IJID Regions 11 (2024) 100375

Contents lists available at ScienceDirect

IJID Regions

journal homepage: www.elsevier.com/locate/ijregi

Pregnant women with chronic hepatitis B virus infection at the assessment of tenofovir disoproxil fumarate prescription: Baseline characteristics of a prospective cohort study in Vietnam

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ARTICLE INFO

Keywords:
HBV
Pregnant women
Vietnam
Tenofovir disoproxil fumarate

ABSTRACT

Objectives: We aimed to determine epidemiological characteristics and serologic markers among chronically hepatitis B virus (HBV)-infected pregnant women during the assessment of tenofovir disoproxil fumarate (TDF) prescription in Vietnam.

Methods: We consecutively recruited 375 pregnant women with chronic HBV (cHBV) infection at week 25±2 of pregnancy, at which time they were assessed for TDF use as pre-prophylaxis and/or pre-treatment at the Hospital for Tropical Diseases in southern Vietnam during December 2019-April 2021. Demographic characteristics, serological biomarkers, and prenatal liver ultrasounds were obtained through interviews and reviews of medical records.

Results: The median age of pregnant women was 29 years (interquartile range: 26-32). More than half of pregnant women (208/375; 55.5%) started TDF for prevention of mother-to-child transmission of HBV and/or treatment of chronic hepatitis B (CHB). Among the pregnant women initiating TDF, 96.1% (198/206) tested positive for hepatitis B e antigen, and 21.6% (45/208) had quantitative hepatitis B surface antigen (qHBsAg) $\leq 10^4$ IU/mL. A relatively strong correlation between qHBsAg and HBV deoxyribonucleic acid (DNA) ($r = 0.81$; 95% CI: 0.76-0.85) was observed in pregnant women starting TDF.

Conclusions: Our results demonstrate the high need for TDF prescription for prevention and/or treatment purposes in pregnant women with cHBV infection. Pregnant women with qHBsAg levels $\leq 10^4$ IU/mL may prioritize HBV DNA testing over qHBsAg to decide on TDF prescription.

Introduction

Globally, an estimated 296 million people were infected with hepatitis B virus (HBV) in 2019 [1], but only 10% and 5% of these HBV infections are clinically diagnosed and receive proper medical interventions, respectively [2]. In 2016, the World Health Assembly targeted an HBV elimination effort aimed at reducing 90% of new infections and 65% HBV-related deaths by 2030 [3]. In many parts of the world, vertical transmission of HBV from mother-to-child is a major mode of infection [1], and the prevention of mother-to-child transmission (MTCT) of HBV thus plays a crucial role in reducing the spread of HBV infection and contributing to the global objective of elimination of HBV by 2030. However, the absence of vital health services and universal healthcare in many developing countries hinders both HBV screening and adequate prevention programs for pregnant women living with HBV, leading to the continued occurrence of new infections in children in these settings [4].

Like other countries in the Southeast Asia region, Vietnam poses a high burden of HBV. Studies with small sample sizes conveniently selected in a limited number of rural areas over 2002-2006 reported a wide range of prevalence (8.8-19.0%) of hepatitis B surface antigen (HBsAg) among the adult population [5,6]. In the 2018-2019 national survey of 25,649 persons aged 18 years or older conducted in 32 provinces across the country, the estimated prevalence of HBsAg was 9.4%, with a slight

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https://doi.org/10.1016/j.ijregi.2024.100375
Received 25 February 2024; Received in revised form 30 April 2024; Accepted 3 May 2024

difference in the prevalence estimates between the rural and urban areas [7]. Maternal HBV infection is a significant transmissible disease in Vietnam, where a high prevalence of HBV (~10%) was reported among pregnant women [8,9]. To reduce the impact of HBV infection, the Vietnamese government launched a comprehensive HBV intervention across the country in 2002, which heavily relied on the universal administration of HBV vaccine at birth and a three-dose primary vaccine series before 4 months of age [10]. In 2019, Vietnam issued its guidelines for diagnosis and treatment of HBV. The critical component of the guidelines includes the use of hepatitis B immunoglobulin (HBIG) at birth for children born from chronically HBV-infected mothers and the administration of tenofovir disoproxil fumarate (TDF) for pregnant women who have a high viral load (HBV deoxyribonucleic acid [DNA] $>10^6$ copies/mL or > 200,000 IU/mL) during the third trimester of pregnancy and continuing until at least 1 month after delivery [11]. The 3-month treatment is expected to decrease the HBV viral load in the mother, thereby limiting the risk of MTCT of HBV. In addition to the purpose of MTCT prophylaxis for HBV, the treatment is also required to treat chronic hepatitis B (CHB) for these pregnant women. Information on the epidemiological characteristics and serologic markers and the need for TDF treatment in pregnant women with chronic HBV (cHBV) infection is crucial in deciding the use of TDF for them. There has been limited reporting of such data in Vietnam.

This study aims to report the epidemiological characteristics and serologic markers of HBV and the need for TDF treatment among pregnant women with cHBV infection prescribed TDF (TDF group) or not (non-TDF group) in Vietnam at a referral tropical disease hospital in the south of Vietnam.

Methods

The study was approved by the Institutional Review Board of the Hospital for Tropical Diseases in Ho Chi Minh City (reference number: 48/HĐĐĐ in 2019). All participants provided written informed consent.

Study design

This prospective cohort study of chronically HBV-infected pregnant women was conducted between December 2019 and April 2021. These women were identified and recruited continuously when they sought MTCT prophylaxis and CHB treatment at an outpatient clinic of the Hospital for Tropical Diseases, a specialist hospital located in Ho Chi Minh City (Figure 1a). The target sample size for this prospective cohort study was 380 participants.

Study population, recruitment, and data collection

Screening evaluations for a potential pregnant woman with HBV infection included the duration of positivity of HBsAg and the availability of results of the HIV and hepatitis C virus (HCV) routinely tested during pregnancy. For clinical purposes, a blood sample was collected to test for HIV and HCV if pregnant women did not have documented testing results during pregnancy. Pregnant women who had an HBsAg for <6 months were additionally tested for immunoglobulin M (IgM) antibody to hepatitis B core antigen (IgM anti-HBc) before recruitment.

Study inclusion criteria were as follows: women who were in week 25±2 of pregnancy; had tested positive for HBsAg for ≥6 months or tested positive for HBsAg for <6 months and negative for IgM anti-HBc; and had tested negative for both HIV and HCV (Figure 1b). Women who were receiving antivirals and those with mental health issues that, in the investigator's judgment, would potentially bias in data collection through interviews were excluded from the study.

At recruitment, face-to-face interviews were held with the participating pregnant women to elicit socio-demographics and self-reports on HBV infection duration, antiviral use, and family history of HBV infection. A review of the existing medical records was also conducted to collect relevant clinical information and diagnostics of a liver ultrasound. After completing interviews, a 6-mL blood sample was collected and tested by laboratories at the Pasteur Institute in Ho Chi Minh City for plasma HBV DNA using real-time polymerase chain reaction (Roche Molecular Systems, New Jersey), quantitative hepatitis B surface antigen (qHBsAg) (Abbott Diagnostics in Sligo, Ireland), and transaminases (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) using Roche's automated biochemical analyzer (Roche, Mannheim, Germany) (Figure 1b).

As per Vietnam's 2019 clinical HBV treatment guidelines, pregnant women with plasma viral load (HBV DNA) above 200,000 IU/mL were prescribed TDF 300 mg q.d. for MTCT prophylaxis that started at week 24-28 of pregnancy and lasted at least 1 month after giving birth. Pregnant women who had HBV DNA less than 200,000 IU/mL but reported a family history of liver cancer or cirrhosis and those with immune clearance or immune escape phase (HBV DNA ≥20,000 IU/mL and HBeAg-positive condition or HBV DNA ≥2000 IU/mL and HBeAg-negative condition; and an increased AST and ALT levels >2 × upper limit of normal [ULN]) also received TDF 300 mg q.d. to treat their CHB. After giving birth, the participating mother was followed up for 12 months to assess HBV DNA and ALT levels. Their newborns received the HBV vaccine and HBIG at birth, followed by a three-dose primary vaccine series at 2, 3, and 4 months. HBsAg and anti-HBs were evaluated when infants were approximately 12 months old.

Statistical analysis

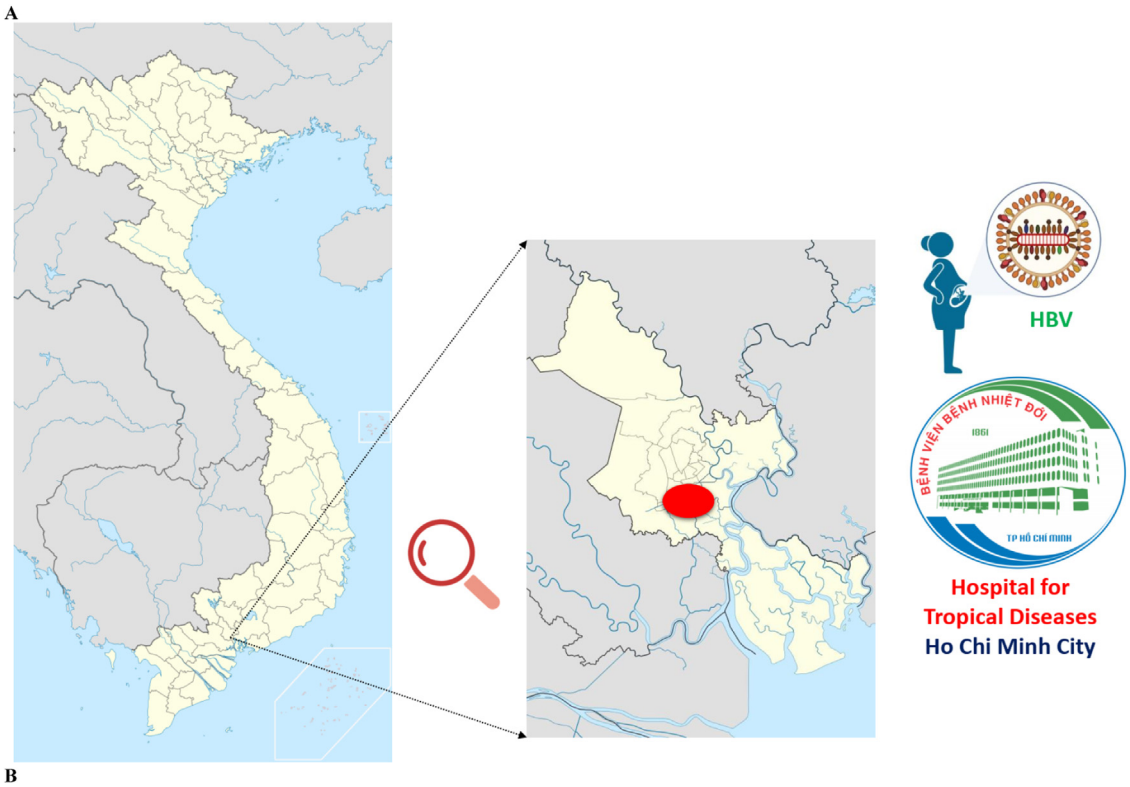
The participants were categorized into two groups, with and without TDF. The participants' characteristics were reported as frequencies and proportions for categorical variables and as means and SDs, or median and interquartile range (IQR), for continuous variables. We performed the Wilcoxon rank sum test and Pearson's chi-squared or Fisher's exact test to examine differences between TDF and non-TDF groups of pregnant women. Pearson's correlation analysis was employed to determine the correlation between qHBsAg and HBV DNA testing. Of note, the 2017 clinical practice guidelines on the management of HBV infection of the European Association for the Study of the Liver [12] and 2019 Vietnam's HBV diagnosis and treatment guidelines [11] recommend the start of TDF for all pregnant women who have HBV DNA >200,000 IU/mL or qHBsAg >4 $\log_{10}$ IU/mL at week 24-28 of gestation for prophylaxis. For this analysis, we used the threshold of 10^4 IU/mL to categorize low or high qHBsAg levels. *P*-values below 0.05 were considered statistically significant. Data were entered using Epi-Data version 3.1 (EpiData Association, Odense, Denmark), and all statistical analyses were carried out using R version 4.1.0 (R Core Team, 2021).

Results

Participants' demographics and medical history

Of 385 chronically HBV-infected pregnant women screened, 375/385 (97.4%) were recruited in the present study, and their demographic and medical characteristics are summarized in Table 1. The median age of participants was 29 years (IQR: 26-32), and up to 21.3% of them (80/375) had a time of HBV diagnosis to recruitment of 10 years or above. Many participants had obtained high-school education or higher (74.1%, 278/375), and 45.0% (169/375) were workers. Nearly half of the participants (48.3%, 181/375) were pregnant with their first child, and 9.1% reported a body mass index of 25 or higher before the pregnancy.

A small proportion of participants had been diagnosed with gestational diabetes (3.7%, 14/375) and steatosis (1.6%, 6/375). There was a substantial proportion of participants reporting their parents, brothers, or sisters with HBV infection (46.4%. 174/375), and a smaller proportion of their partners living with HBV (8.0%, 30/375). About 9.3%



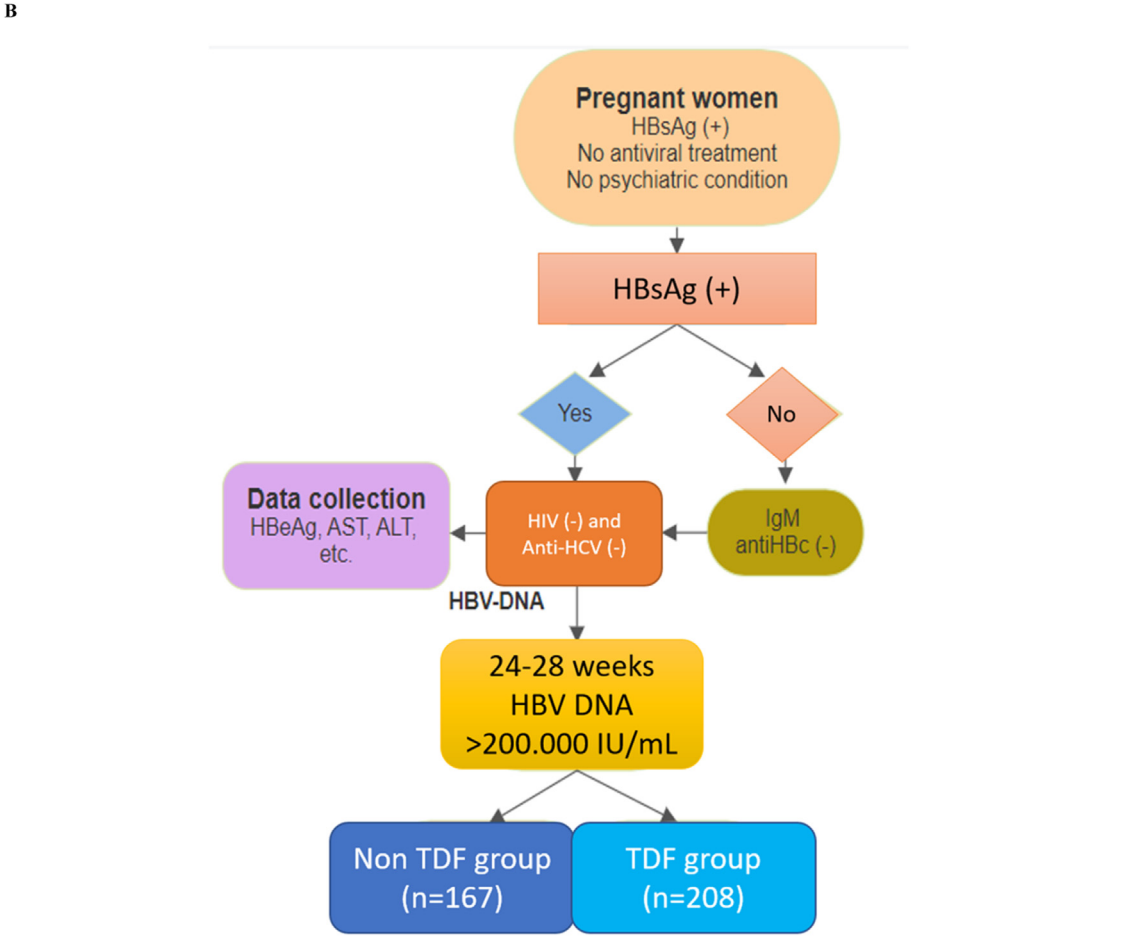


Figure 1. Study setting and follow-up chart of participant selection for the study cohort. The source of map: Wikimedia Commons, available under the Creative Commons CCO license.
ALT, alanine aminotransferase; AST, aminotransferase; TDF, tenofovir disoproxil fumarate; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HBV, hepatitis B virus.

Table 1
Demographics and medical history of pregnant women with chronic hepatitis B virus infection in the tenofovir disoproxil fumarate and non-tenofovir disoproxil fumarate groups.

Variables	Non-TDF (N = 167)	TDF (N = 208)	Total (N = 375)	P-value[a]
Demographics				
Age (year), median (IQR)	30.0 (27.0-34.0)	27.0 (25.0-31.0)	29.0 (26.0-32.0)	<0.001
Education level, n (%)				>0.9
Illiteracy	0 (0)	1 (0.5)	1 (0.3)	
Primary school	1 (0.6)	2 (1.0)	3 (0.8)	
Middle school	42 (25.1)	51 (24.5)	93 (24.8)	
High school	60 (35.9)	77 (37.0)	137 (36.5)	
≥College	64 (38.3)	77 (37.0)	141 (37.6)	
Occupation, n (%)				>0.9
Farmer	1 (0.6)	1 (0.5)	2 (0.5)	
Blue-collar worker	35 (20.9)	45 (21.6)	80 (21.3)	
White-collar worker	39 (23.3)	50 (24.0)	89 (23.7)	
Retail	31 (18.6)	37 (17.8)	68 (18.1)	
Housewife	33 (19.8)	38 (18.3)	71 (19.0)	
Others	28 (16.8)	37 (17.8)	65 (17.3)	
Previous medical conditions and the family and personal history of HBV infection				
Self-reported BMI before pregnancy, n (%)				0.048
<18.5	25 (15.0)	48 (23.1)	73 (19.5)	
18.5-22.9	102 (61.1)	123 (59.1)	225 (60.0)	
23-24.9	23 (13.8)	20 (9.6)	43 (11.5)	
25-29.9	17 (10.2)	13 (6.3)	30 (8.0)	
≥30	0 (0.0)	4 (1.9)	4 (1.1)	
No. of pregnancies, n (%)				0.6
1	77 (46.1)	104 (50.0)	181 (48.3)	
2	68 (40.7)	86 (41.3)	154 (41.0)	
3	19 (11.4)	17 (8.2)	36 (9.6)	
4	2 (1.2)	1 (0.5)	3 (0.8)	
5	1 (0.6)	0 (0)	1 (0.3)	
Gestational diabetes, n (%)	4 (2.4)	10 (4.8)	14 (3.7)	0.2
Steatosis, n (%)	2 (1.2)	4 (1.9)	6 (1.6)	0.7
Time from HBV diagnosis to recruitment, n (%)				0.7
<10 years	133 (79.6)	162 (77.9)	295 (78.7)	
≥10 years	34 (20.4)	46 (22.1)	80 (21.3)	
Past use of antiviral drugs, n (%)				0.015
Yes	12 (7.2)	35 (16.9)	47 (12.5)	
No	152 (91.0)	170 (81.7)	322 (85.9)	
Unknown	3 (1.8)	3 (1.4)	6 (1.6)	
Family history of HBV infection, n (%)				0.3
Yes	70 (41.9)	104 (50.0)	174 (46.4)	
No	51 (30.5)	56 (26.9)	107 (28.5)	
Unknown	46 (27.6)		94 (25.1)	
		48 (23.1)		
Family history of liver cancer/cirrhosis, n (%)	12 (7.2)	23 (11.1)	35 (9.3)	0.2
Partners' status of HBV infection, n (%)				0.3
Infected	12 (7.2)	18 (8.7)	30 (8.0)	
Not infected	70 (41.9)	101 (48.5)	171 (46.0)	
Not tested	85 (50.9)	89 (42.8)	174 (46.0)	

[a] ***P***-values from Wilcoxon rank sum test for discrete variables and Pearson's chi-squared test or Fisher's exact test for categorial variables.BMI, body mass index; HBV, hepatitis B virus; N, number of participants; n, frequency; IQR, interquartile range; TDF, tenofovir disoproxil fumarate.

of participants' family members had a diagnosis of liver cancer and/or cirrhosis.

Of the 375 participating pregnant women, TDF was prescribed for 208 participants (55.5%), and 47 self-reported a previous use of any antivirals (12.5%), primarily for the prevention of MTCT of HBV. Except for age and the past use of antivirals, there were no significant differences in demographic and medical characteristics between TDF and non-TDF groups of pregnant women (Table 1). Of the 375 pregnant women, 155 (41.3%) returned to the hospital for HBV testing for their children, and 20 (5.3%) were successfully contacted to collect the available HBV testing results of their children. HBV infection was identified in 5 of 178 babies born from the 175 mothers (2.8%, 95% CI: 0.9-6.4%).

Serological biomarkers and clinical characteristics

In this cohort, TDF prescription during this pregnancy was mostly for prevention of MTCT of HBV (89.4%, 186/208) due to high plasma viral load (HBV DNA >200,000 IU/mL). Of the remaining 22 pregnant women receiving TDF, 14 participants with high plasma viral load and levels of transaminases >2 × ULN experienced active hepatitis; five with HBV DNA >200,000 IU/mL, normal levels of transaminases and reports of a family history of liver cancer or cirrhosis; three with HBV DNA ≤200,000 IU/mL, normal levels of transaminases and a family history of liver cancer or cirrhosis. In these participants, TDF was initiated in 19 women with HBV DNA >200,000 IU/mL for both the prevention of MTCT of HBV and the treatment of CHB (Table 2).

Table 3 summarizes participants' serological biomarkers and prenatal liver ultrasound characteristics. The proportion of pregnant women who tested positive for HBeAg was 59.5% (222/373). The median qHBsAg of the pregnant women in the study was 5097 IU/mL, and more than half of pregnant women (55.5%, 208/375) had qHBsAg $\leq 10^4$ IU/mL. The median levels of AST and ALT were 20 (IQR: 17-25) and 16 (IQR: 13-22), respectively. Sixteen of the 375 participants (4.3%) had ALT lev-

Table 2
Characteristics of pregnant women with chronic hepatitis B virus infection in the tenofovir disoproxil fumarate group (N = 208).

	HBeAg (N = 206)		qHBsAg (IU/mL) (N = 208)		Reasons for TDF prescription (N = 208)			Total
	Negative	Positive	$\leq 10^4$	$>10^4$	Mother-to-child HBV prophylaxis	CHB treatment [ALT>2 × ULN]	Others: family history of liver cancer or cirrhosis	
Total participants	8	198	45	163	186	14	8	208
HBV DNA (IU/mL)								
<2000	1	1	2	0	0	0	2	2
2000-200,000	2	0	2	0	0	1	1	2
>200,000	5	196	40	163	185	13	5	203
Missing data[a]	0	1	1	0	1	0	0	1

CHB indicates chronic hepatitis B; HBeAg, Hepatitis B e antigen; qHBsAg, quantitative hepatitis B surface antigen; ALT, alanine aminotransferase; N, number of participants; ULN, upper limit of normal; IU/mL, international unit per milliliter; TDF, tenofovir disoproxil fumarate.
[a] This pregnant woman had HBV DNA >200,000 IU/mL tested by a non-study laboratory.

Table 3
Serological biomarkers and prenatal liver ultrasound characteristics of pregnant women in the tenofovir disoproxil fumarate and non-tenofovir disoproxil fumarate groups at recruitment.

Variables	Non-TDF (N = 167)	TDF (N = 208)	Total (N = 375)	P-value[d]
HBeAg (+)[a], n (%)	24 (14.4)	198 (96.1)	222 (59.5)	<0.001
HBV DNA (IU/mL)[b], n (%)				<0.001
<2000	130 (77.8)	2 (1.0)	132 (35.3)	
2000-200,000	37 (22.2)	2 (1.0)	39 (10.4)	
>200,000	0 (0)	203 (98.0)	203 (54.3)	
qHBsAg (IU/mL), median (IQR)	922 (216, 1923)	25,663 (11,771, 38,765)	5097 (923, 27,541)	<0.001
AST (U/L), median (IQR)	19 (16-22)	21 (18-27)	20 (17-25)	<0.001
ALT (U/L), median (IQR)	14 (12-20)	18 (14-27)	16 (13-22)	<0.001
ALT > 2 × ULN, n (%)	2 (1.2)	14 (6.7)	16 (4.3)	0.008
Detection of steatosis on ultrasound[c], n (%)	7 (5.2)	6 (3.8)	13 (4.5)	0.6

[a] Denominator: TDF group and total were 206 and 373, respectively.
[b] Denominator: Non-TDF group, TDF group, and total were 167, 207, and 374, respectively.
[c] Denorminator: Non-TDF group, TDF group, and total were 134, 156, and 290, respectively.
[d] *P*-values from Wilcoxon rank sum test for continuous variables; Pearson's chi-squared test or Fisher's exact test for categorical variables.AST, aspartate aminotransferase; ALT, alanine aminotransferase; HBeAg, Hepatitis B e antigen; qHBsAg, quantitative hepatitis B surface antigen; N, number of participants; n, frequency; IQR, interquartile range; IU/mL, international unit per milliliter; U/L, unit per liter; ULN, upper limit of normal; TDF, tenofovir disoproxil fumarate.

els 2-fold higher than ULN, and 13 (4.5%) were diagnosed with steatosis using ultrasound.

Compared with pregnant women without TDF prescription, pregnant women with TDF had a higher proportion of HBeAg positivity (96.1% vs 14.4%, $p < 0.001$), higher median qHBsAg (25,663 vs 922 IU/mL, $p < 0.001$), and higher median levels of AST (21 vs 19 U/L, $p < 0.001$) and ALT (18 vs 14 U/L, $p < 0.001$). These women were also more likely to have ALT levels 2-fold higher than ULN (6.7% vs 1.2%, $p = 0.008$). Almost all pregnant women without TDF had qHBsAg $\leq 10^4$ IU/mL (97.6%, 163/167), compared to that of 21.6% (45/208) among pregnant women with TDF ($p < 0.001$) (Table 3 and Figure 2).

Correlation between qHBsAg and HBV DNA

Overall, there was a strong correlation between qHBsAg and HBV DNA in pregnant women with cHBV infection at the assessment of TDF prescription ($r = 0.79$, 95% CI: 0.75-0.83). The correlation was also strong in the group of pregnant women with TDF ($r = 0.81$, 95% CI; 0.76-0.85), but it was relatively weak in the group of pregnant women without TDF ($r = 0.24$, 95% CI: 0.09-0.38) (Figure 3).

Discussion

We demonstrate that more than half of pregnant women with cHBV infection need TDF treatment. Despite a strong correlation between HBV DNA and qHBsAg testing in all pregnant women in the study as well as in those receiving TDF, we found that over one in five pregnant women had a high level of HBV DNA, but a qHBsAg level was $\leq 10^4$ IU/mL.

Compared with our results, a much lower proportion of TDF initiation for HBV MTCT prevention or treatment of CHB (18%) was found in a study of 183 participants enrolled at Haiphong Gyneco-Obstetric Hospital in northern Vietnam in 2017-2018. A possible reason for this low proportion is the recruitment at a hospital for women [13]. A high proportion of TDF initiation (67.2%) was reported in a study of 198 chronically HBV-infected pregnant women with HBeAg(+) who sought HBV MTCT prevention services at hospital hepatitis clinics in two tertiary hospitals in Sydney, Australia, during 2006-2019 [14]. It is well-established that despite administration of HBIG and birth-dose HBV vaccine, 10% of newborns whose mothers have a high level of HBV DNA at $>10^6$ copies/mL or >200,000 IU/mL may be infected with HBV [15,16]. With a high proportion of TDF initiation for pregnant women with cHBV infection reported here, enhancement of pre-therapy HBV DNA is of great importance for these women in Vietnam. Currently, the availability of this testing remains limited in urban settings, and due to constraints in laboratory infrastructure and resources available in Vietnam, providing this testing service for HBV-positive pregnant women during pregnancy in other parts of Vietnam is unlikely. Eliminating the vertical transmission of HBV in Vietnam is challenging. There is a need for increased investment, improvement of HBV screening programs, and innovative and cost-effective measures, such as HBV DNA using dried blood spots (DBS), for pregnant women. The DBS sampling for specimen collection was successfully used to improve access to HIV viral load monitoring for patients newly initiated on antiretroviral therapy in remote settings in Vietnam [17,18]. This approach can be used for HBV DNA testing, and it will enhance access to HBV DNA testing services during pregnancy. It may result in a substantial reduction in the risk of vertical transmission of HBV to infants born to HBV-positive pregnant women living in rural and semi-urban settings. It is worth noting that, unlike HIV, low viral loads are relatively common in HBV infection. Using DBS to identify HBV-positive pregnant women with low viral loads could be a challenge.

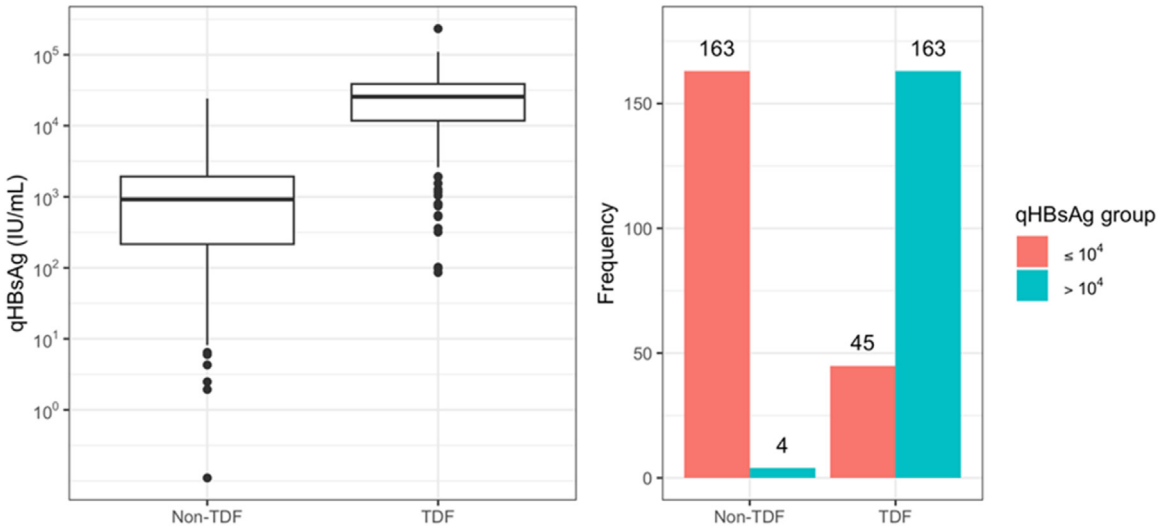


Figure 2. Characteristics of qHBsAg among pregnant women in the TDF and non-TDF groups at the time of screening (n = 375). qHBsAg, quantitative hepatitis B surface antigen; TDF, tenofovir disoproxil fumarate.

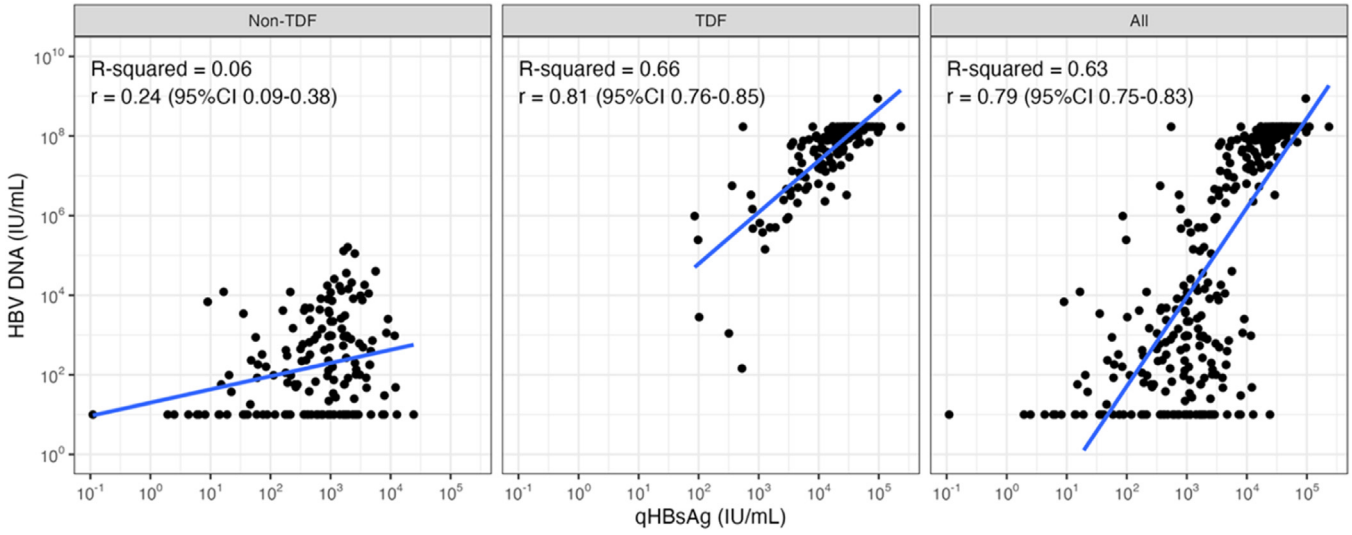


Figure 3. Correlations between qHBsAg and HBV DNA among pregnant women with cHBV infection in non-TDF group, TDF group, and total population (n = 374). One pregnant woman in the TDF group was excluded as tested HBV DNA by a non-study laboratory (HBV DNA = 660,000 IU/mL, qHBsAg = 1917 IU/mL). Black points represent individual HBV DNA and qHBsAg values, while the blue line represents the best fit univariable linear regression of HBV DNA on qHBsAg. The R-squared value quantifies the goodness of fit of the linear regression model, while the *r*-value and its 95% CI are estimates of Pearson's correlation between HBV DNA and qHBsAg values (both on log-scale).
cHBV, chronic HBV; HBV, hepatitis B virus; qHBsAg, quantitative hepatitis B surface antigen; TDF, tenofovir disoproxil fumarate.

Our finding of a strong correlation between qHBsAg and HBV DNA testing was consistent with several previous studies [19–21]. This suggests that cheaper qHBsAg testing (18-22 US dollars per test) could be used as an alternative to HBV DNA (60-70 US dollars per test) for HBV-infected pregnant women living in settings where HBV DNA is not available. In other words, physicians can prescribe TDF for the prevention of MTCT of HBV for pregnant women who have qHBsAg $>10^4$ IU/mL. However, we found that 21.6% of pregnant women whose HBV DNA testing was >200,000 IU/mL had qHBsAg $\leq 10^4$ IU/mL. In such a circumstance in which an HBV-positive pregnant woman has qHBsAg $<10^4$ IU/mL, HBV DNA testing should be further conducted before deciding on no prescription of TDF for them.

In contrast to previous studies conducted in China and Greece [22,23], we found that 4.3% of our participants had ALT >2 × ULN. In addition to HBV DNA testing, transaminases should be tested periodically in untreated HBV-positive pregnant women for timely identification of active chronic hepatitis. By testing transaminases, CHB was identified in our 14 participants, and they were prescribed in a TDF timely fashion for CHB treatment. Another three pregnant women who had normal transaminases and low HBV DNA <200,000 IU/mL were prescribed TDF for CHB treatment purposes due to a family history of liver cancer or cirrhosis. This is in keeping with several treatment guidelines for patients with cHBV infection who do not meet the criteria for viral proliferation and increased transaminases but have a family history of liver cancer or cirrhosis [11,12,24,25].

This study has several limitations. First, our participants were enrolled in a hospital hepatitis clinic at a tertiary Hospital for Tropical Diseases in Ho Chi Minh City, so the findings may not be generalizable nationally. The recruitment of participants who actively sought MTCT prevention and CHB treatment at the study hospital may further lead to biases in estimating the proportion of pregnant women meeting TDF prescription eligibility criteria. Second, our study was probably subjected

to social desirability bias as several demographic, clinical, and behavioral data were collected through self-reporting face-to-face interviews conducted by healthcare workers at the study hospital. Third, HBeAg is mainly collected from pregnant women's medical records, so inconsistencies in testing techniques may exist. Fourth, the inability to test qHBsAg in mothers after giving birth limited our investigation into the change of qHBsAg levels in response to treatment. Future studies are needed to investigate the trend of qHBsAg levels after MTCT prevention and CHB treatment.

Conclusions

Our findings suggest a substantial proportion of pregnant women with cHBV infection require a TDF prescription to prevent MTCT of HBV and/or to treat their CHB. An expansion of TDF for this group, along with efforts to increase awareness of HBV through health promotion programs and timely diagnosis of HBV with effective screening programs, are essential for a reduction of vertical transmission of HBV in Vietnam. With a strong correlation between HBsAg and HBV DNA, physicians may use qHBsAg testing to decide MTCT prevention in areas where HBV DNA testing is not accessible. Notably, for pregnant women with qHBsAg $\leq 10^4$ IU/mL, physicians should base their decisions to start TDF for HBV MTCT prevention on HBV DNA testing results.

Declaration of competing interest

The authors have no competing interests to declare.

Funding

This study was conducted as a part of Dr. Tran Dieu Hien Pham's PhD program and was funded by the Vietnamese Ministry of Health.

Ethical approval

The study was conducted according to the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of the Hospital for Tropical Diseases in Ho Chi Minh City (number: 48/HĐĐĐ, signed on December 02, 2019). Written informed consent was obtained from all participants.

Acknowledgments

This work could not have been completed without the participation of patients with HBV infection. We would like to express our sincere thanks to our colleagues for their tremendous support in the recruitment of patients and data collection. The authors wish to thank Thi Nhu Thuy Nguyen for assistance with data collection and follow-up of participants.

Author contributions

TDHP recruited participants, collected data, made a plan for data analysis, interpreted data, and wrote the first draft of the manuscript with inputs from QDP. KLP performed all statistical data analysis and assisted in the interpretation of findings. QDP contributed to the interpretation of findings and assisted with English language editing. MNN, TBNH, BKD, TPL, and TDN assisted in data collection. QCH and MHL conceived and overviewed the study. All authors contributed to refinement and approved the final version of the manuscript.

Availability of data and materials

Data will be made available on request.

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