論文の内容の要旨

論文題目 Adherence to antiretroviral therapy (ART), self-stigma and depression among people living with HIV (PLWH) in rural Zambia

（ザンビア共和国農村部におけるHIV陽性者の抗レトロウィルス療法に対する服薬遵守及びセルフスティグマと抑うつ症状について）

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Introduction:

AIDS is the leading cause of death in Sub-Saharan Africa. Zambia is among the most severely affected countries in the region. In Zambia, the proportion of people living with HIV (PLWH) has rapidly increased, peaking in the mid 1990s at about 16% but reaching as high as 25% in some urban areas. Although the rate of new HIV infection has decreased, the total number of PLWH continues to rise. Heterosexual sex is the major mode of transmission of HIV in Zambia. In 2004, the Ministry of Health (MoH) has offered antiretroviral therapy (ART) at four clinics in Lusaka. The program expanded and the government declared that the entire ART service package would be provided free of charge in the public sector with a goal of universal access to HIV care and treatment. The concerted efforts have increased the availability of ART in rural Zambia, resulting in increased coverage of nearly 70% by 2009, and the number of sites is expanding. As part of this, mobile ART services were introduced in 2007. The mobile sites are expected to make it easier for PLWH to access ART services. While achievements have been remarkable, challenges remain related to universal coverage in Zambia.

Adherence to ART is crucial for treatment success among PLWH; it has improved the health of people who otherwise would have progressed to AIDS or died. Based on the previous studies, factors influencing adherence can be divided into six key themes: demographic, economic, medication, physical health, interpersonal, and mental health factors. In Zambia, few quantitative studies have investigated associations between ART adherence and these factors, and to the best of my knowledge, no studies have investigated factors related to ART adherence focusing on clients' mental health factors at the early months of treatment.

Thus, this study aimed to identify the factors associated with ART adherence, and to examine the relationship among ART adherence, self-stigma and depression at the early months of treatment in rural Zambia.

Methods:

This is a field based observational longitudinal study. Field surveys were carried out from September 2010 to March 2011 in Mumbwa district, which is located 150 km west of the capital, Lusaka in Zambia. There was one district hospital (DH), one mission hospital and 27 rural health centers (RHCs) in Mumbwa district during the study period. Among the health facilities, ART services were available only at the DH, the mission hospital and eight RHCs.

All ART clients that came to the DH or to one of the eight RHCs where ART services were offered were asked to participate in the study. The eligible population were ART clients who 1) were aged 16 and over; 2) were ART-naïve and newly registered for ART services based on Zambia HIV National Guidelines during September-November 2010; and 3) agreed to give an informed consent. The exclusion criteria included the clients who were too ill to be interviewed. Clients were interviewed at the initiation of treatment as well as at six weeks after the initiation.

Based on a 10% significant level using a two-sided test, with 80% statistical power and 15% self-stigma and depressive symptoms among clients who adhered to ART, the estimated sample size was 216 samples.

The questionnaires covered respondents' socio-demographic characteristics, ART adherence, disclosing status, physical and mental health characteristics, and sexual activities of the respondents. WHO HIV/AIDS stage, weight, CD4 lymphocyte count, TB status were extracted from individual medical records.

Full adherence to ART is defined as when a client had never skipped a prescribed drug and followed time restrictions during the previous four days before the interview. Scores for self-stigma and depression were measured using the 'Internalized AIDS-Related Stigma Scale' and the 'Cognitive/Affective Depression Subscale' respectively. The median of each scale score was used as the cutoff point between the clients who had self-stigma or depressive symptoms and who did not.

Data obtained from the questionnaire surveys were analyzed with SPSS version 19 statistical software. Characteristics of participants were compared between the clients who adhered to ART and who did not by Pearson's chi-square test and Fisher's exact test. Multiple logistic regression analysis was performed to identify the factor associated with ART adherence. Mental health related variables and other variables of which associated significance p value level was less than 0.1 were entered into a multiple logistic regression model. If the variable was highly correlated with the other variable, one of them was removed from the model. Clients' characteristics were also compared between those who had self-stigma or depressive symptoms at the initiation of ART and who did not by Pearson's chi-square test and Fisher's exact test. In addition, association between self-stigma and depressive symptoms at the initiation of ART and the six weeks later was investigated by Spearman rank correlation coefficient.

Ethical clearance for the study was obtained from the ethic review committee of the University of Tokyo, the University of Zambia, and the International Medical Center of Japan. Written informed consents were obtained from respondents at the beginning of the interview after the study was explained to them. They were informed that participation in the study was voluntary. The participants were randomly assigned by one of the eight interviewers, and the name of the interviewer who would interview them was informed before interview. If a participant knew the name, the other interviewer was assigned. Data were recorded in anonymous form to protect confidential information of participants.

Results:

Among the 157 ART clients [94 female, median age 35 years old (range: 18-68)] who were included in this study, 94 (59.9%) were fully adherent and 63 (40.1%) were non-adherent to their drug regimen six weeks after starting ART, respectively. The proportion of those who were adherent to ART was significantly lower among farmers than others ($p=0.038$), but was higher among females and clients who had experienced food insufficiency in the previous 30 days ($p<0.001$).

Fifty-eight (44.6%) of the respondents' spouses were HIV positive and 36 (29.3%) were on ART. Regarding disclosure, 89 (85.6%) disclosed one's HIV status to their spouse. The proportion of those who were adherent to ART at the first six weeks of the treatment was significantly higher among the clients who disclosed it to one's spouse than those who did not (p=0.048).

Over half of clients had self-stigma and depressive symptoms (n=87, 56.5%; n=92, 58.6%). These characteristics did not differ between clients who were adherent and non-adherent for ART by univariate analysis.

In multivariate analysis, full adherence was associated with being female [Adjusted odds ratio (AOR), 6.4; 95% Confidence interval (CI), 1.7-23.5], experience of food insufficiency in the previous 30 days (AOR, 5.7; 95% CI, 1.6-21.2), spouse undergoing ART (AOR, 5.4; 95% CI, 1.4-19.9), self-stigma at the initiation of ART (AOR, 0.1; 95% CI, 0.02-0.6), being more depressed (AOR, 1.1; 95% CI, 1.0-1.3) and having less self-stigma (AOR, 0.6; 95% CI, 0.5-0.9) at the first six weeks compared with at the initiation of ART. Some of the most common reasons for missed doses in this study were being away from home (n=21), food insufficiency (n=20), and being busy with other things like work (n=15).

In addition, association between self-stigma and depressive symptoms was investigated. Self-stigma was positively associated with depressive symptoms at the initiation of ART (r=0.176, p=0.029). The result was also found six weeks after starting ART (r=0.198, p=0.015).

Discussion:

This study described the status of ART adherence by PLWH who started ART and identified the factors associated with ART adherence at the early months of treatment, focusing on mental health issues in a rural setting in Zambia. In this study, 59.9% were considered fully adherent to ART six weeks after starting ART, and the factors positively associated with ART adherence were being female, experiencing food insufficiency in the previous 30 days, spouse undergoing ART, having no self-stigma at the initiation of ART, being more depressed and having less self-stigma after six weeks compared with at the initiation.

Female clients may have more opportunities to access care and start treatment at less advanced stages of HIV, likely through their participation in prevention of mother-to-child transmission (PMTCT) programs launched in 1999 and which expanded in Zambia. Although not determined in this study, sex differences in drug metabolism, distribution, side effects and greater motivation to adhere to ART among female clients could have contributed to the outcome observed.

Experiencing food insufficiency in the previous 30 days from the baseline interview date was found to be a significant determinant for ART adherence although a number of previous studies have reported that food insufficiency is a barrier to ART adherence. This result may be explained by enhanced social support among people living in such extreme poverty that they cannot afford to buy food, which has been indirectly explained as good adherence in Sub-Saharan Africa.

Spousal use of ART was also found to be positively associated with ART adherence. Spouses on ART might play a role as a treatment partner more spontaneously than spouses not on ART because they have a better understanding of ART adherence for their partners and themselves.

Having self-stigma at the initiation of ART, being more depressed and having less self-stigma six weeks after starting ART were associated with ART adherence. Clients who had self-stigma at the initiation of ART might be less enthusiastic about taking their medications. However, access to ART might reduce self-stigma and being on ART might improve clients' physical health, contributing to

improvements in self-image, self-worth and leading to reductions in fears of disclosure and negative public attitudes.

An increase in depressive symptoms six weeks after starting ART was positively associated with ART adherence. Some level of depression may function as a motivator for ART adherence with self-protective alertness about following the medication regimens. The result might also be explained by the 'life in a pill bottle' metaphor and clients might be depressed even when they adhered to their medication regimen. Moreover, clients on ART might feel pressure and experience increased depressive symptoms because incomplete adherence can quickly lead to viral mutation and drug resistance once ART is initiated. Additionally, taking medicines is time consuming, a constant reminder of HIV positive status for life, and conflicts with confidentiality. These factors might worsen depressive symptoms after ART initiation.

This study found an association between self-stigma and depressive symptoms. The result suggests that interventions for improving ART adherence must take into account therapeutic techniques and strategies used in the treatment of self-stigma and depressive symptoms for ART clients.

Conclusions and Recommendations:

ART adherence continues to be a significant behavioral challenge in HIV medical care. Based on adherence to dose and schedule, there was a relatively low level of ART adherence in this rural area where ART services have become widespread. Regarding the feasibility of expanding mobile ART services, more human resources and an increased budget may be needed.

The study showed that female gender, food insufficiency in the previous 30 days and a spouse on ART were associated with full ART adherence. Related to mental health issues, no self-stigma at the initiation of ART, being more depressed and having less self-stigma six weeks after starting ART were also associated. Adherence issues associated with mental health challenges should be addressed through a comprehensive approach to HIV care. Self-stigma reduction interventions should be the priority in this population to enhance adherence to ART. HIV counseling and support services should include clients' self-stigma concerns prior to and during the early months of treatment, providing a better understanding of gender differences in treatment and food security situations among ART clients.