BRIEF REPORT

Hepatitis C Screening in Mothers and Infants Exposed to Opioids

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ABSTRACT

OBJECTIVES: Hepatitis C virus (HCV) is the most common blood-borne pathogen in the United States. In the context of the opioid epidemic, there has been a dramatic rise in perinatal opioid use and the prevalence of HCV infection, which can be transmitted to infants. One national guideline recommends HCV screening for all pregnant women and screening for HCV-exposed newborns after 18 months of age. In this study, we aimed to identify the trends in HCV prevalence and screening among mothers using opioids during pregnancy and infants exposed to HCV infection in utero.

METHODS: Infants with *International Classification of Diseases, Ninth Revision* (779.5) or *International Classification of Diseases, 10th Revision* codes (P96.1) for neonatal abstinence syndrome and in-utero exposure to methadone, buprenorphine, or other opioid medications were identified for this retrospective cohort analysis. Information regarding maternal and infant HCV screening, demographics, and follow-up care was also extracted from the electronic medical record and HealthInfoNet, a statewide database of laboratory results.

RESULTS: Between 2013 and 2018, 769 infants with in-utero opiate exposure were identified. The maternal HCV screening rate increased from 58.1% in 2013 to 90% in 2018. Of the mothers tested for HCV during pregnancy, 257 (47.9%) were HCV-positive. Of the 177 infants eligible for testing by age criteria, 94 (53%) were tested for HCV, and 7 (7.4%) were HCV-positive. We estimate that an additional 10 infants were HCV-positive and undiagnosed.

CONCLUSIONS: Despite the high prevalence of HCV, rates of maternal and infant screening remain suboptimal. This study highlights the need for improved care for this high-risk population of infants born to mothers with opiate use disorder.

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Hepatitis C virus (HCV) is currently the most common blood-borne pathogen in the United States and can cause both acute and chronic infection of the liver.[1] Early HCV detection permits the delivery of appropriate therapies and improves long-term patient outcomes. Although sharing needles is a common cause of HCV transmission, children born to mothers with HCV are also at risk for contracting the disease with a reported vertical transmission rate of 5.8%.[2] As perinatal opioid use continues to increase,[3] so, too, has the incidence of HCV,[4] placing newborns in this population at increased risk.

The 1998 US Preventive Services Task Force guidelines suggest routine screening for individuals who have "ever injected illegal drugs."[5] In 2018, the American Association of the Study of Liver Disease and the Infectious Disease Society of America recommended HCV screening for all pregnant women.[6] The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition recommends screening for HCV-exposed newborns with the HCV antibody test after 18 months of age[7] to avoid falsely detecting maternal immunoglobulin. Infants >18 months old with positive antibody test results should also receive a serum HCV RNA test. If requested by the parents, HCV RNA may be tested as early as 2 months of age; however, positive results should be rechecked after 12 months for confirmation.[7]

Since 2013, the rate of acute hepatitis C infection in Maine has increased 243%, and 62% of the chronic-HCV–affected population has injected drugs intravenously.[8] In the context of the rising opioid epidemic in our state, we investigated the HCV screening rates in pregnancies involving opioid exposure and follow-up screening rates in infants exposed to HCV in utero.

METHODS

This retrospective cohort study was conducted at a tertiary-care center in southern Maine with a birth rate of ~2700 per year. Maternal-infant dyads were identified for the cohort by using the *International Classification of Diseases, 10th Revision* code (P96.1) or *International Classification of Diseases, 9th Revision* code (779.5) for neonatal abstinence syndrome (NAS) in the infant and maternal use of buprenorphine, methadone, or other opioids while pregnant. Multiple demographic and clinical characteristics were extracted from the electronic medical record (EMR), including maternal HCV status during pregnancy and infant HCV screening by using either antibody or polymerase chain reaction RNA testing. Maternal HCV-positivity was highlighted in the infant chart and verified by using antibody screening or RNA testing. Infant HCV-positivity was determined by using a positive antibody screen result followed by a positive RNA test result. Maternal exposures to opiates and multiple other drugs were collected through manual review of the EMR, specifically maternal urine or infant urine and/or meconium toxicology screening. Exposures were compiled from the maternal or infant history and physical examination at the time of admission or maternal self-report. Infants without HCV testing results documented in the EMR were further pursued by using the HealthInfoNet (HIN) database. HIN is a health-information exchange system that synthesizes medical information from separate facilities into a single patient EMR. HIN connects data from all of the hospitals in Maine, >450 ambulatory locations, and the Department of Veterans Affairs. HIN was used to obtain records of infant-lead testing, blood work, immunizations, and well-child services within 18 to 24 months of age as a proxy for follow-up care. The data were recorded in the Tufts University Research Electronic Data Capture database. This received expedited approval from the local institutional review board as nonhuman subjects research.

Differences in the characteristics of groups based on HCV testing status were evaluated by using a χ^2 test of independence. Statistical analyses were performed by using Prism statistical software and SPSS (IBM SPSS Statistics, IBM Corporation).

RESULTS

Prevalence of HCV in Mothers of Infants With NAS

Between June 1, 2013 and March 1, 2018, 769 mother-infant dyads were identified in the EMR as having opiate exposure in utero. The mothers were predominantly white with Medicaid insurance (Table1). In the cohort as a whole, 536 (69.7%) mothers were tested for HCV. Of those tested, the prevalence of HCV across all years of the

TABLE 1 Maternal Characteristics by HCV Screening Status

Maternal HCV Status	HCV−	HCV+	Untested	*P*
n (%)	279 (36.3)	257 (33.4)	233 (30.3)	—
Age, y	28.3	28.8	29.1	.00
Maternal race, white, %	95.0	94.9	97.4	.71
Maternal insurance, %				
Medicaid and/or Medicare	84.9	65.0	71.7	.0001
Commercial	3.6	8.2	9.0	.03
Maternal exposure, %				
Methadone, prescription	22.6	27.2	18.9	.09
Buprenorphine, prescription	62.0	63.4	51.1	.01
Methadone, illicit	2.9	1.6	2.1	.59
Buprenorphine, illicit	7.9	7.0	5.2	.46
Tobacco	83.2	80.5	66.1	<.0001
Marijuana	39.1	40.1	26.2	.0017
Heroin	11.1	16.3	5.6	.0008
Cocaine	10.8	17.9	6.0	.0002
Oxycodone	8.6	4.3	20.6	.04
Hydrocodone	3.6	1.2	9.4	.07

—, not applicable.

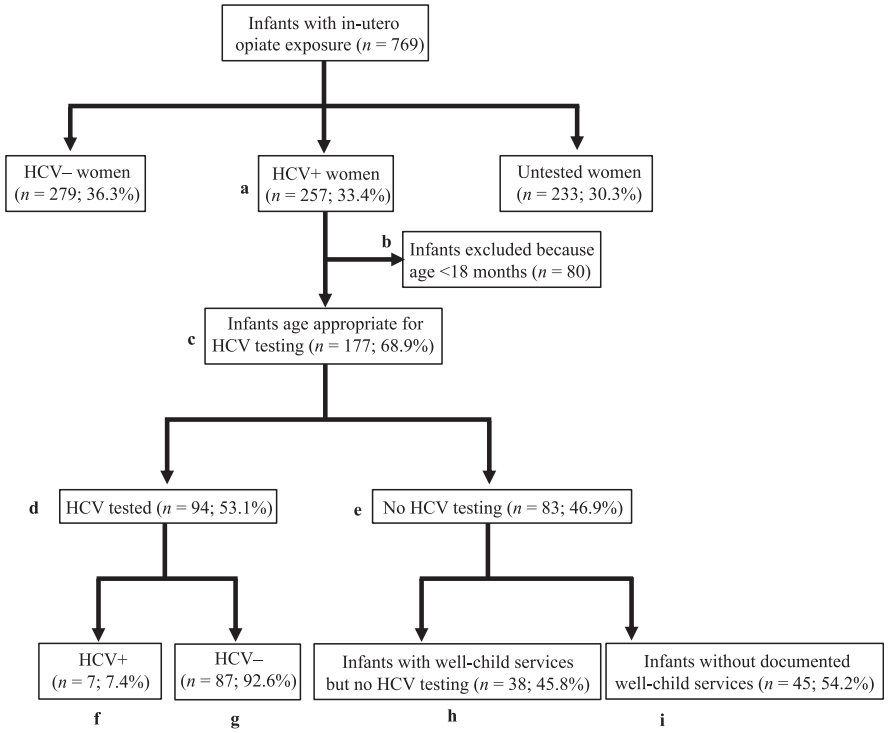

FIGURE 1 Frequency of infant HCV screening after in-utero exposure.

study was 47.9% (n = 257; Fig 1, box a). The maternal perinatal screening rate increased from 58.1% in 2013 to 90% in 2018 (Fig 2A). HCV-infected women were more likely to have used alcohol, cocaine, heroin, and/or amphetamines during their pregnancy.

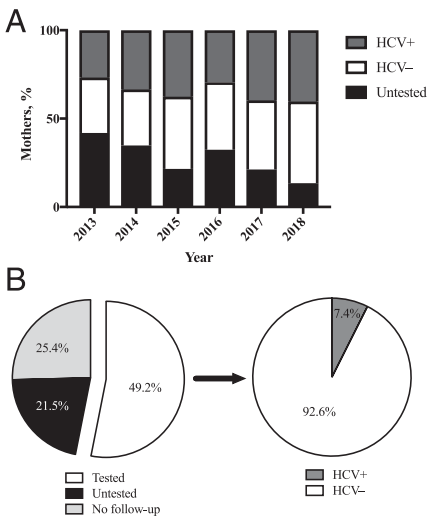

FIGURE 2 A, Maternal HCV status. B, Infant HCV screening and follow-up testing.

Within the untested maternal population, more mothers used short-acting opioids, such as oxycodone and hydrocodone (Table 1).

Screening of Infants Born to HCV-Positive Mothers

Of the 257 infants born to HCV-positive mothers, 80 were born after January 10, 2017, and were ineligible for testing according to the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition recommendation and were thus excluded from subsequent analysis (Fig 1, box b). Of the 177 infants exposed to HCV and eligible for testing according to age criteria, 94 were tested as follows: 76 infants had negative antibody screening results, 8 had negative RNA screening results, 10 received both the antibody and RNA screening, and 7 of these 10 were HCV-positive. Of those who were tested, HCV screening was conducted at a mean age of 2.0 ± 0.7 years, and the observed vertical transmission rate was 7.4% (Fig 2B and Fig 1, box f). There were 38 infants (21.5%) who had documented follow-up care surrounding the 18-month time point for whom there is no evidence of HCV testing (Fig 1, box h). There were an additional 45 infants with no documented follow-up care (Fig 1, box i).

We conducted a sensitivity analysis to estimate the number of infants with undiagnosed HCV infection born to HCV-positive mothers. For the 83 age-eligible but untested infants (Fig 1, box e) born to HCV-positive mothers, we applied the published vertical transmission rate of 5.8%[2] and thus estimate there are an additional 5 untested newborns who are HCV-positive. In a separate analysis of untested mothers, we excluded 70 (30%) mothers taking short-acting opioids, such as oxycodone and hydrocodone, because they were less likely to have engaged in intravenous drug use and have HCV infection (Table 1). We assumed 47.9% of the remaining untested mothers (n = 163) were HCV-positive (n = 78). Using the 5.8% vertical transmission rate, we estimate that an additional 5 infants have unrecognized HCV infection. In summary, 7 infants have been diagnosed with HCV infection, and an estimated additional 10 infants are likely to have the infection but remain undiagnosed at this time.

DISCUSSION

Our results demonstrate improved compliance with recommended maternal HCV testing over time. Although the recommendation for universal screening of pregnant women remains controversial, our study demonstrates the inadequacy of a risk-based screening approach. Even among this high-risk population, a proportion of untested mothers used heroin, demonstrating the gaps in our bedside assessment of clinical risk. In the context of a new guideline released in May 2018 calling for universal maternal HCV screening, we anticipate continued improvement in maternal HCV screening.[6] Early detection of maternal HCV allows for ample opportunity to provide proper education surrounding the risk of vertical transmission and the importance of follow-up screening and care for the child.

Despite the high prevalence of maternal HCV in pregnancies with comorbid

substance use disorder, only 53.1% of infants in this cohort received HCV testing after 18 months of age. The unscreened newborns are at risk for developing chronic hepatitis C infection, hepatocellular carcinoma, and liver failure as well as further unknown transmission of the disease. From the sensitivity analysis, we estimate that 59% of HCV-positive infants are undiagnosed. If this pattern of inadequate testing continues, a serious public health concern is likely to develop, emphasizing the additional serious public health consequences of the opioid epidemic.

Although recent studies have revealed trends toward insufficient infant HCV screening after perinatal exposure,[9,10] little has been done to identify patterns in the growing population of infants born to mothers with substance use disorder. We identified suboptimal maternal and infant screening rates in this high-risk population. We suspect testing rates are reduced because of poor compliance with prenatal care, fragmentation of maternal and infant follow-up care, custody variability, and complex parental addiction and mental health issues. Because this was a retrospective study, the specific reasons for poor follow-up care could not be elucidated. Although we attempted to track whether infants had follow-up care in HIN, the results of all physician visits or laboratory studies may not have been uploaded into this database comprised of centers that voluntarily participate. Regardless, our study points to a role for improved and standardized communication among obstetricians, addiction medicine providers, and pediatricians in both the inpatient and outpatient settings caring for infants with NAS to improve compliance with recommendations for HCV testing.

CONCLUSIONS

As the opioid epidemic continues to grow, the prevalence of hepatitis C is increasing. This study demonstrates that perinatal HCV screening rates for mothers have improved slowly since 2013, whereas the follow-up screening rate in infants remains low. As HCV rates continue to rise, further counseling regarding HCV transmission, treatment, and screening protocols needs to be implemented, including a stronger emphasis on communicating the importance of HCV screening to patients, parents, and providers in the primary care, obstetrics, addiction medicine, and hospital settings. Education of HCV transmission, preventive practices, and screening guidelines should continue to be emphasized to all providers of those in this high-risk population.

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