Impact of Tuberculosis on Maternal and Child Health

Ben J. Marais

1Department of Paediatrics and Child Health, Tygerberg Children's Hospital, Stellenbosch University, Tygerberg, South Africa

(See the article by Gupta et al, on pages 358–362.)

Tuberculosis (TB) is the most important infectious cause of disease and death in women residing in areas where TB is endemic, such as sub-Saharan Africa and Asia [1]. Traditionally, the majority of TB cases reported were in men, but the global human immunodeficiency virus (HIV) epidemic induced major changes in TB epidemiology. The preponderance of HIV-infected women (women account for up to 70% of HIV-infected adults in areas where heterosexual HIV transmission is dominant) may explain why more women than men receive a diagnosis of TB in countries where HIV infections prevalence is high [2]. TB and TB-HIV coinfection are associated with poor pregnancy outcomes, including intrauterine growth retardation, prematurity and fetal death, and infant and maternal disease and death [3].

Although there is general awareness regarding the greatly increased TB risk experienced by immunocompromised individuals, the risk that TB may enhance HIV transmission and/or disease progression is less appreciated. Animal models that explore possible TB-HIV interactions include macaques coinfected with simian immunodeficiency virus and Mycobacterium bovis bacille Calmette-Guerin (BCG). M.bovis BCG infection causes marked T lymphocyte BCG infection with increased plasma viral loads, reduced CD4 cell counts, and accelerated HIV disease progression [4, 5]. Studies evaluating TB-HIV interactions in humans have also demonstrated immune activation, with resultant increases in viral load [6, 7]. Its clinical and epidemiological relevance is less well defined [8], but its potential contribution to HIV pathogenesis and transmission has been recognized [7, 8].

In this issue of the Journal, Gupta et al study the contribution of maternal TB as a risk factor for mother-to-child transmission (MTCT) of HIV infection [9]. Limiting MTCT of HIV infection is a major public health priority, because every infant infected with HIV represents a preventable event. Early initiation of life-long antiretroviral therapy saves lives and improves the outcomes in HIV-infected infants [10], but this comes at a huge cost to the health care system and a multitude of long-term adverse effects. The study by Gupta et al, conducted in India, used data from 783 mother–infant pairs enrolled in the prospective, randomized, placebo-controlled six week extended-dose nevirapine trial [11]. The primary aim of the trial was to compare rates of MTCT with use of a single dose, compared with daily nevirapine for 6 weeks, in breastfed infants. Although TB cases were limited (only 33), the rate of MTCT was significantly higher (30% vs 12%) in mothers with TB. Excluding the 3 cases with prevalent TB, the number of mothers with incident TB (30 of 780) equates to a TB incidence of 3846 cases/100,000 population/year, which is exceptionally high, compared with the expected background TB incidence.

Maternal viral load and CD4 cell count were strongly associated with HIV MTCT. Increased viral load resulting from chronic immune stimulation in patients with TB probably accounts for much of the increased HIV MTCT risk observed; however, a significantly increased risk persisted in multivariate analysis despite correcting for maternal viral load, CD4 cell count, and other relevant factors.

Potential mechanistic explanations for this phenomenon are of interest. One of the reasons why pregnant women are thought to be more vulnerable to developing TB is Th-1 down regulation to accommodate the growing fetus. The strong Th-1 stimulus provided by TB may increase placental inflammation, explaining some of the adverse fetal outcomes observed and the increased risk of in utero HIV MTCT. In fact, the majority of infant HIV infections were detected at delivery (indicating in utero transmission) and in very close proximity to the maternal TB diagnosis. Apart from the significant independent
association demonstrated between maternal TB and infant HIV infection, the clustering of the 2 events (maternal TB diagnosis and infant HIV infection diagnosis) also suggests a possible causal relationship. It demonstrates that prevention of TB among HIV-infected mothers should be considered as part of a well-functioning prevention of HIV MTCT program. The exceptionally high TB disease and transmission risk provides additional motivation to carefully monitor all HIV-infected women for TB during and after pregnancy [12]. More operational research is required to clearly define the feasibility, benefits, and risks of providing routine TB preventive therapy to HIV-infected pregnant mothers in areas where TB is endemic [13].

In 2000, world leaders signed the United Nations Millennium Declaration and agreed to meet 8 Millennium Development Goals by 2015. These included a strong focus on maternal and child health, control of major infectious diseases, and other issues of global importance, such as poverty alleviation, environmental sustainability, and biodiversity protection. From 1995 through 2008, 43 million patients with TB were treated and 36 million were cured through TB control efforts. Despite this achievement, an estimated 9.4 million new cases of TB occurred in 2008, with 1.7 million TB-related deaths (more than half among women) [14]. Although the burden of childhood TB remains poorly quantified, TB clearly has a major impact on child health and under-5 mortality in areas where TB is endemic [1]. A prospective pediatric surveillance study from South Africa demonstrated that TB is a major cause of community-acquired pneumonia not responding to first-line antibiotics [15], and a Zambian autopsy study confirmed TB to be a common cause of death in children, irrespective of their HIV status [16]. These deaths are frequently misclassified as pneumonia-related deaths, because diagnostic facilities and expertise to diagnose childhood TB are limited [17]. There is huge opportunity to improve the provision of preventive therapy and TB diagnostic services to young and vulnerable children, irrespective of their HIV status [13].

It is evident that TB has a major impact on maternal and child health in areas where TB is endemic, with HIV-infected mothers and their young children being particularly vulnerable. This includes direct effects on morbidity and mortality, but also multiple indirect effects that trap people in a vicious circle of poverty and vulnerability [14], even facilitating vertical transmission of HIV, as demonstrated by Gupta et al (9). The renewed focus on maternal and child health as key components of a healthy society is welcomed with enthusiasm, but adequate recognition must be given to the importance of TB control and prevention in areas where TB is endemic.

References