



Published in final edited form as:

J Clin Gastroenterol. 2019 ; 53(10): e424–e430. doi:10.1097/MCG.0000000000001122.

Peripartum Maternal Hepatitis B Care in a U.S. Nationwide Dataset

Matthew S. Chang, MD, MPH^{1,8}, J. Frank Wharam, MB, BCh, BAO, MPH², Fang Zhang, PhD², Robert F. LeCates, MA², Emma Morton-Eggleston, MD, MPH³, Ruth E. Tuomala, MD⁴, Anna E. Rutherford, MD, MPH¹, Muthoka L. Mutinga, MD¹, Karin L. Andersson, MD⁵, Robert S. Brown Jr., MD, MPH⁶, Chinweike Ukomadu, MD, PhD^{1,7}, Emily Oken, MD, MPH²

¹Division of Gastroenterology, Hepatology, and Endoscopy, Brigham and Women's Hospital, Boston, MA. matthew.s.chang@kp.org, arutherford@partners.org, mmutinga@partners.org, cukomadu@partners.org ²Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA. jwharam@post.harvard.edu, fang_zhang@harvardpilgrim.org, robert_lecates@harvardpilgrim.org, emily_oken@harvardpilgrim.org ³West Virginia University Health Sciences Center, Martinsburg, WV. emma.eggleston@wvumedicine.org ⁴Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Boston, MA rtuomala@partners.org ⁵Division of Gastroenterology, Massachusetts General Hospital, Boston, MA kanderson@mgh.harvard.edu ⁶Division of Gastroenterology and Hepatology, Weill Cornell Medical College, New York, NY rsb2005@med.cornell.edu ⁷Current address: Novartis Institutes for Biomedical Research, Cambridge, MA ⁸Current address: Department of Gastroenterology, Kaiser Permanente Northern California, 2350 Geary Blvd, San Francisco, CA 94115, Phone: 415.833.3514, Fax: 415.833.3364, matthew.s.chang@kp.org

Abstract

Background: Hepatitis B virus (HBV) screening during pregnancy is standard of care to prevent vertical transmission to infants, yet the mothers themselves may not receive appropriate follow-up.

Goals: Using a national database, we sought to determine rates of maternal peripartum follow-up with a HBV specialist and identify factors associated with a lack of follow-up.

Method: We identified women who delivered 2000–2012 and were diagnosed with HBV according to International Classification of Diseases-9 codes using a national database (Optum) derived from commercial insurance claims with ~46 million members ages 0–64 in all 50 states. Our primary outcome was follow-up during or after pregnancy with a HBV specialist (gastroenterology/infectious diseases).

Results: The prevalence of HBV was 0.27% (2,558/959,747 pregnancies), and median follow-up was 45 months. Only 21% of women had peripartum HBV specialist follow-up. On multivariable

Corresponding Author: Matthew S. Chang, M.D., M.P.H., Work conducted at: Division of Gastroenterology, Hepatology, and Endoscopy, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, Phone: (617) 732-6389, Fax: (617) 732-6389.

Disclosures:

Dr. Ukomadu is an employee of Novartis. The remaining authors report no conflicts of interest.

regression, predictors of peripartum follow-up at 1-year included younger age (odds ratio [OR] 0.97 per year [95% confidence interval (CI): 0.94, 0.99]), Asian race/ethnicity (OR 1.56 versus white [95% CI: 1.13, 2.17]), and residing in the Northeast (OR 1.70 [95% CI: 1.09, 2.66]) and Midwest (OR 1.73 [95% CI: 1.07, 2.81]) versus West. Predictors of testing for HBV DNA and ALT at 1-year included Asian race (OR 1.72 [95% CI: 1.23, 2.41]), a PCP visit within 2 years of delivery (OR 1.63 [95% CI: 1.19, 2.22]), and peripartum HBV specialist follow-up within 1-year (OR 15.68 [95% CI: 11.38, 21.60]).

Conclusions: Maternal HBV specialist follow-up rates were extremely low in this large, diverse cohort representing all United States regions. Referral to a HBV specialist was the strongest predictor of appropriate postpartum HBV laboratory testing. Follow-up rates may be even lower in uninsured populations.

Keywords

disparity; surveillance; nonadherence; administrative data; pregnancy

Introduction

Screening for chronic hepatitis B virus (HBV) infection during pregnancy to prevent vertical transmission is standard of care and has been recommended since 1988, yet little is known about peripartum maternal outcomes because HBV prevention efforts have largely focused on newborn prophylaxis.^{1, 2} Guidelines from the American Congress of Obstetrics and Gynecology (ACOG) and the American Association for the Study of Liver Diseases (AASLD) recommend that patients with HBV have lifelong care and laboratory testing by a clinician experienced in the management of chronic liver disease, typically a gastroenterologist/hepatologist or infectious disease specialist,³ given the risk of HBV complications such as cirrhosis, portal hypertension, and hepatocellular carcinoma.⁴

Despite these recommendations, our two recent studies found that only 50% of HBV-infected mothers had HBV follow-up either during or after pregnancy.^{5, 6} However, our studies were limited to births in a single health system⁵ and in the state of Massachusetts,⁶ and thus may not be generalizable across the United States (US) because of practice variation and regional differences in HBV prevalence. Further, these samples are likely subject to loss to follow-up. Finally, because of small numbers (n=291 and 983, respectively), we were limited by sample size.

To overcome these limitations, we used a national commercial insurance database (Optum) comprising ~46 million members in all 50 states to determine rates of maternal follow-up with a HBV specialist and identify factors associated with a lack of follow-up.

Materials and Methods

We analyzed administrative data from the Optum database, which is derived from commercial insurance claims representing approximately 4% of insured adults in the US.⁷ We used a rolling cohort enrolled from 2000 to 2012 and identified women who had continuous insurance coverage during pregnancy (the 9 months prior to delivery) and at least

1 month after pregnancy. We included the first pregnancy in the dataset for women who had more than 1 pregnancy captured (index pregnancy). We defined pregnancy and delivery using International Classification of Diseases, 9th revision (ICD-9) and Current Procedural Terminology (CPT) codes (Supplemental Table 1). Follow-up data were available through the end of 2012.

Similar to accepted definitions used in the hepatitis C virus (HCV) claims literature,⁸ we defined a diagnosis of HBV as meeting any one of three criteria: 1) at least 1 inpatient/emergency department ICD-9 code for HBV during the index pregnancy, 2) at least 2 outpatient ICD-9 codes for HBV on different dates during the index pregnancy, or 3) hepatitis B surface antigen (HBsAg) positivity, in the subset of patients who had HBsAg lab results available. We excluded women with any HBV specialist visit prior to the index pregnancy as we sought to study the gap in care among women identified by routine perinatal screening. Previously published claims-based HBV case definitions have typically required only one ICD-9 HBV code,^{9–11} but we chose a more conservative definition to reduce the risk of misclassification, specifically false positive HBV cases, because these would bias our findings towards an artificially low peripartum HBV specialist follow-up rate. To further evaluate our HBV definition, we also conducted a sensitivity analysis by determining HBV specialist follow-up within the subset of women with HBsAg+ results available and comparing it with the overall cohort.

Our primary outcome of interest was HBV specialist follow-up during or after pregnancy, which we defined as a gastroenterologist or infectious disease specialist visit plus a HBV ICD-9 diagnosis code. We evaluated follow-up within 6 and 12 months after delivery (among women with at least 6 and 12 months follow-up, respectively), as well as overall among all included women. We evaluated HBV-related laboratory tests using CPT codes (Supplemental Table 1), which included HBV DNA, e antigen, e antibody, core antibody, core IgM, alanine aminotransferase (ALT), hepatitis A virus antibody, hepatitis C virus antibody or RNA, and human immunodeficiency virus (HIV) antibody. We also determined Papanicolaou testing rates within 6 months after pregnancy, which is recommended by ACOG¹², to provide an internal comparison with HBV specialist follow-up rates.

Predictors of interest included demographics, having a primary care physician (PCP) visit within 2 years before delivery (including only PCP visits that occurred prior to the initial HBV specialist visit), and having a prior pregnancy, which were identified in our prior studies as predictors of HBV follow-up.^{5, 6} Education and poverty were classified based on census block of residence, as individual characteristics are not available in this dataset. We categorized women as from census block groups with below-high-school-education levels of <15%, 15%–24.9%, 25%–39.9%, and 40% and below poverty levels of <5%, 5%–9.9%, 10%–19.9%, and 20%. We included imputed race/ethnicity as a predictor using a validated approach of combining surname analysis and census data that has positive and negative predictive values of approximately 80 and 90 percent.¹³ We classified members as from predominantly white, black, or Hispanic neighborhoods if they lived in a census block group (geocoding) with at least 75% of members of the respective race/ethnicity. We then applied a superseding ethnicity assignment if members had an Asian or Hispanic surname and

classified remaining members as from mixed race/ethnicity neighborhoods.¹⁴ Finally, we also included US region¹⁵ as a predictor of HBV follow-up.

We conducted bivariate analyses to compare characteristics of mothers with and without HBV specialist follow-up. We used the t-test for age, and chi-squared or Fisher's exact test for categorical data, which included race/ethnicity, education, poverty, and US region. We included all variables from our bivariate analyses in two separate multivariable logistic regression models to identify predictors of HBV specialist follow-up at 6 months and at 1 year, restricted to patients with postpartum enrollment of at least 6 months or 1 year, respectively.

Additionally, we used a Cox regression model to identify predictors of HBV specialist follow-up in the entire cohort regardless of follow-up duration while accounting for differential follow-up. We tested the proportional hazards assumption using time-varying covariates for all variables in the initial model and then retained time-varying covariates only for variables that violated proportionality in the final model, using a cutoff of $p < 0.05$.¹⁶

As a secondary outcome, we created a composite variable for the combination of HBV DNA and ALT laboratory testing, since both are necessary for appropriate HBV disease management per AASLD guidelines.⁴ We included all variables and also HBV specialist follow-up at 1 year in a multivariable logistic regression model to identify predictors of HBV DNA and ALT laboratory testing at 1 year, restricted to women at least 1 year of postpartum enrollment. Results were reported as odds ratios (OR) for logistic regression models and hazard ratios (HR) for the Cox regression model with 95% confidence intervals (CI). All statistical analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC). This study was approved by institutional review boards from Partners HealthCare and Harvard Pilgrim Health Care.

Results

Cohort characteristics

The cohort selection process is detailed in Figure 1. The prevalence of HBV in our cohort was 0.27% (2,558/959,747). We excluded 214 women who had seen a HBV specialist prior to the index pregnancy, leaving a final cohort of 2,344 women with HBV diagnosed during pregnancy.

Median follow-up was 45 months (interquartile range [IQR] 23, 77). Overall, only 21% of women with HBV in pregnancy had peripartum HBV specialist follow-up. When stratified by HBV inclusion criteria, as expected, women who met inclusion by the stricter definition of at least 2 outpatient ICD-9 codes for HBV had a higher HBV specialist follow-up rate compared to the other definitions of at least 1 inpatient or ER ICD-9 code, or HBsAg positivity within the subset of the cohort with lab results (47.8% versus 22.8% and 18.2%, respectively, Supplemental Table 2). The majority, 17%, were seen by a gastroenterologist, while 1% were seen by an infectious disease specialist, and 3% were seen by both. Most women, 60%, who received specialist follow-up had their initial HBV specialist visit during pregnancy. When follow-up occurred postpartum, the first HBV specialist visit occurred at a

median of 15 months after delivery (IQR 5, 33). In the sensitivity analysis of women who had HBsAg+ results available, peripartum HBV specialist follow-up was actually slightly worse at 18% (219/1,200), than among the overall cohort (21%).

As a comparison, 42% of women in our cohort had a Papanicolaou test within 6 months postpartum, which was recommended by ACOG as part of routine care at the first postpartum visit during the study period.¹² Women who had a Pap were not more likely than women without a Pap to have HBV specialist follow-up on bivariate analysis (26.5% versus 22.7%, $p = 0.10$). In the logistic regression models, Pap completion was not a predictor of HBV specialist follow up and therefore not included in the final models (data not shown).

HBV specialist follow-up

On bivariate analysis, women with HBV specialist follow-up were more likely to be Asian (47% versus 39%, $p=0.002$) (Table 1). On multivariable logistic regression (Table 2) analysis restricted to women with postpartum enrollment of at least 6 months ($n=1,939$), predictors of peripartum HBV specialist follow-up at 6 months included increasing age as a negative predictor (OR 0.97 per year [95% CI: 0.94, 0.99]) and Asian race as a positive predictor (OR 1.43 versus white [95% CI: 1.05, 1.94]). Education, poverty, region, seeing a PCP within 2 years before delivery, and having a prior pregnancy were not associated with likelihood of follow-up. On analysis restricted to women with postpartum enrollment of at least 1 year ($n=1,546$), predictors of peripartum HBV specialist follow-up at 1 year were similar to those at 6 months (age OR 0.97 per year [95% CI: 0.94, 0.99], Asian race (OR 1.56 versus white [95% CI: 1.13, 2.17]), and also included residing in the Northeast as a positive predictor (OR 1.70 versus West [95% CI: 1.09, 2.66]) and Midwest (OR 1.73 versus West [95% CI: 1.07, 2.81]) (Table 3). Education, poverty, seeing a PCP within 2 years before delivery, and having a prior pregnancy were not predictors.

When allowing for any length of postpartum enrollment by using a Cox regression model (Table 4), positive predictors of overall peripartum HBV specialist follow-up included Asian race (HR 1.54 versus white [95% CI: 1.24, 1.92]), and mixed race/ethnicity neighborhood (HR 1.49 versus white [95% CI: 1.12, 1.98]), while increasing age (HR 0.97 per year [95% CI: 0.96, 0.99]) was a negative predictor. US region was also a predictor, but was found to have a non-proportional hazard, resulting in an increasing HR over time (Supplemental Figure 1a). Education and poverty were not predictors. Seeing a PCP within 2 years before delivery and having a prior pregnancy were also found to have non-proportional hazards, but were not predictors (Supplemental Figures 1b and 1c).

To assess time trends, when we evaluated delivery from 2001–2006 compared to 2007–2012, we found that there was no difference in HBV specialist follow-up on bivariate analysis, 20% versus 22%, respectively (Table 1), but when added to logistic regression models “delivery after 2006” was identified as an independent predictor of HBV specialist follow-up at 6 months (OR 1.86 [95% CI: 1.43, 2.40]) (Table 2) and 1 year (OR 1.79 [95% CI: 1.35, 2.36]) (Table 3) and when added to the cox regression model (HR 1.50 [95% CI: 1.25, 1.81]) (Table 4).

Only 2% (48/2344) of women were on nucleoside/nucleotide therapy peripartum (lamivudine 0.6%, adefovir dipivoxil 0.4%, tenofovir disoproxil fumarate 0.9%, entecavir 0.3%, with patients sometimes switching or taking more than 1 medication). Women with HBV specialist follow-up were more likely to be on therapy than women without (7.2% versus 0.65%, $p = <0.0001$). Among women with HBV specialist follow-up who were on therapy, two-thirds (24/36) had therapy started after establishing HBV specialist care.

HBV-related laboratory testing

In our cohort, 84.8% (814,322/959,747) of women had HBsAg testing during pregnancy, which is consistent with reported rates in the literature.¹⁷ Among all women with HBV in pregnancy, seeing an appropriate specialist was the strongest predictor of receiving HBV-related laboratory testing by 1 year postpartum. The rate of HBV-related testing, including the combined measure of HBV DNA and ALT testing (recommended for HBV disease management by AASLD) was 70% in those with specialist care versus 14% in those without, $p < 0.0001$ (Table 5).⁴ Among women with HBV specialist follow-up (not restricted by a 1 year follow-up interval), 57% (284/500) had HBV DNA and ALT checked before the first specialist visit, compared to 4% (22/500) who had labs checked after their HBV specialist visit, while the remainder did not have labs checked.

In 2006, the Centers for Disease Control and Prevention (CDC) and ACOG^{18, 19} recommended HIV testing during pregnancy in all women, which in our cohort occurred in 79% of women overall and was not different between those with or without HBV specialist care. As a comparison, the CDC reported that only 53.7 to 59.3% of pregnant women were tested for HIV in the US from 2000 to 2010.²⁰ When splitting our cohort using 2006 as a dividing point to assess for time trends, we found that a greater proportion of women had HIV checked if they delivered “after 2006” when compared to “2006 and before” (89% versus 79%, $p < 0.001$). In our cohort, only 62% of women who delivered in 2006 had HIV testing, compared to 94% of women who delivered from 2011 and onwards.

On multivariable logistic regression (Table 6), predictors of testing for HBV DNA and ALT at 1 year included Asian race (OR 1.72 versus white [95% CI: 1.23, 2.41]), seeing a PCP within 2 years before delivery (OR 1.63 [95% CI: 1.19, 2.22]) and having HBV specialist follow-up within 1 year postpartum (OR 15.68 [95% CI: 11.38, 21.60]). Interestingly, “delivery after 2006” was not a predictor of HBV laboratory testing at 1 year.

As a comparison, when we analyzed the group of women who had been excluded for prior HBV specialist care before the index pregnancy, more women had HBV DNA and ALT checked at 1 year if they were new to HBV specialist care (no prior HBV specialist, and did have peripartum follow-up) than when compared to women who never had any specialist care (no prior HBV specialist and no peripartum follow up) or even women who had specialist care prior to pregnancy at (70% versus 14% versus 56%, respectively, Supplemental Table 3). Other HBV-related labs varied in frequency, but the proportion that had HIV testing rate was the same as in women who were included in the study population.

As a sensitivity analysis, when defining HBV as 1 outpatient ICD-9 code (instead of 2 outpatient codes) we found that more patients were defined as having HBV (2,898 versus

2,344) with lower HBV specialist follow-up (544/2,898 [19%] versus 500/2,344 [21%], respectively). The proportion of women who had lab testing, including ALT and HBV DNA, was slightly lower when defining HBV as 1 outpatient ICD-9 code (Supplemental Table 4), but otherwise did not affect the findings from our primary logistic regression model (Supplemental Table 5).

Discussion

This study examines peripartum HBV care following HBV diagnosis during pregnancy within a large, diverse national cohort. Our study found that peripartum HBV specialist follow-up rates are extremely low, only 21%, among women of all socioeconomic backgrounds. Younger age, Asian race, and possibly residence in a mixed race/ethnicity neighborhood and in the US Northeast and Midwest were associated with higher rates of HBV specialist follow-up. Asian race, having a PCP visit within 2 years before delivery and having HBV specialist follow-up were associated with improved testing rates for HBV DNA and ALT.

This suboptimal peripartum HBV care is particularly striking when compared to the impressive near universal (>90%) implementation of newborn prophylaxis for HBV.^{2, 21} This success in preventing vertical transmission has largely developed through the efforts of the CDC and state/local perinatal hepatitis programs, which identify HBsAg+ pregnant women and provide case management during and after pregnancy.^{2, 22} However, despite the tremendous infrastructure that has been established for the newborns, the vast majority of HBV-infected mothers fail to receive HBV specialist care peripartum. These women are missing the opportunity for effective antiviral therapy, during a time of increased risk for hepatic flares,²³ as well as preventative HBV care, such as monitoring for cirrhosis and regular hepatocellular carcinoma screening, as dictated by AASLD guidelines.⁴ It is also important to note that we detected suboptimal HBV laboratory testing; even among women who had HBV specialist follow-up, only 70% of women had HBV DNA and ALT checked within 1 year postpartum. Although HBV specialists are more knowledgeable and are more likely to adhere to guidelines than non-specialists, such as obstetricians and primary care providers, follow-up with a HBV specialist is only the first step to appropriate, lifelong HBV care.²⁴⁻²⁶ In a study of 962 patients with chronic HBV followed at a major academic teaching hospital, 29% did not have at least an ALT and HBV DNA checked annually, while HBV specialists were not much better: 18% and 10% of patients followed by a gastroenterologist or infectious disease specialist, respectively.²⁵ In our cohort, we did find that the failure to have subspecialty care was the strongest predictor of not obtaining appropriate HBV-related testing, which is consistent with findings from prior studies.^{26, 27} It is unclear why follow-up was so poor, but may be related to lack of awareness of the long-term risks resulting from chronic HBV infection, by both patients and providers, particularly given the low prevalence of HBV in the US. Patients and provider education coupled with systematic case management of infected mothers would potentially improve peripartum HBV follow-up, a goal which has already been successfully achieved using these methods with newborns.^{2, 21}

HBV follow-up of infected mothers could also facilitate HBV screening and vaccination efforts for family and close contacts who are at risk for HBV, which is critical to the World Health Organization's goal of eradicating chronic HBV as global health threat by 2030.²⁸ Most HBV screening for non-pregnant adults in the US is organized by independent community organizations, often found in large metropolitan areas with immigrant groups from HBV endemic areas, with few or no programs in the Midwest, Southeast, and Southwest.²⁹ While providing an important service, these groups have limited catchments and are unable to meet the need for screening recommended by the CDC.²⁹ Improved strategies are urgently needed to diagnose chronic HBV, as the prevalence continues to rise with continued immigration from HBV endemic countries, adding an estimated 53,800 cases per year from 2004 through 2008.³⁰ HBV screening programs that start with contacts and families of HBV-infected mothers would be more efficient than current case-finding practices, as they have already been identified by local/state perinatal hepatitis programs. It is especially important that women are connected to medical care during pregnancy and not postpartum to best leverage this existing public health infrastructure. Pregnancy appears to be a key time to connect women to medical care, as we found 60% of women had follow-up during pregnancy, as opposed to after pregnancy when are less likely have regular medical care for themselves while they are busy caring for their newborn. However, the ultimate onus likely falls on the obstetrical providers to refer these women to specialists, or to refer to primary care providers who can refer to specialists.

Our study was limited by biases inherent to administrative claims data, which lack clinical information and are subject to miscoding and selection bias. We attempted to reduce inclusion of false positive HBV cases by adopting more restrictive diagnostic criteria for HBV and did not include women with only a single outpatient ICD-9 code for HBV. This increased the possibility that the patients included truly had chronic HBV, thus reducing the possibility of misclassifying patients who had an erroneous HBV code (for example: coded to have HBV infection when really the patient was just being screened for HBV and did not actually have chronic infection). If anything, our definition might have led to an overestimate in the peripartum follow up rates for hepatitis B, which is actually what we found when we broke down the population by inclusion criteria. While our cohort may have included some false positive HBV diagnoses, we performed a sensitivity analysis on a subset of women with laboratory-confirmed (HBsAg positive) HBV and found that the peripartum HBV specialist follow-up rate was similar to the main cohort (18% versus 21%), supporting the robustness of our overall cohort findings. We identified a number of factors associated with a lack of peripartum maternal HBV follow-up, but were limited in our ability to demonstrate causality given the observational nature of our study. Although most of our socioeconomic status variables were based on census block group of residence, not individual characteristics, this methodology has been validated to accurately detect socioeconomic status gradients, particularly poverty.^{31, 32} Our results were consistent with the findings from our two prior studies, one based in a single hospital system, and the other based in the state of Massachusetts, which also demonstrated inadequate peripartum HBV follow-up. Furthermore, we found that this gap in care was specific to HBV both during and after pregnancy; only 8.4% of women (200/2,344) in our cohort had postpartum HBV specialist follow-up compared to 42% of women who had a Papanicolaou test within 6

months postpartum. One of the limitations of using claims data is that it would be very difficult to know which patients were cared for by PCPs as opposed to simply coding for HBV when the patient does not actually have HBV (such as when screening for HBV). Even conservatively assuming that all of these patients had HBV managed by their PCPs, we still found that at most 288 patients (12%) were potentially managed only by a PCP rather than specialist, which would have been unlikely to alter our findings in a meaningful way. Another limitation of claims data is that it only captures lab tests that were successfully performed and not when lab tests were ordered, but never completed (such as when a patient has an HBV diagnosis, but then does not have the HBV DNA drawn). It can be difficult to identify intent behind lab ordering practices. When we tried to differentiate whether HBV labs were checked before HBV specialist referral, we found that 57% of women had labs checked before the first visit compared to 4%, but it was unclear whether this is because of abnormal lab values were prompting HBV specialist referral, or referring providers who remember to check labs also tend to refer to HBV specialists, or some other reason. It is possible that inappropriate labs, such as anti-HBc IgM, were ordered non-HBV specialists as part of a lab panel or indiscriminately due to insufficient HBV knowledge. This would be consistent with findings from our survey of obstetrician provider practices and knowledge regarding HBV and pregnancy; only 40% and 51% of respondents from 2 major teaching hospitals could accurately identify serologies that were consistent with acute and chronic infection, respectively.³³ Unfortunately, infant records could not be linked to our cohort so we were unable to address infant outcomes, such as HBV vaccination, HBIG administration, and chronic HBV infection status. Lastly, it is possible that not all women who failed to be linked to HBV care in the year following delivery will experience negative consequences; some of these women might establish subsequent HBV care later in life, such as at 40 years of age, and we were not able to capture this with our median follow-up limited to 45 months.

In conclusion, peripartum HBV specialist follow-up rates were only 21% in this nationwide US dataset. Follow-up rates may be even lower in uninsured and more vulnerable populations. Low rates of HBV follow-up might lead to potentially preventable morbidity and mortality from untreated HBV in these mothers and their close contacts. Mechanisms to increase HBV follow-up are needed, such as improved patient and provider education, streamlined referral systems to HBV specialists, and ideally expansion of state perinatal hepatitis programs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Financial Support:

Funding for EO: NICHD K24 HD069408.

This study was funded in part by a Partners HealthCare Patient Care Quality & Safety Center of Expertise Research Grant and a microgrant from the Biomedical Research Institute and the Brigham and Women's Hospital Center for Faculty Development and Diversity's Office for Research Careers.

Data source purchased through grants from the Harvard Pilgrim Health Care Foundation 214168, American Cancer Society 118261-RSGI-10-075-01-CPHPS, and CDC/NIDDK 1U58DP02719.

References

1. Lin K, Vickery J. Screening for hepatitis B virus infection in pregnant women: evidence for the U.S. Preventive Services Task Force reaffirmation recommendation statement. *Ann Intern Med* 2009;874–6. [PubMed: 19528566]
2. Smith EA, Jacques-Carroll L, Walker TY, et al. The national Perinatal Hepatitis B Prevention Program, 1994–2008. *Pediatrics* 2012;129:609–16. [PubMed: 22451702]
3. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 86: Viral hepatitis in pregnancy. *Obstet Gynecol* 2007;110:941–56. [PubMed: 17906043]
4. Lok AS, McMahon BJ. Chronic hepatitis B: update 2009. *Hepatology* 2009;50:661–2. [PubMed: 19714720]
5. Chang MS, Tuomala R, Rutherford AE, et al. Postpartum care for mothers diagnosed with hepatitis B during pregnancy. *Am J Obstet Gynecol* 2015;212:365 e1–7. [PubMed: 25281364]
6. Chang MS, Barton K, Crockett M, et al. Postpartum laboratory follow-up in women with hepatitis B in Massachusetts from 2007–2012. *J Clin Gastroenterol* 2016;50:e60–e64. [PubMed: 27092430]
7. Optum. Clinformatics Data Mart. Available at: <https://www.optum.com/life-sciences/differentiate-products/marketing-analytics/clinformatics-data-mart.html>. Retrieved May 25, 2015.
8. Juday T, Tang H, Harris M, et al. Adherence to chronic hepatitis B treatment guideline recommendations for laboratory monitoring of patients who are not receiving antiviral treatment. *J Gen Intern Med* 2011;26:239–44. [PubMed: 20978862]
9. Fan L, Owusu-Edusei K Jr., Schillie SF, et al. Antiviral treatment among pregnant women with chronic hepatitis B. *Infect Dis Obstet Gynecol* 2014;2014:546165. [PubMed: 25548510]
10. Chen JY, Ma Q, Everhard F, et al. HIV screening in commercially insured patients screened or diagnosed with sexually transmitted diseases or blood-borne pathogens. *Sex Transm Dis* 2011;38:522–7. [PubMed: 21336232]
11. Lee TA, Veenstra DL, Iloeje UH, et al. Cost of chronic hepatitis B infection in the United States. *J Clin Gastroenterol* 2004;38:S144–7. [PubMed: 15602162]
12. American Academy of Pediatrics (AAP) Committee on Fetus and Newborn and American Congress of Obstetricians and Gynecologists (ACOG) Committee on Obstetric Practice, Editors: Riley L, Stark A, et al. *Guidelines for Perinatal Care: Elk Grove Village, 2012.*
13. Fiscella K, Fremont AM. Use of geocoding and surname analysis to estimate race and ethnicity. *Health Serv Res* 2006;41:1482–500. [PubMed: 16899020]
14. Ethnic Technologies. Available at: <http://www.ethnictechnologies.com/>. Retrieved May 25, 2015.
15. United States Census Bureau. Geographic Terms and Concepts - Census Divisions and Census Regions. Available at: https://www.census.gov/geo/reference/gtc/gtc_census_divreg.html. Retrieved 5/23/2014.
16. Bellera CA, MacGrogan G, Debled M, et al. Variables with time-varying effects and the Cox model: some statistical concepts illustrated with a prognostic factor study in breast cancer. *BMC Med Res Methodol* 2010;10:20. [PubMed: 20233435]
17. Schillie SF, Vellozzi C, Reingold A, et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep* 2018;67:1–31.
18. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. *MMWR Recomm Rep* 2006;55:1–17; quiz CE1–4.
19. ACOG Committee Opinion no 596: Committee on Gynecologic Practice: Routine human immunodeficiency virus screening. *Obstet Gynecol* 2014;123:1137–9. [PubMed: 24785878]
20. Massachusetts Department of Public Health. Massachusetts Pregnancy Risk Assessment Monitoring System (PRAMS) 2009/2010 Surveillance Report. Available at: <http://www.mass.gov/eohhs/docs/dph/com-health/prego-newborn/prams-report-09-10.pdf>. Retrieved August 25, 2014.
21. Ross CE, Tao G, Patton M, et al. Screening for human immunodeficiency virus and other sexually transmitted diseases among u.s. Women with prenatal care. *Obstet Gynecol* 2015;125:1211–6. [PubMed: 25932850]

22. Centers for Disease Control and Prevention (CDC). Perinatal Hepatitis B Prevention Coordinators. Available at: <http://www.cdc.gov/hepatitis/Partners/PeriHepBCoord.htm>. Retrieved 11/4/2013.
23. Giles M, Visvanathan K, Lewin S, et al. Clinical and virological predictors of hepatic flares in pregnant women with chronic hepatitis B. *Gut* 2015;64:1810–5. [PubMed: 25431458]
24. Burman BE, Mukhtar NA, Toy BC, et al. Hepatitis B management in vulnerable populations: gaps in disease monitoring and opportunities for improved care. *Dig Dis Sci* 2014;59:46–56. [PubMed: 24052195]
25. Wu Y, Johnson KB, Roccaro G, et al. Poor Adherence to AASLD Guidelines for Chronic Hepatitis B Management and Treatment in a Large Academic Medical Center. *Am J Gastroenterol* 2014;109:867–75. [PubMed: 24732869]
26. Sarkar M, Shvachko VA, Ready JB, et al. Characteristics and management of patients with chronic hepatitis B in an integrated care setting. *Dig Dis Sci* 2014;59:2100–8. [PubMed: 24728968]
27. Ku KC, Li J, Ha NB, et al. Chronic hepatitis B management based on standard guidelines in community primary care and specialty clinics. *Dig Dis Sci* 2013;58:3626–33. [PubMed: 24122622]
28. World Health Organization. Combating hepatitis B and C to reach elimination by 2030. Available at: http://apps.who.int/iris/bitstream/10665/206453/1/WHO_HIV_2016.04_eng.pdf?ua=1. Retrieved April 2, 2017, 2016.
29. Rein DB, Lesesne SB, Leese PJ, et al. Community-based hepatitis B screening programs in the United States in 2008. *J Viral Hepat* 2010;17:28–33. [PubMed: 19674286]
30. Mitchell T, Armstrong GL, Hu DJ, et al. The increasing burden of imported chronic hepatitis B--United States, 1974–2008. *PLoS One* 2011;6:e27717. [PubMed: 22163270]
31. Krieger N, Chen JT, Waterman PD, et al. Geocoding and monitoring of US socioeconomic inequalities in mortality and cancer incidence: does the choice of area-based measure and geographic level matter?: the Public Health Disparities Geocoding Project. *Am J Epidemiol* 2002;156:471–82. [PubMed: 12196317]
32. Berkowitz SA, Traore CY, Singer DE, et al. Evaluating area-based socioeconomic status indicators for monitoring disparities within health care systems: results from a primary care network. *Health Serv Res* 2015;50:398–417. [PubMed: 25219917]
33. Kwong AJ, Chang MS, Tuomala RE, et al. Peripartum Care for Mothers Diagnosed with Hepatitis B During Pregnancy: A Survey of Provider Practices. *Matern Child Health J* 2018.

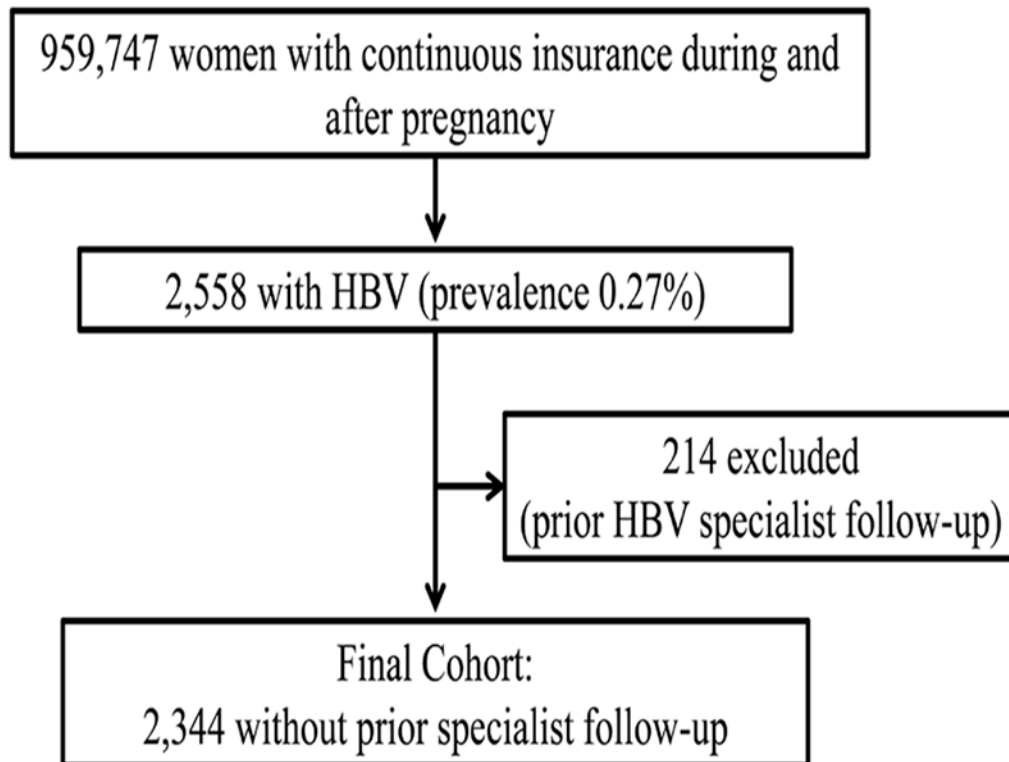


Figure 1.
Cohort selection flow diagram.

Table 1.

Characteristics of women with HBV during pregnancy, with and without HBV specialist follow-up (n=2,344).

	Without HBV specialist follow-up (n=1,844)	With HBV specialist follow-up (n=500)	P-value
Mean age in years (standard deviation)	31.7(5.3)	31.1 (5.0)	0.06
Race/ethnicity, n (%)			0.002
Asian	706 (39%)	237 (47%)	
White	614 (33%)	130 (26%)	
Black	61 (3%)	15 (3%)	
Hispanic	126 (7%)	26 (5%)	
Mixed	328 (18%)	92 (18%)	
Census block group % below high school education, n (%)			0.19
<15%	1072 (58%)	309 (62%)	
15%-24.9%	385 (21%)	105 (21%)	
25%-39.9%	266 (14%)	54(11%)	
40%	113(6%)	32 (6%)	
Census block group % below poverty levels, n (%)			0.38
<5%	807 (44%)	233 (47%)	
5%-9.9%	432 (24%)	122 (24%)	
10%-19.9%	371 (20%)	84 (17%)	
20%	226 (12%)	61 (12%)	
United States region, n (%)			0.35
Northeast	249 (14%)	75 (15%)	
Midwest	439 (24%)	134(27%)	
South	829 (45%)	207 (41%)	
West	323 (18%)	84 (17%)	
Seen by a primary care physician within 2 years of delivery, n (%)	1127(67%)	336 (67%)	0.79
Prior pregnancy, n (%)	360 (20%)	131 (26%)	0.002
Years 2001–2006	920 (80%)	235 (20%)	0.27
Years 2007–2012	924 (78%)	265 (22%)	

Table 2.

Predictors of peripartum HBV specialist follow-up at 6 months* (n=1,939).

Variable	Odds ratio (95% Confidence Interval)
Age (per year)	0.97 (0.94, 0.99)
Race/ethnicity	
Hispanic	1.46 (0.85, 2.52)
Asian	1.43 (1.05, 1.94)
Black	1.10 (0.48, 2.52)
Mixed	1.41 (0.95, 2.09)
White	1.00 (referent)
Census block group below high school education	
<15%	1.43 (0.73, 2.81)
15%-24.9%	1.47 (0.76, 2.85)
25%-39.9%	0.94 (0.49, 1.82)
40%	1.00 (referent)
Census block group below poverty levels	
<5%	0.86 (0.50, 1.45)
5%-9.9%	0.86 (0.51, 1.46)
10%-19.9%	0.74 (0.45, 1.22)
20%	1.00 (referent)
US region	
Northeast	1.29 (0.87, 1.90)
Midwest	1.32 (0.86, 2.03)
South	0.81 (0.56, 1.17)
West	1.00 (referent)
Seen by a primary care physician within 2 years of delivery	0.89 (0.68, 1.16)
Prior pregnancy	0.95 (0.71, 1.28)
Delivery after 2006	1.86 (1.43, 2.40)

* 313 women experience HBV specialist follow-up.

Table 3.

Predictors of peripartum HBV specialist follow-up at 1 year* (n= 1,546).

Variable	Odds ratio (95% Confidence Interval)
Age (per year)	0.97 (0.94, 0.99)
Race/ethnicity	
Hispanic	1.25 (0.69, 2.26)
Asian	1.56 (1.13, 2.17)
Black	1.84 (0.82, 4.14)
Mixed	1.37 (0.88, 2.12)
White	1.00 (referent)
Census block group below high school education	
<15%	0.89 (0.45, 1.79)
15%-24.9%	0.95 (0.48, 1.88)
25%-39.9%	0.73 (0.37, 1.44)
40%	1.00 (referent)
Census block group below poverty levels	
<5%	1.26 (0.69, 2.28)
5%-9.9%	1.26 (0.63, 2.06)
10%-19.9%	0.87 (0.49, 1.54)
20%	1.00 (referent)
US region	
Northeast	1.70 (1.09, 2.66)
Midwest	1.73 (1.07, 2.81)
South	1.11 (0.74, 1.68)
West	1.00 (referent)
Seen by a primary care physician within 2 years of delivery	0.97 (0.73, 1.29)
Prior pregnancy	1.08 (0.80, 1.45)
Delivery after 2006	1.79 (1.35, 2.36)

* 273 women experience HBV specialist follow-up.

Table 4.

Cox regression model for the outcome HBV specialist follow-up* (n=2,344).

Variable	Hazard ratio (95% Confidence Interval)
Age (per year)	0.97 (0.96, 0.99)
Race/ethnicity	
Hispanic	1.06 (0.69, 1.64)
Asian	1.54 (1.24, 1.92)
Black	1.43 (0.81, 2.52)
Mixed	1.49 (1.12, 1.98)
White	1.00 (referent)
Census block group below high school education	
<15%	1.02 (0.64, 1.62)
15%-24.9%	1.00 (0.63, 1.59)
25%-39.9%	0.75 (0.48, 1.19)
40%	1.00 (referent)
Census block group below poverty levels	
<5%	1.03 (0.70, 1.54)
5%-9.9%	1.08 (0.73, 1.61)
10%-19.9%	0.87(0.60, 1.27)
20%	1.00 (referent)
Delivery after 2006	1.50(1.25, 1.81)

* 500 women experience HBV specialist follow-up.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 5.

Laboratory testing at 1 year in women with and without HBV specialist follow-up (n=1,546).

	Without HBV specialist follow-up (n=1,273)	With HBV specialist follow-up (n=273)	P-value*
HBV DNA	15%	74%	<0.0001
E antigen	29%	70%	<0.0001
E antibody	22%	60%	<0.0001
Core antibody	34%	60%	<0.0001
Core IgM	29%	49%	<0.0001
ALT	61%	88%	<0.0001
Hepatitis A virus antibody	24%	47%	<0.0001
Hepatitis C antibody or RNA	38%	60%	<0.0001
HBV DNA and ALT	14%	70%	<0.0001
HIV antibody (during pregnancy)	79%	77%	0.63
HIV antibody (at 1 year postpartum)	80%	78%	0.46

* Fisher's exact test.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 6.

Predictors of HBV laboratory testing (HBV DNA and ALT) at 1 year* (n= 1,546).

Variable	Odds ratio (95% Confidence Interval)
Age (per year)	1.02 (0.99, 1.04)
Race/ethnicity	
Hispanic	0.88 (0.46, 1.69)
Asian	1.72 (1.23, 2.41)
Black	1.26 (0.51, 3.15)
Mixed	1.22 (0.77, 1.94)
White	1.00 (referent)
Census block group below high school education	
<15%	1.78 (0.82, 3.87)
15%-24.9%	1.48 (0.68, 3.19)
25%-39.9%	1.78 (0.84, 3.78)
40%	1.00 (referent)
Census block group below poverty levels	
<5%	0.92 (0.49, 1.71)
5%-9.9%	0.81 (0.44, 1.51)
10%-19.9%	0.76 (0.42, 1.38)
20%	1.00 (referent)
US region	
Northeast	1.26 (0.78, 2.03)
Midwest	0.87 (0.58, 1.29)
South	0.87 (0.58, 1.40)
West	1.00 (referent)
Seen by a primary care physician within 2 years of delivery	1.63 (1.19, 2.22)
Prior pregnancy	0.99 (0.72, 1.35)
HBV specialist follow-up within 1 year postpartum	15.68 (11.38, 21.60)
Delivery after 2006	1.28 (0.96, 1.70)

* 370 women experience HBV DNA and ALT testing.