HCV and pregnancy: is now the time for universal testing?

Steven A Pergam†, Stephen E Hawes, Carolyn M Gardella & Chia C Wang

†Author for correspondence Department of Medicine, University of Washington, Fred Hutchinson Cancer Center, 1100 Fairview Ave. North, D3-100, PO Box 19024, Seattle, WA 98109, USA spergam@fhcrc.org

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'An estimated 40,000 women chronically infected with HCV become pregnant every year in the USA.'

Hepatitis C virus (HCV) affects up to 3% of the world's population [1]. Chronic infection occurs in most HCV-infected patients, causing end-stage liver disease in approximately 20% [2]. Intravenous drug use (IVDU) is the most common risk factor, accounting for 60–80% of cases in the USA. In those without history of IVDU, sexual, household and iatrogenic risk factors are likely modes of transmission [3,4].

Approximately 1.6% of the US population is estimated to be HCV-antibody-positive, but prevalence depends on age and other characteristics of the population [5]. For example, the prevalence in active IV drug users is 80–100% [6]. Seroprevalence rates in pregnant women generally range from 0.6 to 2% [7], but may be as high as 4.4% in inner-city populations [8]. An estimated 40,000 women chronically infected with HCV become pregnant every year in the USA.

The Centers for Disease Control and Prevention (USA) and the American College of Obstetricians and Gynecologists (ACOG) recommend testing at-risk pregnant women for HCV as part of prenatal care. Testing is encouraged for pregnant women with any history of IVDU, those working in high-risk settings, or those with HIV or hepatitis B infection. Women who received a blood transfusion or solid organ transplant before July 1992, received clotting factor concentrates before 1987, underwent long-term dialysis, and those with signs or symptoms of liver disease should also be tested [9,10].

While most experts agree with these recommendations, others advocate for universal HCV testing in pregnancy. In this editorial we address arguments for and against universal testing in the context of recently published data. In the process we review potential complications associated with HCV in pregnancy, identify areas for future research and emphasize the importance of adequate screening in practice.

Arguments for universal testing

Arguments for universal testing of pregnant women focus on;

- The inaccuracy of self-reported drug use in pregnant women
- The prevalence of non-IVDU modes of transmission in pregnant woman
- Inconsistencies in provider screening for HCV-related risk factors and HCV infection
- The benefits of early detection.

Current recommendations depend on the ability to identify at-risk women. Practitioners face challenges identifying these women, particularly in regards to recreational drug use. In high-risk non-pregnant populations for example, under-reporting of drug use can bias prevalence estimates [11]. Eliciting such information in pregnant women may be further hampered by perceived consequences such as legal ramifications and potential loss of custody, leading to inaccurate responses to screening questions. Unsurprisingly, studies demonstrate that self-reporting is an unreliable method to determine drug use in pregnancy [12–14].

Rates of IVDU in HCV-positive pregnant women range between 32 and 50% [15–18], less than the 60–80% reported in HCV-positive patients in the general population [19]. These figures suggest pregnant women may be more likely to acquire HCV infection through non-IVDU exposures. An increased risk of HCV in pregnant women living with partners with HCV or an IVDU history suggests a larger role for sexual or household transmission [17,20]. Even more troubling, up to 40% of pregnant women may have no identifiable risk factor [15].

Obstetricians may also miss opportunities to test at-risk women for HCV. In one study, less than 50% of obstetricians recommended testing patients with histories of IVDU, and only 30% for patients who had recieved blood transfusions prior to 1992 [21]. Furthermore, while 60% of Australian gynecologists routinely tested for HCV, only 20% routinely asked about risk factors for blood-borne infections [22]. Local rates of HCV and HIV, misconceptions about HCV and limited HCV treatment options may influence a provider's likelihood for following testing guidelines.

Universal testing has the advantage of identifying women not captured by current guidelines. Pregnancy is an opportunity to identify women with HCV, many of whom may not have otherwise sought, nor had access, to primary care. Since few are aware of their serologic status [23], early diagnosis could be the most important reason in support of universal testing for HCV. Those identified as HCV-positive could benefit from opportunities for evaluation and treatment, alcohol abstinence and access to primary care and monitoring.

Arguments against universal testing

Since 2–4% of HCV-infected mothers transmit infection to their infants perinatally [7], universal testing would be more strongly advocated if knowledge of maternal status could decrease this risk. Therapy for HCV in pregnancy is currently not recommended due to the potential teratogenicity of current treatment agents [24]. Furthermore, unlike the case for HIV, cesarean section has not been shown to decrease rates of vertical transmission. A few studies suggest decreased rates of perinatal HCV transmission with cesarean section [25], but a large metanalysis found no protective benefit [26].

Others have indicated an increase in HCV transmission through invasive monitoring and prolonged rupture of membranes [27,28], but these findings are debated [25]. Additionally, breastfeeding has not been shown to increase the risk of transmission [29]. If prevention of vertical transmission is a primary goal of early testing, the lack of effective interventions argues against more rigorous efforts to detect maternal HCV infection.

Pregnancy does not appear to impact HCV disease progression, as evidenced by the lack of changes in liver function or level of viremia during pregnancy [30,31]. Perinatally-acquired HCV is also relatively asymptomatic during childhood. In the first year of life greater then 50% of children have elevated liver function tests [32,33], but early clinical symptoms are rare. HCV viremia clears in up to 25% of infected children [33,34]. Hepatic fibrosis and/or minimal to mild hepatitis is present in nearly 75% of infected children on liver biopsy [33,35,36], but progression to cirrhosis and liver transplantation due to HCV during childhood is rare [37]. Information on the progression of disease into adulthood in perinatally-infected children is currently lacking.

While data do not support adverse consequences of pregnancy on the course of HCV infection in mothers, and support a benign natural history for children infected at birth, few studies have examined peripartum effects of HCV infection on maternal and neonatal health. The limited data that are available come to varying conclusions. While maternal HCV was not associated with obstetric complications in a number of studies [23,38,39], one reported that women with HCV viremia had an increased risk of premature rupture of membranes [40]. Two studies demonstrated an increased risk of gestational diabetes in pregnant women with HCV [41,42]. While the known association of HCV infection with insulin resistance in nonpregnant persons [43] suggests a potential biologic plausibility to these observations, further study is needed to confirm these findings.

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Data regarding the effect of HCV on neonatal outcomes is also contradictory. Two studies found no difference in rates of prematurity in children born to HCV-positive women [20,39], while another demonstrated higher rates of prematurity and spontaneous abortion in women with acute hepatitis [44]. A study in HIV-positive women demonstrated higher rates of low birth weight children (<2500 g) born to those coinfected with HCV [42], and another demonstrated higher rates of neonatal intensive care unit admission and need for assisted ventilation [41]. Apgar scores on the other hand, appear to be similar regardless of maternal HCV status [20,23,38,41]. Owing to their narrow scope and retrospective nature, conclusions that can be drawn from these studies are limited.

Perhaps most importantly, costs of identifying a single pregnant woman using universal testing were estimated to be more than twice that of current standard of care [45]. Universal testing of asymptomatic women is not cost–effective, even when modeled under the assumption that primary cesarean section reduces the risk of perinatal transmission, and when costs associated with chronic infection in the mother are taken into account [46]. Unless the potential risks associated with HCV on peripartum outcomes are substantiated, universal testing does not appear to be cost–effective.

Conclusion & future directions

Current studies provide insufficient evidence to advocate for universal testing for HCV, but data do suggest that current screening approaches could be improved. Expanding criteria to include testing women with less common risk factors would enhance identification of those missed by current guidelines. Providing optional testing for pregnant women may be more acceptable for patients concerned about self exposure, and could lead to improved detection of high-risk patients. Finally, increased provider education regarding the risk factors for HCV in pregnancy could also maximize identification of at-risk women.

Reviewing guidelines for testing pregnant women is particularly timely as newer, more effective antiviral therapy for HCV are currently being developed. Such therapies may render it even more essential to identify HCV in pregnancy. Not only providing the opportunity to counsel about the risk of vertical transmission, early testing would take advantage of this limited period of engagement to identify and potentially eradicate HCV in these women.

Further evaluation of the impact of HCV on short- and long-term effects on pregnancy outcomes, longitudinal studies in perinatally acquired infection and treatment options for pregnant women and children are needed. Until then, efforts to increase awareness of the relevance and pitfalls of current recommendations for risk factor driven HCV testing should remain standard care for all providers caring for pregnant women.

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Affiliations

- *Steven A Pergam, MD*
  Department of Medicine, University of Washington, Fred Hutchinson Cancer Center, 1100 Fairview Ave. North, D3-100, PO Box 19024, Seattle, WA 98109, USA
  spergam@fhcrc.org
- *Stephen E Hawes, PhD*
  University of Washington, Department of Epidemiology, WA, USA
- *Carolyn M Gardella, MD, MPH*
  University of Washington, Department of Obstetrics and Gynecology, WA, USA
- *Chia C Wang, MD, MS*
  Virginia Mason Hospital, Department of Medicine, WA, USA