Diabetes and tuberculosis coexist together, and influence each other’s natural history and treatment outcomes significantly. This assumes clinical as well as public health significance. This article describes these associations, and discusses action that can be taken at the primary care level to tackle this challenge.

**Keywords:** Anti-tubercular treatment, Bidirectional screening, Diabetes, Insulin, Metformin.

**Introduction**

‘Diabetic tuberculosis’ is the name we choose to describe the well-documented association between diabetes mellitus and tuberculosis. Asia bears the maximum brunt of ‘diabetic tuberculosis’, with India, China, Indonesia, Pakistan, Bangladesh, Philippines, and Myanmar taking 7 of the top 10 positions in this regard.1

**Epidemiology**

Systematic reviews indicate that the relative risk of tuberculosis in persons with diabetes mellitus is 3.1, as compared to non-diabetics. The odds ratio of tuberculosis varies from 1.2 to 7.8 in case-control studies conducted using persons with diabetes as cases.2,3

Recently published case-control study demonstrates the association of pulmonary tuberculosis and diabetes in Kazakhstan, with adjusted odds ratio of 23.43 or 48.59, depending on the multivariate model used4 Similar data is available from Portugal5 and India.6 Yet another paper from Italy highlights the increasing risk of spread of diabetes and tuberculosis, because of international migration.7

**Pathogenesis**

Various reasons have been put forward to explain the increased susceptibility of persons with diabetes to tuberculosis. These include changes in both humoral and cell-mediated immunity.8 A recent hypothesis states that increase in butyrate concentrations (noted in insulin deficient states) may decrease proinflammatory cytokine response to Mycobacterium tuberculosis infection, while increasing interleukin 10 production.9

**Clinical Impact**

The impact of diabetes on tuberculosis presentation, natural history, and treatment outcomes is multifaceted,8 and is described in Table-1. On the other hand, tuberculosis complicates diabetes by causing hyperglycaemia, which may be refractory until anti-tubercular therapy is initiated. It takes time for both anti-tubercular therapy and anti-diabetic treatment to have an effect. Simultaneous, start of both with aggressive titration of glucose lowering therapy, helps escape the vicious cycle seen in clinical practice.

**Action Plan**

The World Health Organization and the International Union against Tuberculosis and Lung Disease have launched a Collaborative Framework for Care and Control of Tuberculosis and Diabetes.10 This helps policymakers plan strategies to fight diabetic tuberculosis, and provides simple, yet pragmatic guidance for clinicians. This move has been reinforced by the Bali Declaration, which calls for aggressive measures to tackle this co-epidemic.11

**Bidirectional Screening and Management**

People with diabetes should be screened clinically(by history taking) for a chronic cough lasting ≥ 2 weeks, at diagnosis and follow up. Rigorous screening should be carried out in persons with uncontrolled hyperglycaemia. Laboratory and radiological screening should be performed as per national recommendations, with referral where necessary. Persons diagnosed to have ‘diabetic tuberculosis’ should be managed in the same

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**Table:** Impact of diabetes on tuberculosis.

<table>
<thead>
<tr>
<th>Impact</th>
<th>Description</th>
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<tbody>
<tr>
<td>1. Increased risk of</td>
<td>Disease</td>
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<tr>
<td>2. Greater time to sputum culture conversion</td>
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<td>3. Treatment failure</td>
<td></td>
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<td>4. Death</td>
<td></td>
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<tr>
<td>5. Recurrent tuberculosis</td>
<td></td>
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<tr>
<td>6. Change in clinical picture</td>
<td>Extra-pulmonary tuberculosis</td>
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<tr>
<td>7. Lower lobe tuberculosis</td>
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<tr>
<td>8. Cavitatory tuberculosis</td>
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way as euglycaemic or non-diabetic persons detected to have tubercular infection.\textsuperscript{10}

Patients with tuberculosis should be screened for diabetes at the onset of therapy. Tuberculosis is an absolute indication for screening, even though it is not mentioned in the Standards of Medical Care document published by the American Diabetes Association.\textsuperscript{12} The choice of screening/diagnostic tests should be based on availability and feasibility. The tests and cut-off values are similar to those for non-infected populations.\textsuperscript{10} Persons with tuberculosis, detected to have diabetes should be treated appropriately. It must be noted that insulin therapy may be needed at onset, as patients may present with severe cachexia.\textsuperscript{8} Metformin is a calorie restriction mimic,\textsuperscript{13} and may not be the best choice for a newly diagnosed diabetic tuberculosis patient who is severely malnourished, and has loss of appetite, gastrointestinal symptoms, or concomitant renal and/or hepatic impairment.

**Summary**

Bidirectional screening of persons diagnosed to have tuberculosis or diabetes will help in efficient case finding. This, followed by appropriate therapy, will help tackle the epidemics of both tuberculosis and diabetes.

**References**