

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

Endpoints	Statistical methods
Prevalence	Proportion of active TB cases among all HIV-infected children
Incidence	No. of new active TB cases / Total no. of person-years of follow-up (PYFU)
Predictors of active TB	Poisson regression models adjusted for gender and age – incidence rate ratios (IRR)
Survival rates	Estimation: Kaplan-Meier method Comparison HIV with TB vs. HIV with no TB: log-rank test

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

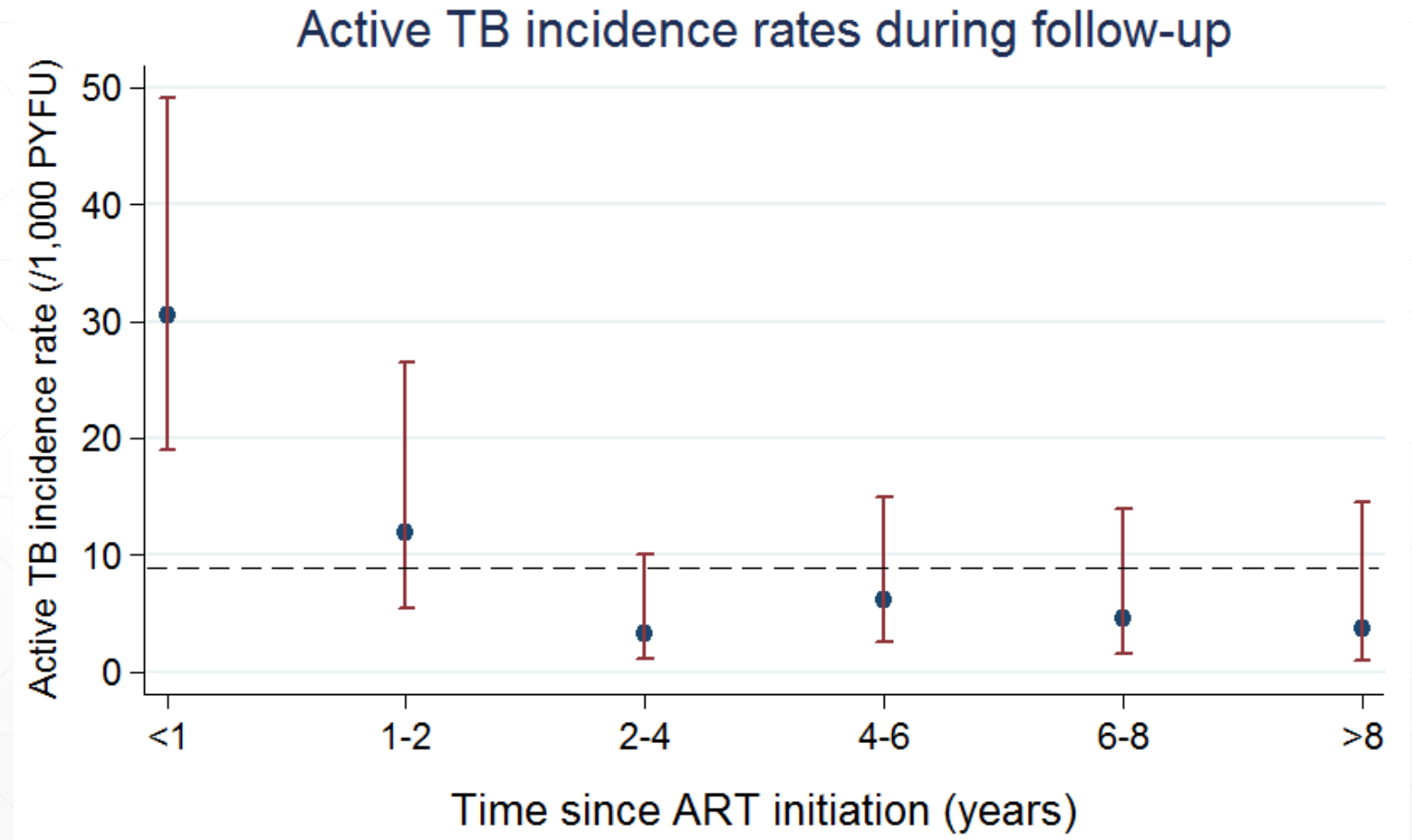
- 59 children diagnosed before ART initiation, and
 - 47 after ART initiation
- = 106/839 (**12.6%**) children diagnosed with active TB
(95% CI: 10.5%-15.1%)
- Manifestation of TB:
 - Pulmonary TB: 65%
 - TB lymph nodes: 16%
 - Other: 19% (mostly TB meningitis, abdominal TB and miliary TB)

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 log₁₀ 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



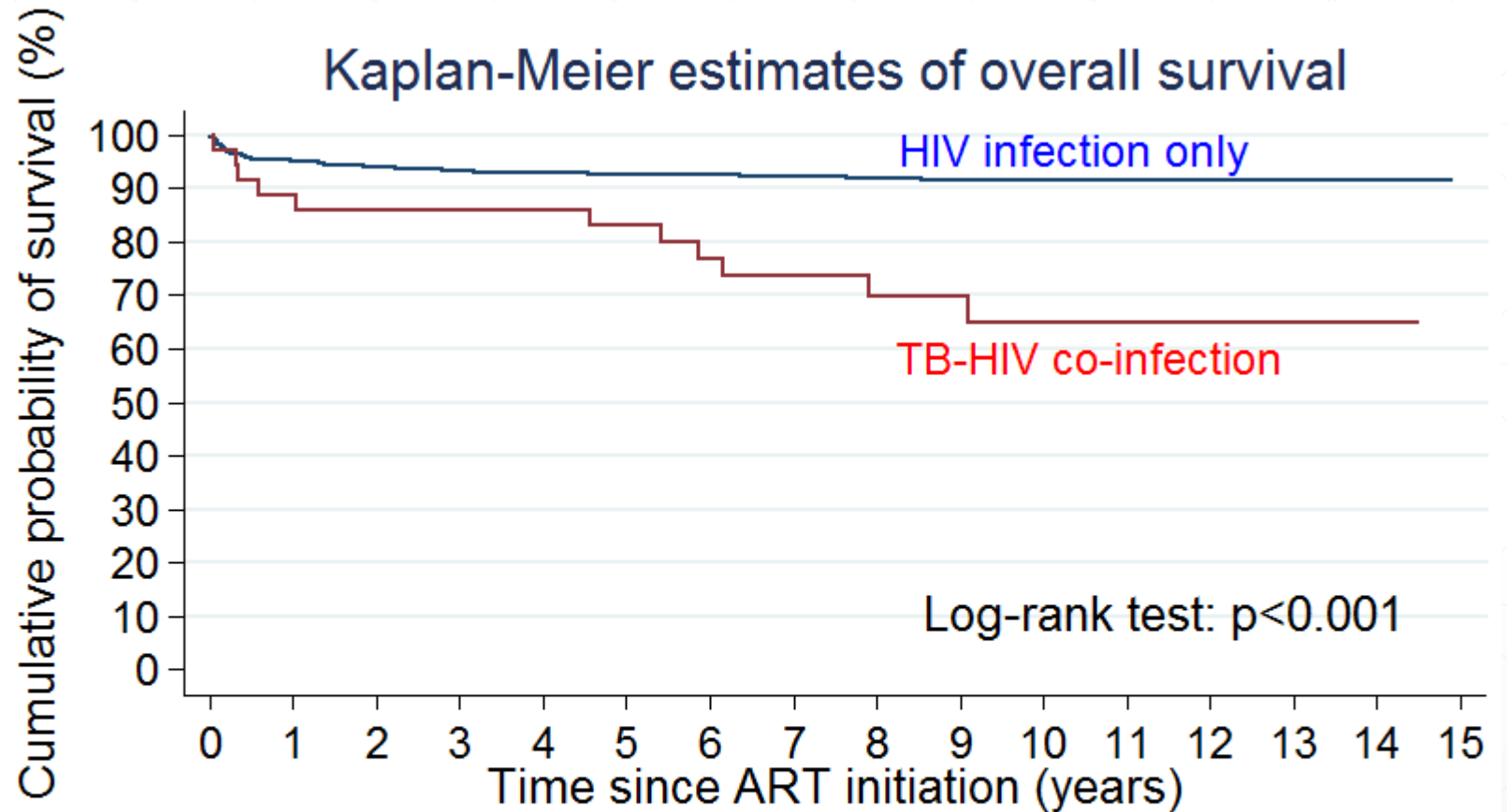
Predictors of active TB infection

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

Risk factors	IRR	P
CD4 cell percentage <5%	3.3	0.003
HIV RNA load >5.5 log ₁₀ copies/mL	2.9	0.01
Hemoglobin levels <11 g/dL	3.4	0.007
Hematocrit levels <32%	2.7	0.007
Lymphocyte count <2,000 cells/mm ³	3.2	0.008
Neutrophil count >3,000 cells/mm ³	2.5	0.02

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



Numbers of children at risk

HIV only	586	477	422	374	272	124	25	6
TB-HIV	36	31	30	25	18	9	3	1

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: US¹: 3% UK²: 5.5%
- Incidence: US¹: 6.1/1,000 PYFU South Africa³: 64/1,000 PYFU
- Mortality: no previous results found

¹Thomas et al., PIDJ 2000

²Cohen et al., HIV Med 2008

³Walters 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)

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