HEPATITIS B VIRUS INFECTION AMONG ANTENATAL CLINIC ATTENDEES AT THE MUHIMBILI NATIONAL HOSPITAL, SEROPREVALENCE AND ASSOCIATED FACTORS

BY

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A dissertation submitted in partial fulfillment of the requirements for the degree of Master of Medicine (Obstetrics and Gynaecology) of the Muhimbili University of Health and Allied Sciences (MUHAS)

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation entitled: **"Hepatitis B Virus infection among Antenatal Clinic attendees at the Muhimbili National Hospital, Seroprevalence and Associated factors,"** in partial fulfillment of the requirements for the degree of Master of Medicine (Obstetrics and Gynaecology) of the Muhimbili University of Health and Allied Sciences

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DEDICATION

This book is dedicated to my husband Nassor and my children Nahir, Satra and Nadir

ABSTRACT

Background:

Hepatitis B virus (HBV) infection is a serious public health problem in sub-Saharan Africa. Vertical transmission is one of the modes of transmission. The risk of transmission increases if the mother is hepatitis B surface antigen (HBsAg) positive and more so if also hepatitis B envelope antigen (HBeAg) positive. Current magnitude of HBV infection at Muhimbili National Hospital MNH is not known, and could be on the increase due to the HIV epidemic, since the two have a shared mode of transmission.

Objectives:

To determine the seroprevalence of HBV infection and associated factors among pregnant women attending Antenatal Clinic at Muhimbili National Hospital.

Methodology:

This was a cross-sectional study conducted at the Antenatal Clinic, Muhimbili National Hospital between 31stAugust and 22nd September 2010. Data including socio-demographic (age, residence, marital status, education level, occupation) sexual history (number of life-time sexual partners), obstetrics (parity) and history of blood transfusion were collected using a structured questionnaire. Blood specimen was collected for detection of HBsAg, HBeAg, IgM antibodies to hepatitis B core antigen (Anti-HBc), antibodies to hepatitis B surface antigen (anti-HBs) and HIV antibodies. Ethical clearance and informed consent were obtained prior to the enrolment in the study. Data were analyzed using the SPSS version 16.0. Fisher's exact tests were used for analysis. A p-value of <0.05 was regarded as statistically significant.

Results:

A total of 310 pregnant women were enrolled in the study. Their overall mean (SD) age was 28.5 (5.4) years. Majority of the women were from the Kinondoni Municipality, married and had primary education. Ninety-six (31.0%) of the women were primigravidae.

Of the 310 women 12 (3.9%) tested positive for HBsAg. Of the 12 women with positive HBsAg, none had detectable anti-HBs antibodies. None had IgM HBcAb, excluding acute HBV infection. In addition, all these women tested negative for HBeAg. The prevalence of HIV infection was 9.7%. Three of 12 (25%) women had HBV and HIV co-infection.

There were no significant differences between those who tested positive and those who tested negative to HBsAg with respect to age, residence, marital status, education level, occupation and parity.

Similarly, there were no statistically significant differences noted between the two groups with regard to number of life-time sexual partners, HIV serostatus and history of blood transfusion.

Conclusion and Recommendation

The seroprevalence of 3.9% HBsAg was of moderate severity according to WHO. This finding would suggest for the introduction of routine screening for HBV to all pregnant women during the antenatal period, and that “at birth dose” vaccination is given to new born babies of mothers found to be HBsAg positive so as to reduce and prevent the spread of infection. However more data is required from larger studies to support the findings so that ultimately this can be recommended as a policy

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LIST OF ABBREVIATIONS/ACRONYMS

AIDS = Acquired Immunodeficiency syndrome

ALAT = Alanine aminotranferase

ART = Anti retro viral therapy

DPT= Diphtheria, pertusis and Tetanus

ELISA = Enzyme linked Immunosorbent assay

HAV = Hepatitis A Virus

HBV = Hepatitis B Virus

HbeAg= Hepatitis B envelope antigen

HbeAb=Hepatitis B envelope antibodies

HBsAg = Hepatitis B Surface Antigen

HBcAg= Hepatitis B core antigen

HBcAb = Hepatitis B core Antibody

HCV = Hepatitis C Virus

HIV = Human Immunodeficiency Virus

IgM = Immunoglobulin M

IgG = Immunoglobulin G

MNH = Muhimbili National Hospital

MUHAS = Muhimbili University of Health and Allied Sciences

NACP= National AIDS Control Program

PCR= polymerase chain reaction

WHO= World Health Organization

1.0 INTRODUCTION

The World Health Organization (WHO) considers hepatitis B virus (HBV) to be second to tobacco among the carcinogens [(1)]. Hepatitis B infection is caused by HBV which is a DNA virus belonging to a family called *Hepadnaviridae* which can cause acute or chronic infection [(2)]. It is estimated that 2 billion people worldwide have been affected of which 350 million people have chronic infection, and 10% of these are in sub-Saharan Africa and East Asia [(1, 3)]. These chronically infected patients may develop complications of liver cirrhosis and hepatocellular carcinoma.

The clinical manifestations of HBV infection in acute infection are either prodromal, or icteric and recovery [(2)]. After the incubation period which varies depending to the type of virus, patients clinically present with chills, headache, nausea, vomiting and may precede jaundice(2-4). The liver becomes tender and enlarged with a right upper quadrant pain. Splenomegaly and adenopathy may also occur in 10% to 20% of cases [(2)]. The recovery to normality clinically and biochemically is a rule in Hepatitis A Virus (HAV) and in almost all HBV infections [(2, 3)]. However, some do remain chronically infected especially with HBV and HCV and may progress to liver cirrhosis and, or to hepatocellular carcinoma[(2, 3)]

Reported consequences of HBV infection in pregnancy include an increased likelihood of occurrence of pre-term delivery and low birth weight [(4)]. Furthermore, HBV infection has been

reported to be associated with threatened preterm labour, antepartum haemorrhage as well as gestational diabetes mellitus [5]

Chronic HBV infection in pregnant women is usually asymptomatic but can be associated with mild liver disease. The outcome depends on the severity of disease and presence of portal hypertension, whose presence indicates poor long term prognosis. In that case, abortion and sterilization should be opted for [4]

Hepatocellular carcinoma is rare in pregnancy due to the late age of presentation in females, the known male predominance, and the decrease in fertility in women with cirrhosis. Oral contraceptives and high parity are known to be at an increased risk. Furthermore, pregnancy is known to worsen the prognosis of patients with hepatocellular carcinoma [6]

The effects of pregnancy on clinical course of HBV infection have been reported to vary from being not altered by pregnancy[4], to exacerbation of disease to fulminant hepatic failure during the peripartum period [7]. Furthermore, alanine aminotranferase (ALAT) and HB viral load have been noted to increase not only postpartum but even in late pregnancy [8]. A follow up study done in Taiwan concluded that subsidence of HBV replication is precipitated by delivery [9]

Diagnosis of HBV infection is confirmed by demonstrating specific antibodies and/or antigen in serum of patients [1]. The most important laboratory test for diagnosis of HBV infection is

HBsAg which is the first antigen to appear, and appears during the incubation period, the prodrome, as well as during acute disease [2, 10]. It appears after infection and disappears after one to two months following jaundice. During convalescence it falls to undetectable levels and if it persists for more than 6 months then this indicates a carrier state and a risk for chronic hepatitis and hepatocellular carcinoma [10]. Presence of HBsAg means that the patient is potentially infectious. Antibodies to HBsAg (Anti-HBs) replace HBsAg as the acute infection resolves, and this indicates immunity in almost 80% of cases after the acute infection [4] This Anti-HBs also appears after HBV vaccination. Some lose these antibodies that are acquired after acute HBV infection and may become susceptible to disease HBV [2]

During the window period, and when the HBsAg has disappeared and HBsAb has not yet appeared, Hepatitis B core antibody (HBcAb) is detectable and can be used for diagnosis. Acute or chronic infection can be differentiated by the presence of Immunoglobulin M (IgM) to HBcAg in acute infection, and Immunoglobulin G (IgG) in chronic infection [2] After the appearance of HBsAg in one or two weeks, the HBcAb starts to be detectable. Very rarely HBcAg will be detected since it is within the HBsAg.

Investigations to be done among patients with HBV infection include the demonstration of Hepatitis B e antigen (HBeAg) which arises during the incubation period, prodrome, acute and to certain patients with chronic phase. It is an important indicator of transmissibility and is replaced by HBeAb, whose presence indicate low transmissibility [10]. DNA polymerase is detected during the incubation period and early in the disease, and is a more sensitive and

quantitative test (for the detection of viral load), although it is very expensive as it needs PCR [4]. Estimation of serum transaminases could also be done, which typically rises from 400 to 4000U/L. Similarly, bilirubin also usually rises in clinical jaundice [4].

In Tanzania the prevalence of HBsAg among pregnant women was reported to vary between 3.5%[11], and 6.3% [12]. However in a neighboring country of Kenya data suggests an increase in prevalence over time to a figure of 9.3% in 2001/2002 [13].

Another study suggested that HIV infected individuals have a higher prevalence of hepatitis B. Co-infection with HIV was reported in 66.7% of the 120 HIV infected pregnant women as compared to 49% among the 157 HIV negative patients [14]. The noted increase in prevalence over time, as well as the high prevalence among HIV infected patients may suggest that there was an influence of HIV on the seroprevalence of HBV. Since HIV is still a public health problem in Tanzania, it is important to have up to date data of HBV infection among pregnant women. The information is also important in relation to the adoption of recommendations made by WHO on screening of pregnant women and offering the at-birth-dose of HBV vaccine to prevent perinatal transmission for those mothers who test positive.

2.0 LITERATURE REVIEW

The reported prevalence of HBV infection among pregnant women in African countries ranges from 6% to 25% (WHO meta-analysis done 2007). However, a study done in Nigeria showed the prevalence to be 4.3%.[15], while in Sudan the prevalence was 5.6% [16]. The reported prevalence of HBsAg in Kenya was 9.3%, while that of HBeAg was 18.8% in a study done in 2001-02. It was concluded in that study that there was a high carrier rate, and it also questioned on the results from the previous studies which reported low prevalence [13].

Tanzania was reported to be one of the countries with high endemicity levels of HBV infection according to the World Health organization WHO. This is defined as a prevalence rate equal to or greater than 8% [1]. In the year 1987, the HBsAg carrier rates in Tanzania were estimated to be 10% and 15% among the general population and pregnant women respectively [17].

Apart from prevalence of 3.5%[11] and 6.3% [12] reported among pregnant women in studies done in mid 1990's, a figure as high as 56.7% was reported by Shao et al in a study done in 1989[14]. In the same study, the seroprevalence of HBsAg in HIV infected pregnant mothers was found to be 66.7% [14]. Matee et al found the prevalence of HBsAg to be 11.0% among blood donors [18] while Nagu found 17.3.% among HIV patients at MNH [19].

Pregnant women are not spared from HBV infection in which case the great concern is that their babies may also be affected. Indeed it is reported that 70%-90% of chronic HBV

infections occur following the acute infections taking place during childhood [2]. In a previous study done by Kibassa et al among pregnant women in Dar es Salaam it was found that the rate of vertical transmission was 11.8% [11]. In another study done in Southern Tanzania the reported perinatal transmission was 8% [12]. Fortunately HBV vertical transmission can be prevented by immunization, and indeed universal immunization has been recommended by WHO since 1991 [1]. In Tanzania universal immunization was introduced in 2002 whereby hepatitis B vaccine is given to infants in combination with diphtheria pertussis tetanus (DPT) at 4,8 and 12 weeks of age [20] .

This is also true in most other countries where the immunization schedule of vaccination against hepatitis B is in combination with DPT vaccination and is given at 4th week of life followed by 2 other doses given at a monthly interval. The WHO has reported that this does not prevent perinatal transmission and hence advised on a 3 doses schedule or a 4 doses schedule [1]. According to the WHO, HBV vaccination for prevention of perinatal transmission needs the first dose to be given within 24 hours of delivery (before the mother has been discharged home). Consequently, routine antenatal screening for HBsAg to all pregnant women, followed by vaccination of their babies at birth has been recommended by WHO [1]. A study done in Cuba showed 95.9% to 99.3% effective prevention of HBV infection if the “at birth” dose of vaccine was given after screening pregnant women for HBsAg [21]. However, in a previous study done in India, 2.25% of children under five were found to be positive for HBsAg despite immunization, and no statistically significant difference was observed between the age groups, suggesting that most of the infections occurred via vertical transmission [22].

In Tanzania Metodi J et al found that 69.3% of the immunized underfive children had HBsAb level>10mIU/mL, a level considered protective. On the other hand, 1.7% of the underfives were found to be HBsAg positive suggesting that vertical transmission occurred despite immunization [23]. The study recommended that a change in hepatitis B vaccination schedule including at birth dose would raise the level of immunity and thus offer protection. Since a post exposure vaccination could break the chain of transmission, identifying children born to HBsAg mothers is very important.

The main modes of transmission of HBV are via blood, during sexual intercourse and perinatally [2]. Vertical transmission from mother to infant in the perinatal period is a major mode of transmission in regions where hepatitis B is endemic through ingestion of maternal fluids (amniotic fluid, vaginal secretions, and blood (2-4). Transplacental transmission is reported to be low, even to those infected mothers on whom amniocentesis has been done to [24, 25]

Although the risk of transplacental transmission is rare, it is known to be increased among HBeAg positive mothers as well as those with high HBsAg titre and HBV DNA level [26]. Some studies suggest that breach of placental barrier could be the cause[27].

With regard to breast feeding the transmission is low and hence it is recommended that HBV infected mothers should be allowed to breastfeed [28].

It is also known that transmission can occur among intravenous drug users, homosexuals, health care personnel, as well as those who receive frequent blood transfusion such as haemophilic patients [2, 3]. A study done in Barcelona showed that there was a higher prevalence among intravenous drug users of 22.5%, whereas among the non intravenous drug users the prevalence was 7.4% [29].

Other factors reported to be associated with acquisition of HBV include increasing age, male gender, low level of education and history of previous surgery, multiple sexual partners, HIV infection, and non use of condoms [30, 31]

Among pregnant women high parity, polygamy, multiple sexual partners and previous history of sexually transmitted disease were shown to be among the significant risk factors for HBV infection in Nigeria [32]. In a study done by Kibassa et al the prevalence showed no association with marital status, previous history of jaundice, history of blood transfusion and age [11]

Since HIV and HBV share the modes of HIV transmission, it is plausible that HBV and HIV co-infection can occur, and this has been documented. Co-infection in Tanzania among HIV infected patients was found to be 17.3% among patients attending the Care and Treatment centre at the MNH [19].

HIV/AIDS is a major global health problem. By the end of 2009, it was estimated that 33.3 million people worldwide were living with HIV and AIDS. Sub-Saharan Africa is the world most severely affected region[33].

In Tanzania As reported in the HIV-AIDS-STI surveillance report of 2009, the overall prevalence of HIV in the general population is 6.5% (7.7% among adult women, and 6.3% among adult male). The prevalence in urban Tanzania is 10.9%, while that in rural areas is 5.3%. [34]. Approximately 30% of these are in need of ART.

Heterosexual sex is the main mode of transmission accounting for 85.0% of all reported cases in 2008. Mother to child transmission was less than 6.0% and blood transfusion was less than 1.0%[34].

Hepatitis B and co-infection with HIV in pregnant women could occur since the modes of transmission are shared. A study done among pregnant women showed that one out of sixteen HIV infected had HBV infection as well. In this study HBV co-infection was also associated with low CD4 count[35]. In Tanzania 66.7% of the 120 HIV positive pregnant women were also positive for HBV, while only 49% of the 157 HIV negative group were HBV positive [14]. On the other hand, in Malawi 71.7% were co-infected [36]. Another study done in Burkina Faso compared co-infection among HIV infected and those who were not and reported the prevalences of 11.6% and 7% respectively [37]. As shown above co-infection is common and also the prevalence is higher among those who are HIV infected compared to non infected ones.

3.0 PROBLEM STATEMENT

HBV infection is a serious public health problem in Sub-Saharan Africa. Tanzania is categorized as a country of high level of endemicity of HBV infection. Current magnitude of HBV infection could be on the increase due to HIV epidemic. Vertical transmission from the mother to the child is one of the major modes of transmission. The rate of transmission increases if the mother is HBsAg positive and even more if she is also HBeAg positive. Furthermore, HBV infection does pose a risk not only to the mother and her newborn but also the sexual partners and health workers as well.

Despite recommendations proposed by WHO since 2002 of screening pregnant women against HBV and universal immunization of all infants against HBV infection[(1)], routine screening of HBV among pregnant women is not practiced in the country and we don't have recent data on the magnitude of the problem. The last study was done more than 10 years ago. Hence recent data is lacking, and this could be influenced by the HIV endemicity which has a shared mode of transmission with HBV. The study done in Kenya 2001-2002 has reported an increase in prevalence of HBsAg and of HBeAg [(13)].

There was thus a need for a study in our setting to get a clearer picture of hepatitis B virus infection in this era of HIV.

4.0 RATIONALE

The introduction of routine hepatitis B screening among pregnant women requires updated data on the magnitude of HBV infection among these women. HBV infected pregnant women are at risk of infecting their babies with a consequence of developing fulminant HBV infection. This can be prevented by giving vaccination against HBV to babies born by mothers who are HBsAg positive immediately after delivery. Current data on the magnitude of HBV among pregnant women in Tanzania is limited including at MNH. This study has provided data on the magnitude of the problem and came out with recommendations for possible measures to be taken.

5.0 OBJECTIVES

5.1 Broad Objective

To determine the seroprevalence of HBV infection and associated factors among pregnant women attending antenatal clinic (ANC) at Muhimbili National Hospital (MNH).

5.2 Specific Objectives

1. To determine the seroprevalence of HBsAg among pregnant women attending ANC at MNH.

2. To determine the seroprevalence of HBeAg among pregnant women attending ANC at MNH

3. To determine the association of social-demographic factors and hepatitis B infection (HBsAg positivity) among pregnant women attending ANC at MNH.

4. To determine the association of previous blood transfusion, number of sexual partners and HIV infection with hepatitis B infection among pregnant women attending ANC at MNH.

6.0 METHODOLOGY

6.1 Study area

This study was conducted at the ANC MNH. MNH is the national hospital of Tanzania located in Dar es Salaam. The ANC at the hospital is conducted between Tuesdays and Fridays. Each of the four firms in the department of Obstetrics and Gynaecology has a specific day of the week to run the ANC. On average, 40 non-paying (public) and 80 paying (private) women per day were attended at the ANC during the study, of whom 75% were pregnant women and 25% were attended for a postnatal follow up. Most of these pregnant women would come for a follow up visit more than once per month, while a few are new attendees. On average 20 pregnant women attended for a follow up visit, and 6 were new attendees in each day of the clinic. Among the usual services provided at the ANC are health education given by Nurses, who also record weights and blood pressure readings at each visit. These are done before the patient enters a Doctor's room. Routine screening for syphilis, blood groups, Rhesus factor, and haemoglobin level determination are also provided. Counseling and screening for HIV, as well as drugs for the prevention of maternal to child transmission of HIV are provided. Presently there are no screening services for HBV during antenatal clinic.

Paying (Private) pregnant mothers were not included in the study, as most were reluctant to be recruited. These are often Doctor-centred and prefer to be attended by their private Doctors and are usually non-cooperative when it comes to be attended by others.

6.2 Study design

This was a hospital based cross-sectional study.

6.3 Study population.

The study population was all pregnant women attending ANC at Muhimbili National Hospital.

6.4 Study Period

The study was conducted between 31st August 2010 and 22nd September 2010.

6.5 Sample size

Sample size for this study was calculated using the formula for cross-sectional study. Based on the 9.3% prevalence of HBsAg infection among pregnant women in the study done in Kenya (13), the formula is:

$n= z^2 p (1-p)/ \varepsilon^2$

Where n =expected minimum sample

z = standard, corresponding to 95% confidence; 1.96

P= prevalence of Hepatitis 9.3%

ε = maximum likely error taken as 4%

Hence, minimum sample size calculated was 202, approximately 310 (after adding 10% for non responders, and adding 10% for the 3 risk factors to be studied)

6.6 Sampling technique

Mothers attending the ANC (excluding those attending for post-natal reasons, and those who were private patients) were consecutively enrolled until the desired sample size was reached. The Research Assistants and researcher did not want to interfere with the flow of the mother in receiving antenatal care. Therefore, the first three women coming from each of the doctors were asked to participate in the study by the two Research Assistants and the investigator. Following their consent, each was interviewed individually and blood sample was taken. A Research Assistant ensured that all mothers coming out of Doctor's rooms were appropriately directed for study inclusion. The research assistants or the researcher picked another woman after finishing the previous one. This continued until the end of the non-paying clinic.

6.7 Data collection methods

Mothers who consented to participate were subjected to a face-to-face interview with the investigator/assistant whereby pre-test counseling was done, and then the questionnaire was filled in to obtain information on socio-demographic characteristics, previous history of blood transfusion and number of sexual partners. Hospital registration number, party, and HIV test results were recorded from the participant's antenatal card. After this a venopuncture was performed and blood collected in a vacutainer tube. Five mls of blood was collected for Hepatitis B serology. Additional 5 mls were taken for HIV testing in those with no HIV test results in their antenatal cards.

A mark was put in the clinic card of all enrolled mothers to avoid repeat inclusions during their subsequent visits.

6.8 Laboratory investigations

Serological testing for HBV was performed at the Central Pathology Laboratory (CPL) at MNH except for determination of HBeAg which was performed at a private hospital (TMJ Hospital). Testing for HIV was performed by the nurse counselors at the MNH ANC.

6.8.1 HBsAg assay

This was performed using microparticle enzymes immunoassay (MEIA) (Abbott/AxSYM, Germany). The presence or absence of HBsAg in the sample was determined by comparing the rate of formation of fluorescent product in the test sample to a cut-off rate determined from previous AxSYM HBsAg mean index calibrator rate. Samples with an index greater or equal to the cut off rate were considered reactive for HBsAg.

6.8.2 HBeAg assay

This was performed using an enzyme-linked fluorescent assay (VIDAS® HBe/Anti-HBe system Biomerieux, France). The results were reported as positive or negative.

6.8.3 Anti-HBc IgM assay

Anti-HBc IgM antibodies were measured using MEIA core (Abbott AxSYM, German). The detection of IgM was done by comparing the rate of formation of fluorescent product in the test sample to the mean index calibrator rate. The value of >1.20 was regarded as reactive for anti-HBc IgM.

6.8.4 Anti-HBs or Anti-HBsAb assay

Anti-HBsAb was determined using MEIA Ag (Abbott/AxSYM Germany). If the concentration of the sample was ≥10 mIU/ml, sample was regarded as having protective antibody levels.

6.8.5 Rapid HIV assays

HIV serostatus was determined using the National rapid HIV testing algorithm. Samples were initially tested with SD HIV-1/2 3.0 Bioline followed by testing of reactive samples on Determine HIV-1/2 test. Sera that were reactive on both tests were considered HIV positive. Discordant results were resolved by a tiebreaker Uni-Gold test.

HIV results were issued to the pregnant women immediately after post-test counseling. Laboratory results for HBsAg, HBcAg IgM, anti-HBsAb, HBeAg were given to the patients either during the next ANC attendance or by special appointments made through phone calls.

6.9 Statistical methods

Data was entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 16.0. The determined proportions were compared using Fishers exact test. A p-value of <0.05 was regarded as significant.

6.10Ethical Considerations

Ethical approval for the study was given by Muhimbili University of Health and Allied sciences (MUHAS) Ethics Committee and permission from MNH management to use patients from the ANC was granted as well.

Information about the study (appendix 1) was delivered to patient and consent obtained then face to face interview was conducted. Informed written consent was obtained from the pregnant women who agreed to participate in the study (appendix 1). For those whose HIV status was not known pre test counseling for HIV was given. Those found to be HIV positive were offered the prevention of mother to child transmission (PMTCT) regimen (Zidovudine 300mg twice daily from 28 weeks of gestation). Those eligible for antiretroviral therapy were referred to the Care and Treatment Clinic (CTC) at MNH for further management. Mothers found to be HBsAg positive were given post test counseling and then referred to the MNH medical clinic for further management (where they were investigated and managed accordingly). Those who were found to be HBV negative or HIV negative, an emphasis on preventive measures was offered. Neonates of those mothers found to be positive for HBV can only be given at birth vaccination to prevent perinatal transmission, however this was not available.

7.0 RESULTS

During the study period of between 31st Aug 2010 and 22nd Sept 2010 a total of 330 pregnant mothers attended the ANC. Out of these, 20 were excluded for various reasons including 2 refusals to be HIV tested and 18 refusals to participate in the study. Three hundred and ten mothers were enrolled in the study. Of the 310 enrolled pregnant women, 12 had positive hepatitis B surface antigen (HBsAg). The Seroprevalence of HBsAg was thus 3.9% (95% CI of 2.1-6.8). The level of anti-HBs antibodies was not detected in all the twelve women who tested positive for HBsAg.

All enrolled mothers had their HIV test results documented in their ANC card, except three of them who were tested at the clinic and all were HIV negative.

Table1. Baseline characteristics of pregnant women who were enrolled in the study. (N=310)

Characteristic	n (%)
Age (years)	
15-20	17 (5.5)
21-30	195 (62.9)
30 and more	98 (31.6)
Residence	
Kinondoni	131 (42.3)
Ilala	105 (33.9)
Temeke	70 (22.6)
Others	4 (1.3)
Marital status	
Single	22 (7.1)
Cohabiting	18 (5.8)
Married	269 (86.8)
Divorced	1 (0.3)
Level of Education	
Non-formal	3 (1)
Primary	158 (51)
Secondary	104 (33.5)
College and university	45 (14.5)
Occupation	
Health sector	23 (7.4)
Petty trader	89 (28.7)
Housewife	119 (38.4)
Non employed	20 (6.5)
Formal employed	45 (14.5)
Others	14 (4.5)
Parity	
0	96 (31)
1-5	213 (68.7)
6 and more	1 (0.3)
History of life-time sexual Partners	
1	168 (54.2)
2-3	119 (38.4)
4 and more	23 (7.4)

The baseline characteristics of the study population are summarized in table 1. The overall mean (SD) age was 28.5 (5.4) years. Of the 310 pregnant women who were studied, 195 (62.9%) were in the age group of 21-30 years, Majority of the women were from the Kinondoni Municipality, were married and had primary level of education. Only Forty-five (14.5%) women had formal employment.

Ninety-six (31.0%) of the women were primigravidae. More than half of the women had one life-time sexual partner.

The sero prevalence of HIV infection was found to be 9.7%.

Table 2. Association between Socio-demographic characteristics of the study participants and HBsAg serostatus (N=310).

Characteristic	Total (100%)	HBsAg +ve n (%)	HBsAg –ve n (%)	p-value
Age (years)				
20 or less	17	-	17 (100)	
21-30	195	10 (5.1)	185 (94. 9**)**	
30 and more	98	2 (2)	96 (98)	0.497
Residence				
Kinondoni	131	5 (3.8)	126 (96.2)	
Ilala	105	3 (2.9)	102 (97.1)	
Temeke	70	4 (5.7)	66 (94.3)	
Others	4	-	4 (100)	0.701
Marital status				
Single	22	-	22 (100)	
Cohabiting	18	-	18 (100)	
Married	275	12 (4.5)	257 (95.5)	
Divorced	1	-	1 (100)	0.82
Level of Education				
No formal	3	-	3 (100)	
Primary	158	5 (3.2)	153 (96.8)	
Secondary	104	6 (5.8)	98 (94.2)	
University/collage	45	1 (2.2)	44 (97.8)	0.644
Occupation				
Health sector	23	-	23 (100)	
Petty trader	89	7 (7.9)	82 (92.1)	
House wife	119	1 (0.8)	118 (99.8)	
Not employed	20	1 (5)	19 (95)	
Formal employed	45	3 (6.7)	42 (93.3)	
Others	14	-	14 (100)	0.073
Parity				
0	96	4 (4.2)	92 (95.8)	
1-5	213	8 (3.8)	205 (96.2)	
6+	1	-	1 (100)	1.00

There were no significant differences between those who tested positive and those who tested negative to HBsAg with respect to age, residence, marital status, education level, occupation and parity. (Table 2)

Table 3. Sexual history, HIV serostatus and history of blood transfusion in relation to HBsAg serostatus among the study participants (N=310)

Characteristic	Total (100%)	HBsAg +ve n (%)	HBsAg -ve n (%)	p-value
No. of Sexual partners				
1	168	4 (2.4)	164 (97.6)	
2-3	119	7 (5.9)	112 (94.1)	
4 and more	23	1 (4.3)	22 (95.7)	0.239
HIV sero status				
Positive	30	3 (10)	27 (90)	
Negative	280	9 (3.2)	271 (96.8)	0.099
History of blood transfusion				
Yes	36*	-	36 (100)	
No	274	12 (4.4)	262 (95.6)	0.373

*nb: Of these 36 women, 25 (69.4%) received blood transfusion once; while the remaining had two or more blood transfusions.

This table compares the sexual history, history of blood transfusion and HIV status between pregnant mothers who tested positive for HBsAg and those who tested negative.

No statistically significant differences were noted between the two groups in terms of number of life-time sexual partners, HIV serostatus and receipt of blood transfusion by the HBsAg serostatus.

Hepatitis Be antigen and HBcAb

All of the 12 pregnant women who tested positive for HBsAg were found to be negative for the HBeAg. Furthermore, they all tested negative for the IgM form of HBcAb, implying that none had acute HBV infection. However, for financial reasons, antibodies against HBeAg were not tested.

8.0 DISCUSSION

This study has found that the seroprevalence of HBsAg among pregnant women at MNH was 3.9%. None of the pregnant women had acute HBV infection. None had detectable antibodies against HBsAg indicating that these women had chronic HBV infection. This level of seroprevalence is in agreement with findings from a previous study, conducted almost 14 years ago, among pregnant women presenting in the labour ward at the same hospital whereby the seroprevalence for HBsAg was 3.5% [(11)]. In the same study, it was found that the overall prevalence of HBsAg in Dar es Salaam city was the same as that found at the MNH [(11)]. The findings of this study indicate that the seroprevalence of HBsAg at the MNH has remained fairly stable over the past 14 years. This relatively stable seroprevalence of HBsAg found among pregnant women over time could possibly be explained by the routine HIV and syphilis screening during antenatal period (which includes pre and post test counseling that includes prevention of sexually transmitted diseases) and strengthened campaigns against HIV, diseases with has a shared mode of transmission with that of HBV. A decrease in HIV incidence from 0.64 in 2001 to 0.54 in 2009 has been reported [(38)]. The overall HIV prevalence in adults was 5.6% in 2009 compared to 7.1% in 2001 [(38)]. The other reason could be the fact that since the emergency of HIV infection all blood transfusion throughout the country is presently subjected to rigorous screening measures for HIV and HBV infections through national blood transfusion services and thus reducing the risk of HBV transmission to recipients of donated blood. In Tanzania, the National Blood Transfusion Services (NBTS) was established in 2004 with the aims of ensuring availability of safe blood and blood products for transfusion. The strategy of blood donation is focused on getting donors at low

risk of HIV, voluntary non-renumerated blood donors, and gradual discouragement of replacement/family donors due to the high-risk of transfusion transmissible agents in replacement/family donors[39]. The use of antiretroviral therapy that contains lamivudine in the country could also possibly contribute to the observed lower prevalence of HBV. Earlier studies have documented the effectiveness of lamivudine in treating chronic infection and also prevention of perinatal transmission [40, 41]. Use of ART among HIV infected patients of whom the majority were women at the MNH has shown that there is an improved access to HIV care and treatment [42], and there is high adherence to ART[43].

It should also be appreciated though that the seroprevalence of HBsAg of 3.9% as reported in the present study is regarded as being of moderate level of HBV infection as per the WHO classification of assessing severity of HBsAg infection in HBV endemic countries. WHO defines low prevalence to be <2%, moderate prevalence as 2-8%, and high prevalence as >8% HBsAg positivity. The WHO therefore recommends universal immunization of all infants to be adopted by all countries irrespective of HBsAg prevalence[1].

Despite the finding of a relatively stable prevalence of HBsAg as found in this study, it is important to note that there has been a report of increasing seroprevalence from a neighboring country. A study conducted in Kenya in 2001-2002 among pregnant women by Okoth et al reported such an increase in HBsAg seroprevalence. Factors that were thought to lead to the increase of seroprevalence were low socio-economic status and female genital mutilation in some provinces in Kenya. Furthermore, in this Kenyan study the consequent perinatal transmission of HBV infection was reported to be high, despite a low HBe antigenaemia of

8.8%, and therefore a high risk of later chronic carrier state and attendant long-term sequalae of chronic liver disease and hepatocellular carcinoma[13]. The fact that female genital mutilation is relatively rare in Dar es Salaam [44], could possibly explain the differences in findings between the current study and the above quoted Kenyan study.

Previous studies conducted at MNH reported higher HBV seroprevalence levels among other populations. The prevalence among blood donors was reported to be 11% [18]. On the other hand, the HBV prevalence among HIV infected patients in 2006 was 17.3% [19]. The national HBV prevalence among blood donors has ranged between 7.1% to 6.1% between 2006 and 2008[45]. The differences from the present study are probably due to the fact that the populations studied are inherently different.

It is known that infection with HBV is predominantly a problem of the resource-limited countries. Whereas the prevalence of HBsAg among pregnant women at a tertiary hospital in the eastern part of Germany was 0.48% [46]. A much higher prevalence of 11.0% has been reported from Guiana [47]. Infection with HBV among pregnant women has been reported in a number of African countries. In Nigeria, the seroprevalence among 1,052 attendees of ANC was reported as 6.08% [48]. On the other hand, HBsAg was detected in 1.5% (23/1,500) pregnant women in Libya [49].

It was found out in this study that all of the 12 women who were HBsAg positive were HBeAg negative. It is known that presence of HBeAg is an important indicator of transmissibility of HBV infection from the mother to the baby [1]. It follows therefore that all these women could

have a low probability of infecting their new born babies or their sexual partners. On the other hand, the presence of antibodies against HBeAg is known to indicate that the person is not infectious at all [(1)]. This could not be done for these women due to financial resources.

Reported rates of vertical transmission of HBV and seroprevalence of HBeAg in Tanzania and neighboring countries are varied. The study by Kibassa et al in Dar-es-salaam reported the rate of vertical transmission of HBV to be 11.8%, but the presence of HbeAg was not detected [(11)]. A study in Kenya reported the prevalence of HBeAg to be 8.8% [(13)]. On the other hand, a study done by Haukenes et al on HBV markers in pregnant women in Dar-es-salaam in 1975 reported that none of the HBsAg positive pregnant women were positive for HBeAg similar to the findings of the current study[(17)].

Chronic carrier state of HBV infection has been associated with the finding of negative HBeAg [(1).] On the other hand, the detection of HBeAg increases the chance of transmissibility of HBV. However, the lack of detection of HBeAg per se should not be taken as indicating total lack of HBV transmissibility. Rather, the presence of HBV infection in pregnant women can lead to the spread and acquisition of infection to newborn babies. It is reported that the perinatally acquired infections account for about 90% of all cases of HBV globally, and can lead to a chronic carrier state and other long-term sequalea [(1)]. It was also found in this study that none of the women had anti-HBsAg antibodies indicating that they were chronically infected.

In order to prevent chronic HBV and hepatocellular carcinoma the WHO has recommended universal immunization, for it is known that the lack of administration of protective antibodies to newborn babies results in the development and progression of the chronic diseases. In Tanzania, vaccination against HBV infection was introduced in 2002 and has been continuing since then. The vaccine is provided together with DPT to babies as 3 doses given at 4, 8 and 12 weeks of age[1, 20]. Despite these efforts, a study done by Metodi J et al in 2008 reported that only about 69.3% of the underfives had protective antibodies post immunization (≥10 mIU/ml), and 1.7% of them were indeed found to be HBsAg positive signifying that perinatal transmission occurs despite the immunization given. These findings from the study by Metodi, and the findings of the current study that HBsAg seroprevalence is still of moderate intensity suggest that it will be beneficial to have routine screening of mothers during the antenatal period so that those found to be HBsAg positive should have their babies administered an at birth dose of vaccination[23]. At birth dose of anti-serum and/ or immunoglobulin gives immediate protection to the newborn babies born to HBsAg positive mothers [1].

It was found in this study that none of the HBsAg positive pregnant women had IgM form of HBcAb, implying that none had acute HBV infection. The IgM form of HBcAb is present during acute infection and tends to disappear approximately 6 months after infection[1]. It is therefore difficult to determine the time point at which these pregnant women became infected with the HBV.

This study found that 3 (25%) of the 12 pregnant women with HBsAg were co-infected with HIV. Indeed, HBV-HIV co-infection has been reported previously. A study done among pregnant women showed that one out of sixteen HIV infected had HBV infection as well [35]. A previous study done in Tanzania reported the prevalence of 66.7% of the 120 had co-infection, while only 49% of the 157 HIV negative group were HBV positive [14]. On the other hand, in Malawi 71.7% were co-infected [36] and in Burkina Faso 11.6% had co-infection [37]. As shown above co-infection is common and also the prevalence is higher among those who are HIV infected compared to non infected ones.

Similar co-infections have also been reported in other study populations, such as the finding of 17.3% by Nagu et al among HIV infected patients in MNH [19]. This is not surprising given their common mode of acquisition. Despite an attempt by this study, no clear risk factors including HIV associated with HBV infection could be established. This is because the study was not powered to demonstrate this

9.0 Study limitations

This study was limited by the fact that it is a hospital based study and that mothers attending the ANC at this tertiary level hospital are a select population of those likely to have obstetric complications. Hence the results can't be generalized for the whole country. Furthermore, the exclusion of private patients could also affect the generalization of findings. This is however minimized by the fact that non-paying patients are a mixture of mothers from low as well as

high socioeconomic status. However, the findings of this study have adequately shed light into the problem of hepatitis B infection among pregnant mothers in MNH, Dar es Salaam.

10.0 CONCLUSION AND RECOMMENDATIONS

In conclusion, this study has found that the seroprevalence of HBV infection among pregnant women in MNH was 3.9%, which is of moderate intensity, and hence it is suggestive of the need to adopt the WHO recommendations in our set up.

It is recommended that further larger studies be performed to support the findings, since the calculated sample size was based on a higher prevalence figure than the level found in the study. This will allow for ultimately coming up with a policy of routine screening for HBV is introduced to all pregnant women during the antenatal period, and that “at birth” dose vaccination with hepatitis B vaccine is given to new born babies of mothers found to be HBsAg positive so as to reduce and prevent the spread of infection.

It is also recommended that health care workers at the MNH be offered Hepatitis B vaccination.

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APPENDIX 1

Title of the Study: Seroprevalence of HBV infection and associated factors among women attending Antenatal Clinic at Muhimbili National Hospital

Consent Form

Dear Participant,

You are being asked to enroll in a cross-sectional study titled seroprevalence of HBV infection and associated factors among women attending Antenatal Clinic at Muhimbili National Hospital. This informed consent form gives you information about the study, which will be discussed with you. Once you understand the study, and if you agree to enroll, you will be asked to sign this consent or make your mark in front of someone. Please note that your participation in this research is entirely voluntary. The main purpose of this research study is to determine the seroprevalence of HBV infection and associated factors among women attending Antenatal Clinic at Muhimbili National Hospital. A total of 310 pregnant women are expected to participate in the study. Once you have agreed to enroll in the study, you will be asked some questions concerning the study and to have blood drawn about two teaspoonful for HBV testing, and other tests like HIV if not done. You will receive pre and post HIV test counseling. You may receive no monetary benefit from this study. However, knowledge gained from this study may help in the management of infectious diseases in the future. If you would like additional information regarding benefits of participating in the study, you may speak with a physician as well. There is no cost to you for enrolling in the study. Your research records will be confidential. You will be identified by a participant identification

number, and 3 initials, and personal information from your records will not be released without your written permission. You will not be personally identified in any publication about this study. If you ever have questions about this study you should contact Dr Sabria Rashid. Tel. 0713210880, Dr Chales Kilewo Tel 0713609136 or Dr Said Aboud Tel 0754 301692 (*Muhimbili University College of Health Sciences, P.O. Box 65015, Dar es Salaam*). If you ever have questions about your rights as a research participant you may contact, *Chairperson of the Senate Research and Publications Committee, Muhimbili University of Health and Allied Sciences, P.O. Box 65001, Dar es Salaam.* If you have read the informed consent or had it read and explained to you and understand the information, and you voluntarily agree to participate in the study, please sign your name or make your mark below.

Volunteer's name	Volunteer's signature	Date
Person obtaining consent	Signature	Date

Utafiti Kuhusu Kiwango cha Maambukizi ya Homa ya Ini na Vihatarishi vya Mambukizi kwa Wajawazito Wanaopima Katika Hospitali ya Taifa ya Muhimbili, Dar es Salaam, Tanzania.

Fomu ya Ridhaa ya Kushiriki Katika Utafiti

Mpendwa Mshiriki,

Unaombwa kujiunga na utafiti mdogo ambao unaoitwa “Utafiti Kuhusu Kiwango cha Maambukizi ya Homa ya Ini na Vihatarishi vya Mambukizi kwa Wajawazito Wanaopima Katika Hospitali ya Taifa ya Muhimbili”**.** Fomu hii ya ridhaa ya kushiriki katika utafiti inakupa maelezo kuhusu utafiti wenyewe ambao utajadiliwa pamoja na wewe. Mara utakapofahamu kuhusu utafiti huu na kama utakubali kujiunga nao, utaombwa kutia saini yako au kuweka alama mbele ya shahidi. Kushiriki katika utafiti huu ni kwa hiari yako. Madhumuni makubwa ya utafiti huu ni kutafuta viwango vya maambukizi ya virusi vya homa ya ini na kwa wajawazito wanaopima Katika Hospitali ya Taifa ya Muhimbili, Dar es Salaam, Tanzania. Jumla ya wagonjwa mia tatu na kumi wanatarajiwa kushiriki katika utafiti huu. Mara utakapokubali kujiunga na utafiti, utaombwa kuchukuliwa kipimo cha damu kiasi cha vijiko viwili vya chai kwa ajili ya kupima maambukizi ya virusi na kuulizwa maswali kuhusu utafiti huo. Utapewa ushauri nasaha kabla na baada ya kupima ukimwi. Hakuna faida kifedha kwa kushiriki katika utafiti huu. Ila matokeo ya utafiti huu yatasaidia katika kuboresha matibabu ya maradhi ya kuambukiza kwako na mtoto pia. Kama utapenda kujua maelezo zaidi kuhusu faida za kushiriki katika utafiti, unaweza kuzungumza na daktari pia. Hakuna malipo yoyote ya kutoa kwa kujiunga na utafiti huu. Kumbukumbu zako za utafiti zitakuwa ni siri ya

wanautafiti. Utatambuliwa kwa nambari ya mshiriki wa utafiti na herufi 3 za mwanzo katika majina yako matatu, na maelezo yako binafsi hayatotolewa kwa mtu mwengine yeyote ila kwa ridhaa yako ya kimaandishi. Hutoweza kutambuliwa na mtu yeyote katika ripoti ya utafiti huu. Kama bado utakuwa na maswali kuhusu utafiti huu, unaweza kuwasiliana na Dr. Sabria Rashid simu nambari 0713210880, Dk. Chales Kileo simu nambari au 0713609186 Dk. Said Aboud kwa simu nambari 0754 301692 (Chuo kikuu cha Sayansi za Afya Muhimbili, SLP 65015, Dar es Salaam). Kama una maswali kuhusu haki zako kama mshiriki wa utafiti, unaweza kuwasiliana Mwenyekiti wa kamati ya utafiti, Chuo kikuu cha Sayansi za Afya Muhimbili, SLP 65015, Dar es Salaam.

Kama umesoma fomu hii ya ridhaa ya kushiriki katika utafiti au umesomewa na kupewa maelezo, uko meelewa na unakubali kwa hiari yako kushriki katika utafiti, tafadhali tia saini yako au weka alama yako hapo chini.

_____	_____	_____
Jina la Mshiriki	Saini ya Mshiriki	Tarehe
_____	_____	_____
Anayechukua ridhaa	Saini	Tarehe

APPENDIX 2

QUESTIONNAIRE

1. Registration no: _____
2. Date of interview: ____/____/_____
3. Name: (initials)_____
4. Tel no: _____
5. Parity: _____
6. Date of birth: _____/____/_____
7. District: _____
8. HIV status:_____
9. Marital status:
    1. Single
    2. Cohabiting
    3. Married
    4. Divorced
    5. Widowed
10. Education level attained
    1. No formal education
    2. Primary school
    3. Secondary school
    4. Post Secondary

11. Occupation _____

    1. Employed at health sector
    2. Petty trader
    3. Housewife
    4. Not employed
    5. Other (mention) _____

12. Have you ever had blood transfusion yes_____ or no_____

13. If yes how many times_____

14. Total number of sexual partners since when started being sexually active ( )