Burden of TB in HIV+ pregnant & postpartum women in Cape Town, South Africa

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Background

- In 2014, there were 3.2 million new cases of TB and 480 000 deaths due to TB in women
- Women of reproductive age are disproportionately affected, and TB during pregnancy has been associated with adverse pregnancy and perinatal outcomes, particularly in the presence of HIV
- However, large research gaps remain regarding TB epidemiology and control in pregnant and postpartum women, and TB receives little attention within pregnancy and PMTCT services
- We investigated the burden of TB before, during, and after pregnancy in a cohort of HIV+ women accessing antenatal care and PMTCT services in Gugulethu, Cape Town

Methods

- Consecutive women attending their first visit at a primary care antenatal clinic completed a brief questionnaire, underwent CD4 enumeration, and had an ultrasound for pregnancy dating
- TB cases were diagnosed via passive detection by routine public sector services based on symptom screening with or without bacteriologic confirmation; TB notification data were obtained for the period extending from 18 months before the estimated date of conception to 6 months postpartum
- Poisson methods were used to compare the incidence of TB per 100 000 person-years (PYs) in the pre-conception period, during pregnancy and postpartum
- A smoothed incidence over time curve was fitted using a Cox proportional hazards model (Figure 1)

Results

- Among 1507 HIV+ women (median age 29 years), 989 initiated ART in pregnancy (66%; median CD4 377 cells/uL, IQR 250-543) and 518 (34%; median CD4 391 cells/uL, IQR 271-527) were on ART at conception (Table 1)
- Overall incidence of TB pre-conception, during pregnancy and postpartum was 2445 (95% CI 1846-3174), 1125 (95% CI 599-1923), and 1611 (95% CI 773-2963) per 100 000 PY, respectively (Table 2)
- Adjusting for age, CD4 cell count, and ART status:
  - **Pregnancy vs pre-conception** - TB incidence was significantly reduced during pregnancy compared to pre-conception (IRR 0.49; CI 0.25-0.90) (Figure 1, Table 4)
  - **Postpartum vs pre-conception** – TB incidence postpartum was reduced compared to pre-conception, (IRR 0.64; 95% CI 0.30-1.39), but was increased slightly relative to pregnancy

Table 1: Description of the cohort at antenatal booking (n=1507)

	All women (n=1507) n (%) or median (IQR)	Women who developed TB (n=79)			
		TB pre-conception (n=56) n (%) or median (IQR)	TB during pregnancy (n=13) n (%) or median (IQR)	TB post-conception (n=10) n (%) or median (IQR)	*p*-value*
Median age (IQR)	29 (25-33)	30 (27-32)	29 (27-32)	30 (27-32)	0.68
Married or cohabiting	844 (56)	22 (39)	5 (38)	5 (50)	0.81
Formal housing	687 (46)	25 (45)	4 (31)	5 (50)	0.59
No of people in house	4 (3-6)	4 (2-6)	4 (3-7)	3.5 (3-5)	0.69
Finished high school	405 (27)	16 (29)	1 (8)	2 (20)	0.32
Employed	557 (37)	15 (27)	4 (31)	2 (20)	0.85
Median CD4	382 (258-536)	309 (212-465)	232 (95-496)	269 (196-463)	0.63
ART status at conception					0.43
Not on ART	989 (66)	22 (39)	7 (54)	7 (70)	
On ART	518 (34)	3 (5)	2 (15)	3 (30)	

*Chi-square or Kruskal-Wallis test | ART: antiretroviral therapy; IQR: inter-quartile range; TB: tuberculosis

- Overall TB incidence was doubled in women with CD4 cell count <200 cells/uL (IRR 1.96; *p*=0.01)
- Incidence was lowest in women on ART in pregnancy (IRR 0.38; *p*=0.021 vs pre-conception without ART) and increased slightly postpartum (IRR 1.50; *p*=0.417 vs during pregnancy)
- 79% of cases were first TB episodes, with 21% retreatment cases (Table 3)
- Retreatment cases accounted for 18%, 23% and 40% of cases in the pre-conception, pregnancy and postpartum periods respectively
- 78% of TB cases were pulmonary, of which 66% were bacteriologically confirmed, and 22% were extrapulmonary, of which 18% were bacteriologically confirmed; this did not vary by pregnancy status

Figure 1: TB incidence per 100000 PYs for the period 18 months pre-conception to 6 months postpartum (n=1507) showing high incidence over time in the pre-conception period, reduction during pregnancy, and slight increase postpartum

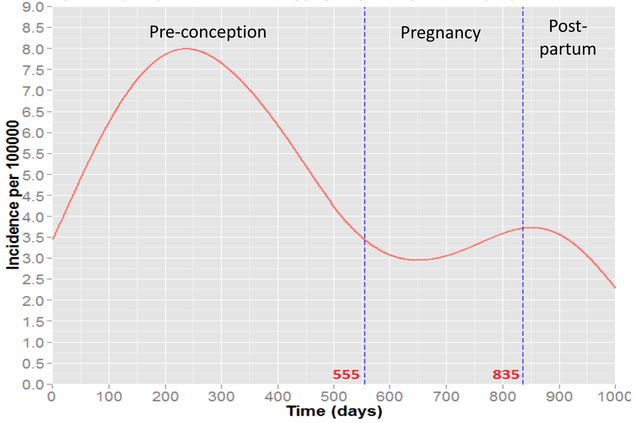


Table 2: Incidence rates for TB by period and ART status

	Pre-conception			Pregnancy			EDD to 24 weeks post-delivery			Total		
	Person-years	TB events (n)	IR/100000 PYs (95% CI)	Person-years	TB events (n)	IR/100000 PYs (95% CI)	Person-years	TB events (n)	IR/100000 PYs (95% CI)	Person-years	TB events (n)	IR/100000 PYs (95% CI)
All women	2292	56	2445 (1846; 3174)	1206	13	1125 (599; 1923)	621	10	1611 (773; 2963)	3269	79	1966 (1559; 2447)
On ART	664	16	2409 (1377; 913)	773	7	968 (389; 1995)	610	10	1640 (787; 3017)	1197	33	1653 (1138; 2321)
Not on ART	1627	40	2458 (1808; 3418)	433	6	1385 (508; 3015)	11	0	-	2072	46	2221 (1667; 3017)

ART: antiretroviral therapy; EDD: estimated date of delivery; CI: confidence interval; IR: incidence rate; PY: person-years; TB: tuberculosis

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Table 3: Description of TB events (n=79)

	All TB (n=79); n (%)	TB pre-conception (n=56); n (%)	TB in pregnancy (n=13); n (%)	TB post-delivery (n=10); n (%)	*p*-value*
Site of disease					
Pulmonary	62 (78)	42 (75)	11 (85)	9 (90)	0.57
Extrapulmonary	17 (22)	14 (25)	2 (15)	1 (10)	
TB category					
New cases	62 (78)	46 (82)	10 (77)	6 (60)	0.32
Retreatment	17 (22)	10 (18)	3 (23)	4 (40)	
ART status during period in which TB diagnosed					
On ART	33 (42)	16 (29)	7 (54)	10 (100)	<0.001
Not on ART	46 (68)	40 (71)	6	0	
Bacteriological confirmation					
Nil	35 (44)	26 (46)	5 (38)	4 (40)	0.84
Any	44 (56)	30 (54)	8 (62)	6 (60)	
Culture results					
Positive	12 (15)	10 (18)	1 (8)	1 (10)	0.60
Negative	6 (8)	3 (5)	2 (15)	1 (10)	
Not done	61 (77)	43 (77)	10 (77)	8 (80)	
Xpert MTB/RIF results					
Positive	28 (35)	17 (30)	6 (46)	5 (50)	0.33
Negative	15 (19)	13 (23)	1 (8)	3 (30)	
Not done	36 (46)	26 (46)	6 (46)	2 (20)	
Smear results					
Positive	14 (18)	9 (16)	3 (23)	2 (20)	0.80
Negative	39 (49)	30 (54)	5 (38)	4 (40)	
Not done	26 (33)	17 (30	5 (38)	4 (40)	

*Chi-squared or Kruskal-Wallis test | ART: antiretroviral therapy; TB: tuberculosis

Discussion

- TB incidence appears reduced in HIV+ women during pregnancy compared to pre-conception; incidence increases postnatally, but not to preconception levels
- Reduced incidence during pregnancy and postnatally may be related to increased ART coverage in these periods
- Limitations of the study include reliance on routine TB case detection data, meaning that only clinically presenting cases are included and dates could be inexact
- The absolute incidence of TB is high throughout; intensified TB case detection interventions in PMTCT services warrant consideration
- Additionally, expanded ART access in pregnancy may further reduce the TB burden in this population

Table 4: Poisson Regression Results

	IRR	95% CI	*p*-Value
Age	1.03	0.99; 1.06	0.18
CD4 >200	1	Reference Category	
CD4 <200	1.96	1.21; 3.18	0.01
No ART	1	Reference Category	
On ART	0.89	0.52; 1.53	0.67
Pre-conception	1	Reference Category	
Pregnant	0.49	0.25; 0.90	0.02
Post-delivery	0.64	0.30; 1.39	0.26

IRR: incidence rate ratio; CI: confidence interval; ART: antiretroviral therapy