Substance Abuse and Tuberculosis
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Co-morbidities in Substance Abuse that Impact Managing TB
Lisa Armitige, MD, PhD
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Co-morbidities in Substance Abuse that Impact Managing TB

Lisa Y. Armitige, M.D., Ph.D.
Medical Consultant
Heartland National TB Center
Associate Professor of Medicine/Pediatrics
University of Texas Health Sciences Center, Tyler, TX

TB control measures

- Patient diagnosed as having TB disease
  - Investigation conducted to identify all contacts of person with TB disease
  - Screen contacts for TB disease and latent infection
    - Treatment of contacts with TB disease and latent infection
      - Treatment care for people with TB disease and complete preventative therapy for contacts with latent infection
    - Substance abuse–related barriers
      - Substance abuse is associated with non-tuberculous mycobacterial disease (NTM, infections) and delayed care seeking (e.g., prolonged infections)
Medical Co-Morbidites

• Tobacco smoke

• Diabetes

• Malnutrition

• Hepatic disease

Global lung health: the colliding epidemics of tuberculosis, tobacco smoking, HIV and COPD
van Zyl Smit et al, Eur Respir J 2010, 35; 27

• In 2006 approximately 5.8 trillion cigarettes were manufactured; an average of 2.4/day for all 6.5 billion inhabitants of earth

• Current estimates of tobacco smoking rates are 49% males, 8% females in low and middle income countries (37% and 21% respectively in high-income countries)

• In 2004, COPD was the 4th leading cause of death worldwide (5.1% of total deaths)

• By 2030, COPD will be the 3rd leading cause of death globally, eclipsing deaths by TB and HIV
Association between Tobacco Smoking and Active Tuberculosis in Taiwan
Hsien-Ho et al AJRCCM 2009, 180; 475

• Prospective cohort study in Taiwan: 17,699 participants, 2001-2004

• Current smoking associated with twofold increased risk of active TB
  – Association stronger for patients < 65 years
  – Significant dose-response relations
    • Cigarettes per day
    • Years of smoking
    • Pack years

Smoking, drinking and incident tuberculosis in rural India: population-based case-control study
Gajalakshmi et al Int J Epidemiol 2009, 38; 1018

• Case-control study from India: 1839 males, 870 females

• NO WOMEN SMOKED or DRANK ALCOHOL!

• 82% TB cases vs 55% of controls smoked
  – RR 2.2 (for alcohol consumption RR 1.5)

• Conclusion: increased incidence of pulmonary TB among those who smoke and among those who drink
Association between Tobacco Smoking and Active Tuberculosis in Taiwan
Hsien-Ho et al AJRCCM 2009, 180; 475

• “The finding that smoking increased the risk of tuberculosis suggests that tobacco control be considered as an important component in the global effort to eliminate tuberculosis”.

• “…policy makers and public health personnel should consider addressing tobacco cessation as part of TB control.”

Systematic Reviews and Meta-analyses evaluating tuberculosis and cigarette smoking

• Slama et al, Int J Tuberc Lung Dis 2007, 11; 1049
  • “Tobacco and tuberculosis: a qualitative systematic review and meta-analysis”

• Lin et al, PLoS Med 2007, 4; e20
  • “Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis”

• Bates et al Arch Intern Med 2007
  • Smokers almost twice as likely to be infected with TB and to progress to active disease. 2/3 studies suggest smokers almost twice as likely to die from TB
Systematic Reviews and Meta-analyses evaluating tuberculosis and cigarette smoking

- Approximately 13% of the TB cases in the world each year may be attributable to tobacco exposure.

- “Tobacco cessation must become an integral part of all TB control programmes.”

Diabetes and TB
Type 2 Diabetes

- Increased risk has been noted in many racial and ethnic populations
  - African Americans
  - Hispanic/Latino Americans
  - Native Americans
  - Asian Americans

- Globally urbanization has fueled an increasing incidence in Africa, India, Asia
  - Areas of world with high rates of tuberculosis

Prevalence of Diagnosed Diabetes by Race/Ethnicity and Age in Persons 18 & Older

<table>
<thead>
<tr>
<th>AGE</th>
<th>White non-Hispanic</th>
<th>Black, non-Hispanic</th>
<th>Hispanic</th>
<th>Other</th>
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<tr>
<td>18 – 44</td>
<td>2.9</td>
<td>3.0</td>
<td>4.3</td>
<td>1.4</td>
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<tr>
<td>45 – 64</td>
<td>10.4</td>
<td>23.8</td>
<td>20.9</td>
<td>13.9</td>
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<tr>
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<td>17.0</td>
<td>33.5</td>
<td>34.8</td>
<td>28.7</td>
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<tr>
<td>Overall</td>
<td>8.3</td>
<td>13.0</td>
<td>11.1</td>
<td>8.1</td>
</tr>
</tbody>
</table>

» Texas Diabetes Fact Sheet, 2009
Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958-2008


At Risk Populations and Behaviors for TB and Diabetes

- HIV/AIDS
- Immune Suppression
- Alcohol and Drug Abuse
- Homeless Population
- Refugees
- Prisoners
- Migrant Farm Workers
- Health Care Workers
- Native Americans
- Hispanics
- Asian / Pacific Islanders
- Blacks
- Older Age
- Unhealthy Diet
- Smoking
- Vitamin D deficiency
- Overweight / Obesity
- Cardiovascular Disease
- Family History
- Polycystic Ovary Syndrome (PCOS)
Linkage Between Tuberculosis and Diabetes

Does Diabetes Impact TB Treatment and Cure?

• Previously thought not to affect treatment

• Four new studies from Baltimore, Texas, Taiwan and Indonesia reveal:
  – Delayed culture conversion
  – Higher mortality
Response to TB Treatment

• Relapse may be more frequent
  – Recent Shanghai study 203 diabetics with TB followed for 2 years after standard treatment

  • 20% relapse rate in patients with DM (most Type 2)
  • 5% relapse rate in patients without DM

  Zhang et al. Jpn J Infect Dis, 2009

Hyperglycemia in Patients with TB

• Blood glucose control may worsen while patients are taking Rifampin
  – Rifampin augments intestinal absorption of glucose
  – Does so in both diabetics and non-diabetics

• Infections impair glucose tolerance early in disease in both diabetics and non-diabetics
  – Independent of rifampin, infection can lead to poor glucose control
Low Blood Levels of Rifampin in Diabetics: Indonesia

- 17 Patients with Diabetes and Tuberculosis

- Rifampin levels decreased 50%
  - Perhaps related to higher BMI in diabetics

- Is a different dose of rifampin needed?
  - Mg/kg?

Response to tuberculosis therapy in Diabetic patients

- Baseline mycobacterial burdens might be higher in diabetic patients than in controls

- Diabetics tend to have modestly longer times to sputum-culture conversion
  - Dooley et al Am J Trop Med Hyg 2009, 80; 634
  - Alisjahbana et al Clin Infect Dis 2007, 45; 428

- Rates of sputum-culture conversion are similar to those of non-diabetic patients by 2-3 months of treatment
TB and Diabetes - Treatment Issues

• **Diabetic neuropathy** at baseline complicates therapy due to INH-related neuropathy
  – Baseline assessment of neuropathy
  – Vitamin B 6 (pyridoxine) to all diabetics on INH or ethionamide

• **Renal insufficiency** is associated with diabetes, especially long standing or poorly controlled diabetes
  – Adjust dose and dosing interval of EMB & PZA in those with Creatinine CI < 30

TB and Diabetes - Treatment Issues

• Diabetics have an increased risk of hepatotoxicity
  – Multiple medications
  – Fatty liver

• Monitoring and education are very important
  – Baseline and monthly liver enzymes

  – Educate regarding risk of liver toxicity, symptoms to watch for, and what to do should these occur
    • Contact provider
    • Hold TB medications until liver injury excluded
Pharmacologic Interactions in patients with tuberculosis and diabetes

- Diabetes does not alter the pharmacokinetics of anti-tuberculosis drugs during the intensive phase of tuberculosis treatment but...

- Diabetic patients had lower rifampin levels c/w controls in the continuation phase of therapy
  - Nijland et al Clin Infect Dise 2006, 43; 848
  - Ruslami et al Antimicro Ag Chemother 2010, 54; 1068

- Rifampin, a potent inducer of drug metabolizing enzymes, can lead to accelerated metabolism of oral hypoglycemic drugs

Malnutrition
Importance of Nutrition in TB Treatment Response

Impact of Poor Nutrition on TB Relapse

- Patients 10% below ideal body weight at diagnosis
  - have a 20% chance of relapse if they don’t regain at least 5% by end of two months of treatment
  - If CXR cavitary & 2 mo sputum culture +, 50% chance of relapse


“Weight gain of 5% or less during the first 2 months of therapy is associated with an increased risk of relapse, even after controlling for other factors.”

Khan Am J Resp Crit Care Med 2006

Lack of Weight Gain and Relapse Risk, TBTC Study 22

- Relapse risk high in those underweight at diagnosis 19.1% versus 4.8%
- Among pts underweight at Dx, weight gain ≤ 5% after 2 mo treatment:
  - Relapse risk 18.4% vs. 10.3%
  - If also cavitary disease: 18.9%
  - If cavitary and + 2 month culture: 50.5%

Hepatitis

• Alcohol

• HIV

• Hepatitis C virus

• Hepatitis B virus

• Combinations of the above

Hepatic Disease

• Difficulties in treating tuberculosis due to potentially hepatotoxic drugs

• Hepatitis B and C virus infections

• Exacerbated by the need for treatment with multiple classes of medications in treating HIV/TB co-infected patients
Thanks!!

Questions?

1-800-TEX-LUNG