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Loss to follow-up and mortality amongst pregnant women referred to a community clinic for antiretroviral treatment

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Summary

In a retrospective cohort analysis, loss to follow-up (LTFU) and mortality rates were compared between pregnant and non-pregnant women referred to a community-based antiretroviral treatment (ART) program in South Africa. While there was no significant difference in adjusted mortality rates between the two groups, the pregnant women had a substantially higher risk of LTFU both pre and on-treatment. This finding highlights the need for programmatic interventions to address retention in care for this patient population.

Keywords

antiretroviral therapy; pregnancy; mortality; loss to follow-up; Africa

Letter

In sub-Saharan Africa, HIV-positive pregnant women are being enrolled in large numbers into the antiretroviral treatment (ART) services. While treatment outcomes such as loss to follow-up (LTFU) and mortality rates have been well described for large ART cohorts in this region [1] little is known of treatment outcomes for this group of patients.

To ascertain losses due to mortality and LTFU for pregnant women, a retrospective cohort analysis was carried out on all ART-naïve, adult women referred for treatment to the Hannan Crusaid Treatment Centre in Gugulethu. This is a large community-based ART service in Cape Town, South Africa which was established in 2002 and has previously been well described [2-4].

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Author's Contributions R. Kaplan wrote the manuscript and contributed to the study design, data collection and data analysis. C. Orrell was responsible for establishing the study cohort, data collection, data interpretation and revising the manuscript. E. Zwane did the statistical analysis and assisted with revising the manuscript. LG Bekker was responsible for establishing the study cohort, data interpretation and data analysis. R. Wood was responsible for study design, analysis, data interpretation and revising the manuscript. All authors have seen and approved the final version of the manuscript.

Conflicts of Interest The authors have no conflicts of interest.

In this study, we looked at mortality and LTFU rates for 2131 HIV infected, ART naïve women from the age of 15 who were referred for ART between 1 Sept 02 to 30 Sept 07. Of the total number of women enrolled, 318 (15%) were pregnant on the date of screening. Overall, this group was younger with less advanced HIV as indicated by a lower median CD4 count and less WHO stage 3 and 4 disease than the non-pregnant women.

Both pre and on-treatment outcomes were included in this analysis, which compared the mortality and LTFU rates between pregnant and non-pregnant women prior to starting and after commencement of ART. For the purpose of this analysis, the pre-treatment LTFU was calculated as the percentage of patients referred for ART who refused treatment or did not return to the clinic. Other pre-treatment losses were due to mortality, patients who accessed ART elsewhere and patients whose treatment was deferred as they did not meet the South African national treatment criteria for triple therapy.

In the pre-treatment analysis there was a crude overall programmatic loss of 19.8% amongst pregnant women as compared to 17.1% amongst non-pregnant women ($p<0.243$). Pre-treatment mortality was significantly lower amongst pregnant women (0.3% vs. 4.7%; $p<0.001$) while the pre-treatment LTFU rate was higher (13.2% vs. 6.0%; $p<0.001$).

An on-treatment analysis was carried out on the 1677 women who started ART. On-treatment LTFU was defined as patients receiving ART who had not attended the clinic for twelve or more weeks. This would equate to having defaulted ART for at least four weeks. Similar to the findings in the pre-treatment period, Kaplan-Meier plots showed that over a 3-year period, cumulative mortality was lower ($p=0.045$) but risk of LTFU was substantially higher ($p<0.001$) for pregnant women when compared to non-pregnant women. (Fig. 1) The differential risk of LTFU between the two groups continued over 3 years.

In a multivariate analysis, mortality was not associated with pregnancy, age or baseline viral load but was associated with WHO Stage and baseline CD4 counts. Conversely, pregnancy and age were independently associated with LTFU but WHO clinical stage, baseline CD4 count and viral load were not. When controlled for the other variables, the relative risk of pregnancy for LTFU was 2.1 (95%CI, 1.4-3.1, $p<0.001$). Younger patients were also at greater risk of LTFU with an adjusted risk of 2.2 (95%CI: 1.3-3.6, $p=0.002$) for women < 25 years when compared to women >35 years old.

The cumulative programmatic LTFU rate for pregnant women was substantial when considering the crude pre-treatment LTFU rate for pregnant women of 13.2% compared to 6.0% for non-pregnant women ($p<0.001$) and the LTFU rate at 3 years on treatment of 32% for pregnant women as opposed to 13% for non-pregnant women ($p<0.001$).

The high LTFU rates in this analysis are consistent with the findings presented by Wang et al, who reported patient characteristics associated with LTFU for 1507 patients starting ART at four community care sites in South Africa. Over a median follow-up period of 11.4 months, they described a higher on-treatment LTFU rate for pregnant women when compared to non-pregnant women and men [5].

In ART programs, LTFU rates have been shown to be influenced by programmatic characteristics, with the provision of a free service and a comprehensive treatment support system identified as contributing to higher patient retention rates [1,6,7] The Hannan Crusaid Treatment Centre offers a free service and has an intensive treatment support program conducted by trained peer counselors who provide in-clinic counseling as well as an outreach service in the form of home visits [7-8]. This includes an active patient tracing system for defaulting patients and ensures high retention rates when compared to other developing world programs [1]. Overall LTFU rates at other community clinics with less intensive support

systems may be higher. Pregnancy however is still likely to be a risk factor for LTFU in these programs.

The reasons pregnant women defaulted treatment were not ascertained from this study. Pregnant women do however have a number of common characteristics which could result in a higher LTFU rate. Many of them have had a recent HIV diagnosis during their antenatal assessments leaving them little time to process their diagnosis or deal with the issues around the disclosure of their HIV-status to their spouse and family members. They may therefore not be adequately prepared to start ART. They are also undergoing a major life-altering event. Of note however is that while the increased LTFU rate for pregnant women occurs from the start of treatment, it continues as a relatively constant hazard for the 3 years of follow-up, indicating that the mother's circumstances post delivery continues to influence adherence to the program.

This high LTFU rate is of particular concern as it will not only impact on the morbidity and mortality of the mother but is also likely to result in an increased risk of HIV transmission to the child and may be detrimental to the future care of the child. This analysis points to the need for a more focused intervention to ascertain why these patients are at higher risk of defaulting treatment. It also identifies pregnant women as a special sub-group of patients who may require additional longitudinal interventions for programmatic retention.

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Not pregnant:	1431	1098	883	671	493	308	207
Pregnant:	246	183	142	115	88	57	31

Figure 1.

(a) Survival from date of starting ART for pregnant and non-pregnant women.

The Kaplan-Meier plot shows a comparison of survival rates for pregnant and non-pregnant women from start of ART, with losses due to mortality at 3 years of 5% for the pregnant women and 11% for the non-pregnant women. ($p=0.045$)

(b) Cumulative proportion not lost to follow-up for pregnant and non-pregnant women.

The Kaplan-Meier plot shows cumulative proportion of pregnant and non-pregnant women who were not LTFU. At 3 years on ART, 32% of the pregnant women and 13% of the non-pregnant women were LTFU. ($p<0.001$)