Updates From A Tuberculosis Incidence Cohort Study In Infants, Western Kenya

Grace Kiringa 1, MD
*Videlis Nduba*1,2 *MD, MPH*
Anja Van't Hoog 1,3 *MD*, *MSc*
Anthony Hawkridge 4 *MD*
*Kayla Laserson*1 *ScD*
1KEMR/CDC Research and Public Health Collaboration
2KEMRI/Centre for Respiratory Disease Research
3University of Amsterdam
4Aeras Global TB Vaccine Foundation

KEMRI/CDC
Research And Public Health Collaboration

EDCTP

Background

- Study conducted in an area under continuous Demographic Surveillance
- 80% of births occur at home in the study area
- TB case notification rate 440/100.000
- HIV prevalence 15% (KAIS 2007)

Defining the Problem

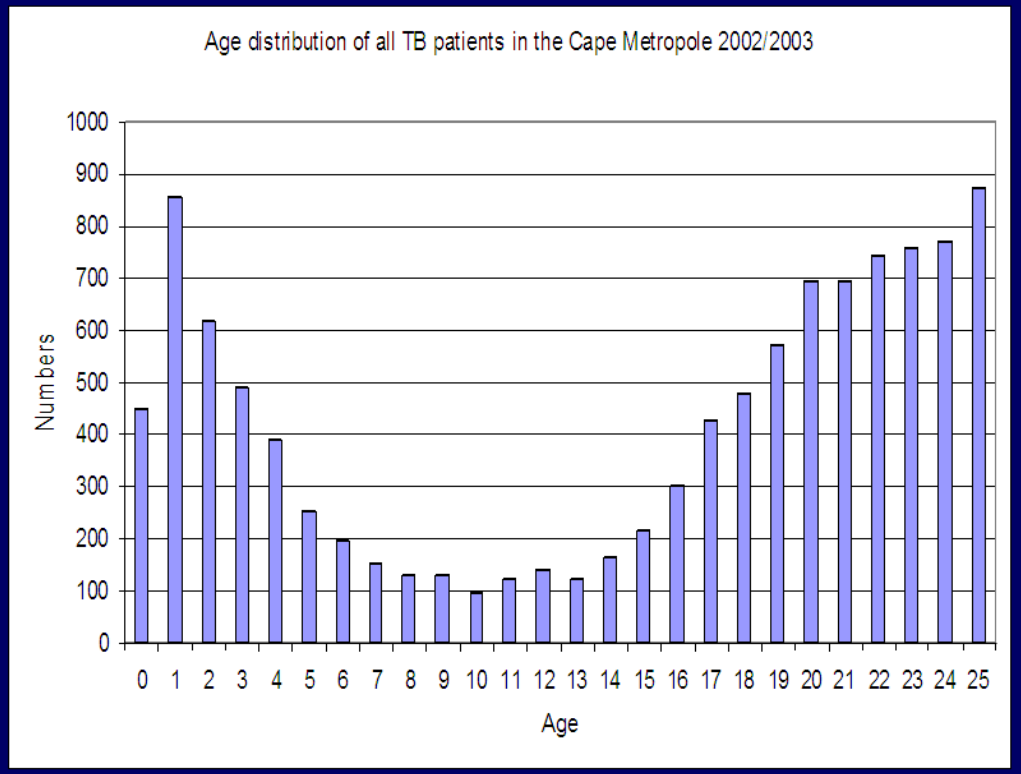
- TB in young children is under diagnosed especially in resource-constrained settings
- Kenya <15 years TB notification rate is 1.1%; forms 2.8% of total smear(+) case notification (WHO 2008)
- TB diagnosis in infants generally difficult-why?
  - Difficult to obtain sputum
  - Paucibacillary disease, are smear and culture –ve
  - Bacteriologic confirmation (cultures) requires expensive, complex lab facilities
  - TB score charts low sensitivity and specificity in settings with high rates of malnutrition and HIV due to confounding clinical symptoms and reduced Tuberculosis skin test (TST) sensitivity
  - The radiographic features in infants are less typical than in adults

Why epidemiological studies?

- To guide assumptions that will be made in planning for a vaccine trial
- To provide reliable estimates of TB incidence, Infant Mortality Rate (IMR) and explore IMR reduction strategies
- Build staff, laboratory and diagnostic capacity to conduct a clinical trial

Infants as target population

- Newborns provide an opportunity to prevent both TB infection and disease
- The risk of severe forms of TB is highest in infants and TB disease peaks at 2 years in infancy
- BCG vaccine does not prevent pulmonary tuberculosis
- Infants a good target group for more effective TB vaccines



Study Objectives (1)

PRIMARY OBJECTIVE

Determine the incidence of definite and probable TB in infants

Definite TB-culture positive TB from any body fluid or tissue, or Mycobacteria TB identified on smear of sputum, gastric washing, urine, blood, CSF, or any other bodily fluid or tissue

Probable TB-suggestive radiological and clinical TB in absence of a positive culture

Study Objectives (2)

SECONDARY OBJECTIVES

- Determine Infant Mortality rate.
  - all cause mortality rate
  - TB related mortality rate
- Determine the rate of adverse BCG reactions
  - suppurative lymphadenitis
  - disseminated BCG disease

Methods

KAREMO DIVISION 3600births/year

SCREENING

- Ineligible-5%
- Declined-5%
- Deaths-10%

ENROL 2900infants+BCG vaccination + antenatal history questionnaire for mother's serostatus

6wk PCR for HIV

4monthly follow up visits for 1-2 years

Health records surveillance

Case Verification Ward for TB suspects investigation.

TB INCIDENCE

Determining TB suspects & Cases

Follow Up

(6 week; 4 monthly)

With questionnaire asking about

- contact
- Symptoms
- Hospitalisation history-meningitis

Health Record Surveillance

(Checking TB registers, TB lab for participants/contacts)

TB Suspects-admitted to a Case Verification Ward for:-

- Induced sputum (2)
- Gastric Aspirate (2) } Taken 1 day apart
- TST
- Quantiferon*
- Chest radiograph
- PCR/Rapid HIV test
- Keith Edward Score

TB CASES – definite/probable/possible

Results (1)

SCREENING-884

- Deferred 5%
- Ineligible 3.6%
- Declined 5%

ENROLLED-767=85%

Sero exposed infants=112/(14%)of 733 mothers who knew their status

ENROL 2900infants → give BCG vaccinations

- Hospital=150(19%)
- home 577(75%)
- Pending 40(6%)

6wk -440/468*=94%retention rate

4month 24/31*=77%retention rate

Health Record Surveillance

6wk HIV PCR +ve(12).4.4%

Total tested at 6 wks=272

TB suspects=40 (5%)

Results (2)

TB SUSPECTS = 40

History of contact

4 = 1%

TB symptoms 2 = .05%

History of hospitalisation e.g malnutrition, lower respiratory tract infections 34 = 85%

TB suspects investigated = 19.

Remainder (21) 6 died, 3 - have travelled, 8 are < 2 mths, 4 deferred.

Definite TB cases-awaiting culture results

Challenges

- Finding newborns, in an area with 80% home deliveries, within 72 hours so as to offer BCG vaccination within 96 hours
- Cultural practices that prohibit a newborn from being seen by strangers until after 4 days-lead to delayed BCG vaccination and enrolment

Lessons Learnt

- Use of designated community members and Traditional Birth Attendants to notify births are an effective way of finding newborns, shortly after birth.
- Extensive community mobilisation through village barazas, village elder's meetings, women's groups meetings are necessary to develop an understanding of cultural norms.

Discussion

- Despite 80% of deliveries occurring at home, its still feasible to enrol and vaccinate infants at home, through careful planning and community involvement.
- A large no of home enrolments still come for health facility follow up visits as shown by high turn up at 6 weeks. However, It's too early to conclude on outcomes and retention
- Establishment of complete diagnostic work up for diagnosis of TB in infants will determine the proportion of TB in children aged 0-2 years.

Acknowledgements

- EDCTP
- KEMRI/CDC Research and Public Health Collaboration
- AERAS TB GLOBAL VACCINE FOUNDATION
- KNCV Dutch TB foundation
- Ministry of Health-Siaya District Hospital