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Pregnancy in Women with HIV in a Tuberculosis Preventive Therapy Trial

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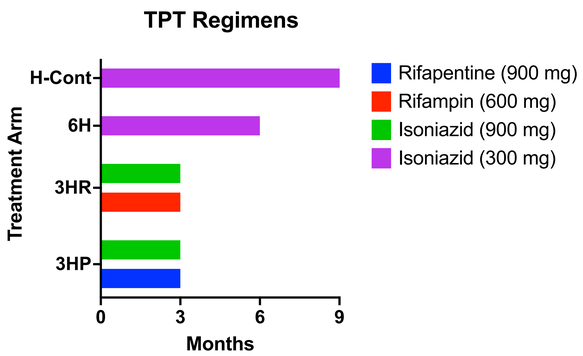
BACKGROUND

Tuberculosis (TB) preventive therapy (TPT) is recommended for people with HIV infection, including during pregnancy. The impact of TPT exposure at conception and during pregnancy is poorly documented.

We assessed the overall frequency of incident pregnancies and the pregnancy outcomes among women who had documented TPT exposure periconceptually and/or in their 1st trimester in a large trial in PLHIV in South Africa

METHODS

We report pregnancy outcomes among South African women with HIV enrolled in a randomized trial of 4 TPT regimens. Descriptive statistics and risk ratios were assessed to examine relationships between study regimens and outcomes.



Rifamycin based TB preventive treatment regimens are associated with increased risk of pregnancy events compared to isoniazid regimens.

RESULTS

- 216/896 women (24%) conceived during the study. Women who conceived were younger (27.9 vs 31.3 years) and had higher CD4 counts (589.1 vs 536.7).
- The odds of pregnancy were higher in women in the rifamycin-containing arms than the isoniazid arms (3HP: 1.73, p = 0.001; 3HR: 1.55, p = 0.017) despite increased contraceptive use compared to the standard 6H therapy.
- Pregnancy events in both rifamycin arms were associated with increased overall contraceptive use (3HP vs 6H: RR = 1.76, p = 0.004; 3HR: RR = 1.53, p = 0.04). When stratified by contraceptive method, only barrier contraceptive use in the 3HP arm was associated with an increased risk of pregnancy (RR = 1.75, p = 0.012).
- 34 women became pregnant while taking preventive treatment (8 rifamycin, 26 isoniazid monotherapy). Pregnancy outcomes in these women were: 17 (50%) mother/baby healthy, 3 (9%) spontaneous abortions, 6 (18%) elective abortions, 1 (3%) premature delivery, 2 (6%) neonatal deaths [1 rifamycin and 1 isoniazid], and 5 (15%) unknown.

Treatment Arm	Pregnancy Events n/N (%)	RR (95% CI)	P value	Adjusted** RR (95% CI)	P value
All Participants	212/896 (23.6%)	--	--	--	--
6H*	44/260 (16.9%)	--	--	--	--
3HP	75 /256 (29.3%)	1.73 (1.25, 2.41)	0.001	1.69 (1.23, 2.34)	0.001
3HR	66/252 (26.2%)	1.55 (1.10, 2.18)	0.013	1.51 (1.08, 2.10)	0.017
H-Cont	27/128 (21.1%)	1.25 (0.81, 1.90)	0.331	1.21 (0.79, 1.85)	0.375

Count of Delivery	Delivery Results						
Arm	Healthy	Spontaneous Abortion	Elective Abortion	Premature Birth	Infant Death	Unknown	Grand Total
3HP	1 (2.9%)		2 (5.9%)			1 (2.9%)	**4 (11.8%)**
3HR	2 (5.9%)	1 (2.9%)			1 (2.9%)		**4 (11.8%)**
6H	1 (2.9%)		1 (2.9%)	1 (2.9%)			**3 (8.8%)**
H-Cont	13 (38.2%)	2 (5.9%)	3 (8.8%)		1 (2.9%)	4 (11.8%)	**23 (67.6%)**
Grand Total	**17 (50.0%)**	**3 (8.8%)**	**6 (17.6%)**	**1 (2.9%)**	**2 (5.9%)**	**5 (14.7%)**	**34 (100%)**

CONCLUSIONS

- Pregnancy was common in women receiving TPT and more frequent in women receiving rifamycin-based regimens.
- Given the high rate of pregnancy seen in several TPT trials, the exclusion of pregnant women and/or prohibition of pregnancy from trials may not be effective, but instead, be directly studied in this population.
- To prevent TB disease, safer shorter preventive treatments such as the 1- to 3- month rifapentine-based regimens should be given to women living with HIV, including those who are pregnant.

Acknowledgments

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Figure 1. Pregnancy Risk Stratified by Treatment Arm

