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Evaluating Women's Preferences for Hepatitis C Treatment During Pregnancy

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There is a rising prevalence of hepatitis C (HCV) among women of child-bearing age nationally, which prompted a recommendation by national guidelines to screen all women for HCV during pregnancy. Women with HCV during pregnancy are at risk of perinatal transmission of HCV. Directly acting antiviral (DAA) therapy during pregnancy can potentially reduce the risk of perinatal transmission as well as cure women while they are engaged in antenatal care. However, data on the safety and efficacy of DAAs during pregnancy are limited. We aimed to evaluate the preferences of women with HCV regarding potential DAA treatment during pregnancy. We conducted a survey of women with a history of HCV followed in the University of California, San Francisco HCV clinic and in the Women's Interagency HIV Study (most of whom are coinfected with HIV) to determine their preferences for DAA treatment during pregnancy. A total of 141 women completed the survey. Sixty percent reported that they would be willing to take antepartum DAA therapy if it lowered the risk of perinatal transmission. Only 21% reported that they would agree to take DAA therapy during pregnancy for self-cure; 20% of women stated that they would not, yet indicated that they might change their minds if there were more human data available regarding use of DAAs during pregnancy. In multivariable analysis, having a previous history of taking DAAs and being of childbearing age at the time of the survey were associated with willingness to take DAA medication during pregnancy (odds ratios 4.29 and 4.11, respectively). *Conclusion:* These results point to the need for further investigation of the role of HCV therapy during pregnancy. (*Hepatology Communications* 2018;2:1306-1310)

There is an increasing rate of hepatitis C virus (HCV) infection among women of child-bearing age in the United States, and a parallel increase in anti-HCV detection in children under the age of 2 years (despite evidence of under-screening children of mothers with HCV), likely reflecting perinatal transmission of HCV.[1,2] As a result, last month, the American Association for the Study of Liver Diseases and Infectious Diseases Society of America identified women with HCV during pregnancy as a key population for screening and updated national guidelines to recommend universal HCV screening in women during pregnancy.[3] Engagement of women in care during pregnancy provides an opportune time to identify and potentially treat HCV. Furthermore, antiviral treatment during pregnancy may reduce perinatal transmission of HCV and the community burden of HCV. Most direct-acting antivirals (DAAs) have been labeled pregnancy-safe based on animal studies, but none are currently approved for use in humans during pregnancy.[4] To better understand the feasibility of

Abbreviations: CI, confidence interval; DAA, direct-acting antivirals; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IQR, interquartile range; OR, odds ratio; UCSF, University of California, San Francisco; WIHS, Women's Interagency HIV Study.

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studying DAA therapy in pregnancy, it is critical to evaluate preferences of women with HCV regarding the use of antiviral therapy during pregnancy. Therefore, we conducted a survey of women with current or previous chronic HCV infection, evaluating their views on the potential benefit versus harm of DAAs in pregnancy.

Methods

We conducted a survey in the San Francisco Bay Area of women over the age of 18 with current or previous chronic HCV infection. Women seen in the University of California, San Francisco (UCSF) HCV treatment clinic who provided their email address were invited to participate in the online survey; three serial invitations were sent during May 2017. The Women's Interagency HIV Study (WIHS) follows women who are infected with human immunodeficiency virus (HIV) and at risk for HIV infection. Women with current or previous chronic HCV infection who presented for a study visit in September 2017 completed the interview-administered survey during their study visit. Survey questions included demographics, pregnancy history, and past medical history, including HCV disease history (see Supporting Information). Responses to any of the questions included in the survey were optional. Three key questions asked participants whether they would take DAA therapy during the third trimester of pregnancy to reduce perinatal transmission, whether they would self-cure HCV even if it did not decrease mother-to-child transmission, and whether they would obtain treatment while health insurance coverage is available. Eight-six percent of the study participants answered the first two of these questions; 83% answered the third. A composite primary endpoint was a response of "Yes" to any of these three key questions. Survey questions were designed to be at a sixth-grade reading level and included pictorial representations of known data on the risks for perinatal transmission of HCV. Univariable and multivariable logistic regression to assess factors associated with willingness to take DAAs during pregnancy was performed (predictive factors with a $P < 0.1$ in the univariable analysis were included in the multivariable analysis). The study was approved by the UCSF Institutional Review Board.

Results

Of the 329 UCSF clinic women who were invited to participate, 121 (37%) completed the survey. Twenty of 20 women from WIHS responded to the survey questions. Characteristics of the study participants are given in Table 1. The median age was 60 (interquartile range [IQR] 56, 64), and 11% were 45 years of age or less at the time of the survey. Nearly two-thirds (62%) of the women were Caucasian and 15% were African American. Thirty-five percent had a bachelor's degree or higher education level. Most (85%) had received HCV treatment in the past. Fourteen percent were HIV coinfected and 34% had a reported history of cirrhosis. The latter reflects the tertiary referral practice at UCSF.

With regard to pregnancy history, 74% had a history of at least one pregnancy in the past, with 23% reporting a history of previous pregnancy complication. Of those responding to the question about knowledge of their HCV status during their pregnancies, 15 of 85

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TABLE 1. CHARACTERISTICS OF WOMEN PARTICIPATING IN THE SURVEY

	UCSF Cohort (n = 121)	WIHS Cohort (n = 20)	Overall (n = 141)
Median age (IQR)	61 (55, 64)	60 (59, 65)	60 (56, 64)
Childbearing age (< 45 years)	15 (14%)	1 (5%)	16 (11%)
Race			
African American	9 (7%)	12 (60%)	21 (15%)
White	86 (71%)	1 (5%)	87 (62%)
Other	26 (21%)	7 (35%)	33 (23%)
Education level			
High school	19 (16%)	17 (85%)	36 (26%)
< 4 years college	52 (43%)	3 (15%)	55 (39%)
Bachelor's degree	24 (20%)	0	24 (17%)
Advanced degree	24 (20%)	0	24 (17%)
Marital status			
Single	19 (16%)	6 (32%)	25 (18%)
Widowed	8 (7%)	4 (20%)	12 (9%)
Married	54 (46%)	6 (32%)	60 (44%)
Divorced	36 (31%)	3 (16%)	39 (29%)
HIV positive	2 (2%)	18 (90%)	20 (14%)
Taking any chronic medication	67 (57%)	20 (20%)	87 (62%)
HCV history			
Previously treated	104 (87%)	15 (79%)	119 (85%)
Cirrhosis	46 (38%)	2 (10%)	48 (34%)
Pregnancy history			
Pregnant in past	86 (73%)	18 (90%)	104 (74%)
Complications	24 (20%)	8 (40%)	32 (23%)
Miscarriage	19 (16%)	4 (5%)	23 (16%)
Premature birth	4 (3%)	5 (25%)	9 (6%)
Low birth weight	5 (4%)	2 (10%)	7 (5%)
Birth defect	0	0	0
Pregnant while HCV positive	15 (18%); n = 85	3 (18%); n = 17	18 (1%); n = 102
Baby with HCV	4 (5%); n = 82	1 (6%); n = 18	5 (5%); n = 100

(18%) in the UCSF clinic group and 3 of 17 (18%) in the WIHS were aware of their positive HCV status during their pregnancies. Of the participants who answered the question of whether they had a child with hepatitis C, 4 of 82 (5%) reported having a child with HCV.

Women were asked whether they would consider taking medication for HCV during the third trimester of pregnancy to lower the chance of perinatal HCV, after being provided with information on the known risks of perinatal transmission. Of the 121 respondents, 60% answered yes: 56% of the 102 respondents with HCV mono-infection and 79% of the 19 respondents with HIV/HCV coinfection. When asked whether they would consider taking medication during pregnancy for self-cure even if it did not decrease perinatal transmission of HCV, 26 of 122 respondents (21%) answered yes. Of those that responded no, 20 of 96 (20%) answered that they would consider taking medication if there were more studies performed in human patients testing the use of DAAs during pregnancy. When asked whether their decision to take medication during pregnancy would be influenced by whether they only had health insurance during pregnancy, 63 of 117 (54%) responded that they would make sure to take antiviral therapy during pregnancy while they had health insurance, if possible. Finally, when asked what they would do if they were already on DAAs and became pregnant, 55 of 119 (46%) responded that they would continue the medication, 54 of 119 (45%) would stop the medication, and 10 of 119 (8%) would terminate the pregnancy.

In univariable analysis, race, advanced education level, having cirrhosis, and having a history of

TABLE 2. UNIVARIABLE AND MULTIVARIABLE PREDICTORS OF WILLINGNESS TO TAKE HCV MEDICATION DURING PREGNANCY

	Univariable Analysis, OR (95% CI)	Multivariable Analysis, OR (95% CI)
African American race	1.75 (0.61, 5.0)	
Advanced education level*	0.91 (0.40, 2.10)	
Childbearing age (< 45 years)	3.40 (0.92, 12.54)†	4.29 (1.10-16.70)‡
Previous history of taking HCV medications	2.92 (1.07-7.97)†‡	4.11 (1.32-12.72)‡
Married	0.52 (0.26-1.04)	
Cirrhosis	0.68 (0.34-1.39)	
HIV positive	2.25 (0.77-6.59)†	2.96 (0.94-9.37)
History of pregnancy complications	1.73 (0.73-4.13)	

*College or higher.
†$P < 0.1$, included in multivariable analysis.
‡$P < 0.05$.

pregnancy complications were not associated with a willingness to take DAA medications (odds ratio [OR] 1.75, 95% confidence interval [CI] 0.61-5.0; OR 0.91, 95% CI 0.40-2.10; OR 0.68, 95% CI 0.34-1.39; and OR 1.73, 95% CI 0.73-4.13, respectively) (Table 2). Being of childbearing age (less than 45 years old) and being HIV positive were not significantly associated (OR 3.40, 95% CI 0.92-12.54; and OR 2.25, 95% CI 0.77-6.59, respectively) with willingness to take DAAs during pregnancy. Having a previous history of taking HCV medications was significantly associated with a greater willingness to take medications during pregnancy (OR 2.92, 95% CI 1.07-7.97). In the multivariable analysis, being of childbearing age and having a previous history of taking DAAs remained independently associated with a willingness to take medication during pregnancy, with OR 4.29 (95% CI 1.10-16.70) and OR 4.11 (95% CI 1.32-12.72), respectively.

Discussion

More than half of the women surveyed would be willing to take HCV medication during pregnancy if it were to decrease the risk of perinatal transmission, despite only 5% reporting a known personal history of perinatal transmission of HCV. Fewer (21%) would take DAAs solely for self-cure, with many expressing that they would consider changing their minds if more clinical studies were performed in humans, suggesting that women are more motivated by prevention of perinatal transmission of HCV rather than self-cure during pregnancy, and that they would be more comfortable taking medications if human data on safety and efficacy were obtained. Being of childbearing age was associated with a greater willingness to take HCV medications during pregnancy. Although we acknowledge that the number of women in this age range was small, our finding could suggest that HCV infection might be of greater concern in women who may have acquired infection more recently and might be more likely to transmit HCV infection, highlighting the importance of linking HCV detection and treatment in settings such as prenatal clinics. Another possible reason is that younger women are more likely to have knowledge only of DAAs for the treatment of HCV (versus interferon/ribavirin) and have a more favorable viewpoint of the tolerability of the treatment of HCV. History of previously taking HCV treatment was associated with willingness to take medication during pregnancy, suggesting that first-hand knowledge about the safety and efficacy of HCV medications made patients more amenable to taking medications during pregnancy. There was a trend toward significance of coinfection with HIV being associated with willingness to take medication during pregnancy (OR 2.96, 95% CI 0.94-9.37), implying that women with HIV, who are possibly more accustomed to taking medication during pregnancy to decrease perinatal transmission of infections, would be more comfortable taking DAAs during pregnancy. Although the number of women with HIV coinfection in our study was small, targeting antiviral therapy in this group may be important given that the risk of perinatal transmission of HCV of HCV has been reported to be about 15% in HCV/HIV coinfected mothers compared with the approximate 5% reported in HCV-positive mothers.[5]

There are a few limitations to this study. Because participation was voluntary and participants were able to opt out of answering questions, results may not be entirely representative of the patient population. In addition, the cohort consisted almost entirely of patients who were not currently pregnant, which may have made their answers to questions regarding decisions during pregnancy not entirely representative of what they would choose had they actually been pregnant at the time of the survey. However, although the

cohort had an older median age than women of childbearing age, most of them had DAA treatment experience and a history of pregnancy, and therefore had realistic and informed perspectives on the treatment of HCV as well as considerations relating to pregnancy.

These results point to the need for further investigation of the role of HCV therapy during pregnancy. Despite little data on the safety and efficacy of HCV treatment during pregnancy, women expressed willingness to take HCV medications during pregnancy to prevent perinatal transmission. There are currently no results on the safety and efficacy (from the standpoint of perinatal transmission as well as maternal cure) available. Additional unanswered questions regarding HCV treatment prepartum and postpartum—including optimal timing and duration of treatment, recommendations surrounding breastfeeding while potentially on therapy, and which of the DAAs would be most optimal to use—still remain to be answered. As the number of women being screened for HCV during pregnancy increases after implementation of universal pregnancy screening in the United States, women who screen positive will be turning to providers to guide the management of the virus during pregnancy. Use of DAAs during pregnancy will be a key aspect to address in counseling mothers.

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Supporting Information

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