Perspectives on maternal and infant outcomes of pregnant people treated for DR-TB

Marian Loveday

WHO Regional Consultation Lusaka

27 – 29 September 2022



Pregnant People with DR-TB: A Complex and Under-Served Population

- Increased physical vulnerability to all forms of TB;
- Exclusion from studies and, as a result, access to innovation;
- "Limited information" means counseling often creates additional anxiety;
- Fear-based infection control practices lead to discriminatory and harmful practices;
- Result is that pregnant people with DR-TB feels confused, scared, isolated and alone.

RESEARCH ARTICLE "Take the treatment and be brave": Care experiences of pregnant women with rifampicin-resistant tuberculosis Marian Lovedayo^{1,2}*, Sindisiwe Hlangu¹, Jennifer Furin³ 1 HIV Prevention Research Unit, South African Medical Research Council, KwaZulu-Natal, South Africa, 2 CAPRISA-MRC HIV-TB Pathogenesis and Treatment Research Unit, Doris Duke Medical Research Institute, University of KwaZulu-Natal, Durban, South Africa, 3 Department of Global Health and Social Medicine, Harvard Medical School, Boston, Massachusetts, United States of America * marian.loveday@mrc.ac.za Abstract Background There are few data on the on the care experiences of pregnant women with rifampicin-resis tant TB. Objective To describe the treatment journeys of pregnant women with RR-TB-including how their care experiences shape their identities-and identify areas in which tailored interventions are needed Editor: Jennifer Zelnick, Touro College and Methods Accepted: November 5, 2020 system in which treatment was received Results 1) the experience of physical symptoms or changes; 2) the experience of the "mothering"



Citation: Loveday M, Hlangu S, Furin J (2020) "Take the treatment and be brave": Care experiences of pregnant women with rifampicin resistant tuberculosis, PLoS ONE 15(12): e0242604. https://doi.org/10.1371/journal. pone.0242604

University System, UNITED STATES

PLOS ONE

Received: May 6, 2020

Published: December 21, 2020

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process: therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available her https://doi.org/10.1371/journal.pone.0242604

Copyright: © 2020 Loveday et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which nermits unrestricted use distribution and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: The primary data is not available as open access was not approved by the South African Medical Research Council Human Research Ethics Committee. However, the

In this qualitative study in-depth interviews were conducted among a convenience sample from a population of pregnant women receiving treatment for RR-TB. This paper follows COREQ guidelines. A thematic network analysis using an inductive approach was per-

formed to analyze the interview transcripts and notes. The analysis was iterative and a cod ing system developed which focused on the care experiences of the women and how these experiences affected their perceptions of themselves, their children, and the health care

Seventeen women were interviewed. The women described multiple challenges in their treatment journeys which required them to demonstrate sustained resilience (i.e. to "be brave"). Care experiences required them to negotiate seemingly contradictory identities as both new mothers-"givers of life"-and RR-TB patients facing a complicated and potentially deadly disease. In terms of their "pregnancy identity" and "RR-TB patient identity" that emerged as part of their care experiences, four key themes were identified that appeared to have elements that were contradictory to one another (contradictory areas). These included:

Key recommendations

Management of Drug-Resistant Tuberculosis in Pregnant and Peripartum People: **A FIELD GUIDE**

First Edition, September 2022



Photo courtesy of Chris Tabu at @TabuCapital

- Free family planning services;
- Pregnant people should be routinely screened using WHO recommended diagnostic tests;
- Compassionate counselling and support for either continuing or terminating a pregnancy when a pregnant person is diagnosed with DR-TB;
- Effective treatment should include new, repurposed and 3rd generation fluoroquinolones even if data on the newer drugs is limited.
- Avoid drugs with known reproductive toxicity pretomanid and the injectables.
- Anyone who has been on effective treatment is no longer infectious after two weeks, so:
 - The routine standard of care should be provided to pregnant people. Discriminatory infection control practices should not be enforced.
 - $\circ\;$ Newborns should not be separated from their mothers.
 - Newborns should be breastfed if this is the choice of the postpartum parent.
 - The rare exceptions are those started very recently on DR-TB treatment or those who are lost to follow-up.
- Adherence challenging post-partum supportive compassionate counselling necessary.





Figure 3. Pooled Proportion of Pregnancy Outcomes Among Patients With Multidrug-Resistant Tuberculosis

Original Investigation | Infectious Diseases

Treatment Outcomes Among Pregnant Patients With Multidrug-Resistant Tuberculosis A Systematic Review and Meta-analysis

Kefyalew Addis Alene, PhD; Megan B. Murray, ScD, MD; Brittney J. van de Water, PhD; Mercedes C. Becerra, ScD; Kendalem Asmare Atalell, MSc; Mark P. Nicol, PhD; Archie C. A. Clements, PhD

10 studies (275 patients)

Treatment outcomes:

- Treatment success: 72.5%
- Death: 6.8% ٠
- Loss to follow up: 18.4% ٠
- Treatment failure: 0.6% Lzd associated with treatment success.

Pregnancy outcomes:

- Favorable pregnancy outcomes: 73.2%.
- Preterm birth: 9.5% ٠
- Pregnancy loss: 6.0% ٠
- Low birth weight: 3.9% ٠
- Stillbirth: 1.9%

Source	ES (95% CI)	Does not favor outcome	Favors outcome	Weight, %
Preterm				
Shin et al. ²² 2003	0.0 (0.0-41.0)			2.4
Palacios et al. ²¹ 2009	2.6 (0.1-13.8)			4.0
Tabarsi et al. ²⁰ 2011	0.0 (0.0-52.2)		T	2.0
van der Walt et al. ¹⁷ 2020	0.0 (0.0-13.7)			3.7
Mokhele et al, ¹⁴ 2021	55.0 (31.5-76.9)			➤ 3.5
Loveday et al. ¹⁵ 2021ª	25.7 (17.8-34.9)			4.5
Subtotal: / ² = 87.7%: P <.001	9.5 (0.0-29.0)			20.0
Pregnancy loss	,			
Shin et al. ²² 2003	0.0 (0.0-41.0)			2.4
Palacios et al. ²¹ 2009	13.2 (4.4-28.1)			4.0
Tabarsi et al, ²⁰ 2011	0.0 (0.0-52.2)			2.0
van der Walt et al, ¹⁷ 2020	8.0 (1.0-26.0)			3.7
Mokhele et al, ¹⁴ 2021	20.0 (5.7-43.7)			3.5
Loveday et al, ¹⁵ 2021 ^a	3.7 (1.0-9.1)		· -	4.5
Subtotal: <i>I</i> ² = 38.1%; <i>P</i> = .15	6.0 (1.3-12.9)			20.0
Low birth weight			_	
Shin et al, ²² 2003	0.0 (0.0-41.0)			2.4
Palacios et al, ²¹ 2009	7.9 (1.7-21.4)			4.0
Tabarsi et al. ²⁰ 2011	0.0 (0.0-52.2)			2.0
van der Walt et al, ¹⁷ 2020	0.0 (0.0-13.7)			3.7
Mokhele et al, ¹⁴ 2021	0.0 (0.0-16.8)			3.5
Loveday et al, ¹⁵ 2021 ^a	30.3 (21.8-39.8)			4.5
Subtotal: <i>I</i> ² = 85.6%; <i>P</i> <.001	3.9 (0.0-18.7)			20.0
Stillbirth				
Shin et al, ²² 2003	0.0 (0.0-41.0)			2.4
Palacios et al, ²¹ 2009	2.6 (0.1-13.8)			4.0
Tabarsi et al, ²⁰ 2011	0.0 (0.0-52.2)			2.0
van der Walt et al, ¹⁷ 2020	4.0 (0.1-20.4)		- **	3.7
Mokhele et al, ¹⁴ 2021	0.0 (0.0-16.8)			3.5
Loveday et al, ¹⁵ 2021ª	5.5 (2.0-11.6)	-	- -	4.5
Subtotal: I ² = 0.0%; P = .92	1.9 (0.1-5.1)		\$	20.0
Neonatal death				
Shin et al, ²² 2003	0.0 (0.0-41.0)			2.4
Palacios et al, ²¹ 2009	0.0 (0.0-9.3)			4.0
Tabarsi et al, ²⁰ 2011	0.0 (0.0-52.2)		• i	2.0
van der Walt et al, ¹⁷ 2020	0.0 (0.0-13.7)			3.7
Mokhele et al, ¹⁴ 2021	5.0 (0.1-24.9)		-	3.5
Loveday et al, ¹⁵ 2021 ^a	0.0 (0.0-3.3)			4.5
Subtotal: I ² = 0.0%; P = .56	0.0 (0.0-0.2)			20.0
Heterogeneity: P = .003 Overall effect: I ² = 80.8%; P <.001	3.5 (0.6-7.8)			100.0
			5 10 15 20 25 30 35 40 45 50 55	60

Proportion

A comparison of maternal treatment, pregnancy and infant outcomes: 1st cohort vs 2nd cohort



	1 st cohort	2 nd cohort
Still on treatment		11
Maternal treatment outcomes	N=58	N=27
Favourable treatment outcomes	41 (71%)	16 (59%)
Unfavourable treatment outcomes	17 (29%)	11 (41%)
LTFU	11 (19%)	8 (30%)
Pregnancy outcomes	N=49	N=32
Live births	45 (92%)	32 (100%)
Favourable pregnancy outcomes	24 (49%)	19 (59%)
Unfavourable pregnancy outcomes	25 (51%)	13 (39%)
Foetal and neonatal deaths	4	0
Preterm < 37 weeks	13 (29%)	9 (28%)
Low birth weight < 2500g	20 (45%)	10 (31%)
Infant outcomes	N=41	N=23
Favourable infant outcomes	36 (88%)	18 (78%)
Weight gain: Thrive normally	36 (88%)	17 (74%)
Unfavourable infant outcomes	5 (12%)	5 (23%)
Developed TB in 1 st year of life	0	3 (13%)

New developments, but back to basics

New developments – an example

- Low BDQ exposure in ante- and postpartum women
- BDQ significantly accumulates in breast milk
- Breastfed infants received equivalent mg/KG doses of BDQ as their mothers

High infant plasma concentrations could have implications for infant safety vs potentially protective in infants exposed to DR-TB

Court R, Gausi K, Mkhize B, et al. Bedaquiline exposure in pregnancy and breastfeeding in women with rifampicin-resistant tuberculosis. Br J Clin Pharmacol 2022;88:3548-58

Challenges

LTFU: Same in shortened BDQ regimen as in 18 – 24-month regimen with an injectable.

Increasing resistance to new drugs.

Back to basics:

- Supportive adherence counselling
- Family centered/differentiated/wholistic management throughout treatment journey
- TB programme not rocket science

But can an effective TB programme be implemented within a weak health system?



Acknowledgements

All DR-TB patients, health care workers and managers in the TB programme and research collaborators.

Funders

South African Medical Research Council (SAMRC)

Thank you





