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Predictors of Adherence and Disclosure of HIV Status to Sexual Partners among HIV Positive Adults under HAART in Amhara Region, North-West Ethiopia; Application of Joint Models

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Abstract

Background: The rate of prevalence of HIV among adults has been increasing in Sub-Saharan African countries over the last decade. The objective of this study was to identify the joint predictors of cART adherence and disclosure of HIV status among HIV infected adults at Felege Hiwot teaching and specialized hospital, North-West Ethiopia.

Methodology: A retrospective cohort of longitudinal data was conducted on 792 randomly selected patients in the study area. A joint model was used to identify predictor variables. The two response variables under the current investigation were cART adherence and disclosure of HIV status. Binary logistic regression was conducted for separate models.

Results: Among the predictors, the age of patients (AOR=1.020, 95% CI: (1.016,1.191); p-value=0.005), the number of follow-ups (AOR=1.014, 95% CI: (1.023, 1.030); p-value<0.0001). CD4 cell count (AOR=0.981; 95% CI: (0.765, 0.971), p-value<0.01), marital status (AOR=1.013; 95% CI: (1.002, 1.015), p-value=0.006), female patients (AOR=1.014; 95% CI; (1.001, 1.121), p-value<0.007), rural (AOR=0.982; 95% CI; (0.665, 0.998), p-value=0.004), non-educated adult patients (AOR=0.950, 95% CI; (0.92, 0.98). p-value=0.003), non-existence of social violence (AOR=1.012, 95% CI: (1.008, 1.234), p-value<0.01), an adult with non-opportunistic diseases (AOR=1.021, 95% CI; (1.002, 1.042). p-value=0.001) significantly affected the two response variables jointly.

Conclusion: Several variables that affected both disclosures of HIV status and adherence to cART had been identified in the current investigation. Due attention should be given to younger patients, rural residents, and non-educated patients to disclose the disease status and to have a long life with the virus.

Keywords: HIV • cART adherence • Disclosure • Joint model • Dietary adherence • HIV transmission

Introduction

HIV continues to be a serious global public health problem for 36.7 million people to live with HIV, for 1.8 million new infections and 1 million people to be died from HIV related illnesses [1]. Among these, bout 19.4 million people are testified to live with HIV in Sub-Sahran Africa [2].

The infection of HIV is the leading public health related problem in Ethiopia. Amhara region, one of the eleven regions in the country, accounts the highest number of people living with the HIV. In the region, overall incidence rate of new HIV infection is 6.9 per 1000 tested population [3]. Disclosing own HIV status is

one of the indicators of behavioural changes and crucial to reduce the transmission of the virus from infected to non-infected individuals. Disclosing the HIV status facilitates for cART adherence to be effective. Hence, if HIV infected adult disclosed own HIV status, an individual can adhere properly the time, medication and dietary instruction prescribed by the health staff [4]. Disclosure of the HIV status is one indicator of behavioral changes of the adults and this further leads to be cART adherent.

Self-disclosure of the HIV disease status is generally have important effects on an individual's health, lower stress, and leads to

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better psychological relief [5]. In the case of HIV/AIDS, individuals who disclose their HIV status are in a better health conditions in terms of reproductive choices as well as psychosocial readiness [6].

Disclosure of the HIV status facilitates other behaviors like strict combine antiretroviral therapy (food, time and medicatin) that may improve the management of HIV. Previous studies indicate that individuals who disclosed their disease status have better adherence to cART treatments. Previously conducted studies, indicate that disclosure may increase opportunities to receive social support, which may help individuals cope and recover from physical illness, and decrease depressive symptoms due to HIV-related indications and finally leads to be cART adherent [7]. Disclosure of HIV status to all societies living around them is crucial for avoidance of HIV transmission and helps for good cART adherence [8]. Hence, the two responses namely disclosure of HIV status and combine Antiretroviral Therapy (cART) are highly correlated and one is the compliment of the other. Previous studies indicate that HIV infected individuals who disclosed the HIV status are free from mental depression and stress to take his/her medication on time without fear of other individuals living together [9]. This indicates that disclosure facilitates the conditions for adherence to cART [10]. This why the joint predictors of the two responses was initiated. A number of key issues may raise in the study of adherence to cART and disclosure of HIV status determinants affecting jointly, and the development of interventions. Addressing these issues may provide valued information about which patients are most at risk for non-adherence and about how adherence can be improved. It is well known that patients hidden own disease status may not take treatment medication on time if he/she are with another individual at a time around them and this further leads to be fail to medication [11]. Joint models are used to make analysis for the joint behavior of the two response variables at the same time [12]. Many previous studies had used joint models for repeated outcomes of longitudinal responses and time to event [13]. Such studies did not consider two longitudinal and correlated outcomes observed repeatedly from the same subject and lacked multivariate analysis of two observed results. Joint modeling between two repeated measures has benefits in reducing type I error rates in numerous tests with repeated observation on the same subject and advances efficiency in approximating the unknown parameters [14].

As far as an author's knowledge is concerred, no research has been conducted on the joint predictors of the two correlated longitudinal outcome variables in the study area. Therefore, the current investigation was conducted with objective of detecting the joint predictors of disclosure of HIV status and adherence to cART(dietary, time and medication). The result obtained in current investigation helps for health professional to conducted health related education and to design interventional strategy.

Materials and Methods

Study site and population: The study was conducted at Felege-Hiwot teaching and specialized hospital located in North-western Ethiopia, Amhara region. The hospital is a referral hospital in which many patients referred from district hospitals in the region. The hospital has regional laboratory where all HIV results in different district hospitals in the region are collected, processed and organized to send to Ministry of health. There are about 6 thousand HIV infected adults treated at the hospital whose enrollment was between

Septembers to Jun/2012. Among these, about 2 thousands were under ART.

Study design: A retrospective cohort study design was conducted to assess joint predictors of disclosure of HIV status and cART adherence among HIV infected adults enrolled in the first 10 months of 2012 and followed-up to June 2017. Both separate and joint models were used in data analysis.

Inclusion criteria: Adult patients, whose ages were 15 years and above, enrolled in the first 10 months of 2012 and started cART in the hospital from September 2012 to June 2017 with a minimum of 2 follow-up visits at Felege-Hiwot referral, teaching and specialized hospital, were included under this study.

Sample size and sampling technique: Out of the targeted population, 792 were selected using stratified random sampling technique considering their residence area as strata using 95% level of confidence and 5% marginal error [15].

Data quality and analysis strategy: The quality of the data was controlled by data controllers from ART section of the hospital. Traing about the way how to follow up the quality of data was given to data controllers by the ministry of health. Pilote test on the consistency research questions was conducted on 35 random samples and some modifications on the questionnaires were made on the final data collection sheet

Data collection tools and extraction procedures: Before the required data has been collected, there was a discussion with the health staff at ART section in the hospital about the variables included in this investigation. The required data was extracted from each participants chart using data extraction format. The format was developed by an author in consultation with health staffs. Data analysis was conducted using Statistical System Analysis (SAS) software version 9.2.

Variables under investigation

Response variable: The longitudinal response variables for current study were disclosure of HIV status and adherence to cART. Bothe of the two response variables were binary in nature and measured as follows; if an individual disclosed the HIV status to families, friends and relatives including sexual partner, it is level as disclosed (yes), otherwise not (no). On the other hand if a patients adhered at least 95 % the prescribed cART (time, dietary and medication), it is cART adherent (yes) otherwise, non-adherent (no).

Predictor variables: The independent variables for the two outcomes were age in years, gender (male, female), marital status (living with partner, living without partner), ownership of cell phone (yes, no), weight in kilogram, baseline CD4 cell count in cells/mm³, disclosure of the disease (yes, no), educational status (non-educated, educated), residential area (rural, urban), WHO stages (stage 1, stage 2, stage 3 and stage 4), cART adherence (adheret, non-adherent), level of income (low, middle and high), follow up times/ visits (1,2...23), existence of mental depression/stress (yes, no), social discrimination (yes, no), special support for patients disclosed the disease (yes, no).

Impact of dropouts on the analysis: Patients who defaulted from cART treatment develops drug resistant virus and ultimately leads to bad response from the treatment and finaly resulted to be died. Missing observations were tested using logistic regression to assess the missing values were independent of the past result.

Model selection: In model selection, all predictors were considered in the model and fitted each product term obtained from predictors one at a time which helps to assess interaction effect of covariates on the response variable.

Before conducting joint model, separate models were done for each response using binary logistic regression models for each the two responses [16]. The covariance structure and the magnitude of residual errors were also measured in model selection. In this regard, the model with the smallest within individual residual inconsistency was selected [17].

Models used separate analysis of the two outcomes

In this investigation, analysis of binary data in terms of the binomial distributions with logit transformation was conducted. The result is a binomial response conducted with logistic regression model with logit link function.

First, the binary random variable Y with probabilities $P(Y=1)=\pi$ and $P(Y=0)=1-\pi$ was considered. Then recalled that the random variable, Y has the binomial (n, π) as:

$$P(Y = y) = {n \choose y} \pi^{y} (1 - \pi)^{n - y}, y = 0, 1, 2, ..., n$$
(1)

Where, π_i depends on a vector of observed covariates x_i and let π_i be a linear function of the covariates as $\pi_i=\beta_0+\beta_1X_1+...+\beta_kX_k$.

The probability π_i has to be between zero and one, but the linear predictor can take any real value. The solution for such problem is model the transformation as a linear function of the covariates and one can do this in two steps.

First: The probability π_i to be the odds defined as: odds_i= $\pi_{i/1+}$ π_i

Second: Calculating the logit or log-odds was expressed as:

$$\log it(\pi_i) = \log\left(\frac{\pi_i}{1-\pi_i}\right) = \beta_0 + \beta_1 x_1 + \dots + \beta_k x_k$$
(2)

The above formula has the effect of removing the floor restriction. This is known as logistic regression model that follows a linear model. In this model, the effect of a unit change in X_j is to increase/decrease the log-odds by an amount β_j keeping the other predictors constant.

Formulation of joint modelling

To construct a joint model of two outcome variables, Let y_{1ij} be the first response (Disclosure of HIV status) and y_{2ij} be the second response (adherence to cART).

For bivariate response vector for the same subject i, let

 $y_{1ij}=(y_{1i1},y_{1i2},...,y_{1ini})^T$ and $y_{2ij}=(y_{2i1},y_{2i2},...,y_{2ini})$ to be repeated measures for the two responses

Where $y_{kij} = (y_{1ij}^{T}, y_{2ij}^{T})^{T}$ (k=1,2)

Assume that the general model for the two responses is of the form [18,19]:

$$y_{kij} = \mu_{ki}(\eta_i) + \varepsilon_{ij} = h^{-1}(X_{kij}^T \beta + Z_{kij}^T \alpha_{kij}) + \varepsilon_{kij}$$
(3)

Where μ_i is specified in terms of fixed and random effects and ϵ_{kij} is the error term.

The nature of response, y_{kij} , determines the components of an inverse link function h⁻¹(.). In (3) X_{kij} and Z_{kij} are $(2n_i \times p)$ and $(2n_i \times q)$ dimensional matrices of known covariate values for individual i, and β is a p-dimensional vector of unknown regression coefficients. Furthermore, α_{kij} ~N (0,H) are q-dimensional random effects. For fitting joint models for variables of interests, a general first order of the variance-covariance matrix of y_{ij} is given as [20]:

$$\operatorname{Var}(y_{ij}) = \Delta_{ij} Z_{ij} H Z_{ij}^T \Delta_{ij}^T + v_{ij}$$
(4)
with $\Delta_{ij} = \left(\frac{\partial \mu_i}{\partial \eta_i}\right) \alpha_i = 0$ and $v_{ij} = \emptyset_{ij}^{1/2} A_{ij}^{1/2} R_{ij}(\theta) A_{ij}^{1/2} \Theta_{ij}^{1/2}$

Where, A_{ij} is the diagonal matrix containing the variances generated from the generalized linear model specification $Y_{kij}(k=1,2)$ provided that the random effects $\alpha_{ij}=0$, σ_{ij} is a diagonal matrix with the over dispersion parameters along the diagonal and $R_{ij}(\theta)$ is correlation matrix.

When exponential family specification is used for all components, with canonical link $\Delta_{ij}=A_{ij}$, then Generalized Linear Mixed effect Model (GLMM) has the variance-covariance matrix of the form:

$$\operatorname{Var}(y_{ij}) = \Delta_{ij} Z_{ij} H Z_{ij}^{T} \Delta_{ij}^{T} + \emptyset_{ij}^{1/2} A_{ij}^{1/2} R_{ij}(\theta) A_{ij}^{1/2} \emptyset_{ij}^{1/2}$$
(5)

When there are no residual correlations ($R_{ij}(\theta)=I$), the model is said to be purely random effects or conditional independence and the variance-covariance matrix of Y_{ii} in (5) is reduced to

$$\operatorname{Var}\left(y_{ij}\right) = \Delta_{ij} Z_{ij} H Z_{ij}^{T} \Delta_{ij}^{T} + \emptyset_{ij}^{1/2} \Delta_{ij} \,\emptyset_{ij}^{1/2} \tag{6}$$

If there are no random effects, a marginal model is obtained and the variance-covariance for (6) becomes:

$$\operatorname{Var}(y_{ij}) = \emptyset_{ij}^{1/2} A_{ij}^{1/2} R_{ij}(\theta) A_{ij}^{1/2} \emptyset_{ij}^{1/2}$$
(7)

Hence, we can have two possible alternatives for formulation of joint model namely the conditional argument approach and direct formulation approach. In the conditional argument approach, joint model can be formulated by factor out of the given distribution as marginal and conditional components with introduction of probit approach. In the direct formulation approach, the plancket-dal approach (placket latent variable) can be considered for modeling bivariate responses.

The joint generalized linear mixed model assumes that each outcome and the univariate models are combined through specification of joint multivariate distribution for all random effects.

For the assessment of the relation between two responses (disclosure of HIV status and adherence to cART), the joint GLMM model was fitted. In this model, the association between the two outcomes was quantified through the random effect given that separate random intercept for each outcome variable has been conducted and merging them by imposing joint multivariate distribution on the random intercept.

Results

Among the sample of 792 patients: 40.9% were rural residents; 50.6% were females; 56.3% were living with their partner; 21% of the patients disclosed their disease status to family members, 49.2% were owners of cell phones, 25.5% were cART adherent, only 11.5% had high income and 20.6% had no education. Among the participants, 20.7% declared that there was social discrimination by societies living with them and 53.8% said that there was special social support for those patients disclosed their disease. Some of the participants (47.3%) declared that there was mental depression/stress because of the drug at initial time of the cART. The average (median) weight was 58 kg (IQR: (52, 64)), average years of all patients was 36 years (IQR: (28, 48)). The average

(median) baseline CD4 cell count for all patients was 134 cells/ $\rm mm^3$ (IQR: (113,180). The baseline characteristics of respondents are indicated in Table 1.

In the analysis, among the patients who disclosed the disease (65%) reported that they got better social support from communities around them. Similarly, mental depression of participants was also invented using Beck's depression inventory scale at each visit and 178 (22.5%) were mentally depressed.

The nature of missingness pattern in current investigation was tested using logistic regression model and known to be monotone (dropouts). The pattern indicates that there was no missing observation in the first two visits and the number of dropouts increased linearly as follow-up times/visits increased. The result in this regard revealed that dropouts were not affected by the previous outcomes (χ^2 1=0.3018, p=0.762). Hence, the trend of missingness was Missed Completely at Random (MCAR).

| Variable | | Average | No (%) |
|---|------------------------|-----------------|------------|
| Weight (kg) | | 58.1 (45-70) | - |
| Base line CD4 cells/ mm ³ | | 148.7 (113-180) | - |
| Age (years) | | 74.3 (48-78) | |
| Follow-up times | | 23 visits | |
| First month/initial CD4 cell count change/mm ³ | | 16.6 (12-26) | - |
| Sex | Male | | 392 (49.4) |
| | Female | | 400 (50.6) |
| Educational status | Non-educated | | 163 (20.6) |
| | Educated | | 629 (79.4) |
| Residence area | Urban | | 468 (59.1) |
| | Rural | | 324 (40.9) |
| Marital status | Living with partner | | 446 (56.3) |
| | Living without Partner | | 346 (43.7) |
| Existance of social discrimination | Yes | | 164 (20.7) |
| | No | | 628 (79.3) |
| Special support for patients disclosed disease | Yes | | 426 (53.8) |
| | No | | 366 (46.2) |
| Existance of mental deperession/stress at initial | Yes | | 375 (47.3) |
| time | No | | 417 (52.7) |
| WHO HIV stages | Stage I | | 101 (12.8) |
| | Stage II | | 259 (32.7) |
| | Stage III | | 199 (25.1) |
| | Stage IV | | 233 (29.4) |
| Disclosure of HIV status | Yes | | 166 (21.0) |
| | No | | 426 (79.0) |
| Ownership of cell phone | yes | | 390 (49.2) |
| | | | |

| | No | 402 (50.8) |
|-------------------|--------------|------------|
| Adherence to cART | Adherent | 202 (25.5) |
| | Non-adherent | 590 (74.5) |

Table 1. Baseline socio-demographic, economic and clinical variables (n=792).

Missing data were handled using multiple computation separately before construction of joint models as shown in Table 2. technique. Parameter estimates for the two responses was inducted

| Parameter | Disclosure of HIV stat | us | | Adherence to cART | Adherence to cART | | |
|------------------------------|--------------------------|-----------|---------|-------------------|-------------------|----------|--|
| | Estimates | St. error | p-value | Estimates | St. error | p-value | |
| Intercept | 3.014 | 0.703 | <0.01* | 0.922 | 0.245 | <0.01* | |
| Age | 0.022 | 0.611 | 0.003* | 0.122 | 0.013 | <0.01* | |
| Weight | -0.023 | 0.814 | 0.001* | 0.031 | 0.016 | <0.01* | |
| Baseline CD4 cell count | 0.011 | 1.413 | <0.001 | 0.022 | 0.014 | <0.01 | |
| Number of follow-ups 0.0 |)32 | 0.943 | <0.001* | 0.033 | 1.038 | <0.01* | |
| Marital status (Ref.=Withou | ut partner) | | | | | | |
| With partners | 0.023 | 1.603 | 0.005* | -0.012 | 0.051 | 0.021* | |
| Sex (Ref.=Male | | | | | | | |
| Female | 0.015 | 0.713 | <0.001 | 0.014 | 1.104 | < 0.001* | |
| Existance of social discrim | ination (Ref.=Yes) | | | | | | |
| No | 0.046 | 1.435 | <0.001 | -0.132 | 1.023 | 0.002* | |
| Special support for patients | s disclosed disease (Ref | .=Yes) | | | | | |
| No | -0.031 | 0.763 | 0.002 | -0.031 | 0.231 | 0.031* | |
| Existance of mental depere | ession/stress (Ref.=Yes) | | | | | | |
| No | 0.021 | 0.923 | 0.013 | 0.021 | 0.231 | 0.003* | |
| Residence area (Ref.=Urba | an | | | | | | |
| Rural | -0.016 | 0.921 | 0.046 | -0.135 | 1.432 | 0.148 | |
| Level of education (Ref.=E | ducated) | | | | | | |
| Non-educated | -0.024 | 0.814 | <0.021* | -0.125 | 0.156 | 0.512* | |
| Ownership of cell phone (F | Ref.=No) | | | | | | |
| Yes | -0.035 | 1.906 | <0.018* | 0.725 | 1.091 | <0.014* | |
| WHO stages (Ref.=Stage I | V) | | | | | | |
| Stage I | -0.138 | 0.818 | <0.016* | -0.194 | 1.013 | 0.072 | |
| Stage II | -0.142 | 1.916 | <0.073 | 0.246 | 0.092 | 0.026 | |
| Stage III | -0.19 | 1.715 | <0.059 | 0.158 | 0.096 | 0.094 | |

*significant at 5% level of confidence

Table 2. Parameter estimates for marginal models for disclosure of HIV status and adherence to cART.

The results in Table 2 show the separate or marginal models for the two variables of interests, considering binary logistic regression for both responses. From the main effects, age, weight, baseline CD4 cell count, the number of follow-up visits, sex, marstat, existence of social discrimination, social support, existence of stress and cell phone ownership considerably influenced both outcomes.

To assess the joint determinants of the two responses, a joint multivariate distribution becomes more relevant. Developing models for the two response variables with uncorrelated random intercepts gives results for an initial parameter estimate. The results obtained by applying this procedure are

indicated in Table 3. The analysis was conducted using loglikelihood functions with the Laplace approximation. The conditional independence of random-effects models conducted in this analysis showed that the GLMMs approach could be extensive separate random-effect for each response. The SAS procedure that uses generalized mixed effect models allow the joint distribution to be constructed for the random effects from the two separate models. The conditional independence of random effects model considered the following components:

 $y_{1ij} \, \text{stands}$ for j^{th} observation on disclosure of HIV status for the i^{th} patient.

 $y_{2ij}\ \text{stands}$ for $j^{th}\ \text{observation}$ on adherence to cART for the $i^{th}\ \text{patient.}$

logit $(\mu_{1i})=X^{T}_{1ii}\beta+\alpha_{1i}$.

logit
$$(\mu_{2i})=X^{T}_{2ii}\beta+\alpha_{2i}$$

 $\alpha_{ii} = (\alpha_{1ii}, \alpha_{2ii})^T \sim \text{MVN} (0, \text{H}) \text{ where } \text{H} = ((\sigma_1^2 \rho \sigma_1 \sigma_2 \rho \sigma_1 \sigma_2 \sigma_2^2))$

This shows the way how to construct multivariate longitudinal data by supposing separate random effects from a generalized mixed approach for each outcome variable. The formulation of a joint model by striking a joint multivariate distribution helps in developing a joint multivariate distribution in the random effects of the two separate models. Parameter estimates for the conditional independence of random intercept model for disclosure of HIV status data and adherence to cART is indicated in Table 2.

As shown in Table 2, age of patients, weight, CD4 cell count at baseline, the number of follow-ups, cell phone ownership, existence of social support, social discrimination, existence of stress and sex significantly affected both response variables. The fact that these are identical signs for the two predictors indicates that they are positively correlated to each other. Hence, a patient who disclosed the HIV status can be adherent to cART and an adherent to cART patient encourages to be disclosed the HIV status.

| Parameter | Disclosure of HIV status | | | | Adherence to cART | | |
|-----------------------------------|--------------------------|-----------|--------------------|-----------|-------------------|--------------------|--|
| | Estimates | St. error | p-value | Estimates | St. error | p-value | |
| Intercept | 3.014 | 0.003 | <0.01* | 0.922 | 0.245 | <0.001* | |
| Age | 0.025 | 0.011 | 0.003* | 0.122 | 0.013 | <0.001* | |
| Weight | -0.021 | 0.014 | 0.001* | 0.031 | 0.016 | 0.001* | |
| Baseline CD4 cell count | 0.014 | 0.013 | <0.001* | 0.022 | 0.014 | <0.001* | |
| Number of follow-ups 0 | .032 | 0.043 | <0.001* | 0.033 | 0.038 | 0.012* | |
| Marital status (Ref.=Witho | out partner) | | | | | | |
| With partners | 0.023 | 0.035 | 0.005* | -0.012 | 0.051 | 0.021* | |
| Sex (Ref.=Male | | | | | | | |
| Female | 0.01 | 0.016 | <0.001 | 0.014 | 0.104 | <0.001 | |
| Existance of social discrir | nination (Ref.=Yes) | | | | | | |
| No | 0.046 | 0.435 | <0.001 | -0.132 | 0.023 | 0.002* | |
| Special support for patien | ts disclosed disease (| Ref.=Yes) | | | | | |
| No | -0.031 | 0.763 | 0.002 | -0.031 | 0.231 | 0.031* | |
| Existance of mental depe | ression/stress (Ref.=Y | es) | | | | | |
| No | 0.021 | 0.923 | 0.013 | 0.021 | 0.231 | 0.003 [*] | |
| Residence area (Ref.=Urt | an | | | | | | |
| Rural | -0.015 | 0.016 | 0.045 [*] | 0.134 | 0.013 | 0.014 | |
| Level of education (Ref.=I | Educated) | | | | | | |
| Non-educated | -0.026 | 0.015 | <0.012* | -0.125 | 0.154 | 0.012* | |
| Ownership of cell phone (Ref.=No) | | | | | | | |
| Yes | -0.034 | 0.204 | <0.013* | 0.725 | 0.091 | <0.013* | |
| WHO stages (Ref.=Stage | IV) | | | | | | |
| Stage I | 0.137 | 0.015 | <0.014* | -0.192 | 0.013 | 0.072 | |
| Stage II | 0.146 | 0.016 | <0.041 | 0.246 | 0.094 | 0.025 | |

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|--|-------|-------|---------|-------|-------|-------------------------------|--|--|
| Stage III | 0.104 | 0.014 | <0.015* | 0.156 | 0.092 | 0.092 | | |
| *significant at 95% CI for both outcomes | | | | | | | | |

Table 3. Parameter estimates for conditional independence of random intercepts model with disclosure of HIV status data and adherence to cRRT data.

However, the results in Table 3 revealed that, the conditional independence assumption was not flexible (it is restrictive) and considering the conditional dependence assumption provides a relaxed assumption and it gives an alternative approaches by re-considering the joint random intercepts model with potentially associated errors.

Introducing the restricted dependence of one outcome in terms of the other using a linear predictor provides and formulates joint predictors of two longitudinal response variables with the possible error values created. This approach is also helpful to evaluate the observed correlation between the two responses increasing from the association of the random intercepts. Hence, a generalized linear mixed model was fitted for disclosure of HIV status as a variable of interest including adherence to cART in the linear predictor. Table 4 indicates that disclosure of HIV status is positively correlated with adherence to cART (p-value <0.001). That is, if the status of HIV was disclosed, an individual disclosed the disease can strictely adheres the prescribed medication by the health staff respected the due date, time and dietary instruction without fear of any one. On the other hand, if patients adhere to cART medication properly, then they would have a motivation to disclose the disease status to families, friends, relatives or sex partners [18,19]. Finally, the parameter estimates of disclosure of HIV status considering adherence to cART as a linear predictor is indicated in Table 4.

Table 4 indicates that, predictors like age of patients, baseline CD4 cell count, the number of followed-up visits, marital status, and sex, residence area, and cell phone ownership, existence of social support, social discrimination, mental stress, and level of adherence to HAART had significant effect on the variable of interest.

As, age of patients increased by one year, the expected number of the oddis of being disclosed the status status was increased by 2%assuming that the other things remain constant (AOR=1.020, 95% CI: (1.016, 1.191); p-value=0.005). similarly, as the number of follow-up visits increased by one unit, the expected value of the odds of being disclosed the disease was increased by 1.4% provided that patients adhere properly to the prescribed medication by health staff (AOR=1.014, 95% CI: (1.023, 1.030); p-value <0.0001). As baseline CD4 cell count increased by cell/mm³, the expected value of odds of being exposed the HIV status was decreased by 1.9% given the other covariates constant (AOR=0.981; 95% CI: (0.765, 0.971), p-value<0.01).

Marital status had significant effect for the variable of interest. Hence, comparing patients living with their partner and without partners, patients living with their partners have high possibility of disclosing the disease to families, friends and relatives including sexual partners. The expected possibility of odds of being disclosed the HIV status by patients living with partners was increased by 1,3%as compared to patients living without partners (AOR=1.013; 95% CI: (1.002, 1.015), p-value=0.006).

Comparing female HIV infected patients with males, the expected number of being disclosed the HIV status by female was increased by 1.4 than males given the other covariates constant (AOR=1.014; 95% CI; (1.001, 1.121), p-value <0.007). However, the expected number of odds of being disclosed the HIV status by rural patients was decreased by 1.8% as compared to urban patients, given the other covariates constant (AOR=0.982; 95% CI; (0.665, 0.998), p-value=0.004).

The expected odds of being disclosed the HIV status by noneducated adult patients was decreased by 5% as compared to educated adults, keeping the other things constant (AOR=0.950, 95%Cl; (0.92. 0.98). p-value=0.003).

Similarly, The expected odds of being disclosed the HIV status by cART non-adherent adult patients was decreased by 6% as compared to cART adherent adults, keeping the other things constant (AOR=0.940, 95% CI; (0.61. 0.97). p-value<0.001).

Existence of social violence had statistical significant effect for HIV positive adults not disclosed the status HIV disease for sexual partners. Hence, the expected odds of being disclosed the HIV status for sexual partners by HIV infected individuals, where there is no social violence, was increased by 1.2% as compared to those HIV infected adults living with the societies, where there is social violence, keeping the other things constant (AOR=1.012, 95% CI: (1.008, 1.234), p-value <0.01).

The expected odds of being disclosed the HIV status by nonopportunistic diseases adult patients was increased by 2.1 % as compared to opportunistic infectious disease adults, keeping the other things constant (AOR=1.021, 95% CI; (1.002. 1.042). p-value=0.001).

WHO stages had also statistically significant effect for the disclosure of the level of the HIV status for sexual partners. Hence, the expected odds of being disclosed the HIV status by adult patients whose WHO stage 1 was decreased by 11.3% as compared to WHO stage 4 keeping the other variables constant. Similarly, the expected odds of being disclosed the HIV status by adult patients whose WHO stage 2 was decreased by 12.2% as compared to WHO stage 4 keeping the other variables constant and the expected odds of being disclosed the HIV status by adult patients whose WHO stage 3 was decreased by 9.5% as compared to WHO stage 4 keeping the other variables constant.

| Parameter | Estimates | St. error | Adjusted Odds Ratio (AOR) | Wald 95% | CI | p-value |
|-----------|-----------|-----------|------------------------------|----------|-------|---------|
| Intercept | 3.011 | 0.037 | 20.29 | 51.53 | 58.62 | <0.001* |

| Age | 0.022 | | 0.267 | 1.02 | 1.016 | | 1.19 | 0.005* | | | |
|--|---------------------------------------|--------------------|-------|-------|-------|-------|-------|---------|---------|--|--|
| Weight | -0.026 | | 0.865 | 1.024 | 0.015 | | 1.01 | 0.082 | | | |
| Baseline CD4 cell count | -0.023 | | 0.764 | 0.981 | 0.765 | | 0.97 | <0.001* | | | |
| Follow-up times | 0.014 | | 0.517 | 1.014 | 1.023 | | 1.03 | <0.001* | | | |
| Marital status (R | Aarital status (Ref.=Without partner) | | | | | | | | | | |
| With partners | 0.011 | 0.715 | | 1.013 | 1.002 | | 1.015 | 0.006 | | | |
| Sex (Ref.=Male | 9) | | | | | | | | | | |
| Female | 0.014 | 0.453 | | 1.014 | 0.015 | | 1.02 | 0.007 | | | |
| Existence of soc | al discrimination (Re | .=Yes) | | | | | | | | | |
| No | 0.046 | 0.435 | | 1.041 | 1.001 | | 1.121 | <0.001* | | | |
| Special support f | or patients disclosed | disease (Ref.=Yes) | | | | | | | | | |
| No | -0.034 | 0.546 | | 0.97 | 0.765 | | 0.998 | <0.001* | | | |
| Existence o mental depression/ stress (Ref.=Yes | | | | | | | | | | | |
| No | 0.011 | 0.462 | | 1.01 | 1.001 | | 1.131 | 0.001* | | | |
| Opportunistic infectious disease (Ref. Yes) | | | | | | | | | | | |
| No | 0.021 | 0.082 | | 1.021 | 1.002 | | 1.042 | 0.001* | | | |
| Residence area (Ref.=Urban | | | | | | | | | | | |
| Rural | -0.021 | 0.011 | | 0.982 | 0.965 | | 0.998 | 0.004* | | | |
| Level of education | on (Ref.=Tertiary educ | ation) | | | | | | | | | |
| Non-educated | -0.052 | 0.012 | | 0.951 | 0.924 | | 0.987 | 0.003* | | | |
| Level of income | (Ref.=High income) | | | | | | | | | | |
| Middle income | -0.01 | 0.013 | | 0.991 | 0.015 | | 1.012 | 0.006 | | | |
| Low income | -0.014 | 0.006 | | 0.992 | 0.986 | | 1.102 | 0.103 | | | |
| Ownership of cell phone (Ref.=Yes) | | | | | | | | | | | |
| No | -0.024 | 0.307 | | 0.982 | 0.525 | | 0.997 | <0.001* | | | |
| Adherence to cART (Ref.=Ad hent) | | | | | | | | | | | |
| Non-adherent | -0.063 | 0.514 | | 0.944 | 0.614 | 0.973 | | | <0.001* | | |
| WHO stages (Ref.=Stage IV) | | | | | | | | | | | |
| Stage I | 0.124 | 0.013 | | 1.136 | 1.123 | 1.142 | | | 0.062 | | |
| Stage II | 0.123 | 0.012 | | 1.132 | 1.124 | 1.052 | | | 0.061 | | |
| Stage III | 0.102 | 0.043 | | 1.118 | 0.092 | 1.103 | | | 0.093 | | |
| *significant at 95 | % CI for both outcom | es, eβ=AOR | | | | | | | | | |

Table 4. Parameter estimates for disclosure of HIV status data using a linear predictor.

Discussion

The current study tried to identify factors affecting jointly for disclosure of HIV status and adherence to cART for HIV positive adults under cART. The extent of disclosure of the HIV status indicates that 79% of them did not disclose the HIV status for people around them. Similarly, the level of adherence to cART indicates that only 25.5% the patients are adherent to cART. Potential joint predictors of disclosure of the HIV status and cART adherent have been identified as discussed below. Age significantly affects the level of disclosure of the HIV positive status for people living with HIV. As age increase, the disclosure levels of the disease status also increase. It is known that, sexual intercourse decrease as age of individual increase and this may encourage disclosing the disease to people living around them. Hence, being older, the HIV infected individuals are more likely to have a steady sexual partner, and this contributes to increase the rate of disclosure. Older HIV positive patients with high probability of disclosing the disease encouraged the patient to be more adherent without any

fearness of others living together. Another previously conducted research indicates that younger age group may not go for HIV testing and such people may not disclose their status unknowingly.

HIV positive people with high number of CD4 cell count fells comfort ability and healthiness as compared to those with low number of CD4 cell count and such people consider themselves as HIV negative and they need not to accept the diagnosis result given by the health staff. Hence, they are not volunteer to disclose their HIV status. The non-disclosure status of HIV positive adults with high number of CD4 cell count leads for its less probable of being adherent to cART. The result in this regard is consistent with another previously conducted investigation.

As visiting time of the heath institution increase, HIV positive adults are encouraged to disclose the disease status because of their awareness and health related education they got on every visiting time at health institutions. This result is similar with another previous research. When HIV positive adults visit the health institution as prescribed by the health staff, such people might be exposed by other individuals during visiting and communication with such people encourages disclosing the disease. Visiting times have also positive effect for patients being adherent for cART because of education and counseling given to patients at each vising time.

Marital Status also significantly affects the degree of disclosure of HIV status. HIV positive adults living with partner increase their willingness to disclose the status of their disease as compared to adults living without partner. The potential reason for this might be the fact that adults living with their partners feel more concern about the health care of partners. Disclosure of the disease for adults living with partners might help to each other as reminder to cART adherent and also important to remind the date when the partner should visit the heath institution. The result in this regard is similar with previously conducted research and contradicted with another research. Hence, this result needs further investigation. Disclosure of HIV status empowers couples to make knowledgeable reproductive health varieties that may ultimately lower the number of unplanned pregnancies among HIV positive couples, and even reduce the risk of HIV transmission from mother to child.

Female HIV positive adults are more likely to disclose the disease status to their partners as compared to males. The possible reason for this might be the fact that males need multiple partners as compared to females. Such needs discourage males to disclose the disease status and they need to hide the disease. Another reason may be the fact that females are willing to disclose their HIV status due to their responsibility of their concern for their partners' health or to avoid their guilt. The experience gained from pills taking for family planning contributed for females being cART adherent. This result is supported by previous research and contradicted with another investigation. The reason on the contradicted result is that females hide their disease because of their fairness of being stigma and discrimination. This result also needs further investigation.

Urban HIV positive adults are more likely to disclose the disease status as compared to rural HIV positive adults. Urban patients might have better understanding on disclosing the disease to get social support from the government and communities around them. The culture at rural area is stricter as compared to urban and the HIV positive adults disclosed the disease status might be discriminated by the society because of the reason that societies at rural area lack information how and when the disease is transmitted from one individual to another.

Social violence has significant effect for the HIV people not disclosed the disease status to their sexual partners. The potential reason for this might be that, HIV infected adult fear the trend that those individuals disclosed the disease violated by people living together. Social-violence also contributed negative effect for HIV patients to be non-adherent (Patients may not take pills whenever individual are there).

Education plays significant role for the variation of disclosure level of HIV status. Educated people are more likely to disclose the disease to people around them. The potential reason for this might be the fact that such people have more information about use of disclosing the disease to the society especially to their sexual partner. Knowledge on how to prevent HIV transmission is important to disclose the HIV status and this encourages to disclose the disease and this disclosure leads the patients to be adherent for CART.

Conclusion

Majority of the participants (79%) under investigation did not disclose the HIV status which is a creditable strategy that will target those not likely to disclose will have to be evolved. Considering adherence to cART, only 25.5% were adherent to cART. Hence, the two low performance outcomes require great effort to identify, joint predictors of the two responses.

Common joint predictors were indified in current investigation and the association between the two responses indicates that the two responses are highly correlated to each other. Patients who decided to disclose the disease are committed to be adherent to cART without fear of any one living with them.

Due attention should be given for patients not disclosed the disease status and for non-adherent to cART HIV positive adults. Hence, health related education for HIV positive adults is crucial to disclose the HIV status and to be adherent to cART to have long live with the virus.

Knowledge on HIV transmission is also important to reduce the violence and discrimination of those HIV positive adults not disclosed their disease status. Special support for those HIV infected individuals disclosed the disease may encourage the others to disclose their disease status without fear and anxiety. This further helps to be adherent to CART

This research was not without limitation, the data were taken on one treatment site, including the other treatment sites may provide additional information about the prevalence and predictors associated with why HIV infected individuals not disclose their HIV status to sexual partners, friends, and relatives and generally to the society.

Competing interests

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