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

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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 rate of maternal death, pregnancy loss, and a significant prevalence of low-birthweight infants. Anti-tubercular drugs such as bedaquiline and clofazimine have long half-lives and the impact of in-utero exposure is largely unknown. There is little information to help women, their family members, and clinicians make informed decisions about DR-TB treatment during pregnancy.

Methods

Data on pregnancy outcomes were systematically collected as part of a pharmacovigilance programme supporting a clinical trial (TB-PRACTECAL; N=552) and a prospective cohort (endTB; N=2,906). We present the birth outcomes as reported to investigators by participants.

Ethics

The endTB and TB-PRACTECAL studies were both approved by the local ethics committees in all recruiting countries and by the MSF Ethics Review Board. endTB was approved by the Partners Healthcare Human Research Committee, Boston, USA, and TB-PRACTECAL was approved by the London School of Hygiene and Tropical Medicine Ethics Committee, UK.

Results

Between 01 April 2015 and 31 December 2021, 58 pregnancies in 53 women were notified from 10 different countries, predominantly Uzbekistan (14), Kazakhstan (13) and Pakistan (9). In 13 cases, pregnancy occurred after completion of tuberculosis treatment. Patients became pregnant a median of 260.5 (range, 0-727) days from treatment start; five women were 5-32 weeks pregnant at treatment start. There were no maternal deaths. 17.0% (9/53) of mothers changed or interrupted treatment during pregnancy. Treatment outcome was successful in 97.3% (36/37) of others in endTB and 100% (7/7) of mothers who completed follow-up in TB-PRACTECAL. Pregnancy outcome was known in 52 cases: 20 elective abortions, three miscarriages and 30 live births (one twin pregnancy). There were no stillbirths. Of the 30 live births, 29 occurred in mothers ever exposed to bedaquiline, 16 to clofazimine, 11 to a second-line injectable, 10 to pretomanid, and 7 to delamanid. Birth weight was known in 24/30 (80.0%) babies. Median weight was 3,015 (range, 1,270 to 4,200) grams. Two babies were born prematurely at 30 and 31 weeks. Low birthweight was reported in seven (29.2%; 7/24) babies. One low-birthweight baby died within four months of birth from complications unrelated to tuberculosis. One baby was treated for DR-TB. There were no reported birth malformations.

Conclusion

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. A global registry is urgently needed to assist parents and clinicians with decision-making.

Conflicts of interest

The endTB project was funded by UNITAID (Geneva, Switzerland). Provision of delamanid within the endTB project was partially funded through a donation from Otsuka Company (Kyoto, Japan).

Nathalie has set up and is managing the pharmacovigilance unit for MSF, which ensures appropriate detection, monitoring, follow-up and prevention of adverse drug reactions, notably in multidrug resistant tuberculosis projects, with focus on the TB-PRACTECAL clinical trial and the endTB project and clinical trials.