

Risk factors for tuberculosis in household contacts of smear positive TB in Senegal: *preliminary results*

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Background

- Detection of *M.tb* infection by Tuberculin Skin Test (TST) has limitations :
 - variable sensitivity
 - poor specificity : cross-reaction with environmental mycobacteria and previous BCG vaccine
- Diagnostic based on interferon- γ release assays (IGRA) using ESAT-6/CFP-10 (EC) are promising but their capacity to predict active TB need to be evaluated.
- The African TB VACcine (AFTBVAC) project in Senegal: pre-vaccine cohort study to estimate epidemiological determinants of TB infection and disease

Objectives

1. To determine the incidence and risk factors for active tuberculosis (TB) amongst Household Contacts (HHC) of smear positive pulmonary tuberculosis cases;
2. To assess the value of an in-house IGRA for the prediction of tuberculosis, in comparison with TST.



Methods : inclusion

- Study area: Dakar, Senegal (West Africa)
 - TB estimated incidence: 132/100,000/year
 - HIV sero prevalence: 0.7%



- TB Index cases : newly detected smear-positive pulmonary TB patients older than 18 recruited at two urban health centres
- Household Contacts (HHC)
 - Extended family living in the same compound than TB case (> 3 months)
 - HHC inclusion :
 - Individual interview with standardized questionnaire
 - TST : Mantoux method
 - In house IGRA (random sample of 11 contacts/household)

Methods : HHC follow-up

- Active Follow-up : scheduled home visits by trained field workers each 6 months during 24 months
 - symptoms and signs suggestive of TB
 - TST at 12th month
 - In house ELISPOT : at 12th & 24th month
- Passive follow-up : HHCs encouraged to self-refer to the chest clinic for any symptom

TB suspects

- All HHCs referred by field assistants or self referred if:
 - symptoms suggestive of TB
 - TST ≥ 15 mm
- TB confirmation
 - Examination by experienced chest physician
 - Sputum smear and CXR
 - Any other investigations as needed

Results

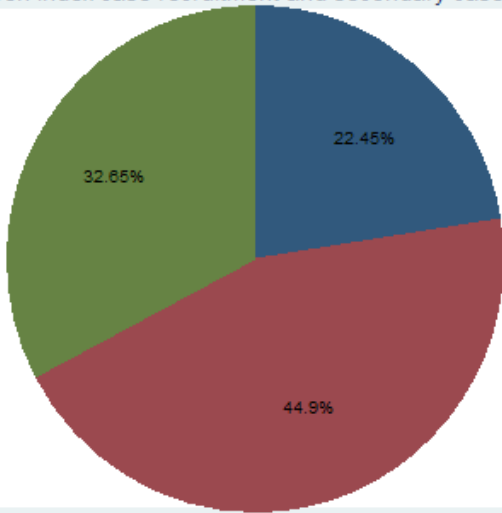
- **154 TB Index cases**
- **1990 HHCs**
 - Sex ratio (M/F) : 0.9 (931/1059)
 - Age (mean, range) : 23 years (6 m - 90 yrs)
 - TST: 1838 performed (152 not read)
 - 722 Elispot performed at baseline
- **49 secondary cases** detected → estimated incidence:
1,230/100,000 p-y

Secondary TB cases (N= 49)

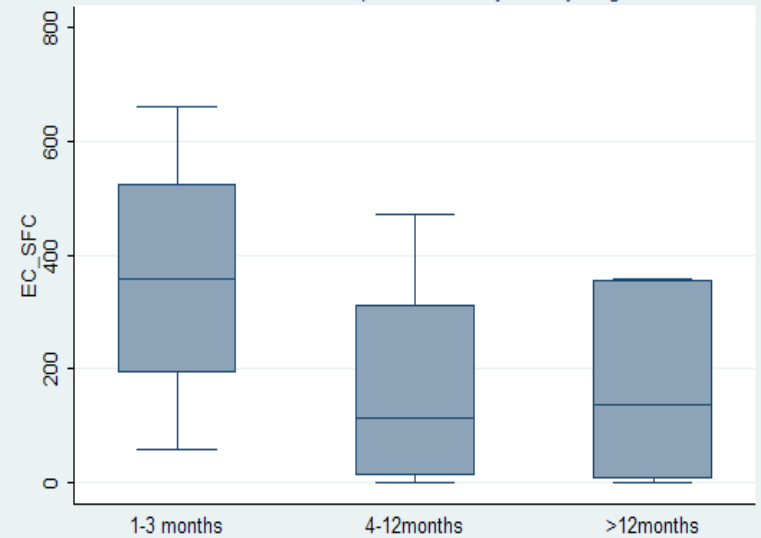
- Characteristics
 - Age (years) : mean 26; median 23 (6m-70y)
 - Sex ratio (M/F) : 0.9 (23/26)
- TB localisation:
 - Pulmonary : 39 (80%)
 - Extrapulmonary : 6 (12%)
 - Both : 4 (8%)
- Smear results:
 - Smear +ve : 36 (73.5%)
 - Culture +ve : 37 (75.5%)

Secondary TB cases : timing

time between index case recruitment and secondary cases detection



median of EC SFC Elispot baseline by time by diagnostic



Risk of active TB according to positive response at baseline

Test	Cut-off	# test positive at baseline (%)	# TB among positive test	OR [IC95]
TST (n = 1838)	10 mm	1173 (63.8)	37	2.1 [1.1-4.1]
	15 mm	572 (31.1)	27	3.4 [1.9-6.3]
EC Elispot (n= 762)	20 SFC	448 (58.8)	16	1.9 [0.7-4.9]
	30 SFC	377 (49.5)	15	2.2 [1.1-5.6]

Validity of TST and EC-ELISPOT for development of TB within 24 months

Test	TST		EC Elispot	
	10mm	15mm	20 SFC	30 SFC
Sensibility	82%	60%	73%	68%
Specificity	37%	70%	42%	51%

Risk factors analysis

Variables	Univariate OR [IC95]	<i>p</i>	Multivariate OR [IC95]	<i>p</i>
Age (years)				
- 1-4	1		1	
- 5-14	0.7 [0.2-2.9]	0.015	0.7 [0.1-3.1]	0.27
- 15-49	2.8 [0.8-9.0]		1.8 [0.5-6.3]	
- >= 50	1.3 [0.3-6.3]		1.2 [0.2-6.2]	
Former history of TB				
- No	1		1	
- Yes	10.1 [4.8-21.1]	< 10⁻⁵	8.0 [3.5-18.6]	< 10⁻⁵
Tabac				
- No	1		1	
- Yes	2.8 [1.3-6.2]	0.006	2.2 [0.9-5.3]	0.08
Contact with case during the day				
- < 4 h	1		1	
- 4-8 h	1.5 [0.6-3.6]	0.04	1.4 [0.5-3.6]	0.07
- > 8 h	3.2 [1.5-6.8]		2.5 [1.1-5.8]	
Proximity with the case at night time				
- Other space	1		1	
- Same bed/same room	3.4 [1.9-6.0]	< 10⁻⁵	2.6 [1.3-4.9]	0.004

Conclusion

- Development of TB in HHCs of smear-positive TB cases is associated with the degree of exposure to the case
- In our setting, TST and in-house ESAT-6/CFP-10 IGRA appear to be comparable in their ability to predict the development of active TB amongst HHCs of TB smear positive patients
- Further research is needed to estimate the predictive value of IGRAs

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Thank you for your attention