Research Article
Viral Hepatitis

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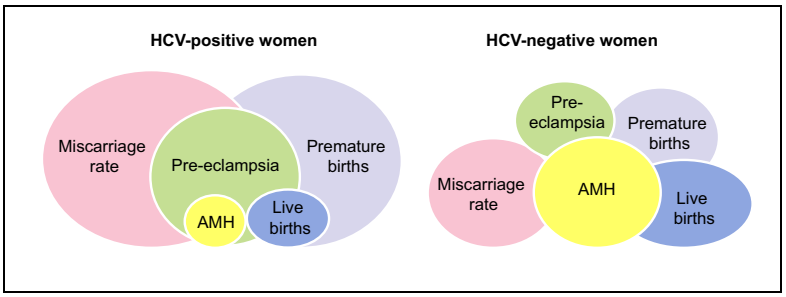
Premature ovarian senescence and a high miscarriage rate impair fertility in women with HCV

Graphical abstract



Highlights

- Women of child-bearing age who are HCV positive undergo premature ovarian senescence.
- Such women have fewer live births, and higher rates of miscarriage and gestational diabetes.
- Total fertility rate in women who are HCV positive *vs.* the general population is 0.7 *vs.* 1.37.
- Miscarriage rate is significantly reduced by successful HCV treatment.
- Antivirals should be tested for their effects on other adverse pregnancy outcomes.

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Lay summary

Most new cases of HCV infection are among people who inject drugs, many of whom are young women in their child-bearing years. Women of reproductive age who are HCV+ display markers of ovarian senescence. This is associated with an increased burden in terms of infertility and adverse pregnancy outcomes, including stillbirth, miscarriage, fewer live births, and gestational diabetes. Early viral suppression with therapy is likely to mitigate these risks.

http://dx.doi.org/10.1016/j.jhep.2017.08.019
 J. Hepatol. 2018, 68, 33–41

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Premature ovarian senescence and a high miscarriage rate impair fertility in women with HCV

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Background & Aims: Premenopausal women who are HCV positive (HCV+) have failing ovarian function, which is likely to impact their fertility. Thus, we investigated the reproductive history, risk of infertility, and pregnancy outcomes in women of childbearing age who were HCV+.

Methods: Three different groups were studied: (1) Clinical cohort: 100 women who were HCV+ and also had chronic liver disease (CLD), age matched with 50 women who were HBV+ with CLD and with 100 healthy women; all women were consecutively observed in three gastroenterology units in hospitals in Italy; (2) 1,998 women who were HCV+ and enrolled in the Italian Platform for the Study of Viral Hepatitis Therapies (PITER); (3) 6,085 women, who were mono-infected with HCV, and 20,415 women, who were HCV−, from a large de-identified insurance database from the USA. Measurements: total fertility rate (TFR) defined as the average number of children that a woman would bear during her lifetime. To define the reproductive stage of each participant, levels of anti-Müllerian hormone (AMH) and 17β-estradiol were measured.

Results: Clinical cohort: women who were either HCV+ or HBV+ had similar CLD severity and age at first pregnancy. Based on a multivariate analysis, women who were HCV+ had a higher risk of miscarriage than those who were HBV+ (odds ratio [OR] 6,905; 95% CI 1.771–26.926). Among women who were HCV+, incidence of miscarriage was correlated with median AMH level (1.0 ng/ml). Achieving a sustained virologic response (SVR) after antiviral treatment reduced the risk of miscarriage (OR 0.255; 95% CI 0.090–0.723). In the PITER-HCV cohort, miscarriage occurred in 42.0% of women (44.6% had multiple miscarriages). TFR for women who were HCV+ and between 15 and 49 years of age was 0.7 *vs.* 1.37 of Italian population of the same age range. In the US cohort: compared with women who were HCV−, women who were HCV+ positive were significantly more likely to have infertility (OR 2.439; 95% CI 2.130–2.794), premature birth (OR 1.34; 95% CI 1.060–1.690), gestational diabetes (OR 1.24; 95% CI 1.020–1.510), and pre-eclampsia (OR 1.206; 95% CI 0.935–1.556), and were less likely to have a live birth (OR 0.754; 95% CI 0.622–0.913).

Conclusions: Ovarian senescence in women of childbearing age who are HCV+ is associated with a lower chance of live birth, greater risk of infertility, gestational diabetes, pre-eclampsia and miscarriage. Such risks could be positively influenced by successful HCV cure.

Keywords: Anti-Müllerian hormone; Antiviral therapy; Sustained viral response; HBV; HCV.
Received 5 March 2017; received in revised form 24 August 2017; accepted 27 August 2017; available online 5 September 2017

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