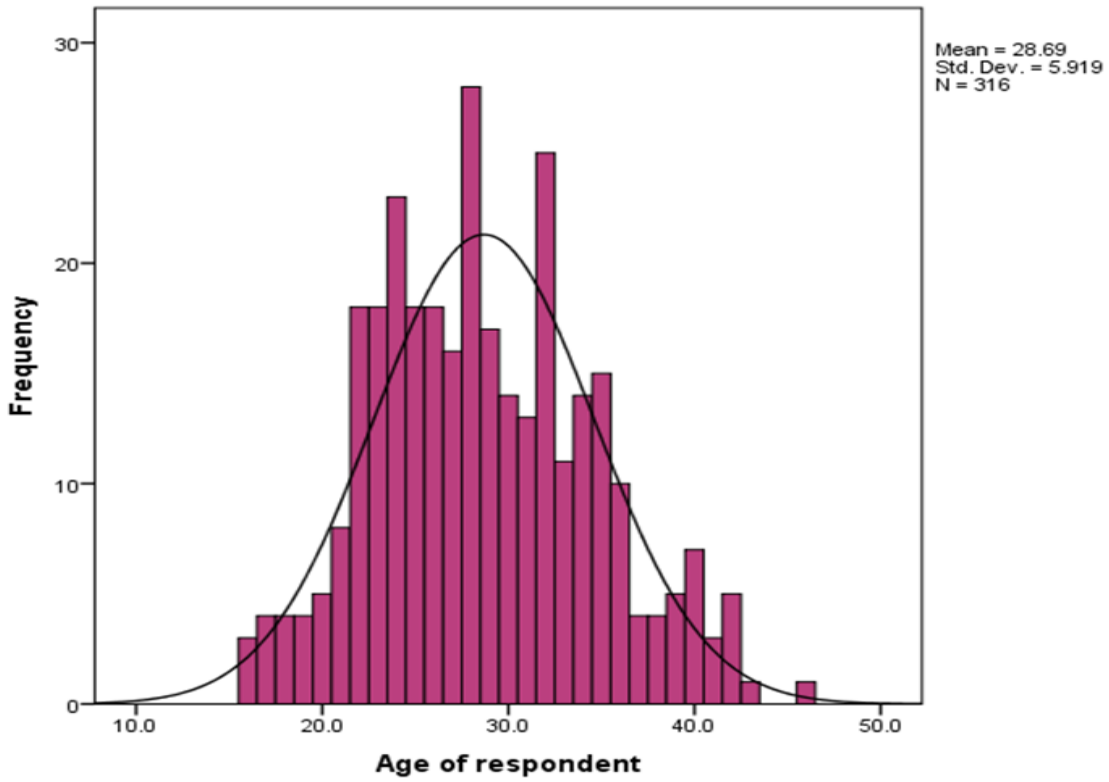
Recalling some events in the past was a challenge for some of the study participants especially on the question on vaccination.

CHAPTER FOUR: RESULTS

4.1 Socio-demographic characteristics of the study participants

Respondent age followed a normal distribution curve with mean of 28.7 years (SD = 5.92) [Figure 1]. The minimum age was 16 years and maximum 46 years. Categorized, there were 87 (27.5%) respondents less than 24 years old, 174 (55.1%) between 25 – 34 years old, and 55 (17.4%) aged 35 years or above. There were 42 (13.3%) single women and 274 (86.7%) married women, and this difference in proportional distribution was statistically significant (P<0.001). There were 82 (25.9%) women with parity 0, 81 (25.6%) with parity 1, 69 (21.8%) with parity 2, 46 (14.6%) with parity 3, and 38 (12%) with parity 4 or more

Figure 1: Respondent age distribution



There were 59 (18.7%) respondents in formal employment, 45 (14.2%) in informal employment, while the greater majority 212 (67.1%) were not employed. A larger proportion of the respondents, 312 (98.7%), were Christians. There was only 3 (0.9%) Muslims and 1 (0.3%) Hindu. A greater majority of the respondents were from high density residential areas, 181/316 (57.3%). There were 77 (24.4%) respondents from

medium density areas, 33 (10.4%) from low density areas, and 25 (7.9%) from rural areas.

4.2 Respondent antenatal card results

The distribution of HIV positive respondents was 158 (50%) and HIV negative also 158 (50%). Among the HIV positive respondents, 147 (93%) were on combined anti-retroviral therapy (cART) and 11 (7%) were not on cART. More than half of the respondents had been on cART for more than 12 months. There were 43(29.3%) respondents who had been on cART for less than 6 months, and 21 (14.3%) had been on cART for between 6 and 12 months. Out of the 147 respondents on cART there were 106 (72.1%) who started cART before pregnancy while 41 (27.9%) had started cART during the current pregnancy.

There were 11 (3.5%) respondents who were HBV positive and 305 (96.5%) HBV negative, and this difference in proportional distribution was statistically significant ($P<0.001$). Thus, the prevalence of HBV in pregnant women attending antenatal at UTH was 3.5%. There were only 2 (0.6%) respondents who reported to have ever been vaccinated against HBV, 242 (76.6%) had never been vaccinated, and 72 (22.8%) were not sure (Table 1).

Table 1: Respondent characteristics frequency distribution

Variable	Frequency	Percentage
Age Group		
Less than 24 years	87	27.5
25 - 34 years	174	55.1
35 and above years	55	17.4
Marital status		
Single	42	13.3
Married	274	86.7
Parity		
0	82	25.9
1	81	25.6
2	69	21.8
3	46	14.6
4+	38	12
Gravida		
1-2 Pregnancies	143	45.3
3-4 Pregnancies	124	39.2
5 or more pregnancies	49	15.5
Education level		
None	16	5.1
Primary	78	24.7
Secondary	143	45.3
Tertiary	79	25
Employment		
Formal	59	18.7
Informal	45	14.2
Not employed	212	67.1
Residence		
High Density	181	57.3
Medium Density	77	24.4
Low Density	33	10.4
Rural Density	25	7.9
HBV status		
Negative	305	96.5
Positive	11	3.5
Ever vaccinated against HBV		
Yes	2	0.6
No	242	76.6
I don’t know	72	22.8
Age		
(n,mean,SD)	316, 28.7, 5.92	

4.3 Bivariate and multivariate analysis for association with HBV infection

Bivariate analysis for the association with HBV infection was conducted and results shown in Table 2. There were only two study variables moderately associated with HBV infection at 10% significance level; residential density with P = 0.09 and respondent age with P = 0.10. HIV status was not associated with HBV infection, P = 0.99 (Table 2).

Residential density and age were entered into a logistic regression model and the results presented in Table 3. When comparing any two respondents with age difference of 1 year, the older respondent had on average 7% increased odds for infection with HBV [Odds Ratio (OR) = 1.07, 95% confidence interval (CI) = 0.97 - 1.18], however, this was not statistically significant P = 0.17. Compared to respondents from rural areas, respondents from high density areas had on average 79% reduced odds for HBV infection but this was not statistically significant (OR = 0.21, CI = 0.03 – 1.34, P = 0.10). Respondents from medium density areas had 39% reduced odds for HBV infection but this was not statistically significant (OR = 0.61, CI = 0.10 – 3.58, P = 0.58), and respondents from low density areas had 29% reduced odds for HBV infection but this also was not statistically significant (OR = 0.71, CI = 0.09 – 5.53, P = 0.75) [Table 3].

Table 2: Bivariate analysis for association with HBV infection

Variable	HBV negative		HBV positive		P-value
	n	%	n	%	
Age Group					
Less than 24 years	86	28.2%	1	9.1%	0.34[f]
25 - 34 years	167	54.8%	7	63.6%	
35 and above years	52	17.0%	3	27.3%	
Marital status					
Single	41	13.4%	1	9.1%	0.99[f]
Married	264	86.6%	10	90.9%	
Parity					
0	80	26.2%	2	18.2%	0.68[f]
1	79	25.9%	2	18.2%	
2	67	22.0%	2	18.2%	
3	43	14.1%	3	27.3%	
4+	36	11.8%	2	18.2%	
Gravida					
1-2 Pregnancies	139	45.6%	4	36.4%	0.77[f]
3-4 Pregnancies	119	39.0%	5	45.5%	
5 or more pregnancies	47	15.4%	2	18.2%	
Education level					
None/Primary	91	29.8%	3	27.3%	0.68[f]
Secondary	139	45.6%	4	36.4%	
Tertiary	75	24.6%	4	36.4%	
Employment					
Formal	55	18.0%	4	36.4%	0.33[f]
Informal	44	14.4%	1	9.1%	
Not employed	206	67.5%	6	54.5%	
Residence					
High Density	178	58.4%	3	27.3%	0.09[f]
Medium Density	73	23.9%	4	36.4%	
Low Density	31	10.2%	2	18.2%	
Rural Density	23	7.5%	2	18.2%	
HIV status					
Negative	152	49.8%	6	54.5%	0.99[f]
Positive	153	50.2%	5	45.5%	
Age					
mean, SD	28.6, 5.93		31.5, 5.15		0.10[t]

[f]=Fisher's exact test; [t]=Independent Samples T-test

Table 3: Logistic regression predicting HBV infection

Variable	Unadjusted Odds Ratio (95%CI)	Adjusted Odds Ratio (95% CI)	P-value
Age	1.09 (0.98 - 1.20)	1.07 (0.97 - 1.18)	0.17
Residence			
Rural	1	1	
High Density	0.19 (0.03 - 1.22)	0.21 (0.03 - 1.34)	0.10
Medium Density	0.63 (0.11 - 3.67)	0.61 (0.10 - 3.58)	0.58
Low Density	0.74 (0.10 - 5.67)	0.71 (0.09 - 5.53)	0.75

Among the respondents with HIV infection, 5 (3.2%) were con-infected with HBV while 153 (96.8%) were not co-infected with HBV, p=0.76 (Table 4).

Table 4: Prevalence of HBV in HIV positive and HIV negative women

Variable	HIV negative	HIV positive	P- value
HBV negative	152 (96.2%)	153 (96.8%)	
HBV positive	6 (3.8%)	5 (3.2%)	0.76
Total	158 (100%)	15800%)	

3.1 Bivariate analysis for association with HBV co-infection

Among the 158 HIV positive patients 5/158 (3.2%) were co-infected with HBV. Bivariate analysis for association with HBV co-infection was conducted. At 5% significance level, ART status was significantly associated with co-infection (P=0.04) and residential classification was marginally associated with co-infection (P=0.05). Table 5 presents the Fisher's exact test analysis results.

Table 5: Fisher's exact test for association with HBV co-infection

Variable	No Co-infection		Co-infection		P-value
	n	%	n	%	
Age Group					
Less than 24 years	43	28.1%	0	0.0%	0.35
25 - 34 years	77	50.3%	3	60.0%	
35 and above years	33	21.6%	2	40.0%	
Marital status					
Single	24	15.7%	0	0.0%	0.99
Married	129	84.3%	5	100.0%	
Parity					
0	32	20.9%	1	20.0%	0.27
1	42	27.5%	1	20.0%	
2	40	26.1%	0	0.0%	
3	19	12.4%	2	40.0%	
4+	20	13.1%	1	20.0%	
Education level					
None	7	4.6%	0	0.0%	0.45
Primary	46	30.1%	3	60.0%	
Secondary	76	49.7%	1	20.0%	
Tertiary	24	15.7%	1	20.0%	
Employment					
Formal	23	15.0%	1	20.0%	0.65
Informal	25	16.3%	1	20.0%	
Not employed	105	68.6%	3	60.0%	
Residence					
High Density	96	62.7%	1	20.0%	0.05
Medium Density	29	19.0%	3	60.0%	
Low Density	17	11.1%	0	0.0%	
Rural Density	11	7.2%	1	20.0%	
On ART					
Yes	144	94.1%	3	60.0%	0.04
No	9	5.9%	2	40.0%	
How long on cART					
Less than 6 months	42	29.2%	1	33.3%	0.99
Between 6 and 12 months	21	14.6%	0	0.0%	
More than 12 months	81	56.3%	2	66.7%	
cART started before pregnancy					
Yes	104	72.2%	2	66.7%	0.99
No	40	27.8%	1	33.3%	

4.5 Logistic regression analysis predicting HBV co-infection

Backward logistic regression with residence and cART was conducted and only cART status was independently associated with co-infection. Compared to women not on cART, women on cART had on average 91% reduced odds for HBV co-infection, odds ratio = 0.09, 95% confidence interval = 0.01 – 0.63, P-value = 0.02.

CHAPTER FIVE: DISCUSSION

This study found that the overall prevalence of Hepatitis B among the pregnant women attending antenatal at the University Teaching Hospital was 3.5%. Comparing between the HIV positive and HIV negative, the prevalence of HBV was 3.2% and 3.80% respectively showing no statistical significance (P=0.76). There was no significant association between HBV infection and socio demographic factors. However, being on cART appeared to have a protective effect on acquisition of new HBV infection.

The 3.5% prevalence of HBV among the women attending antenatal at the UTH found in the study, puts it among the intermediate endemic regions, (classified as: low 0.1-2%, intermediate 2-10% and high endemic regions 10-20%) as suggested by other earlier studies done on HBV in Zambia which include; Oshitani, et al. (1996), who found that the HBsAg positivity among pregnant women was 6.5%, Siame, (2006), who found 9.3% prevalence among 97 HIV positive pregnant women admitted to labour ward in Kitwe and Mwambungu, Siulapwa, Mampi (2015) who found the seroprevalence of HBV among blood donors at Lewanika General Hospital in Mongu at 6.74%. The 3.5% may seem to have dropped when compared to other earlier studies done in Zambia, possibly because of the introduction of anti-retroviral medication for HIV treatment which are also effective against HBV. The anti-retroviral drugs were not yet available in the public health when Oshitani, et al, conducted their study. The other studies mentioned above though recently done, such as Siame, (2006) only looked at the HIV positive pregnant women and the other one was among the blood donor population. The study considered only the patients in the outpatient antenatal clinic of UTH which a referral hospital and thus excluded other patients coming in as emergencies like those in labour. Most of the surrounding referring clinics do not offer routine screening of hepatitis B in Zambia and therefore, with this still high prevalence calls for more efforts from the policy makers. This prevalence is also, comparable with other studies in Africa showing intermediate endemicity. Thumbiran, et al. (2014) reported a 5.3% HBV prevalence among pregnant women in South Africa. In Yaoundé, Cameroon, Fomulu, et al. (2013), found the HBV prevalence at 7.7%. In Ethiopia, Zenebe et al. (2014) found 3.8% prevalence of HBV infection, In Nigeria, Ajayi, (2013) found 6.9% prevalence for

HBsAg. Elsheikh, (2007), in Sudan found 5.6% prevalence of HBV in pregnant women and while, Simpore, et al. (2006) in Burkina Faso found the prevalence of HBV in pregnant women was 9.8%.

Comparing the prevalence between the HIV positive and HIV negative, the study found HBV seropositivity was 3.2% and 3.80% respectively showing no statistical significance (P=0.76). The finding is in agreement with similar studies in the sub Saharan region which showed no significant difference in the prevalence of HBsAg seropositivity between HIV positive and HIV negative subjects such as Oshitani et al, 1996, Rouet, et al 2004 and Simpore, et al 2006. The expectation would have been to see a higher prevalence among HIV positive since HIV and HBV share common modes of transmission and it is known that HBV is more transmissible than HIV (Alter, 2006). The WHO, 2015, suggests that in counties where HBV prevalence is high (>5%), infection is usually acquired perinatally or during early childhood, and precedes HIV infection in most cases. As such the prevalence of chronic hepatitis B in HIV positive persons is close to that observed in the general population. This as well calls for stronger concerted efforts to prevent perinatal transmission of hepatitis B by routinely screening all pregnant women and administration of birth dose vaccines to babies born to mothers who are seropositive to HBsAg. The finding may seem to contradict Barth, et al. (2010), who in a systematic review and meta-analysis of sixty studies of Hepatitis B/C and HIV in sub-Saharan Africa found that among HIV-infected individuals, the mean HBsAg prevalence rate were 15% and then concluded that many HIV-positive individuals in sub-Saharan Africa are HBV co-infected and that HIV is associated with a higher prevalence of HBV in this region. However, similar other recent studies have shown a lower coinfection of HBV and HIV. Thumbiran, et al. (2014) South Africa, reported a 3.1% HBV/HIV co-infection prevalence in pregnant women similar to this study. In Nigeria, Ajayi, (2013), found an even low (0.8%) coinfection with of HIV and HBV.

There was no significant association between HBV infection and socio demographic factors (i.e. parity, marital status, education level, employment status, religion). This finding is similar to Elsheikh, (2007), in Sudan who found that 5.6% of pregnant women were positive for HBsAg irrespective of their age, parity and socio-demographic characteristics. In this study however, there were two study variables with some degree of association with HBV infection at 10% significance level; but not

statistically significant. Residential density with P = 0.09 and respondent age with P = 0.10. When comparing any two respondents with age difference of 1 year, the older respondent had on average 7% increased odds for infection with HBV [OR = 1.07, 95% CI = 0.97 - 1.18], however, after logistic regression, this was not statistically significant P = 0.17. The possible explanation would be that the older one gets the more exposure to HBV as they become sexually active and have a higher chance of having multiple sexual partners and other risk behaviors such as injectable drug use. Also for residential areas, when respondents where compared to those from rural areas , respondents from high density areas had on average 79% reduced odds for HBV infection (OR = 0.21, CI = 0.03 – 1.34, P = 0.10). Respondents from medium density areas had 39% reduced odds for HBV infection (OR = 0.61, CI = 0.10 – 3.58, P = 0.58), and respondents from low density areas had 29% reduced odds for HBV infection (OR = 0.71, CI = 0.09 – 5.53, P = 0.75). This finding is similar to Oshitani et al, (1996) who also that HBsAg positivity ranged from 3.3% to 13.6% among the sites, with higher prevalence in the rural district hospitals than urban health centres in Lusaka. This call for rolling out of routine HBV screening countrywide especially in the densely populated areas

Among the 5 HBV/ HIV positive mothers 3(60%) were on cART and 2(40%). The study found that being on cART was independently associated with HBV/HIV co-infection. Compared to women not on cART, women on cART had on average 91% reduced odds for HBV co-infection, (OR = 0.09, 95% CI = 0.01 – 0.63, P = 0.02). This finding therefore suggests that being on cART may have a role in preventing new HBV infections in the HIV positive pregnant women since the ARVs that are used in the first line cART in Zambia (Tenofovir, Lamivudine) have anti-HBV activity. The duration of being on cART did not seem to have any association. 67% of those coinfected with HBV/HIV were on cART for more than 12 months and 33% for less than six months. It would have been interesting to follow up these patients with HBeAg measurements to characterise their infectivity. The presence of a positive HBeAg test would indicate active HBV replication and high infectivity. Antiretrovirals are effective inhibitors of HBV replication and seldom result in cure, and therefore clearance of HBsAg is rare (WHO, 2015). Long term therapy is required to delay the progression of cirrhosis, reduce incidence of hepatocellular carcinoma and improve long term survival (WHO, 2015). Thus being on cART and

not duration on cART appeared to be the important protective factor in terms of acquisition of new HBV infection.

There were 0.6% respondents who reported to have been vaccinated against HBV, 76.6% had not been vaccinated, and 22.8% were not sure. The HBV vaccine in Zambia was introduced in the national expanded programme on immunization (EPI) in 2005 as part of the pentavalent vaccine (which includes, vaccine against diphtheria, tetanus, pertussis, haemophilus influenza and Hepatitis B) also known as DPT-HepB-Hib. It is given every four weeks in three doses from the age of six weeks. This could in part explain why the majority of the participants reported not being vaccinated. The other explanation would be cost of the vaccine, lack of awareness or knowledge about HBV which unfortunately was not tackled in this study. With the background of an intermediate endemicity of hepatitis B in pregnant women, there is need for health education and routine screening of all pregnant women for hepatitis B during antenatal care.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

The prevalence of hepatitis B infection among pregnant women attending antenatal at UTH was 3.5% falling in the intermediate endemic group. There was no significant difference in the HBV prevalence between the HIV positive and HIV negative pregnant women (3.2% and 3.8% respectively). Being on cART had on average 91% reduced odds for HBV co-infection, suggesting that cART may have a role in preventing new HBV infections in the HIV positive pregnant women. There was no association between HBV infection and socio-demographic factors.

6.2 Recommendations

1. The Ministry of Health should ensure that all pregnant women regardless of their HIV status, socio-demographic factors or vaccination status should routinely be screened for Hepatitis B as is recommended by the World Health Organization.
2. The Ministry of Health through medical stores Limited should make sure Hepatitis B vaccine and Immunoglobulin is made available to hospitals so that neonates from mothers who test positive for HBsAg especially those that are also positive for HBeAg receive the birth dose vaccine within twelve hours of birth.
3. All antenatal clinics should ensure that counselling of all pregnant women on hepatitis B is done concurrently as the HIV counselling is taking place to increase awareness.
4. Treatment of all HIV positive women with antiretroviral drugs should be encouraged as it seems to have a protective effective on the acquisition of HBV infection. A large multi-centre study is however, necessary to explore this association.

REFERENCES

Adesina, O., Oladokun, A., Akinyemi, O., Adedokun, B., Awolude, O., Odaibo, G., Olaleye, D. and Adewole, I., 2010. Human immuno-deficiency virus and hepatitis B virus coinfection in pregnancy at the University College Hospital, Ibadan. African journal of medicine and medical sciences, 39(4), pp.305-310.

Ahmed, S.D., Cuevas, L.E., Brabin, B.J., Kazembe, P., Broadhead, R., Verhoeff, F.H. and Hart, C.A., 1998. Seroprevalence of hepatitis B and C and HIV in Malawian pregnant women. Journal of Infection, 37(3), pp.248-251.

Ajayi, B.B., Ajayi, O.D., Dawurung, J.S. and Hamidu, I., 2013. Seroprevalence of some sexually transmitted infections among antenatal attendees in university of Maiduguri teaching hospital, Maiduguri-Nigeria. Annals of Biological Research, 4(2), pp.141-145.

Alter, M.J., 2006. Epidemiology of viral hepatitis and HIV co-infection. Journal of hepatology, 44, pp.S6-S9. Am J Obstet Gynecol. 2016 Jan;214(1):6-14. Doi: 10.1016/j.ajog.2015.09.100. Epub 2015 Oct8.

Andersson, M.I., Maponga, T.G., Ijaz, S., Barnes, J., Theron, G.B., Meredith, S.A., Preiser, W. and Tedder, R.S., 2013. The epidemiology of hepatitis B virus infection in HIV-infected and HIV-uninfected pregnant women in the Western Cape, South Africa. Vaccine, 31(47), pp.5579-5584.

Barth, Roos E., et al. "Hepatitis B/C and HIV in sub-Saharan Africa: an association between highly prevalent infectious diseases. A systematic review and meta-analysis." International Journal of Infectious Diseases 14.12 (2010): e1024-e1031.

Beasley, R.P., Shiao, I.S., Stevens, C. and Meng, H.C., 1975. Evidence against breast-feeding as a mechanism for vertical transmission of hepatitis B. The Lancet, 306(7938), pp.740-741.

Elsheikh, R.M., Daak, A.A., Elsheikh, M.A., Karsany, M.S. and Adam, I., 2007. Hepatitis B virus and hepatitis C virus in pregnant Sudanese women. Virology Journal, 4(1), p.1.

Euler, G.L., Wooten, K.G., Baughman, A.L. and Williams, W.W., 2003. Hepatitis B surface antigen prevalence among pregnant women in urban areas: implications for testing, reporting, and preventing perinatal transmission. Pediatrics, 111(Supplement 1), pp.1192-1197.

Ezegbudo, C.N., Agbonlahor, D.E., Nwobu, G.O., Igwe, C.U., Agba, M.I., Okpala, H.O. and Ikaraoha, C.I., 2004. The seroprevalence of hepatitis B surface antigen and human immunodeficiency virus among pregnant women in Anambra State, Nigeria. Shiraz E-Medical Journal, 5(2), pp.4-8.

Fomulu, N. J., Morfaw, F. L., Torimiro, J. N., Nana, P., Koh, M. V., & William, T. (2013). Prevalence, correlates and pattern of Hepatitis B among antenatal clinic attenders in Yaounde-Cameroon: is perinatal transmission of HBV neglected in Cameroon? BMC Pregnancy and Childbirth, 13, 158.

Gambarin-Gelwan, M., 2007. Hepatitis B in pregnancy. Clinics in liver disease, 11(4), pp.945-963.

Gasim, G.I., 2013. Hepatitis B virus in the Arab world: where do we stand?. Arab Journal of Gastroenterology, 14(2), pp.35-43

Gilson, R.J., Hawkins, A.E., Beecham, M.R., Ross, E., Waite, J., Briggs, M., McNally, T., Kelly, G.E., Tedder, R.S. and Weller, I.V., 1997. Interactions between HIV and hepatitis B virus in homosexual men: effects on the natural history of infection. AIDS, 11(5), pp.597-606.

Hahné, S.J., Veldhuijzen, I.K., Wiessing, L., Lim, T.A., Salminen, M. and van de Laar, M., 2013. Infection with hepatitis B and C virus in Europe: a systematic review of prevalence and cost-effectiveness of screening. BMC infectious diseases, 13(1), p.1.

Kapembwa, K.C., Goldman, J.D., Lakhi, S., Banda, Y., Bowa, K., Vermund, S.H., Mulenga, J., Chama, D. and Chi, B.H., 2011. HIV, hepatitis B, and hepatitis C in Zambia. Journal of Global Infectious Diseases, 3(3), p.269.

Kourtis, A.P., Bulterys, M., Hu, D.J. and Jamieson, D.J., 2012. HIV–HBV coinfection—a global challenge. New England Journal of Medicine, 366(19), pp.1749-1752

Kumar, S., Balks, M.,Williamson, C.,Castillo, E.,and Money,D.M. (2010) Disorders of the liver, biliary system and exocrine pancreas in pregnancy. In: Raymond, O.P., Micheal, F.G.,and William, C. (eds.) de Swiet's Medical Disorders in Obstetric Practice. 5th edition. 9600 Garsington Road, Oxford,OX4 2DQ, UK, 111 River Street, Hoboken, NJ 07030-5774, USA

Landes, M., Newell, M.L., Barlow, P., Fiore, S., Malyuta, R., Martinelli, P., Posokhova, S., Savasi, V., Semenenko, I., Stelmah, A. and Tibaldi, C., 2008. Hepatitis B or hepatitis C coinfection in HIV-infected pregnant women in Europe. HIV medicine, 9(7), pp.526-534.

Levy M and Koren G, 1991. Hepatitis B vaccine in Pregnancy: maternal and fetal safety. American journal of perinatology 8(03), 227-232.

Mangani, C.B., 2011. HIV and the Risk of Hepatitis B Co-infection in Sub-Saharan Africa: A Systematic Review and Meta-analysis (Doctoral dissertation, University of Malawi).

Oshitani, H., Kasolo, F.C., Mpabalwani, M., Mizuta, K., Luo, N.P., Suzuki, H. and Numazaki, Y., 1996. Prevalence of hepatitis B antigens in human immunodeficiency virus type 1 seropositive and seronegative pregnant women in Zambia. Transactions of the Royal Society of Tropical Medicine and Hygiene, 90(3), pp.235-236.

Ranger-Rogez, S. and Denis, F.O., 2004. Hepatitis B mother-to-child transmission. Expert review of anti-infective therapy, 2(1), pp.133-145.

Reddick, K.L.B., Jhaveri, R., Gandhi, M., James, A.H. and Swamy, G.K., 2011. Pregnancy outcomes associated with viral hepatitis. Journal of viral hepatitis, 18(7), pp.e394-e398.,

Rouet, F., Chaix, M.L., Inwoley, A., Msellati, P., Viho, I., Combe, P., Leroy, V., Dabis, F. and Rouzioux, C., 2004. HBV and HCV prevalence and viraemia in

HIV-positive and HIV-negative pregnant women in Abidjan, Côte d'Ivoire: The ANRS 1236 study. Journal of medical virology, 74(1), pp.34-40.

Simpore, J., Savadogo, A., Ilboudo, D., Nadambega, M.C., Esposito, M., Yara, J., Pignatelli, S., Pietra, V. and Musumeci, S., 2006. Toxoplasma gondii, HCV, and HBV seroprevalence and co-infection among HIV-positive and-negative pregnant women in Burkina Faso. Journal of medical virology, 78(6), pp.730-733.

Siame, G. 2006. Hepatitis B and hepatitis C prevalence in HIV positive pregnant women. Retrovirology,3,pp.1-1

Sullivan, K. M., Dean, A., & Soe, M. M. (2009). OpenEpi: A Web based Epidemiologic and Statistical Calculator for Public Health. Public Health Reports, 124 (3), 471–474.

Söderström, A., Norkrans, G. and Lindh, M., 2003. Hepatitis B virus DNA during pregnancy and postpartum: aspects on vertical transmission. Scandinavian journal of infectious diseases, 35(11-12), pp.814-819.

Terrault, N.A. and Jacobson, I.M., 2007, August. Treating chronic hepatitis B infection in patients who are pregnant or are undergoing immunosuppressive chemotherapy. In Seminars in liver disease (Vol. 27, No. S 01, pp. 018-024). Copyright© 2007 by Thieme Medical Publishers.

Thumbiran, N.V., Moodley, D., Parboosing, R. and Moodley, P., 2014. Hepatitis B and HIV co-infection in pregnant women: Indication for routine antenatal hepatitis B virus screening in a high HIV prevalence setting. SAMJ: South African Medical Journal, 104(4), pp.307-309.

Thio, C.L., Seaberg, E.C., Skolasky, R., Phair, J., Visscher, B., Muñoz, A. and Thomas, D.L., 2002. HIV-1, hepatitis B virus, and risk of liver-related mortality in the Multicenter Cohort Study (MACS). The Lancet, 360(9349), pp.1921-1926.

Tse, K.Y., Ho, L.F. and Lao, T., 2005. The impact of maternal HBsAg carrier status on pregnancy outcomes: a case–control study. Journal of hepatology, 43(5), pp.771-775.

World Health Organization, 2002. hepatitis B. [Online], Available: http://apps.who.int/iris/bitstream/10665/67746/1/WHO_CDS_CSR_LYO_2002.2_HEPATITIS_B.pdf, [29.02.2016, 11:27, AM]

World Health Organisation, 2015. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection.[Online], Available: http://www.who.int/hiv/pub/hepatitis/hepatitis-b-guidelines/en/. [13.04.2018, 20:30,]

Xu, D.Z., Yan, Y.P., Choi, B.C., Xu, J.Q., Men, K., Zhang, J.X., Liu, Z.H. and Wang, F.S., 2002. Risk factors and mechanism of transplacental transmission of hepatitis B virus: A case-control study. Journal of medical virology, 67(1), pp.20-26.

Zhang, L, Gui XE, Teter C, Zhong H, Pang Z, Ding L, Li F, Zhou Y and Zhang L., 2014 Effects of hepatitis B immunization on prevention of mother to infant transmission of hepatitis B virus and the immune response of infants towards hepatitis B vaccine. Vaccine. 2014 Oct 21: 32(46): 6091-7.doi: 10.1016/j. vaccine. 2014.08.078. Epub 2014 Sep 18.

Zenebe, Y., Mulu, W., Yimer, M. and Abera, B., 2014. Sero-prevalence and risk factors of hepatitis B virus and human immunodeficiency virus infection among pregnant women in Bahir Dar city, Northwest Ethiopia: a cross sectional study. BMC infectious diseases, 14(1), p.1.

APPENDICES

Appendix A: Participant information sheet

TITLE: A comparative study of the prevalence of hepatitis B in the HIV positive and negative pregnant women at the UTH, Lusaka

My name is Dr. Victor Sichone, a postgraduate student at the University of Zambia, School of Medicine. I am conducting a research on the above subject at the University Teaching Hospital (UTH), Obstetrics and Gynaecology department, as part of the requirement for the award of a Master's Degree in Medicine. I am here by inviting you to take part in this study.

PURPOSE: the study would like to find out the overall prevalence of Hepatitis B virus infection, its co-infection with HIV and the social demographics factors associated with HBV infection in pregnant women attending antenatal at UTH. The information obtained may then be used to lobby policy makers to make available routine screening of HBV in all pregnant women in Zambia, and also help allocate resources needed to prevent mother to child transmission of HBV i.e. HBV vaccine and immunoglobulin (HBIG).

EXPLANATION OF THE PROCEDURE: You have been invited to this study because you qualify to participate in this study. If you agree to take part in the study, you will be asked some questions to help us know you better while some other information concerning you, will be extracted from your medical records (antenatal card). A blood sample will be collected from you for the purpose of testing for Hepatitis B. The results for this test will be ready on your next antenatal visit and will be communicated to you. Appropriate referral to the hepatitis B experts will be made if you test positive and necessary advice will be given to help prevent infection to the baby. Participation in the study is voluntary. You are free to withdraw at any time without risk of compromising on the standard medical care. The information obtained from you will not be shared with anyone not involved in the study.

BENEFITS: You will know your Hepatitis B status and appropriate referral to the Hepatitis B experts will be made if you test positive. Advice and other necessary arrangements to prevent transmission of the HBV to the new-born will be given if found to be positive for HBV infection. Overall the information obtained will be used

to lobby policy makers to make available HBV vaccine and HBIG from the policy makers.

RISKS: Less than minimal risk such as needle prick will be encountered in this study. The procedure will be done under sterile conditions with necessary expertise.

If you agree to take part, please sign the consent form which will allow us to enroll you in this study. If you have any questions please contact us on the addresses below.

Principal Researcher

Dr. Victor Sichone

Cell: 0966 636524

University Teaching Hospital

Department of OBGY

P/Bag RW1X,

LUSAKA.

The Chairperson

UNZA Biomedical Research Ethics Committee

Phone: 0211-256067

Ridgeway Campus

P.O.BOX 50110

LUSAKA

Appendix B: Participant consent form

TITLE: A comparative study of the prevalence of hepatitis B in the HIV positive and HIV negative pregnant women at the UTH, Lusaka

I have read and understood the information concerning the study and was given an opportunity to ask questions which were answered. I therefore voluntarily consent to take part in this study.

Name:

_____

Signature: _____ Date: _____

Right Thumb Print: _____ Date: _____

Witness

Name:

_____

Signature: _____ Date: _____

Right Thumb Print: _____ Date: _____

Name of person taking consent:

_____

Signature: _____ Date: _____

Appendix C: Assent form for participants under 18 years

My name is Dr Victor Sichone, a postgraduate student from the University of Zambia, School of Medicine. I am conducting a study titled: A comparative study of the prevalence of hepatitis B in the HIV positive and negative pregnant women at the UTH, Lusaka. I am asking you to take part in this research so that we can know the prevalence of HBV at UTH. If you agree to be in this study, you will be asked some questions to complete a survey. Some of the questions will ask on sensitive issues, and may make you feel uncomfortable. You are free not to answer questions you are not comfortable with. Furthermore, no one will be able to know how you responded to the questions. Please talk about this study with your parents before you decide whether or not to participate. I will also ask your parents to give their permission for you to participate. Even if your parents give consent, you can still decide not to participate No one will be upset with you if you don't want to participate or if you change your mind later and want to stop.

You may ask me any questions about this study, feel free to call me at any time on 0966 636524 or talk to me the next time you see me.

By signing below, you are agreeing to participate with the understanding that your parents have given permission for you to take part in the study and because you want to. You and your parents will be given a copy of this form to sign as an agreement to participate in this study.

Name:

_____

Signature: _____ Date:

_____

Right Thumb Print: _____

Date:_____

Appendix D: Questionnaire

TITLE: A comparative study of the prevalence of hepatitis B in the HIV positive and negative pregnant women at the UTH, Lusaka

Initials:_____ Study no.:_____ Age: _____

Marital Status: _____ Parity: _____ Gravida_____

Please tick or enter in the appropriate space.

SOCIO-DEMOGRAPHICS

1. Education Level

0. None **( )** 1. Primary **( )** 2. Secondary **( )** 3. Tertiary **( )**

2. Are you employed?

0. Formal **( )** 1. Informal **( )** 2. Not employed **( )**

3. What religion are you?

0. Christian **( )** 1. Muslim **( )** 2. Hindu **( )** 3. Other **( )**

4. Residence (write name of place of stay) _____

0. High density **( )** 1. Medium density **( )** 2. Low density **( )** 3. Rural density **( )**

ANTENATAL CLINIC

5. What is your HIV Status (from antenatal card)? _____

6. Are you on cART?

0. Yes **( )** 1. No **( )** 2. N/A **( )**

7. If **YES** above, for how long have you been on cART? _____

1)less than 6months 2) 6-12 months 3) more than 12 months

8. Was cART started before pregnancy?

0. Yes **( )** 1. No **( )** 2. N/A **( )**

9. Hepatitis B status:_____

1) Negative 2) Positive

10. Have you ever been vaccinate against Hepatitis B Virus?

0. Yes **( )** 1. No **( )** 2. I don't know **( )**