

Obstetricians' and gynecologists' knowledge, education, and practices regarding chronic hepatitis B in pregnancy

Bolin Niu^a, Dina Halegoua-De Marzio^b, Jonathan M. Fenkel^b, Steven K. Herrine^b

Thomas Jefferson University Hospital; Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA, USA

Abstract

Background In pregnant women with high viral loads, third-trimester initiation of antiviral agents can reduce the risk of vertical transmission. We aimed to assess obstetricians' and gynecologists' (OB-GYN) knowledge and clinical practice when treating pregnant women with chronic hepatitis B virus (HBV).

Methods All program directors (PDs) from 250 US OB-GYN residency programs were invited to anonymously complete an 18-item questionnaire. Descriptive statistics were calculated and analyzed.

Results A total of 323 participants responded, including both PDs (n=51, response rate 21%) and residents (n=272, response rate 11%). Responding PDs (62% university-based vs. 32% community-based) came from various practice types. All PDs and 95.2% of residents reported screening for chronic HBV in pregnant patients on the first prenatal visit. A majority of PDs (85.5%) and residents (85%) correctly interpreted HBV serologies. Referral patterns showed that 66.7% of PDs and 65.5% of residents refer to a specialist regardless of viral load. A minority of respondents (19.6% PDs and 12.6% residents) knew that third-trimester antiviral therapy is recommended for women with high viral loads (>200,000 IU/mL). Few respondents had prescribed HBV antivirals (9.8% PDs and 6.0% residents), with residents more commonly prescribing tenofovir and less frequently lamivudine. Half the PDs believed trainees from their programs were comfortable managing HBV in pregnancy, but only 41.8% of residents reported being comfortable managing pregnant patients with HBV.

Conclusion OB-GYNs report screening almost all pregnant patients for chronic HBV, though significant gaps still exist in practitioner comfort and training regarding the management of HBV during pregnancy.

Keywords Hepatitis B virus, pregnancy, obstetricians and gynecologists, survey, education, practice

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Introduction

Between 800,000 and 1.4 million people in the United States are infected with the hepatitis B virus (HBV) [1].

Department of Medicine, Division of Gastroenterology and Hepatology, ^aThomas Jefferson University Hospital (Bolin Niu); ^bSidney Kimmel Medical College at Thomas Jefferson University (Dina Halegoua-De Marzio, Jonathan M. Fenkel, Steven K. Herrine), Philadelphia, PA, USA

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Correspondence to: Dina Halegoua-De Marzio, MD, Division of Gastroenterology and Hepatology, Thomas Jefferson University Hospital, 480 Main, 132 South 10th Street, Philadelphia, PA 19107, USA, e-mail: dina.halegoua-demarzio@jefferson.edu

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HBV is a major risk factor for hepatocellular carcinoma, leading to 50% of cases worldwide. There is an estimated prevalence of 0.7-0.9% of chronic HBV among pregnant women in the US, with >25,000 neonates at risk for chronic infection annually [2,3].

Obstetricians and gynecologists (OB-GYNs) perform a key role in the prevention of mother-to-child transmission (MTCT). To provide optimal care of pregnant women who are HBV carriers, OB-GYNs need appropriate knowledge, education, and practice in the management of these patients.

The Centers for Disease Control and Prevention and the American College of OB-GYNs (ACOG) have both published recommendations for screening for HBV among pregnant women [5], calling for hepatitis B surface antigen (HBsAg) as the initial serological testing for all pregnant women, followed by hepatitis B e-antigen (HBeAg), HBV DNA viral load, and alanine aminotransferase (ALT). If HBeAg is positive, HBV DNA >20,000 IU/mL, or ALT \geq 19 IU/L, then the

patient should be referred to a specialist immediately during pregnancy.

The 2016 American Association for the Study of Liver Diseases (AASLD) guidelines suggest antiviral therapy to reduce the risk of perinatal transmission of hepatitis B in pregnant women with an HBV DNA level >200,000 IU/mL (>1 million copies/mL) [4]. The 2016 Society for Maternal-Fetal Medicine consensus recommends third-trimester HBV viral load testing and antiviral therapy over a greater range of viral load (HBV DNA >1 million to 100 million copies/mL) compared to the AASLD recommendation.

The current survey aimed to determine the knowledge, education, and practices of OB-GYNs regarding HBV in pregnant women. In addition, we determined referral patterns and thresholds for OB-GYNs to treat patients with HBV.

Materials and methods

Participants

All program directors (PDs) from the 250 US OB-GYN residency programs were invited via e-mail to complete an 18-item online survey. E-mail addresses for PDs were obtained from the American Medical Association FREIDA web site. OB-GYN residents, contacted via e-mail by their PDs, were also invited to participate.

Survey and administration

An 18-item survey was sent to PDs to obtain demographic information and assess their knowledge, clinical practice, and residency program education with regard to pregnant women with chronic HBV. A slightly different 18-item survey was written for trainees to obtain demographic information and assess knowledge, clinical practice, and comfort level when treating pregnant women with chronic HBV. The survey was first piloted at several programs and adjusted from feedback. Exemption status was obtained from Thomas Jefferson University's Institutional Review Board. Question responses included agree, disagree, or unsure. Many questions allowed for free-text comments. In January 2016, all participants were contacted via e-mail with a cover letter describing the study and a link to the Survey Monkey Website. Follow-up emails were sent at 4 and 8 weeks after the initial e-mail to encourage participation. Anonymized responses were stored in a database for analysis.

Statistical analysis

Descriptive statistics, including means for continuous variables and frequencies for categorical variables, were calculated. The chi-squared test for significance was employed.

Results

Characteristics of responders

A total of 323 participants from ACGME-accredited OB-GYN residency programs across the US responded to the survey (Table 1). The respondents included both PDs (n=51, response rate of 21%) and residents (n=272, response rate of 11%). The responding resident cohort exhibited a diversity of experience, with equal distribution across postgraduate years (PGY) of training. Responding PDs came from varied practice settings, including university-based (62%), community-based (32%), and military-based (6%).

Practice patterns and peripartum management

All PDs and 95.2% of residents reported screening for chronic HBV in pregnant patients on the first prenatal visit. Referral patterns showed that 66.7% of PDs and 65.5% of residents referred to a specialist regardless of viral load. A minority of respondents (19.6% PD, 12.6% residents) knew that third-trimester antiviral therapy is recommended for women with high viral loads (>1 million copies/mL or 200,000 IU/mL). Few respondents had prescribed antivirals for HBV (9.8% PD, 6.0% residents). Residents more commonly prescribed tenofovir (75%) and less frequently lamivudine (16.7%). In contrast, more PDs prescribed lamivudine (60%) and fewer tenofovir (40%). Furthermore, most PDs (98%) and residents (83.1%) disagreed that HBV was an indication for Cesarean section (C-section) (Table 2).

Education and interpretation of HBV serologies

Half of PDs believed residents from their programs were comfortable in managing HBV in pregnancy, but only 41.8% of residents reported being comfortable managing these patients (Table 2). Only 23.5% of training programs have dedicated teaching about HBV in pregnancy. With respect to years of training, the percentage of residents who felt comfortable managing HBV increased with post-graduate year: PGY 1 (22%), PGY 2 (28%), PGY 3 (42%), and PGY 4 (69%) (Fig. 1). A majority of PDs and residents interpreted HBV serologies correctly (Table 3).

Discussion

Because screening based on risk factors alone will miss many cases of HBV, universal screening for HBV during pregnancy at the first prenatal visit has been recommended by the ACOG and the US Preventative Services Task Force for many years [5]. In our study, all PDs and over 95% of residents screened for HBV appropriately at the first prenatal visit.

Despite appropriate screening, significant gaps exist in residents' comfort and education in the management

Table 1 Characteristics of responding PDs and residents

Responders' characteristics	% PDs	% Residents
Overall		
Survey response rate	20.4	11.0
Gender		
Male	37.3	10.9
Female	62.7	89.1
Practice type		
Community-based medical center	32	27.6
University-affiliated medical center	62	72.4
Group practice	4	0
Other	2	0
Practice setting		
Urban	88.2	93
Rural	11.8	7
MFM		
MFM specialty training	15.7	2.6
Geographical distribution		
New England (CT, MA, ME, NH, RI, VT)	7.8	9.8
Mid-Atlantic (NJ, NY, PA)	15.7	25.8
East North Central (IL, IN, MI, OH, WI)	25.5	20.7
West North Central (IA, KS, MN, MO, ND, NE, SD)	9.8	11.3
Mountain (AZ, CO, ID, MT, NV, NM, UT, WY)	9.8	2.9
Pacific (AK, CA, HI, OR, WA)	7.8	8.7
South Atlantic (DE, DC, FL, GA, MD, NC, SC, VA, WV)	3.9	14.5
East South Central (AL, KY, MS, TN)	9.8	2.5
West South Central (AR, LA, OK, TX)	9.8	3.6
Trainee year		
PGY 1		24.4
PGY 2		26.2
PGY 3		24.7
PGY 4 and beyond		24.7

PD, program director; MFM, maternal-fetal medicine; PGY, postgraduate year

of pregnant patients with HBV, though improvement is seen as they progress through years of training. Even in their last year of training, only 69% of PGY-4 residents felt comfortable managing a pregnant patient with HBV. This may be related to a lack of clinical exposure, with less than half of residents reporting an adequate amount of clinical exposure to HBV patients. In addition, less than a quarter of programs offer a didactic session on HBV. Better educational initiatives could potentially decrease MTCT rates further.

Maternal infection with HBV is a major cause of MTCT [6]. A recent study found that a maternal HBV DNA level >1 million copies/mL at delivery is the most important predictor of *in utero* MTCT and hepatitis B immune globulin

prophylaxis failure [7]. The newest guideline from the Society for Maternal-Fetal Medicine recommends third-trimester HBV viral load testing and antiviral therapy if viral load is >6-8 log₁₀ (1 million to 100 million) copies/mL [8]. In 2012-2013, the European Association for the Study of the Liver and the United Kingdom's National Institute for Health and Care Excellence have published similar guidelines, recommending treatment in those with HBV viral load >6-7 log₁₀ (1 million to 10 million) copies/mL [9,10].

With respect to the choice of antiviral therapy, the American Association for the Study of Liver Diseases' revised guidelines in 2009 for the treatment of chronic HBV call for tenofovir and entecavir to be first-line agents, with lamivudine no longer a first-line agent as there has been

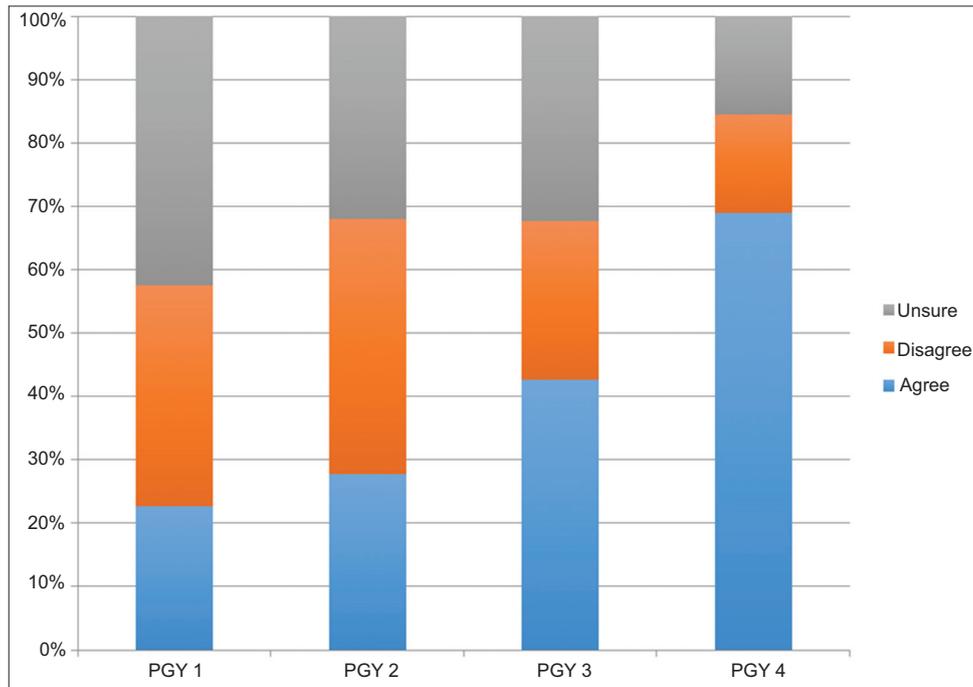


Figure 1 Resident responses to “I feel comfortable managing pregnant patients with chronic hepatitis B” across post-graduate years (PGY)

Table 2 Summary of selected survey responses from PDs and residents

Survey questions	Response	PD response % (n=51)	Resident response % (n=275)	Chi-square P-value
C-section is indicated in the setting of maternal HBV	Agree	2.0	5.1	0.018
	Disagree	98.0	83.1	
	Unsure	0.0	11.8	
There is a dedicated teaching session for managing hepatitis B in pregnancy at my program	Agree	23.5	32.5	<0.001
	Disagree	70.6	41.0	
	Unsure	5.9	26.6	
Trainees from my program are comfortable managing a pregnant patient with hepatitis B	Agree	51.0	41.2	0.265
	Disagree	29.4	28.7	
	Unsure	19.6	30.1	
The patient population in my program provides adequate clinical exposure for trainees with regard to HBV in pregnancy	Agree	54.9	42.3	0.017
	Disagree	41.2	37.5	
	Unsure	3.9	20.2	

PD, program director; HBV, hepatitis B virus; C-section, cesarean section

concern about resistance [11]. Tenofovir has been shown to be associated with no increase in congenital abnormalities or differences in infant growth parameters at birth compared to an untreated control group [12]. The newest guideline from the Society for Maternal-Fetal Medicine recommends tenofovir as a first-line agent in pregnant women who are candidates for antiviral therapy [8]. Interestingly, a majority of PDs who have prescribed antivirals selected lamivudine as their agent of choice, while the majority of residents

selected tenofovir. It is likely that the new guidelines have been disseminated faster to those who are currently in training.

Perinatal HBV infection occurs when the infant comes into contact with vaginal blood and secretions during delivery. A Chinese systemic review that included 789 patients showed a significant decrease in vertical transmission associated with elective C-section (10.5%) compared to vaginal delivery (28.0%) [13]. However, that review included many studies

Table 3 Interpretations of HBV serologies

Type of HBV serology	% PD correct	% Resident correct
Chronic hepatitis B infection	94	86
Prior infection with hepatitis B, now resolved	80	78.8
Immune to hepatitis B from vaccination	82.4	90.1

PD, program director; HBV, hepatitis B virus

Summary Box

What is already known:

- Mother-to-child transmission of hepatitis B virus (HBV) occurs when maternal HBV viral load is higher than 1,000,000 copies/mL
- Third-trimester initiation of antiviral agents reduces the risk of vertical transmission

What the new findings are:

- Our survey of all Obstetricians' and Gynecologists' (OB-GYN) residency programs in the United States shows almost all OB-GYNs screen pregnant patients for HBV
- A minority of OB-GYN respondents knew that third trimester antivirals are recommended for women with high viral loads
- Less than half of residents report that they are comfortable managing patients with HBV
- Less than a quarter of residency programs have dedicated teaching about HBV in pregnancy

that did not report maternal HBV DNA viral load. Currently, the OB-GYN literature does not support chronic HBV as an indication for C-section [8]. The majority of PDs and residents in our survey reported similar opinions regarding C-section.

Although we surveyed PDs and residents in the entire US, the major limitations of our study include the recall bias inherent in survey studies and the slightly low response rates. We elected to survey PDs as representative of physicians in practice. However, this may not be accurate, as PDs are perhaps more knowledgeable about changing guidelines than are their non-teaching colleagues.

Overall, despite excellent self-reported screening for hepatitis B in pregnant women, OB-GYN knowledge and education regarding management, especially in patients with higher viral loads during the third trimester, is still lacking. Improvement in education and dissemination of guidelines can further decrease vertical transmission in this vulnerable population.

References

1. Masters BR. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Eighth Edition (2015) Eds: Bennett JE, Dolin R, Blaser MJ. ISBN: 13-978-1-4557-4801-3, Elsevier Saunders. *Graefes Arch Clin Exp Ophthalmol* 2016;**254**:2285-2287.
2. Kubo A, Shlager L, Marks AR, et al. Prevention of vertical transmission of hepatitis B: an observational study. *Ann Intern Med* 2014;**160**:828-835.
3. Din ES, Wasley A, Jacques-Carroll L, Sirotkin B, Wang S. Estimating the number of births to hepatitis B virus-infected women in 22 states, 2006. *Pediatr Infect Dis J* 2011;**30**:575-579.
4. Terrault NA, Bzowej NH, Chang KM, Hwang JP, Jonas MM, Murad MH; American Association for the Study of Liver Diseases. AASLD guidelines for treatment of chronic hepatitis B. *Hepatology* 2016;**63**:261-283.
5. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 86: Viral hepatitis in pregnancy. *Obstet Gynecol* 2007;**110**:941-956.
6. Burk RD, Hwang LY, Ho GY, Shafritz DA, Beasley RP. Outcome of perinatal hepatitis B virus exposure is dependent on maternal virus load. *J Infect Dis* 1994;**170**:1418-1423.
7. Pan CQ, Duan ZP, Bhamidimarri KR, et al. An algorithm for risk assessment and intervention of mother to child transmission of hepatitis B virus. *Clin Gastroenterol Hepatol* 2012;**10**:452-459.
8. Dionne-Odom J, Tita AT, Silverman NS; Society for Maternal-Fetal Medicine (SMFM). #38: Hepatitis B in pregnancy screening, treatment, and prevention of vertical transmission. *Am J Obstet Gynecol* 2016;**214**:6-14.
9. European Association For The Study Of The Liver. EASL clinical practice guidelines: Management of chronic hepatitis B virus infection. *J Hepatol* 2012;**57**:167-185.
10. National Clinical Guideline Centre (UK). Hepatitis B (Chronic): Diagnosis and management of chronic hepatitis B in children, young people and adults [Internet]. London: National Institute for Health and Care Excellence (UK); 2013 [cited 2016 Dec 16]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK254250>
11. Lok AS, McMahon BJ. Chronic hepatitis B: update 2009. *Hepatology* 2009;**50**:661-662.
12. Greenup AJ, Tan PK, Nguyen V, et al. Efficacy and safety of tenofovir disoproxil fumarate in pregnancy to prevent perinatal transmission of hepatitis B virus. *J Hepatol* 2014;**61**:502-507.
13. Yang J, Zeng XM, Men YL, Zhao LS. Elective caesarean section versus vaginal delivery for preventing mother to child transmission of hepatitis B virus—a systematic review. *Virol J* 2008;**5**:100.