Seroprevalence of HBsAg among pregnant woman and rate of vertical transmission in 3 teaching hospitals in Addis Ababa

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ABSTRACT

BACKGROUND
HBV and HIV are the two most important viral infectious agents which share common modes of transmission and which can seriously affect the health of both the pregnant women and her baby. Vertical transmission of HBV from the mother to her baby is the most important modes of transmission in Africa. Neonates who contract the virus from their mother have more than 90% chance of becoming chronic carriers and this can be prevented by vaccinating the baby immediately after delivery. There are only few studies on the prevalence and rate of vertical transmission of HBV during pregnancy in Addis Ababa.

OBJECTIVE
To determine the seroprevalence of HBsAg during pregnancy and its rate of vertical transmission.

METHODS
A cross sectional study was conducted from May to September 2014 in three teaching hospitals in Addis Ababa. A total of 530 pregnant women were included in the study. Sociodemographic factors and explanatory variables were collected with structured questionnaire. HBsAg were tested with ELISA and HIV was tested by Rapid test kits following national HIV test algorithms. The mothers with HBsAg positivity were also tested for HBeAg and followed till they deliver and cord blood was tested for HBsAg with ELISA.

RESULTS
24/530(4.5%) were tested positive for HBsAg and of these 2(8.3%) were also positive for HBeAg. Of mothers with HBsAg 4(16.7%) were also positive for HIV. 17/530(3.2%) were tested positive of HIV and 4(23.5%) were also positive for HBsAg. Being single pregnant women (AOR=6, 95CI,1.5-22.8) and having HIV (AOR=5.6, 95CI,1.4-22.1) has statistically significant relationship with Positivity for HBsAg. Having HBsAg was the only variable associated with having HIV (AOR=6, 95CI, 1.7-21.5). All cord blood tested for HBsAg were negative.

CONCLUSIONS
The prevalence of HBV among pregnant mothers in Addis ababa is of intermediate endemicity. The prevalence of HIV among pregnant women of Addis ababa is 3.2% and 16.6% of those mothers with HBV also has HIV. Single pregnant women and those pregnant women with HIV
were more likely to test positive for HBsAg. There was no perinatal transmission in this study and the perinatal outcome of pregnant women with HBsAg seems to be not adversely affected.

1. Introduction

Hepatitis B virus infection is one of the most important public health problems all over the world. Approximately 2 billion people worldwide have been infected with the hepatitis B virus (HBV) and approximately 350 million people have chronic infection of Hepatitis B which may develop into acute, fulminant, cirrhosis and liver carcinoma (1,2).

In high prevalence areas, the transmission of hepatitis B virus from mothers to neonates is the main route of transmission of hepatitis B (3,2,4). In the absence of immunoprophylaxis 90% of infants who get infected during pregnancy, delivery or breastfeeding, become chronic carriers of HBV (3,4). Even if the provision of active and passive immunization soon after birth will reduce the rate of vertical transmission of hepatitis B virus, immunoprophylaxis is not 100% protective and up to 2% of infants can still become infected, where the maternal viral load is high. Meanwhile, according to WHO data of 1985, an estimated 73-100% of infants were born to mothers with positive HBeAg and HBsAg (2,4). This makes the vertical transmission of hepatitis B a global health problem that needs serious attention, particularly in moderate to high endemic areas like Africa and Asia with low public awareness on HBV (2,11,6).

Globally of the 350 million who have chronic infection, 15-25% will die from chronic liver disease (liver cancer and cirrhosis) at least 1 million deaths per year, Young children who become infected with HBV are the most likely to develop chronic infection and there is 25% mortality in perinatally acquired disease (2).

Hepatitis B-associated hepatocellular carcinoma is probably the most common tumor affecting males in sub sub-Saharan Africa (2,11).

1.1 Epidemiology

Global distribution of hepatitis B is divided into 3 categories: mildly endemic areas such as Northern Europe, North America and Australia, where the HBV carrier status is less than 0.1%. Moderately endemic areas such as eastern Europe, the Mediterranean, South America and West Asia where the carrier status is about 5%, and severely endemic areas such as China, Southeast Asia, the Pacific, and Africa where up to 20% are estimated to be chronic carriers (1,2).

Overall, approximately 45% of the global populations live in areas of high chronic HBV prevalence (1,2).
Transmission of hepatitis B virus can be vertical or horizontal. In Africa, which is one of the hyperendemic HBV regions, it was found that infection with hepatitis B virus (HBV) is transmitted vertically and horizontally (7,4,8,9).

There are approximately 50 million chronic carriers of HBV in Africa with a 25% risk of mortality. In sub-Saharan Africa, the carriers rate ranges from 9-20% (2,10,11).

Chronic hepatitis B infection is an important health issue in Eastern Asia. In a serological survey in China in 2006, HBsAg carrier status was around 7.18% (46). In Taiwan, the HBsAg carrier status was found to range from 10 to 20%, whiles in Taipei it was about 5% among infants increasing to 10% by the second birthday (4,6,9,12).

The rate of transmission was found to increase with age and infection rates as high as 50% were noted at the age of 15 years (2).

The incidence of hepatitis B in pregnant women varies widely, averaging around 10%. The rate of transmission of HBV from the mother to the baby ranges from 0.12% to 60% (6,13). Research in Southeast Asia showed that the HBsAg prevalence in the population ranges between 4-13% (13). An estimated 40-50% of them are chronic carriers and were proven
having obtained the infection during birth (8,9). North America, southern Europe and the Oceania region are areas with low prevalence (approximately 0.1% of the population), and HBV obtained in many teens and adults (2).

1.2 Virology

Hepatitis B virus belongs to the family of Hepadnaviruses. The virus particle (virion) consists of a capsule of lipids on the outside and an icosahedral nucleocapsid core composed of proteins. The diameter of the particle size is 42 nM. The core nucleocapsid genome consists of DNA, and is sometimes called "Dane particle".

The viral genome consists of double-stranded DNA with 3200 nucleotides. Another core component of HBV is the core antigen (HBcAg) and HBeAg which is a glycoprotein with a light molecular weight.

The viral envelope containing HBsAg, consists of one major protein and two other proteins. HBsAg aggregates are often found in large quantities in the serum during infection. They can have a spherical or filamentous shape with an average diameter of 22 nm and can contain parts of the nucleocapsid. When HBV DNA in the serum then active infection is proven.

In the liver of infected patients, HBcAg, HBeAg, and HBV DNA are found in the nucleus of infected hepatocytes, whereas HBsAg is found in the cytoplasm.

Hepatitis B virus replication involves a reverse transcription step and this is something that is unique among DNA viruses. During viral replication, viral RNA transcripts positively incorporate into the mature core particle at the end of the cycle of replication (2,8).

Figure 2: Structure of HBV, ChangMH. *Hepatitis B Virus infection*, science direct 2007, 12:160-7.
1.3 MODES OF TRANSMISSION

The predominant mode of transmission of HBV varies in different geographical areas. Perinatal infection is the predominant mode of transmission in high prevalence areas. In comparison, horizontal transmission, particularly in early childhood, accounts for most cases of chronic HBV infection in intermediate prevalence areas, while unprotected sexual intercourse and intravenous drug use in adults are the major routes of spread in low prevalence areas (2,3,4).

<table>
<thead>
<tr>
<th>Carrier rate, percent</th>
<th>High (≥8 percent)</th>
<th>Intermediate (2-7 percent)</th>
<th>Low (≤1 percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geographic distribution</td>
<td>Southeast Asia; China; Pacific islands; sub-Saharan Africa; Alaska (Eskimos)</td>
<td>Mediterranean basin; eastern Europe; central Asia; Japan; Latin and South America; Middle East</td>
<td>United States and Canada, western Europe; Australia; New Zealand</td>
</tr>
<tr>
<td>Predominant age at infection</td>
<td>Perinatal and early childhood</td>
<td>Early childhood</td>
<td>Adult</td>
</tr>
<tr>
<td>Predominant mode of infection</td>
<td>Maternal-infant; percutaneous</td>
<td>Percutaneous; sexual</td>
<td>Sexual; percutaneous</td>
</tr>
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PERINATAL TRANSMISSION

Perinatal transmission is the Commonest route in developing countries and is Very effective, the probability of transmission is as high as 90% if the mother is HBeAg positive. Perinatally acquired HBV is more likely to be chronic infection in as high as 95% and Has 25% mortality because children develop CLD early (2,3,4).

Maternal-infant transmission may occur in utero, at the time of birth, or after birth. The high protective efficacy (95 percent) of neonatal vaccination suggests that most infections occur predominantly at or before birth(2,3,4).
The high frequency of perinatal transmission in endemic areas is probably related to the high prevalence (40 to 50 percent) of HBeAg in women of reproductive age. These women remain infectious because of the slow rate of HBeAg seroconversion during the first two decades of life (21,45). Studies in Chinese children prior to introduction of universal vaccination of newborns have found HBeAg in as many as 90 percent below the age of 5, and up to 80 percent below the age of 20(28). The cumulative rate of spontaneous HBeAg clearance is estimated to be only 15 percent after 20 years of infection, leaving many women of childbearing age still highly infectious(8,12).

**Mechanisms of Perinatal transmission**

Women of childbearing age in high prevalence area constitute a reservoir for HBV perinatal transmission which is associated with a very high rate of chronicity (8). The vertical transmission is influenced by several factors such as maternal levels of HBV-DNA, HBeAg, variations in gene S of hepatitis B virus (HBV), duration of labor, and neonatal immune deficiency (14,28,30). Gestational age during hepatitis B infection is an important factor affecting infant outcome (45).

**The role of the Placental barrier**

Intrauterine infection is rare, less than 5% occurring in infants born to mothers with positive HBsAg and HBeAg. Research in Taiwan revealed that, over a period of 10 years only 2.4% of 665 infants born to mothers who were both HbsAg and HBeAg positive, only 2.4% were HBsAg positive at birth(14,28). Rupture of blood vessels in the mother and the placental barrier breakdown is the main route leading to perinatal (vertical) hepatitis B infection (28,45). Intrauterine infection with HBV is caused by a damage of placental barrier (30).

The mother to fetus transmission rate varies from 0.6 to 20%. This variation is depending upon many factors such as the time of onset of hepatitis in mother. There is a higher incidence of transmission (76%) in the third trimester or early post-partum, compared to the transmission (10 %) in the first or second trimester (2,8).

It has been reported that the rate of transmission of HBV in mothers with positive HBeAg is about 90% and about 85% of the infants will become chronic carriers (2,8).

Xu et al. examined 101 placental tissues from pregnant women at term by in-situ hybridization immunohistochemistry and obtained the following results: HBsAg was found in 34 placentas (33.7%), HBeAg in 38 placentas (37, 6%), HBCAg in 21 placentas (20.8%) and HBV-DNA in 45 placentas (44.6%)(30). Intrauterine Infection was found in eight of the 101 women. Intrauterine HBV infection correlated with the presence of the virus in villous capillary endothelial cells lining the fetal parts than other placental linings (30).
The effect of Mode of delivery

Prolonged labor has an influence on the risk of vertical transmission from mother to her fetus, which revealed a linear correlation between the incidence of HBsAg in the cord and the length of first stage of labor of which the correlation can be observed if the first stage lasts ≥ 9 hours. Evaluation of 447 infants born to HBsAg-positive mothers revealed that 24.9% (96/385) of vaginally born babies had HBV infection compared to about 10% delivered by caesarean section (14).

However, in other studies no significant association between the mode of delivery and transmission of HBV was found, and no difference between vaginal delivery and caesarean section was observed (35).

There is no evidence that cesarean section prevents maternal-infant transmission. Thus, Cesarean section should not be routinely recommended for carrier mothers (14).

The effect of Viral load

The risk for HBV transmission through the placenta depends on HBeAg positivity, titer of HBsAg and HBV-DNA levels. In one study, the mother's level of HBV DNA > 10^8 copies/ml was associated with increased risk of intrauterine infection (9). Wiseman et al. reported that perinatal HBV transmission occurs only when the levels of HBV DNA exceeds 10^8 copies/ml (or about 1.7 x 10^7 IU/ml) and if the mother is HBeAg positive.

Determination of HBV-DNA plays an important role in the management and administration of HBV vaccination; however this is 15 times more expensive than that of HBsAg. Sun Kui-xia et al. conducted a study on the correlation between HBsAg and HBV-DNA. It was found that in HBeAg-positive pregnant women there was a correlation between the levels of HBsAg and HBV-DNA regardless of age and genotype (2,4,22).

HBsAg examination can be used as predictors of HBV-DNA levels: it has been shown that HBsAg levels of more than 4.1 log IU/ml are a predictive value for HBV-DNA levels ≥ 7.0 log IU/ml in HBeAg positive women. This would be less expensive than HBV-DNA examination (22).

The effect of Immunoprophylaxis

Universal vaccination in newborns with active and passive immunoprophylaxis has dramatically reduced the prevalence of hepatitis B. In contrast, without immunoprophylaxis up to 90% of infants born to HBeAg positive mothers become chronically infected. However, and even in cases of appropriate prophylaxis with HBV immunoglobulin (HBIG) and HBV vaccination, a significant risk (10%) of vertical transmission remains, particularly in mothers with high viral load (serum HBV DNA >10 6–7 IU/ml) and positive HBeAg status (11,13,16,17).
Sun Kui-Xia et al. reported that out of 975 infants born to HBsAg-positive mothers, 25 infants (2.6%) were identified to have suffered perinatal transmission despite the HBV vaccine and HBIG given at birth, one month and six months, respectively (22). In total 96% (24/25) of the newborns’ mothers had HBV-DNA levels ≥ 107 log IU/ml and were HBeAg positive. Mothers with high HBV-DNA levels have a high risk of transmitting HBV to their babies (22).

Some previous studies addressed that increasing doses of hepatitis B vaccine or HBIG can reduce the rate of transmission (16,17).

**Other modes of transmission of HBV are:**

**Bloodborn:** Mainly related to transfusion of non tested blood or test done during ‘Window period’ (see below) (8).

**Sexual:** Sexual transmission remains the major mode of spread of HBV in developed countries. Sexual transmission of hepatitis B can be prevented by vaccination of spouses and steady sex partners in individuals with monogamous partners, and safe sex practice including use of condoms in subjects with multiple partners (2,8).

**Horizontal:** Children may acquire HBV infection through horizontal transmission via minor breaks in the skin or mucous membranes or close bodily contacts with other children. In addition, HBV can survive outside the human body for a prolonged period; as a result, transmission via contaminated household articles such as toothbrushes, razors, and even toys may be possible (2,8).

**Percutaneous:** Percutaneous transmission usually happens among intravenous drug users who share syringes and needles. Certain practices like acupuncture, tattooing, and body piercing have also been associated with transmission of hepatitis B (2,8).

**Nosocomial:** HBV is the most commonly transmitted blood-borne virus in the healthcare setting. Transmission generally occurs from patient to patient, health care personnel to patients or from patient to health care personnel via contaminated instruments or an accidental needle stick (2,8).

**Paternal:** From genotypic and phylogenetic analysis, transmission of HBV from father to infants is possible. Some studies have detected HBV in sperm, but there is no clinical evidence to support that "infected" sperm results in transmission of HBV infection to the fetus (2,8).

**Breastfeeding:** Breastfeeding does not appear to increase the risk of transmission. Although HBV DNA has been detected in the colostrum of HBsAg positive mothers, a study on 147 infants born to carrier mothers revealed no evidence for a relationship between breastfeeding and the subsequent development of chronic HBV infection in the babies (46).
1.4 Clinical features

The spectrum of clinical manifestations of hepatitis B virus (HBV) infection varies in both acute and chronic disease. During the acute phase, manifestations range from subclinical or anicteric hepatitis to icteric hepatitis and, in some cases, fulminant hepatitis; during the chronic phase, manifestations range from an asymptomatic carrier state to chronic hepatitis, cirrhosis, and hepatocellular carcinoma. Extrahepatic manifestations can also occur with both acute and chronic infection (8).

Acute phase

Approximately 70 percent of patients with acute hepatitis B have subclinical or anicteric hepatitis, while 30 percent develop icteric hepatitis. The disease may be more severe in patients coinfected with other hepatitis viruses or with underlying liver disease(2,8).

Fulminant hepatic failure is unusual, occurring in approximately 0.1 to 0.5 percent of patients. Fulminant hepatitis B is believed to be due to massive immune-mediated lysis of infected hepatocytes. This explains why many patients with fulminant hepatitis B have no evidence of HBV replication at presentation(2,8).

The incubation period lasts one to four months. A serum sickness-like syndrome may develop during the prodromal period, followed by constitutional symptoms, anorexia, nausea, jaundice, and right upper quadrant discomfort. The symptoms and jaundice generally disappear after one to three months, but some patients have prolonged fatigue even after normalization of serum aminotransferase concentrations(2,8).

Laboratory testing during the acute phase reveals elevations in the concentration of alanine and aspartate aminotransferase levels (ALT and AST); values up to 1000 to 2000 int. unit/L are typically seen during the acute phase with ALT being higher than AST. The serum bilirubin concentration may be normal in patients with anicteric hepatitis. The prothrombin time is the best indicator of prognosis. In patients who recover, the normalization of serum aminotransferases usually occurs within one to four months. A persistent elevation of serum ALT for more than six months indicates a progression to chronic hepatitis(2,8).

Clinical manifestations of acute Viral Hepatitis In pregnancy

Liver is susceptible to noxious stimuli especially in 2nd and 3rd trimesters. A serum sickness-like syndrome may develop during the prodromal period, followed by constitutional symptoms, anorexia, nausea, jaundice, and right upper quadrant discomfort. These symptoms are generally nonspecific and indeed common during pregnancy except the presence of jaundice. If a pregnant mother has jaundice and she has serologic markers for HBV and if there is no obvious cause for her symptoms and jaundice then it can be taken as acute viral hepatitis (8,18,19).

Acute hepatitis has 35% chance of preterm delivery.

Fulminant course occurs more during pregnancy especially if co infected with HDV which has mortality as high as 85%.
Hepatitis in pregnancy is to be differentiated from HELLP syndrome, AFLP and cholestasis of pregnancy.

**Criteria for diagnosing acute viral hepatitis caused by HBV in pregnancy are seropositivity for HBsAg and:**

1. Recent onset of jaundice and
2. No other cause accountable for jaundice e.g., Pre-eclampsia, Eclampsia, Cholestasis of pregnancy, Severe infections, Malaria, Drugs etc. and
3. Serum transaminase levels at least more than three times normal (8,18,19).

**Chronic phase:**

The presence of HBsAg for > 6 months indicates chronic infection. Many patients with chronic hepatitis B are asymptomatic (unless they progress to decompensated cirrhosis or have extrahepatic manifestations), while others have nonspecific symptoms such as fatigue. Pregnancy is well tolerated in chronic carriers (8,19,24).

**1.5 Disease progression:**

The sequelae of chronic HBV infection vary from an inactive carrier state to the development of cirrhosis, hepatic decompensation, hepatocellular carcinoma (HCC), extrahepatic manifestations, and death. The prognosis appears to vary with the clinical setting and The progression is faster and common in Perinatally acquired infection in infants. The rate of progression is 95% in infants, 35% in toddlers, 5% in Adults (43).

The progression is also faster and common in Those Co infected with HIV & or HCV & or HDV. This is because They have Higher HBV viral loads, Decreased hepatitis B e antigen (HBeAg) seroconversion, and Exaggerated liver injury because there is Faster and more severe liver fibrosis, faster Cirrhosis, HCC and Untreated HIV has More liver related deaths (8,31,34,36,37,42,43).

Because of the above reasons Both should be screened if infected with one of them before starting treatment because it influence the response to antiretroviral therapy and thus Both should be treated regardless of CD4 count, And the Drug Regimen should be effective against both infections. A first-line regimen including tenofovir and either lamivudine or emtricitabine in HIV-1/HBV co-infected patients is preferred (42,43).

**1.6 Diagnosis**

The diagnosis of hepatitis B virus (HBV) infection was revolutionized by the discovery of Australia antigen, now called hepatitis B surface antigen (HBsAg). During the ensuing two decades, serologic assays were established for HBsAg and other HBV antigens and antibodies. Advances in molecular biology techniques led to the development of hybridization and polymerase chain reaction (PCR) assays for direct determination of hepatitis B virus DNA (HBV DNA). The diagnosis of HBV infection can also be made by the detection of HBsAg or hepatitis B core antigen (HBcAg) in liver tissues by immunohistochemical staining and of HBV DNA by Southern hybridization, in-situ hybridization, or PCR (8).
SEROLOGIC MARKERS — Infection with HBV is associated with characteristic changes in the serum levels of hepatitis B antigens and antibodies.

Hepatitis B surface antigen and antibody — Hepatitis B surface antigen (HBsAg) is the serologic hallmark of HBV infection. It can be detected by radioimmunoassays (RIA) or enzyme immunoassays (EIA).

HBsAg appears in serum 1 to 10 weeks after an acute exposure to HBV, prior to the onset of hepatic symptoms or elevation of serum alanine aminotransferase (ALT). In patients who subsequently recover, HBsAg usually becomes undetectable after four to six months. Persistence of HBsAg for more than six months implies chronic infection. It is estimated that less than 1 percent of immunocompetent adult patients with genuine acute hepatitis B progress to chronic infection. Among patients with chronic HBV infection, the rate of clearance of HBsAg is approximately 0.5 percent per year (8).

The disappearance of HBsAg is followed by the appearance of hepatitis B surface antibody (anti-HBs). In most patients, anti-HBs persists for life, thereby conferring long-term immunity. In some patients, however, anti-HBs may not be detectable until after a window period of several weeks to months, during which neither HBsAg nor anti-HBs can be detected. At this time, the serologic diagnosis may be made by the detection of IgM antibodies against hepatitis B core antigen (IgM anti-HBc).

HBV can be classified into seven genotypes and four major serotypes. All HBV serotypes share one common antigenic determinant: "a." These serotypes have epidemiologic significance. Antibodies to the "a" determinant confer protection to all HBV serotypes (8).

Coexistence of HBsAg and anti-HBs has been reported in approximately 24 percent of HBsAg positive individuals. In most instances, the antibodies are unable to neutralize the circulating virions. These individuals should therefore be regarded as carriers of the hepatitis B virus(8).

Hepatitis B core antigen and antibody — Hepatitis B core antigen (HBcAg) is an intracellular antigen that is expressed in infected hepatocytes. It is not detectable in serum. Anti-HBc can be detected throughout the course of HBV infection(8).

During acute infection, anti-HBc is predominantly of IgM class. IgM anti-HBc is the sole marker of HBV infection during the window period between the disappearance of HBsAg and the appearance of anti-HBs. The detection of IgM anti-HBc is usually regarded as an indication of acute HBV infection.

However, IgM anti-HBc may remain detectable up to two years after the acute infection. Furthermore, the titer of IgM anti-HBc may increase to detectable levels during exacerbations of chronic hepatitis B. This can present a diagnostic problem, incorrectly suggesting acute hepatitis B, particularly in endemic areas in which many HBsAg-positive patients presenting with acute hepatitis actually have exacerbations of chronic hepatitis B. Other common causes of acute exacerbation of chronic hepatitis B are superinfection with hepatitis D virus (delta virus) or hepatitis C virus.
IgG anti-HBc persists along with anti-HBs in patients who recover from acute hepatitis B. It also persists in association with HBsAg in those who progress to chronic HBV infection.

**Hepatitis B e antigen and antibody** — Hepatitis B e antigen (HBeAg) is a secretory protein that is processed from the precore protein. It is generally considered to be a marker of HBV replication and infectivity. The presence of HBeAg is usually associated with high levels of HBV DNA in serum and higher rates of transmission of HBV infection from carrier mothers to their babies and from patients to health care workers (2,8).

HBeAg to anti-HBe seroconversion occurs early in patients with acute infection, prior to HBsAg to anti-HBs seroconversion. However, HBeAg seroconversion may be delayed for years to decades in patients with chronic HBV infection. In such patients, the presence of HBeAg is usually associated with the detection of high levels of HBV DNA in serum and active liver disease. However, HBeAg-positive patients with perinatally acquired HBV infection may have normal serum ALT concentrations and minimal inflammation in the liver.

Seroconversion from HBeAg to anti-HBe is usually associated with a decrease in serum HBV DNA and remission of liver disease. However, some patients continue to have active liver disease after HBeAg seroconversion. Such individuals may have low levels of wild type HBV or HBV variants with a stop codon in the precore or dual nucleotide substitutions in the core promoter region that prevent or decrease the production of HBeAg (8).

**SERUM HBV DNA ASSAYS** — Qualitative and quantitative tests for HBV DNA in serum have been developed to assess HBV replication. The sensitivity limit of these assays depends upon the techniques used. The range of linearity also varies. Currently, most HBV DNA assays use real-time PCR techniques, report results in IU/mL, have lower limit of detection around 20 IU/mL and a range of linearity up to 8 log(10) IU/mL.

Recovery from acute hepatitis B is usually accompanied by the disappearance of HBV DNA in serum as determined by hybridization or DNA assays. However, HBV DNA may remain detectable in serum for many years if tested by PCR assays. This observation suggests that the virus persists after "recovery" but is controlled by the immune system.

The major clinical role of serum HBV DNA assays in patients with chronic HBV infection is to assess HBV replication and candidacy for antiviral therapy. Indication for HBV treatment is based on the presence of active liver disease and high HBV DNA levels. A cutoff of 100,000 copies/mL or 20,000 IU/mL has been proposed for treatment initiation in HBeAg positive patients, and a lower threshold (2000 IU/mL) for HBeAg negative patients(2,8,24).

Acute infection is diagnosed by the presence of HBeAg, HBsAg and HBV DNA, IgM anti-HBc and HBsAg. Recovery is accompanied by normalization of the serum ALT, the disappearance of HBV DNA, HBeAg to anti-HBe seroconversion, and subsequently HBsAg to anti-HBs seroconversion and switch from IgM to IgG anti-HBc. Thus, previous HBV infection is characterized by anti-HBs and IgG anti-HBc (8).
Chronic infection characterized by Persistence of HBsAg for more than six months after acute infection, persistence of HBeAg, HBsAg, and HBV DNA in the circulation. Anti-HBs is not seen in approximately 20 percent of patients and a non-neutralizing form of anti-HBs can be detected.

HBeAg-negative patients who have normal serum ALT and low (<2000 IU/mL) or undetectable HBV DNA are considered to be in an inactive carrier state (8).

**Occult HBV infection** — There exists a subset of patients with occult HBV infection defined as the presence of detectable HBV DNA by PCR in patients who are negative for HBsAg. Such patients have been further subclassified as having "seropositive" or "seronegative" HBV depending upon whether they are positive or negative for other HBV markers, most commonly anti-HBc. Most of these patients have very low or undetectable serum HBV DNA levels accounting for the failure to detect HBsAg. Infections with HBV variants that decrease HBsAg production or have mutations in the S gene with altered S epitopes that evade detection in serology assays for HBsAg are uncommon. HBV DNA is often detected in the liver and transplantation of livers from these persons can result in de novo HBV infection(80).

![Serologic responses to HBV infection](image)

**Figure 3:** Serologic response to HBV infection, ChangMH. Hepatitis B Virus infection, science direct 2007,12:160-7.

**Diagnosis of Vertical transmission**

Mother-to-infant transmission of HBV remains to be intensively studied. Currently, there is still no recognized diagnostic standard for HBV infection of infants. HBsAg, HBeAg, can traverse placental barrier but rarely. The sensitivities of methods of diagnosing vertical transmission is different. Even prenatal expression of HBV DNA and HBsAg does not necessarily show postnatal infection. Cord blood expression of even HBV DNA is not definitive as children may be found uninfected at followup. One method of diagnosing vertical infection is post delivery follow up. The problem with post delivery follow up and diagnosis of persistent infection is it would be difficult to differentiate between horizontal and vertical transmission. HBsAg may be
used as a main seromarker in determining vertical transmission to substitute the role of HBV-DNA due to the cost (4,5,10,13,14,16).

Some of the methods of diagnosing vertical transmission in the literature are Cord blood HBV viral load >100,000 IU/ml, Cord blood HBsAg titer >250 IU/ml, 3rd day peripheral blood HBsAg titer > or same as cord blood titer, Cord blood is HBsAg and HBV DNA positive and the neonate is negative for HBsAg –Ab at 1 month of age, Cord blood HBV DNA positivity, Cord blood positivity for HBsAg in mother who is HBeAg positive, Cord blood positivity for HBsAg in mother who has acute infection in third trimester or high maternal HBV Viral load and the other method is to follow the neonate for about a year for markers of infection(4,5,10,13,14,16,21,22,28,41).

1.7 Screening of HBV

Different organizations have different indications for screening but all agree pregnant mothers and Those who are at risk should be screened (2,8).

The Rationale for screening HBV is that HBV causes Serious infection with significant health burden and sequelle and there is Effective diagnostic method which is ELISA that is 99.58 specific and 100% sensitive for HBsAg and there is Effective preventive method (2,8,11,16,17).

Screening of pregnant mothers is seriously indicated for many reasons. There is effective method of preventing perinatal transmission which is a major mode of transmission. The other reason why pregnant mothers should be screened is pregnancy is an Opportunity for health promotion and preventive medicine because most mothers come to health facility during pregnancy who would not otherwise come. It also creates an opportunity to Vaccinateserodiscordant couples and Link them to medical evaluation and treatment.

The advantages of making HBsAg testing routine during early pregnancy include the ability to identify HBV carrier mothers that is not dependent on the healthcare provider’s ability in identifying high-risk women or ordering HBsAg as a special test; So if a pregnant woman knows her status before delivery she can protect her baby and her partner but if she is not screened during pregnancy when she is likely to visit health facility then she is unlikely to be screened thereafter and she will lose the golden opportunity to protect her baby (2,8).

1.8 Treatment

When women in the childbearing age require antiviral therapy, the issue of pregnancy must be discussed before starting treatment. In pregnant women with chronic HBV infection who need antiviral therapy, the liver disease stage of the mother and potential benefit of treatment must be weighed against the risk to the fetus. IFN-based therapy is contraindicated because of its antiproliferative effect; the only choice is a nucleoside (NRTI) or nucleotide analogue (NtRTI) (24). Therapy with NRTI during pregnancy may be considered if the benefit seems to be higher than the risk. Tenovofir and Telbivudine are classified as category B drugs (no risk in animal studies, but unknown in humans), whereas Lamivudine,
Adeovir, and Entecavir are classified as category C drugs (teratogenic in animals, but unknown in humans) by the US FDA (24).

Studies have shown that antiviral therapy administered in late pregnancy may further reduce the risk of perinatal HBV infection from highly viremic mothers, as compared with passive-active immunization alone (24).

However, the extent of benefit, the threshold of serum HBV DNA level for initiating therapy, the optimal time to start therapy, the appropriate choice of an antiviral agent, and the optimal duration of therapy need to be further studied before they are applied in the algorithm of hepatitis B in pregnant women (24).

1.9 Prevention

HBV is a preventable virus and HBV associated HCC is a preventable carcinoma (2).

**Preventing vertical transmission**

This is a very important step in prevention of HBV in the community especially in developing countries. Some of the strategies include Screening all pregnant mothers and using HBV vaccine which is 75% effective alone and HBV vaccine combined with HBV immunoglobulin which is 93% effective. Both should be given within 12 hours of delivery but the faster the better (2, 8, 11, 16, 17).

The use of Lamivudine in third trimester to prevent vertical transmission is controversial (24).

If HBsAg status of the mother is unknown give vaccine to the neonate then screen the mother and give HBVIG to the neonate only if the mother is HBsAg positive (2).

Cesarean section, Avoiding Breast feeding to prevent perinatal transmission are generally not recommended but controversial when the viral load is >100,000IU/ml (14, 16, 24, 46).

Other methods of preventing HBV transmission are: Vaccinating of partners of serodiscordant couples, Using Barrier methods, Screening of all blood products, Non recycling of injection needles and Post exposure prophylaxis with vaccine and immunoglobulin (2, 8, 11, 16, 17).
2. Statement of the problem

HBV is a highly contagious and dangerous virus with serious sequelae.

In developing countries major mode of transmission is Perinatal and the risk is as high as 90% if the mother is HBeAg positive.

There is a 93.6% ANC coverage by skilled attendant in Addis ababa which shows most pregnant mothers come to Health facility. This is very important opportunity for preventive, health promotional and therapeutic intervention (EDHS 2011).

The Rationale to screen HBV in high risk non pregnant populations is that HBV is a serious infection with significant health burden and sequelae, there is effective diagnostic method which is ELISA that is 99.58 specific and 100% sensitive for HBsAg and there is effective preventive method (2,8,11,16,17).

Screening of pregnant mothers is seriously indicated for many reasons: There is effective method of preventing perinatal transmission which is a major mode of transmission. The other reason why pregnant mothers should be screened is pregnancy is an opportunity for health promotion and preventive medicine because most mothers come to health facility during pregnancy who would not otherwise come. It also creates an opportunity to vaccinate serodiscordant couples and link them to medical evaluation and treatment (2,8).

The advantages of making HBsAg testing routine during early pregnancy include the ability to identify HBV carrier mothers that is not dependent on the healthcare provider’s ability in identifying high-risk women or ordering HBsAg as a special test; So if a pregnant woman knows her status before delivery she can protect her baby and her partner but if she is not screened during pregnancy when she is likely to visit health facility then she is unlikely to be screened thereafter and she will lose the golden opportunity to protect her baby.

Knowing the prevalence of HBV specifically during pregnancy is vital for 2 reasons:

1. Major mode of transmission in developing countries is perinatal and the best way of assessing the prevalence in the general population is studying its prevalence in pregnant mothers, especially the prevalence of highly infectious mothers and quantifying the rate of perinatal transmission.

2. The prevalence is not necessarily the same as non-pregnant mothers. Pregnancy is a certain proof of sexual activity which can transmit HBV and non-pregnant populations include those who are using effective contraception including barrier methods which can prevent HBV or those who are not sexually active at all.

So screening of all pregnant mothers is critical and If we screen, knowing the burden of the problem is vital for its value for policy makers and it should continuously be updated. In Ethiopia there are only few studies on the prevalence of HBV during pregnancy and rate of vertical transmission.
3. LITERATURE REVIEW

An electronic review of the literature was made on Pubmed and WHO regional databases with keywords: Hepatitis B AND Pregnancy AND Africa, Hepatitis B AND Vertical transmission, Hepatitis B AND HIV.

The retrieved literature was sorted in a way that the socioeconomic status of the country that the research was conducted in could probably match the Ethiopian setup and these data’s were used to compare for the prevalence of HBV but researches all over the world were used for scientific evidences and explanations.

Overall, approximately 45% of the global populations live in areas of high chronic HBV prevalence (1,2).

Transmission of hepatitis B virus can be vertical or horizontal. In Africa, which is one of the hyperendemic HBV regions, it was found that infection with hepatitis B virus (HBV) is transmitted vertically and horizontally (4,8,11,23).

There are approximately 50 million chronic carriers of HBV in Africa with a 25% risk of mortality. In sub-Saharan Africa, the carriers rate ranges from 9-20% (2,10,11,23).

Chronic hepatitis B infection is an important health issue in Eastern Asia. In a serological survey in China in 2006, HBsAg carrier status was around 7.18% (9). In Taiwan, the HBsAg carrier status was found to range from 10 to 20%, while in Taipei it was about 5% among infants increasing to 10% by the second birthday (4,6,9).

The rate of transmission was found to increase with age and infection rates as high as 50% were noted at the age of 15 years (2).

The incidence of hepatitis B in pregnant women varies widely, averaging around 10%. The rate of transmission of HBV from the mother to the baby ranges from 0.12% to 60% (2,3,4,6,7,23). Research in Southeast Asia showed that the HBsAg prevalence in the population ranges between 4-13% (9). An estimated 40-50% of them are chronic carriers and were proven having obtained the infection during birth (9).

North America, southern Europe and the Oceania region are areas with low prevalence (approximately 0.1% of the population), and HBV obtained in many teens and adults (2).

In Africa there are multiple studies on the prevalence of HBsAg during pregnancy (2,3,4,6,7,23,26,27,32,33,37,39,44). The main method used for the diagnosis of HBsAg in the pregnant mothers is ELISA.

The prevalence of HBsAg during pregnancy in Africa ranges from 6.5% to 25% (23).
The prevalence of HBeAg during pregnancy in Africa ranges from 2.7 to 19.8% (23).

The literatures on the seroprevalence of HBsAg during pregnancy in African countries is summarized in the following table.

<table>
<thead>
<tr>
<th>Sn.</th>
<th>Year</th>
<th>Country</th>
<th>Design</th>
<th>SETTING</th>
<th>SAMPLE</th>
<th>HBsAg,%</th>
<th>HBeAg%</th>
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<tr>
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<td>2000</td>
<td>Burkina faso</td>
<td>CS</td>
<td>»</td>
<td>917</td>
<td>10.7</td>
<td>18.2</td>
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<tr>
<td>3</td>
<td>2004</td>
<td>Ivory coast</td>
<td>CS</td>
<td>»</td>
<td>1002</td>
<td>9</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>2001</td>
<td>Mali</td>
<td>CS</td>
<td>»</td>
<td>829</td>
<td>15.5</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>1995</td>
<td>Malawi</td>
<td>CS</td>
<td>»</td>
<td>253</td>
<td>13</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>1995</td>
<td>Zambia</td>
<td>CS</td>
<td>»</td>
<td>2095</td>
<td>6.5</td>
<td>16.1</td>
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<tr>
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<td>CS</td>
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<td>692</td>
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<td>15</td>
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<tr>
<td>10</td>
<td>1985</td>
<td>Senegal</td>
<td>CS</td>
<td>»</td>
<td>1442</td>
<td>9.8</td>
<td>19.8</td>
</tr>
</tbody>
</table>

Table 2, seroprevalence of HBsAg and HBeAg during pregnancy, Calvintiyou, *prevalence of HBV in pregnancy and vertical transmission rate in Africa*, systematic review, 2007, WHO.

The literature in ETHIOPIAN SETTING:

Ethiopian national hepatitis study showed that 10.8% of young males from all regions of the country were positive for HBsAg (18).

A community based seroepidemiological survey of Addis Ababa, Ethiopia has shown a 7% seroprevalence for HBsAg, higher in males than females (19).
Another study done in Ethiopia has shown an overall HBsAg prevalence of 6.2% and infection occurring early in life and continuing to increase gradually without leveling off (25).

Published information's on the seroepidemiology of HBV infection among pregnant women are sparse and these reports were mainly from Addis Ababa which was done in 1988 showed 5% (26).

Another study from Jimma which was done in 2005 showed a 3.7% seroprevalence of HBsAg during pregnancy(27).

The seroprevalence of HBsAg at attendants of Antenatal care at Debretabor Hospital was 5.3 % in 2004 (44).

The literature on rate of vertical transmission:

Mother-to-infant transmission of HBV remains to be intensively studied. Currently, there is still no recognized diagnostic standard for HBV infection of infants. HBsAg, HBeAg, can traverse placental barrier but rarely. The sensitivities of methods of diagnosing vertical transmission is different. Even prenatal expression of HBV DNA and HBsAg does not necessarily show postnatal infection. Cord blood expression of even HBV DNA is not definitive as children may be found uninfected at follow up.

One method of diagnosing vertical infection is post-delivery follow up. The problem with post-delivery follow up and diagnosis of persistent infection is it would be difficult to differentiate between horizontal and vertical transmission. HBsAg may be used as a main seromarker in determining vertical transmission to substitute the role of HBV-DNA due to the cost (3,4,5,10,13,14).

Some of the methods of diagnosing vertical transmission in the literature are Cord blood HBV viral load >100,000IU/ml, Cord blood HBsAg titer >250IU/ml, 3rd day peripheral blood HBsAg titer > or same as cord blood titer, Cord blood is HBsAg and HBV DNA positive and the neonate is negative for HBsAg –Ab at 1 month of age, Cord blood HBV DNA positivity, Cord blood positivity for HBsAg in mother who is HBeAg positive, Cord blood positivity for HBsAg in mother who has acute infection in third trimester or high maternal HBV Viral load and Follow the neonate for about a year for markers of infection (3,4,5,10,13,14,16,17,21,22,28,30,41,45).

The most widely used method for Diagnosis of vertical transmission of HBV are: Most studies used cord blood HBsAg (16,21,23,26), Others used cord blood DNA PCR (10,41,45), Still others followed exposed neonate for about a year with viral markers (3).

There are different studies with different methods on the rate of vertical transmission in Africa and it ranges from 7 to 57.8% (23). Some of the studies on the rate of vertical transmission are summarized in the following table.
<table>
<thead>
<tr>
<th>Sn</th>
<th>year</th>
<th>country</th>
<th>Design</th>
<th>Setting</th>
<th>Sample</th>
<th>HBsAg,%</th>
<th>Vertical transmission,%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1993</td>
<td>Senegal</td>
<td>Cohort</td>
<td>Hospital</td>
<td>152</td>
<td>13.8</td>
<td>7</td>
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<tr>
<td>2</td>
<td>1975</td>
<td>S.A</td>
<td>Cohort</td>
<td>»</td>
<td>630</td>
<td>0.16</td>
<td>12.5</td>
</tr>
<tr>
<td>3</td>
<td>2000</td>
<td>Egypt</td>
<td>Cohort</td>
<td>»</td>
<td>352</td>
<td>15.3</td>
<td>51.8</td>
</tr>
<tr>
<td>4</td>
<td>1999</td>
<td>Tanzania</td>
<td>Cohort</td>
<td>»</td>
<td>980</td>
<td>6.3</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 3: The rate of vertical transmission in Africa, Calvin tiyou, *prevalence of HBV in pregnancy and vertical transmission rate in Africa*, systematic review, 2007, WHO.
4. Objectives:

4.1 General objective:
Determine the Seroprevalence of HBsAg during pregnancy and rate of vertical transmission in pregnant mothers in 3 teaching hospitals in Addis Ababa.

4.2 Specific objective:
4.2.1 Determine the prevalence of active infection of HBV during pregnancy in the three teaching hospitals in Addis Ababa.

4.2.2 To describe immediate perinatal outcome of neonates born to HBsAg positive mothers in the three teaching hospitals in Addis Ababa.

4.2.3 Determine the prevalence of HIV during pregnancy in the three teaching hospitals in Addis Ababa.

4.2.4 Determine the rate of co-infection of HIV and HBV during pregnancy in the three teaching hospitals in Addis Ababa.

5. Methodology

5.1 Study design:
This study is a Cross-sectional study that was conducted in the three teaching hospitals in Addis Ababa from May, 2014 to September 2014.

5.2 Study area:
This is a Hospital based study at the three teaching hospitals in Addis Ababa, TikurAnbessa specialized Hospital, Zewditu Memorial Hospital, Ghandi Memorial Hospitals.

Tikuranbessa specialized hospital is located in Lidetasubcity and is a teaching hospital of Addis ababa University with high number of deliveries per month with patients coming from all over the country and all over the city. It is the largest hospital in the country with multiple specialites and departments working together for the best advantage of the patients. For example it is a hospital that is giving the most specialized obstetrics and Gynecology care including Radical surgeries, Chemotherapies and it is the only place in the country where there is Radiotherapy.

Ghandi Memorial Hospital is located in Cherkossucity and is a hospital run under Addis Aababa Health bureau and is an affiliate hospital with Addis ababauniversity. It is known by High number of deliveries, as high as 550 deliveries per month and it is a hospital that was praised and rated number one in the country for best obstetrics and gynecology service in 2014 by Ministry of Health.
Zewditu Memorial hospital is also run under Addis Ababa health bureau and is affiliate of Addis Ababa University. It is located in Cherkossubcity and is working hard to excel its service and it was recently joined by the department of obstetrics and gynecology of Addis Ababa University.

5.3 Study populations:

Source population: Pregnant women following or delivering at the above three teaching hospitals.

5.4 Sampling: Sampling was done with Single proportion formula and is based on 5.3 % prevalence of HBsAg during pregnancy from FissehaWalle, Daniel Asrat, prevalence of HBsAg among pregnant women attending antenatal care service at debre-tabor hospital,2004, 2% error of margin And 10% Non-response rate.

Sample size:

\[ n = \frac{(z_{\alpha/2})^2 \cdot p \cdot (1-p)}{d^2} \]

Where n = sample size

\[ P = 0.053 \quad (44) \quad d = 0.02 \quad (2\% \text{ error of margin}) \]

\[ z_{\alpha/2} = 1.96 \quad (\text{standard normal probability for } 95\% \text{ CI}) \]

\[ n = 482 \]

10% non-response rate added, \( n = 530 \)

5.5 Inclusion criteria:

All pregnant mothers attending ANC or delivering who are at or beyond 28 weeks of gestation. The reasons for this are, Negative tests at first or early second trimester should be repeated for the mother can be infected thereafter, First or early second trimester infections are unlikely to cause vertical transmission with only 10% risk and We wanted to analyze vertical transmission that is we have to wait until the woman delivers so if we include those at first or early second trimesters would not have time to wait until they deliver.

5.6 Ethical consideration:

Ethical clearance was obtained from research and publication committee of the Department of Obstetrics and Gynecology, Faculty of Medicine, AAU.

TAH,GMH,ZMH Hospitals where the study was conducted were notified by official letters.

Verbal consent was obtained from respondents and data was collected confidentially. No name was written on the questionnaire.
5.7 Data collection:

Data collectors, 1 physician/Intern & 1 nurse were trained for half a day on the questionnaire and the proceedings and the questionnaire was pretested by the data collectors. After the quality and simplicity of the questionnaire was assured the data collectors were given the questionnaire.

The data was collected at the Antenatal care clinic of each hospital.

The data collectors introduced themselves and explained to patients the objective of the study stressing on the benefit of being tested for HBsAg during pregnancy and what will be done if the mother is positive.

The data collectors explained to the patient that no names will be written on the questionnaire and confidentiality is protected and got Verbal consent.

Once the pregnant woman agreed to participate in the study, The data was filled in the questionnaire starting from identification of the woman but not her names and continued by stating her past obstetrics history, Risk factors for HBV and History of Current pregnancy. After this the data collectors revised the patients’ card for the presence and the date of test of HIV and HBsAg and ordered the investigation if not already done. If the tests were already done, Tests done at first or early second trimesters were repeated. When patients come with results the data was filled in the structured questionnaire.

The data collectors finished the phase one of the data collection which has the primary aim of identifying those mothers with markers for HBV and HIV. Then each mother who were positive for HBsAg were contacted by phone and evaluated by the principal investigator.

The woman who was found to be HBsAg positive were evaluated for the presence of Jaundice, RUQ pain or Tenderness, those mother with the above symptoms were screened for HBeAg and SGOT, SGPT & we looked for other obvious causes of jaundice eg. Drugs, Malaria, hypertension. For mothers who did not had those symptoms and signs, only Serology for HBeAg was tested. When the above results were at hand the questionnaire was filled and a slip (anexe-) was given to the patient and it was also attached to the patient card. We also counseled the mothers so that their partners should also be tested for HBsAg and if they were found to be positive they should be vaccinated for HBV.

The mother was counseled to deliver in the hospital where she was having ANC care and she was counseled to show the slip describing that she is HBsAg positive and cord blood is to be tested for HBsAg and was told to remind the delivery attending physicians to send HBsAg test from cord blood and to give HBV Vaccine for the neonate immediately after delivery or call the principal investigator with the name and phone number of the principal investigator that was written clearly on the slip that was given to the pregnant mother. The prescriptions for the HBV Vaccine and the request for cord blood serology for HBsAg were given to the mothers.
The labor ward community of the three teaching hospitals during the study period was asked for assistance to the study by taking cord blood for HBsAg for those mothers who come with the slip describing their status or call the principal investigator whenever such a mother was admitted for delivery.

When the cord blood serology for HBsAg test result was available the questionnaire was completed and the slip collected and the mother were linked to medical side and the neonate to pediatrics side for further evaluation and follow-up.

Conceptual Framework

- Screen for HIV with rapid test kits & for HBsAg with ELISA.

  HBsAg POSITIVE:

  - Screen for HBeAg.
  - Clinical evaluation for Acute hepatitis
  - Counsel and give prescriptions for HBV VACCINE
  - Attach a SLIP to the woman’s card and Give a SLIP describing her status
  - Counsel to deliver in the above hospitals and to remind attending physicians or call the principal investigator when she is admitted for delivery.

  Complete questionnaire = DONE

- HBsAg NEGATIVE

- At delivery Screen cord blood for HBsAg.
- LINK the mother to Medical side and the neonate to Pediatrics side if cord blood is positive for HBsAg.

Figure 4. Conceptual framework.
5.8 Data entry and analysis:
The collected questionnaires was checked for completeness, coded, entered in to SPSS 20 statistical software package, cleaned, recoded and analyzed by the principal investigator.

Descriptive statistics was used to summarize data. Proportions and the corresponding 95% CI is presented.

Mean and standard deviation was used for numerical variables.

Frequency was used for categorical variables.

Bivariate analysis was done for each variable in the study each at a time and those variables with P value of < 0.2 were taken in to multivariate logistic regression to test for association.

Adjusted odds ratio with 95% confidence interval presented and those with P value of < 0.05 in multivariate analysis were considered significantly associated.

5.9 Variables
5.9.1 Independent variables:
The independent variables are Age, Marital status, Educational status, Occupation, Parity, Mode of delivery, Gestational age at delivery, History of Tattoos, Blood transfusion, History of Multiple sexual partners.

5.9.2 Dependent variables:
The dependent variables are Maternal HBsAg, HBeAg, HIV status, Cord blood HBsAg status.

5.10 Operational definitions:
Active HBV infection: Serum HBsAg & HBeAg positive by ELISA.

Acute viral hepatitis: Maternal serum HBsAg positivity and Recent onset of jaundice and No other cause accountable for jaundice E.g., pre-eclampsia, eclampsia, cholestasis of pregnancy, severe infections, drugs etc. And Serum transaminase levels at least more than three times normal.

Vertical transmission:
Cord blood positive for HBsAg in mothers positive for HBsAg and HBeAg.
Cord blood positive for HBsAg in mother with acute viral hepatitis.

6. BENEFICIARIES OF THE RESEARCH:
Will be submitted to AAU-MF / OBGYN DEPARTEMENT as partial fulfillment of specialty certificate.

May be used by policy makers.
7. BUDGET

- **Data collectors:**
  
  Per dime: $15 \times 530 = 7950$ ETB

- **Stationary:**
  - Printing questionnaire: $0.4 \times 595 = 238$ ETB
  - Pens, 3 bags = $200$ ETB

- **Data entry & Analysis:** $1500$ ETB

TOTAL = $9863$ ETB., Source of the money is the principal investigator.

8. Work plan

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<td>3 Obtaining ethical clearance</td>
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<td>4 Data collection</td>
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<td>7 Preparing final thesis</td>
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<td>8 Public defense</td>
<td>Investigator</td>
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</table>

Figure 5. Work plan.
9. RESULT

The mean age of the pregnant mothers studied is 27.9±4.3, the minimum age is 16 years and the maximum age is 40 years. Most of the study participants were in the age range 23-28,245 (46.2%), and the rest comprises 29-34 years, 193 (36.4%), 35-40, 37 (7%), 16-22, 55 (10.4%).

Most of the study subjects were from Addis Ababa, 520 (98.1%) and only 10 mothers (1.9%) were from outside Addis Ababa.

Majority of the study participants were married, 504 (95.1%), 20 were single (3.8%), 6 were separated (1.1%).

243 (45.9%) were educated up to secondary school, 139 (26.3%) went to college, 116 (21.9%) stop school at primary school and 31 (5.9%) were illiterate.

308 (58.1%) were orthodox Christian, 132 (24.9%) Muslims, 86 (16.2%) Protestants, 3 (0.6%) Catholics.

Most of the pregnant mothers are private employee, 203 (38.4%), followed by unemployed 166 (31.4%), government employees were 158 (29.9%), 2 mothers were student (0.4%).

The mean monthly income for the study group is 2140 birr ± 1673, the minimum being 300 and 20,000 is the maximum. The Mode is 1500. Most of the mothers earn 1000-1999 birr per month, 189 (35.7%).

438 (82.6%) of the mothers did not own the house they were living in, 17.4% do own their house.

117 (22.1%), 52 (9.8%), 5 (0.9%) had history of multiple sexual partners, tattoo and blood transfusion respectively.

Of the 530 pregnant women 183 (34.5%) were primigravid and 226 (44.7%) were nulliparous.

422 (79.6%) did not have history of abortions, 91 (17.2%) had 1 abortion, 16 (3%) had 2 abortions and of the abortions majority are induced.

<1% of the study participants had history of still birth, ENND, LNND and ectopic pregnancy.

The mean gestational age of the pregnant women in the study is 35.77±3.8 weeks. The significant proportions of the mothers 169 (32.1%) were in the gestational age range of 28-34 weeks.

Of the 530 pregnant women screened 17 mothers (3.2%) were seropositive for HIV and 24 (4.5%) were positive for HBsAg.

Of those with HBsAg only 2 (8.3%) had seropositivity for HBeAg and none had acute clinical hepatitis.
4 were also positive for HIV thus the confection rate among those with HBsAg being 16.7% and the prevalence of HIV/HBV coinfected mothers is 0.75%.

18(75%) of mothers with markers for HBV delivered by SVD and the rest by cesarean section. 21(87.5%) of HBV exposed babies had first minute APGAR score 8 and above, 3(12.5%) had first minute APGAR of 7. The mean baby weight is 3216.6±310.2gm. Most of the babies, 20(83.3%) weighted between 2500-3500gm, 3(12.5%) babies between 3600-3999gm, 1 baby weighted 4000gm.

Mean gestational age at delivery is 39.6±1.6 weeks. Majority of the babies, 11(45.8%) were delivered at gestational age between 37-39 weeks, 9(37.5%) between 40-41, 4(16.7%) between 42-43 weeks.

All the 24 cord blood tests were negative for HBsAg serology.

Table 4. Sociodemographic characteristics of pregnant women attending antenatal clinic of 3 teaching hospitals in Addis Ababa, 2014 (n=530).

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<thead>
<tr>
<th>VARIABLES</th>
<th>NUMBER/PERCENT</th>
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<tr>
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<td>23-28</td>
<td>245(46.2)</td>
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<tr>
<td>29-34</td>
<td>193 (36.4)</td>
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<td>35-40</td>
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</tr>
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</tr>
<tr>
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</tr>
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</tr>
<tr>
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</tr>
<tr>
<td>Married</td>
<td>504(95.1)</td>
</tr>
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<td>Separated</td>
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<td><strong>4.Educational status</strong></td>
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</tr>
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</tr>
<tr>
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<td>College</td>
<td>139(26.3)</td>
</tr>
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</tr>
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<td>VARIABLE</td>
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</tr>
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<td>6</td>
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<td><strong>4. Gestational age in weeks</strong></td>
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</tr>
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<td>169(32.1)</td>
</tr>
<tr>
<td>35-37</td>
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</tr>
<tr>
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<td>167(31.7)</td>
</tr>
<tr>
<td>40-42</td>
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</tr>
<tr>
<td>&gt;42</td>
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Table 6. Prevalence of HBV and HIV in pregnant women attending antenatal clinic of 3 teaching hospitals in Addis ababa, 2014 (n=530).

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<th>HBsAg VARIABLE</th>
<th>HIV NEGATIVE N(%)</th>
<th>HIV POSITIVE N(%)</th>
<th>HIV POSITIVE N(%)</th>
<th>HIV NEGATIVE N(%)</th>
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<td>8(47.1)</td>
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<td>187(36.5)</td>
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<td>3(17.6)</td>
<td>34(6.6)</td>
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<td></td>
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<td></td>
<td></td>
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<td>234(45.7)</td>
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<td></td>
<td></td>
<td></td>
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<td>127(25.1)</td>
<td>5(20.8)</td>
<td>1(5.9)</td>
<td>131(25.5)</td>
</tr>
<tr>
<td>Orthodox</td>
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<td>17(70.8)</td>
<td>14(82.4)</td>
<td>294(57.3)</td>
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<tr>
<td>Catholic</td>
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<td>0</td>
<td>0</td>
<td>3(0.6)</td>
</tr>
<tr>
<td>Protestant</td>
<td>84(16.4)</td>
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<td>2(11.8)</td>
<td>84(16.4)</td>
</tr>
<tr>
<td>other</td>
<td>1(0.2)</td>
<td>0</td>
<td>0</td>
<td>1(0.2)</td>
</tr>
<tr>
<td>5.Occupation</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Government employee</td>
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<td>5(20.8)</td>
<td>9(52.9)</td>
<td>149(29.1)</td>
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<td>Private employee</td>
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<td>9(37.5)</td>
<td>4(23.5)</td>
<td>199(38.9)</td>
</tr>
<tr>
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<td>10(41.7)</td>
<td>4(23.5)</td>
<td>162(31.6)</td>
</tr>
<tr>
<td>Student</td>
<td>2(0.4)</td>
<td>0</td>
<td>0</td>
<td>2(0.4)</td>
</tr>
<tr>
<td>6.Income/Birr</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1000</td>
<td>147(29.6)</td>
<td>8(33.3)</td>
<td>6(37.5)</td>
<td>149(29.6)</td>
</tr>
<tr>
<td>1000-3000</td>
<td>248(50)</td>
<td>15(62.5)</td>
<td>8(50)</td>
<td>255(50.6)</td>
</tr>
<tr>
<td>&gt;3000</td>
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<td>1(4.2)</td>
<td>2(12.5)</td>
<td>100(19.8)</td>
</tr>
<tr>
<td>7.Own your home?</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Yes</td>
<td>91(18)</td>
<td>1(4.2)</td>
<td>3(17.6)</td>
<td>89(17.3)</td>
</tr>
<tr>
<td>No</td>
<td>415(82)</td>
<td>23(95.8)</td>
<td>14(82.4)</td>
<td>424(82.7)</td>
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<tr>
<td>8.Gestatinal age in weeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28-34</td>
<td>167(33.2)</td>
<td>2(8.3)</td>
<td>1(5.9)</td>
<td>168(32.9)</td>
</tr>
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<td>35-37</td>
<td>138(27.4)</td>
<td>14(58.3)</td>
<td>8(47.1)</td>
<td>144(28.2)</td>
</tr>
<tr>
<td>Age Group</td>
<td>Positive</td>
<td>Active</td>
<td>Acute</td>
<td>Total</td>
</tr>
<tr>
<td>-----------</td>
<td>----------</td>
<td>--------</td>
<td>-------</td>
<td>-------</td>
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<tr>
<td>38-40</td>
<td>159(31.6)</td>
<td>8(33.3)</td>
<td>7(41.2)</td>
<td>160(31.4)</td>
</tr>
<tr>
<td>40-42</td>
<td>38(7.6)</td>
<td>0</td>
<td>1(5.9)</td>
<td>37(7.3)</td>
</tr>
<tr>
<td>&gt;42</td>
<td>1(0.2)</td>
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<td>1(5.9)</td>
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</table>

### 9. Abortion Numbers

<table>
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<th>Active</th>
<th>Acute</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>404(79.8)</td>
<td>18(75)</td>
<td>11(64.7)</td>
<td>411(80.1)</td>
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<tr>
<td>1-2</td>
<td>101(20)</td>
<td>6(25)</td>
<td>6(35.3)</td>
<td>101(19.7)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>1(0.2)</td>
<td>0</td>
<td>0</td>
<td>1(0.2)</td>
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</table>

### 10. Parity

<table>
<thead>
<tr>
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<th>Positive</th>
<th>Active</th>
<th>Acute</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>226(44.7)</td>
<td>10(41.7)</td>
<td>10(58.8)</td>
<td>226(44.1)</td>
</tr>
<tr>
<td>1-2</td>
<td>256(50.6)</td>
<td>11(45.8)</td>
<td>7(41.2)</td>
<td>260(50.7)</td>
</tr>
<tr>
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<td>24(4.7)</td>
<td>3(12.5)</td>
<td>0</td>
<td>27(5.3)</td>
</tr>
</tbody>
</table>

### 11. Gravidity

<table>
<thead>
<tr>
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<th>Positive</th>
<th>Active</th>
<th>Acute</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>178(35.2)</td>
<td>5(20.8)</td>
<td>4(23.5)</td>
<td>179(34.9)</td>
</tr>
<tr>
<td>2</td>
<td>169(33.4)</td>
<td>8(33.3)</td>
<td>7(41.2)</td>
<td>170(33.1)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>159(31.4)</td>
<td>11(45.8)</td>
<td>6(35.3)</td>
<td>164(32)</td>
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</tbody>
</table>

#### 10. Discussion

In this study, 4.5% of the pregnant mothers were positive for HBsAg, making intermediate prevalence according to WHO classification. The prevalence of Active hepatitis among positives for HBsAg with seropositivity for HBeAg is 8.3%. There was no pregnant woman with acute clinical hepatitis. This prevalence is lower than some African countries, 11.4%, 9.7%, 8%, 6.5% in Burkina Faso (48), Cameroon (53), Mali (39) and Niger (52) respectively and is higher than some countries like India 0.9% (51), Libya 1.5% (55). Compared to similar studies in the country, it is higher than those from Jimma, 3.7% (27), Bahir Dar, 3.8% (54) and comparable to study done in Addis Ababa 26 years ago, 5% (26) and DebreTabor 5.3% (44).

The prevalence of HBeAg among those who have HBsAg is also lower than some African countries 18.2%, 16.1% in Burkina Faso and Zambia respectively and higher than some 5.2%, 3.3%, 2.7% in Cameroon, Zimbabwe and Democratic republic of Congo respectively (23).

The differences in the prevalence in these diverse populations can be due to differences in cultural and behavioral characteristics of the pregnant woman studied.

The age specific prevalence is highest in the age group 29-34 which comprises to 50% of those positives for HBsAg but there is no statistically significant association.

The income of the studied pregnant women was classified in to three categories for analysis using SPSS generated percentiles which showed the 25th centile income is 1000 Birr, the 50th centile, 1500 Birr and the 75 centile being 3000 Birr.
The highest proportions of pregnant women with HBsAg were who went till secondary school, orthodox Christian, unemployed and who earn >1000 birr but there was no statistically significant association with all of demographic characteristics except Marital status which has strong and statistically significant relationship with positivity for HBsAg which was further confirmed with multivariate analysis. Single pregnant women being 6 times more likely to be infected with HBV(AOR=6.95CI,1.5-22.8). This may be due to single pregnant women are more likely to be exposed to risk factors for HBV like unprotected sex and multiple sexual partners than women who are married.

All the variables in the study were tested for association with HBV infection with bivariate analysis one at a time and Income, history of multiple sexual partner, blood transfusion, educational status being illiterate, being single and having HIV had association with p value < 0.2 and all these were tested together for association with multivariate logistic regression and only being single and having HIV continued to have significant association, those having HIV are 5.6 times more likely to have HBV(AOR=5.6,95CI,1.4-22.1). This can be due to similar modes of transmission and similar risk factors for both HIV and HBV. This is in agreement with other studies which also showed that women with HIV are at increased risk of getting HBV (34),(36),(37),(42).

The prevalence of HIV in pregnant mothers was found to be 3.2% and among those who were positive for HBsAg rate of co infection with HIV was 4 (16.7%) and among those who were HIV positives the rate co infection with HBsAg is 23.5%. The prevalence of HBV/HIV co infected pregnant woman is 0.75%. These figures are lower than those seen at Bahir Dar where the prevalence of HIV was 6.6% (54) and Co infection rate of HBV in seroreactive mothers for HIV being 19% and infection with HIV in among those with HBsAg 33.3% and prevalence of mothers with HIV and HBV was 1.25%(54). Although the difference is not exaggerated, these differences can be due to differences in patient characteristics of the pregnant women studied.

All the variables in the study were tested for association with HIV each at a time and Marital status and seropositivity for HBV had association with p value < 0.2 and both were evaluated further together for association with multivariate logistic regression and only having HBV was statistically associated with having HIV, those having HBV were 6 times more likely to get HIV as well (AOR=6, 95CI, 1.7-21.5).

In mothers who were seroreactive for HBsAg and followed till delivery there was no preterm delivery, No still birth, No small for gestational age baby and 87.5% of the babies had first minute APGAR of 8. Most of the mothers (75%) delivered by SVD and Mean gestational age at delivery was 39.6±1.6 weeks and mean birth weight is 3216.6±310.2gm. This is in contrast to other studies which showed increased rate of preterm delivery (47) and in agreement with studies showing seropositivity for HBsAghas no direct effect on perinatal outcome (49).

The number of babies exposed to HBV in this study is small, 24 and is difficult to conclude on perinatal outcome of mothers with HBsAg.

All 24 babies exposed for HBV were tested for cord blood HBsAg with ELISA and all were negative for HBsAg. This is in contrast to other studies showing cord blood seropositivityof
0.96% in Nigeria (32), 0.9% in Libya (55) and similar to other study which showed zero cord blood seropositivity for HBsAg in turkey (50).

Although the sensitivity of ELISA for detection of HBsAg is excellent DNA PCR could have been more specific which we were not able to do because of no set up for the test in the country at the time of the study.

Table 7. Association of selected explanatory variables and HBV infection among pregnant mothers in 3 teaching hospitals in Addis ababa, 2014, n=530.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>POSITIVEN/%</th>
<th>NEGATIVEN%</th>
<th>CPVALUE</th>
<th>COR/95CI</th>
<th>AOR/95CI</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
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<td></td>
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<td>0.007</td>
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<td>1</td>
<td>1</td>
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<td></td>
<td></td>
</tr>
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<td></td>
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<td></td>
</tr>
<tr>
<td>YES</td>
<td>1(4.2)</td>
<td>4(0.8)</td>
<td>0.136</td>
<td>5.5(0.6-50.7)</td>
<td>5.2(0.5-52)</td>
<td>0.16</td>
</tr>
<tr>
<td>NO</td>
<td>23(95.8)</td>
<td>502(99.2)</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Tatoo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>3(12.5)</td>
<td>49(9.7)</td>
<td>0.65</td>
<td>1.3(0.38-4.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>21(87.5)</td>
<td>456(90.3)</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. HIV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POSITIVES</td>
<td>4(16.7)</td>
<td>13(2.6)</td>
<td>0.001</td>
<td>7.6(2.27-22)</td>
<td>5.6(1.4-22.3)</td>
<td>0.014</td>
</tr>
<tr>
<td>NEGATIVES</td>
<td>20(83.3)</td>
<td>493(97.4)</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Income</td>
<td></td>
<td></td>
<td></td>
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</tr>
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</table>
11. Conclusion

The prevalence of HBV among pregnant mothers in Addis Ababa is of intermediate endemicity.

The proportions of mothers who have both HBeAg and HBsAg are small (8.3%).

The prevalence of HIV among pregnant women of Addis Ababa is 3.2% and 16.6% of those mothers with HBV also has HIV.

Single pregnant women and those pregnant women with HIV were more likely to test positive for HBsAg.

There was no perinatal transmission in this study and the perinatal outcome of pregnant women with HBsAg seems to be not adversely affected.

12. Limitation of the study

We used non probability sampling method which might result in sampling bias.

13. Recommendations

All pregnant women should be screened for both HIV and HBV during ANC.

Partners of pregnant women who test positive for HBsAg should be counseled to get tested and get HBV Vaccine if found to be negative.

Women who test positive either for HBV or HIV should be specifically screened for the other because of significant rate of co infection.

The baby of mothers with HBV should be given HBV Vaccine and HBVIG immediately after delivery and arrangements should be made before delivery.

Health education about risk factors and mode of transmission of HBV and HIV should be given to pregnant women in particular and all peoples generally.

Further study specifically case control study comparing pregnant women with HBV and those without should be done to evaluate the effect of HBV on perinatal outcome.
Further study specifically cord blood HBV DNA testing of mothers with HBV or long term follow up of babies exposed for HBV for markers of HBV infection should be done to evaluate rate of perinatal transmission.

14. Annex

14.1 Questionnaire

Date: Hospital:Card No.:Roll No:_____

1. Sociodemographic information

1.1 Age:______ 1.2 Address:_____________Phone No.____________________
1.7.1 Monthly income:____________________
1.7.2 Own your home? 1.YES 2. NO

2. Risk factors for HBV

2.1 History of multiple sexual partner 1. YES 2. NO
2.3 History of blood transfusion 1. YES 2. NO
2.4 History of Tatoo 1.YES 2. NO

3. Past obstetric history

3.1 Parity: ____ 3.2 Abortion ____ 3.2.1 Induced ____ 3.2.2 Spontaneous ____ 3.3 Ectopic pregnancy: ____ 3.4 Stillbirth: ____ 3.5 ENND: ____ 3.6 LNND: ____ 3.7 No.of alive children:_____

4. Current pregnancy

4.1 Gravidity: ____ 4.2 GA: ____ By Date / from Ultrasound / by Physical examination

5. Rapid test for HIV: 5.1 CTRR 5.2 CTNR

6. Serology for HBsAg: 6.1 POSITIVE 6.2 NEGATIVE
✓ If Serology for HBsAg is Negative = FINISHED THANKS.
✓ IF Serology for HBsAg is POSITIVE: CONTINUE TO THE END OF QUESTIONNAIRE.

7. **Serology for HBsAg:**
   - 7.1 POSITIVE
   - 7.2 NEGATIVE

8. **Jaundice&/or RUQ pain &/or Tenderness:**
   - 8.1 YES
   - 8.2 NO

9. IF YES TO Question no.8
   - 9.1 SGOT ________
   - 9.2 SGPT ________

10. **Clinical Acute Hepatitis:**
    - 10.1 YES
    - 10.2 NO

10. **Birth outcome:**
    - 10.2 Indications for CS or Instrumental delivery. .................................................................
    - 10.3 GA at delivery: .......10.4 Weight: .......Gram
    - 10.5 APGAR SCORE: ....... & .......at 1st and 5th minute.

11. **CORD BLOOD FOR HBsAg:**
    - 1. POSITIVE
    - 2. NEGATIVE
14.2 SLIP given to the pregnant women who were positive for HBsAg

Hospital: ______________________
Card No.: ______________________
• This client is HBV carrier and a study subject on sero-prevalence and vertical transmission of HBV.
• Please take cord blood to test for HBsAg.
• Please give the baby HBV Vaccine immediately after delivery.
• Principal investigator:
  ❖ Dr. Sisay Kirba
  ❖ Contact address: 0911794838/0913733261

❖ Birth outcome:
• Indications for CS or Instrumental delivery ________________________________
• GA at delivery: ________________
• Weight: ________________ Gram.
• APGAR SCORE: ______ & ______ at 1st and 5th minute.
❖ CORD BLOOD FOR HBsAg:
  1. POSITIVE  2. NEGATIVE
14.3 Consent form

Hello My name is ______________ we are conducting a study on HBV during pregnancy and its transmission from pregnant mothers to their baby during pregnancy and delivery.

Knowing HBV status during pregnancy help to protect your baby and your partner and you will have the chance for further evaluation. Even if you don’t participate in this study it is strongly recommended that you are tested for HBV.

All of the investigations that you will be asked to undergo are primarily for your and your baby’s benefit and what we are interested is how many of pregnant mothers have markers for HBV and how many of them transmit it to their baby.

If you are positive for markers of HBV, we will do some clinical evaluations and some investigations and we will test the baby’s cord blood for markers of HBV immediately after delivery and we will give HBV Vaccine to the baby to protect the baby.

Participation in the study is confidential and no names will be mentioned in the questionnaire to be filled.

Participation in the study is optional and disagreeing to participate in the study will not result in any harm or will not affect the service you get from the hospital.

Are you willing to participate in the study?

1. NO
2. YES

IF YES  Proceed to the questionnaire.
References


41. World Health Organization. 2010. Revision of Antiretroviral therapy for HIV infection in adults and adolescents. WHO/ART.


