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High TB Risk in HIV-Positive Patients on Second line Antiretrovirals in Pune, India

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Background

- Tuberculosis (TB) continues to be the leading cause of opportunistic infection and death among HIV-infected patients [1].
- With the increasing coverage and a 2-4% rate of virologic failure on first line antiretroviral treatment (ART) regimens globally, the number of patients who will need second-line ART containing protease inhibitor (PI) based regimens is increasing. [2]
- But, globally data gaps exist on risk of TB among HIV-infected patients receiving second line ART regimens.
- India's national program has rolled out free second line ART for HIV-infected people failing NNRTI based regimens [3].
- While a recent report showed 11% incident TB rate among patients on first line ART regimens [4], no data are available on the TB incidence among those receiving second line regimens in India.
- India has the 3rd largest absolute burden of HIV and 2.1 million HIV infections.

Methods

- **Study design**: Prospective cohort of 405 HIV-infected, on 2nd line ART.
- **Study Site**: BJ Government Medical College (BJGMC) - Sassoon General Hospital (SGH) public health sector ART center in Pune, India.
- **Eligibility criteria**: Patients receiving PI (boosted atazanavir or lopinavir)-based second line ART regimens for first line ART failure.
- Patients already on TB treatment on 2nd line ART initiation or patients with history of prior TB were excluded.
- TB was diagnosed either clinically or microbiologically by acid-fast bacillus smear as per the national program guidelines.
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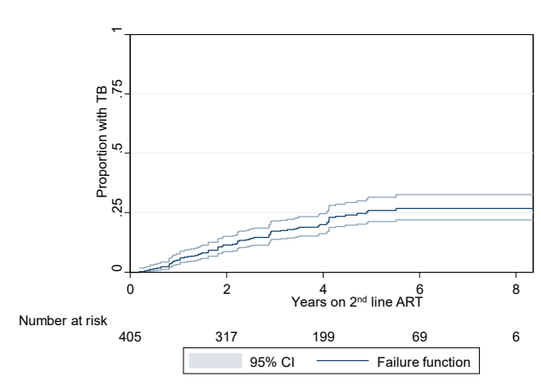
Table: TB Incidence rates by risk factors associated RRs

Risk Factor	Person-years of follow-up	Incidence rate (95% CI)/1000 PY	uIRR (95% CI); p-value	aIRR; p-value
Sex				
Male	939	79.9 (62.9 – 100.2)	Ref	Ref
Female	621	16.1 (0.77 – 29.6)	0.20 (0.10 – 39.4); p < 0.01	3.45 ; p = 0.01
Age (years)				
< 30	347	48.9 (28.5 – 78.3)	Ref	Ref
> 30	1212	56.1 (43.6 – 71.1)	1.15 (0.67 – 1.97); p = 0.61	0.94; p = 0.84
Marital Status				
Other*				
Married	354	28.3 (13.5 – 52.0)	Ref	Ref
Single	586	52.8 (35.9 – 75.0)	1.87 (0.90 – 3.90); p = 0.09	0.88; p = 0.78
	619	71.1 (51.7 – 95.4)	2.52 (1.24 – 5.10); p = 0.01	1.08; p = 0.87
Employed				
No	67	0	Cannot be calculated	Not Included
Yes	1348	60.1 (47.7 – 74.7)		
ART at registration				
No	1051	51.4 (38.6 – 67.1)	Ref	Ref
Yes	317	81.9 (53.5 – 119.9)	1.59 (0.99 – 2.56); p = 0.06	1.51; p = 0.10
WHO Stage				
I and II	473	50.7 (32.5 – 75.5)	Ref	Not Included
III and IV	1048	54.4 (41.2 – 70.5)	1.07 (0.66 – 1.74); p = 0.78	
BMI (kg/m^2)				
Normal	495	74.7 (52.6 – 103.0)	Ref	Not Included
Underweight	448	53.6 (34.3 – 79.7)	0.72 (0.42 – 1.21); p = 0.21	
Overweight	33	121.6 (33.1 – 311.4)	1.63 (0.62 – 4.29); p = 0.32	
CD4/100 cells/cumm decrease			1.08 (0.99 – 1.18); p = 0.07	1.04; p = 0.47
Unit decrease in hemoglobin			1.26 (1.09 – 1.45); p = 0.002	1.17; p = 0.009

Methods continued..

- Study outcome was new TB diagnosis after initiating 2nd line ART
- Univariable and Multivariable Poisson regression analysis was performed to assess independent risk factors of TB.

Figure: Kaplan-Meier Estimate of TB incidence on 2nd line ART



Results

- Of 405 patients on 2nd line ART, median age was 35, 66% were males, and 85 (21%) developed TB.
- The overall TB incidence rate (95% CI) was 54.5/1000 (43.5 – 67.4) person-years (PY) on second line ART.
- Median (IQR) time to incident TB was 1.92 (1.04 – 2.93) years after second line ART initiation (**Figure**).
- In multivariate model adjusted for age, sex, CD4 count at registration, male sex (3.45, 1.33 – 9.09, p=0.01), and unit decrease in hemoglobin from baseline hemoglobin (1.17; 95% CI, 1.04 – 1.32, p = 0.009) were independently associated with incident TB.
- CD4 <350 cells/cumm showed 3-fold risk for incident TB, but did not meet statistical significance (6.19; p = 0.69)
- All-cause case-fatality was 26.7 (95% CI, 8.7 – 62.3) /1000 PY among TB co-infected patients receiving 2nd line ART.

Conclusions

- Our study documents a high TB incidence and mortality among patients receiving second line PI-based ART.
- Since the high TB incidence on second line ART pose treatment challenges due to drug interactions between rifampin and PIs, long recommended World Health Organization's TB prevention strategies such as isoniazid prophylaxis need to be prioritized among all HIV-infected patients in India and other high TB burden countries.

References

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