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ORIGINAL ARTICLE

Seroprevalence of Hepatitis B virus in pregnancy women at the time of delivery

Seroprevalencia de virus Hepatitis B en gestantes al momento del parto

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What do we know about the subject matter of this study?

HBV infection in the newborn (NB) is the main risk factor, up to 90%, for progression to chronic disease, so diagnosis in pregnant women is essential for the prevention of vertical transmission of HBV.

What does this study contribute to what is already known?

It provides data on HBV seroprevalence in all pregnant women seen at the time of delivery in one of the main hospitals of the Valparaíso region, before the MINSAL strategies of vaccination against HBV in newborns and universal screening for HBV in pregnant women, establishing a baseline reference to evaluate the results of these strategies locally.

Abstract

Worldwide, there is an alert due to the increase in the seroprevalence of hepatitis B virus (HBV). This can cause up to 3.5% of chronic diseases, of which 40% present secondary complications and/or early death. **Objective:** To determine the seroprevalence of HBV in pregnant women at the time of delivery. **Patients and Method:** Observational, descriptive, cross-sectional study with cross-association between 2018 and 2019 at the *Hospital Carlos Van Buren* (HCVB), in Valparaiso, Chile. All pregnant women admitted for delivery care or with an immediate newborn who had HBV surface antigen study were included. Data were collected from the pregnant woman (age, nationality, education level, parity, type of delivery, and peripartum HIV-syphilis serology) and the newborn (gestational age, weight, and APGAR score). Inferential and multivariate analysis was performed using the Stata software. **Results:** 1,355 pregnant women were analyzed. 87.7% were Chilean, 5.5% Haitian, 4.2% Venezuelan, and 2.6% were of other nationalities. 0.3% were positive for HBV. The prevalence of HBV in Chileans was 0.08% and in Haitians 4%. Haitian

Keywords:
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nationality was at higher risk of HBV (OR = 83) vs. Chilean nationality (p = 0.0001). None presented coinfection with HIV and/or syphilis. **Conclusions:** HBV seroprevalence in HCVB pregnant women was 0.3%, similar to that described in the general population in Chile. There was no coinfection with other sexually transmitted diseases. The only predictor of HBV infection was Haitian nationality.

Introduction

Worldwide, there is an alert for the increasing seroprevalence of the Hepatitis B virus (HBV), estimating that one-third of the world's population has been exposed to the virus. Of these, 3.5% progress to chronic disease[1], and of the latter, up to 40% present secondary complications and/or early death[2]. Although chronic cases are mostly concentrated in Africa and Asia, the current high mobility of the population makes it necessary to implement global measures[3]. Therefore, the World Health Organization (WHO) published the "Global Health Sector Strategy on Viral Hepatitis 2016-2021"[3], such as HBV screening in pregnant women and the administration of combined prophylaxis (HBV immunoglobulin plus HBV vaccine) in newborns (NB) before 12 hours of life, which has demonstrated to reduce chronic infection from up to 90% to less than 10%[4]. These goals have been adhered to by the Chilean Ministry of Health (MINSAL), with the initiation of screening in pregnant women and the administration of the HBV vaccine in the newborn.

In Chile, according to the 2009-2010 National Health Survey (ENS) there is a prevalence of 0.15% (95%CI 0.04 - 0.53) in the general population, which is considered low endemicity[5]. There are other studies in blood banks and at-risk populations (people with immunodeficiency and dialysis) with variable prevalence (up to 30%). Few data are available on pregnant women, with a maximum prevalence of 0.3%[6]. It should be noted that pregnant women with HBV infection are at higher risk of gestational diabetes and antepartum hemorrhage, in addition to increasing the risk of premature delivery and low APGAR score in the NB[7,8,9]. Additionally, the presence of coinfection with the Human Immunodeficiency Virus (HIV) has been described in 1% and, at the same time, people with HIV have a 7.4% prevalence of HBV[1].

In 2009, Chile updated the HBV epidemiological surveillance standard, observing a significant increase in the notification rate secondary to the rescue of positive cases not reported from blood banks and clinical laboratories (private and public), revealing the underreporting of cases before its existence[10]. Added to this is the increase in immigration from countries with a higher HBV endemicity, estimating that at the end of 2020, 1,462,103 foreigners were residing in Chile, mostly from Venezuela, Peru, Haiti, Colombia, and Bolivia[11]. Of these, Peru and Colombia have intermediate endemicity (2.1% and 2.3%, respectively), and Haiti has high endemicity (13.6%)[12]. In this context of probable underdiagnoses at the national level and after a chance diagnosis of HBV infection in some pregnant women, the *Hospital Carlos Van Buren* (HCVB) of Valparaiso began universal screening of pregnant women entering the antepartum unit at the end of 2018. The objective of this study was to determine the HBV seroprevalence of pregnant women attending delivery care or in the immediate newborn period to HCVB.

Patients and Method

A descriptive observational cross-sectional study with cross-association was conducted between October 24, 2018, and May 31, 2019. The sample consisted of all pregnant women admitted to the HCVB of Valparaiso for delivery care or in the immediate newborn period. Non-probabilistic sampling was performed by random clustering. The inclusion criteria were pregnant women admitted to the HCVB for delivery or in the immediate newborn period, and the exclusion criterion was pregnant women with unavailable HBV surface antigen (HBsAg). The variables collected were nationality, parity, type of delivery, and HBV, HIV, and syphilis serology of the pregnant woman, in addition to gestational age, weight, and APGAR score of the NB.

In the context of a low national prevalence according to the ENS, and with the authorization of the ethics committee, the "Delivery Database" was used, an electronic file that was provided to the researchers already anonymized in a spreadsheet in order to include all the patients and avoid loss of cases. The HBV serology study was performed with the RAPID RESPONSE™ (BTNX Inc., Canada), a rapid test for HBsAg (qualitative technique by immunochromatography) with sensitivity > 99.9% and specificity of 99.9%[13]. For qualitative variables, relative and absolute frequencies were determined and for quantitative variables, measures of central tendency and dispersion were determined.

In the inferential analysis, proportion comparison test and Chi² test of independence were performed, and confidence intervals were determined. In the multivariate analysis, binary logistic regression was used to see the role of the independent variables in seroprevalence. *P*-values < 0.05 were considered significant. All analyses were performed in Stata 15.0 software licensed from *Universidad de Valparaiso*.

Results

The sample consisted of, 1366 pregnant women admitted for delivery care or in the immediate newborn period. After applying the exclusion criterion, the sample consisted of 1355 pregnant women (loss < 0.8%).

Table 1 summarizes the sociodemographic characteristics of the pregnant women.

Of the 1,355 pregnant women, 0.3% (n = 4) tested positive for the HBsAg rapid test. A total of 87.7% (n = 1188) of the pregnant women were Chilean, 5.5% (n = 75) Haitian, 4.2% (n = 57) Venezuelan, and 2.6% (n = 35) of other nationalities. The prevalence of HBV in Chilean pregnant women was 0.08% (n = 1) and in Haitian pregnant women 4.00% (n = 3). There were no HBsAg-positive pregnant women of other nationalities.

The pregnant women were multiparous in 60.81% (n = 824) and primigravidae in 39.19% (n = 531). All HBsAg-positive pregnant women were primigravidae.

Vaginal delivery was performed in 63% (n = 854) and cesarean section in 37% (n = 501). The route of delivery of the HBsAg-positive pregnant women was: 2 emergency cesarean sections, 1 vaginal delivery, and 1 instrumental delivery (forceps).

Of the 4 HBsAg-positive pregnant women, none had HIV and/or syphilis coinfection.

Gestational age, weight, and APGAR score at 1' and 5' minutes of the NB showed low variability, without following a normal distribution, due to the large number of outliers present. The mean gestational age in the 4 NBs born to HBsAg-positive pregnant women was 38.5 ± 1.3 weeks. The mean weight was 3302.5 ± 350.8 gr. The APGAR score was 9 at 1 and 5 minutes. There was no significant relationship between HBV positive (as independent variable) in the pregnant woman and the NB status (gestational age, weight, and APGAR score at 1 and 5 minutes as dependent variables).

When analyzing the variables for association with the presence of HBV (as a dependent variable), it was observed that the Haitian nationality of the pregnant woman was significant, with the risk of HBV positive outcome being 83 (OR) times higher than in pregnant women of Chilean nationality (*p*-value: 0.000).

Table 1. Sociodemographic characteristics of pregnant women treated at the time of delivery at the Carlos Van Buren Hospital between October 24, 2018, and May 31, 2019 (N = 1,355)

Age (N = 1,354)	27.55 ± 6.3 years
Education (N = 1,352)	
- Non	5 (0.4%)
- Incomplete primary	40 (3.0%)
- Complete primary	86 (6.4%)
- Incomplete secondary	216 (16.0%)
- Complete secondary	628 (46.4%)
- Incomplete university	211 (15.6%)
- Complete university	166 (12.3%)
Nationality (N = 1,355)	
- Chile	1.188 (87.68%)
- Haiti	75 (5.54%)
- Venezuela	57 (4.21%)
- Otra*	35 (2.58%)
Parity (N = 1,355)	
- Primigravida	531 (39.19%)
- Multiparous	824 (60.81%)

Qualitative variables are expressed as an absolute number (percentage) and quantitative variables as mean ± standard deviation. *Other Nationalities: Argentina, Bolivia, Brazil, China, Colombia, Ecuador, Nicaragua, Peru, Dominican Republic.

Discussion

In Chile, there are few studies on HBV seroprevalence, most of them more than 10 years old and/or focused mainly on populations at risk of HBV infection. This study provides relevant information on pregnant women, a group of interest for the application of HBV prevention strategies in the NB, before the beginning of HBV vaccination in the NB as a program in 2019 and universal HBV screening in pregnant women in 2021[14]. These perinatal Hepatitis B prevention strategies are considered cost-effective, with a cost-effectiveness ratio of CLP$2,600 per quality-adjusted life year[15]. For this, the application of universal screening in pregnant women is fundamental since knowing the HBsAg status of the pregnant woman determines that the application of the vaccine to the NB occurs within 12 hours after delivery in 84% of the cases versus when the HBV serological status of the pregnant women is not known, where only 28% of the newborns are vaccinated within the first 24 hours of life[16].

The HBV seroprevalence obtained from, 1,355 pregnant women was 0.3%, within the range determined in the 2009-2010 ENS for the general population in Chile[5] and other studies[6, 17-20]. In comparison with studies in pregnant women without differenti-

ation by risk factors, it is observed that it is in the highest value described (0.3%)[6]. This result was lower than that obtained in a recent study in pregnant women with risk factors (2.4%), highlighting that in Chilean pregnant women with risk behaviour, it was 0.66% and in Haitian pregnant women (nationality that concentrated 91.1% of the seropositive foreign nationals) it was 3.5%[21]. It is important to consider that performing a search based on the presence of risk factors would be insufficient, given that these are only recoverable as antecedents in 62% of patients infected with HBV[22].

The multivariate analysis determined that the Haitian origin of the pregnant woman resulted in an increased risk of HBV infection (OR = 83; $p < 0.000$). This result should be interpreted with caution given the wide confidence interval (95%CI 7.16 - 962.35), the low number of HBsAg-positive pregnant women, and the study design, which is not ideal for this type of association.

60.8% of the pregnant women were multiparous, but all the HBsAg-positive pregnant women were primiparous. This condition offers the opportunity for future pregnancies to have an adequate follow-up, treatment, and the application of all the necessary measures for the prevention of vertical transmission.

There were no cases of co-infection with HIV or syphilis in any of the HBsAg-positive pregnant women. This could be explained by the low number of HBV cases detected, since there is evidence of a higher prevalence of HIV in patients with HBV (1%)[1].

In NBs, there was no difference in relation to gestational age, weight, or APGAR score at 1 and 5 minutes between HBsAg-positive versus -negative pregnant women. This would support a previous study that states that the pregnant women carrier of HBsAg does not affect the condition of the NB[9].

Chile has progressively optimized the strategies for the prevention of vertical transmission of HBV:

- In 2005, HBV vaccination of infants (aged 2, 4, and 6 months) was initiated, benefiting to date children under 19 years of age. This is relevant since most women of childbearing age are not immunized against HBV except for those belonging to certain risk groups[23], increasing the probability of chronic infection in case of exposure.
- A booster dose at 18 months was initiated in 2009.
- Since 2015, the Perinatal Guide includes the suggestion of immunoprophylaxis (HBV vaccine plus HBV immunoglobulin) for newborns born to HIV-positive mothers.
- Since April 2019, the vaccination schedule of newborns against HBV to be administered within the first 24 hours of life has begun, with a coverage goal of 95%. It is important to consider that this measure is insufficient given that the most important component of immunoprophylaxis is the administration of immunoglobulin and compliance with immunoprophylaxis before 12 hours of life. The vaccine administered as the only strategy manages to protect only 64% of HBV-exposed NBs from chronic HBV infection[24,4].
- In September 2021, HBV screening of pregnant women in the first prenatal check-up in primary care was initiated. It includes collecting the viral load in HBV-positive cases, the eventual use of antivirals, and the application of prophylaxis of the NB before 12 hours of life[14,24,4].
- Finally, in 2022, the "Technical Standard for the Prevention of Vertical Transmission of Hepatitis B" was published, providing an integrated national guideline for the care of the HBV-positive pregnant woman and her child[25].

After these results, it is important to maintain continuous monitoring of compliance with the "Technical Standard for the Prevention of Vertical Transmission of Hepatitis B" at the national level, both in public and private health centers. In addition, to continue adding evidence of HBV seroprevalence, recognizing that those studies before 2018 may not be representative of the current reality.

The limitations of the study are the risk of information bias given that the database used was made with the information obtained from each pregnant woman in the antepartum or immediate puerperium unit, so that the confirmation of HBV infection, which requires confirmation by the ISP in the case of positive screening, was not recorded in this database, nor was it possible to recover the subsequent result since it is an anonymized database, which translates into a possible overestimation of cases due to false positives. For the same reason, it was not possible to obtain follow-up data for NBs born to HBV-positive mothers. Finally, there is a risk of information bias, given that the data is entered into the database by the midwife in charge of the antepartum unit, which could result in transcription errors or information omission.

In conclusion, there is little evidence of HBV seroprevalence in pregnant women. This is the first study carried out on all pregnant women seen at one hospital center in Chile, obtaining a result similar to that described in the general population by the ENS 2009-2010. The only predictor of HBV infection in this study was the Haitian nationality of the pregnant woman (OR = 83). There was no co-infection with HIV or syphilis.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: This study was approved by the respective Research Ethics Committee, which, according to the study's characteristics, has accepted the non-use of Informed Consent.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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