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National-level evaluation of viral load outcomes of HIV-infected pregnant women: closing the gaps towards eliminating mother-to child transmission of HIV in South Africa

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A NATIONAL-LEVEL EVALUATION OF VIRAL LOAD OUTCOMES OF HIV-INFECTED PREGNANT WOMEN: CLOSING THE GAPS TOWARDS ELIMINATING MOTHER-TO-CHILD TRANSMISSION OF HIV IN SOUTH AFRICA

Abstract

Background

In the words of Burton *et al.*, South Africa's prevention of mother-to-child transmission of HIV (PMTCT) programme has been an ever-changing landscape since inception in 2004. The national PMTCT programme rose from humble beginnings, fraught with delays and AIDS denialism to become the largest programme in the world. One and half decades later, the programme has documented unprecedented reduction in new paediatric HIV infections, shifting efforts from prevention to elimination of mother-to-child transmission of HIV (eMTCT). However, the road to eMTCT in South Africa is considerably challenged.

The World Health Organization defines eMTCT as the attainment of <50 new paediatric infections per 100 000 live births at the end of the breastfeeding period. By 2017, the national intra-uterine case rate alone, was five times the elimination target, with postnatal transmissions expected to contribute a further 1.5 times the intra-uterine case rate by the end of the breastfeeding period. Since maternal viral load (VL) is the strongest predictor of MTCT risk, this research project sought to provide a national description of maternal viraemia as a key driver of vertical transmission, in order to establish a baseline from which to improve virological control during pregnancy and postpartum periods to facilitate eMTCT in South Africa.

Methods

This thesis comprises of four publications conducted using data from two cohorts: a national level synthetic cohort from the National Health Laboratory Service's Corporate Data Warehouse (NHLS CDW) and a sub-national level cohort of pregnant women living with HIV (WLHIV), delivering in four tertiary obstetric units in Gauteng province (Gauteng cohort). Using the Thembisa Model and data triangulated from five HIV-related and demographic data sources, Publication 1 (Chapter 3), set the scene for the case for eMTCT by describing the provincial distribution of target populations for eMTCT (women of reproductive age, 15-49 years and adolescent girls and young women, 15-24 years; stratified by HIV status) in 2018.

In order to assess maternal VL suppression rates in the public sector, a cohort of women of reproductive age living with HIV (WRLHIV) was identified from the NHLS CDW between 2016-2017. Due to lack of a pregnancy marker within the NHLS CDW, syphilis screening in association with ward

type and/or post-pregnancy cervical screening and/or infant birth HIV test and/or positive β-hCG was used to identify pregnant from non-pregnant WRLHIV. Fractional polynomial models described longitudinal changes in maternal VL during pregnancy and the postpartum periods, while spline regression determined factors associated with maternal VL decline during follow up (Publication 2, Chapter 4). Maternal VL suppression rates observed from the national level synthetic cohort were validated against the Gauteng cohort in 2018 (Publication 3, Chapter 5). The geospatial distribution of maternal viraemia at delivery was described using ArcGIS and a negative binomial regression model assessed population-level determinants of vertical transmission within the national PMTCT programme using the national level synthetic cohort during the study period (manuscript in preparation 1, Chapter 6). Lastly, an evaluation of maternal VL testing coverage and compliance to national VL testing guidelines was assessed from the Gauteng cohort in 2018 (Publication 4, Chapter 7).

Results

In 2018, 74% of all WRLHIV were located in Gauteng, KwaZulu-Natal, Western Cape, Eastern Cape, Limpopo and Mpumalanga provinces. The same provinces also accounted for 87% of all AGYW living with HIV during the study period. These data suggested that the need for eMTCT is greatest in these six of the nine provinces in the country.

Regarding maternal viraemia (VL ≥50 copies/mL), a steady decline in viraemia was observed from presentation at the first antenatal care visit (fANC) to delivery and postpartum nationally. However, proportions with viraemia were 54% at first HIV VL measurement during pregnancy, 37% at delivery and 34% postpartum, when eMTCT requires sustained maternal VL suppression from conception through pregnancy until breastfeeding cessation. Importantly, 43% of ART-experienced pregnant WRLHIV were viraemic at fANC visit while two thirds of women not on ART at fANC visit were still viraemic after three months of ART use. At delivery, the proportion with maternal viraemia was similar to that of known pregnant WLHIV in Gauteng province, suggesting representativity of the study population to pregnant WRLHIV in the country. Notably, the community VLs of pregnant WRLHIV at all time points were higher than those of non-pregnant WRLHIV. Maternal viraemia during the postpartum period, high maternal seroprevalence, women initiating ART late in pregnancy and/or incident maternal HIV during pregnancy were significant population-level drivers of MTCT during the study period, while early booking (<20 weeks gestation) for ANC among pregnant women was associated with a decline in vertical transmission. Implementation of maternal VL monitoring guidelines during pregnancy and postpartum was poor as observed in Gauteng province. Less than 5% of pregnant WLHIV received VL monitoring according to national guidelines while >80% had no

evidence of VL monitoring during the antenatal period. However, if women received VL monitoring during the antenatal period, they were more likely to be virally suppressed at delivery and receive VL monitoring postpartum. Lastly, we observed provincial differences in sustaining VL suppression into the postpartum period, with KwaZulu-Natal, Western Cape and Free State the best performing provinces.

Conclusions

Maternal VL suppression rates during pregnancy, delivery and postpartum were poor in spite of high ART coverage during the study period. Results emphasize the need for closer monitoring of and rapid response to elevated maternal VL during pregnancy, delivery and postpartum for the attainment of eMTCT in South Africa. These findings provide baseline data on maternal virologic responses within the national PMTCT programme and have informed the development of routine surveillance reports for near real-time monitoring of VLS rates among pregnant WLHIV from the NHLS CDW. Based on these data, targeted interventions to improve PMTCT outcomes with ongoing NHLS CDW monitoring are recommended to achieve eMTCT.