

Determinants of Adherence to Antiretroviral Treatment among HIV Patients in Ethiopia

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Abstract

This study investigated factors of adherence to Antiretroviral Treatment (ART), factors or variables that can discriminate between adherent and non-adherent patients on ART were selected. Simple structured questionnaire was employed. The study sample consisted of 145 HIV patients who received ART in the Shashemene General Hospital (SGH). Using self report measure of adherence in the two weeks of study period, 81% of the patients on ART were adherent whereas 19% of the patients were non adherent. The major reasons of non-adherence were: forget to take (28.6%), confused on how and when to take (17.9%) and feel depressed (14.2%). Using discriminant analysis, depression, poor NGO support and HIV serostatus disclosure were identified as barriers of adherence while transportation problem, strong NGO support, good reception in the service area and high CD4 count were identified as facilitators of adherence. To improve adherence of patients on ART, it was recommend that the current ART program should strive to manage depression before and after the initiation of ART and also strong linkage between NGOs which are working in care and support program must be established.

Key Words: Antiretroviral, Adherence, Non Adherence, Discriminant Analysis

Introduction

HIV/AIDS is an epidemic that affects every part of the globe. According to the latest figures, it is estimated that 39.5 million people are living with HIV. There were 4.3 million new infections in 2006 with 2.8 million (65%) of these occurring in Sub-Saharan Africa.

(UNAIDS/WHO AIDS epidemic update: December 2006). One of the countries hit by HIV/AIDS epidemic in this region is Ethiopia. Based on the official figures, 1.3 million people are living with the virus, 744,100 are orphaned due to AIDS, and 277,800 are in need of antiretroviral treatment (ART) in 2005. Antiretroviral treatment (ART) refers to treatment of HIV infection using combination of antiretroviral drugs. The introduction of highly active antiretroviral therapy (HAART) in 1996 was a turning point for millions of people who are living with HIV/AIDS. Although it cannot cure HIV/AIDS, antiretroviral (ARV) has dramatically reduced mortality and morbidity, prolonged lives, and improved the quality of life of many people living with HIV/AIDS in third world countries. Notwithstanding these benefits, patients often default in adhering to treatment prescription for the following reasons: pill burden, food and fluid restriction, temporal side effects such as nausea, vomiting, diarrhea and fatigue; and long lasting side effects such as neuropathy, lipotrophy/lipodystrophy, and metabolic disfunction. The treatment has to be taken regularly for the rest of the patient's life with maximum adherence (95% and above) in order to obtain the full benefit of the treatment. Adherence below 95% is associated with a poor viral load or low CD4 count and response, and with faster disease progression (Peterson, 2000). Level of adherence below this threshold value is referred to as non adherence. Unfortunately, non adherence to treatment is common in patients receiving ART treatment.

After the introduction of the free ART program in Ethiopia in 2005, non adherence to medication has become a major problem. The paper is therefore concerned with investigating the general characteristics of adherence and non adherence patients in Shashemene General Hospital, Shashemene, Oromia regional state, Ethiopia. In addition, the paper is to develop a statistical model that can discriminate the case population into adherent group and non adherent group.

The Data

A combination of survey data and transcription from hospital records were employed in this study. The latter was used to retrieve data on type of regimen, disease stage, CD4 count and duration of therapy. The hospital's ART register was the sole sampling frame because ART register is exhaustive, non-repetitive, and traceable list of patients on ART. The data covers all HIV/AIDS patients attending ART medication program in Shashemene General Hospital who came to the hospital for their regular drug refill and some of them for medical follow up during the month of May (May 1 to May 30, 2007). A structured questionnaire was designed and administered to gather information on demographic, social support, treatment characteristics, patient characteristic and service provision variables.

Adherence was also measured using the self report adherence measure included in the questionnaire. Medical records were inspected in order to collect additional clinical information about the patient. Adherence was measured over two days, four days, one week and two weeks recall of medication intake. The level of adherence required for effective HIV therapy is high. Levels below 95% are consistently associated with a poor viral load or CD4 response, and with faster disease progression (Patterson, 2000). Therefore, a patient is considered in this study non adherent if he missed at least one dose from his daily medication and missed dose timing (Liu H et al., 2006) in two hours delay.

Before selecting the study sample from the sampling frame, those who started the medication in Shashemene General Hospital and those who had been transferred from other facilities were given sequential order number. A simple random sampling procedure was then applied on this list. During the sampling process the hospital's appointment record logbook was also used in order to select the patients who were going to come on that data collection day. During the random sampling process patients who did not come at the time of the study were substituted by the next random number. The patients who were

selected by simple random sampling procedure were contacted during their visit to the hospital. The observation (Y_i) were follows:

$$Y_i = 1, \text{ if the patient is non adherent}$$

$$= 0, \quad \text{if the patient is adherent}$$

$$\text{For population, } Y = \sum_{i=1}^N Y_i = A, \quad \bar{Y} = \frac{\sum Y_i}{N}$$

$$= \frac{A}{N} = P$$

where P is proportion of non adherent patients and A denote the total number of non adherent patients. Using the defaulter rate as an estimator of non - adherence rate of Shashemene General Hospital it was estimated P to be 9.1%, that is $p=0.091$. Assume that the proportion estimate, p, is normally distributed with absolute margin of error $d = p-P$, then sample size n can be calculated by

$$n = \frac{Z^2 PQ}{1 - \frac{1}{N} + \frac{Z^2 PQ}{Nd^2}}$$

If we put $n_0 = \frac{Z^2 PQ}{d^2}$, then we get

$$n = \frac{n_0}{1 - \frac{1}{N} + \frac{n_0}{N}}$$

Where $Q = 1-P$ and Z is the upper bound of two tailed $(1 - \alpha)$ 100% Confidence interval of standard normal distribution. In practice the population parameters P must be estimated while the other factors Z

and d usually is set by the investigator. Since population parameter (P) is unknown, calculate n_0 by using the estimate of the non adherence. That is, $p=0.091$, $Z= 1.96$ for 95% confidence interval estimation and d to be 0.04, then

$$n_0 = \frac{Z^2 p(1-p)}{d^2} = \frac{(1.96)^2(0.091)(.909)}{(0.04)^2} = 198.6 \cong 199$$

To calculate n , the total sample size of the study. The total population of patients on antiretroviral (ARV) drug at the time of investigation was 540.

$$n = \frac{n_0}{1 + \frac{n_0}{N}} = \frac{199}{1 + \frac{199}{540}} = 145.36 \cong 145 \text{ patients (26.9\% of N)}$$

Therefore, a total sample size of 145 patients representing 26.9 % of the population was selected.

Sample Profile and Characteristics: Demographic and Socio-Economic Variables

The study sample was comprised of women (61.9%) and men (38.8%). The majority of the participants (48.1%), were either separated or widowed, and the rest are still married (42.9%) or never married (19%). The participants' ethnicity comprises the major ethnic groups in the country, Oromo (34.4%), Amhara (36.7%), South nations and nationalities people (or SNNP) (22.4%), and Tigray (6.1%). As regard religious affiliation: Orthodox (54.4%), Protestant (29.3%) and Muslim (16.3%). The majority of the respondents were unemployed (75.5%). Approximately 89% of the participants reported their monthly income as: no income (32%), below 100 birr (57.1%). Some of the respondents who reported below 100 birr said they do not have income but they were using informal income earning mechanisms like baking traditional "ambasha" and selling. As for education the majority of the respondents (72.8%) were either elementary or high school drop outs and 21.1%

reported either no education (illiterate) or basic education. More than one half of the respondents (56.5%) live in a rented house. The rest 32% owned a house, 9.5% were homeless (that is, they were living with their family and friends) and 2% live in NGO shelter.

Treatment Characteristics

The health status of the respondents at the time of the study was assessed using treatment characteristic variables such as disease stage, CD4 count and duration of the Therapy. Almost one half of the respondents were on WHO stage III (47.6%) followed by WHO stage II (27.9%) , WHO stage VI (13.6%), WHO stage I(9.5%) and only two respondents reported not having disease stage. Above one third of the respondents (34%) reported from 101 to 200 CD4 cell count, from 201 to 300 CD4 cell count (25.9%), above 300 CD4 cell count (23.1%) and less than 100 CD4 cell count(17%). More than one third of the respondents reported from six to twelve months of duration of therapy (42.9%) and the rest; from two to six months (28.6%), from twelve to thirty six months (25.9%) and less than two months (2.7%).

Patient characteristics

The health status of the respondents can also be described using the depression status of the respondent. According to the scaling mechanism – five point Likert scale, the bottom two item scales correspond to having depression and the rest not having depression in the study period. Therefore, 24.5% reported having depression and the rest do not have depression in the study period.

Regimen complexity

The type of regimen and the side effect encounter due to this regimen which shows drug complexity, in many literatures is a predictive of adherence to treatment. All except one of the respondents were on first line regimen, twice daily intake and three or two doses per intake. This shows no problem with pill burden or food or fluid restriction. But one of the respondents reported that she is taking five doses. More than one half of the respondents (59.2%) were on 1a30/40(D4T/3TC/NVP), about quarter of the respondents were on 1b30/40 (D4T/3TC/EFV), 1c (AZT/

3TC/NVP) (8.2%), and 1d (AZT/3TC/EFV) (6.8%). Almost half of the respondents reported no side effect (46.3%). Among those who had encountered, 13.6% reported head ache, 12.9% reported fatigue, 7.5% had nausea and vomiting and the rest other side effects.

Disclosure Status, ART Knowledge, and Service Provision and Accessibility

Disclosure status of the respondent can be described using two variables such as disclosure to family (spouse, children, mother, father, and relatives) and disclosure to community (neighbors, "Edir" and public gathering). Majority (79.6%) of the respondents have disclosed their HIV status to spouse, children, mother, father, or relatives. 69.7% have disclosed to their community. More than half of the respondents reported that confidentiality of the ART service is very good; while the rest fear that their status has been known as they come to the hospital. 64.7% of the respondents reported that service hour delay has been a problem and the rest said there is no problem with service hour. Majority (96.6%) of the respondents reported sympathetic and good reception service provision. That is, the sum of the lowest three ranks in the likert scale. 83.0% reported that transportation to the hospital is a big problem as the hospital is 12km from Shashemene town.

Adherence to ART

Some of the respondents (2%) have totally discontinued the medication in the study period. 17% had missed at least one dose of medication and dosage timing. Majority of the respondents (54.4%) reported they had missed medication but not in the study period. 25.5% of the respondents reported they had not missed starting from the beginning of the ART therapy. Non adherent respondents claimed that they didn't understand when and how to take medication during their first month of start of medication. The mean adherence rate of the Shashemene General Hospital was calculated using weighted average and was found to be 84.62 %.

Discriminant Analysis

Discrimination and classification are multivariate techniques concerned with separating distinct sets of objects or observations and allocating new objects (observations) to previously defined groups. There are two goals of discrimination and classification, the first one is to describe graphically or algebraically the deferential features of objects(observations) from several known collections (populations).The second goal is to sort objects (observations) into two or more labeled classes, that is, deriving a rule that can be used to optimally assign new objects to the labeled classes.

In order to differentiate between the barriers of adherence and facilitators of adherence, data analysis was made for adherent and non adherent patients separately. The data was divided into two: those who did not adhere to the treatment in the past two weeks prior to the assessment and those of who adhere to the treatment. The variables which were identified as the loaded variables on HIV serostatus status disclosure, home based care and psychological well being in the factor analysis were used. Socio demographic variables were analyzed but were not significant and were automatically excluded by the SPSS stepwise discriminant analysis. The cost function of the SPSS default value was used in the analysis.

Probably the most common application of discriminant function analysis is to include many measures in the study, in order to determine the ones that discriminate between groups. A "model" on how best to predict which group a case belongswas meant to be developed. In stepwise discriminant function analysis, a model of discrimination is built step-by-step. Specifically, at each step all variables are reviewed and evaluated to determine which one will contribute most to the discrimination between groups. That variable will then be included in the model, and the process starts again.

The stepwise procedure is "guided" by the respective F to enter and F to remove values. The F value for a variable indicates its statistical

significance in the discrimination between groups, that is, it is a measure of the extent to which a variable makes a unique contribution to the prediction of group membership.

Case 1: Adherent Patients

Prior to data analysis, it was assumed that good service provision, strong social support, HIV serostatus disclosure and high CD4 count, no transportation problem and good NGO support were facilitators of adherence. But after the data analysis it was found that the facilitators of adherence included: good reception, strong NGO support, high CD4 count and free transportation mechanism. The model that significantly discriminates among groups of adherent patients is derived as:

$$Y = -0.449 X_1 + 0.796 X_2 + 0.244 X_3 + 0.538 X_4$$

Where Y denote adherent group, X_1 is transportation problem, X_2 is reception, X_3 is CD4 count and X_4 is NGO support.

Fisher's linear discriminant function was used for each of the three groups of adherent patients. There are three classification models for each group. The classification power of the studies analysis was investigated using the classification matrix which shows 66.4% of the original group cases classified correctly. Let S_1 be those adherent patients who has been considered to adhere the treatment "Some of the time". Let S_2 be those who had been considered to adhere to the treatment "Most of the time". And finally let S_3 be those who had been considered to adhere to the treatment "All of the time". Then following the above argument the Fisher's linear discriminant function for each of the groups is given by:

$$S_1 = -16.233 + 1.38 X_1 + 5.084 X_2 + 2.556 X_3 + 1.979 X_4$$

$$S_2 = -11.655 + 2.002 X_1 + 3.627 X_2 + 2.099 X_3 + 1.082 X_4$$

$$S_3 = -13.904 + 1.406 X_1 + 3.207 X_2 + 3.076 X_3 + 2.087 X_4$$

These functions can now be used to assign fresh cases to their

respective groups.

Case 2: Non Adherent Patients

The variables earlier identified as facilitators of adherence were valuable information for the analysis of the data on non adherent patients. Prior to the data analysis transportation problem, depression, lack of NGO support, and poor service quality were assumed to be the crucial barriers to adherence. After the data analysis the variables that qualified to be in the discriminating model which are equally identified as barriers of adherence included: depression, NGO support and HIV serostatus disclosure. These variables have significantly discriminated between the two groups of non adherent patients and also observed that there was a good canonical correlation between the variables and the dependent variable. Finally the model that can discriminate significantly between the groups of non adherent patients can be given as:

$$Y = 0.935 X_1 + 0.805 X_2 - 0.683 X_3$$

Where the dependent variable Y is adherent to treatment and the independent variables are: depression, community disclosure and NGO support denoted by X_1 , X_2 , and X_3 respectively.

The study further classified the non adherent patients using the two group Fisher's linear discriminant function, into two groups of non adherent patients. There were two classification models for each group. The classification power of the analysis was investigated using the classification matrix which showed 89.3% of the original group cases classified correctly. Let S_1 be those non adherent patients who said they had taken the medication "none of the time". Similarly let S_2 be those who said "A little of the time". Then following the above argument Fisher's linear discriminant function for the two groups are:

$$S_1 = -17.054 + 4.669 X_1 + 3.275 X_2 - 1.022 X_3$$

$$S_2 = -7.251 + 2.523 X_1 + 1.787 X_2 + 0.525 X_3$$

These functions can now be used to assign fresh cases of non adherence patients to their respective groups.

Conclusion

Adherence to antiretroviral medications is critically important for the success of therapy in patients who are on ART. The mean adherence rate of a patient in the hospital has been observed to be 84.62%. This study also found that 19% of the respondents are non adherent to antiretroviral drugs which is an indication of a need to closely monitor this problem in the area. The study have identified a number of socio-demographic and economic variables which were associated with adherence to ART in the univariate analysis such as occupation, income, and level of education, depression and service hour. Whereas in the discriminant analysis only depression, NGO support, CD4 count, transportation problem, reception and community disclosure variables predicted satisfactory adherence to treatment.

To improve adherence of the patients the intervention areas has to focus on patient related factors like depression. Psychiatric consultations and appropriate treatment should be more systematically offered to socially vulnerable patients. Interventions to improve ART adherence should address transportation problem, a strong collaboration in terms of information exchange with other NGOs, and a frequent CD4 count disclosure has to be made for the HIV patients.

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