論文の内容の要旨

論文題目 Adherence to the prevention of mother-to-child transmission of HIV (PMTCT) program among women living with HIV in Zambia

（ザンビア共和国における HIV 陽性女性の母子感染予防プログラムへのアドヒアランス）

大川　純代

Introduction

Prevention of mother-to-child transmission of HIV (PMTCT) is one of the most important strategies to reduce the global burden of HIV/AIDS. If any antiretroviral (ARV) intervention is not used, 30 to 45% of breastfeeding infants are exposed to the risk of HIV infection. To avoid this, WHO revised the PMTCT guidelines in 2010, and has addressed to reduce the risk of HIV transmission to less than 5% among breastfeeding infants.

Zambia is one of the highest HIV prevalence countries in the world. HIV has been the top –ranked cause of years of life lost in the last decade, its prevalence is estimated as 14% among adults in 2007, and pediatric HIV infections accounts for 10% of all HIV infections. To improve such situation, Zambian government developed the new national guidelines in 2010 based on Option A of the WHO 2010 guidelines. Furthermore, they plan to adopt Option B+ protocol (providing lifelong antiretroviral therapy (ART) to all HIV- positive mothers) in 2013. However, since the revised guidelines were introduced, no study has been conducted to assess the longitudinal ARV adherence. Risk factors for non-adherence have not been well explored, either.

The objectives of the study were to assess a probability of adherence to ARV and to identify the risk factors for non-adherence in HIV-positive pregnant women and postnatal mothers until 24 weeks postpartum under the 2010 national guidelines.

Methods

A prospective cohort study was conducted in Chongwe district, from June 2011 to October 2012. Overall 389 HIV positive mothers were enrolled in the study, and 321 were included in the analysis. Adherence status was defined as "non-adherence" if a mother has missed any prescribed drug, or has not followed their prescribing schedule at least once in the past four days to the interview, or if medication

interruption was detected at interview. Mothers on ARV prophylaxis regimen were assessed on the basis of their own adherence during pregnancy and adherence in administering nevirapine to their infants from birth to 24 weeks postpartum. Mothers on ART regimen were assessed on the basis of their own adherence over the assessment period. The participants had interviews a maximum of four times including pregnancy (wave 1), 1-5 week (wave 2), 6-23 weeks (wave 3), and 24-52 weeks (wave 4) postpartum. A participant was treated as loss to follow up, if she missed any scheduled interview within a wave.

The incidence of non-adherence to ARV was calculated using the time from the start of an observation to detection of non-adherence (the event). The recurrent event model was adopted to analyze the potential repeated event to control for the effect of loss to follow up. As proxy date when censorship occurred, a midpoint between the date of previous observation and regular cut-off point of the current observation was applied to all failure events. The regular cutoff points were defined as follows: one week postpartum for wave 2; six weeks postpartum for wave 3; and 24 weeks postpartum for wave 4. Sensitivity analysis for midpoint censorship was done to test the effect of time definition on the study outcome by comparing results for censoring at the midpoint (main model) with the regular cutoff point (alternative model). The proportional hazards assumptions were assessed using Schoenfeld residuals and log-log survival plot. The incidence of non-adherence was calculated using Log-rank test, and the probability of remaining adherent was plotted with a Kaplan-Meier survival curve. The Cox proportional hazards regression model was tested in a backward stepwise model-building procedure to identify risk factors for non-adherence.

Results

The probability of remaining adherent decreased over the assessment period: 0.54 (95% confidence interval (CI), 0.49-0.59) at 60 days; 0.30 (95% CI, 0.26-0.34) at 120 days; 0.19 (95%CI, 0.16-0.23) at 180 days; and 0.12 (95%CI, 0.10-0.15) at 240 days. The proportional hazard assumptions for the Cox proportional hazards regression model were not seriously violated. The multiple regression analysis showed that mothers attending the primary health centers with ART services (hazard ratio (HR): 0.71, 95% CI: 0.57-0.88) and mothers attending the primary health centers without ART services (HR: 0.58, 95% CI: 0.46 – 0.74) were less likely to be non-adherent than mothers attending the referral health center. As for individual factor, mothers newly diagnosed as HIV-positive during the pregnancy were more likely to be non-adherent than mothers who had already known their HIV-positive status (HR: 1.24, 95% CI: 1.03-1.50). The secondary analysis demonstrated that different time definitions for censorship affected the confidence intervals, but did not make any changes in directions of the hazard ratios.

Conclusions

This study was the first operational evaluation on longitudinal ARV adherence for PMTCT controlling for the effect of loss to follow-up after the Zambian government revised the national guidelines in 2010. Maternal ARV adherence seriously declined over the assessment period. Especially,

mothers attending the referral health facility showed higher incidence of non-adherence than those attending the primary health facilities. New HIV diagnosis during pregnancy was also a crucial risk factor for non-adherence.

Toward implementing Option B+ regimen, ART services should be also expanded to all primary health facilities to prevent loss to follow-up and treatment interruption. Training and careful task-sifting for health workers and volunteers are feasible responses to improve the quality of PMTCT services at the referral health center. Meanwhile, HIV testing and treatment before pregnancy is a potential strategy for mothers newly diagnosed as HIV-positive to overcome negative effects of the first HIV diagnosis on medication adherence, as considering cost-effectiveness in implementing such strategies.

To achieve elimination of mother-to-child transmission of HIV, not only prescribing ARVs, but comprehensive interventions to reduce loss to follow-up and improve maternal ARV adherence are needed.