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Hepatitis C Virus Detection and Management After Implementation of Universal Screening in Pregnancy

Sarah Boudova

Danielle Tholey
Thomas Jefferson University

Elizabeth Ferries-Rowe

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Sarah Boudova, MD, PhD; Danielle M. Tholey, MD; Elizabeth Ferries-Rowe, MD

BACKGROUND: Accurately identifying cases of hepatitis C virus has important medical and public health consequences. In the setting of rising hepatitis C virus prevalence and highly effective treatment with direct-acting antivirals, the Society for Maternal-Fetal Medicine guidelines recently changed to recommend universal screening for hepatitis C virus during pregnancy. However, there is little data on the influence of this policy change on case identification and management.

OBJECTIVE: We aimed to examine the influence of universal hepatitis C virus screening on our patient population. Our primary objective was to determine if there was a difference in the detected hepatitis C virus prevalence after the policy change. Our secondary objectives were to determine which factors were associated with a positive test for hepatitis C virus and to examine postpartum management of pregnant patients living with hepatitis C virus, including the (1) gastroenterology referral rate, (2) treatment rate, (3) infantile hepatitis C virus screening rate, and (4) factors associated with being referred for treatment.

STUDY DESIGN: We conducted a single-center, retrospective cohort study of deliveries that occurred before (July 2018—June 2020) and after (July 2020—December 2021) the implementation of universal hepatitis C virus screening. Information on hepatitis C virus and HIV status, if patients were screened for hepatitis C virus, history of intravenous drug use, and basic demographic information were abstracted from the electronic medical records. A subset of patients was administered a questionnaire regarding hepatitis C virus risk factors. For all patients who tested positive for hepatitis C virus, information on if they were referred for treatment in the postpartum period and if their infant was screened for hepatitis C virus were abstracted from the electronic medical records.

RESULTS: A total of 8973 deliveries occurred during this study period. A total of 71 (0.79%) patients had a detectable viral load. With implementation of universal screening, hepatitis C virus screening rates increased from 5.78% to 77.25% of deliveries ($P<.01$). The hepatitis C virus prevalence rates before and after universal screening was implemented were 0.78% and 0.81%, respectively ($P=.88$). There were significant demographic shifts in our pregnant population over this time period, including a reduction in intravenous drug use. A subset of 958 patients completed a hepatitis C virus risk factor questionnaire, in addition to undergoing universal hepatitis C virus screening. Ten patients screened positive with universal screening; only 8 of these individuals would have been identified with risk-based screening. Among the patients with a detectable viral load, 67.61% were referred for treatment and 18.75% were treated. A multivariate logistic regression model indicated that intravenous drug use was associated with significantly decreased odds of being referred for treatment (odds ratio, 0.14; 95% confidence interval, 0.04—0.59; $P=.01$). At the time of our evaluation, 52 infants were at least 18 months old and thus eligible for hepatitis C virus screening. Among these infants, 8 (15.38%) were screened for hepatitis C virus, and all were negative.

CONCLUSION: Following the practice shift, we saw a significant increase in hepatitis C virus screening during pregnancy. However, postpartum treatment and infant screening remained low. Intravenous drug use was associated with a decreased likelihood of being referred for treatment. Pregnancy represents a unique time for hepatitis C virus case identification, although better linkage to care is needed to increase postpartum treatment.

Key words: direct-acting antiviral, HCV, hepatitis C virus, intravenous drug use, pregnancy, universal screening, vertical transmission

From the Department of Obstetrics and Gynecology Indiana University School of Medicine, Indianapolis, IN (Drs Boudova and Ferries-Rowe); Division of Gastroenterology and Hepatology, Sidney Kimmel Medical College, Thomas Jefferson University Hospital, Philadelphia, PA (Dr Tholey).

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Patient consent was not required because no personal information or details were included.

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Corresponding author: Sarah Boudova, MD, PhD. sarah.boudova@jefferson.edu

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Why was this study conducted?

The Society for Maternal-Fetal Medicine recently changed its guidelines to recommend universal screening for hepatitis C virus (HCV) during pregnancy. There are little data on the influence of universal screening on case identification and management.

Key findings

Universal HCV screening during pregnancy was rapidly adopted with rates increasing from 5.78% to 77.25%. Despite increased HCV screening during pregnancy, the rates of treatment (18.75% of eligible patients) and infant screening (15.38% of eligible infants) remained low. Intravenous drug use was associated with decreased odds of referral for treatment postpartum.

What does this add to what is known?

This study adds to the small body of literature that shows low rates of postpartum treatment of and infant screening for HCV despite rapid adoption of universal HCV screening. We identified intravenous drug use as a barrier to referral for postpartum treatment.

Introduction

Hepatitis C virus (HCV) is a major cause of morbidity and is responsible for causing cirrhosis, hepatocellular carcinoma, and death.[1] HCV prevalence is rising in the United States, particularly among reproductive-aged adults.[2,3] The rate of HCV infection among pregnant persons increased 16-fold between 1998 and 2018, reaching 5.3 cases per 1000 deliveries.[4] A national database showed that 0.73% of pregnant individuals were living with HCV.[2]

Identifying HCV during pregnancy has consequences for the patient, infant, and population. Treatment is considered curative now. Although there is no recommendation for treatment during pregnancy, accurately identifying patients living with HCV during pregnancy allows for close follow-up, postpartum treatment, and appropriate neonatal screening. Perinatal transmission is the primary source of pediatric HCV, and it is estimated that the majority of cases go unidentified.[5–9] Postpartum treatment has the benefit of interrupting community transmission of the virus and ensuring that subsequent pregnancies are not at risk.

Until recently, the Society for Maternal-Fetal Medicine (SMFM) and the Centers for Disease Control and Prevention (CDC) recommended risk-based HCV screening during pregnancy.[10] However, it is imperfectly applied and fails to identify a large proportion of patients living with HCV.[11–16] In addition, with new medications, universal screening is highly cost-effective.[17,18] Thus, between 2020 and 2021, the CDC and the SMFM updated their guidelines to recommend universal screening during every pregnancy.[19,20]

We examined the influence of this policy change on our patient population.

Materials and Methods

Study design

We conducted a retrospective cohort study of data on deliveries that occurred between July 1, 2018, and December 31, 2021 at the Sidney and Lois Eskenazi Hospital (Eskenazi Hospital) in Indianapolis, IN. Ethical approval was obtained from the Indiana University Institutional Review Board (IRB) and the Eskenazi Health Research Department. The study was deemed IRB exempt by the Indiana University IRB because it was secondary research for which consent was not required. All data were recorded and analyzed anonymously.

Study population

On July 1, 2020, universal screening for HCV during pregnancy was introduced at the Eskenazi Hospital in Indianapolis, IN. HCV screening was added to the standard prenatal laboratory set and providers were instructed to perform HCV antibody (Ab) screening on any patients who had not received the HCV screening test as part of their prenatal laboratory analyses. Screening was performed using a serological HCV Ab assay, and if positive, a quantitative HCV viral titer polymerase chain reaction (PCR) assay was performed. There was no standardized protocol in place to facilitate a referral to gastroenterology——it was left to the discretion of the provider to facilitate the referral. On February 4, 2021, a questionnaire on HCV risk-factors (Supplemental Figure 1) was added to the routine first antenatal visit workflow. All deliveries that occurred at the hospital during the study period were included in the analysis. This included deliveries with no prenatal care.

Data collection

Information on the baseline patient characteristics, including age, ethnicity, race, insurance type, and gravidity, were abstracted from the electronic medical records (EMRs). Data on race and ethnicity were collected to examine if any populations were affected disproportionately more. Maternal risk factors for HCV, including HIV status and history of intravenous drug use (past and/or present), were also gathered from the EMRs. In addition, data on if the pregnant patient was screened for HCV during the prenatal period and on maternal HCV infection were collected. For patients with multiple pregnancies during the study period, each pregnancy was recorded as a separate event. Records from outside hospitals were not reviewed. There were 22 pregnancies with no recorded gravidity or parity. All patients were screened for HIV during the prenatal period. Among the patients with a detectable HCV viral load, the EMRs were manually reviewed, and data were abstracted on if the patient was referred for treatment in the postpartum period, if the patient was treated, if they achieved viral clearance, and if the infant was screened for HCV as of June 30, 2022. In our

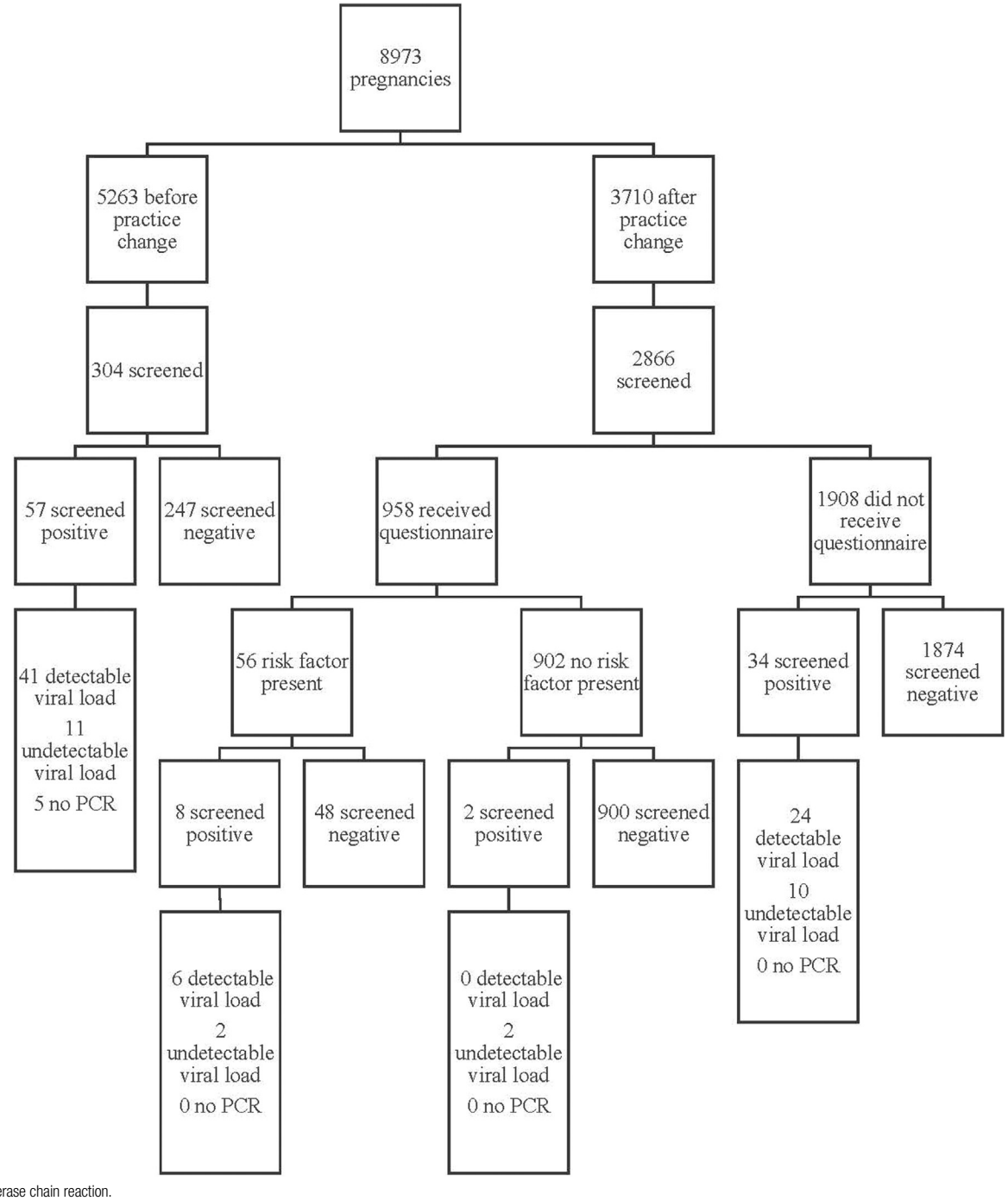
hospital system, patients were routinely referred to the gastroenterology department for treatment of HCV.

For those patients who delivered after February 4, 2021, information was collected on if the HCV risk factor questionnaire was completed and what the results of the questionnaire were. The HCV risk factor questionnaire was administered by medical assistants at the time of the intake appointment. The questionnaire was in English and a phone interpreter service was used to communicate with non-English–speaking patients.

Study outcomes

The primary study outcome was the prevalence of patients with a detectable HCV viral load. Secondary outcomes included HCV screening rate and result, gastroenterology referral rate, treatment rate, infant screening

FIGURE 1
Study flow diagram



PCR, polymerase chain reaction.

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TABLE 1
Patient characteristics

Characteristic	Total (n=8973)	Deliveries before July 2020 (n=5263)	Deliveries after July 2020 (n=3710)	*P* value[a]
Maternal age, mean (SD)	27.90 (6.40)	27.84 (6.33)	28.00 (6.49)	.26[b]
Race, n (%)				
American Indian or Alaska Native or Native Hawaiian	27 (0.30)	18 (0.34)	9 (0.24)	<.01
Asian	98 (1.09)	58 (1.10)	40 (1.08)	
Black or African American	3678 (40.99)	2220 (42.18)	1458 (39.30)	
More than one race	629 (7.01)	371 (7.05)	258 (6.95)	
Other Pacific Islander	144 (1.60)	75 (1.43)	69 (1.86)	
Other race[c]	12 (0.13)	3 (0.06)	9 (0.24)	
Unknown or declined to report	1992 (22.20)	1031 (19.59)	961 (25.90)	
White	2393 (26.67)	1487 (28.25)	906 (24.42)	
Ethnicity, n (%)				
Hispanic, Latino/a, or Spanish origin	3729 (41.56)	2093 (39.77)	1636 (44.10)	<.01
Non-Hispanic, Latino/a, or Spanish origin	5107 (56.92)	3107 (59.03)	2000 (53.90)	
Unknown or declined to report	137 (1.53)	63 (1.20)	74 (1.99)	
Insurance, n (%)				
Commercial	786 (8.76)	481 (9.14)	305 (8.22)	<.01
HIP	2036 (22.69)	1226 (23.29)	810 (21.83)	
Health Advantage	318 (3.54)	146 (2.77)	172 (4.63)	
Incarcerated	27 (0.30)	11 (0.21)	16 (0.43)	
Medicaid	4450 (49.59)	2487 (47.25)	1963 (52.91)	
Medicare	50 (0.56)	31 (0.59)	19 (0.51)	
Other[c]	16 (0.18)	12 (0.23)	4 (0.11)	
Self-pay	885 (9.86)	645 (12.26)	240 (6.47)	
Sliding fee	405 (4.51)	224 (4.26)	181 (4.88)	
Nulliparous, n (%)[d]	2122 (23.71)	1235 (23.56)	887 (23.91)	.70
Intravenous drug use, n (%)	37 (0.41)	28 (0.53)	9 (0.24)	.04
Persons living with HIV, n (%)	47 (0.52)	34 (0.65)	13 (0.35)	.06

HIP, Healthy Indiana Plan; *SD*, standard deviation.

[a] Chi-square tests were used unless otherwise indicated.; [b] Student's *t* test was used.; [c] Listed as other in the electronic medical record.; [d] A total of 8951 pregnancies with data available on parity.

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TABLE 2
HCV screening and prevalence

HCV screening parameters	Total (n=8973)	Deliveries before July 2020 (n=5263)	Deliveries after July 2020 (n=3710)	*P* value[a]
Screened for HCV, n (%)	3170 (35.32)	304 (5.78)	2866 (77.25)	<.01
Screened positive for HCV, n (%)	101 (1.13)	57 (1.08)	44 (1.19)	.65
Detectable viral load, n (%)	71 (0.79)	41 (0.78)	30 (0.81)	.88

HCV, hepatitis C virus.

[a] Chi-square tests were used.

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rate, and predictors of treatment referral status.

Statistical analysis

Continuous variables were analyzed using mean, standard deviation (SD), and Student's *t* tests. Categorical variables were analyzed using percentage and chi-squared tests. $P<.05$ was considered statistically significant. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using logistic regression models. Multivariate logistic regression models incorporated whether the outcome occurred before or after the policy change and any variable with a $P<.05$ in the univariate analysis. Statistics were performed using Stata/SE 17.0 for Windows (StataCorp, College Station, TX). Graphs were generated in GraphPad Prism version 9.5.0 for Windows, (GraphPad Software, San Diego, CA, www.graphpad.com).

Definitions

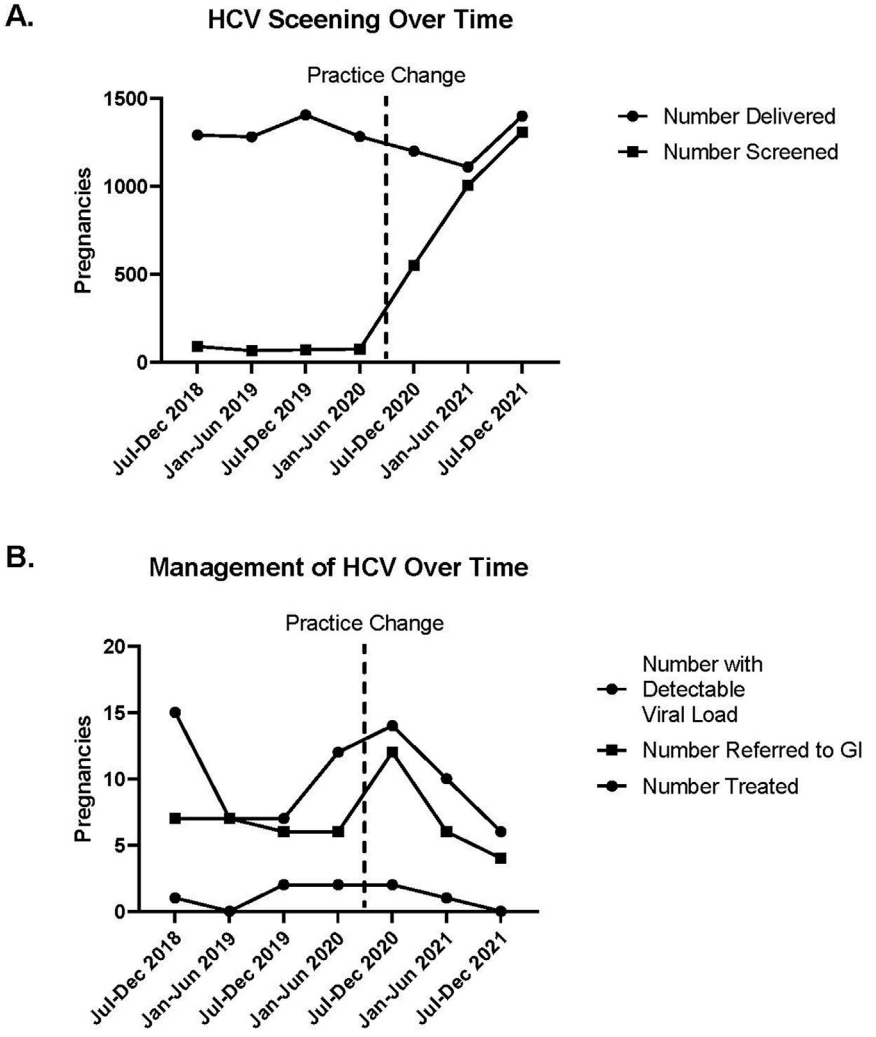
A delivery was defined as occurring in a person living with HCV if there was a detectable viral load with PCR analysis. HCV screening was defined as any pregnant person who was tested for HCV using Ab or PCR. A positive screening result was defined as a reactive HCV Ab result or a detectable viral load with PCR analysis. Intravenous drug use was defined as any pregnancy in which the woman had intravenous drug use recorded in her problem list. Race and ethnicity were defined based on what was reported in the EMR. The category of other was how the patient was identified in the EMR. Insurance type included Healthy Indiana Plan (HIP), a managed care health plan and consumer-directed model that provides an account, similar to a health savings account offered by the state of Indiana, to patients with low-income who may or may not qualify for Medicaid or Medicare, and Health Advantage, a charity insurance provided by Eskenazi Hospital for patients with low-income, and commercial insurance, incarcerated insurance, Medicaid, Medicare, self-pay, sliding fee, and other as indicated in the EMR. Insurance type was based on the insurance the patient had at the time of delivery.

Results

A total of 8973 deliveries occurred at the Eskenazi Hospital between July 1, 2018, and December 31, 2021. Before the practice change on July 1, 2020, there were 5263 deliveries of which 304 (5.78%) were screened for HCV. Of the 3710 deliveries that occurred after the policy change, 2866 (77.25%) pregnancies were screened for HCV. A subset of 958 patients were screened dually with the addition of an HCV risk factors questionnaire (Figure 1).

The average patient age at delivery was 27.90 (SD, 6.40) years. The population was diverse with the most common races reported as Black or African American (40.99%) and White (26.67%), with 41.56% of the cohort identifying as Hispanic, Latino/a, or Spanish ethnicity. The most common insurance payor was Medicaid (49.59%). Intravenous drug use was identified on the problem list for 37 (0.41%) patients, and 47 (0.52%) were living with HIV (Table 1). After the

FIGURE 2
HCV screening and management over time



A, HCV screening over time. **B**, Management of HCV over time. The *dashed lines* indicate the timing of practice change from risk-based to universal screening. The Y axis shows the number of pregnancies and the X axis shows time, divided into half-year segments.

GI, gastroenterology; *HCV*, hepatitis C virus.

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policy change, the racial, ethnic, and insurance profiles of the population changed significantly. Patients were more likely to have an unreported race, have Hispanic ethnicity, and have Medicaid insurance (Table 1). There was also a significant decline in intravenous drug use (0.53% to 0.24%; *P*=.04) (Table 1).

Among the 8973 deliveries that occurred over the entire study period, 3170 (35.33%) were screened for hepatitis C virus. A total of 101 (1.13%) screened positive for Abs to HCV, and 71 (0.79%) had a detectable viral load. Five patients had a positive antibody test but did not have a viral load test conducted. A total of 25 patients with positive antibody tests had an undetectable viral load. Significantly more pregnancies were screened for HCV after the practice change (5.78% before vs 77.25% after; *P*<.01) (Table 2). Examining the adaptation of the practice change over time, universal screening was widely adopted within 6 months (Figure 2, A). The detected HCV prevalence increased from 0.77% to 0.81% after the practice change, although this rise did not achieve statistical significance (*P*=.88) (Table 2), and there was no noticeable trend over time (Figure 2, B).

Among the 71 pregnancies of patients detected to be living with HCV, the average maternal age was 28.82 (SD, 5.05) years (Table 3). The majority of these patients were White (83.10%),

TABLE 3
Characteristics of patients based on HCV status

Characteristic	Patients living with HCV with detectable viral load (n=71)	HCV uninfected (n=3099)	HCV unscreened (n=5803)	*P* value[a]
Maternal age, mean (SD)	28.82 (5.05)	28.24 (6.47)	27.71(6.37)	<.01[b]
Race, n (%)				<.01
American Indian or Alaska Native or Native Hawaiian	0	9 (0.29)	18 (0.31)	
Asian	0	34 (1.97)	64 (1.10)	
Black or African American	2 (2.82)	1247 (40.24)	2429 (41.86)	
More than one race	5 (7.04)	202 (6.52)	422 (7.27)	
Other Pacific Islander	2 (2.82)	57 (1.84)	85 (1.46)	
Other race[c]	0	9 (0.29)	3 (0.05)	
Unknown or declined to report	3 (4.23)	774 (24.98)	1215 (20.94)	
White	59 (83.10)	767 (24.75)	1567 (27.00)	
Ethnicity, n (%)				<.01
Hispanic, Latino/a, or Spanish origin	2 (2.82)	1345 (43.40)	2382 (41.05)	
Non-Hispanic, Latino/a, or Spanish origin	66 (92.96)	1692 (54.60)	3349 (57.71)	
Unknown or declined to report	3 (4.23)	62 (2.00)	72 (1.24)	
Insurance, n (%)				<.01
Commercial	1 (1.41)	244 (7.87)	541 (9.32)	
HIP	45 (63.38)	689 (22.23)	1302 (22.44)	
Health Advantage	1 (1.41)	152 (4.90)	165 (2.84)	
Incarcerated	8 (11.27)	11 (0.35)	8 (0.14)	
Medicaid	7 (9.86)	1608 (51.89)	2835 (48.85)	
Medicare	0	19 (0.61)	31 (0.53)	
Other[c]	0	6 (0.19)	10 (0.17)	
Self-pay	9 (12.68)	215 (6.94)	661 (11.39)	
Sliding fee	0	155 (5.00)	250 (4.31)	
Nulliparous, n (%)[d]	10 (14.08)	705 (22.77)	1407 (24.33)	.04
Intravenous drug use, n (%)	15 (21.13)	19 (0.61)	3 (0.05)	<.01
Persons living with HIV, n (%)	0	25 (0.81)	22 (0.38)	.024

HCV, hepatitis C virus; *HIP*, Healthy Indiana Plan; *SD*, standard deviation.

[a] Chi-square tests were used unless otherwise indicated.; [b] Analysis of variance was conducted.; [c] Listed as other in the electronic medical record.; [d] Only 8951 pregnancies with data on gravidity.

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non-Hispanic, Latino/a, or Spanish origin (92.96%), and had HIP insurance (63.38%). Based on EMR data, 15 (21.13%) of these patients had a history of intravenous drug use and none were co-infected with HIV (Table 3). The average viral titer was 3,057,050 IU/mL (SD 6,459,751 IU/mL; range, 54 -3.60×10^7 IU/mL). The characteristics of patients who were determined to be living with HCV were similar before and after the shift to universal screening (Supplemental Table 1).

Patients living with HCV had significantly different racial, ethnic, and insurance demographics than HCV-uninfected and unscreened patients and were more likely to have a history of intravenous drug use (Table 3, Supplemental Table 2). In a multivariate logistic regression analysis in which these variables were adjusted for, the timing of delivery before the implementation of universal HCV screening in 2020 was not significantly associated with having a detected HCV infection (OR, 0.75; 95% CI, 0.44−1.29; *P*=.30) (Table 4).

After the implementation of routine questionnaire administration for HCV risk factors, 2335 deliveries occurred. Among these pregnancies, 1009 (43.21%) patients were administered the questionnaire. A subset of 958 pregnancies had universal screening and were administered the risk-factor questionnaire. At least 1 risk factor was reported in the questionnaire for 56 (5.85%) of these patients. Among those individuals, 8 had a positive antibody screen. An additional 2 patients who had an HCV infection were identified with the universal screening. Six patients had a detectable viral load. All 6 of these patients had risk factors identified in the questionnaire (Figure 1). The most common risk factor identified with the questionnaire was incarceration (3.55%), followed by blood exposures in an unregulated setting (2.09%). Similar to what was noted in the the EMRs, 1.04% of patients reported intravenous drug use (Table 5).

Among the 71 patients who had a detectable viral load, 48 (67.61%) were referred to gastroenterology for treatment during the postpartum period. Ultimately, 9 (18.75%) received treatment and 1 (2.08%) spontaneously cleared the virus. At the time of the analysis, 2 patients were still being treated, and 7 had an undetectable viral load. Six patients were treated with glecaprevir/pibrentasvir and 3 were treated with sofosbuvir/velpatasvir. Patients who were referred for treatment were significantly older (29.83 vs 26.70 years; *P*=.01), less likely to be nulliparous (8.33% vs 26.09%; *P*=.04) and less likely to have a history of intravenous drug use (12.50% vs 39.13%; *P*=.01) than those who were not referred for treatment. Insurance payor, race, ethnicity, and screening timepoint were not significantly different between patients who were and those who were not referred to gastroenterology (Table 6).

TABLE 4
Multivariate logistic regression model examining the impact of the policy change on the odds of testing positive for HCV (having a detected infection) in comparison with testing negative or going unscreened while controlling for other factors associated with testing positive for HCV[a]

Factors	OR (95% CI)	*P* value
Delivery before July 2020	0.75 (0.44−1.29)	.30
Race, n (%)		
American Indian or Alaska Native or Native Hawaiian	—	
Asian	—	
Black or African American	Ref	
More than 1 race	70.18 (12.92−381.29)	<.01
Other Pacific Islander	63.9 (8.39−486.94)	<.01
Other race[b]	—	
Unknown or declined to report	16.56 (2.52−108.90)	<.01
White	70.64 (17.00−293.54)	<.01
Ethnicity, n (%)		
Hispanic, Latino/a, or Spanish origin	Ref	
Non-Hispanic, Latino/a, or Spanish origin	30.15 (6.81−133.49)	<.01
Unknown or declined to report	41.81 (5.52−316.87)	<.01
Insurance, n (%)		
Commercial	Ref	
HIP	26.61 (3.62−195.442)	<.01
Health Advantage	21.22 (1.20−374.77)	.04
Incarcerated	160.85 (18.28−1415.22)	<.01
Medicaid	5.18 (0.63−42.83)	.13
Medicare	—	
Other[b]	—	
Self-pay	19.65 (2.44−158.06)	.01
Sliding fee	—	
Intravenous drug use	11.84 (5.41−25.91)	<.01

CI, confidence interval; *HCV*, hepatitis C virus; *HIP*, Healthy Indiana Plan; *OR*, odds ratio.

[a] See Supplemental Table 2 for univariate analysis that identified demographic factors included.; [b] Listed as other in the electronic medical record.

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TABLE 5
HCV risk-factor questionnaire

Risk factor reported by patient	Yes, n (%)	No, n (%)	Declined to answer, n (%)
Injected illegal drugs (even once)	10 (1.04)	947 (98.85)	1 (0.10)
Snorted illegal drugs	13 (1.36)	938 (97.91)	7 (0.73)
Long-term hemodialysis	0	951 (99.26)	7 (0.73)
Blood exposures in an unregulated setting (eg, tattoo received outside of licensed parlor or medical procedures done in settings without strict infection control policies)	20 (2.09)	926 (96.66)	12 (1.25)
Blood transfusions or organ transplants before July 1992	2 (0.21)	948 (98.96)	8 (0.84)
Received blood clotting factor concentrates produced before 1987	0	948 (98.96)	10 (1.04)
Received blood products from donors who later tested positive for HCV	0	948 (98.96)	10 (1.04)
Incarceration	34 (3.55)	914 (95.41)	10 (1.04)
Seeking evaluation or care for sexually transmitted infections including HIV	5 (0.52)	941 (98.23)	12 (1.25)
Unexplained chronic liver disease	2 (0.21)	945 (98.64)	11 (1.15)
Any of the above risk factors	56 (5.85)	—	—

HCV, hepatitis C virus.

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In a multivariate logistic regression model that included age, parity, intravenous drug use, and if delivery occurred before the HCV screening practice change, age was associated with a 1.18-fold increased odds (95% CI, 1.02−1.36; *P*=.03) of referral, and intravenous drug use was associated with significantly decreased odds of referral (OR, 0.14; 95% CI, 0.04−0.59; *P*=.01) (Table 7). There was no association between referral to gastroenterology and implementation of universal screening (Table 7) and there was no noticeable trend over time (Figure 2, B).

Among the 71 pregnancies with a detectable viral load, 52 infants were at least 18 months old, and thus eligible for HCV screening at the time of the data extraction. Among these infants, 8 (15.38%) had screening documented in the EMRs. All 8 infants screened negative for HCV.

Comment

Principal findings

Following the introduction of universal screening, we saw a rapid increase in the HCV screening rate from 5.78% to 77.25% (*P*<.01). HCV prevalence increased from 0.77% to 0.81% but was not significantly different. Although 67.61% of patients living with HCV were referred for treatment, only 18.75% were treated and only 15.38% of infants were screened. Intravenous drug use was associated with decreased odds of referral for postpartum treatment.

Results in the context of what is known

There have been a few studies in which risk-based and universal HCV screening were compared directly in the general-risk population. Our data are consistent with retrospective studies in Alabama and London that observed nonsignificant increases in HCV prevalence when risk-based screening (0.27%−0.6%) was compared with universal screening (0.28%−0.86%).[21,22] However, demographic changes in our population over the study may have led to a lower proportion of true positives, thereby limiting our ability to detect a difference. White race and history of intravenous drug use (characteristics associated with HCV infection[9]) were less common in the period after the practice change. We used a multivariate logistic regression model to control for these factors; however, delivery after the policy change was still not significantly associated with an increased likelihood of HCV infection. This may be because of a nationwide decline in HCV in reproductive-aged individuals during the study period.[23] Inherent biases in who is screened for HCV may have continued to play a role in our results because universal screening was not perfectly applied. We further administered an HCV risk factor questionnaire to a subgroup of the universal screening cohort to more directly compare which individuals would have been identified with risk-based vs universal screening. Among these patients, 5.78% reported any risk factors for HCV. Risk-based screening only identified 8 of the 10 patients who screened positive for HCV, although it did capture all 6 viremic patients. Given the limited number of patients administered the questionnaire, it is likely that universal screening identified multiple cases of HCV that would have been missed by risk-based screening alone.

We also observed gaps in infant follow-up. Our observed HCV-exposed

TABLE 6
Characteristics of patients who were and were not referred for treatment

Characteristic	Total (n=71)	Referred (n=48)	Not referred (n=23)	*P* value[a]
Maternal age, mean (SD)	28.82 (5.05)	29.83 (5.15)	26.70 (4.16)	.01[b]
Race, n (%)				.19
American Indian or Alaska Native or Native Hawaiian	0	––	––	
Asian	0	––	––	
Black or African American	2 (2.82)	2 (4.17)	0	
More than one race	5 (7.04)	5 (10.42)	0	
Other Pacific Islander	2 (2.82)	2 (4.17)	0	
Other race[c]	0	––	––	
Unknown or declined to report	3 (4.23)	1 (2.08)	2 (8.70)	
White	59 (83.10)	38 (79.17)	21 (91.30)	
Ethnicity, n (%)				.28
Hispanic, Latino/a, or Spanish origin	2 (2.82)	2 (4.17)	0	
Non-Hispanic, Latino/a, or Spanish origin	66 (92.96)	45 (93.75)	21 (91.30)	
Unknown or declined to report	3 (4.23)	1 (2.08)	2 (8.70)	
Insurance, n (%)				.58
Commercial	1 (1.41)	1 (2.08)	0	
HIP	45 (63.38)	31 (64.58)	14 (60.87)	
Health Advantage	1 (1.41)	1 (2.08)	0	
Incarcerated	8 (11.27)	4 (8.33)	4 (17.39)	
Medicaid	7 (9.86)	6 (12.50)	1 (4.35)	
Medicare	0	––	––	
Other[c]	0	––	––	
Self-pay	9 (12.68)	5 (10.42)	4 (17.39)	
Sliding fee	0	––	––	
Nulliparous, n (%)	10 (14.08)	4 (8.33)	6 (26.09)	.04
Intravenous drug use, n (%)	15 (21.13)	6 (12.50)	9 (39.13)	.01
Delivery before July 2020	0	26 (54.17)	15 (65.22)	.38

HIP, Healthy Indiana Plan; *SD*, standard deviation.

[a] Chi-square tests were used unless otherwise indicated.; [b] Student's *t* test was used.; [c] Listed as other in the electronic medical record.

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TABLE 7
Logistic regression model of factors associated with being referred to gastroenterology

Factors associated with referral	OR (95% CI)	*P* value
Maternal age	1.18 (1.02–1.36)	.03
Nulliparous	0.30 (0.06–1.56)	.15
Intravenous drug use	0.14 (0.04–0.59)	.01
Delivery before July 2020	1.00 (0.30–3.33)	1.00

CI, confidence interval; *OR*, odds ratio.

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infant screening rate of 15.38% is on the lower end of the roughly 15% to 40% range reported in the literature.[5–9] It is possible that we are underestimating screening rates because of infants being treated outside of our healthcare system. Alternatively, these low screening rates may be a consequence of the absence of documentation of perinatal exposure, inadequate maternal counseling regarding postnatal screening importance, or accidental omission of screening because of the delayed 18-month screening

recommendation. However, higher screening rates are possible. Early nucleic acid–based testing, improved transitions in care, coupling care to substance use disorder treatment, or a multidisciplinary clinic model could increase HCV-exposed infant screening.[24,25]

Clinical implications

Universal screening for HCV was rapidly adopted in our hospital with more than three-quarters of pregnancies screened within a year after the policy shift, demonstrating feasibility and acceptance. However, management outcomes remained suboptimal. Only 67.61% of our patients with HCV were referred for treatment in the postpartum period and only 18.75% of patients received treatment. Previous literature has documented similar outcomes with 75% of patients referred and 9% treated.[21]

There are many potential structural, patient, and provider barriers to treatment. We found that patients with a history of intravenous drug use were significantly less likely to be referred for treatment. This may reflect stigma, provider concerns regarding adherence, or denials by insurance companies. Our data are consistent with drop-offs in the treatment cascade shown by others.[26] Innovative approaches to treatment are needed. One possible model is linkage to care with co-located HCV and opioid use disorder treatment. HCV treatment initiation was increased from 17.07% (n=28/164) to 52.00% (n=13/25) in a study that used this approach.[27]

Research implications

Improvements in HCV treatment and infantile screening rates are critical. Antepartum HCV treatment could help to decrease the proportion who are lost to follow-up and potentially prevent vertical transmission.[28–31] Although a phase 1 trial demonstrated the safety and efficacy of ledipasvir/sofosbuvir during pregnancy, no HCV medications are currently recommended for use during the antepartum period.[32] Until then, linkage to care in multidisciplinary obstetric-gastroenterology clinics, co-located treatment of HCV and opioid used disorder, point-of-care testing, treatment of non–breast feeding patients during the insured postpartum period, and surveys evaluating barriers to postpartum treatment may prove useful. It will be valuable for future studies to identify factors that influenced postpartum treatment and successful treatment, including insurance coverage of treatment.

Strengths and limitations

Our study is limited by its sample size, accuracy of EMR data, limitation to a single hospital system, and the before and after study design. Differences in characteristics of the universal HCV screening population may mask significant differences in HCV prevalence. Alternatively, our mild increase in HCV prevalence may have reflected a true rise in prevalence because of temporal factors rather than a rise in detection because of increased screening. With regards to postpartum treatment and infant screening, it is possible that patients and their infants transferred their care to a different hospital system where they received care and thus were not captured in our follow-up data, making it likely that we underestimated these rates. A larger, multicenter study would be more generalizable and could be powered to examine vertical transmission and postpartum HCV treatment rates. Despite these limitations, our study demonstrated the feasibility of universal screening in pregnancy and identified areas for improvement in the management of patients who screen positive. We further identified factors associated with a lack of referral to postpartum treatment.

Conclusion

With aggressive approaches to case identification, we have the opportunity to potentially eradicate HCV.[28,33,34] Universal screening during pregnancy is of paramount importance because it presents a unique opportunity to diagnose and refer patients to treatment when they have regular access to healthcare. Yet, postpartum HCV treatment and infant screening rates remain low. While we await recommendations for HCV treatment during pregnancy, linkage to care initiatives will be vital. ■

CRediT authorship contribution statement

Sarah Boudova: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Elizabeth Ferries-Rowe:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Conceptualization. ■

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.xagr.2024.100317.

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