Active TB in HIV-infected children in Thailand: Prevalence, incidence and mortality

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Background

- In 2012, worldwide: 530,000 new TB cases among children
  74,000 HIV-negative children died from TB
- However, data on pediatric TB-HIV co-infection (prevalence, incidence, mortality) are scarce
- Risk factors for active TB in HIV-infected children may need to be better known
Objectives

▪ Estimate the prevalence and incidence of active TB in children with HIV in a large HIV pediatric cohort in Thailand

▪ Identify predictors at ART initiation of active TB infection

▪ Estimate the burden of TB in terms of mortality in HIV-infected children
Study design and population

- Study design
  Data from the observational prospective cohort study (PHPT cohort) of 882 HIV-infected children on ART in 37 hospitals across Thailand

- Study population
  839 HIV-infected children < 15 years old enrolled in the PHPT cohort between 1999 and 2012
Diagnosis of TB

For this study we relied on the pediatrician’s diagnosis, based on:

- Medical history and epidemiologic context
- Clinical examination
- Tuberculin skin test
- Chest X-ray
- Sputum smear and culture
- Gastric aspirate
## Statistical methods

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<td>Prevalence</td>
<td>Proportion of active TB cases among all HIV-infected children</td>
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<td>Incidence</td>
<td>No. of new active TB cases / Total no. of person-years of follow-up (PYFU)</td>
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<td>Predictors of active TB</td>
<td>Poisson regression models adjusted for gender and age – incidence rate ratios (IRR)</td>
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<td>Estimation: Kaplan-Meier method Comparison HIV with TB vs. HIV with no TB: log-rank test</td>
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Potential predictors at ART initiation

- Demographics
  - Gender
  - Age
  - BMI-for-age (WHO)
  - Enrollment period

- Laboratory values
  - HIV RNA load
  - CD4 %
  - Complete blood counts
Prevalence of active TB infection

- 59 children diagnosed before ART initiation, and
- 47 after ART initiation

= 106/839 (12.6%) children diagnosed with active TB
  (95% CI: 10.5%-15.1%)

- Manifestation of TB:
  - Pulmonary TB: 65%
  - TB lymph nodes: 16%
  - Other: 19% (mostly TB meningitis, abdominal TB and miliary TB)
Population for active TB incidence and mortality estimation

- 622 children with no TB diagnosed at ART initiation
- Median follow-up: 7.7 years (IQR: 3.6 – 9.8)
- 22% were lost to follow-up, 21% withdrew and 9% died

Characteristics at ART initiation:
- 55% female
- Median age: 6.2 years (IQR: 1.8 – 9.7)
- Median HIV RNA load: 5.2 log_{10} copies/mL (IQR: 4.7 – 5.7)
- Median CD4 percentage: 9% (IQR: 2% – 16%)

Median follow-up from ART initiation to active TB diagnosis: 1.1 year (IQR: 0.1 – 4.1)
Incidence of active TB infection

- Overall incidence rate: 9.0 cases/1,000 PYFU (95% CI: 6.5 – 12.4)
- Most active TB cases diagnosed shortly after ART initiation
Predictors of active TB infection

Risk factors at ART initiation associated with a higher risk of active TB infection (adjusting for gender and age)

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<tr>
<th>Risk factors</th>
<th>IRR</th>
<th>P</th>
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<tr>
<td>CD4 cell percentage &lt;5%</td>
<td>3.3</td>
<td>0.003</td>
</tr>
<tr>
<td>HIV RNA load &gt;5.5 log_{10} copies/mL</td>
<td>2.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Hemoglobin levels &lt;11 g/dL</td>
<td>3.4</td>
<td>0.007</td>
</tr>
<tr>
<td>Hematocrit levels &lt;32%</td>
<td>2.7</td>
<td>0.007</td>
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<tr>
<td>Lymphocyte count &lt;2,000 cells/mm³</td>
<td>3.2</td>
<td>0.008</td>
</tr>
<tr>
<td>Neutrophil count &gt;3,000 cells/mm³</td>
<td>2.5</td>
<td>0.02</td>
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</table>
Overall survival rates

- Overall survival at the end of follow-up:
  - HIV with no TB: 91%
  - HIV with TB: 65%
- Risk of death 4.1 times higher in HIV-infected children with TB
Summary

In this cohort

▪ Prevalence of active TB: 13%

▪ Overall incidence rate: 9/1,000 PYFU

▪ TB cases usually diagnosed within the first year after ART initiation

▪ HIV RNA, CD4% and CBC at ART initiation = good predictors of active TB

▪ Risk of death 4 times higher in HIV-infected children with TB
Discussion

Previous studies in HIV-infected children

- Prevalence: US$^1$: 3%  UK$^2$: 5.5%
- Incidence: US$^1$: 6.1/1,000 PYFU  South Africa$^3$: 64/1,000 PYFU
- Mortality: no previous results found

$^1$Thomas et al., PIDJ 2000
$^2$Cohen et al., HIV Med 2008
$^3$Walters et al., BMC Ped 2008
Limitation

Difficult evaluation and interpretation of the burden of TB-HIV co-infection in children

- TB diagnosis is challenging (children with HIV often have other pulmonary infections / may have multiple and concurrent infections)
  - TB can be missed or over diagnosed

- This burden may greatly vary across areas (depending on TB and HIV endemicity levels, ART coverage)
Acknowledgments

▪ The Global Fund to Fight AIDS, Tuberculosis and Malaria
▪ Oxfam GB THAA51
▪ Ministry of Public Health, Thailand
▪ Institut de Recherche pour le Développement (IRD), France

▪ All children who participated in the PHPT cohort study and their caregivers