Universal Screening of Pregnant Women for Hepatitis C: The Time Is Now

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The epidemiology of hepatitis C virus (HCV) has changed significantly over the last decade. Once most prevalent among older adults, the current burden has disproportionately affected young adults including women of childbearing age (WOCA). The Society for Maternal-Fetal Medicine recently issued guidelines that made no change in the recommendation to screen pregnant women based on risk factors. The current burden in young adults including WOCA supports a change in strategy away from risk-based screening to universal HCV screening in pregnancy. Universal screening offers several advantages that position us for a future where HCV treatment in pregnancy can happen and offers us progress toward the elimination of HCV.

Keywords. hepatitis C virus; pregnancy; universal screening; mother-to-child transmission; direct-acting antivirals.

Hepatitis C virus (HCV) is widely acknowledged as a national and global health problem and is the leading single infectious cause of mortality in the United States [1]. While previously considered a problem focused largely on predominantly male veterans and “baby boomers,” the cohort born between 1945 and 1965, the epidemiology of HCV has changed tremendously over the last decade, driven by tremendous increases in nonurban young adults associated with injection drug use in the United States. This new wave of HCV infections has occurred largely in young adults and teenagers of both sexes. Embedded within the young adult population are women of childbearing age (WOCA), a group that raises the unique issue of mother-to-child transmission (MTCT) of the virus. Current public health policy endorses universal screening for baby boomers and risk-based screening for all other groups including pregnant women. While all pregnant women are universally screened for human immunodeficiency virus (HIV), hepatitis B virus (HBV), and many other infections, HCV is notably absent from this list. The Society of Maternal-Fetal Medicine (SMFM) and the American College of Obstetrics and Gynecology have recently reaffirmed the position of risk-based screening of pregnant women [2]. Others have advocated that now is the time to implement universal screening

[3–6]. In sharp contrast to the SMFM document, we argue that universal screening of pregnant women should be adopted based on the current epidemiology of HCV, the recommendation for change in obstetrical practices for women known to have HCV infection, and the availability of highly efficacious treatment regimens for these women after they give birth [2]. This practice will best position providers for what is coming in the near future and allow for early identification of infants at risk. Universal HCV screening of pregnant women has now been recommended by the American Association for the Study of Liver Diseases/ Infectious Diseases Society of America (AASLD/IDSA) HCV guidance panel along with each society [7].

CHANGING EPIDEMIOLOGY

An informed policy for HCV screening should be based on the most recent epidemiology of the epidemic. Several recent publications highlight the disproportionate burden of HCV in young adults linked to the national opioid epidemic and specifically in WOCA. While certain localities reported increasing rates of HCV among young people, the Centers for Disease Control and Prevention (CDC) in 2014 described the increasing number of cases of HCV nationally and the associations with nonurban locale, white individuals, current/prior drug use, and an equal distribution among men and women [8–11]. A subsequent CDC study described HCV seroprevalence nationally by using data from a national referral laboratory to develop population-level estimates [12]. These data showed that national prevalence estimates from 2011 to 2014 increased from 132 to 169/100 000 tested samples, with Kentucky prevalence estimates soaring from

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275 to 862/100 000 tested samples. In 2017, CDC authors used the same national referral laboratory data to examine national trends for HCV among WOCA [13]. A significant increase in HCV detections from 2011 to 2014 was demonstrated across the entire United States. Current estimates indicate 29 000 HCV-infected women giving birth to 1700 infected infants yearly, far exceeding prior projections [14]. Overall, 1.34% of the female population aged 15–44 years were HCV antibody positive with marked geographic consistency (1.25% South, 1.36% Northeast, 1.37% West, 1.63% Midwest). These trends document the increasing risk among WOCA and have been described individually in several states across the country [15, 16]. These reports not only demonstrate the massive increases in HCV cases but also demonstrate that no single region of the country is affected in isolation and that regions within states may have dramatically different rates of HCV. None of these articles were referenced in the recent SMFM publication.

THE CASE FOR UNIVERSAL SCREENING

Beyond the changes in epidemiology, what factors support the case for universal screening? First, risk-based screening has been repeatedly demonstrated to miss many cases of HCV infection [4, 17, 18]. Either providers do not ask about risk factors or patients do not volunteer this information. In a detailed look at the results of the 2017 CDC article mentioned above, the HCV antibody positive rate in tests sent from obstetricians was 0.37%, far lower than any other provider group listed (pediatrics, 1%; primary care, 1.62%; infectious diseases, 6.57%; and gastroenterology, 14.69%) [13]. A superficial analysis might suggest that obstetricians are not seeing HCV-infected patients. However, given the risk-based screening recommendation and the much lower rate than in other settings, the more likely explanation is that the HCV-infected patients are not being questioned and therefore not being identified. The only published survey regarding screening and counseling practices among obstetrician–gynecologists showed numerous gaps that would limit the effectiveness of risk factor–based screening alone [19]. Anecdotally, many obstetricians in high-prevalence states are independently screening all pregnant women for HCV. Risk-based screening also has the potential to create an ethical challenge for providers, as uncovering information about drug use carries implications for child custody and could prevent honest and open communication to facilitate care for at-risk women. It should be noted that similar arguments in favor of risk-based screening were made years ago when the issue of universal HBV screening of pregnant women was raised. The same failure of that strategy was documented, and the universal screening policy was adopted and accepted, even though at-risk women are rare in some practices [20, 21]. It is likely that HCV infection will be more common in standard obstetric practices than unidentified HBV or HIV infection. Unless risk factor–based screening is validated as effective, which has not been shown in any population, universal screening is much more likely to identify

the full burden of cases. These issues are not unique to pregnancy, and a recent study estimated that 1-time universal screening of all young adults (including WOCA) would be cost effective [22].

Second, many young women may consistently seek medical care only during pregnancy. As has been previously noted for HIV and anecdotally by many HCV experts, the compliance of pregnant women for testing and follow-up is higher as they consider the future of unborn children [23, 24]. Studies have shown that after delivery, this compliance wanes, and reengaging these women in care can be difficult [24].

Third, universal testing could be easily packaged within the current prenatal screening practices. HCV antibody testing could be performed with intake laboratory testing, and pooling of samples for batch testing could be done to reduce the cost of testing and lower the rate of low-level false-positive testing.

Fourth, knowledge of HCV status could influence provider decisions and patient behavior. Providers could make more informed decisions about a woman's HCV status and plan appropriately during delivery to avoid invasive procedures known to promote HCV transmission (eg, scalp electrode monitoring). Changes in obstetrical practice for women known to be HCV infected are recommended in the previously referenced SMFM guideline. Yet, without universal screening, some infected women will not have the benefit of these recommendations, perhaps putting their newborns at unnecessary risk for MTCT. Additionally, a woman with knowledge of her status could be offered harm-reduction counseling, may be more motivated to cease engaging in high-risk behavior (injection drug use), and could engage injection partners to seek testing and care for themselves. If identified early, she could also be referred for evaluation and planned HCV therapy while still pregnant and perhaps while still covered by public insurance during pregnancy. A recently presented abstract showed that early identification of HCV in pregnant women did lead to increases in completed referral visits [25]. Ideally, this kind of intervention could be delivered in a public health–clinical care partnership model similar to those in place for HIV and HBV.

Fifth, this knowledge could also help facilitate the evaluation of HCV-exposed infants, as it is well known that the vast majority of these infants never undergo follow-up testing [26].

Finally, treatment of HCV can be life extending. Chronic HCV infection is associated with, on average, 20 years of lost life expectancy; screening during pregnancy allows identification and treatment that restores this loss. Identifying all infections during pregnancy would provide a unique opportunity to enhance maternal long-term health.

REFUTING THE COMMON ARGUMENTS MADE AGAINST UNIVERSAL SCREENING

A variety of arguments have been made against universal HCV screening of pregnant women. One common concern is that an identified HCV-infected pregnant woman does not currently

have any (intrapartum) treatment options. Direct-acting antivirals (DAAs), now in use for HCV, have safety profiles that are similar to those of other antivirals that are already widely used in pregnant women including, zidovudine, lamivudine, tenofovir, and valacyclovir. Ribavirin, with its teratogenic potential, is no longer part of regimens used for primary treatment of HCV. While DAAs have not yet been approved for use in pregnancy, it is indisputable that finding HCV-infected women during pregnancy is a necessary first step. It is also critical to alert clinicians to test the newborns for infection. A woman who is identified as infected could be treated for HCV after pregnancy and be cured of her infection. The power of cure should be extremely compelling. In the current era of injection drug use and increasing HCV cases, the best public health strategy to reduce the prevalence and incidence of HCV is identification and treatment of as many young adults as possible to reduce the reservoir of individuals able to infect others. With respect to intrapartum HCV treatment, we strongly emphasize the word “currently” in that sentence as DAAs have this potential with short enough treatment lengths to fit into late pregnancy. There is currently an ongoing clinical trial of DAAs in pregnant women that will inform this practice in the near future (Clinicaltrials.gov #NCT02683005).

Despite the current lack of treatment options, the SMFM has recommended avoidance of fetal scalp monitoring, prolonged rupture of membranes, episiotomies, and chorionic villus sampling in HCV-infected pregnant women [2]. Careful clearance of maternal blood and secretions prior to neonatal vitamin K administration might also be considered. The risk imposed by amniocentesis in women with HCV should be factored into the informed consent for this procedure. It is also important to communicate the lack of evidence supporting elective cesarean section deliveries in HCV-infected women in order to avoid unnecessary risk and expense.

Another argument against universal HCV screening is the need to manage or retest “false-positive” antibody results. While 15%–25% of women who have HCV antibody may be negative for serum HCV RNA, and a small fraction of women may be “false positive,” all positive HCV screening tests need follow-up HCV RNA testing to assess for chronic infection, just as HIV and HBV antibody screening tests need confirmation with Western blot or nucleic acid testing [27]. Antibody-positive screening tests, true or “false,” like any screening test, need confirmation. It should be noted that a positive HCV antibody test may be a surrogate marker for past or present injection drug use and should lead to counseling for harm reduction and syringe access to reduce future risk of reinfection.

The third argument is that the additional cost of testing would be a burden. Given that blood samples are already obtained early in pregnancy for complete blood count, blood typing, rubella, and hepatitis B and HIV testing, there would

be no additional visit or phlebotomy required for adding HCV testing. In the past, a strategy for pooling samples for batch testing was used as a means to lower screening costs and potentially lower the rate of false-positive tests for low prevalence conditions [28]. However, the cost of the anti-HCV test (an enzyme-linked immunosorbent assay test) is quite modest [29], and the cost-effectiveness of conventional screening is expected even in very low prevalence populations [22]. Many of these concerns have already been addressed for HIV, HBV, and several other infections, all of which are much less prevalent than HCV and all of which lead to fewer infections in infants than HCV does now.

Finally, concerns are often raised that universal screening could lead to an increase in cesarean section rates due to concerns for transmission. It is worth noting that cesarean section has never been shown to be protective against HCV MTCT [30–32]. Cesarean section is not recommended in HCV-infected pregnant women unless it is indicated based on other obstetric risk factors. This is the position outlined in the SMFM document as well as in the AASLD/IDSA recommendations for management of HCV in pregnancy [2, 7].

THE POWER OF DIRECT-ACTING ANTIVIRAL THERAPIES AND A GLIMPSE INTO A POTENTIAL FUTURE

DAAs have revolutionized HCV therapy in a very short amount of time. HCV treatment used to rely on complicated treatments of prolonged duration, with serious side effects, that only led to successful outcomes half the time [33]. DAAs are oral, once-daily, well-tolerated medications that can be given for as little as 8 weeks and lead to HCV “cure” more than 95% of the time [34–36]. While still high, costs of these therapies are coming down. From 2014 to 2018, state Medicaid program restrictions on DAA therapy based on fibrosis score or sobriety status have been liberalized slowly [37]. If proven safe and effective during pregnancy, these high cure rates with rapid suppression of HCV viremia combined with a short duration of 8 weeks means that treatment could easily be achieved late in pregnancy but prior to delivery. Because the presence of viremia is the only absolute risk factor for HCV MTCT, if a pregnant woman were to be cured of her HCV infection, any risk of transmission to the infant would be eliminated [30, 31]. This outcome would obviate the need for screening their exposed infants. The discussion of treatment during pregnancy gets a bit ahead of the discussion of universal screening, as we first have to put systems in place to identify HCV-infected women and draw attention to the need to treat them during this time. Pharmaceutical companies will not consider this population for therapy unless we as providers demand it of them and demonstrate that we will use these drugs during pregnancy. The status-quo approach of risk-based screening does not position us for this strategy, but universal screening does.

WHY NOW?

Why should we start universal screening now as opposed to a few years from now when the data show that the wave of HCV infections will far exceed the current figures of 29 000 pregnant women and 1700 infected infants [13]? Aside from the previously stated fact that the current epidemiology justifies the change, it takes considerable time to get to the point where patients are actually being tested in accordance with the recommendations. Studies have repeatedly demonstrated that despite baby-boomer screening being the recommendation since 2012, many adults born from 1945–1965 are still not being screened for HCV [38]. The sooner we start, the sooner we reach our goal of eliminating HCV as a public health problem in the United States. The longer we wait, the more opportunities to identify HCV-infected WOCAs are missed [39].

CONCLUSIONS

The time is now for universal screening of pregnant women for HCV. The current epidemiology nationwide justifies it, and the potential limitations can be mitigated with thoughtful strategies for implementation. DAAs enable a future where pregnant women could be treated once identified, and universal screening of pregnant women is a critical first step to that future. The AASLD/IDSA has issued a recommendation for universal screening, and the hope is that other stakeholder professional organizations will do the same. This is an opportunity for obstetricians and other providers who evaluate pregnant women to play a critical role in contributing to the elimination of HCV in the United States.

Notes

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