# The association of chronic hepatitis B infectivity with fetomaternal outcome: A retrospective cohort study in a tertiary hospital

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## ABSTRACT

**Background:** Hepatitis B infection on pregnancy has been linked to preterm labor, risk of prematurity, low birth weight, and the occurrence of gestational diabetes mellitus.

**Objective:** To determine the association between Chronic Hepatitis B infectivity and fetomaternal outcome such as preterm birth, low birth weight, gestational diabetes and preeclampsia among pregnant patients admitted in a Tertiary Hospital.

**Methodology:** A retrospective cohort study was done among pregnant women diagnosed with chronic hepatitis B infection admitted in a tertiary hospital from January 1, 2014 to December 31, 2018. The association of Hepatitis B infectivity and fetomaternal outcomes namely preterm birth, gestational diabetes, preeclampsia and low birth weight was determined

**Results:** Chronic Hepatitis B infection had 1.43% prevalence among the study group. 149 patients were able to able to fulfill the inclusion criteria. Pregnant women with high infectivity Hepatitis B infection tend to be younger, have lower BMI, have lesser gravidity and parity than patients who are nonreactive to Hepatitis B e-antigen. AST and ALT were also higher among those with high infectivity Hepatitis B. However, there was no significant difference among the two groups in terms of elevated ALT. There was no significant association between Hepatitis B infectivity and fetomaternal outcomes such as preeclampsia, gestational diabetes mellitus, preterm birth and low birth weight. There is no increased risk for patients with high infectivity for preeclampsia, gestational diabetes mellitus, and low birth weight. There appears to be an excess risk in the likelihood of preterm birth/labor among those women who have a high infectivity Hepatitis B infection during pregnancy.

**Conclusion:** The prevalence of chronic hepatitis B infection among Filipino pregnant women admitted in a tertiary hospital was 1.43% from 2014 to 2018. There was no association between chronic hepatitis B infectivity and preeclampsia, Gestational diabetes mellitus. There seems to be an increased risk for HBeAg positive patients for preterm birth preterm labor, and occurrence of low birth weight, but was not statistically significant in the study population.

*Keywords: chronic hepatitis B infectivity, fetomaternal outcome*

## INTRODUCTION

Hepatitis B virus belongs to the Hepadnaviridae family, and primarily affects the liver. The hepatocellular injury brought about during hepatitis B infection is due to the immune response to the antigens presented by the hepatitis B virus. Great concern has been focused on its progress into the chronic state, since it can lead to development of chronic liver disease, and hepatocellular carcinoma.[1] The appearance of hepatitis B surface antigen (HBsAg) is noted to be the hallmark of hepatitis B infection, and is the first serum marker that appears during the incubation period. A diagnosis of Chronic hepatitis B infection is given when HBsAg remains persistent in a period of 6 months and the seroconversion of anti-HBc IgM to a negative result.[1]

Researches focusing on the impact of hepatitis B infection on pregnancy have linked Hepatitis B infection with preterm labor, risk of prematurity, low birth weight, and the occurrence of gestational diabetes mellitus;

while other studies have found no association with these outcomes[2]. Routine screening as part of prenatal care has been advocated to identify neonates who are supposed to be given both active and passive immunization, as this has been noted to decrease the risk of the neonate to acquire hepatitis B infection[3]. In addition to controlling the number of individuals being infected with Hepatitis B virus, health care practitioners particularly obstetricians, must also know the impact of such an infection in the course of pregnancy. It is then important to generate more information regarding its effect in pregnancy among Filipino women, specifically with its level of infectivity as indicated by the positivity of HBeAg. Positive HBeAg denotes high infectivity, while a nonreactive test denotes low infectivity.

Fetomaternal outcomes such as preeclampsia, gestational diabetes mellitus, preterm labor and low birth weight may bring about fetomaternal morbidity and mortality. Hence establishing hepatitis B infection as one of the predictors for such outcomes among Filipino pregnant women will be of sound clinical value.

Ideally, the viral load should be obtained during pregnancy, as part of the management of patients with chronic hepatitis B infection. This value is essential in identifying which among the patients should be given treatment. However, many patients are not able to avail such tests due to the high cost of hepatitis B viral load. Nevertheless, the importance of seropositivity in HBeAg could not be underestimated as it has been associated with higher hepatitis B viral load, and reflects replication of the hepatitis B virus. Furthermore, HBeAg has also been noted to be able to cross the placenta, hence with an increased rate of maternal transmission and association with fetomaternal sequelae[4].

Hepatitis B Virus is a DNA virus, surrounded by an envelope which is comprised of lipoproteins and a core composed of double stranded DNA. This core is surrounded completely by a surface antigen or the HBsAg. This increases in patients with hepatitis B infection and is released into the blood circulation and becomes detectable in the blood, either during an acute or chronic infection[1]. The focus of this study would be the Hepatitis B virus e- antigen, which is associated and correlates with the DNA polymerase activity of hepatitis serum levels. Its persistence has been found to correlate well with hepatitis B infectivity and prognosis. Patients with hepatitis B infection who are positive for HBeAg have been noted to be at risk to develop chronic active hepatitis[1]. In cases where a mother is both HBsAg positive and at the same time positive for the e-antigen, maternal to child transmission goes as high as 90% in newborns without the benefit of hepatitis B vaccination and Hepatitis B immunoglobulin[1].

According to the latest data by the World Health Organization, Hepatitis B infection remains to be a global health problem as of 2018, with an estimate of about 257 million individuals affected worldwide[5]. Chronic hepatitis B infection is noted to have high prevalence in the Philippines, occurring in about 10.4% of the national population, or an estimate of about 10.6 million individuals are infected. Due to the high prevalence of hepatitis in the country, the Philippines is then classified to be hyperendemic for Hepatitis B infection[6].

The aim of this retrospective cohort study is to determine the association of Chronic hepatitis B infectivity, as evaluated by having reactive and nonreactive HBeAg, with four fetomaternal outcomes such as gestational diabetes mellitus, preeclampsia, low birth weight and preterm labor among Filipino pregnant women who were admitted and delivered in a tertiary hospital. The study would also be able to compare the sociodemographic characteristics between the two groups. This study would also be able to determine the prevalence of chronic hepatitis B infection among pregnant women admitted in the department of obstetrics and gynecology from 2014 to 2018.

## MATERIALS AND METHODS

A retrospective cohort study on pregnant patients diagnosed with chronic hepatitis B infection was done for a period of 5 years, from January 1, 2014 to December 31, 2018. The list of admitted patients, which includes patients not in labor and those who delivered in the institution, were reviewed. This was recorded through the masterlist of admissions and ward reports. All patients properly identified with a diagnosis of chronic hepatitis B infection were included in the study (Total Enumeration). The patients with medical records that could not be retrieved or not in file were excluded from the study. The charts of the patients were then screened according to the following inclusion and exclusion criteria.

### A. Inclusion Criteria

- Patients with Chronic hepatitis B infection who were admitted (shall include patients not in labor) and delivered in the Department of Obstetrics and Gynecology in the Philippine General Hospital from January 1, 2014 to December 31, 2018
- Singleton pregnancy

### B. Exclusion Criteria

The study will not include patients who have the following characteristics:

- Patients with known systemic comorbid illnesses aside from preeclampsia and Gestational Diabetes Mellitus
- Patients with acute hepatitis B infection

- Patients who have other known sexually transmitted infections
- Patients with no hepatitis profile or liver function test results
- Those reactive for Hepatitis A and Hepatitis C infection

Clinical and demographic data were obtained from the obstetrical sheet previously completed by the residents in charge, and were transcribed into a database to maintain anonymity. The clinical information taken included the patients' age, marital status, educational attainment, and body mass index. Laboratory results such as Liver function test, hepatitis profile and Hepatitis B Virus DNA were also recorded.

The patients who were able to fulfill the inclusion criteria were grouped according to their diagnosis: Those with chronic hepatitis B infection with low infectivity were assigned to group A, while those with high infectivity were assigned to group B. Pregnancy outcomes among the two groups were assessed such as the occurrence of preterm birth, presence of low birth weight infants, preeclampsia and gestational diabetes mellitus. The data taken were placed in a case report form which was approved by the research ethics board, and encoded in excel form, and placed in a USB. The case report forms and USB are being kept in a secure cabinet in the Section of Infectious Diseases office, which is accessible only to the researcher and research assistant. This is in compliance to the guidelines for privacy and confidentiality indicated in the Data Privacy Act of 2012 and 2017 National Ethical Guidelines for Health Related Research (NEGHHR).

The prevalence of Hepatitis B infection among pregnant women from 2014 to 2018 was estimated. Point and interval estimates of these proportions were also determined with a trend analysis of proportions performed to determine patterns in the prevalence of the condition.

In order to provide an overview of the study population, descriptive statistics such as mean and standard deviation were used for numerical data variables, while frequency and percentage was then used for categorical variables.

A series of chi-square test of association and independent t-test were used to determine the differences in the clinico-demographic characteristics across those women with high and low infectivity Hepatitis B infection.

Initially, a logistic regression method was to be performed, but the inability to account for differences between the two groups with the variables has rendered such analysis to be avoided. Chi square test was done to determine if there was an association between the level of infectivity and the fetomaternal outcomes. The relative risks for the clinically important outcomes using the high and low infectivity as a stratifying variable were also estimated, as well as their confidence intervals.

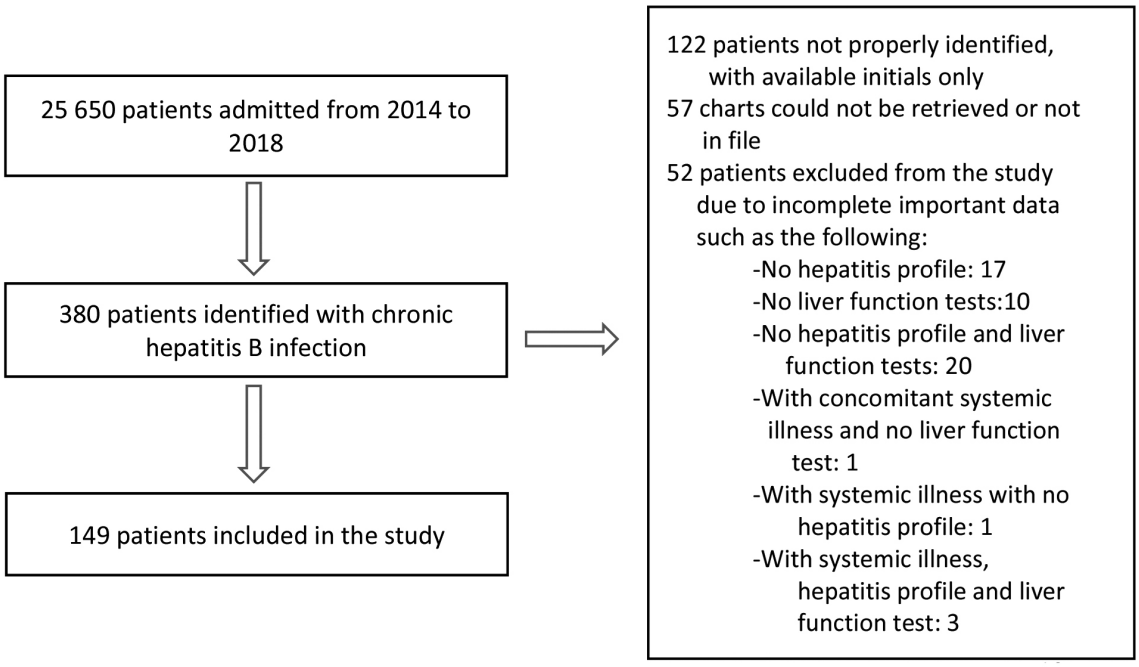
The level of significance for all sets of analysis was set at a p-value of less than 0.05 using two-tailed comparisons.

## RESULTS

There were a total of 380 patients with chronic hepatitis B infection from a total of 26, 560 pregnant women admitted and delivered in the Department of Obstetrics and Gynecology from January 1, 2014 to December 31, 2018. Screening for Hepatitis B Infection is part of the routine prenatal check-up for all pregnant patients. It is requested in the institution upon admission if it has not yet been requested as out-patient basis prior to admission or delivery.

This data was derived from the ward report and masterlist submitted by the residents to the department. The patients in the ward report who were not included in the masterlist were only identified through their initials. Other data such as the case numbers were also not indicated, hence leading to difficulty in identification of the patients and failure of retrieval of some of the charts. Upon request of retrieval from the medical records, 57 charts were noted to be not in file. This is also in consideration that majority of the charts were from 2014 have already been placed in the storage area of the medical records. Upon review of the charts, 52 patients had incomplete data, such as hepatitis profile and liver function tests, hence could not be included in the study. A total of 149 patients were included in the study, and qualified for data analysis. Given the hypothesized increased risk of preterm labor or birth by 21% among those who are HBeAg (+) than those who are HBeAg (-) according to a study done by Ma et al, the sample size of the current study involving 149 patients yielded 80%, with a level of confidence set at 95%.

Based on the census data, a total of 380 patients were diagnosed with chronic hepatitis B infection among the total number of pregnant patients admitted in the department from January 2014 to December 2018. This presents a five-year prevalence of 1.43%, with a 95% confidence interval of 1.29 to 1.58%. This was derived from the total number of Obstetric admissions in the tertiary hospital from 2014 to 2018 (Table 1). Data reveals a consistent increasing trend from 2015 to 2016 (p=.0026), where from 0.72% prevalence of Hepatitis B, it went up to 1.31% in 2016. Likewise, an increasing trend was also observed from year 2016 (1.31%) up to 2017 where prevalence was increase to 2.12%. The prevalence from 2017 to 2018 decreased to 1.82%, but its difference in previous year was not statistically significant (p=.0.2849). (Table 1)




The current sample includes 149 pregnant women who have Hepatitis B infection. with more than half of them noted to have low infectivity (n= 100, 67.11%) and the remaining have reactive HBeAg result (n= 49, 32.89%). Most of the patients with chronic hepatitis B infection were from 18 to 30 years of age (n=82, 55%), single (n=89, 59%), were able to reach high school level (n=88, 59%), and were multiparous (n=108, 81%). (Table 2)

In comparison of patients between patients with high and low infectivity, pregnant women positive for HBeAg were noted to be younger ($\chi 2$: 18.38, p<0.01), have lower BMI (t: 2.10, df: 102.7, p: 0.04); have lesser gravidity (z: 2.57, p: 0.01); parity (z: 2.90, p<0.01; $\chi 2$: 11.06, p<0.01), than patients who were nonreactive to Hepatitis B e-antigen. (Table 3)

The values of liver function tests done namely AST and ALT in units are higher among those with high infectivity Hepatitis B( AST p<0.01, ALT p=0.04). However when comparing the number of patients with elevated ALT between the two groups, the difference was noted to be not statistically significant (p=0.22) (Table 4). It can also be noted that only eleven patients were able to have an HBV DNA done, with the majority of these patients in group A, with nonreactive HBeAg (Table 4). Patients with nonreactive HBeAg had a range of values from <6 IU/ml to 141 IU/ml, and one result of 8,865,000 IU/ml. The highest HBV DNA noted in this group, measured at 8,865,000 IU/ml. The patient was given tenofovir to decrease the possibility of maternal to child transmission of hepatitis B infection. Only three patients with reactive HBeAg had reactive HBV DNA results, which were noted to be a 1.2 IU/ml, 8500 IU/ml and 11,500 IU/ml respectively.

There was no noted significant association between the fetal and maternal outcomes namely the occurrence of preeclampsia, gestational diabetes mellitus, among patients with chronic hepatitis B infection with high

**Table 1.** Distribution of Chronic Hepatitis B Cases in the Obstetric Population in PGH from 2014 to 2015 and Trend Analysis

| Year | Hepatitis B Cases Identified | Annual Number of Obstetric Patients Seen | Prevalence Proportion | p value | Year being Compared | Trend |
|---|---|---|---|---|---|---|
| 2014 | 56 | 5, 139 | 1.09% | | | |
| 2015 | 35 | 4, 876 | 0.72% | 0.0513$^{ns}$ | 2014-2015 | No Change |
| 2016 | 80 | 6, 102 | 1.31% | 0.0026* | 2015-2016 | Increasing |
| 2017 | 134 | 6, 330 | 2.12% | 0.0005* | 2016-2017 | Increasing |
| 2018 | 75 | 4, 113 | 1.82% | 0.2849$^{ns}$ | 2017-2018 | No Change |
| Total | 380 | 26, 560 | 1.43% | | | |

**Table 2.** Baseline characteristics of the study population

| | | # of Patients | % | p value |
|---|---|---|---|---|
| **Age** | **30 and Below** | 83 | 55.7% | 0.0495* |
| | <17 | 1 | 0.7% | |
| | 18-30 | 82 | 55.0% | |
| | **31 and Above** | 66 | 44.3% | |
| | 31-45 | 65 | 43.6% | |
| | >45 | 1 | 0.7% | |
| **Marital Status** | Single | 89 | 59.7% | 0.0008* |
| | Married | 60 | 40.3% | |
| **Educational Attainment** | **Below College Level** | 95 | 63.8% | 0.0001* |
| | No Formal Education | 1 | 0.7% | |
| | Elementary | 6 | 4.0% | |
| | High School Level | 88 | 59.1% | |
| | College Level | 54 | 36.2% | |
| Gravidity/Parity | Primapara | 41 | 27.5% | 0.0001* |
| | Multipara | 108 | 72.5% | |

**Table 3.** Baseline Characteristics of patients with Low infectivity and High Infectivity

| Characteristics | Low Infectivity | High Infectivity | p-value |
|---|---|---|---|
| **Age** | | | |
| 15-17 years old | - | 1 (2.04%) | |
| 18-30 years old | 44 (44%) | 38 (77.55%) | <0.01* |
| 31-45 years old | 55 (55%) | 10 (20.41%) | |
| 46-50 years old | 1 (1%) | - | |
| **Marital Status** | | | 0.22 |
| Single | 56 (56%) | 33 (67.35%) | |
| Married | 44 (44%) | 16 (32.65%) | |
| **Educational Attainment** | | | |
| No formal education | 1 (1%) | - | 0.64 |
| Elementary Level | 5 (5%) | 1 (2.04%) | |
| High school Level | 60 (60%) | 28 (57.14%) | |
| College Level | 34 (34%) | 20 (40.82%) | |
| *Weight in kilograms* | 65 ± 10.82 | 61 ± 10.19 | 0.04* |
| **Body-mass Index Category** | 27.24 ± 4.35 | 25.76 ± 4.08 | 0.05* |
| Normal | 32 (32%) | 20 (40.82%) | |
| Overweight | 50 (50%) | 19 (38.78%) | 0.15 |
| Obese I | 13 (13%) | 10 (20.41%) | |
| Obese II | 5 (5%) | - | |
| **OB Score** | | | |
| Gravidity | 3 (1-9) | 2 (1-6) | 0.01* |
| Primipara | 19 (19%) | 22 (44.9%) | <0.01* |
| Multipara | 81 (81%) | 27 (55.10%) | <0.01* |

infectivity and those with low infectivity using the chi square test (Table 5). It can be noted that there appears to be an increase risk in the likelihood of preterm birth/labor, and low birthweight among those women who have a high infectivity Hepatitis B infection during pregnancy. However, the increased risk in this group was noted to be not statistically significant. Similarly, there was no increase in the risk of developing preeclampsia and gestational diabetes mellitus among patients who were positive for HBeAg. (Table 6)

## DISCUSSION

According to the data released by the World Health Organization, Chronic Hepatitis B infection continues to be a threat to public health due to its high prevalence, affecting about 257 million worldwide[5]. In a study by Gish et al in 2016, the highest prevalence of hepatitis B infection

**Table 4.** Laboratory and Diagnostic Characteristics of the Study Population

| Characteristics | Low Infectivity | High Infectivity | p-value |
|---|---|---|---|
| With HBV-DNA Result | 8 (8%) | 3 (6.12%) | |
| HBV-DNA in IU/mL | 6 to 8, 865, 000 | 1.22 to 11, 500 | |
| AST Level in units/mL | 25.09 ± 7.38 | 33.73 ± 16.57 | <0.01* |
| ALT Level in units/mL | 22.72 ± 9.86 | 26.84 ± 11.88 | 0.04* |
| Elevated | 3 (3%) | 4 (8.16%) | 0.22 |

**Table 5.** Distribution of Feto-maternal Outcomes among Women with Chronic hepatitis B Low and High Infectivity

| Outcomes | Low Infectivity | High Infectivity | p-value |
|---|---|---|---|
| Preterm Labor | 10 (10%) | 8 (16.67%) | 0.29 |
| Preterm Birth | 9 (9.09%) | 6 (12.77%) | 0.49 |
| Birthweight in grams<br>*Low birthweight*<br>*Term Low Birthweight* | <br>13 (13.13%)<br>5 (5.05) | <br>8 (17.39%)<br>3 (6.52) | <br>0.50<br>0.72 |
| Pre-eclampsia | 15 (15%) | 6 (12.24%) | 0.65 |
| Gestational Diabetes | 8 (8%) | 2 (4.08%) | 0.36 |

**Table 6.** Relative Risk of Feto-maternal Outcomes among Women with Chronic Hepatitis B Infection

| Outcomes | Relative Risk | 95% Confidence Interval | p-value |
|---|---|---|---|
| Preterm Labor | 1.44 | 0.81-2.57 | 0.18 |
| Preterm Birth | 1.27 | 0.65-2.50 | 0.34 |
| Low birthweight | 1.32 | 0.59–2.97 | 0.52 |
| Term Low birth weight | 1.29 | 0.32-5.17 | 0.72 |
| Pre-eclampsia | 0.85 | 0.41-1.75 | 0.43 |
| Gestational Diabetes | 0.59 | 0.17-2.07 | 0.30 |

was noted in the reproductive age, 18.1% noted in among Filipinos aged 20-29, and 17.6% for those 30 to 39 years of age. The Philippines is still a hyperendemic country for hepatitis B infection. The reason for such was pointed to limited access to health care, inadequate screening, and vaccination in the country, such that chronic hepatitis B infection was more common among patients with lower socioeconomic status and educational attainment[3]. In the data released by the World Health Organization as of July 2018, the Philippines had a high burden of disease of about 10.4% of the total population. This relays a total of 10.6 million Filipinos who have chronic hepatitis B infection[6].

A total of 380 patients had chronic hepatitis B infection among 26, 560 pregnant women admitted and delivered in the Department of Obstetrics and Gynecology from 2014 to 2018. This entailed a five-year prevalence of 1.43% of chronic hepatitis B infection, with a 95% confidence interval of 1.29 to 1.58%. This still represents a significant disease burden among the obstetric population in the current institution. There was also an increasing prevalence of cases identified through the years via the trend analysis of proportions (Table 2). This could be the result of various factors such as increased reporting and routine performance of hepatitis antigen testing. It could also be due to the increase in the subsidy provided in the tertiary hospital, as laboratory tests were provided by Philhealth. There was decrease in the prevalence from 2017 to 2018, from 2.12% to 1.82%. This, however was found to be not statistically significant (p value=0.2849) (Table 1). The decrease could be accounted for by the renovation of the OB GYN complex, resulting to a decrease in the total number of admissions. This prevalence in the obstetric population is lower, but remains comparable with South East Asian countries with high prevalence of chronic hepatitis B infection. China, which is hyperendemic for Hepatitis B infection, has a prevalence rate of 2-8 % in women of reproductive age[7]. The prevalence rate noted in the study conducted is higher than countries with low prevalence rate, such in the United States, occurring 0.4 % in the obstetric population[7].

In a study done by Carpio et al in 2014, risk factors associated with the disease were studied among pregnant women seeking prenatal care in the Out-patient department of Philippine General Hospital. The study

revealed that seropositivity was present in 9.6% out of 768 pregnant women. It was also noted that the occurrence of hepatitis B infection directly proportional to the patient's age, and was seen more in married women, multiparas, and those with history of miscarriages[8].

In the data gathered in this study, hepatitis B infection was seen more in single women, eighteen to thirty years of age, and able to reach high school level (n=88, 59%). Similar to the study done in the same institution in 2014, hepatitis B infection was more common among multiparous women. The difference in the findings from the previous study may be explained by the greater number of patients involved in the current study. Moreover, the current study involved all pregnant patients admitted in the tertiary hospital during the 5 year period.

In the data gathered, Socio-demographic data between HBeAg positive and negative patients were similar in terms of marital status, and educational attainment. Differences were only noted in terms of age, BMI, and gravidity. Patients with positive HBeAg were noted to be younger patients ($\chi 2$: 18.38, $p<0.01$), have lower BMI (t: 2.10, df: 102.7, p: 0.04); have lesser gravidity (z: 2.57, p: 0.01); parity (z: 2.90, $p<0.01$; $\chi 2$: 11.06, $p<0.01$), than patients are nonreactive to Hepatitis B e-antigen. (Table 3)

It can also be noted that only eleven patients were able to have an HBV DNA done, with the majority of these patients in group A, with nonreactive HBeAg (Table 4). The highest HBV DNA noted in this group, measured at 8,865,000 IU/ml. The reason for having highly elevated viral load in HBeAg negative patients is that she may be in the immune-escape phase. This may be due to mutations that occur in the virion particles, rendering it not able to express Hepatitis b e-antigen. This then may lead to progressive damage to the hepatocytes 9. The patient was given tenofovir to decrease the possibility of maternal to child transmission of hepatitis B infection.

There was a noted difference in the liver function tests namely Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) between the two study groups. It was found to be higher among patients who were HBeAg positive, compared to those who were seronegative, and was noted to be statistically significant (Table 4). Seven patients were noted to have elevated ALT levels, but were noted to be less than twice of the upper normal limit. The elevated ALT, which is a more specific marker for liver injury, were also noted to be not statistically significant between the two groups. Hepatitis B virus infection does not directly damage the cells of the liver, but rather, the hepatocellular injury brought about during hepatitis B infection is due to the immune response to the antigens presented by the hepatitis B virus[1]. Changes in pregnancy renders the patient to be in the immune tolerance phase, which is characterized by a positive hepatitis B antigen, elevated hepatitis B virus DNA but with normal liver function tests[9]. Hepatic flares, defined as an increase in the ALT three to five times as that of the upper normal limit, was found to be more commonly seen among patients who were HBeAg positive[2]. The statistically significant increase in the liver function test values among patients with high infectivity then entails closer monitoring postpartum, when immune reconstitution takes place.

A meta-analysis was done by Ma et al in 2017, which included 22 observational studies which studied the correlation of HBsAg reactive status of pregnant women with preterm labor. The occurrence of preterm labor was postulated to be either due to the inflammatory response elicited in the placenta in cases of hepatitis B infection. HBeAg, which reflects viral replication, is also linked to a higher viral load. Results showed an 18 % increase in preterm birth among those who were positive for HBsAg as compared to those who were seronegative. The risk increases to 21 % for those with positive result for HBeAg.[10] HBeAg has been noted to be able to cross the placenta, hence an increased risk rate of fetomaternal sequelae. Reddick et al conducted a 10-year study in the Unites States with patients with Hepatitis B infection. The fact that Hepatitis B virus DNA has been noted to be positive in the placenta of infected women, implies the ability of Hepatitis B Virus to pass through the placental barrier, and can bring about inflammatory response in the placenta[11].

In the current study, it was noted that among patients diagnosed with chronic hepatitis B infection, there was no association of seropositivity of HBeAg and preterm labor in the study group. However, there appears to be an excess risk in the likelihood of preterm birth/labor, among those women who have a high infectivity Hepatitis B infection during pregnancy. The increased risk however, was noted to be not clinically significant, with the p-value of more than 0.05 (Table 6).

A study by Lao et al noted that Hbsag carrier status was an independent risk factor for the development of gestational diabetes mellitus, with no association with maternal body mass index or their parity. This study noted that hepatitis B infection in pregnant women carried an increased risk of 24% for the development of gestational diabetes mellitus. The association of diabetes mellitus and chronic hepatitis B infection was linked to the increase in production of tumor necrosis alpha, which renders a patient to have insulin resistance[12]. The high prevalence rate of gestational diabetes among pregnant Filipino women makes ethnicity itself a risk factor for developing the disease during pregnancy. According to Asian Federation of endocrine Societies Study Group on Diabetes in Pregnancy (ASGODIP), the prevalence of gestational diabetes among Filipino women is at 14%[13]. Despite this high prevalence, gestational diabetes was found only in

10 patients among the study population in the current study. There was also no association of HBeAg positivity with gestational diabetes mellitus, nor an increased risk for developing the disease.

Hypertension in pregnancy implicates a high risk for maternal morbidity and mortality. It is found in about 5-10% of pregnant women, and many risk factors have been linked to its occurrence such as primiparity, obesity, personal and family history of preeclampsia, ethnicity, age of more than 40 years old, and smoking[14]. In a meta-analysis done in Qi-tao et al in 2016 studied the relationship of chronic hepatitis B infection and the occurrence of preeclampsia among Asian women. The study showed a decreased incidence of preeclampsia of about 23%. The postulated possible explanation for such decrease in the risk for was that hepatitis B virus increases MMP's or Matrix Metalloproteinases, which enhances trophoblastic invasion of the spiral artery, hence decreases the incidence of preeclampsia among pregnant women in the Asian region, where hepatitis B infection is more prevalent[15]. In the current study, there was no noted association of the incidence of preeclampsia among women who were positive for HBeAg as compared with patients with low infectivity. There was also no increase in the risk for developing preeclampsia in patients positive for HBeAg.

A 20-year by Safir et al in 2010, found that there was an increase in the occurrence of low birth weight infants among mothers with hepatitis B infection, since it renders the patient to be in a chronic inflammatory state[16]. In this current study done, there was no association noted between HBeAg seropositivity and the occurrence of low birth weight. There was an increase in the risk for low birth weight for patients who had high infectivity, but was noted to be not statistically significant. Given the knowledge that its occurrence of low birth weight could also be brought about by preterm birth, the relative risk for the occurrence of term low birth weight among newborns was noted. The risk was also noted to be increased for having term low birth weight among HBeAg positive patients, but was not statistically significant.

The study done is a retrospective cohort study, hence has several limitations. In compliance to the data privacy act, only initials of the patients were retrieved from the ward report of the department, rendering 122 patients or 32% of the total number of patients with hepatitis B infection unidentified, and hence charts were not retrieved from the medical records. On the other hand, some of the retrieved charts had incomplete data such as hepatitis profile and liver function tests which are included in the exclusion criteria of the study.

## CONCLUSION

In this study, the five-year prevalence chronic hepatitis B infection among the obstetric population admitted in a tertiary hospital was 1.43% from January 2014 to December 2015. This prevalence in the obstetric population is lower, but remains comparable with Southeast Asian countries which are hyperendemic for hepatitis B infection. There was also a significant increase in the prevalence of cases identified through the years which could be the result of increased reporting, hepatitis antigen testing and subsidy with the availability of Philhealth.

In the data gathered, Socio-demographic data between group A and B were similar in terms of marital status, and educational attainment. HBeAg positive women tend to be younger, have lower BMI, have lesser gravidity and than patients who are nonreactive to Hepatitis B e-antigen. There was a noted difference in the liver function tests namely AST (Aspartate aminotransferase) and ALT (Alanine aminotransferase) were found to higher among patients who were HBeAg positive, compared to those who were seronegative, and was noted to be statistically significant. Seven patients were noted to have elevated ALT levels, but were noted to be less than twice of the upper normal limit. The statistically significant increase in the liver function tests among patients with high infectivity then implies closer monitoring postpartum, when immune reconstitution takes place, thus an increase in the possibility of a hepatic flare.

There was no noted association between HBeAg positive result and fetomaternal outcomes namely the occurrence of preeclampsia, gestational diabetes mellitus, among patients with chronic hepatitis B infection.

There appears to be an excess risk in the likelihood of preterm birth/labor, and low birth weight among those women who have a high infectivity Hepatitis B infection during pregnancy. The increased risk however, was noted to be not clinically significant.

Conduction of a retrospective study remains to be a challenge since it relies on previously gathered data. A more organized recording of data is recommended in the conduction of such researches, for easier and faster retrieval of patients' medical records.

It is likewise important to reiterate the importance of requesting HBV DNA among patients with chronic hepatitis B infection. A correlation of the level of HBV DNA, liver function tests, and maternal to child transmission of hepatitis B infection may be recommended for future studies. ■

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