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Household Contact Tracing of Adult Pulmonary TB Patients in India: Prevalence of TB Infection and Disease

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Background

- WHO recommends systematic screening of high risk populations for tuberculosis infection (TBI) and disease as a key strategy for eliminating TB[1]
- Household contacts (HHC) of pulmonary TB cases are at high risk of contracting TBI and progressing to active disease[2]
- QuantiFERON-TB Gold in Tube (QGIT) and tuberculin skin test (TST) are commonly used tools for the detection of tuberculosis infection (TBI), but may yield differential results impacting eligibility for TB preventive therapy[3]
- Among HHC of newly diagnosed adult pulmonary TB cases in India, we sought to –
  1. Measure the proportion with TBI by TST and/or QGIT
  2. Measure discordance between TST and QGIT results

Methods

- We enrolled asymptomatic HHCs of newly diagnosed adult PTB cases at BJGMC, Pune and NIRT, Chennai, India from January 2014 to September 2016
- HHC were defined as individuals living in the same house as the index case during the 3 months prior to diagnosis of TB and were enrolled within 1 month of the index case being diagnosed with TB
- HHCs underwent TST (Span Diagnostics) and QGIT (Qiagen) testing at enrollment

TST:
- 2TU or 5TU of purified protein derivative (PPD) was placed intradermally and read 48-72 hours after placement by trained study staff
- Induration ≥ 5mm was defined as a positive TST[4]

QGIT:
- Approximately 1mL of blood was collected in standard QGIT tubes and incubated at 37°C for 16-24 hours
- INF-γ response ≥ 0.35 IU/mL defined as a positive QGIT

- Concordance between QGIT and TST (both 5mm and 10mm cutoffs) was assessed using % agreement and Kappa statistics
- TST (5mm cutoff) and/or QGIT positivity was assessed by HHC and index case characteristics using Fischer's exact test
- Logistic regression models were used to identify factors associated with TST (5mm cutoff) and QGIT discordance – defined as having either a positive TST and negative QGIT OR a negative TST and positive QGIT

Results

- 694 HHCs were enrolled from 346 households (HHC : Index = 2)
- 6 (1%) had culture confirmed TB disease at enrollment and were excluded from our analysis

Figure-1: Proportion of HHCs with a positive TST and/or QGIT

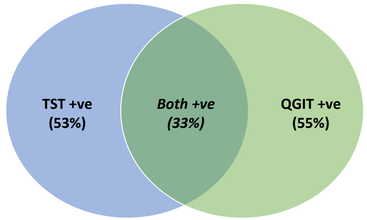
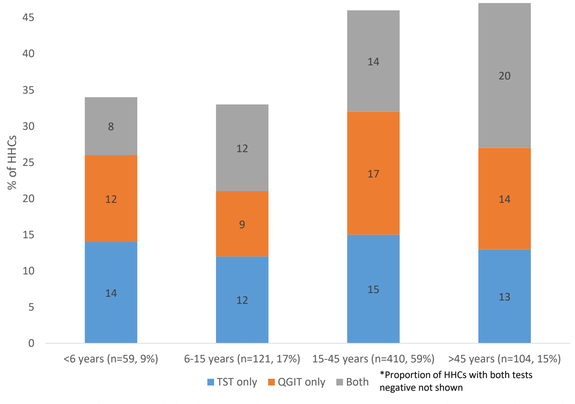


Figure-2: Proportion of HHCs with a positive TST and/or QGIT by age



- Proportion of HHCs with both TST and QGIT tests positive increased with age (***p=0.01***)

Table-1: % agreement and Kappa statistic for QGIT and TST

TST	QGIT Positive	QGIT Negative	Total	% agreement	Kappa (95% CI)
5mm cutoff					
Positive	232 (34%)	134 (19%)	366 (53%)	59%	0.17 (0.09 - 0.24)
Negative	151 (22%)	174 (25%)	325 (47%)		
10mm cutoff					
Positive	109 (16%)	23 (3%)	132 (19%)	57%	0.19 (0.14 - 0.24)
Negative	274 (40%)	285 (41%)	559 (81%)		
Total	383 (55%)	308 (45%)	691 (100%)		

- Poor concordance was noted between QGIT and TST results

Results

Table-2: Factors associated with TST and/or QGIT positivity

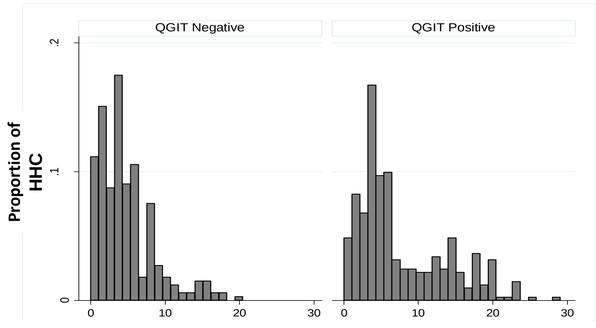
Characteristics	Total N (%)	TST+ve QGIT+ve N (%)	TST+ve QGIT-ve N (%)	TST-ve QGIT+ve N (%)	TST-ve QGIT-ve N (%)	P-value
HHC						
Sex						
Female	376 (54)	124 (53)	78 (58)	86 (57)	88 (51)	0.51
Male	315 (46)	108 (47)	56 (42)	65 (43)	86 (49)	
Smoking						
Never	228 (82)	65 (77)	39 (76)	38 (76)	86 (90)	0.13
Former	13 (5)	7 (8)	2 (4)	3 (6)	1 (1)	
Current	38 (14)	12 (14)	8 (16)	9 (18)	9 (9)	
HIV						
No	239 (97)	88 (97)	24 (100)	72 (96)	55 (96)	0.99
Yes	8 (3)	3 (3)	0	3 (4)	2 (4)	
DM						
No	461 (92)	159 (89)	94 (93)	116 (94)	92 (93)	0.45
Yes	42 (8)	20 (11)	7 (7)	8 (6)	7 (7)	
BCG scar						
No	153 (30)	65 (35)	36 (38)	25 (25)	27 (23)	***0.02***
Yes	349 (70)	121 (65)	58 (62)	77 (75)	93 (78)	
Contact						
Shares a bed	196 (28)	79 (34)	30 (22)	45 (30)	42 (24)	
Shares a room	281 (41)	96 (41)	54 (40)	57 (38)	74 (43)	0.37
Shares a house	185 (27)	50 (22)	43 (32)	42 (28)	50 (29)	
Other	13 (2)	4 (2)	3 (2)	2 (1)	4 (2)	
Index Case						
Cough						
No	11 (2)	0	7 (6)	1 (1)	3 (2)	***0.001***
Yes	651 (98)	223 (100)	119 (94)	148 (99)	161 (98)	
AFB smear						
Negative	189 (27)	50 (22)	28 (21)	42 (28)	69 (40)	***<0.001***
Positive	502 (73)	182 (78)	106 (79)	109 (72)	105 (60)	
Cavitation						
No	271 (50)	91 (48)	67 (57)	49 (43)	64 (55)	0.10
Yes	268 (50)	100 (52)	51 (43)	65 (57)	52 (45)	

AFB - Acid fast bacilli , DM – Diabetes mellitus

- HHC of index cases who had cough or were smear positive for AFB were more likely to have both TST and QGIT positive
- TST and QGIT discordance was associated with the index case not having cough (OR=3.83, 95%CI 1.00-14.58, p=0.04) or having an AFB smear grade of 3+ (OR=3.74, 95%CI 1.24-11.20, p=0.01)
- After adjusting for age, sex and having an index case with cough, AFB smear grade of 3+ remained a significant predictor of TST and QGIT discordance (aOR=3.98, 95%CI 1,31-12.10, p=0.01)
- HHCs of index cases with an AFB smear grade of 3+ were more likely to have a TST-ve and QGIT+ve discordance (9 of 16, 56%) compared to a TST+ve and QGIT-ve discordance (2 of 16, 13%) (p<0.001)

Results

Figure-3: Distribution of TST induration by QGIT result



- Median (IQR) TST induration in HHC with a positive QGIT = 6 (4-12) mm
- Median (IQR) TST induration in HHC with a negative QGIT = 4 (2-6) mm

Conclusions and Implications

- Nearly a third of HHCs of newly diagnosed adult pulmonary TB patients in India had both TST and QGIT positive for TBI
- Poor concordance was noted between QGIT and TST at both a 5mm and a 10mm cutoff
- Index cases who had cough or a smear positive for AFB were more likely to have HHCs with both TST and QGIT positive for TBI and should be considered for systematic screening and TB preventive therapy

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