



Diabetes Mellitus (DM) and Tuberculosis (TB)

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At the 2016 TB Update held on June 8, Pinnacle Health Medical Director for Diabetes Dr. Renu Joshi gave a presentation titled "Management of Tuberculosis and Diabetes." Because diabetes is now recognized as a significant risk factor for TB and much of the information presented was new to many in the audience, the key points of Dr. Joshi's talk are summarized in the following paragraphs.

An association between diabetes and TB was noted in the medical literature as early as the 1930s, but controversy remains as to the direction of any causal relationship. As noted by the World Health Organization in 2011, "... diabetes can worsen the clinical course of TB, and TB can worsen glycemic control in people with diabetes."

The convergence of diabetes and TB poses a global public health issue. In 1980, the prevalence of diabetes in high-income countries was significantly greater than in low-income countries. Since then, not only has the prevalence of diabetes increased significantly worldwide, but the prevalence rates in low- and high-income countries are now comparable. Add in the high prevalence of TB in many low-income countries, and the limited resources available in those countries to treat both diseases, and the 'double burden' to public health organizations is readily apparent.

Diabetes Global Prevalence*

- A total of **422** million people worldwide were living with diabetes in 2014, increasing to **439** by 2030.
- In 2012, diabetes was the direct cause of 1.5 million deaths.
- WHO projects that diabetes will be the seventh leading cause of death in 2030.
- In 1980, diabetes prevalence was highest in high-income countries; now it is similar in both high- and low-income countries.

*WHO Diabetes Summit 2014

DM and TB

- In 2013, **15 percent** of all adult cases of TB worldwide were associated with DM, which corresponds to over 1 million cases of diabetes-associated TB per year.*
- There is a much higher association in specific areas like Asia (20 percent)** and along the Texas-Mexico border (28 percent)***
- Prevalence will increase due to the increase in DM over the next decade, especially in the lower income population.

* Lancet Diabetes Endocrinology 2014; 2: 730-738

** Thorax 2010; 65: 578-81

*** Bull world health organ 2011;89:352-9

Biologically, diabetes creates a more favorable environment for the conversion of TB to active disease. Simply stated, bacteria love sugar, and hyperglycemia provides a rich medium for the growth of bacilli. Diabetes also affects immune system metabolism — increasing interleukin 10 and cytokines and decreasing T-cell lymphocytes — in ways that make it more difficult to kill *M. tuberculosis* bacilli. Compared to non-diabetic persons, patients with diabetes have a higher risk of latent TB infection, are more likely to have pulmonary TB than extra pulmonary TB, are more likely to have TB in the lower lobes of the lungs, and have more cavity lesions. Even worse, patients with poorly controlled diabetes, as measured by their hemoglobin A1C level, typically present with more advanced TB disease, have a **four times higher** rate of TB relapse as well as a **four times higher** rate of death during TB treatment.

Diabetes and the drugs used to treat it can alter the efficacy and tolerability of TB medications. When used together, the side effect profile for diabetes and TB medications may worsen; the hepatotoxicity of rifampin may be higher; the efficacy of TB drugs may be lessened by drug-drug interactions; and the greater risk of renal disease with diabetes can result in a higher risk of nephrotoxicity with TB medications.

TB and TB drugs may also have a negative effect on diabetes. All TB medications can result in hyperglycemia and increased insulin resistance, though there is some evidence this is a temporary effect. Rifampin is known to reduce the efficacy of several diabetes medications (except insulin and metformin) by activating P450 system enzymes, resulting in increased metabolism.

In light of the emerging co-epidemic of diabetes and TB, enhanced screening of both patient groups should be considered:

- Persons with diabetes—and especially those with poorly controlled hyperglycemia—should be tested for TB infection with either the PPD skin test or a blood test (QFT-Gold; T-Spot) and, if positive, screened for TB symptoms (such as a bad cough that lasts for three weeks or more, fatigue, loss of appetite, weight loss, or night sweats). Patients with symptoms should then be evaluated for active TB consistent with the CDC Guidelines.
- Patients with TB infection or disease should similarly be screened for diabetes consistent with national guidelines (i.e., A1C > 6.5 or fasting blood glucose > 126). For TB patients diagnosed with diabetes, insulin may be the mainstay of treatment, since it is not affected by rifampin.

When treating latent TB infection (LTBI) or active TB in patients with diabetes, consider that a longer duration of therapy may be needed due to the effect of drug-drug interactions on treatment efficacy. Drug-drug interactions are also associated with a higher risk of side effects, making treatment adherence more challenging. While DOT is the standard of care for treating *active* TB cases, it may also be helpful for certain LTBI patients with diabetes.

Lastly, due to the higher rate of TB recurrence in patients with diabetes, continued TB screening may be advisable for these patients even after they complete their TB treatment.

Take Home Messages*

- **Tuberculosis treatment**
 - Increased duration of treatment and weight-adjusted doses of antituberculous drugs might be necessary.
- **Diabetes treatment**
 - Different approaches might be needed for newly diagnosed and previously diagnosed diabetes.
- **Treatment adherence**
 - Disease symptoms, high pill burden and side-effects could compromise treatment adherence in patients with both diseases. DOT is required in many cases.

* Lancet Sept 2014 Vol 2

Take Home Messages (continued)

- **Monitoring**
 - Intense monitoring and follow-up might be needed because of an increased likelihood of toxic effects of drugs, treatment failure and relapse rates.
 - Active tuberculosis screening might be worthwhile in patients with diabetes who previously had tuberculosis because of high recurrence rates.