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EDITORIAL COMMENTARY

Treatment of Hepatitis C During Pregnancy: We Are Approaching a "Tipping Point"

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Over the last 15 years, chronic hepatitis C virus (HCV) infection has evolved from a difficult-to-treat condition using interferon therapy to one that is readily treated with once-daily oral direct-acting antivirals (DAAs), resulting in viral cure for nearly all patients [1, 2]. While the uptake of DAA treatment among the general population has continued to progress over the years, there is one subpopulation who has been left far behind: pregnant women [3]. Research on DAA use in pregnancy had been virtually nonexistent with a paucity of papers studying this population. Most official guidelines still do not recommend treatment, but the AASLD/IDSA HCV guidelines committee has endorsed an individualized shared-decision making approach [4, 5]. Some recent studies in pregnancy have demonstrated the same viral cure rates as nonpregnant patients with no significant safety concerns in the patients or their offspring [6–8]. These results suggest we as providers of HCV treatment are approaching a "tipping point" toward widespread treatment in pregnancy. The potential benefits of treatment during pregnancy have been discussed in detail elsewhere, but briefly they include maternal cure, potential elimination of vertical transmission events, short treatment duration that aligns well with prenatal care schedules, and high patient engagement during pregnancy [3, 9]. Despite the positive results of prior studies of HCV treatment in pregnancy, there has been 1 major lingering issue. Virtually, all of the studies have been conducted using the combination of sofosbuvir and velpatasvir [6, 10, 11]. While this combination is highly efficacious and well tolerated, it is often not the first choice regimen of treaters and payors due to its higher cost and longer treatment duration (12 weeks). Research in pregnancy with the more commonly used regimen of glecaprevir–pibrentasvir (G/P) with a shorter duration of 8 weeks has been notoriously absent. That is, until now.

In this issue of *Clinical Infectious Diseases*, McCrary et al report their experience using G/P for treatment in pregnancy in a clinic they established to treat chronic hepatitis C in pregnant patients with known substance use disorder [12]. Their results highlight their attempt to address the "real-world" issues that plague HCV treatment efforts. To eliminate the need for additional in-person visits, study visits were conducted via telemedicine. They dispensed the entire 8-week course of DAAs at the initiation of treatment. They performed follow-up testing as early as 4 weeks after therapy (SVR4), which is an evolving standard to improve confirmatory test rates compared to the established standard of 12 weeks (SVR12) [13]. Their bottom-line results were very promising: 100% SVR in those who were tested, no safety events among the pregnant patients or their infants, and no detected vertical transmission events. We must acknowledge the limitations of this work. Only 10 patients completed treatment, with 9 achieving confirmed SVR4; furthermore, only 6 infants underwent follow-up testing. Despite these limitations, the successful treatment outcomes in this small group of patients should pave the way for larger studies of G/P (such as the IMPAACT 2041 study that is currently open to enrollment) while also supporting more informed shared decision-making between providers and patients regarding the use of G/P during pregnancy.

What happens now? Hopefully, a few things. With these data, more providers will engage in treatment discussions with their pregnant patients. The outcomes of what we anticipate will be successful treatment can be shared with others via an established registry, such as the TiP-HepC registry sponsored by the Coalition for Global Hepatitis Elimination (https://www.globalhep.org/projects-research/treatment-pregnancy-hepatitis-c). These data can be assembled into evidence briefs to inform future shared decision-making discussions. Ultimately, this may lead to a firm recommendation by all involved specialty societies (AASLD, IDSA, ACOG, SMFM, and others) to establish

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treatment during pregnancy as the default approach. However, increased treatment uptake is contingent upon appropriate prenatal screening. Most patients are still not tested in accordance with current guidelines [14, 15]. Results from the McCrary study demonstrate that patients who undergo screening are often tested later in pregnancy than is desirable for an efficient DAA treatment course. What will enable more testing? Better patient engagement and support, particularly for those individuals with substance use disorders. We still need robust point-of-care testing, allowing patients and providers to make immediate, informed treatment decisions [16, 17]. Other countries, such as Australia, have embraced this approach in various settings to accelerate viral hepatitis elimination [18]. With a stated goal of elimination, the United States has taken steps in this direction but is still far behind where it needs to be.

McCary et al should be commended for taking these important early steps toward expanding HCV treatment during pregnancy. The rest of us need to continue this momentum by identifying and implementing strategies that incorporate some or all of their practices, thereby increasing access to DAA treatment for pregnant patients. We must also continue to advocate for society guidelines that are rapidly updated to reflect emerging evidence that demonstrates the safety and efficacy of HCV treatment during pregnancy.

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