Pregnancy outcomes in patients undergoing drug-resistant tuberculosis treatment in two closely monitored cohorts

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Conflict of Interest:
The author has declared no conflict of interest.

Photo: Emilie Régnier

Ethical approval, funding sources & drug donations

endTB & TB-PRACTECAL approved by MSF Ethics Review Board and local committees in implementing countries.

TB-PRACTECAL approved by London School of Hygiene and Tropical Medicine Ethics Committee.

endTB approved by Partners Healthcare Human Research Committee.

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TB-PRACTECAL was funded by MSF. The TB Alliance donated the first batch of pretomanid before its commercialisation.

Photo: Jean-Pierre Amigo

Introduction

- Drug-resistant tuberculosis (DR-TB) carries significant morbidity and mortality risk. Care of DR-TB in pregnancy is even more challenging.
- A recent meta-analysis* examining the impact of DR-TB on pregnancy outcomes found a higher-than-expected rates of maternal death (7.5%), pregnancy loss (10.6%), and a significant prevalence of low-birthweight infants (23.7%).
- Anti-tubercular drugs such as bedaquiline and clofazimine have long half-lives and the impact of in-utero exposure is largely unknown – pregnant women being often excluded from clinical trials.
- There is little information to help women, their families and clinicians make informed decisions about DR-TB treatment during pregnancy.

*Alene KA, Jegnie A, Adane AA. Multidrug-resistant tuberculosis during pregnancy and adverse birth outcomes: a systematic review and meta-analysis. *BJOG*. 2021;128(7):1125-1133. doi:10.1111/1471-0528.16573

Methods

Data on pregnancy outcomes were systematically collected as part of a pharmacovigilance program supporting:

TB Practecal
Innovating MDR-TB Treatment

An **interventional Phase II-III clinical trial**
in 3 countries,
sponsored by MSF,
N=552, 40% women:

- Pregnant at baseline excluded,
- Double contraception required,
- Case by case decision on retention in the trial if pregnant.

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A **prospective observational cohort**
in 17 countries, national TB programs with consortium of MSF, Partners in Health and Interactive Research and Development,
N=2'906, 36% women.

- Pregnant at baseline included,
- Contraception recommended,
- Case by case regimen design.

We present the **birth outcomes as reported to investigators by participants** between 01 April 2015 and 31 December 2021.

MEDECINS SANS FRONTIERES

Pregnancy data collection form available: http://endtb.org/resources/pharmacovigilance

SCIENTIFIC DAYS


BELARUS
KAZAKHSTAN
KYRGYZSTAN
GEORGIA
DPRK
UZBEKISTAN
HAITI
ARMENIA
BANGLADESH
VIETNAM
ETHIOPIA
PAKISTAN
INDONESIA
PERU
KENYA
MYANMAR
SOUTH AFRICA
LESOTHO
TB-PRACTECAL
endTB observational cohort

Results – *Mothers*

- 58 pregnancies in 53 women were notified from 10 different countries, predominantly Uzbekistan (14), Kazakhstan (13) & Pakistan (9). There were no maternal death.

Characteristics	endTB Obs. cohort	TB-PRACTECAL	Total
#Pregnant women	37	16	53
#Pregnancies	42*	16	58
Mean mother age (years)	27.9	25.2	27.1
#Pregnant at DR-TB tx start	5 (14%)		5 (9%)
#Pregnant after DR-TB tx completion	1 (3%)	12 (75%)	13 (25%)
Median (min-max) days on DR-TB tx at pregnancy start	219 (0-678)	329 (104-727)	261 (0-727)
#Mothers changed/interrupted DR-TB tx	9 (24%)		9 (17%)
DR-TB tx outcome			
Favourable	36 (97%)	7	43
Not yet assigned		*9*	*9*
Death	1 (3%)		1

DR-TB tx=drug resistant tuberculosis treatment.
*5 women in endTB were pregnant more than once.

Results – *Outcome of pregnancies*

Pregnancy outcome was known in 52 of 58 pregnancies:

- **30** live births (1 twin pregnancy) - 2 babies born prematurely at 30 and 31 weeks.
- **20** elective abortions,
- **3** early miscarriages: 6, 8, 12-14 weeks, respectively
- No stillbirths.

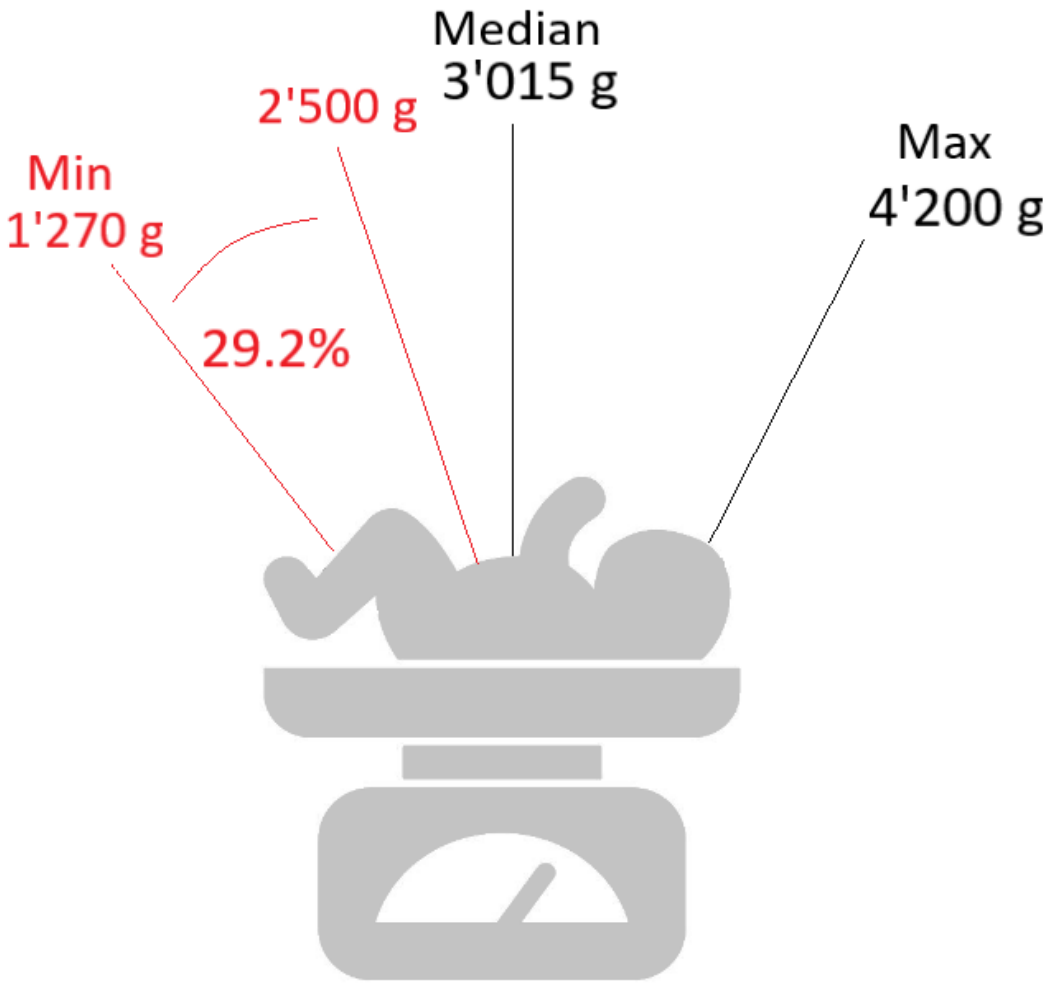
Of the 30 live births:

- 29 occurred in mothers ever exposed to bedaquiline,
- 16 to clofazimine,
- 11 to second-line injectable,
- 10 to pretomanid,
- 7 to delamanid.

Photo: Bithin Das

Results – *Neonates*

- Birth weight known in 24 of 30 (80%) babies:
- 1 low-birthweight baby died at 4 months from complications unrelated to TB.
- 1 baby treated for DR-TB.
- No reported birth malformations.



Conclusions, limitations and next steps!

These results support evidence that **effective DR-TB treatments may improve maternal outcomes and prevent perinatal transmission**.

How these perinatal outcomes compare to other cohorts not affected by TB in these settings or exposed to different TB treatments needs exploration.

The factors contributing to low birthweight in babies born to mothers with DR-TB requires further research.

Photo: IRD

Acknowledgments

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Photo: TB-PRACTECAL