Effect of HIV on Latent TB Screening of Pregnant Women in Pune, India

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BACKGROUND

- The World Health Organization (WHO) recommends isoniazid preventive therapy (IPT) for all HIV-infected people, including pregnant women.[1]
  - Both HIV[2] and pregnancy[3] increase the risk of converting from latent TB infection (LTBI) to active TB disease.
- Many programs, including Brazil and South Africa, are considering LTBI tests to identify who will benefit most from IPT.
  - Use of the tuberculin skin test (TST) us hampered by operational challenges and supply shortages.
  - The role of the newer interferon gamma release assay (IGRA) in high burden countries is still unclear.[4]
- Immune changes of both HIV and pregnancy may impact the performance of the two most commonly used immune-based LTBI tests– the tuberculin skin test (TST) and the IGRA.[5]
- **We compare the performance of the TST versus the IGRA in HIV-infected and –uninfected pregnant women in India, where ~40% of the population has LTBI.[6]**

METHODS

We performed a cross-sectional study of 128 HIV-infected pregnant women and 158 HIV-uninfected pregnant women to compare the perfomance of the TST versus an IGRA (QuantiFERON® TB Gold In-tube (QGIT))

Study population: Pregnant women seeking antenatal care in their 2nd or 3rd trimester.

Study Site: Antenatal clinic at Sassoon General Hospital, an urban, public government hospital in Pune, India

Enrollment Visit:
- Sociodemographic questionnaire administered by trained counselors.
- Medical/obstetric history questionnaire, including WHO-recommended TB symptom screen, administered by trained nurses.
- TST and QGIT testing by trained nurses and lab staff, respectively

Analysis:
- Agreement was measured using the kappa statistic with the following definitions: 0.20-0.39= fair agreement; 0.40-0.59= moderate agreement
- Percent positivity with binomial exact 95% confidence intervals was estimated.
- Odds ratios (OR) for risk factors of test positivity and discordance were estimated using a logistic regression model adjusting for education, location of home, number of adults in the household, TB contact, gestational age (GA), and HIV.

RESULTS

Table 1. Participant characteristics by HIV status

Characteristic	HIV-infected (n=125)	HIV-uninfected (n=158)	p value
Sociodemographics			
Location of residence			0.005
Urban/periurban	110 (85%)	150 (94%)	
Rural	18 (14%)	8 (5%)	
Joint family	54 (42%)	115 (73%)	<0.005
Median adults in the home (IQR)	2 (2-4)	4.5 (3-6)	0.0001
Median children in the house (IQR)	1 (0-2)	1 (0-2)	0.29
Employed for pay	26 (20%)	15 (9.5%)	0.009
Education level ≤4th grade	26 (20%)	20 (12%)	0.08
Medical/Obsetric History			
Median gestational age, wks (IQR)	25 (21-30)	26 (23-30)	0.38
Median CD4 (per mm3)	518 (384-685)	-	
Taking antiretroviral treatment	50 (39%)	NA	
TB History			
Positive TB symptom screen	12 (9.7%)	11 (6.9%)	0.39
Positive household TB symptom screen	12 (9.4%)	30 (19%)	0.02
Known TB contact	10 (7.8%)	4 (2.5%)	0.03
Prior/current use of INH	0 (0%)	0 (0%)	

Table 2. LTBI test results by HIV status

LTBI test result	HIV-infected (n=125)	HIV-uninfected (n=158)	p value
TST			0.57
Positive	15 (11%)	27 (17%)	0.20
Negative	99 (77%)	117 (74%)	0.52
Did not return	14 (10%)	14 (8%)	0.55
QGIT			0.45
Positive	38 (29%)	51 (32%)	0.63
Median IFN-γ (IU/mL),(IQR)	3.2 (1.2-9.7)	2.7 (1.1-5.5)	0.28
Negative	88 (68%)	103 (65%)	0.52
Indeterminate	2 (1.5%)	4 (2.5%)	0.69
TST+/QGIT+	9 (7%)	21 (15%)	0.08
Median IFN-γ (IU/mL), (IQR)	9.3 (3.4-10)	3.9 (2.5-5.6)	0.14
TST+/QGIT-	6 (4.6%)	6 (4.2%)	0.70
Median IFN-γ (IU/mL), (IQR)	0.12 (0.40-0.18)	0.18 (0.1-0.26)	0.33
TST-/QGIT+	24 (18%)	25 (17%)	0.92
Median IFN-γ (IU/mL), (IQR)	1.85 (1.1-4.4)	2.28 (1.1-3.7)	0.95
TST-/QGIT-	73 (57%)	88 (62%)	0.82
Median IFN-γ (IU/mL), (IQR)	0.1 (0.07-0.16)	0.19 (0.05-0.9)	0.79
Kappa	0.22 (0.03-0.40)	0.40 (0.24-0.56)	

Figure 1. Comparison of TST vs QGIT results, by HIV status

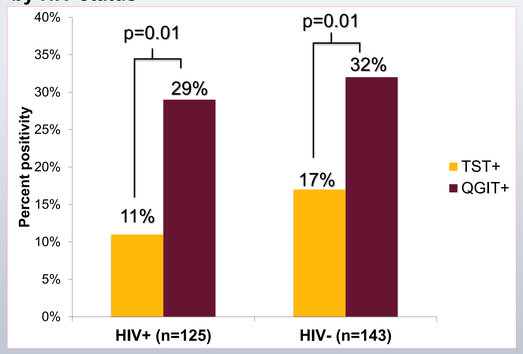
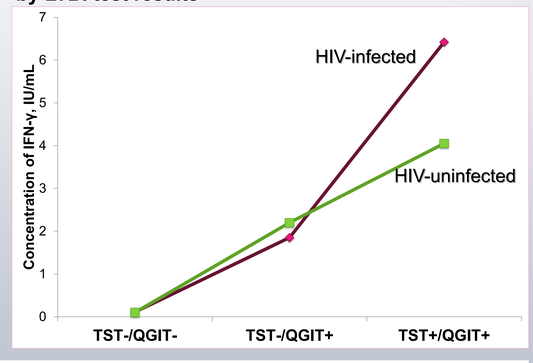


Figure 2. Concentration of IFN-γ in pregnant women, by LTBI test results



- *Figure 1*: Compared to HIV-uninfected women, HIV-infected women had lower TST positivity (p=0.2) and lower QGIT positivity (p=0.63).
- *Figure 2*: HIV-infected women with TST-/QGIT+ discordance produced significantly less IFN-γ than those with TST+/QGIT+ results (1.8 vs 6.4 IU/mL, p=0.02). There was trend towards this in the HIV-uninfected women (2.2 vs 4.0 IU/mL, p=0.12)
- In multivariate analysis, a positive QGIT was associated with having a known TB contact (aOR 2.9, 95% CI: 1-8.9, p=0.05)
  - A positive TST was not associated with a known TB contact (aOR 1.0, 95%CI 0.20-5.4, p=0.93)

CONCLUSIONS

1. Discordance between the IGRA and TST is common in pregnant women, regardless of HIV status.
   - The IGRA returned significantly more positive results than the TST in both HIV-infected and HIV-uninfected pregnant women.
   - A positive IGRA was also associated with having a known TB contact and more closely matched LTBI prevalence in the general population of India.
2. HIV-infected women with TST-/IGRA+ discordance produced lower amounts of IFN-γ when stimulated with TB antigens, suggesting that insufficient IFN-γ disproportionately impairs TST performance.
3. Reliance on the TST for LTBI screening in antenatal programs would result in 50% fewer HIV-infected women being treated with IPT.

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