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Statistical Analysis of Factors Associated With Mortality among HIV Infected Adult Patients under Antiretroviral Therapy (ART) In Hossana District Queen Elleni Mohamad Memorial Hospital, SNNPR, Ethiopia

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Abstract : Even though the use of ART has brought a significant reduction in the mortality and morbidity of patients living with HIV/AIDS, a number of patients still die after the start of ART. The main objective of this study was to identify and describe factors associated with mortality among HIV infected patients who are taking ART in Hossana District Queen Elleni Mohamad Memorial Hospital. The data for the study was obtained from Hossana District Queen Elleni Mohamad Memorial Hospital ART clinic. The HIV infected patients ≥ 15 years of age and who are under ART from March 2009 up to May 2015 were included in the study. So as to meet our objective standard logistic regression and multilevel logistic regression models were used. A total of 400 adult HIV infected patients who are taking ART were included in the study. Out of these patients, 18.75% of them were dead. The results obtained from standard logistic regression analysis showed that age, level of education, alcohol, baseline weight, woreda, TB status and baseline CD4 count were found to be significant factors of mortality of HIV infected patients taking ART in Hossana District Queen Elleni Mohamad Memorial Hospital. The multilevel logistic regression analysis showed that the variance of the random component related to the intercept term was found to be statistically significant implying variation in mortality of HIV infected patients among the woredas where they live. It was also found that age, level of education, alcohol, baseline weight, TB status and baseline CD4 count were significant determinants of variations of mortality of HIV infected patients among woredas. However, the factors that had significant effect on mortality of the patients did not show underlying variations across woredas. Health workers should be cautious when a patient has lower baseline CD4 and lower baseline weight. Health workers also need to support those patients with no or little education by continuous awareness creation of taking care of themselves and knowing what factors facilitate death. And also patients who drink alcohol need to be given advice to reduce excessive drinking.

Key Words: Mortality of HIV infected patients, Multilevel Logistic Regression model, Random Intercept Logistic Regression Model.

INTRODUCTION

AIDS-related illnesses remain one of the leading causes of death globally and are projected to continue as a significant global cause of premature mortality in the coming decades [1].There are 34.2 million people living with HIV, 2.5 million new HIV infections and 1.7 million deaths due to AIDS in 2011 worldwide. Out of the total number of people living with HIV/AIDS in 2011, 30.7 million are adults, 16.7 million are women and about 3.4 million are children below the age of 15. From the total of 1.7 million deaths in 2011, about 230,000 are children below 15 years of age while the rest are adults [2].

Sub-Saharan Africa has the most serious HIV and AIDS epidemic in the world. In 2010, about 68% of all people living with HIV resided in sub-Saharan Africa, a region with only 12% of the global population. Sub-Saharan Africa also accounted for 70% of new HIV infections in 2010, although there was a notable decline in the regional rate of new infections. The epidemic continues to be most severe in southern Africa, with South Africa having more people living with HIV (an estimated 5.6 million) than any other country in the world. Almost half of the deaths from AIDS-related illnesses in 2010 occurred in southern Africa. AIDS has claimed at least one million lives annually in sub-Saharan Africa since 1998. Since then, however, AIDS-related deaths have steadily decreased, as free antiretroviral therapy has become more widely available in the region. The total number of new HIV infections in sub-Saharan Africa has dropped by more than 26%, down to 1.9 million from the estimated 2.6 million at the height of the epidemic in 1997 [3]. Regional HIV and AIDS statistics shows that there are 23.5 million (22.2 million-24.7 million) adults and children living with HIV, 1.7 million adults and children newly infected with HIV, 1.2 million adult and child death due to AIDS and 4.8% adult prevalence of HIV in sub Saharan Africa in 2011 [4].

In 2011, over half (56%) of HIV patients of sub-Saharan Africans in need of ART were receiving it [4], in 2012 this increased to 68 % [5]. It is widely acknowledged that increasing access to ART will dramatically decrease the impact of HIV in this region [6].

In Ethiopia since the first two AIDS case reported in 1986, the prevalence rate has continuously increased until the year 2000 when it begun to show some decline [7]. Adult HIV prevalence in 2009 was estimated to be between 1.4% and 2.8% in the country. Prevalence was 1.8% for males and 2.8% for females, and women accounted for 59% of the HIV-positive population. There were an estimated 131,145 new HIV infections and 44,751 AIDS-related deaths of which females accounted for 57% of the total infections and deaths. The total estimated number of HIV-positive pregnant women and annual HIV positive births in the same year were 84,189 and 14,140, respectively. There were an estimated 72,945 children less than 15 years old living with HIV, out of which 20,522 needed ART. Due to the combined effect of poverty and AIDS, more than 5.4 million children under the age of 18 years were orphaned out of which 855,720 lost at least one parent due to AIDS [8].

The Antiretroviral (ARV) drugs improve the quality of HIV infected persons by helping them to stay well much longer than they otherwise would. The drugs slow down the replication of HIV within the body. Although the treatments are not a cure and continue to present new challenges with respect to side-effects and drug resistance ART as disease modifying therapy for established HIV infection has produced dramatic effects on morbidity and mortality among HIV AIDS patients. As a result of the widespread use of ART, the HIV AIDS pandemic which was once regarded as an infectious disease with an almost universal fatal outcome has been transformed into a manageable chronic infectious disease [9-10].

A fundamental component of working towards the goal of providing, by 2010, universal access to antiretroviral treatment for patients with acquired immunodeficiency syndrome (AIDS) is an increased and secured production of antiretroviral drugs (ARTs) in order to meet the increased demand from lower- and middle-income countries. The vast majority of adults (96%) were reported to be receiving first-line regimens. Reporting compliance was very high for this group, with information on the specific regimens used available for 97% of this set of patients. The programs reported that 95% of all adults receiving first line regimens were using regimens consistent with the preferred first-line approach including: Stavudine (d4T) lamivudine (3TC) Nevirapine (NVP) (61%), Zidovudine (ZDV) +3TC+NVP (16%), ZDV+3TC+ efavirenz (EFV) (9%), and d4T+3TC+EFV (8%). Less than 1% of these groups were reported to be taking either alternative first-line regimens, including the triple nucleoside combinations of ZDV+3TC+abacavir (ABC) and d4T+3TC+ABC, or taking regimens not considered or not recommended by WHO [11].

Objective of the study

General objective

The general objective of this study is to identify and describe factors associated with mortality among HIV infected patients who are taking ART in Hossana District Queen Elleni Mohamad Memorial Hospital.

Specific objectives

The specific objectives of the study were:

- ✓ To identify the effect of demographic, socio-economic, behavioral and clinical factors on mortality of HIV infected patients taking ART.
- ✓ To identify the factors that may explain the variation in mortality among HIV infected patients taking ART.
- ✓ To provide information for concerned bodies on the factors that facilitate mortality of HIV infected patients taking ART.

DATA AND METHODOLOGY

Sample size and Sampling technique /Sampling procedures

The sample size for this study was 400 based on the interest of the researcher. The sample was selected by using stratified random sampling technique by grouping patients by woreda where they live. The sample size in each woreda was determined in proportion to the size of the woreda (the number of patients in the woreda), termed as proportional allocation (Hossana town administration 71, Lemmo 51, Anlemmo 45, Misha 53, Angecha 37, Duna 33, Lera 45, Gombora 36, Soro 29). Finally, using ART unique identification number of eligible patients, a simple random sample of patients was taken from each woreda.

Eligibility Criteria

Inclusion criteria:

- ✓ HIV infected patients aged 15 years or older and have started ART
- ✓ HIV infected patients with complete intake form, registers and follow up form

Exclusion criteria:

- ✓ Diagnosis made outside of the hospital
- ✓ Loss to follow up (withdraw, transfer out)

Data collection procedures (Instrument, personnel, data quality control)

The data were extracted from the available standard national medical registers which have been adopted by Federal Ministry of Health (FMOH) to be uniformly used by clinicians to simply identify and document clinical and laboratory variables. The registers include pre-ART register and follow up form, ART intake form, patients' card and death certificate complemented by registration by home visitors. Two days training was given for supervisors and data collectors. The overall activity was controlled by the researcher. Data quality was controlled by designing the proper data collection materials and through continuous supervision. The completed data collection forms were examined for completeness and consistency during data management, storage and analysis. The data were collected by data clerks working in the clinic and coded and analyzed using the statistical packages STATA and SAS.

Variables of the study

The variables of interest that were considered in the analysis are the response (dependent) variable and the explanatory (independent) variables.

Response (Dependent) variable

Response variable is the HIV infected patient mortality. It is dichotomous variable coded as 1 if a patient is dead and 0 if a patient is alive.

Explanatory (Independent) variables

Several explanatory variables were used as predictors of mortality of HIV infected patients taking ART. These variables are classified as Demographic factors (Age, Sex, Marital status), Socio-economic factors (Residence, Level of educational and Woreda), Behavioral factors (Tobacco and Alcohol) and Clinical factors (WHO clinical stage, Baseline CD4 counts, Baseline weight, Antiretroviral regimen, and TB status).

Methods of Data Analysis

In this study standard logistic regression analysis was used to investigate the effect of each predicator variable on the mortality of HIV infected patients and multilevel logistic regression analysis was also used to investigate existence of variation in mortality of HIV infected patients among the woredas where they live and identify the factors that explain the variation in mortality of HIV infected patients among woredas.

Logistic Regression Model

Logistic regression is part of a family of models called the Generalized Linear Model used when the response variable is qualitative in nature or categorical and independent variables may be either continuous or categorical. Unlike discriminant analysis, the logistic regression does not have the requirements of the independent variables to be normally distributed, linearly related, nor equal variance within each group [12]. The logistic regression model is supported by variety of link functions, which include the logit, clog-log, log and probit. For logistic regression, least squares estimation is not capable of producing minimum variance unbiased estimators for the actual parameters instead maximum likelihood estimation is used to solve for the parameters that best fit the data. Binary logistic regression is the form of regression which is used when the dependent variable is dichotomous and the independent variables are of any type [13].

Let Y_{nx1} be a dichotomous outcome random vector with categories 1 (HIV infected patient taking ART is dead) and 0 (HIV infected patient taking ART is alive). Let X be an n x (k+1) matrix denote the collection of k-predictor variables of Y, i.e.

$$X=\begin{pmatrix}1 & x_{11} & \cdots & x_{1k}\\ 1 & x_{21} & \cdots & x_{2k}\\ \vdots & \vdots & \ddots & \vdots\\ 1 & x_{n1} & \cdots & x_{nk}\end{pmatrix},\quad \beta=\begin{pmatrix}\beta_0\\ \beta_1\\ \vdots\\ \beta_k\end{pmatrix},\quad Y=\begin{pmatrix}y_1\\ y_2\\ \vdots\\ y_n\end{pmatrix}$$

Where, X -is the design matrix

β - is the vector of unknown coefficients of the covariates and intercept

Let π denote the proportion of success (Death of HIV infected patient taking ART).

Then, the conditional probability that the i^{th} patient mortality given patient characteristics X_i is given by:

$$\pi_i = p(y_i = 1/x_i) \ldots\ldots\ldots\ldots\ldots(1)$$

In logistic regression analysis, it is assumed that the explanatory variables affect the response through a suitable transformation of the probability of the success. This transformation is a suitable link function of π_i, and is called the logit-link, which is defined as:

$$\log it(\pi_i) = \log(\frac{\pi_i}{1-\pi_i}) \ldots\ldots\ldots\ldots(2)$$

The transformed variable $\log it(\pi_i)$ is related to the explanatory variables as:

$$\text{logit}(\pi_i) = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \ldots + \beta_k x_{ki} = X_i^{'}\beta \;.(3)$$

Where,

$\beta = (\beta_0 + \beta_1 + \beta_2 \ldots + \beta_k)'$ are parameters

$X_i = (1, X_{1i}, X_{2i}, \ldots, X_{ki})'$ i = 1, 2, 3,... n

The probability of success is expressed as follows:

$$\pi_i = p(Y_i = 1/x_{1i}, x_{2i}, \ldots, x_{ki}) = \frac{e^{X'_i}\beta}{1+e^{X'_i}\beta} \ldots.(4)$$

Then, odds of success is given as follows

$$odds\ (Y_i = 1) = \frac{\pi_i}{1-\pi_i} = e^{X'_i\beta} \ldots.(5)$$

Estimation of Logistic Regression Model

The most commonly used method of estimating logistic regression parameters is method of Maximum Likelihood. The method of maximum likelihood yields values for the unknown parameters which maximize the probability of obtaining the observed set of data. In order to apply this method we first construct a function, called the likelihood function. This function expresses the probability of the observed data as a function of the unknown parameters. The maximum likelihood estimators of these parameters are chosen to be those values that maximize this function. Thus, the resulting estimators are those which agree most closely with the observed data. We describe how to find these values from the logistic regression model. Since each y_i represents a bernoulli count in the i^{th} population, the probability distribution function of Y_i is given by:

$$f(y_i) = \pi^{y_i}(1-\pi)^{1-y_i} \ldots\ldots\ldots\ldots(6)$$

$Y_i = 0$ or 1 and i =1, 2, 3, …, n

Then the likelihood function is the joint probability distribution of all *n* observations:

$$l(\beta) = \prod_{i=1}^{n} \pi^{y_i}(1-\pi)^{1-y_i} \ldots\ldots\ldots\ldots..(7)$$

The principle of maximum likelihood states that we use as our estimate of parameter the value which maximizes the expression in equation (7).However, it is easier mathematically to work with the log of equation (7). This expression, the log likelihood, is defined as:

$$L(\beta) = \ln[l(\beta)] = \sum_{i=1}^{n}\{y_i \ln(\pi) + (1-y_i)\ln(1-\pi)\} \;..(8)$$

The maximum likelihood estimates are the values for β that maximize the likelihood function in equation (8). Through maximization of the log-likelihood function we can theoretically estimate the parameter vector β. But the equation is nonlinear in β, and as a result the estimates do not have a closed form expression. Therefore, β can be obtained by maximizing using iterative algorithm method[14].

Multilevel Logistic Regression Model

Multilevel models have become popular for the analysis of a variety of problems. Multilevel models are specifically geared toward the analysis of data that have a hierarchical or cluster structure. Such data arise routinely in various fields, for instance in educational research with pupils nested within schools, family studies with children nested within families.

Multilevel analysis is a statistical approach for the analysis of data with complex patterns of variability, with a focus on nested sources of variability. The best way to the analysis of multilevel data is an approach that represents within the group as well as between group relations within a single analysis. It can take into account the variability associated with each level of the hierarchy [15]. It can also estimate both between group and within group variations, and help to figure out how those levels interact with each other. For this study variation in mortality of HIV infected patients taking ART within woredas means that not only unexplained variation between HIV infected patients taking ART but also unexplained variation between woredas. Such variation can be analyzed through statistical models known as random coefficients models.

Multilevel logistic regression model can be used to predict a dichotomous dependent variable from a set of independent variables. It can be employed in the simplest case without explanatory variables (usually called the Empty model) and also with explanatory variables by allowing only the intercept term(called Random intercept model) or both the intercept and slopes (called Random coefficient model) to vary randomly, and the coefficients are assumed to follow a multivariate normal. In this study for the sake of simplicity of discussion on multilevel logistic regression model, two-level models were used in such a way that HIV infected patient is level-one and woreda where the patients live is level-two.

The Random Intercept Logistic Regression Model

The random intercept logistic regression model expresses the logit of p_{ij}, as a sum of a linear function of the explanatory variables and random group-dependent deviation U_{0j}.

Assume k explanatory variables $X_1, X_2,...X_k$. The values of X_h (h=1,2,…,k) are indicated in the usual way by $X_{hij} (h = 1,2,...,k; i = 1,2,...,n_j; j = 1,2,...,N)$. Since some or all of these variables could be level-one variables, the success probability is not necessarily the same for all individuals in a given groups. Therefore, the success probability depends on the individual as well as on the group, and is denoted by p_{ij}. The outcome variable is expressed as the sum of success probability and a residual term ε_{ij}.

$$\log it(P_{ij}) = \left(\frac{P_{ij}}{1-P_{ij}}\right) = \beta_{0j} + \beta_1 x_{1ij} + \beta_2 x_{2ij} + ... + \beta_k x_{kij} \quad \text{……………………………(9)}$$

Equation (9) does not include a level-1 residual because it is an equation for the probability P_{ij} rather than for the outcome Y_{ij} [16].

By letting $\beta_{0j} = \beta_0 + U_{0j}$ in equation (9) we have the following:

$$\log it(P_{ij}) = \beta_0 + \sum_{h=1}^{k} \beta_h x_{hij} + U_{0j} \quad \text{……....(10)}$$

Or

$$p_{ij} = \frac{e^{\beta_0} + \sum_{h=1}^{k} \beta_h x_{hij} + U_{0j}}{1 + e^{\beta_0} + \sum_{h=1}^{k} \beta_h x_{hij} + U_{0j}} \quad \text{……….….(11)}$$

Where, $\beta_0 + \sum_{h=1}^{k} \beta_h x_{hij}$ is the fixed part of the model and U_{0j} is the random part of the model. Thus, unit difference between the x_h values of two individuals in the same group is associated with a difference of β_h in their log-odds, or equivalently, a ratio of exp (β_h) in their odds. The deviations U_{0j} are mutually independent with zero mean and variance σ_0^2.

STATISTICAL DATA ANALYSIS AND DISCUSSION

Descriptive Analysis

A total of 400 HIV infected patients aged 15 years or older taking ART in Hosana District Queen Elleni Mohamad Memorial Hospital were eligible for this study. Among the patients, 75 (18.75%) were dead while 325(81.25%) are alive. Summary statistics of factors associated with mortality of HIV infected patients are presented in Table 1.

According to Table 1, the proportion of mortality of HIV infected patients taking ART in Hossana Disrict Queen Elleni Memorial hospital varies from one woreda where they live to the other. For instance, the highest percentage of mortality was observed in Hossana town adminstration (26.8%) followed by Anlemmo woreda (24.4%) where as the lowest percentage was observed in Lera worea (11.1%) followed by Duna woreda(12.1%).

Similarly, the proportion of mortality of HIV infected patients taking ART varies by place of residence: urban and rural. The higher percentage of mortality (19.8%) of patients was observed in urban areas, and relatively smaller percentage of mortality (17.6%) is observed in rural areas.

The proportion of the mortality of HIV infected patients varies by sex and age groups. The percentage mortality of male patients is higher (21.0%) than the percentage mortality of female patients (16.9%).With regard to their age, the percentage of mortality of patients was higher for patients aged 40 or older years (22.5%) than below 40 years (17.5%).

The proportion of mortality of HIV infected patients taking ART also varies by marital status. For example, the highest percentage of mortality of patients was observed for patients who were separated (40.0%) followed by Widowed (25.6%) while lowest percentage of mortality was observed for patients who were married (14.3%) followed by Divorced (16.7%).

The proportion of mortality of HIV infected patients taking ART varies by level of education. The percentage of mortality of patients was highest for patients who have no education (22.6%) as opposed to the lowest percentage of mortality of patients for those patients whose level of education was secondary or above (15.0%).

The proportion of mortality of HIV infected patients taking ART also varies with their TB status. The percentage of mortality of patients was higher for patients who were TB positives (37.3%) while the lower percentage of mortality of patients was observed for patients who were TB negatives (11.7%).

Table 1: Summary of descriptive statistics of mortality of HIV infected patients taking ART

Variables	**Categories**	**Dead**			
		No	**Yes**	**Total**	**Percentage of death**
Woreda	Hossana town administration	52	19	71	26.8%
	Lemmo	44	7	51	13.7%
	Anlemmo	34	11	45	24.4%
	Misha	41	12	53	22.6%
	Angecha	31	6	37	16.2%
	Duna	29	4	33	12.1%
	Lera	40	5	45	11.1%
	Gombora	30	6	36	16.7%
	Soro	24	5	29	17.2%
Sex	Female	182	37	219	16.9%
	Male	143	38	181	21.0%
Age	Below 40	241	51	292	17.5%
	40 or older	84	24	108	22.2%
Residence	Rural	159	34	193	17.6%
	Urban	166	41	207	19.8%
Marital Status	Never married	63	18	81	22.2%
	Married	198	33	231	14.3%
	Separated	15	10	25	40.0%
	Divorced	20	4	24	16.7%
	Widowed	29	10	39	25.6%
Level of education	No education	65	19	84	22.6%
	Primary	130	33	163	20.2%
	Secondary or above	130	23	153	15.0%
Tobacco	No	254	40	294	13.6%
	Yes	71	35	106	33.0%
Alcohol	No	254	47	301	15.6%
	Yes	71	28	99	28.3%
Baseline weight	Less than 50 kg	108	41	149	27.5%
	50 kg or above	217	34	251	13.5%
WHO Clinical stage	Stage I	93	11	104	10.6%
	Stage II	107	19	126	15.1%
	Stage III	102	39	141	27.7%
	Stage IV	23	6	29	20.7%
TB Status	Negative	256	34	290	11.7%
	Positive	69	41	110	37.3%
Antiretroviral Regimen	d4t-3TC-NVP or d4t-3TC-EFV	65	29	94	30.9%
	AZT-3TC-NVP or AZT-3TC-EFV	119	27	146	18.5%
	TDF-3TC-NVP or TDF-3TC-EFV	141	19	160	11.9%
Baseline CD4 count	Less than 200	123	49	172	28.5%
	200 or above	202	26	228	11.4%

Table 2: Results of Logistic Regression Analysis for mortality of HIV Infected Patients

Parameter	Estimate	Standard error	Wald chi-quare	df	Pr > ChiSq	OR	95% C.I of OR	
Intercept	-2.1281	0.4021	28.0016	1	0.024*	-	-	
Age			8.1068	1	0.013*			
Below 40(Ref)								
40 or older	0.5479	0.1924	8.1068	1	0.013*	1.7296	1.1323	1.9159
Woreda			71.3591	8	0.014*			
Hossana(Ref)								
Lemmo	-1.2691	0.3016	17.7015	1	0.029*	0.2811	0.0899	0.8789
Anlemmo	-0.3937	0.2115	3.4519	1	0.442	0.6745	0.2475	1.8384
Misha	-1.7376	0.4864	12.7481	1	0.031*	0.1759	0.0315	0.7212
Angecha	-0.6617	0.6065	1.1864	1	0.275	0.5160	0.1572	1.6938
Duna	-0.9383	0.6486	2.0768	1	0.147	0.3913	0.1098	1.3949
Lera	-1.2322	0.6101	4.0691	1	0.043*	0.2917	0.0882	0.9643
Gombora	-2.8982	0.6322	21.0014	1	0.002*	0.0551	0.0103	0.6262
Soro	-0.9176	0.6496	1.9749	1	0.158	0.3995	0.1118	2.4270
Led			37.8264	2	0.028*			
No education(Ref)								
Primary	-1.2399	0.3942	9.8717	1	0.043*	0.2894	0.0346	0.7093
Secondary or above	-2.0629	0.4147	24.7295	1	0.007*	0.1271	0.0275	0.1557
Alch			14.3186	1	0.000*			
No(Ref)								
Yes	1.2099	0.3194	14.3186	1	0.000*	3.3535	1.7931	6.2715
Baslinwt			7.9649	1	0.012*			
Less than 50(Ref)								
50kg or above	-0.8612	0.3049	7.9649	1	0.031*	0.4226	0.2325	0.7682
TBStas			18.7618	1	0.000*			
Negative(Ref)								
Positive	1.3231	0.3052	18.7618	1	0.000*	3.7551	2.0644	6.8303
BaslinCD4			11.0624	1	0.032*			
Less than 200(Ref)								
200 or above	-1.4118	0.4243	11.0624	1	0.032*	0.2437	0.1922	0.5016

(* =Significant at 5% level) and (Ref =Reference category)

Logistic Regression Analysis of Mortality HIV infected Patients

Multiple logistic regression analysis was used to analyze the effect of each of independent variables on mortality of HIV infected patients while controlling for the other independent variables. Stepwise method of variable selection procedure was employed to select the important determinants of mortality of HIV infected patients. The significance of individual parameter estimates were tested using Wald test. A negative sign in column labeled estimate indicates an inverse relationship of explanatory variable with the log odds of the dependent variable whereas a positive coefficient column labeled estimate indicates a positive relationship to the log odds of the dependent variable.

The result presented in Table 2 is interpreted in terms of odds ratio. Odds ratios greater than one indicate that the event is more likely to happen in the comparator than in the reference category, odds ratios of one indicate the event is exactly as likely to occur in the two categories, while odds ratios less than one indicate that the event is less likely to happen in the comparator than in the reference category.

According to Table 2, age, woreda, level of education, alcohol, baseline weight, TB status and baseline CD4 count were found to be significant predictors of mortality of HIV infected patients at 5% level of significance but Anlemmo woreda, Angecha woreda, Duna woreda and Soro woreda are insignificant when compared to Hossana town administration.

The estimated model is given by:

$$logit(\hat{p}) = \beta_0 + \sum_{h=o}^{1} \beta_{1h} Age_h + \sum_{i=0}^{8} \beta_{2i} Wrda_i + \sum_{j=o}^{2} \beta_{3j} Led_j + \sum_{k=0}^{1} \beta_{4k} Alch_k + \sum_{l=0}^{1} \beta_{5l} Baslinwt_l + \sum_{m=0}^{1} \beta_{6m} TBStas_m + \sum_{n=0}^{1} \beta_{7n} BaslinCD4_n$$

Where, $\hat{p}$ = predicted probability of mortality of HIV infected patient, β_0 = constant, Age_h = Age of Patient h, $Wrda_i$ = Patient's woreda i, Led_j = Level of education j, $Alch_k$ = Alcohol k, $Baslinwt_l$ =

Baseline weight l, $TBStas_m$ = TB status m , $BaslinCD4_n$ = Baseline weight n.

The value of explanatory variable for each category is taken as 1 if the given variable falls in the corresponding category. For instance, Age_h= 1 for patient's age h and Age_h= 0 for others age groups. Similarly, each of the other variables takes value 1 if it falls within the corresponding level of category. Based on the result revealed in Table 2, the regression equation consisting of the significant variables is given by:

$$\begin{aligned} logit(\hat{p}) = & -2.1281 + 0.5479Age_{\geq 40} - 1.2691Wrda_{Lemmo} - 0.3937Wrda_{Anlemmo} \\ & - 1.7376Wrda_{Misha} + \cdots - 0.9176Wrda_{Soro} - 1.2399Led_{Primary} \\ & - 2.0629Led_{Secondary}or_{Above} + 1.2099Alch_{Yes} - 0.8612Baslinwt_{\geq 50kg} \\ & + 1.3231TB_{Positive} - 1.4118BaslinCD4_{\geq 200} \end{aligned}$$

In Table 2, binary logistic regression analysis revealed that HIV infected patients who aged 40 years or older were 1.7296 times more likely to die than those patients who aged below 40 years. Thus, patients who aged 40 years or older were 72.96% (OR=1.7296, 95% CI: 1.1323, 1.9159) more likely to die than those patients who aged below 40 years controlling for other variables in the model.

HIV infected patients who live in Lemmo woreda were 0.2811 times (OR=0.2811, 95% CI: 0.0899, 0.8789) less likely to die than those patients who live in Hossana town controlling for other variables in the model. Thus, patients who live in Lemmo woreda were 71.89% less likely to die compared to patients who live in Hossana controlling for other variables in the model. Also, patients who live in Misha woreda were 0.1759 times (OR=0.1759, 95% CI: 0.0315, 0.7212) less likely to die than those patients who live in Hossana town. Similarly, patients who live in Lera woreda and Gombora wored were 0.2917 times (OR=0.2917, 95% CI: 0.0882, 0.9643) and 0.0551 times (OR=0.0551, 95% CI: 0.0103, 0.6262) respectively less likely to die compared those patients who live in Hossana town controlling for other variables in the model.

HIV infected patients whose level of education was primary were 0.2894 times (OR=0.2894, 95% CI: 0.0346, 0.7093) less likely to die compared to patients who had no education controlling for other variables in the model while patients whose level of education was secondary or above were 0.1271 times (OR=0.1271, 95% CI: 0.0275, 0.1557) less likely to die compared to patients who had no education controlling for other variables in the model.

HIV infected patients whose baseline weight was 50 kg or above were 0.4226 times(OR=0.4226, 95% CI: 0.2325, 0.7682) less likely to die compared to patients whose baseline weight was less than 50 kg controlling for other variables in the model. Also, patients who were TB positive were 3.7551 times (OR=3.7551, 95% CI: 2.0644, 6.8303) more likely to die compared to patients who were TB negative controlling for other variables in the model. Similarly, patients who drink alcohol were 3.3535 times (OR=3.3535, 95% CI: 1.7931, 6.2715) more likely to die compared to those patients who do not drink alcohol controlling for other variables in the model.

HIV infected patients whose baseline CD4 count was 200 or above were 0.2437 times(OR=0.2437 , 95% CI: 0.1922, 0.5016) less likely to die compared to those patients whose baseline CD4 count was less than 200 controlling for other variables in the model.

Multilevel Logistic Regression Analysis

In the multilevel logistic regression analysis two-level clusters were used with woredas as the level-two units and HIV infected patients as the level-one units i.e. HIV infected patients are nested within woredas. This study was done basically expecting that there is variation in mortality among the woredas. The multilevel logistic regression analysis was used for analysis of the effect of demographic, socio-economic, behavioral and Clinical variables on mortality of HIV infected patients.

A chi-square test was applied to assess the heterogeneity in the proportion of mortality of HIV infected patients taking ART in Hossana Queen Elleni Mohamad memorial hospital among 9 woredas where the patients live. The test yields χ^2= 31.74 which is greater than χ^2_{tab} =15.507 at 8 degree freedom with P-value = 0.0001 implying that there is heterogeneity among woredas where the patients live with respect to mortality of HIV infected patients taking ART in Hossana District Queeen Eleni Mohamad Memorial Hospital.

Multilevel Empty Logistic Regression Analysis

The multilevel empty logistic regression model contains no explanatory variables. The deviance based on Chi-square is the difference in -2*log likelihood between an empty model without random effect (-2LL=386.06206) and an empty model with random effect (-2LL =382.02234) =4.0397 which is greater than χ^2_{tab} (1) =3.841 with p-value= 0.032 at 5% level of significance. This implies that an empty logistic regression model with random intercept is better than an empty model without random intercept.

In multilevel logistic regression model, the average overall odds of HIV infected patients mortality is estimated to be β_0 = -1.47552 and the variance of the random intercept is estimated to be σ^2_0 =0.0333485 which is significant at 5% level of significance indicating that the variations of mortality of HIV infected patients among woredas was non-zero (Table 3). Also, Intra correlation coefficient (ICC) in the empty model is estimated at 0.0100346 which is found to be significant at 5% level of significance suggesting about 1.003% of the variation in mortality of the patients taking ART in Hossana District Queeen Eleni Mohamad Memorial Hospital could be attributed to differences across woredas.

Random Intercept Logistic Regression Analysis

In the random intercept model the intercept is allowed to vary across woredas and the effects of predictors of HIV infected patients are the same for each woreda. Based on deviance based Chi-square, the difference between deviance of multilevel empty logistic regression model and multilevel random intercept logistic regression model, random intercept logistic regression model was found to give a better fit as compared to the multilevel empty logistic regression model. The deviance based Chi-square = 75.49126 is greater than χ^2 = 14.0671 at 7 degree of freedom with P-value = 0.0000. This indicates that after controlling all predictor variables, the intercept varied across the woredas i.e. the variations of mortality of HIV infected patients among woredas where they live was non-zero. The variance of random intercept of the multilevel random intercept logistic regression model was estimated to be 0.0324 which is decreased by about 0.0009 as compared to that of multilevel empty logistic regression model (Table 4). This reduction indicates that there is a contribution of inclusion of fixed independent variables on variations of mortality of HIV infected patients across woredas. The intra correlation coefficient for this model is found to be 0.00976 implying 0.976% of the variation in mortality of HIV infected patients can be explained by grouping patients in woredas.

Table 3: Result of multilevel empty logistic regression model

Fixed Part	**Coefficient**	**S.E**	**Z-value**	**P-value**	**[95% Conf. Interval]**
β_0 =Intercept	-1.47552	0.141608	-10.42	0.000*	-1.753066 -1.197973
Random Part	**Variance Component**	**S.E**	**Z-value**	**P-value**	**[95% Conf. Interval]**
σ_0^2	0.0333485	0.0261593	1.27	0.016*	0.0005687 0.37756
ICC(ρ)	0.0100346	0.0196158	0.52	0.024*	0.00000983 0.9927858
BIC=398.0053, Log likelihood = -191.01117					

(*=Significant at 5% level of significance)

According to Table 4, age, level of education, alcohol, baseline weight, TB status and baseline CD4 count were found to be significant predictors of mortality of HIV infected patients at 5% level of significance indicating effects on mortality of HIV infected patients and also contributing to mortality variations of HIV infected patients among woredas where they live.

Table 4: Result of parameter estimate of multilevel random intercept logistic model

Fixed Part	**Coeff.**	**Std.Err.**	**Z**	**P>|Z|**	**OR**	**[95% CI of OR]**
Age						
Below 40(Ref)						
40 or older	0.5483	0.1901	2.88	0.006*	1.7303	1.0273 1.9242
Led						
No education(Ref)						
Primary	-1.2468	0.3914	-3.19	0.023*	0.2874	0.0189 0.8315
Secondary	-2.0819	0.4086	-5.10	0.002*	0.1247	0.0433 0.2578
Alcohol						
No(Ref)						
Yes	1.2482	0.3167	3.94	0.000*	3.4841	1.7874 6.4526
Baslnwt						
Less than 50kg(Ref)						
50 kg or above	-0.8927	0.3032	-2.94	0.012*	0.4095	0.2251 0.9287
TBStas						
Negative(Ref)						
Positive	1.3642	0.3045	4.48	0.000*	3.9126	2.1179 6.9107
BaslnCD4						
Less than 200(Ref)						
200 or above	-1.4321	0.4125	-3.47	0.003*	0.2388	0.2043 0.6004
Constant	-2.6258	0.4030	-6.52	0.014*		
Random part	**Variance Componen t**	**Std.Err.**	**Z**	**P>|Z|**	**[95% Conf. Interval]**	
σ_0^2	0.0324423	0.029782	1.09	0.034*	0.0271 0.7325	
ICC (ρ)	0.0097646	0.029411	0.33	0.041*	0.0002 0.4771	
AIC	328.5311, BIC=372.4372 , Log likelihood = -153.26554					

(*= Significant at 5%) and (Ref =Reference category)

Table 5: Comparison of Multilevel Logistic Regression Models with respect to AIC and BIC

Model	AIC	BIC
Empty model	390.0223	398.0053
Random Intercept	328.5311	372.4372
Random coefficient(Age)	351.3457	383.2347
Random coefficient(Led)	352.5308	384.4198
Random coefficient(Alcohol)	349.5192	381.4082
Random coefficient(Baslinwt)	352.0138	383.9028
Random coefficient(TB status)	351.9070	383.7960
Random coefficient(BaslinCD4)	352.5308	384.4198

The result in Table 4 revealed that the odds of death of HIV infected patients who aged 40 or older years is 1.7303 times (OR=1.7303, 95% CI: 1.0273, 1.9242) higher than patients aged below 40 years controlling for other variables in the model. The odds of death of patients who drink alcohol is 3.4841 times (OR=3.4841, 95% CI: 1.7874, 6.4526) higher than patients who do not drink controlling for other variables in the model. Similarly, the odds of death of patients who are TB positive is 3.9126 times (OR=3.9126, 95% CI: 2.1179, 6.9107) higher than patients who are TB negatives controlling for other variables in the model.

The odds of death of patients whose level of education are primary and secondary or above are reduced by 71.26% and 87.53% respectively compared to patients with no education controlling for other variables in the model. The odds of death of patients whose baseline weight is 50 kg or above is reduced by 59.05% compared to patients whose weight less than 50 kg controlling for other variables in the model. Similarly, the odds of death of patients whose CD4 count is 200 or above is reduced by 76.12% patients whose CD4 count is less than 200 controlling for other variables in the model.

Random Coefficient Multilevel Logistic Regression Analysis

In random coefficient multilevel logistic regression model both intercept and slopes are allowed to vary across woredas. We analyzed for each of the explanatory variable separately to check the significance of effect of those variables which are significant on mortality of HIV infected patients in logistic regression analysis. The deviance based chi-square test was used to test whether the effect of age, level of education, drinking alcohol, baseline weight, TB status, and baseline CD4 count varies across woredas. The deviance based chi-square test statistic is calculated as two times the difference in the log likelihood values between the model with and without the random slope.

The p-value for each predictor corresponding to deviance based chi-square test is greater than 0.05 indicating that the variance of random slope of each variable is not significantly different from zero at 5% level of significance. This implies that the coefficients of all variables do not vary across woredas.

Multilevel Logistic Regression Model Comparison

The model with smallest AIC and BIC is considered as the best model. Accordingly, random intercept logistic regression model is the best model to explain variation of mortality of HIV infected patients taking ART in Hossana District Queen Elleni Mohamad Memorial Hospital among woredas as compared to other multilevel models.

CONCLUSION AND RECOMMENDATION

Conclusion

This study revealed that the effect of demographic, socio-economic, behavioral and clinical factors on mortality of HIV infected patients. The result of multiple logistic regression revealed that age, level of education, alcohol, baseline weight, TB status and Baseline CD4 count and Woreda had significant effect on mortality of HIV infected patients who are taking ART in Hossana District Queen Elleni Mohamad Memorial Hospital.

The multilevel logistic regression models was applied and showed that there were mortality variation of HIV infected patients among woredas where they live. This variation among woredas is accounted by the random intercept of the model. Moreover, the overall variance of the constant term in both multilevel empty logistic regression model and multilevel random intercept logistic regression model was found to be significant implying the presence of mortality variation across woredas. Age, level of education, alcohol, baseline weight, TB status and baseline CD4 count were significant determinants of variations of mortality of HIV infected patients among woredas.

Among the models that were applied in this study, the multilevel random intercept logistic regression model best fits to the data for mortality of HIV infected patients who are taking ART in Hossana District Queen Elleni Mohamad Memorial Hospital.

Recommendation

Based on the results of this study the following recommend-ations are suggested.

- ✓ Health workers should be cautious when a patient has lower baseline CD4 and lower baseline weight.
- ✓ Level of education of the patients has an important role in increasing their quality of life (reduction of mortality). Health workers need to support those patients with no or little education by continuous awareness creation of taking care of themselves and knowing what factors facilitate death.
- ✓ Patients who drink alcohol need to be given advice to reduce excessive drinking.

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REFERENCES

1. UNAIDS (2008). Report on Global AIDS Epidemic-Google Book: Website:http://www.unaids.org/en/media/unaids/contentassets/dataimport/pub/global report/2008/jc1510.
2. UNAIDS/WHO (2012). *Core Epidemiology Slides*. Geneva, Switzerland.
3. UNAIDS (2011).*World AIDS Day Report*. Geneva, Switzerland.
4. UNAIDS (2012). Global Report: UNAIDS Report on the Global AIDS Epidemic 2012.
5. UNAIDS (2013).Global Report: UNAIDS Report on the Global AIDS Epidemic 2013.
6. Thirumurthy, H., and Lester, R. T. (2012). Bulletin of the World Health Organization, 90(5), 390-392.
7. Merso, F. (2008).Women & Girls and HIV/AIDS in Ethiopia.
8. Federal HIV/AIDS Prevention and Control Office (2010). Report on progress towards implementations of the UN declaration of commitment on HIV/AIDS.Ethiopia, Addis Ababa.
9. WHO (2003). Scaling-up antiretroviral therapy in resource-limited settings. Treatment guideline for a public health approach.2003 revision.
10. Palella, F., Deloria-Knoll, M., Chmiel, J., Moorman, A., Wood, K., Greenberg, A. and Holmberg, S.D. (2003). Ann Intern Med.; 138(8):620-626.
11. Françoise, R., Chris, D., Stephen, K., Sigrid, T., Joseph, P. (2006). Use of antiretroviral therapy in resource-limited countries: distribution and uptake of First and second line regimens. Department of HIV/AIDS, World Health Organization, CH-1211 Geneva 27, Switzerland; Email:theryf@who.int.
12. Fidell, B. and Tabachnick, L. (2007). Using multivariate statistics (5th ed.). Boston . Montreal: Pearson/A & B. ISBN 0-205- 45938-2.
13. Hosmer, W. and Lemeshow, S. (2000), Applied Logistic Regression.2nd Ed., John Wiley and Sons, New York.
14. Agresti, A. (1996). An Introduction to Categorical data Analysis. New York. John Wiley and Sons.
15. Qian, S., Cuffney, T., Alameddine, I., McMahon, G. and Reckhow, K., Ecology, 91(2), 355-361, 2010.
16. Snijders, T. and Bosker, R., 1999. Multilevel modeling: An introduction to basic and advanced multilevel modeling.