Original Research

Reported Prevalence of Maternal Hepatitis C Virus Infection in the United States

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OBJECTIVE: To quantify the reported prevalence and trend of maternal hepatitis C virus (HCV) infection in the United States (2009–2017) and identify maternal characteristics and obstetric outcomes associated with HCV infection during pregnancy.

METHODS: We conducted a population-based retrospective cohort study of all live births in the United States for the period 2009 through 2017 using National Center for Health Statistics birth records. We estimated reported prevalence and trends over this time period for the United States. We also evaluated demographic factors and pregnancy outcomes associated with maternal HCV infection for a contemporary U.S. cohort (2014–2017).

RESULTS: During the 9-year study period, there were 94,824 reported cases of maternal HCV infection among 31,207,898 (0.30%) live births in the United States. The rate of maternal HCV infection increased from 1.8 cases per 1,000 live births to 4.7 cases per 1,000 live births (relative risk [RR] 2.7, 95% CI 2.6–2.8) in the United States. After adjusting for various confounders in the contemporary U.S. cohort (2014–2017), demographic characteristics associated with HCV infection included non-Hispanic white race (adjusted RR 2.8, 95% CI 2.7–2.8), Medicaid insurance (adjusted RR 3.3, CI 3.2–3.3), and cigarette smoking (adjusted RR 11.1, CI 10.9–11.3). Co-infection during pregnancy with hepatitis B (adjusted RR 19.2, CI 18.1–20.3), gonorrhea, chlamydia, or syphilis were also associated with maternal HCV infection. Obstetric and neonatal outcomes associated with maternal HCV infection included cesarean delivery, preterm birth, maternal intensive care unit admission, blood transfusion, having small-for-gestational-age neonates (less than the 10th percentile) birth weight, neonatal intensive care unit admission, need for assisted neonatal ventilation, and neonatal death.

CONCLUSION: The reported prevalence of maternal HCV infection has increased 161% from 2009 to 2017.

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Hepatitis C virus (HCV) affects 2–5 million people in the United States and is a major cause of morbidity and mortality in the United States, with increasing incidence and shifting demographics as a result of the opioid epidemic.[1–5] The incidence of acute HCV infection has increased dramatically in geographic regions and populations most affected by the opioid epidemic, such as young persons and those residing Appalachian states and rural areas.[2,6–11] Hepatitis C rates among pregnant women in Ohio, Tennessee, and West Virginia have been reported to be 9, 10.0, and 22.6 per 1,000 live births as of 2014, reaching approximately 8% in some counties.[10,11] It is estimated that intravenous drug use accounts for approximately 60% of HCV transmission in the United States, with blood transfusion before 1992 as the next biggest risk factor.[8] However, 50% of individuals with HCV infection do not report either a history of illicit drug use or blood transfusion.[8] Additionally, the true prevalence of HCV infection is likely underreported; the Centers for Disease Control and Prevention (CDC) estimates actual cases are

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Data for this study were provided by the National Center for Health Statistics, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program.

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likely 13.9 times the number of reported cases in any year.[8] Previously, treatment of HCV infection was limited to interferon and ribavirin, which are contraindicated in pregnancy. In 2013, however, direct-acting antiviral therapies were approved by the U.S. Food and Drug Administration and have increased in availability and yield cure rates of 95–99%.[12–14]

Despite these promising new treatment modalities, the CDC, the Society for Maternal-Fetal Medicine (SMFM), and the American College of Obstetricians and Gynecologists (ACOG) do not recommend universal screening in pregnancy, because pregnant women traditionally have no greater risk of acquiring HCV infection than nonpregnant women and interventions to prevent mother-to-child transmission are lacking.[15,16] Current guidelines from these organizations support risk factor-based screening.[15]

In this study, our primary objective was to evaluate the trend in reported maternal HCV infection prevalence over the 9-year period (2009–2017). Secondary objectives were to identify maternal characteristics and obstetric outcomes associated with maternal HCV infection in the United States using a contemporary subgroup of the cohort (2014–2017).

METHODS

We conducted a population-based retrospective cohort study of all live births with reported HCV infection status in the United States over a 9-year period (2009–2017). This study was exempt from review by the Institutional Review Board at the University of Cincinnati, because the data used do not meet criteria for human subject research by federal standards. The data for this study were obtained from the U.S.-linked birth–death database of live birth records provided by the National Center for Health Statistics after review and approval by the CDC. The live birth records obtained for these analyses used the newest version of the national birth certificate form (2003 U.S. Standard Certificate of Live Birth).[17]

All variables were abstracted from the individuals medical, prenatal, and delivery records according to the National Vital Statistics System Guide for Completing the Facility Worksheets for the Certificate of Live Birth in the United States.[17,18] The exposure variable for this study, maternal HCV infection is one of five infections tracked on the U.S. birth certificate form. Small-for-gestational age (SGA) birth weight was defined as birth weight less than the 10th percentile.[19]

The study population included all singleton deliveries, as well as the first order birth in each multifetal delivery, corresponding to one mother for each delivery event. Women who delivered multiple times during the study period were counted as unique live births. Women with missing data regarding maternal HCV infection status (n=40,892, 0.3%) or who delivered at 20 0/7 weeks of gestation or less or at 43 6/7 weeks of gestation or more (n=18,776, 0.1%) were not included in this analysis.

The reported rate of maternal HCV infection for each year of the study period was presented along with the annual reported rates of other tracked infections (hepatitis B, gonorrhea, chlamydia, and syphilis). The annual reported maternal HCV infection rates were presented across the study period (2009–2017) for individual U.S. states, with HCV infection rates exceeding 1% in 2017. Additionally, annual rates for U.S. states with HCV infection rates that increased by more than 100% between 2009 and 2017 were also presented. A heat map of reported maternal HCV infection prevalence for each U.S. county (3,146) of the continental United States was created for each year (2009–2017) of the study period to visually demonstrate geographic trends in HCV infection prevalence and distribution. Maps were generated with R tmap, a framework for data visualization with R 3.6.1. County maternal HCV infection rates were based on maternal residence at time of birth and were presented as a yearly percentage of deliveries reported as HCV infection–positive among deliveries with a recorded HCV infection status. All reported prevalence rates were derived from National Center for Health Statistics data.

Baseline differences in demographic characteristics and obstetric and neonatal outcomes were compared between women with HCV infection and those without HCV infection using a subgroup of the cohort (2014–2017). *T* test and χ^2 were used for statistical comparison of continuous and categorical data, respectively. We performed multivariate logistic regression analyses to estimate the association between maternal HCV infection and various maternal, obstetric, and neonatal characteristics and outcomes. Women with multifetal pregnancies were counted only once in the adjusted analyses. Differences between HCV infection status cohorts noted in univariate comparisons were included in the full model and sequentially removed in a stepwise fashion to attain a model of both statistically influential and biologically plausible covariates. We defined significant differences as comparisons with *P*-values of less than 0.05 and 95% CIs not inclusive of the null value of 1.0. Statistical analyses were performed using Stata 15.

RESULTS

During the 9-year study period (2009–2017), there were 94,824 reported cases of maternal HCV infection among 31,207,898 (0.30%) live births in the United States with reported HCV infection status (Table 1). The reported prevalence of maternal HCV infection increased 161% from 1.8 cases per 1,000 live births to 4.7 cases per 1,000 live births (relative risk [RR] 2.7, CI 2.6–2.8) from 2009 to 2017 (Table 1). Maternal HCV infection was the second most prevalent and most rapidly increasing infection in the United States, as reported on the birth certificate form (Appendix 1, available online at http://links.lww.com/AOG/B681). In 2009, there were no states reporting maternal HCV infection rates of at least 10 per 1,000 live births. As of 2017, nine states (18%) reported maternal HCV infection rates at least 10 per 1,000 live births. An additional 16 states observed maternal HCV infection rate increases of greater than 100% between 2009 and 2017 (Appendix 2, available online at http://links.lww.com/AOG/B681). There were minimal missing data on reported HCV infection status after 2013 (Appendix 3, available online at http://links.lww.com/AOG/B681). A county-level heat map of reported maternal HCV infection prevalence within the continental United States for 2017 demonstrates the geographical distribution of HCV infection burden (Fig. 1). A heat map of reported HCV infection prevalence for each individual year in the study period (2009–2017) was also created for visual representation of HCV infection trends (Appendix 4, available online at http://links.lww.com/AOG/B681).

For the contemporary cohort (2014–2017) analyses (Fig. 2), there were numerous demographic differences between women with and without reported HCV infection during pregnancy (Table 2). Women with HCV infection were less likely to be at the extremes of age (younger than 20 or 35 years or older). They were more likely to have pregestational diabetes, chronic hypertension, and be underweight (body mass index [BMI, calculated as weight in kilograms divided by height in meters squared] less than 18.5). Among the maternal cohort with HCV infection, 79.7% of women were of non-Hispanic white race compared with 52.1% in the non-HCV cohort. The reported prevalence of maternal HCV infection increased 204% from 2.4 cases per 1,000 live births to 7.3 cases per 1,000 live births among non-Hispanic white women during the study period (Fig. 3). Women with HCV infection were less likely to be married, had lower educational attainment, and were more likely to use Medicaid insurance (Table 2). Women with HCV infection were more likely to smoke cigarettes (61.4 vs 7.3%, rate difference 54.1%, $P<.001$) compared with women without HCV infection. Women in the cohort with HCV infection were more likely to live in county residential population sizes of less than 250,000 people (county sizes 100,000–250,000; 50,000–100,000; 25,000–50,000; 10,000–25,000, and less than 10,000) and were less likely to live in counties with population sizes of at least 500,000 (Appendix 5, available online at http://links.lww.com/AOG/B681).

Women with HCV infection were more likely to have co-infection with hepatitis B, chlamydia, syphilis, and gonorrhea (Table 3). The total reported number of maternal HCV infection cases exceeded both the number of reported hepatitis B and syphilis cases combined from 2014 to 2017 (Appendix 6, available online at http://links.lww.com/AOG/B681). The maternal cohort with HCV infection had higher rates of preterm birth (17.0 vs 8.7%, rate difference 8.3%,

Table 1. Maternal Hepatitis C Virus Infection Rates in the United States, 2009–2017

Delivery Year	Live Births*	Maternal HCV Infection	No Maternal HCV Infection	HCV Infection Status Not Reported
2009	2,727,351	4,779 (0.18) (0.17–0.18)	2,722,572	19,721 (0.72)
2010	3,055,884	6,107 (0.20) (0.19–0.20)	3,049,777	16,449 (0.54)
2011	3,267,934	6,900 (0.21) (0.21–0.22)	3,261,034	17,787 (0.55)
2012	3,411,640	8,011 (0.23) (0.23–0.24)	3,403,629	13,927 (0.41)
2013	3,480,199	7,865 (0.23) (0.23–0.24)	3,472,334	13,047 (0.37)
2014	3,768,607	12,718 (0.34) (0.33–0.34)	3,755,889	14,006 (0.37)
2015	3,838,062	14,496 (0.38) (0.37–0.39)	3,823,566	9,057 (0.24)
2016	3,873,781	16,229 (0.42) (0.41–0.43)	3,857,552	8,700 (0.22)
2017	3,784,440	17,719 (0.47) (0.46–0.48)	3,766,721	9,129 (0.24)
Total	31,207,898	94,824 (0.30)	31,113,074	121,823 (0.4)

HCV, hepatitis C virus.
Data are n or n (%) (95% CI).
* With HCV infection status recorded.

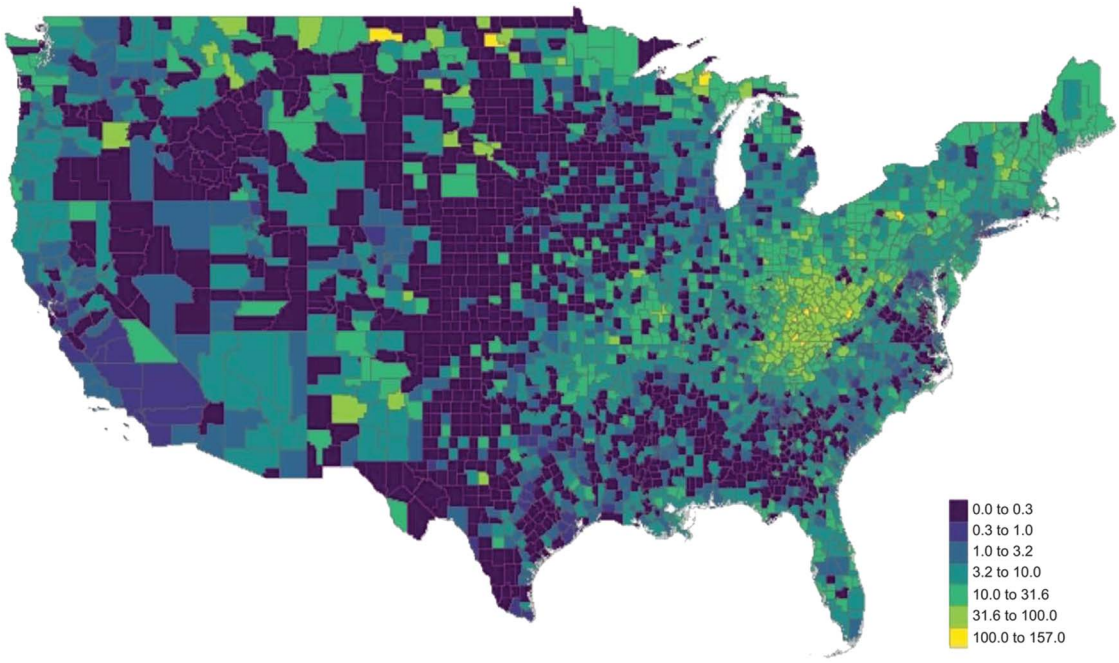

Fig. 1. Heat map of maternal hepatitis C prevalence (per 1,000 live births) at the county level within the continental United States in 2017.

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$P<.001$) and, as expected, lower birth weights (3,034 vs 3,287 g, weight difference 253 g, $P<.001$) compared with the cohort without HCV infection. However, after correcting for gestational age, higher rates of SGA birth weights were observed for the cohort with HCV infection as compared with the cohort without HCV infection (18.2 vs 9.5%, rate difference 8.7%, $P<.001$).

Women with HCV infection were more likely to have more adverse maternal outcomes including blood transfusion, intensive care unit (ICU) admission, unplanned hysterectomy, and uterine rupture as compared with women without HCV infection (Table 3). The composite adverse maternal outcome rate (including transfusion, ICU admission, unplanned hysterectomy, and uterine rupture) was 1.1 vs 0.4% (rate difference 0.7%, $P<.001$) between the cohorts with and without HCV infection, respectively. Neonates in the cohort with maternal HCV infection were more likely to be admitted to the neonatal intensive care unit and had lower 5-minute Apgar scores. Neonatal assisted ventilation, surfactant use, and antibiotic administration were more common in the cohort with HCV infection. Neonatal death was rare, although it was more common in the cohort with HCV infection (0.34 vs 0.22, $P<.001$, Table 3).

Absolute, crude, and adjusted relative risks of factors associated with reported maternal HCV infection were described for the contemporary cohort (Table 4). In the multivariate logistic regression model adjusted for age, race, year of delivery, maternal comorbidities, insurance status, cigarette smoking, BMI, parity, and prior cesarean birth, we estimated the association of various maternal factors and obstetric outcomes with maternal HCV infection. Maternal HCV infection was associated with non-Hispanic white race (adjusted RR 2.8, CI 2.7–2.8), cigarette smoking (adjusted RR 11.1, CI 10.9–11.3), county residential population size 100,000 or less, Medicaid insurance, and not receiving any prenatal care before delivery. Concurrent infections during pregnancy including hepatitis B (adjusted

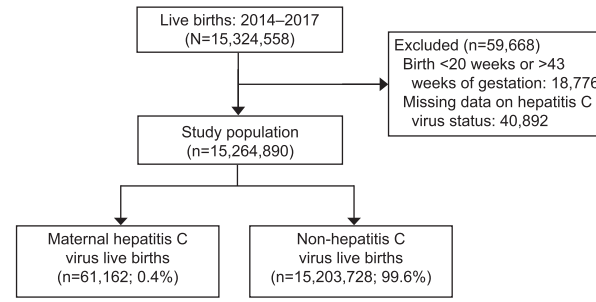

Fig. 2. Flow diagram of study population.

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Table 2. Maternal Characteristics of Hepatitis C Virus– and Non–Hepatitis C Virus–Affected Pregnancies

Characteristic	HCV (n=61,162)	Non-HCV (n=15,203,728)	*P*
Age (y)	28 (25–32)	29 (24–33)	<.001
Teen (younger than 20 y)	1,230 (2.0)	873,619 (5.8)	<.001
Advanced maternal age (35 y or older)	7,811 (12.8)	2,502,080 (16.5)	<.001
Prepregnancy diabetes	710 (1.2)	127,211 (0.8)	<.001
Gestational diabetes	2,926 (4.8)	886,651 (5.8)	<.001
Chronic HTN	1,590 (2.6)	256,787 (1.7)	<.001
Gestational HTN or preeclampsia	3,415 (5.6)	865,155 (5.7)	.296
Prepregnancy BMI (kg/m^2)	28.2±15.5	28.9±14.0	<.001
BMI category			
Underweight (less than 18.5)	3,201 (5.5)	526,992 (3.6)	<.001
Normal (18.5–24.9)	30,369 (51.7)	6,592,225 (44.7)	
Overweight (25.0–29.9)	14,498 (24.7)	3,826,179 (25.9)	
Obese class I (30.0–34.9)	6,567 (11.2)	2,086,533 (14.2)	
Obese class II (35.0–39.9)	2,565 (4.4)	1,010,103 (6.9)	
Obese class III (40.0 or higher)	1,581 (2.7)	708,447 (4.8)	
Race			
Non-Hispanic white	48,721 (79.7)	7,927,310 (52.1)	<.001
Non-Hispanic black	2,892 (4.7)	2,161,667 (14.2)	
Non-Hispanic Asian	770 (1.3)	958,060 (6.3)	
Hispanic	4,976 (8.1)	3,556,295 (23.5)	
Other	3,803 (6.2)	590,396 (3.9)	
Social factors			
Married	15,032 (24.7)	8,838,815 (60.0)	<.001
Less than 12th-grade education	15,654 (26.0)	2,130,022 (14.2)	<.001
Medicaid	47,320 (78.3)	6,484,281 (42.9)	<.001
Prenatal factors			
Parity	1 (0–2)	1 (0–2)	<.001
Nulliparous	15,747 (25.8)	5,906,993 (38.9)	<.001
History of prior cesarean birth	12,153 (19.9)	2,229,287 (15.1)	<.001
History of preterm birth	5,180 (8.5)	448,129 (3.0)	<.001
Cigarette smoking	36,929 (61.4)	1,101,519 (7.3)	<.001
No prenatal care	3,412 (5.9)	228,556 (1.6)	<.001
Maternal county residential population			
1,000,000 or more	7,539 (12.3)	4,346,988 (28.7)	<.001
500,000–1,000,000	10,429 (17.1)	3,143,114 (20.7)	
250,000–500,000	8,678 (14.2)	2,247,634 (14.8)	
100,000–250,000	12,005 (19.6)	2,330,489 (15.4)	
50,000–100,000	8,953 (14.7)	1,277,248 (8.4)	
25,000–50,000	8,047 (13.2)	1,023,267 (6.8)	
10,000–25,000	4,547 (7.4)	629,600 (4.2)	
Less than 10,000	934 (1.5)	167,122 (1.1)	

HCV, hepatitis C virus; HTN, hypertension; BMI, body mass index.
Data are median (interquartile range), n (%), or mean±SD unless otherwise specified.

RR 19.2, CI 18.2–20.3), gonorrhea (adjusted RR 2.9, CI 2.7–3.1), syphilis (adjusted RR 5.9, CI 5.3–6.6), and chlamydia (adjusted RR 1.5, CI 1.5–1.6) were associated with maternal HCV infection. Maternal HCV infection was also associated with cesarean delivery, preterm birth, SGA birth weight, maternal ICU admission, and blood transfusion (Table 4). Neonatal intensive care unit admission, assisted ventilation, and neonatal death were also associated with maternal HCV infection, even after adjustment for gestational age at delivery and birth weight (Table 4).

DISCUSSION

Reported maternal HCV infection has increased 161% from 2009 to 2017 in the United States, more than any other maternal infection tracked on the birth certificate, despite being the only infection not universally screened for in pregnancy. Maternal HCV infection was also associated with various adverse perinatal outcomes including SGA birth weight, preterm birth, cesarean delivery, neonatal intensive care unit admission, and neonatal death at the time of birth certificate filing, even after adjusting for various comorbidities and socioeconomic status. The mechanisms for these

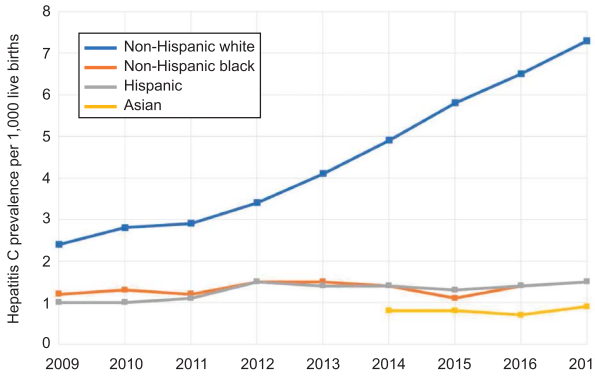

Fig. 3. Racial trends in maternal hepatitis C prevalence per 1,000 live births.

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observed adverse outcomes are largely unknown and may be attributable to underlying HCV infection–related placental vasculitis[20] or another unaccounted-for confounder such as intravenous drug use. Although intravenous drug use may be a plausible major driving force behind these results, similar perinatal outcomes have been reported previously by Pergam et al,[21] even after adjusting for maternal drug use.

In the absence of universal screening, actual maternal HCV infection rates could be higher owing to both underreporting on the birth certificate form and underdiagnoses owing to current screening guidelines.[22] A recent systematic review indicates that only half of individuals with HCV infection are diagnosed or aware, and less than 6% of eligible candidates for curative antiviral (direct-acting antiviral) therapy are receiving treatment in the United States.[23] Our study indicates that between 10,000 and 20,000 women with HCV infection give birth every year in the United States. Ly et al, using Quest laboratory testing from 2011 to 2014, estimated that there were 29,000 pregnancies complicated by maternal HCV infection annually, suggesting that 1,700 neonates were born each year with HCV infection.[24] This was calculated by applying the prevalence rate in the Quest data (2.1 million reproductive-aged women) to the average number of pregnancies each year in the United States. Therefore, the prevalence rate of 0.73% may be overestimated if these tests were performed in women with a high a priori risk based on current screening guidelines. In contrast, we observed a reported maternal HCV infection prevalence of 0.25% (2011–2014) among all U.S. live births, which may be underestimated given current screening guidelines.

Recently, there has been debate in the medical community regarding the adoption of universal HCV infection screening in pregnancy,[25] given the ineffectiveness of risk factor-based screening and recent epidemiologic trends.[24–29] The arguments for universal screening include that 1) many cases of HCV infection are missed with a risk factor–based screening approach; 2) pregnancy provides an opportune time to screen because adherence to medical care is enhanced; 3) batch testing is already performed in pregnancy and would be easy to adopt; 4) there is a possibility of intervening while avoiding invasive procedures (ie, scalp electrode monitoring and invasive prenatal diagnostic testing); 5) it offers the ability to refer for HCV infection treatment evaluation while patients are still pregnant and publicly insured; and 6) it provides an opportunity to identify and refer HCV-exposed neonates, because many do not undergo follow-up testing, as outlined by Jhaveri et al.[25] Because vertical transmission rates are estimated between 2% and 8%, and chronic HCV infection is associated on average with 20 years of lost life expectancy, screening and potentially curative antiviral therapy postpartum may reduce this societal cost.[25] As such, the American Association for the Study of Liver Disease and the Infectious Diseases Society of America have issued guidelines that recommend universal testing for HCV infection at the initiation of prenatal care (IIB, C rating) in their 2018 update.[30] The current CDC and ACOG guidelines recommend risk based screening.[15,16] These guidelines were published in 2006 and 2007, respectively, before the current opiate epidemic, though they were recently reaffirmed by SMFM.[31] These recommendations were founded on lower seroprevalence rates and no preventative measures available to lower the risk of vertical HCV infection of neonates. The more current recommendation by SMFM in 2017 bases the reaffirmation of the CDC and ACOG recommendations on the lack of data regarding cost-effectiveness of universal screening and the current lack of approved treatments in pregnancy.

The incremental cost of universal HCV infection screening for pregnant women is estimated to be $53.20 per person ($202,160,000/year, assuming 3.8 million births/year).[32] Chaillon et al demonstrated the cost-effectiveness of universal HCV infection screening in pregnancy with treatment after completion of pregnancy in all treatment eligibility scenarios, with a mean incremental cost-effectiveness ratio less than $3,000 per quality-adjusted life-year gained; this remained cost-effective with an HCV infection prevalence as low as 0.07%.[32] In our study using National Center for Health Statistics data, there were no individual states with maternal HCV infection rates of less than 0.07%, with the mean reported rate of maternal HCV infection in 2017 at 0.47%, a more than 6-fold

Table 3. Obstetric Characteristics and Neonatal Outcomes of Hepatitis C Virus– and Non–Hepatitis C Virus–Affected Pregnancies

Characteristic	HCV (n=61,162)	Non-HCV (n=15,203,728)	*P*
Cesarean delivery	21,697 (35.5)	4,743,394 (31.2)	<.001
Primary cesarean delivery	10,941 (22.4)	2,724,680 (21.1)	<.001
Operative vaginal delivery	1,777 (2.9)	481,638 (3.2)	<.001
Induction of labor	16,927 (27.7)	3,740,252 (24.6)	<.001
Antenatal corticosteroids	2,572 (4.2)	294,143 (1.9)	<.001
Antibiotics in labor	18,390 (30.1)	3,643,780 (24.0)	<.001
Chorioamnionitis	656 (1.1)	228,875 (1.5)	<.001
Co-infections			
Hepatitis B	1,647 (2.7)	33,017 (0.2)	<.001
Syphilis	428 (0.7)	12,675 (0.08)	<.001
Chlamydia	2,636 (4.3)	277,887 (1.8)	<.001
Gonorrhea	838 (1.4)	40,436 (0.3)	<.001
Delivery characteristics			
Gestational age at delivery (wk)	39 (37–39)	39 (38–40)	<.001
Preterm birth (wk)			
Less than 37	10,422 (17.0)	1,328,299 (8.7)	<.001
Less than 34	2,943 (4.8)	359,044 (2.4)	<.001
Less than 28	534 (0.9)	86,464 (0.6)	<.001
Multifetal gestation	1,133 (1.9)	263,527 (1.7)	.024
Birth weight (g)	3,034±617	3,287±574	<.001
	3,062 (2,675–3,425)	3,311 (2,975–3,630)	<.001
Low birth weight (less than 2,500 g)	9,984 (16.3)	1,087,457 (7.2)	<.001
Very low birth weight (less than 1,500 g)	1,243 (2.0)	181,791 (1.2)	<.001
SGA (less than 10th percentile)	11,110 (18.2)	1,447,791 (9.5)	<.001
LGA (greater than 10th percentile)	2,863 (4.7)	1,320,326 (8.7)	<.001
Maternal hospital transfer	1,123 (1.8)	71,743 (0.5)	<.001
Composite maternal adverse outcome*	694 (1.1)	67,263 (0.4)	<.001
Blood transfusion	451 (0.7)	46,510 (0.3)	<.001
ICU admission	273 (0.5)	21,520 (0.1)	<.001
Unplanned hysterectomy	60 (0.1)	5,965 (0.04)	<.001
Uterine rupture	44 (0.07)	4,252 (0.03)	<.001
Neonatal outcomes			
NICU admission	13,452 (22.1)	1,209,447 (8.0)	<.001
Neonate transferred	2,701 (4.4)	161,629 (1.1)	<.001
5-min Apgar score less than 7	1,963 (3.2)	290,649 (1.9)	<.001
Neonatal death†	209 (0.34)	33,037 (0.22)	<.001
Assisted ventilation	4,923 (8.1)	546,208 (3.6)	<.001
Surfactant administration	748 (1.2)	60,734 (0.4)	<.001
Antibiotics for suspected sepsis	3,378 (5.5)	328,442 (2.2)	<.001

HCV, hepatitis C virus; SGA, small for gestational age; LGA, large for gestational age; ICU, intensive care unit; NICU, neonatal intensive care unit.

Data n (%) or median (interquartile range) unless otherwise specified.

* Includes blood transfusion, ICU admission, unplanned hysterectomy, and uterine rupture.

† Neonatal death at the time of birth certificate completion.

higher prevalence than required for cost-effectiveness. Additionally, reported maternal HCV infection rates have statistically increased on a year-to-year basis since 2013 (2013–2014; 47.8%, 2014–2015; 11.8%, 2015–2016; 10.5%, 2016–2017; 11.9%) an average of 20.5% per year. Since 2009, the overall maternal HCV infection rate has increased 161%.

Limitations to this study include the fact that our data were obtained from birth certificate records, which are likely to underestimate maternal HCV infection because universal screening is not recommended currently by obstetric care provider societies. Additionally, data regarding illicit drug use, including intravenous drug use disorder, are not known from this data source. Intravenous drug use infectious sequelae may also be accountable for a substantial proportion of the poor obstetric and neonatal outcomes observed (ie, sepsis, endocarditis) in this study rather than the result of direct cellular damage caused by the hepatitis virus. Lastly, as the analysis of factors

Table 4. Characteristics and Outcomes Associated With Maternal Hepatitis C Virus Infection

	HCV Infection Absolute Risk (%)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Maternal characteristics			
Non-Hispanic white race	0.6	3.6 (3.5–3.7)	2.8 (2.7–2.8)
Medicaid	0.7	4.8 (4.7–4.9)	3.3 (3.2–3.3)
Cigarette smoker	3.2	20.2 (19.8–20.5)	11.1 (10.9–11.3)
No prenatal care	1.5	3.9 (3.8–4.1)	2.3 (2.2–2.4)
County residential population less than 100,000	0.7	2.3 (2.2–2.3)	1.2 (1.2–1.2)
Co-infectious characteristics			
Hepatitis B infection	4.8	12.7 (12.1–13.4)	19.2 (18.1–20.3)
Gonorrhea	2.0	5.2 (4.9–5.6)	2.9 (2.7–3.1)
Chlamydia	0.9	2.4 (2.3–2.5)	1.5 (1.5–1.6)
Syphilis	3.3	8.4 (7.7–9.3)	5.9 (5.3–6.6)
Obstetric outcomes			
Cesarean delivery	0.5	1.2 (1.2–1.2)	1.1 (1.1–1.2)
Preterm birth	0.8	2.1 (2.1–2.2)	1.6 (1.6–1.6)
SGA (less than 10th percentile)	0.8	2.1 (2.1–2.2)	1.3 (1.3–1.3)
Maternal admission to ICU	1.3	3.2 (2.8–3.6)	2.5 (2.2–2.8)
Blood transfusion	1.0	2.4 (2.2–2.7)	1.8 (1.7–2.0)
Newborn outcomes*			
NICU admission	1.1	3.3 (3.2–3.3)	2.6 (2.5–2.6)
Neonatal death†	0.4	1.6 (1.4–1.8)	1.3 (1.1–1.5)
Assisted ventilation	0.9	2.3 (2.3–2.4)	1.8 (1.7–1.8)

HCV, hepatitis C virus; RR, relative risk; SGA, small for gestational age; ICU, intensive care unit; NICU, neonatal intensive care unit.
Regression model (adjusted RR) includes the following covariates: maternal age, race, year of delivery, pregestational diabetes, chronic hypertension, Medicaid, cigarette smoking, body mass index, parity, and prior cesarean birth.
* Model additionally adjusted for gestational age at birth.
† Neonatal death at the time of birth certificate completion.

associated with maternal HCV infection use a cohort of more than 15 million women, differences observed between women with and without HCV infection are likely to be statistically significant, but not necessarily clinically significant.

Despite these limitations, this study is inclusive of every birth in the United States with reported HCV infection status, and highlights important national, regional, and demographic trends in maternal HCV infection. Our findings demonstrate that maternal HCV infection is the most rapidly increasing infectious disease among those tracked on the birth record. The reported prevalence rates observed in this study, substantively exceed the threshold for cost effectiveness now that postpartum curative therapies are available. Because universal screening is not widely endorsed, our research group is developing an interactive map of reported maternal HCV infection prevalence within the continental United States at the state and county level, which will be available for use by local health care providers and policy makers. It will be important to continually evaluate maternal HCV infection prevalence in the United States given the rapidly shifting dynamic between rising rates of maternal HCV infection and increasing availability and affordability of curative therapies.

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