Scientists discover new information about diabetes' link to tuberculosis

October 14 2008

New evidence discovered by researchers at The University of Texas School of Public Health Brownsville Regional Campus shows that patients with Type 2 diabetes may be at increased risk of contracting tuberculosis because of a compromised immune system, resulting in life-threatening lung infections that are more difficult to treat.

Blanca I. Restrepo, Ph.D., assistant professor of epidemiology; and Susan P. Fisher-Hoch, M.D., professor of epidemiology; and Joseph B. McCormick, M.D., regional dean, previously reported that Type 2 diabetes was the leading risk factor for tuberculosis (TB) in the United States/Mexico border area. Several other studies in Asia and elsewhere have confirmed this observation.

The UT School of Public Health team has now led three new studies that revealed key findings:

-- Type 2 diabetes, especially Type 2 diabetes involving chronic high blood sugar, is associated with altered immune response to TB, and this was particularly marked in patients with chronically high blood sugar.
-- Patients with diabetes and TB take longer to respond to anti-TB treatment.
-- Patients with active tuberculosis and Type 2 diabetes are more likely to have multi-drug resistant TB.

The World Health Organization estimates that 180 million people in the world have diabetes, and that number is expected to double by 2030.

Also, according to the WHO, each person with active, untreated TB infects on average 10 to 15 people per year. "You do the math and it adds up to a major public health threat," McCormick said. "If you have Type 2 diabetes in an area with high rates of TB, your chances of getting TB goes up. In countries where a third of the population is infected with TB, this becomes a real issue."

In a recently published study in linical Infectious Diseases, researchers reported that the immune systems of patients with Type 2 diabetes and tuberculosis respond differently compared with patients with TB alone. "This immune impairment may be what makes patients with diabetes so susceptible to TB," said Fisher-Hoch, whose career as a scientist was recently honored with a Hall of Fame Award from Women In Technology International.

Restrepo and her colleagues found that innate and type 1 cytokine responses were significantly higher in patients with tuberculosis who had diabetes than in the control group of patients with TB and no diabetes. The effect was consistently and significantly more marked in diabetic patients with chronic hyperglycemia, or uncontrolled high blood sugar. Diabetes results in the body's ineffective use of insulin. If left uncontrolled, the chronic high sugar in the bloodstream can affect the critical immune system and damage the body's systems, especially the nerves, the retina of the eyes and blood vessels.

"These findings are the opposite of what we were expecting," Restrepo said. "These innate and type 1 cytokines are typically associated with TB protection, but in patients with diabetes, it appears the cytokines are not effective. Diabetics may have more advanced TB with more bacteria, and hence, more stimulation for secretion of type 1 cytokines."

The researchers wrote, "More detailed knowledge of the underlying mechanisms should focus on the effect of chronic hyperglycemia on the

immune response to help in understanding the enhanced susceptibility of diabetic patients with tuberculosis."

In a second study, which was published in an October issue of the American Journal of Tropical Medicine and Hygiene, the researchers demonstrated that diabetic patients with TB were more likely to take longer to clear the TB bacterium during the first phase of treatment than TB patients who are not diabetic. Using data from 469 TB patients in south Texas, those with diabetes had a five-day delay in mycobacterial clearance within the first 60 days of treatment.

"Despite the goal of global eradication by the year 2050, in 2004, there were an estimated 8.9 million new cases of TB worldwide," the researchers wrote. "Our data showed that adult onset diabetes mellitus (also known as Type 2 diabetes) seems to interfere with sterilization of pulmonary TB by drug therapy. By 2030, it is estimated that 336 million of the world's population will have diabetes mellitus, many in TB-endemic countries. Diabetes on this scale may impact TB control. Prospective studies are needed to define more clearly the consequences for transmission among diabetes patients and the prevention and therapeutic measures that might be taken to lessen the effect."

A third study demonstrated that patients with diabetes were more at risk of developing multi-drug resistant tuberculosis. In an Epub abstract online in Scandinavian Journal of Infectious Diseases, researchers reported that almost 6 percent of patients living along the Texas-Mexico border had TB that was resistant to rifampin and isoniazid, common medications for tuberculosis. Of those with multi-drug resistant tuberculosis, 30 percent also had Type 2 diabetes. "It is possible that impaired immunity in Type 2 diabetes increases susceptibility to infection with resistant strains," the abstract states.

McCormick, the senior author of all three papers, said these research

findings shed new light on a long-known correlation between diabetes and tuberculosis. "It opens a door to doing something about it," said McCormick, the university's James H. Steele Professor. "We can educate physicians and offer more TB screenings. We have an opportunity to make sure patients are diagnosed correctly and that there is no delay in diagnosis."

Fisher-Hoch said the research could help diagnosis TB patients who previously would not be considered at risk for contracting the airborne, contagious disease. "The classic TB patient in this country is a younger male in an urban setting who may have alcohol and drug abuse problems and be HIV-infected," she said. "Our research shows older female patients who have never been in jail and have no history of alcohol and drug abuse or HIV infection are at risk of contracting TB if they have diabetes."

"I think we are illuminating a very important association between TB and diabetes that had pretty well been overlooked," Fisher-Hoch added. "The public health aspect is that we are trying to make sure we can prevent and treat these patients, and when they are TB-infected, treat them better."

Fisher-Hoch recommends that medical professionals screen patients for TB if they have diabetes and a chronic cough. She also recommends that patients with Type 2 diabetes take precautions. "If they are visiting an area where there is a lot TB, they need to be careful," she said. "TB spreads in crowded places with poor ventilation."

Source: University of Texas