

Diagnosis of latent TB infection in HIV-infected pregnant women – “Baby Steps” towards better TB control in pregnancy.

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Despite significant reductions in incidence, the global burden of Tuberculosis is immense. In 2014 there were an estimated 9.6 million new cases, accounting for 1.1 million deaths and with an estimated 1.2 million (12.5%) of these being HIV infected (1). Although TB is more common amongst men, globally TB is a leading cause of death amongst women of child-bearing age(1). The higher risk of TB during pregnancy, as well as adverse outcomes for mother and child have been previously recognised(2–5) and are potentially related to the physiological partial inhibition of the cellular immune system necessary to tolerate the fetus(6, 7).

There is evidence of treatment delays for TB in pregnancy, possibly related to diagnostic difficulties because of symptom masking by the pregnancy and greater reluctance for diagnostic tests, particularly imaging as well as general lack of awareness(4, 5). These delays may be one explanation for the poorer outcomes of TB for mother and child.

Short of a better vaccine and to maximise our chance to decrease morbidity and mortality from TB among pregnant women, it will be necessary to prevent TB disease before it occurs. To accomplish this task, we will need to improve our understanding of the performance of available diagnostic tools for latent TB infection (LTBI) in pregnancy as well as develop new ones so that individuals at high risk for developing TB disease that would benefit from treatment during pregnancy or in the post-partum period can be identified. Whilst differences in diagnostic properties between interferon gamma release assays (IGRAs) and tuberculin skin tests (TSTs) have been previously demonstrated in various populations (8), including HIV-negative pregnant women(9), the evidence of LTBI test properties and concordance in pregnant populations is scarce, particularly in the group for which it may be most needed, those who are HIV-infected.

This month's journal presents research from Mathad and colleagues which provides valuable new insights into the behaviour of Quantiferon (QFT, an ELISA-based IGRA) and the TST in HIV-infected women during pregnancy(10). In their linked cross-sectional and longitudinal studies, the authors examined the positivity and association of these two immunological tests with active TB progression, as well as their discordance with each other among 252 HIV-infected, pregnant women. They found a rather large discordance between the two LTBI tests with IGRA demonstrating a higher positivity rate as well as the finding of a better association between IGRA positivity and TB disease progression. In their longitudinal study, the authors also demonstrated that individuals with QFT positive/TST negative discordance had lower quantitative interferon gamma and interleukin-2 responses compared with those with concordant results and observed a decrease in quantitative interferon gamma concentration during the course of the pregnancy and postpartum. The latter novel findings would support the hypothesis of a weakening of T-cell mediated immune response during the course of the pregnancy, something which could explain the higher risk of active TB observed in late pregnancy and postpartum(4) as well as provide some insights as to the best timing for administering these tests .

Of course, this paper has a number of limitations. It is a small study, and although it demonstrated a larger number of women with active TB outcomes, it did not have enough statistical power to firmly demonstrate predictive values of disease progression between the LTBI tests or combinations thereof. There are other limitations, such as the lack of information on important confounders including co-morbidities, antiretroviral use or potential other relevant co-infections, such as with helminths. This means that results will require validation with well-designed large prospective studies.

Nonetheless, the interesting and highly relevant findings of this paper provide new insights into the complex immunology of HIV-infected pregnant individuals and offer direction for new research aimed at reducing the burden of TB in pregnancy. Much remains to be done, including immunological, epidemiological and operational research to inform important policy decisions about LTBI testing, and treatment in pregnancy, but this paper provides an important step toward greater TB control in high risk HIV infected pregnant women.

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