Labour pains: eliminating HCV in women and children

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Hepatitis C virus (HCV) is a major global public health problem and a leading cause of death worldwide.[1] However, HCV is a problem that can be remedied with enough public health investment. Curative treatment with safe, short-course, direct-acting antivirals has been available for several years, and elimination is in reach.[2] Thus, the priority now is to identify and treat all those who are infected, reduce morbidity and mortality, and prevent new infections, including those that are acquired through mother-to-child transmission.

Ellen Dugan and colleagues[3] provide an important contribution to the field with their modelled estimates of 2019 global prevalence of HCV in women of childbearing age (15–49 years). Dugan and colleagues[3] found that almost 15 million women aged 15–49 years might be living with HCV, accounting for a fifth of the global population with viraemic HCV. Importantly, the authors estimated prevalence at a national and regional level. The huge burden of infections in predominantly low-income and middle-income countries is striking, with China, Pakistan, Russia, and India accounting for nearly half the global HCV infections in women of childbearing age. This wealth imbalance in the global distribution of infections has implications for how we target women for testing, treatment, and prevention of onward transmission to infants. There are also implications for the prevention of reinfection, given that the primary driver of transmission is unsafe health-care practices in many low-income and middle-income settings.[2]

The authors recommend preconception test and treat strategies, suggesting that routine gynaecological visits for the general population of women are a way to identify those with HCV. Although this approach might be feasible in high-income countries, with delivery through established cervical screening programmes, it might not be feasible or cost-effective in many low-income and middle-income countries, where gynaecological access is rarely available. For example, some of the countries estimated to have the highest burden of HCV also have a high burden of cervical cancer,[4] reflecting failures in rolling out cervical screening and vaccination against human papillomavirus. Even in high-income settings with concentrated HCV epidemics like the USA, HCV testing linked to gynaecological visits is likely to miss women at the highest risk of HCV, namely those who inject drugs.[5] Other universal health interventions include community-based mass HCV screening and treatment programmes, as in Egypt, although these efforts exclude pregnant and lactating women because of the paucity of treatment options available to them.

In high-income countries, universal antenatal (or prenatal) HCV testing has been shown to be cost-effective,[6] and is now recommended in the USA.[5] However, as direct-acting antivirals have yet to be approved in pregnant or lactating women due to sparse safety data, these groups have been completely left out of the treatment cascade, creating a huge gap in treatment access. Small studies suggest that direct-acting antiviral regimens without ribavirin, given in the second and third trimester of pregnancy, are safe, with a high rate of maternal cure, no vertical transmissions, and few (often mild) adverse effects,[7,8] but much larger trials are needed to confirm these findings. In the meantime, the strategy is to keep women linked into care post-partum and treat them after they stop breastfeeding. Unfortunately, all evidence to date (mainly from high-income settings) show very poor engagement in the post-partum care cascade,[9] and engagement could be worse in many low-income and middle-income countries like Pakistan, where women breastfeed for a median of 2 years. This treatment gap serves as a gender imbalance and effectively obstructs women from benefitting from the advantages of cure; aside from the harmful effects of HCV on maternal and infant outcomes, there is also the risk of vertical transmission to successive children.[10] Importantly, there are no treatment options for infants younger than 3 years, and the net result is that few women and children with HCV are receiving timely treatment, and so they remain at risk of progressive liver disease.

Dugan and colleagues' paper is important because it clearly shows how women of childbearing age need to be recognised as a key risk population for HCV prevention, treatment, and cure, if we are serious about elimination.[3] Multiple approaches are needed to diagnose and treat all women of childbearing age, including mass community-based screening and treatment programmes and universal antenatal

screening, which is the cornerstone of maternal and child health. Additionally, the risk of reinfection needs to be reduced through continued focus on improving safety in medical practices. However, these efforts will have little benefit without well conducted, large clinical trials to ascertain the safety of direct-acting antivirals in pregnancy and during the lactation period, which have the potential to cure the mother and prevent HCV in the baby. Such trials are crucial in paving the way for equitable access to treatment for all women living with HCV.

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