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Birth Outcomes Among People with Hepatitis C in Pregnancy — Three U.S. States, 2018–2021

Kate R. Woodworth¹, Suzanne M. Newton¹, Ayzsa Tannis², Megan R. Reynolds¹, Emily O. Olsen¹, Lindsey Sizemore³, Heather Wingate³, Lauren Orkis⁴, Bethany Reynolds⁴, Nicole Longcore⁵, Nadia Thomas⁵, Shin Y. Kim¹, Lakshmi Panagiotakopoulos⁶, Carolyn Wester⁶, Dana Meaney Delman¹, Suzanne M. Gilboa¹, Van T. Tong¹

¹Division of Birth Defects and Infant Disorders, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA, USA

²Eagle Global Scientific, LLC, San Antonio, TX, USA

³Tennessee Department of Health, Nashville, TN, USA

⁴Pennsylvania Department of Health, Pittsburgh, PA, USA

⁵New York State Department of Health, Albany, NY, USA

⁶Division of Viral Hepatitis, National Center for HIV, Viral Hepatitis, STD and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA

Abstract

Introduction—There are limited and conflicting data regarding the impact of hepatitis C in pregnancy on adverse birth outcomes.

Methods—Using the Surveillance for Emerging Threats to Pregnant People and Infants Network (SET-NET), a large surveillance cohort, we describe birth outcomes among a cohort of people with HCV in pregnancy in total and by reported substance use.

Results—Among 1418 infants, 89% were born to people with reported substance use during pregnancy. The proportion born preterm was 20%, 13% were small-for-gestational age and 34% of term infants required intensive care.

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[✉]Kate R. Woodworth, setnet@cdc.gov.

Author Contributions Dr. Woodworth and Ms. Tong conceptualized the analysis, drafted the initial manuscript, and reviewed and revised the manuscript. Ms. Newton and Ms. Tannis carried out all analyses and reviewed and revised the manuscript. Ms. Longcore, Dr Orkis, Ms. B. Reynolds, Ms. Sizemore, Ms. Thomas, and Ms. Wingate collected the data, assisted in interpreting findings, and critically reviewed and revised the manuscript. Drs Gilboa, Olsen, Meaney-Delman, Panagiotakopoulos, Wester, Ms. Kim, and Ms. M. Reynolds assisted in interpreting findings and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Ethics Approval This activity was reviewed by the Centers for Disease Control and Prevention and conducted consistent with applicable federal law and policy (*45 C.F.R. part 46.102(1) and 102(e)(1); 42 U.S.C. Section 241(d); 5 U.S.C. Sect. 552a*).

Conflict of Interest The authors report no conflicts of interest.

Disclaimer The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The Surveillance for Emerging Threats to Pregnant People and Infants Network does not collect information on sex or gender of the birthing individual. The term “maternal” are used in this publication to describe characteristics of people who are or were recently pregnant for clarity, but birthing individuals may be of any gender.

Conclusions—Assessments of recent changes to recommendations for HCV screening in pregnancy should evaluate the impact on maternal access to care for both HCV treatment as well as comorbidities such as substance use disorder which may contribute to adverse birth outcomes.

Keywords

Hepatitis C; Adverse pregnancy outcomes; Preterm birth; Substance use

Objective

The incidence of hepatitis C virus (HCV) infection in reproductive-aged adults in the United States has risen in parallel with injection drug use associated with the opioid crisis. (Centers for Disease Control and Prevention, 2023) Universal screening for hepatitis C is recommended during each pregnancy.(Schillie et al., 2020) There are limited and conflicting data regarding the impact of HCV infection on pregnancy and infant outcomes beyond perinatal transmission.

Among a surveillance cohort of people with HCV infection during pregnancy, we describe maternal demographics, pregnancy characteristics, complications, and birth outcomes. We compare these outcomes by maternal substance use.

Methods

Pregnant people with HCV infection who had a live birth during 2018–2021 were reported to the Surveillance for Emerging Threats to Pregnant People and Infants Network by three U.S. jurisdictions (New York State, excluding New York City; Allegheny and Washington Counties, Pennsylvania; and Tennessee). Inclusion criteria were people with a positive nucleic acid test for HCV ribonucleic acid during pregnancy or in the 12 months pre-pregnancy without evidence of subsequent negative testing or treatment, or those who gave birth to an infant with positive HCV test results. Substance use was ascertained through birth certificates, provider notes, ICD-10 codes, and urine drug screening reports. Substance use in pregnancy was defined as use of 1 categories of the following: tobacco, alcohol, cannabis, opioids obtained illicitly or used in a manner not prescribed, and other illicit substances (e.g., methamphetamines, cocaine). Outcomes included preterm birth (< 37 weeks gestation), small-for-gestational age (SGA), neonatal intensive care unit (NICU) admission, possible birth defects, and neonatal abstinence syndrome (NAS). Statistical analyses were conducted using SAS Version 9.4 (Cary, NC). This activity was reviewed by the Centers for Disease Control and Prevention and conducted consistent with applicable federal law and policy (*45 C.F.R. part 46.102(l) and 102(e)(1); 42 U.S.C. Section 241(d); 5 U.S.C. Sect. 552a*).

Results

Three jurisdictions reported 1393 pregnancies among 1303 people (90 people had > 1 pregnancy) meeting inclusion criteria, with data reported as of September 15, 2023. Median age was 29 years (interquartile range [IQR] 26–33), and most pregnant people with HCV infection had public insurance (89%) (Table 1). Of those with available information on

prenatal care (91%), 17% initiated care in the third trimester or had none. Any substance use during pregnancy was common (89%, with 63% using 2 categories of substances). The most frequently reported substances were tobacco (86%) and illicit opioids (41%). Of those with reported substance use during pregnancy, 50% also were treated with Medication for Opioid Use Disorder.

The 1393 pregnancies resulted in 1418 liveborn infants. The proportion of infants born preterm was 20% (15% 34–36 weeks, 5% <34 weeks) and 13% were SGA. Among term infants, 34% were admitted to a NICU. 6% of infants had a birth defect, and 35% had a diagnosis of NAS. Frequencies of infants born preterm were 21% among infants born to people with reported substance use and 13% without (Table 1). Infants born to people with reported substance use had a higher frequency of adverse outcomes than those without reported substance use. After controlling for insurance and trimester of prenatal care initiation, this difference remained significant for SGA (adjusted prevalence ratio [aPR] 1.9, 95% confidence interval [CI] 1.04, 3.60) and NICU admission among term infants (aPR 4.0, 95% CI 2.27, 7.10). Among infants born to people with reported substance use, frequency of NAS was 40%.

Discussion

The proportion of infants born preterm within this cohort (20%) was higher than the general population of each of the three states in 2018–2021 (9.3, 9.3, and 11.1% in New York, Pennsylvania, and Tennessee respectively)(National Center for Health Statistics, 2022). Frequency of preterm birth among those without reported substance use was less pronounced (12.6%). Other reports have described increased risk of preterm birth and SGA among people with hepatitis C (Rossi et al., 2020) but often lacked the ability to control for substance use, which is common among people with HCV infection. However, an analysis of a population-based cohort in Sweden found that even after adjusting for tobacco and alcohol or other substance use, HCV infection during pregnancy was associated with an increased risk of preterm birth, though no increased risk of lower birth weight, SGA, or birth defects (Stokkeland et al., 2017). It is not clear if the association between HCV infection and adverse birth outcomes is related to unmeasured confounders (e.g., other exposures, social determinants of health) or infection; more data may help inform these relationships.

This analysis has several limitations. First, the analysis was limited to pregnancies resulting in a live birth, and we are unable to assess frequency of pregnancy loss. Second, comprehensive ascertainment of substance use is challenging due to stigma associated with substance use, especially during pregnancy. Third, birth defects were likely under-ascertained given reporting only at birth hospitalization.

Continuing to examine how screening for hepatitis C during pregnancy can increase maternal access to curative hepatitis C treatment, and the identification and treatment of comorbidities such as substance use disorder which contribute to adverse pregnancy and infant outcomes could help inform future research.

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Significance

Incidence of hepatitis C in pregnancy is increasing. Prematurity, small-for-gestational age, and intensive care unit admission were common among this surveillance cohort of infants born to people with hepatitis C in pregnancy with high frequency of substance use. Assessments of recent changes to recommendations for HCV screening in pregnancy should evaluate the impact on maternal access to care for both HCV treatment as well as comorbidities such as substance use disorder which may contribute to adverse birth outcomes.

Table 1
Maternal characteristics, pregnancy complications, and infant outcomes by known substance use among people with HCV infection in pregnancy – three U.S. states^a, Surveillance for Emerging Threats to Pregnant People and Infants Network, 2018–2021 (N = 1393)

	Total N (%)	Substance use n (%)	No reported substance use n (%)	p-value ^b
Pregnancies	1393	1234 (88.6)	159 (11.4)	
Age at pregnancy outcome (years)				
Median (IQR)	29 (26–33)	29 (26–33)	29 (26–33)	0.78
24	212 (15.2)	188 (15.2)	24 (15.1)	0.81
25–29	529 (38.0)	471 (38.2)	58 (36.5)	
30–34	438 (31.4)	383 (31.0)	55 (34.6)	
35	214 (15.4)	192 (15.6)	22 (13.8)	
Race and Ethnicity^c				
Black, Non-Hispanic	39 (2.9)	36 (3.0)	3 (2.0)	0.66
Hispanic	18 (1.3)	15 (1.3)	3 (2.0)	
White, Non-Hispanic	1264 (94.2)	1125 (94.2)	139 (93.9)	
Multiple or other	21 (1.6)	18 (1.5)	3 (2.0)	
Missing	51	40	11	
Insurance				
Public	1201 (88.9)	1077 (89.8)	124 (81.6)	0.002
Private	134 (9.9)	107 (8.9)	27 (17.8)	
Other/None/Self-pay	16 (1.8)	15 (1.3)	1 (0.7)	
Missing	42	35	7	
Education level				
Less than high school	208 (16.5)	188 (16.8)	20 (14.1)	0.09
High school graduate	502 (39.9)	441 (39.5)	61 (43.0)	
Some college	370 (29.4)	337 (30.2)	33 (23.2)	
College degree	179 (14.2)	151 (13.5)	28 (19.7)	
Missing	134	117	17	
Trimester of prenatal care initiation				
First	707 (55.8)	600 (53.4)	107 (74.8)	< 0.0001
Second	348 (27.5)	325 (28.9)	23 (16.1)	

	Total N (%)	Substance use n (%)	No reported substance use n (%)	p-value ^b
Third	113 (8.9)	106 (9.4)	7 (4.9)	
None	99 (7.8)	93 (8.3)	6 (4.2)	
<i>Missing</i>	126	110	16	
Parity				0.73
Nulliparous	291 (21.4)	256 (21.2)	35 (22.4)	
Multiparous	1072 (78.7)	951 (78.8)	121 (77.6)	
<i>Missing</i>	30	27	3	
Substance use in pregnancy				
Alcohol	129 (9.3)	129 (10.5)	-	
Tobacco	1066 (76.5)	1066 (86.4)	-	
Cannabis	482 (34.6)	482 (39.1)	-	
Illicit opioids	511 (36.7)	511 (41.1)	-	
Other illicit substances	506 (36.3)	506 (41.0)	-	
Medication for Opioid Use Disorder	611 (43.9)	611 (49.5)	-	
Prescription opioids	42 (3.0)	42 (3.4)	-	
Underlying conditions and complications	497 (39.4)	428 (35.3)	69 (44.2)	0.03
Obesity ^d	227 (17.4)	192 (16.7)	35 (23.5)	
Chronic hypertension	90 (7.0)	80 (7.0)	10 (6.8)	
Pregestational diabetes mellitus	30 (2.3)	24 (2.0)	6 (4.0)	
Hypertensive disorders of pregnancy ^e	115 (9.0)	99 (8.7)	16 (11.1)	
Gestational diabetes	110 (8.6)	90 (7.9)	20 (13.6)	
Cholestasis during pregnancy	63 (6.0)	54 (5.6)	9 (10.2)	
<i>Missing</i>	26	23	3	
Infants	1418	1258 (88.7)	160 (11.3)	aPR and 95% CI^f
Gestational age				
Median (IQR)	38.7 (37.0–39.3)	38.6 (37.0–39.1)	39.0 (37.4–39.4)	0.01
Term (≥ 37 weeks)	1125 (80.0)	986 (79.1)	139 (87.4)	0.01
Preterm (< 37 weeks)	281 (20.0)	261 (20.9)	20 (12.6)	
Late preterm (34–36 weeks)	209 (14.9)	191 (15.3)	18 (11.3)	
Early preterm (< 34 weeks)	72 (5.1)	70 (5.6)	2 (1.3)	

	Total N (%)	Substance use n (%)	No reported substance use n (%)	p-value ^b
<i>Missing</i>	12	11	1	
Median birth weight in grams (IQR)	3020 (2650–3370)	2972.5 (2610–3330)	3282.0 (2900–3700)	< 0.0001
Small-for-gestational age^g	183 (13.3)	173 (14.2)	10 (6.5)	0.008
<i>Missing</i>	42	37	5	
Neonatal intensive care unit admission				
Term (< 37 weeks)	369 (34.2)	358 (37.8)	11 (8.3)	< 0.0001
Length of stay (median, IQR)	15 (7–22)	15 (7–23)	5 (4–11)	0.008
Preterm (< 37 weeks)	191 (70.5)	181 (72.1)	10 (50.0)	0.04
Length of stay (median, IQR)	18 (11–28)	18 (11–28.5)	10 (8–13)	0.08
<i>Missing</i>	62	55	7	
Possible birth defects^h	86 (6.1)	81 (6.4)	5 (3.1)	0.1
Neonatal abstinence syndrome	500 (35.3)	500 (39.8)	0 (0)	< 0.0001

Abbreviations aPR, adjusted prevalence ratio; HCV, hepatitis C virus; IQR, interquartile range

^aNew York state (excluding New York City), Pennsylvania, and Tennessee

^bStatistical testing was conducted using Chi Square tests to assess differences for categorical variables (except for race and ethnicity where Fishers Exact test was used). Wilcoxon-Mann-Whitney test was used to test for differences in medians.

^cRace and ethnicity were reported from birth certificate or medical records.

^dPregestational obesity was defined as body mass index ≥ 30 kg/m².

^eHypertensive disorders of pregnancy was inclusive of gestational hypertension, preeclampsia, eclampsia, or Hemolysis, Elevated Liver enzymes and Low Platelets (HELLP) syndrome.

^f<10th percentile for weight based on sex and gestational age as defined by INTERGROWTH-21st.

^gAscertained through ICD-10 codes reported during birth hospitalization or linkages with state birth defect registry (Tennessee). Birth defects included congenital cerebral cysts ($n = 6$), other congenital malformations of the nervous system ($n = 7$), orofacial clefts ($n = 4$), congenital malformations of the face and neck ($n = 2$), atrial septal defects ($n = 35$), ventral septal defects ($n = 9$), other congenital malformations of the cardiac septa ($n = 6$), stenosis of the pulmonary artery ($n = 11$), other congenital malformations of great arteries ($n = 4$), other congenital malformations of the circulatory system ($n = 5$), congenital malformations of the digestive system ($n = 2$), congenital malformations of the urinary system ($n = 6$), gastroschisis ($n = 2$), polydactyly or syndactyly ($n = 3$), other congenital malformations and deformations of the musculoskeletal system ($n = 4$), and chromosomal abnormalities ($n = 5$). Some infants had more than one birth defect reported