SENSITIVITY COMPARISON OF TWO COMMERCIAL INTERFERON-GAMMA
RELEASE ASSAYS IN PULMONARY TUBERCULOSIS

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Key words: QuantiFERON, T-SPOT.TB, T-cell, interferon-gamma, pulmonary
tuberculosis

Running head: Sensitivity of IGRAs in pulmonary TB

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ABSTRACT

There are few head-to-head comparisons of the commercial interferon-gamma release assays (IGRAs). We compared the performance of the T-SPOT. TB and QuantiFERON Gold In-tube (QFT-IT) in patients with culture-proven pulmonary tuberculosis. Blood was drawn for both assays within 14 days of starting anti-tuberculosis treatment. The QFT-IT indeterminate rate was 3.5%; the T-SPOT. TB failure rate was 1.4%. There was poor agreement between the IGRAs (kappa 0.257) among the 270 patients with valid results for both tests. The sensitivities of the T-SPOT. TB and QFT-IT were 94.1% and 83.0% respectively, with a significant difference in the performance of the assays (McNemar test p=0.001). Factors independently associated with indeterminate QFT-IT results were age >= 60 years (OR 11.18, 95% CI 1.841-67.823, p=0.009), female sex (OR 7.47, 95% CI 1.517-36.733, p=0.013) and non-Chinese (ie. Indian or Malay) race (OR 7.89, 95% CI 1.585-39.267, p=0.012). The QFT-IT was significantly less sensitive in patients >= 60 years old (OR 0.41, 95% CI 0.181-0.918, p=0.030), and in Indian compared to Chinese patients (OR 0.27, 95% CI 0.073-0.990, p=0.048). The T-SPOT. TB was significantly less sensitive in Malay (OR 0.23, 95% CI 0.063-0.815, p=0.023) and Indian patients (OR 0.09, 95% CI 0.017-0.429, p=0.003) compared to Chinese. The performance of both assays was not significantly altered in diabetics. The diminished sensitivity of the IGRAs in persons of Malay and Indian race merits further study.
INTRODUCTION

The commercial T-cell based interferon-gamma (IFN \( \gamma \)) release assays (IGRAs) represent a long-awaited advancement in the field of TB diagnostics. These assays, which measure IFN \( \gamma \) responses to the Mycobacterium tuberculosis (tb)-specific antigens early secretory antigenic target 6 (ESAT-6) and culture filtrate protein 10 (CFP-10), are widely anticipated to replace the century-old tuberculin skin test (TST) (4,15,25,27). The IGRAs are marketed as the T-SPOT.\( \text{TB} \) (Oxford Immunotec, Abingdon, UK), the QuantiFERON-TB Gold (QFT-G) and QuantiFERON-TB Gold In-tube (QFT-IT) (Cellestis, Carnegie, Victoria, Australia). The QFT-IT measures the IFN \( \gamma \) response to Rv2654 (TB 7.7) antigen in addition to ESAT-6 and CFP-10.

Apart from their operational advantages over the TST, the IGRAs have demonstrated superior specificity (approaching 100%) over the TST in previously BCG-vaccinated persons (3,17,21) and would be especially useful in overcoming the problem of false positive TST responses due to cross-reactivity with \( M. \text{bovis} \) BCG vaccine. Regarding the sensitivity of the IGRAs, in the absence of a gold standard for latent TB infection (LTBI), most studies have utilized exposure gradient to the infectious source case in contact investigations or active TB as surrogate markers for LTBI. Using exposure gradient, the T-SPOT.\( \text{TB} \) or its precursor versions have been shown to correlate better with exposure than the TST in point-source contact investigations in low incidence settings (8,26,30). Although it is recognized that active and latent TB states may manifest different T-cell immune responses to the \( M. \ \text{tb} \)-specific antigens, and that there is potential...
diminution of the cell-mediated immune response in active TB, many
investigators have nonetheless utilized active TB as a surrogate for LTBI. A
meta-analysis of studies using this surrogate showed a pooled sensitivity of 76%
for QFT-G / QFT-IT, versus 88% for ELISPOT / T-SPOT. TB, and 70% for TST
using various cut-off readings (20).

To date, there have been few published head-to-head comparisons of the
T-SPOT. TB and QFT-G / QFT-IT. Three such studies in active TB have reported
superior sensitivity of the T-SPOT. TB over the QFT-G (9,18,11), while a study in
paediatric patients showed equivalent sensitivity of the T-SPOT. TB and QFT-IT
(7). A head-to-head study comparing the T-SPOT. TB, QFT-IT and TST in non-
BCG-vaccinated subjects in a point-source contact investigation in the
Netherlands showed both IGRAs to be significantly associated with hours of
exposure (the QFT-IT more so than the T-SPOT. TB), while the TST at cut-off
>=15 mm did not show any association (1).

Although both the T-SPOT. TB and QFT-IT measure T-cell IFN \( \gamma \)
responses to similar \( M. \ tb \)-specific antigens over a 16 to 24 hour incubation
period, they are based on different technology platforms. The T-SPOT. TB is
based on the enzyme-linked immunospot (ELISpot) methodology and requires
the isolation and incubation of peripheral blood mononuclear cells (PBMCs) and
standardization of 250,000 PBMCs in each of its test wells. The QFT-IT has
technical and logistical advantages over the T-SPOT. TB, as the stimulation of T-
cell IFN \( \gamma \) response in whole blood is carried out in tubes pre-coated with the \( M. \)
tb antigens. Although incubation followed by centrifugation are time critical
steps, IFN-γ detection, using the enzyme-linked immunosorbent assay (ELISA) method, is time flexible and may be delayed for up to 4 weeks. However, as the background ‘noise’ is higher, a “Nil” control is required in an attempt to adjust for this background, heterophile antibody effects, and non-specific IFN-γ in blood samples. The T-SPOT. TB may be more laborious but the use of a standardized number of washed PBMCs presumably contributes to the greater sensitivity reported in the literature.

We compared the performance of the T-SPOT. TB and the QFT-IT in a cohort of culture-proven pulmonary TB (pTB) patients treated at the Singapore TB Control Unit (TBCU). We used baseline data collected as part of a larger study evaluating these assays for monitoring response to TB treatment and predicting relapse.

**METHODS**

This study was approved by the Domain Specific Institutional Review Board of the National Healthcare Group. The study population comprised patients evaluated and treated for pulmonary TB at the Singapore TBCU, the national referral centre where approximately 60% of the country’s cases are treated. The study subjects were prospectively recruited between April 2006 and May 2007. All participants gave informed consent.

Patients deemed likely to have pTB based on clinical and radiological findings were recruited within 2 weeks of starting TB treatment. At least two sputum specimens were obtained on separate days for acid-fast bacilli (AFB)
smears and TB culture and drug sensitivity testing prior to starting treatment.

Peripheral venous blood was drawn for both IGRA's at the time of recruitment. Tuberculin skin tests (TST) were performed at the discretion of the attending physician. HIV testing was routinely offered. Random blood glucose and liver enzymes were routinely performed prior to starting treatment. As the main study required patients to be followed up for at least two years for relapse, those in whom overall prognosis was guarded (eg. the frail elderly, or with co-existing advanced malignancy), or who did not reside permanently in Singapore were excluded from the study. Data on patient demographics, co-morbidities, bacteriological status, and radiological findings were captured. The treating physicians were blinded to the patients' IGRA results.

**T-SPOT.TB assay**

Blood was collected in dedicated tubes (BD vacutainer 10 ml plus Lithium Heparin) tubes and sent to the laboratory at room temperature within six hours of sampling. The assay was performed and interpreted according to the manufacturer's instructions. The test result was considered positive if either or both of Panel A (containing ESAT-6 antigen) or Panel B (containing CFP-10 antigen) had six or more spots than the negative control and this number was at least twice the number of spots in the negative control. The test was considered failed if the negative control spot count was > 10, or if there were < 20 spots in the positive control and both Panel A and B were non-reactive according to the criteria above. Spots were counted with an ELISpot reader (AID, Strasberg, Germany) and manually verified.
QFT-IT assay

Blood was collected in three heparinised 1 mL tubes provided as part of the kit; the ‘antigen’ tube contained TB specific stimulating antigens (ESAT-6, CFP-10 and TB7.7), the mitogen (positive control) tube contained phytohemaglutinin, the third was a ‘nil’ control tube. The assay was performed and interpreted according to the manufacturer’s instructions.

Statistical Analysis

Data obtained from questionnaires were entered and analyzed using SPSS version 15. The outcome of the two IGRA (T-SPOT.\(TB\) /QFT-IT) was compared using the McNemar test. Kappa test was used to evaluate the agreement between the two IGRA.

The association between characteristics of subjects and indeterminate QFT-IT tests and positive T-SPOT.\(TB\) and QFT-IT results was evaluated using the Chi-square test or Fisher’s exact test. Odds ratios (OR)s were estimated, and the logistic regression model was constructed to adjust for confounding factors and to obtain the adjusted ORs.

RESULTS

We recruited 350 participants treated for pTB at the TBCU from April 2006 to May 2007. \textit{Mycobacterium tuberculosis complex} (MTC) was isolated from the sputa of 286 (81.7\%) patients. Non-tuberculous mycobacteria (NTM) was isolated from the sputa of 13 patients, one of whom had dual growth (i.e. MTC and NTM). Of the 51 sputum culture-negative patients, 38 were deemed active
pTB on radiological and clinical grounds, and 13 patients were eventually deemed not to have pTB.

Characteristics of patients with sputum culture-positive pTB (n=286)

The patients’ median age was 48.6 years (range 17 to 77 years). There were 74 females (25.9%). The majority of patients were Chinese (195 or 68.2%), followed by Malay (67 or 23.4%), Indian (14 or 4.9%) and other races (10 or 3.5%). Diabetes mellitus was the most common co-morbidity, occurring in 103 patients (36.0%). Of the 238 subjects with known HIV status, seven were HIV-positive. Two patients had end-stage renal failure, and one had malignant disease.

Thirteen patients had indeterminate or failed IGRA results: nine had indeterminate QFT-IT alone, one had indeterminate QFT-IT and failed T-SPOT. TB, and three had failed T-SPOT. TB results. Three patients were recruited after having received more than 14 days of TB treatment. The above patients were excluded from the sensitivity analysis which was performed on 270 culture-proven cases with positive or negative results for their T-SPOT. TB and QFT-IT tests taken within 14 days of starting TB treatment (figure 1). Of these, the vast majority (79%) were IGRA tested within seven days.

Patients with indeterminate / failed IGRA results

The rate of indeterminate QFT-IT was 3.5% (10/286). All the indeterminate results had mitogen minus nil values < 0.5 IU/ml and antigen minus nil values < 0.35 IU/ml. The T-SPOT. TB failure rate was 1.4% (4/286). Three failed results had positive control counts of < 20 SFCs and counts of <= 6
SFCs in both antigen wells, while one had a negative control count of > 10 SFCs. Of the 10 patients with indeterminate QFT-IT results, one had failed T-SPOT.\textit{TB}, one had negative T-SPOT.\textit{TB}, and eight had positive T-SPOT.\textit{TB} results. The patient with indeterminate QFT-IT and failed T-SPOT.\textit{TB} results was a 75-year-old Malay diabetic man who was HIV-negative. Seven of the 10 patients with indeterminate QFT-IT and two of the four patients with failed T-SPOT.\textit{TB} were diabetics.

Factors independently associated with indeterminate QFT-IT results were age $\geq$ 60 years (OR 11.18, 95% CI 1.841-67.823, $p=0.009$), female sex (OR 7.47, 95% CI 1.517-36.733, $p=0.013$) and non-Chinese race (ie. Indian / Malay) (OR 7.89, 95% CI 1.585-39.267, $p=0.012$) (Table 1). Diabetes was significantly associated with indeterminate QFT-IT on univariate analysis; however, this association was not found on multivariate analysis.

**Comparison of T-SPOT.\textit{TB} and QFT-IT results in 270 patients**

The T-SPOT.\textit{TB} was positive in 254 (94.1%) and the QFT-IT in 224 (83.0%) subjects. There was a statistically significant difference in the performance of the two assays (McNemar test $p=0.001$) (table 2). There was poor agreement between the two assays (kappa 0.257). There was no significant difference in the sensitivity of the T-SPOT.\textit{TB} between those tested within seven days and those tested at eight to 14 days of treatment (93.4% vs 96.5%, $p=0.536$). Similarly, no difference was seen in the sensitivity of the QFT-IT between these two groups (83.1% vs 82.5, $p=0.909$). TSTs were performed for
217 patients. The TST sensitivity was 72.8% taking >= 15 mm as the cut-off and
94.9% taking >= 10 mm as the cut-off.

The T-SPOT.\textit{TB} was significantly less likely to be positive in Malay (OR
0.23, CI 0.063-0.815, p=0.023) and Indian patients (OR=0.09, CI 0.017-0.429,
p=0.003) compared to Chinese patients. As all the HIV-infected patients were T-
SPOT.\textit{TB} positive, analysis for this variable could not be performed (table 3).

The QFT-IT was significantly less likely to be positive in those >= 60 years of age
(OR=0.41, 95% CI 0.181-0.918, p=0.03) and in Indian compared to Chinese
patients (OR 0.27, 95% CI 0.073-0.990, p=0.048) (table 4).

Quantitative IGRA results for Chinese vs non-Chinese patients

Comparison of the quantitative T-SPOT.\textit{TB} results between Chinese and
non-Chinese patients showed a statistically significant difference in the median
number of spot-forming cells (SFCs) above negative control in response to
ESAT-6 (32.5 vs 17 SFCs/2.5 x 10^5 PBMCs, p=0.003), but not to CFP-10 (37.5
vs 34 SFCs/2.5 x 10^5 PBMCs, p=0.613). There was no significant difference in
the quantitative QFT-IT results of Chinese versus non-Chinese patients (median
IFN\textgamma 2.4 vs 1.8 IU/ml, p=0.521).

Concordance / discordance in IGRA results

Two hundred and eighteen patients (80.7%) were T-SPOT.\textit{TB} / QFT-IT
positive; 36 (13.3%) were T-SPOT.\textit{TB} positive / QFT-IT negative, 6 (2.2%) were
T-SPOT.\textit{TB} negative / QFT-IT positive, and 10 (3.7%) were both T-SPOT.\textit{TB} /
QFT-IT negative. The last group comprised a disproportionately high number of
Malays (4/10) and Indians (4/10). The percentage of patients with dually negative
tests among the various races was 6.3% in the Malays, 16.7% in the Indians and 2.2% in the Chinese. There were no HIV-infected, renal failure or cancer patients who tested negative with both T-SPOT.\textit{TB} / QFT-IT.

\section*{DISCUSSION}

Head-to-head comparison of the two commercial IGRAs showed poor agreement between the two assays and a significant difference in their performance in our cohort of 270 culture-proven pTB patients. The T-SPOT.\textit{TB} was more sensitive than the QFT-IT (94.1\% versus 83.0\%). The sensitivity of the QFT-IT was significantly diminished in patients \(\geq 60\) years old. We found a disparity in the performance of the IGRAs in different races. Both assays were significantly less sensitive in Indians, with the T-SPOT.\textit{TB} also less sensitive in Malays, compared to Chinese patients. Indeterminate QFT-IT results were more likely in persons \(\geq 60\) years old, female and non-Chinese. The performance of the IGRAs was not significantly affected by the presence of diabetes.

It was not the aim of this present study to evaluate the clinical utility of the IGRAs in diagnosing or ruling out active TB. Rather, we took the opportunity to compare the performance of the two commercial IGRAs in culture-proven TB cases utilizing baseline data from a cohort of pTB patients recruited into a main study evaluating the utility of the IGRAs in monitoring treatment response and predicting relapse. Many of our subjects at enrollment were clinically obvious cases of active pTB in whom the use of the IGRAs as a diagnostic aid would not be necessarily indicated. As the aim of the main study required successful
treatment completion and a follow-up period of at least two years, we had
excluded patients with advanced age, extreme frailty and severe illness. Our
study findings would thus not illuminate on the sensitivities of the IGRAs in such
patients. Nevertheless, we believe that this comparative analysis still provides
potentially useful information regarding the performance of the two commercial
IGRAs.

To our knowledge, this is the largest cohort of culture-proven TB patients
in whom head-to-head comparison of the T-SPOT. TB and QFT-IT has been
reported. The sensitivities of the T-SPOT. TB and QFT-IT in our patients with
active TB reiterates that of previous publications (20). The T-SPOT. TB’s
consistently superior sensitivity is likely explained by the required 250,000
PBMCs in each of its test wells; whereas the measurement of IFNγ in the
supernatent of whole blood in the QFT-IT would adversely affect this assay’s
performance in immunosuppressed persons with low T-cell counts. Our relatively
low QFT-IT indeterminate rate of 3.5% compared to others (9,10) may be due to
our exclusion of frail elderly and severely ill patients. Despite this, we still found a
higher indeterminate rate and diminished sensitivity of the QFT-IT in our older
patients (ie. those > 60 years of age). The higher indeterminate QFT-IT rate in
our female patients is unexplained. Although the sensitivity of the QFT-IT was not
significantly diminished in our HIV-infected patients, there was a difference
(which could be clinically important) in its performance compared to the T-
SPOT. TB in these patients, the QFT-IT being positive in 4/7, vs 7/7 for T-
SPOT. TB. The 100% sensitivity of the T-SPOT. TB in our albeit small number of
HIV-infected patients is consistent with the findings of other reports regarding this assay's undiminished sensitivity in patients with HIV infection or haematological malignancies using active TB or exposure as surrogates for LTBI (5,19,23). It may be argued that lowering the positivity threshold of the QFT-IT should increase its sensitivity to that of the T-SPOT.\textit{TB}. This will, however, be at the expense of reduced specificity. This issue could not be addressed in this study as we did not seek to compare the performance of these assays in healthy controls.

The particular influences of racial and genetic factors on the performance of the commercial IGRAs have not been well-studied in the clinical setting. It has been previously shown that the responses to ESAT-6 and CFP-10 varied between individuals with different HLA-DR types (2). A study in West African twins also reported that memory T-cell responses to “short-term culture filtrate” and peptides from the ESAT-6 protein are subject to genetic regulation (13). We showed, for the first time, a disparity in the performance of the commercial IGRAs among different racial groups, with an increased likelihood of indeterminate QFT-IT results in Malays and Indians compared to Chinese patients, and diminished T-cell responses to the \textit{M.tb}-specific antigens in Malays (with the T-SPOT.\textit{TB} assay) and Indians (with both T-SPOT.\textit{TB} and QFT-IT) compared to Chinese. Another novel finding was the different quantitative T-cell responses to the individual antigens in the T-SPOT.\textit{TB} assay, with the Chinese patients showing significantly greater quantitative responses to ESAT-6, but not to CFP-10, compared to the non-Chinese. The disparity in T-cell responses
among these different races merits further study as this would have potential
implications in the use and interpretation of the IGRAs among different
populations as well as in the field of TB vaccine research and development.

The performance of the IGRAs in patients with diabetes, an important TB
risk factor, has not been widely reported. Diabetes is poised to be the “next
epidemic”, with the number of people with this condition worldwide projected to
increase from 171 million in 2000 to 366 million in 2030 (28). Southeast Asia and
the Western Pacific region are at the forefront of the diabetes epidemic (12) and
we anticipate that this situation would render TB control in these high TB burden
regions an even greater challenge. Singapore has the highest incidence of
diabetes in Asia with a prevalence of 8.2%, which increased with age to 28.7%
among those 60 years and above (24). Although the presence of diabetes was
not independently associated with diminished performance of either IGRA, a
substantial proportion of patients with indeterminate QFT-IT or failed T-SPOT.\textit{TB}
results were diabetic. Whether the degree of diabetic control affected T-cell
response to the \textit{M. tb}-specific antigens was not specifically addressed by our
study design.

In conclusion, head-to-head comparison of the T-SPOT.\textit{TB} and QFT-IT in
270 culture-positive pTB patients showed superior sensitivity of the T-SPOT.\textit{TB}
over the QFT-IT using the manufacturers’ cut-offs. The performance of the QFT-
IT was diminished in patients above 60 years of age. Our finding of decreased
sensitivity of the IGRAs in patients of Indian or Malay race (as compared to
Chinese) highlights the need for further studies pertaining to the use and interpretation of these assays in different racial groups.

ACKNOWLEDGEMENTS

We thank all the patients who participated in the study. We also thank laboratory technician Ms Agampodi Pereira, Nursing Office Kwee-Yin Han and all medical and nursing staff of the TBCU.

Source of financial support:

This work was supported by the National Medical Research Council grant 1004 / 2005 from the Singapore Ministry of Health.
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Int J Tuberc Lung Dis. 9:1242-1247
Figure legend

Figure 1: There were 350 patients enrolled. The final analysis was performed on 270 sputum culture-positive subjects after exclusion of 51 culture-negative patients, 13 patients with NTM disease, 13 patients with indeterminate/failed IGRA results and 3 patients who were recruited after having received more than 14 days of treatment.
Subjects enrolled
N=350

- 51 culture-negative patients (38 clinical pTB, 13 not pTB)
- 13 patients with NTM

Culture-proven pTB
N=286

- 13 patients with indeterminate / failed IGRA results
  - Nine indeterminate QFT-IT
  - Three failed T-SPOT
  - One indeterminate QFT-IT and failed T-SPOT

- Three patients recruited after > 14 days of TB treatment

Culture-proven pTB with positive or negative IGRA results at <= 14 days of TB treatment
N=270
Table 1. Univariate and Multivariate analyses of patient characteristics associated with indeterminate QFT-IT results (10/280)

<table>
<thead>
<tr>
<th>Patient and Disease Characteristics</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>QFT Indeterminate</td>
</tr>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 60</td>
<td>227</td>
<td>6(2.6)</td>
</tr>
<tr>
<td>&gt;= 60</td>
<td>53</td>
<td>4(7.5)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>209</td>
<td>5(2.4)</td>
</tr>
<tr>
<td>Female</td>
<td>71</td>
<td>5(7.0)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>189</td>
<td>3(1.6)</td>
</tr>
<tr>
<td>Non Chinese</td>
<td>91</td>
<td>7(7.7)</td>
</tr>
<tr>
<td><strong>HIV status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative / Unknown</td>
<td>273</td>
<td>10(3.7)</td>
</tr>
<tr>
<td>Positive</td>
<td>7</td>
<td>0(0.0)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>180</td>
<td>3(1.7)</td>
</tr>
<tr>
<td>Yes</td>
<td>100</td>
<td>7(7.0)</td>
</tr>
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</table>

* **unable to estimate risk as there were no indeterminate QFT results in the HIV-infected group**
Table 2. Number of positive and negative QFT-IT and T-SPOT. *TB* tests

<table>
<thead>
<tr>
<th>T-SPOT. <em>TB</em></th>
<th>QFT-IT</th>
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<tbody>
<tr>
<td></td>
<td>Results</td>
<td>Negative</td>
<td>Positive</td>
<td>Total</td>
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<tr>
<td>Negative</td>
<td>10</td>
<td>6</td>
<td></td>
<td>16</td>
</tr>
<tr>
<td>Positive</td>
<td>36</td>
<td>218</td>
<td></td>
<td>254</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>224</td>
<td></td>
<td>270</td>
</tr>
</tbody>
</table>

McNemar test $p<0.001$
Table 3. Univariate and Multivariate analysis of patient characteristics associated with positive T-SPOT. TB results (254/270)

<table>
<thead>
<tr>
<th>Patient and Disease Characteristics</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>T-SPOT Positive No. (%)</td>
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<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 60</td>
<td>221</td>
<td>208 (94.1)</td>
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<td>&gt;= 60</td>
<td>49</td>
<td>46 (93.9)</td>
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<tr>
<td><strong>Gender</strong></td>
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<td></td>
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<tr>
<td>Male</td>
<td>204</td>
<td>191 (93.6)</td>
</tr>
<tr>
<td>Female</td>
<td>66</td>
<td>63 (95.5)</td>
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<tr>
<td><strong>Ethnicity</strong></td>
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<tr>
<td>Chinese</td>
<td>186</td>
<td>180 (96.8)</td>
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<tr>
<td>Malay</td>
<td>63</td>
<td>57 (90.5)</td>
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<tr>
<td>Indian</td>
<td>12</td>
<td>9 (75.0)</td>
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<tr>
<td>Others</td>
<td>9</td>
<td>8 (88.9)</td>
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<tr>
<td><strong>HIV status</strong></td>
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<td></td>
</tr>
<tr>
<td>Negative / Unknown Unknown</td>
<td>263</td>
<td>247 (93.9)</td>
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<td><strong>Diabetes mellitus</strong></td>
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<td></td>
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<tr>
<td>No</td>
<td>177</td>
<td>165 (93.2)</td>
</tr>
<tr>
<td>Yes</td>
<td>93</td>
<td>89 (95.7)</td>
</tr>
</tbody>
</table>

* Unable to estimate risk as the T-SPOT. TB was 100% positive in the HIV-infected group
Table 4. Univariate and Multivariate analyses of patient characteristics associated with positive QFT-IT results (224/270)

<table>
<thead>
<tr>
<th>Patient and Disease Characteristics</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
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<td></td>
<td>Total</td>
<td>QFT Positive No. (%)</td>
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<td>QFT Positive No. (%)</td>
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<tr>
<td><strong>Age (years)</strong></td>
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<tr>
<td>&lt; 60</td>
<td>221</td>
<td>188 (85.1)</td>
</tr>
<tr>
<td>&gt;= 60</td>
<td>49</td>
<td>36 (73.5)</td>
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<tr>
<td><strong>Gender</strong></td>
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<tr>
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<td>166 (81.4)</td>
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<tr>
<td>Female</td>
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<td>58 (87.9)</td>
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<td>Indian</td>
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<td>Others</td>
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<tr>
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<td>75 (80.6)</td>
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