T-SPOT®.TB Test for Latent Tuberculosis Infection Diagnosis and Treatment Guidance in Thai Healthcare Professionals

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Abstract

Background: Data on efficacy of T-SPOT®.TB Test (T-SPOT) in diagnosing latent tuberculosis infection (LTBI) and guiding isoniazid preventive therapy (IPT) among healthcare professionals (HCP) in tuberculosis (TB)-endemic settings is limited.

Methods: A prospective study was conducted among Thai HCP undergoing T-SPOT in June 2016 (initial screening) and June 2017 (follow-up). Nine-month isoniazid preventive therapy (IPT) was offered among the HCP with positive T-SPOT. The incidence of TB and the rates of conversion and reversion of T-SPOT were evaluated during the one-year follow-up period (June 2016 to June 2017).

Results: A total of 140 HCP underwent initial T-SPOT; the median age was 27 years (IQR 25-31 years), 89% were female and 23 (16%) were T-SPOT-positive. Eighty nine HCP (64%) had both initial and follow-up T-SPOTs. Among the 89 HCP, the initial and follow-up rates of T-SPOT positivity were 19% (N = 17) and 24% (N = 21), respectively. The conversion and reversion rates were 10% (N = 9) and 6% (N = 5), respectively. All of the 9 HCP (100%) with T-SPOT conversion reported significant contacts with patients who had active pulmonary TB without using appropriate personal protection equipment. During the 1-year follow-up period, incidence of TB were significantly higher among HCP with T-SPOT conversion compared to HCP with persistent positive T-SPOT, HCP with T-SPOT reversion and HCP with persistent negative T-SPOT [22 vs. 8 vs. 0 vs. 0 cases/100 person-years; P<0.001]. Of the 17 HCP with positive initial T-SPOT, 8 (47%) completed IPT. The incidence of TB was significantly lower and the T-SPOT reversion rate was significantly higher among HCP completing IPT compared to HCP declining or not completing IPT (0 vs. 11 cases/100 person-years; P<0.001 and 63% vs. 0%; P=0.009, respectively).

Conclusions: T-SPOT could be used for diagnosing LTBI, guiding IPT and identifying HCP with subsequent risk for TB. The serial T-SPOT may be used for evaluating IPT efficacy.

Background

- Healthcare professionals (HCPs) are at increased risk for tuberculosis (TB) acquisition through occupational exposure.
- Screening and treating latent tuberculosis (LTBI) among HCPs are essential to prevent subsequent development of active TB.
- T-SPOT®.TB is an interferon-γ release assay used for diagnosis of LTBI among HCPs.
- However, data on efficacy of T-SPOT®.TB in diagnosing LTBI and guiding isoniazid preventive therapy (IPT) among HCPs in TB-endemic settings is limited.

Methods

Population: Healthcare professionals
Settings: Thammasat University Hospital, a 600-bed tertiary-care hospital in Pathumthani, Thailand
Design: A prospective cohort study
Study period: 1 June 2016 to 30 June 2017
Inclusion criteria:
- All HCPs participating in the annual health screening program

Exclusion criteria:
- Having prior or current TB
- Currently on treatment for TB or LTBI
- Having any LTBI testing within the last 12 months

LTBI test:
- T-SPOT®.TB (Oxford Immunotec Ltd., U.K.) at baseline and a year later

Outcomes:
- TB incidence
- Conversion and reversion
- Changes in numbers of spots in the test

Figure: Study flow of the participants

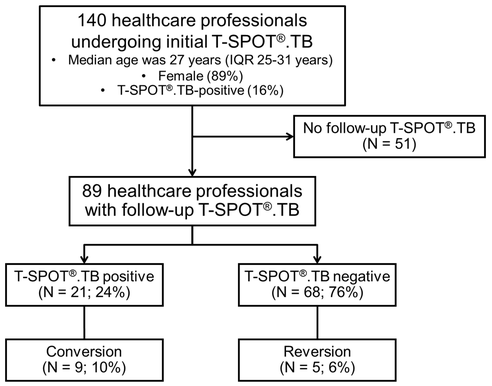

Table 2 Characteristics of the 89 HCPs during 1-year follow-up stratified by initial and follow-up T-SPOT®.TB results

Characteristics	Positive to Positive (N = 12)	Positive to Negative (N = 5)	Negative to Positive (N = 9)	Negative to Negative (N = 63)	P
Tuberculosis (TB) contact	11 (92)	5 (100)	9 (100)	59 (94)	0.90
Most common type of patients contacted					0.48
Smear positive pulmonary TB	8 (67)	4 (80)	4 (44)	42 (69)	
Smear negative pulmonary TB	1 (8)	0 (0)	4 (44)	13 (21)	
High-risk patients[a]	3 (25)	1 (20)	1 (11)	6 (10)	
Frequency of TB contact					0.72
One time	0 (0)	0 (0)	0 (0)	3 (5)	
Two to five times	2 (17)	2 (40)	0 (0)	17 (28)	
Six to ten times	1 (18)	1 (20)	1 (11)	8 (13)	
More than 10 times	8 (67)	2 (40)	8 (89)	31 (51)	
Total duration of TB contact					0.41
Less than one hour	2 (17)	2 (40)	1 (11)	17 (28)	
One to ten hours	2 (17)	1 (20)	3 (33)	17 (28)	
Eleven to fifty hours	1 (8)	1 (20)	2 (22)	5 (8)	
Fifty-one to one hundred hours	0 (0)	0 (0)	2 (22)	2 (3)	
More than one-hundred hours	6 (50)	1 (20)	1 (11)	18 (30)	
Close TB contact within 1 meter					0.37
Never	1 (8)	1 (20)	0 (0)	4 (7)	
Rarely	2 (17)	2 (40)	0 (0)	19 (31)	
Sometimes	2 (17)	1 (20)	3 (33)	12 (20)	
Often	4 (33)	0 (0)	5 (56)	13 (21)	
Always	3 (25)	1 (20)	1 (11)	13 (21)	
Respiratory contact with secretion from patients with pulmonary TB					0.19
Never	1 (8)	2 (40)	0 (0)	5 (8)	
Rarely	3 (25)	2 (40)	1 (11)	25 (41)	
Sometimes	2 (17)	0 (0)	2 (22)	9 (15)	
Often	3 (25)	0 (0)	3 (33)	10 (16)	
Always	3 (25)	1 (20)	3 (33)	12 (20)	
Use of N95 mask when contacting patients with pulmonary TB					0.50
Never	2 (17)	1 (20)	0 (0)	6 (10)	
Rarely	3 (25)	0 (0)	0 (0)	7 (12)	
Sometimes	0 (0)	1 (20)	2 (22)	3 (5)	
Often	3 (25)	2 (40)	4 (44)	17 (28)	
Always	4 (33)	1 (20)	3 (33)	28 (46)	
TB incidence (cases/100 patient-year)	8.33	0	22.22	0	**0.004**

Data are in numbers (%) unless indicated otherwise.
[a]Include homeless persons, HIV-infected persons, and patients with drug abuse

Results

Table 1 Baseline characteristics of the 89 healthcare professionals stratified by initial and follow-up T-SPOT®.TB results

Characteristics	All (N = 89)	Positive to Positive (N = 12)	Positive to Negative (N = 5)	Negative to Positive (N = 9)	Negative to Negative (N = 63)	P[a]
Age (years, median, IQR)	27 (25-32)	33 (31-39)	26 (24-31)	26 (25-28)	27 (25-32)	**0.004**
Female sex	79 (89)	10 (83)	5 (100)	8 (89)	56 (89)	0.80
Working duration (months, median, IQR)	48 (25-97)	120 (70-215)	38 (22-79)	42 (29-73)	36 (19-96)	**0.03**
History of tuberculosis contact	86 (97)	12 (100)	5 (100)	9 (100)	60 (95)	0.73
Most common type of patients contacted						**0.03**
Smear positive pulmonary tuberculosis	57 (64)	6 (50)	0 (0)	7 (78)	44 (70)	
Smear negative pulmonary tuberculosis	18 (20)	3 (25)	2 (40)	2 (22)	11 (18)	
High-risk patients[b]	14 (16)	3 (25)	3 (60)	0 (0)	8 (13)	
Frequency of tuberculosis contact since working						0.26
One time	1 (1)	0 (0)	0 (0)	0 (0)	1 (2)	
Two to five times	14 (16)	0 (0)	0 (0)	0 (0)	14 (22)	
Six to ten times	3 (3)	1 (8)	1 (20)	0 (0)	1 (2)	
More than 10 times	68 (76)	11 (92)	4 (80)	9 (100)	44 (70)	
Total duration of tuberculosis contact since working						0.55
Less than one hour	11 (12)	2 (17)	1 (20)	0 (0)	8 (13)	
One to ten hours	20 (23)	1 (8)	2 (40)	3 (33)	14 (22)	
Eleven to fifty hours	11 (12)	1 (8)	2 (40)	1 (11)	7 (11)	
Fifty-one to one hundred hours	8 (9)	1 (8)	0 (0)	2 (22)	5 (8)	
More than one-hundred hours	36 (40)	7 (58)	0 (0)	3 (33)	26 (41)	
Close tuberculosis contact within 1 meter						0.33
Never	3 (3)	0 (0)	0 (0)	0 (0)	3 (5)	
Rarely	19 (21)	2 (17)	1 (20)	2 (22)	14 (22)	
Sometimes	14 (16)	0 (0)	3 (60)	1 (11)	10 (16)	
Often	35 (39)	6 (50)	1 (20)	5 (56)	23 (37)	
Always	18 (20)	4 (33)	0 (0)	1 (11)	13 (21)	
Respiratory contact with secretion from patients with pulmonary tuberculosis						0.06
Never	9 (10)	1 (8)	3 (60)	1 (11)	4 (6)	
Rarely	18 (20)	1 (8)	1 (20)	2 (22)	14 (22)	
Sometimes	15 (17)	1 (8)	1 (20)	1 (11)	12 (19)	
Often	26 (29)	5 (42)	0 (0)	4 (44)	17 (27)	
Always	21 (24)	4 (33)	0 (0)	1 (11)	16 (25)	
Use of N95 mask when contacting patients with pulmonary tuberculosis						0.30
Never	9 (10)	3 (25)	1 (20)	0 (0)	5 (8)	
Rarely	7 (8)	3 (25)	0 (0)	0 (0)	4 (6)	
Sometimes	24 (27)	3 (25)	1 (20)	2 (22)	18 (29)	
Often	26 (29)	2 (17)	2 (40)	3 (33)	19 (30)	
Always	23 (26)	1 (8)	1 (20)	4 (44)	17 (27)	

Table 3 One-year outcomes among the 17 T-SPOT®.TB-positive HCPs who had completed and not completed isoniazid preventive therapy (IPT)

Outcomes	Completed IPT (N = 8)	No or not completed IPT (N = 9)	P
Tuberculosis incidence (case/100 patient-year)	0	11.11	**<0.001**
T-SPOT®.TB reversion (%)	5 (63)	0 (0)	**0.009**
Median changes in number of spots in T-SPOT®.TB (IQR)			
Panel A- nil	-4 [-1-(-8)]	-3 [18-(-27)]	0.96
Panel B – nil	-13 [1-(-18)]	-4 [11-(-37)]	0.82

Conclusion

- **HCPs who had persistently positive T-SPOT ®.TB and test conversion were at higher risk of TB development than those with persistently negative T-SPOT ®.TB and test reversion.**
- **The incidence of TB was significantly lower and the T-SPOT reversion rate was significantly higher among HCPs completing IPT compared to HCPs declining or not completing IPT.**
- **T-SPOT ®.TB could differentiate HCPs who had different risks for TB acquisition**
- **The test could be used for diagnosing LTBI and guiding IPT to prevent active TB**
- **The serial T-SPOT may be used for evaluating IPT efficacy as the reversion occurred frequently among HCPs completing IPT.**

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