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BRIEF REPORT

Real-World Experience of Hepatitis C Treatment With Glecaprevir-Pibrentasvir During Pregnancy

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(See the Editorial Commentary by Jhaveri on pages e537–8.)

Guidelines endorse antenatal hepatitis C virus treatment following shared decision making. No clinical trial or real-world data exist for glecaprevir-pibrentasvir (GLE/PIB). We report our experience with prenatal GLE/PIB in 14 patients. Ten patients completed treatment; all achieved virologic response by or at delivery, with no maternal or neonatal safety concerns.

Keywords. hepatitis C; pregnancy; perinatal infections; direct-acting antivirals.

Hepatitis C virus (HCV) guidelines published by the Infectious Diseases Society of America (IDSA) and the American Association for the Study of Liver Diseases (AASLD) state that direct-acting antivirals (DAAs) may be considered during pregnancy through shared decision making [1]. No specific regimen is recommended, and pregnancy-specific data for most DAA regimens remain limited. Early studies of sofosbuvir-velpatasvir and sofosbuvir-ledipasvir in pregnancy demonstrated 100% cure with no perinatal transmissions or significant safety events [2, 3]. However, there are no data on glecaprevir-pibrentasvir (GLE/PIB) outcomes in pregnant persons to date. This report of a retrospective series describes the outcomes in pregnant patients with HCV infections who initiated GLE/PIB between 14 and 32 weeks' gestation through shared decision making.

METHODS

Starting in March 2024 at our institution, infectious diseases and maternal-fetal medicine physicians followed IDSA/AASLD guidance on shared decision making, offering pregnant patients the option of prenatal HCV treatment after the first trimester or deferring until post partum. We reviewed all adult patients with pregnancies complicated by HCV who started GLE/PIB treatment at 14–32 weeks' gestational age (GA) from March 2024 through August 2025 at our Midwestern tertiary care center. We restricted the review to patients starting treatment during this time frame to include those who started after the first trimester but would have received a meaningful duration of medication before delivery, as the GLE/PIB course is 8 weeks long.

We collected baseline information from the electronic medical records for patients prescribed GLE/PIB, including age, race, ethnicity, insurance type, medical comorbid conditions, and prior and current pregnancy complications. We also collected data on HCV risk factors, HCV RNA level, HCV genotype, the fibrosis-4 index [4], and GA at treatment initiation for those who started treatment. We reviewed records to determine the cause of any documented discontinuation of GLE/PIB. We collected the following treatment outcomes among patients completing treatment: on-treatment HCV RNA levels; on-treatment aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total bilirubin levels; on-treatment documented adverse effects; HCV RNA levels at or by delivery; and sustained virologic response (SVR) at 4 weeks (SVR4) and 12 weeks (SVR12).

For maternal outcomes we collected the incidence of intrahepatic cholestasis of pregnancy (ICP) and gestational diabetes mellitus (GDM) diagnosed after treatment initiation. Delivery outcomes included preterm delivery (defined as delivery before 37 weeks' GA), GA at delivery, and obstetric hemorrhage. We reviewed the records of infants born to patients who completed treatment to collect the following neonatal outcomes: low birth weight (defined as <2500 g at birth), stillbirth, admission to the neonatal intensive care unit, and perinatal transmission of HCV (defined as detectable HCV RNA at ≥2 months of age).

This study was approved by the Washington University School of Medicine institutional review board.

RESULTS

A total 14 patients were prescribed GLE/PIB in pregnancy from 14 to 32 weeks GA during the study period. Of these women, 10 (71%) reported treatment completion. Baseline characteristics

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Table 1. Characteristics and Outcomes Among Patients Completing Glecaprevir-Pibrentasvir Treatment During Pregnancy

Pretreatment Characteristics and Treatment Outcomes	Patients, No. (%)[a] (N = 14)
Characteristics	
Age, mean, years	31
Race/ethnicity	
African American	2 (14)
White	11 (79)
Native American	1 (7)
Hispanic ethnicity	0 (0)
Insurance—Medicaid	14 (100)
Comorbid conditions	
OUD	8 (57)
On MOUD (methadone or buprenorphine)	4
Stimulant use	4 (29)
Marijuana use	2 (14)
Nicotine use	8 (57)
Hypertension	2 (14)
Maternal cardiac disease	2 (14)
Serious mental illness	3 (21)
Pretreatment complications	
GDM	2 (14)
Cholestasis of pregnancy	1 (7)
Syphilis	1 (7)
Substance use during pregnancy	4 (29)
Fetal anomaly	1 (7)
HCV-related factors	
HCV RNA, mean (range), IU/mL	2 786 021 (17 600–10 600 000)
Genotype	
1a	3 (22)
3	2 (14)
4	1 (7)
Unknown	8 (57)
FIB-4 score <1.45	14 (100)
Risk factor	
Drug use	9 (64)
Endemic region	1 (7)
Unknown	4 (29)
Prior known HCV-affected pregnancy	4 (29)
GA at initiation, mean (range), wk (n = 13)	25 (18–31)
Treatment-related outcomes (n = 10)	**n (%)**
Maternal outcomes	
HCV RNA undetectable at/by delivery	10 (100)
On-treatment HCV RNA undetectable (n = 8)	8 (100)
On-treatment ALT, AST, and total bilirubin levels normal (n = 9)	9 (100)
Achieved SVR4 or better (n = 9)	9 (100)
Achieved SVR12 (n = 5)	5 (100)
Pregnancy outcomes	
Preterm delivery (GA <37 wk)	0 (0)
GA at delivery, mean (range), wk	38 (37–39)
New cholestasis of pregnancy (n = 9)	0 (0)
New GDM (n = 8)	0 (0)
Intrapartum/postpartum hemorrhage (n = 10)	0 (0)
Neonatal outcomes	
Low birth weight (<2500 g)	0 (0)
Neonatal death or stillbirth	0 (0)
NICU admission	0 (0)
Perinatal transmission (n = 6)	0 (0)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; FIB-4, fibrosis-4; GA, gestational age; GDM, gestational diabetes mellitus; HCV, hepatitis C virus; MOUD, medications for opioid use disorder; NICU, neonatal intensive care unit; OUD, opioid use disorder; SVR4, sustained virologic response at 4 weeks; SVR12, sustained virologic response at 12 weeks.

[a]Data represent no. (%) of patients unless otherwise specified.

of the 14 patients who were prescribed GLE/PIB are shown in Table 1. None had HIV, hepatitis B, cirrhosis, or multifetal gestation. Preexisting complications documented before GLE/PIB initiation included trisomy 21 (n = 1), ICP (n = 1), and diet-controlled GDM (n = 2). Notably, 4 women (29%) had prior pregnancies complicated by HCV, and all patients were publicly insured. Treatment initiation occurred at an average GA of 25 weeks.

Among the 4 individuals who were prescribed but did not complete treatment, 3 discontinued GLE/PIB within the first week, and 1 did not start but instead deferred to post partum. Reasons for reported discontinuation included loss of medication after 1 dose at 25 weeks (n = 1) and anxiety and concern for fetal well-being after 1 dose in 1 patient and 5 doses in another (n = 2). The first patient delivered just before 37 weeks' GA with active substance use; the other 2 patients delivered at term. There were no reported safety concerns.

Outcomes in the 10 patients who completed therapy are also listed in Table 1. All patients had an undetectable viral load by delivery. On-treatment liver function test results were available in 8 of 10 individuals with no AST, ALT, or total bilirubin elevations observed. One patient experienced nausea managed with oral antiemetics; the remaining patients who completed the course had no reported adverse effects documented. SVR data were available in 9 of 10 individuals, with all achieving SVR4 or better. The 10th individual had undetectable HCV RNA during treatment prior to delivery but did not present for follow-up SVR laboratory testing. There were no known treatment failures.

No patients were reported to have developed new ICP or GDM or experienced obstetric hemorrhage after initiation of GLE/PIB. In 1 patient with preexisting AST and ALT elevations these values normalized on treatment. It is unknown whether the patient with ICP improved with therapy. All pregnancies ended with delivery at term, with no reported neonatal safety concerns. Six of the 10 exposed infants had available screening, with no perinatal transmissions observed.

DISCUSSION

This retrospective report describes outcomes in 14 pregnant individuals started on GLE/PIB in the second or third trimester of pregnancy, of whom 10 successfully completed therapy. These findings suggest that GLE/PIB may be effective, safe, and well tolerated in pregnancy. They findings also support the IDSA/AASLD guidelines stating that DAAs may be offered to pregnant patients though shared decision making.

This report offers the first data on antenatal GLE/PIB outcomes and contributes to the growing evidence base supporting the safety and efficacy of DAAs in this population. Although limited by its small and retrospective design, our real-world cohort includes medically and socially complex patients with comorbid conditions that reflect modern HCV-affected pregnancy cohorts [5], such as preexisting pregnancy complications, fetal anomalies, history of preterm deliveries, and substance use. Safety and efficacy outcomes in this cohort were comparable to those in similarly sized phase 1 studies of sofosbuvir-velpatasvir and sofosbuvir-ledipasvir [2, 3].

However, clinical trial data on antenatal GLE/PIB is urgently needed. Two of 3 individuals were prescribed treatment but discontinued it, changing their mind due to anxiety, concern for fetal well-being, and lack of safety information. Although sofosbuvir-based regimens may have more existing clinical trial data obtained during pregnancy, GLE/PIB is often an insurance-preferred agent with a shorter duration, fewer potential refills to coordinate, and no interactions with antacids often used in pregnancy. Patients may also prefer a shorter course than used with sofosbuvir-based regimens. These may be critical facilitators to successful HCV treatment in the relatively limited time span of pregnancy, in which delays risk loss to care, treatment opportunities and obstetric complications, particularly in a population with a high rate of public insurance coverage limited to pregnancy. Our findings offer timely, practice-based evidence to help clinicians and pregnant patients weigh the risks and benefits of antenatal GLE/PIB treatment through shared decision making as we await prospective trial data from IMPAACT 2041 (now enrolling).

These findings are particularly important because the annual rate of acute HCV tripled in the United States from 2008 to 2018, fueled by substance use [6]. In addition to long-term hepatic morbidity, HCV in pregnancy is associated with adverse obstetric outcomes, including perinatal transmission (estimated at 8%) [7], ICP, preterm birth, and neonatal death [8]. HCV also affects obstetric delivery management. Current obstetric guidelines recommend avoiding certain procedures that may be associated with perinatal transmission in viremic pregnancies [9]. Unfortunately, the current paradigm of referral for postpartum treatment has been a failure, with <6% of Medicaid recipients with opioid use disorder receiving DAAs by 6 months post partum [10]. Treatment during pregnancy may mitigate this cycle by reducing HCV-associated adverse obstetric outcomes, perinatal transmission, and postpartum loss to follow-up.

Our study provides some important public health findings in pregnancy. Earlier SVR data (ie, SVR4 vs SVR12) was more feasible. SVR4 can be obtained prior to delivery in individuals starting therapy in the late second or early third trimester, as opposed to SVR12 data, which may require postpartum follow-up with associated loss to care. For example, the mean GA at DAA initiation in our study was 25 weeks, which would put SVR12 at 45 weeks—after delivery. If treatment was initiated at a GA of 18 weeks, SVR12 would be at 38 weeks. As the IDSA/AASLD increasingly recognize SVR4 as an acceptable end point for adults without advanced liver disease [11], this shorter-term measure may likewise be appropriate for inclusion in pregnancy registries to inform evidence-based best practices. Thus, the addition of SVR4 data should be considered in future studies as ongoing clinical trials of DAAs during pregnancy assess only SVR12, limiting comparisons.

Our study does have several limitations, highlighting the importance of ongoing clinical trials. First, the study is retrospective and therefore limits our ability to rigorously assess for safety concerns and obtain complete follow-up data, like SVR12. For similar reasons we could not obtain pharmacokinetic data that may inform more detailed assessment of efficacy and infant safety. In addition, the study includes only 10 individuals who completed treatment, limiting generalizability. Finally, while this cohort started treatment at 25 weeks' GA on average, the optimal timing of antenatal HCV treatment remains unknown. For example, we waited until after the anatomy scan at 18–20 weeks' GA to start treatment, but the need for this is uncertain. Prospective studies like IMPAACT 2041 are urgently needed to guide best practices to optimize maternal and fetal health.

In conclusion, our findings provide real-world data supporting the IDSA/AASLSD guidelines stating that DAAs, including GLE/PIB, may be offered to pregnant patients with HCV. Additional studies are needed to improve uptake of share decision-making approaches to offering DAA treatment in pregnancy, in order to improve patient outcomes and reduce perinatal transmission of HCV.

Notes

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