

# #863 Tuberculosis-Associated Immune Reconstitution Disease: Incidence, Risk Factors and Impact in an ART Programme in South Africa



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## UPDATED ABSTRACT

**Objective:** To determine the burden and impact of immune reconstitution disease (IRD) associated with tuberculosis (TB) among patients initiating antiretroviral treatment (ART) in sub-Saharan Africa. **Design:** Retrospective analysis of a study cohort enrolled over 3 years within a community-based ART service in South Africa.

**Methods:** Patients receiving treatment for TB at the time ART was initiated (n=160) were studied. Cases of TB-associated IRD during the first 4 months ART were ascertained.

**Results:** The median baseline CD4 cell count was 68 cells/μl (IQR=29-133) and ART was initiated after a median of 105 days (IQR=61-164) from TB diagnosis. Although IRD was diagnosed in just 12% patients (n=19) overall, 32% (n=12) of those who started ART with 2 months of TB diagnosis developed IRD.

Pulmonary involvement was observed among 84% (n=16) and intra-abdominal manifestations were also common (37%). Overall, 4% (n=7) of the cohort required secondary level health-care for IRD and 2 (1%) patients died. In multivariate analysis, risk of IRD was strongly associated with early ART initiation and low baseline CD4 cell count. Of patients with CD4 counts <50 cells/μl, the proportions who developed IRD following initiation of ART within 0-30, 31-60, 61-90, 91-120 and >120 days of TB diagnosis were 100%, 33%, 14%, 7% and 0%, respectively.

**Conclusions:** The risk of TB-associated IRD in this setting is very high for those with low baseline CD4 cell counts initiating ART early in the course of antituberculosis treatment. However, most cases were self-limiting; overall secondary health-care utilisation and mortality risk from IRD were low.

## CLINICAL MANIFESTATIONS

- (a) Exacerbation of existing disease manifestations (n=10)  
deterioration of pulmonary TB (n=9)  
deterioration of cervical lymphadenopathy (n=1)
- (b) Development of new disease manifestations at another anatomic site with or without exacerbation of existing disease (n=7)  
cervical lymphadenopathy (n=1).  
hepatomegally (n=2).  
intra-abdominal lymphadenopathy (n=1).  
tuberculous terminal ileitis with perforation and peritonitis (n=1).  
cervical and intra-abdominal lymphadenopathy, hepatomegally and splenic micro-abscesses (n=1).  
tuberculous arthropathy of left hallux (n=1).
- (c) IRD resulting in death (n=2)  
death due to deterioration of disseminated TB with pulmonary, intra-abdominal and bone marrow involvement

### Programme Impact

- Most cases were self-limiting
- Cohort utilisation of secondary health care due to TB IRD was low (4% of TB patients)
- Deaths due to TB IRD = 1.3% of patients

## SETTING

Guguletu- Nyanga District, Cape Town, South Africa

Population: 419 000

HIV prevalence : 28.5%

TB incidence approx. 1,400 / 100,000 / yr



## RISK FACTORS: MULTIVARIATE ANALYSIS

	RR of IRD	95% CI	P
Age <sup>1</sup> a	1.03	0.93-1.13	0.596
Sex			
Female	1.00		
Male	3.07	0.74-12.74	0.123
Baseline CD4 count <sup>a,b</sup>	0.983	0.970-0.997	0.018
Baseline viral load <sup>b</sup>	2.39	0.68-8.34	0.172
TB site			
Pulmonary	1.00		
Extrapulmonary	0.59	0.12-3.00	0.525
TB diagnosis to ART delay (days)			
> 90	1.00		
61-90	6.64	1.20-36.5	0.030
31-60	10.6	1.88-59.5	0.007
0-30	69.5	9.94-485.6	< 0.001

a. Continuous variables analysed to show RR associated with 1-unit change in variable.  
b. 100 cells/μl decrease associated with a 5.3-fold increase in RR.

## PATIENTS AND OUTCOMES

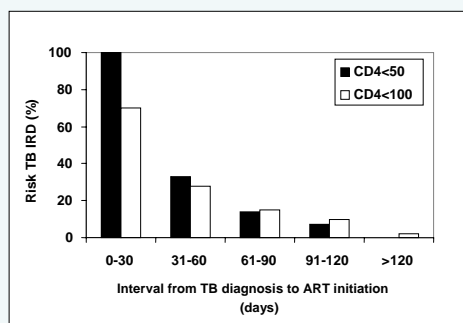
### Definition of TB IRD:

- Patients with prevalent TB pre-ART
- Documented response to TB Rx
- Clinical deterioration of TB after starting ART
- Other causes excluded, including
  - non-compliance with TB Rx
  - another OI
  - MDR TB
  - drug adverse effect

### Cohort:

N=160 patients with TB  
Median CD4 = 68 cells/μl  
ART: d4T, 3TC, EFV  
Retrospective analysis  
Outcomes at 16 weeks ART  
Alive on ART = 89%  
Transfer-out / LTFU = 1%  
Deaths = 10%

## RISK IRD STRATIFIED BY CD4 COUNT AND DELAY IN INITIATION ART



## CASES OF IRD

19 total cases

= 12% of all TB patients

starting ART developed IRD

= 32% of TB patients starting

ART within 2 months of TB

diagnosis developed IRD

Patient characteristics	TB-IRD cases (n=19)	IRD-free patients (n=141)	P
<b>Baseline characteristics</b>			
Median age (years)	35	32	0.60
Female [n (%)]	11 (58)	105 (74)	0.13
Median CD4 count (cells/μl)	31	74	0.003
<b>Patients in CD4 cell categories (cells/μl) [n (%)]</b>			
> 150	0	26 (18)	
100-149	2 (11)	28 (20)	
50-99	5 (26)	42 (30)	
< 50	12 (63)	45 (32)	0.03
Median viral load (log copies/ml)	5.13	4.96	0.27
Extrapulmonary TB (%)	4 (21)	40 (28)	0.59
<b>Time from TB diagnosis to ART (days)</b>			
Median	40	117	< 0.001
<b>Patients in time categories [n (%)]</b>			
> 120	1 (5)	64 (45)	
91-120	2 (11)	28 (20)	
61-90	4 (21)	23 (16)	
31-60	5 (26)	20 (14)	
0-30	7 (37)	6 (4)	
<b>Follow-up at 4 months</b>			
Median change in CD4 count (cells/μl)	83	88	0.97
Proportion with VL < 400 copies/ml (%)	100	96	0.47

## CONCLUSIONS

- Risk of TB-associated IRD is very high for those with low baseline CD4 cell counts initiating ART early in the course of TB Rx
- The overall proportion of patients with TB IRD was relatively low as many were starting ART after several months TB Rx
- Most cases were self-limiting, but occasional deaths do occur
- Overall contribution of TB IRD to mortality and secondary health care utilisation was low. This burden may increase if ART is initiated earlier among these patients



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