

Discordances between TST and IGRA to detect latent tuberculosis infection in paediatric contacts of drug-resistant tuberculosis patients

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BACKGROUND

- Accurate **diagnosis** of latent tuberculosis infection (LTBI) in paediatric contacts of TB is **important** for management.
- There is **no gold standard** for LTBI diagnosis
- Two tests are available for the diagnosis of LTBI:
 - **TST**: tuberculin skin test
 - **IGRA**: in vitro T-cell based interferon-gamma release assay
- Studies comparing IGRA and TST in adults suggest **IGRA is more specific**
- **More data are needed** on the performance of these tests in Drug Resistant (DR) children.

OBJECTIVES

- Primary:**
- To measure the agreement between TST and IGRA in detecting LTBI in paediatric contacts of patients with drug-resistant pulmonary TB in Armenia.
- Secondary:**
- To determine the agreement between TST and IGRA according to the age group.
 - To assess factors associated with discordant TST/IGRA results.

METHODS

- Design and population:**
- Data from a prospective cohort study of paediatric contacts (<15 years) of DR-TB cases in Armenia.
 - Study conducted between June 2012 and December 2016 (children were followed during 2 years).
- Study procedures:**
- Parallel performance of TST and IGRA test at initial assessment
 - TST test:
 - Same brand of tuberculin (PPD RT 23 SSI, 2 T.U./0.1 ml solution for injection) during the full course of study
 - Reading TST done 72 hours after administration by the study doctor
 - TST considered positive if induration ≥ 10 mm or 5mm in HIV infected or malnourished children
 - IGRA test:
 - ELISA test QTF-Gold (IFN- gamma)
 - Blood collection, incubation and testing according to the manufacturer standard operating procedure
 - Quality control every six months (Immunology Quality Services of the United Kingdom National External Quality Assessment Service)

RESULTS

Inclusions

- Inclusions: 150 children from June 2012 to December 2014
- IGRA and TST results available in 99/150 (66.0%)

Children characteristics

	Inclusions (N=99) n (%)
Age, median in years [IQR]	7 [1.3-13.9]
Age groups	
- 0-4 years	29 (29.3)
- 5-15 years	70 (70.7)
Girls	52 (52.5)
BCG vaccination	99 (100)
BCG scar present	46 (46.5)
Malnourished	5 (5.1)
HIV positive	0/3 (0)
Smear positivity index case	66 (66.7)
Household contact with index case	77 (77.7)

RESULTS (continuation)

Latent TB infection rate according to TST and IGRA results

- LTBI according to TST: 56/99 (56.5%, 95%CI: 46.6-66.5)
- LTBI according to IGRA: 53/99 (53.5%, 95%CI: 43.5-63.5)

Agreement between TST and IGRA test for detecting LTBI

Concordance between TST and IGRA:

- Overall: 82.8% (kappa=0.65, 95%CI: 0.45-0.84)
- Children 0-4 years: 89.7% (kappa=0.79; 95%CI: 0.43-1.15)
- Children 5-14 years: 80.0% (kappa=0.59; 95%CI: 0.36-0.85)

	IGRA+ n (%)	IGRA- n (%)	All n (%)
All children			
- TST+	46 (46.4)	10 (10.1)	56 (56.6)
- TST-	7 (7.1)	36 (36.4)	43 (43.4)
- All	53 (53.5)	46 (46.5)	99 (100)
Children 0-4 years			
- TST+	13 (44.8)	1 (3.4)	14 (48.3)
- TST-	2 (6.9)	13 (44.8)	15 (51.7)
- All	15 (51.7)	14 (48.3)	29 (100)
Children 5-15 years			
- TST+	33 (47.1)	9 (12.9)	42 (60.0)
- TST-	5 (7.1)	23 (32.9)	28 (40.0)
- All	38 (54.3)	32 (45.7)	70 (100)

*difference between two age groups is not statistically significant (p>0.05)

Factors associated with discordant TST and IGRA results

- Regression analysis did not identify any factor associated with discordant TST/IGRA results.

	Univariate analyses		
	OR	95 % CI	p
Age category			
0-4 years	1.00		
5-15 years	0.46	0.12-1.75	0.255
BCG scar			
absent	1.00		
present	0.97	0.34-2.76	0.957
Smear positivity of index case			
negative	1.00		
positive	2.72	0.93-7.88	0.066
Type of contact with the index case			
non-household	1.00		
household	0.44	0.14-1.38	0.161

*nutritional status was not included in the model, since all 5 malnourished children had concordant results

- Among IGRA positive children, we did not find differences between those TST positive and those TST negative.

	IGRA+/TST+ n=46	IGRA+/TST- n=7	p
Age category			
0-4 years, % (n)	28.3 (13)	28.6 (2)	
5-15 years, % (n)	71.7 (33)	71.4 (5)	1.000
BCG scar			
absent	52.2 (24)	42.9 (3)	
present	47.8 (22)	57.1 (4)	0.704
Smear positivity of index case			
negative	8.7 (4)	14.3 (1)	
positive	91.3 (42)	85.7 (6)	0.522

CONCLUSION

- Agreement between TST and IGRA among DR-TB paediatric contacts was fairly good.
- The additional benefit of IGRA for identifying LTBI is questionable.
- However, the use of TST alone would have missed 7% of LTBI cases regardless of the age of the child's contacts.